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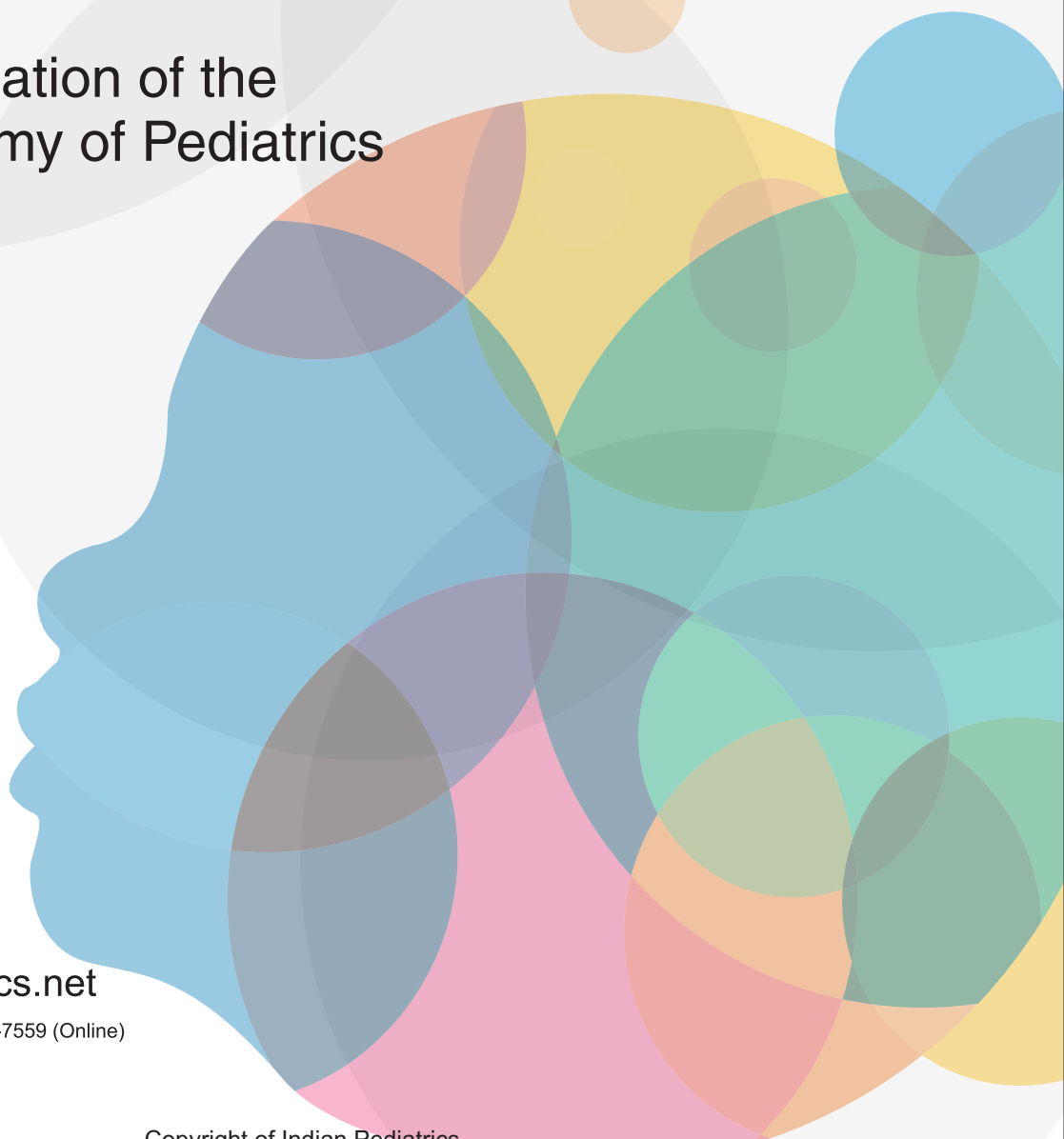

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Indian Pediatrics

Editor-in-Chief Pooja Dewan

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PRESIDENT'S PAGE

Protecting Tiny Minds: The Battle Against the Unhealthy Influence of Food Advertising on Eating Habits of Children

GV Basavaraja
President, Indian Academy of Pediatrics
basavgv@gmail.com

As we embark on a new year, let us collectively aspire for joy and health for children from all over the world. In this article, we delve into a critical topic concerning the impact of advertisements on the impressionable minds of children, particularly how it influences their eating habits and preferences.

Young minds, characterized by curiosity and susceptibility to suggestions, become targets of advertisers, who invest significant resources to ensure that their products capture the attention of this demographic [1]. Despite the potential harm to their health, children often find themselves drawn to these products, creating a concerning link between advertising and unhealthy consumption patterns.

Numerous studies have established connection between childhood obesity and exposure to advertising [2]. This issue demands our attention, in the light of the staggering increase in childhood obesity cases by 11 million, since 2000 [3]. The implications of this extend beyond physical health, affecting education, quality of life, and have psychological consequences. Overweight and obesity are the major risk factors for a broad range of non-communicable diseases (NCDs), including cardiovascular diseases, diabetes, musculoskeletal disorders and cancer.

Recognizing the severity of the issue, organizations such as the World Health Organization and the United Nations Children's Fund have collaborated to develop a comprehensive toolkit and guide for policymakers. As responsible members of the Indian Academy of Pediatrics (IAP), it is incumbent upon us to promote and implement these tools actively. Our duty goes beyond treatment – we must prioritize prevention, so as to safeguard the well-being of future generations.

Now with childhood obesity on the rise, active participation by our fraternity is necessary to tackle it as a major health issue and not just ignore it as a lifestyle choice. The IAP has also stressed on many of these issues in its previous guidelines on junk foods [4]. Measurement of body mass index (BMI) as well as waist circumference should be routinely inculcated in clinical practice. Parents and children have always been a single unit in pediatrics, so educating them of the impending risks is essential for curbing this disease. Need for a balanced diet and all its components should also be explained in detail to the family.

To effectively address the challenge of balancing child rights and content regulation, we need to navigate a delicate balance between protecting the rights of children and imposing restrictions on content. While advocating for freedom, we must also recognize the responsibility to shield young minds from potentially harmful influences. This delicate equilibrium is essential for creating an environment that fosters healthy development.

Our collective responsibility as IAPians transcends the confines of medical treatment. It extends to advocacy, prevention, and shaping a future where children can grow up in environments that nurture their well-being. Let us actively champion the WHO-UNICEF toolkit, guide policymakers, and strive to strike the right balance in our pursuit of safeguarding the health and future of tiny budding minds.

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FROM THE EDITOR'S DESK

Standing on the Shoulders of Giants!

As I assume charge as the Editor-in-Chief of *Indian Pediatrics*, I feel overwhelmed and humbled. My 16 years of association with the journal in different capacities has not only honed my writing and editing skills, but has also helped me develop a more scientific and methodical perspective. But, I am aware that I am stepping into the boots of the thirteen illustrious *Past Editors* who have worked with utmost sedulity and integrity to build *Indian Pediatrics* into a resource to reckon with. The bar is set high and I have a lot to learn. For this I seek support from the readers of *Indian Pediatrics*, who are our greatest strength. It will be my endeavour to give maximum chances to all our readers to showcase their research work in *Indian Pediatrics*, without compromising the scientific rigor or ethical standards. I envisage *Indian Pediatrics* as a stable influence for all authors in their academic journey and hope to build a lasting and fruitful collaboration with all authors.

Original research has been the forte of *Indian Pediatrics* and we aim to publish more of them in the coming years. We will make all efforts to further expand our horizons and in the upcoming issues we will start some newer sections. We will be introducing '*Ethisection*' which aims at stimulating reflection on ethics issues among readers through a case-based discussion highlighting various ethical dilemmas encountered in clinical, publishing or administrative domains. We also will be introducing a section entitled '*Bridging Borders*' with a vision to highlight the challenges in healthcare of children within and outside India, attributed to global as well as region-specific problems like war, climate change, migrant population, cultural practices and poverty. This section will feature ideas from around the world that can inspire and guide efforts to decrease the inequity in global healthcare standards. We also plan to start '*Symposium*' which will comprise of a series of state-of-the-art articles that will cover specific topics in child health comprehensively. We believe this will not only apprise the readers about any recent advances in that field, but also enlighten them about clinical practice protocols. The other sections like Perspective, Journal Club, Guidelines, Clinicopathological Conference, Research Letters, Updates and Images will continue to be published. While we expand our horizons, we will also add a bit of colour in our scientific lives by introducing a few cosmetic changes in *Indian Pediatrics*. We hope to receive an honest and constructive feedback from our readers to enable us to improve with each passing day.

In the current times of rapid progress and research in diagnostics and therapeutics, there is a need for high publishing speed to prevent the results of a study from becoming outdated. I will try my best to expedite the review process and will aim for a still lesser lag time for editorial decisions and publication. Simultaneously, we will also make efforts to ensure more articles are listed electronically ahead of printing. It gives me a sense of great pride in informing our readers that *Indian Pediatrics Case Reports* (*IP CaRes*), the quarterly journal of the *Indian Academy of Pediatrics* (IAP), has now been indexed with the Directory of Open Access Journals (DOAJ), thanks to the perseverance of the entire editorial team of *IP CaRes*.

Keeping our tradition alive, we plan to continue with the workshops on '*Art and Science of Paper Writing*' to stimulate the budding authors and reviewers. We also envisage starting '*Workshops on Systematic Reviews*', a need which came to the fore during the COVID-19 pandemic when doing clinical research became a limitation and authors sought to satiate their penchant for research by doing systematic reviews. It was also a time, when several universities permitted post-graduates to do systematic reviews as a part of their thesis submission, and thus hailing a new trend.

In the coming year, we intend to bring out the fourth volume of '*Best of Indian Pediatrics*', publish a compendium of '*Rational Diagnostics*' which was a hugely popular section and bring out a coffee table book on '*Clinical Images*' published in *Indian Pediatrics* over the last 20 years. I am sure these books will be particularly useful for post-graduate students and practitioners.

The changing landscape of publishing industry has made our task as editors tougher. With the ability to generate papers "good enough" for academic journals, large language models like ChatGPT have led to an infodemic threat in public health. While artificial intelligence (AI) can detect plagiarism, AI-generated

original content including the "*deepfake*" photos, voice clones and videos, are often imperceptible to even the trained human eyes, mind and ears. With the AI wreaked havoc, the well-intentioned editorial policies are likely to remain symbolic unless regulatory laws and appropriate tools are developed soon. Ironically, we will need more robots to tackle this AI-enabled disinformation.

I will strive continuously to keep the Journal policies and practices in synchrony with the mission of the *Academy*. With a spirited editorial board which provides both zeal and direction for the content, a robust peer review process and a supportive *Academy*, we will march ahead.

Pooja Dewan
Editor-in-Chief, Indian Pediatrics, 2024-2026
ip.editor@iapindia.org

Consensus Statement of the IAP - Neurodevelopmental Chapter On Neurodevelopmental Disorders Habilitation Process: Strategic Plan for Prevention, Early Detection and Early Intervention

MKC Nair,[1] Shabina Ahmed,[2] Kawaljit Singh Multani,[3] Mohamed Ismail PM,[4] SS Kamath,[5] Samir H Dalwai,[6] Zafar Meenai, [7] Praveen Suman,[8] Shambhavi Seth,[9] Leena Srivastava,[10] Roopa Srinivasan,[11] Maria Lewin,[12] Sanjay K,[13] Lal DV,[14] N Udayakumar,[15] Babu George,[16] Beena Koshy,[17] Leena Deshpande,[18] S Sitaraman,[19] Manju GE,[20] Jeeson C Unni,[21] Abraham K Paul,[22] Sreetama Chowdhury,[23] NK Arora,[24] PS Russell[25]

[1]NIMS-SPECTRUM-Child Development Research Centre (CDRC) NIMS Medicity, Thiruvananthapuram, Kerala and Emeritus Professor, Allied Health Science, NICHE, Kumarakovil, Kanyakumari District, Tamil Nadu; [2]Chairperson, Neurodevelopment Chapter, Indian Academy of Pediatrics, Guwahati, Assam; [3]Hony Secretary, Neurodevelopment Chapter, Indian Academy of Pediatrics, Ghaziabad, Uttar Pradesh; [4]Rainbow Clinic, Kochi, Kerala; [5]Indira Gandhi Co-op Hospital, Kochi, Kerala; [6]New Horizons Child Development Centre, Mumbai, Maharashtra; [7]Ummeid Group of Child Development Centers, Bhopal, Madhya Pradesh; [8]Child Development Centre, Sir Ganga Ram Hospital, New Delhi; [9]Bright Beginnings Child Development Centre, New Delhi; [10]Bharati Vidyapeeth Medical College & Hospital, Pune, Maharashtra; [11]Ummed Child Development Centre, Mumbai, Maharashtra; [12]Unit of Hope, Child Development Centre, St John's Bengaluru, Karnataka; [13]Child Development Centre, IGICH, Bengaluru, Karnataka; [14]Child Development Centre, Saveetha Medical College, Chennai, Tamil Nadu; [15]Karthikeyan Child Development Unit, SRIHER, Chennai, Tamil Nadu; [16]Child Development Centre, Trivandrum, Kerala; [17]Child Development Centre, CMC Vellore, Tamil Nadu; [18]Child Development Centre, Navi Mumbai, Maharashtra; [19]Child Development Centre, Jaipur, Rajasthan; [20]Prateeksha Child Development Centre, Pusphpagiri Institute of Medical Sciences, Thiruvalla, Kottayam District, Kerala; [21]Child Development Centre, Aster Medicity, Kochi, Kerala; [22]Cochin Hospital, Kochi, Kerala; [23]NIMS-SPECTRUM-Child Development Research Centre (CDRC) NIMS Medicity, Thiruvanthanapuram, Kerala; [24]Inclen Trust International, Okhla, Delhi; [25]Department of Psychiatry, CMC Vellore, Tamil Nadu.

ABSTRACT

Justification: Neurodevelopmental disorders, as per DSM-V, are described as a group of conditions with onset in the development period of childhood. There is a need to distinguish the process of habilitation and rehabilitation, especially in a developing country like India, and define the roles of all stakeholders to reduce the burden of neurodevelopmental disorders.

Process: Subject experts and members of Indian Academy of Pediatrics (IAP) Chapter of Neurodevelopmental Pediatrics, who reviewed the literature on the topic, developed key questions and prepared the first draft on guidelines. The guidelines were then discussed by the whole group through online meetings, and the contentious issues were discussed until a general consensus was arrived at. Following this, the final guidelines were drafted by the writing group and approved by all contributors.

Objectives: These guidelines aim to provide practical clinical guidelines for pediatricians on the prevention, early diagnosis and management of neurodevelopmental disorders (NDDs) in the Indian settings. It also defines the roles of developmental pediatricians and development nurse counselor.

Statement: There is a need for nationwide studies with representative sampling on epidemiology of babies with early NDD in the first 1000 days in India. Specific learning disability (SLD) has been documented as the most common NDD after 6 years in India, and special efforts should be made to establish the epidemiology of infants and toddlers at risk for SLD, where ever measures are available. Preconception counseling as part of focusing on first 1000 days; Promoting efforts to organize systematic training programs in Newborn Resuscitation Program (NRP); Lactation management; Developmental follow-up and Early stimulation for SNCU/ NICU graduates; Risk stratification of NICU graduates, Newborn Screening; Counseling parents; Screening for developmental delay by trained professionals using simple validated Indian screening tools at 4, 8, 12, 18 and 24 months; Holistic assessment of 10 NDDs at child developmental clinics (CDCs) / district early intervention centre (DEICs) by multidisciplinary team members; Confirmation of diagnosis by developmental pediatrician/developmental neurologist/child psychiatrist using clinical/diagnostic tools; Providing parent guided low intensity multimodal therapies before 3 years age as a center-based or home-based or community-based rehabilitation; Developmental pediatrician to seek guidance of pediatric neurologist, geneticist, child psychiatrist, physiatrist, and other specialists, when necessary; and Need to promote ongoing academic programs in clinical child development for capacity building of community based therapies, are the chief recommendations.

Correspondence to: Dr. Kawaljit Singh Multani, Hony Secretary, Neurodevelopment Chapter, Indian Academy of Pediatrics, Ghaziabad, Uttar Pradesh.
kawaljit000@gmail.com

Keywords: *Autism, ADHD, Diagnosis, Developmental delay, Management, Rehabilitation*

Bio-psychosocial development is a dynamic inter-relationship between genetic, brain, cognitive, emotional and behavioral processes most active during the early developmental phase; any significant and persistent disruption to this dynamic process through environmental and biological risk, in the first 1000 days of life (F-1000-D) can lead to neurodevelopmental disorders and consequent disability [1]. Habilitation process through series of early intervention for high-risk babies has been recommended in the revised status of the convention on the rights of persons with disabilities [2] and has been promoted by the National Health Mission (NHM) [3]. Habilitation process by its primary, secondary and tertiary preventive approaches, from the care of high-risk conception and pregnancy to the first two years of life, minimizes the risk outcomes much before the rehabilitation process. Whereas, habilitation is the process of prevention of impairment (e.g., birth asphyxia) going on to disability, rehabilitation prevents disability going on to handicap [4]. While both processes are needed in the Indian subcontinent in an organized manner, the lack of habilitation process results in a systematic error in the delivery of very early services for babies at high risk in rural and urban India [5,6].

This Consensus Statement of the Indian Academy of Pediatrics Chapter of Neurodevelopmental Pediatrics (IAP NDP) will emphasize on the habilitation process as a very early developmental services model. The statement will discuss the epidemiology of at risk of developing neurodevelopmental disorders (NDD) and early NDD; the delivery model with a modified district early intervention centre (DEIC); the evidence-based practice in the habilitation process; and, the projected effectiveness in the context of IAP and National Health Program in India.

This statement has to be taken as a way to practice and enhance the envisaged models of Rashtriya Bal Swasthya Karyakram (RBSK), especially the district early intervention centre model, during the first thousand days of the life of a baby at risk. The recommendation of this consensus statement should be understood in close conjunction with consensus guidelines on the diagnosis and management of global development delay [7]. We have made efforts to harmonize the two related dimensions of global development delay and habilitation, so as to synergize the clinical care in delays and early disabilities.

PROCESS

Conceptualization and topic selection: There have been well evidenced consensus statements/guidelines/practice parameters from the various official organizations that focus on the prevention of NDD and rehabilitation of children with NDD in India. There is a need to provide the practitioners with a consensus statement for the habilitation process that is specific to first thousand days of the life of a baby but with overarching effect on many of documents available. This IAP-NDP chapter guidelines will conceptualize habilitation from three perspectives: *i*) early stimulation vs intervention, *ii*) habilitation vs rehabilitation, and *iii*) first 1000 days (prevention of delay and active therapy for identified delay).

Literature review: We performed a systematic literature review of systematic reviews, meta-analysis and randomized control trials, for a ten year period (January, 2013-September, 2022), in the PUBMED, SCOPUS and Cochrane Library using the terms: ("neurodevelopmental disorders"[MeSH Terms] OR ("neurodevelopmental"[All Fields] and "disorders" [All Fields]) OR "neurodevelopmental disorders"[All Fields]) and ("India" [MeSH Terms] OR "India" [All Fields] OR "India's"[All Fields] OR "India's"[All Fields])) and ((meta-analysis [Filter] OR randomized controlled trial [Filter] OR review [Filter]) and (2013:2022[pdat])) and retrieved 258 studies (k = 258). Finally, we extracted details on: (1) epidemiology of NDD in India (k = 485), (2) disability resources available in India (k = 105), (3) prevention (k = 187), (4) early diagnosis (k = 159), (5) early intervention (k = 102), (6) ways of harmonizing this Consensus Statement and RBSK model, especially the District Early Intervention Centre Model (DEIC) (k = 8). In addition to all this data, the literature was hand-searched for appropriate studies not published online before the mentioned ten-year period, which included conference presentations as well.

Building the Consensus: There were two work groups, composed of general pediatricians, pediatricians with special interest in NDD, child and adolescent psychiatrists, occupational therapist, developmental therapist and specialist nurses. Their age ranged from 21 to 65 years and experience in NDD varied between 2-32 years. Modified delphi technique was used to arrive at the consensus and draft the recommendations among the experts by the facilitator (MKC) (**Fig. 1**). The facilitator and various experts of the IAP-NDP Chapter met as two workgroups; one group met online (during pandemic) and another group met in-person later in Kochi, Kerala, India. The facilitator co-ordinated both the work groups and finally drafted the recommendations with a panel consisting of selected experts. Consensus was defined as 'agreement' if ≥ 75% of the members of the workgroups had concordance and 'disagreement' if < 25% of members had concordance, and included in the subsequent round.

Building the evidence base: The inclusion of studies to provide evidence for consensus was based on Guidelines of the Oxford Centre for Evidence-Based Medicine

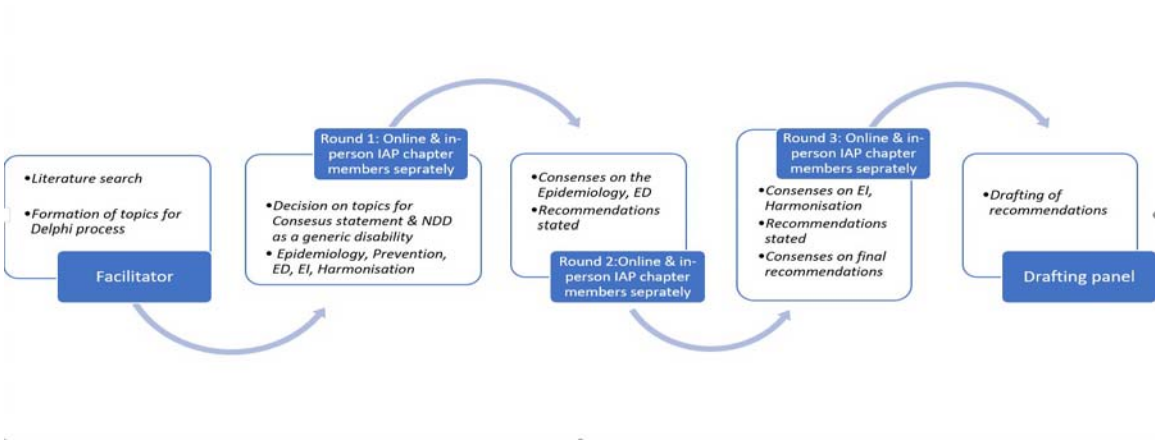

Fig. 1 The modified Delphi technique used for developing the consensus statement.

(Levels of Evidence, March 2009) by the multidisciplinary experts. The conversion of the evidence to recommendation was done following the GRADE protocol and drafted by the drafting panel.

Drafting the recommendation: The consensus statement was drafted and reported based on the ACCORD (Accurate Consensus Reporting Document) reporting standards [8]. If appropriate studies were not available from India, recommendations from other official organizations in India or international organizations were adopted.

CONSENSUS STATEMENT

A. The Epidemiology of At Risk of NDD

This section reviews the epidemiology of various risks in babies, mothers or family context and poverty at various stages of their first thousand days of life. Research studies have identified advanced maternal age (27-106% risk), maternal antepartum bleeding (81% risk), maternal prenatal medication use (46% risk), first order pregnancy (61% risk) [9], meconium aspiration (RR: 7.34), feeding difficulties (RR: 3.35) [10] as risk factors for NDDs in the antenatal and early neonatal period. Prematurity and low birth weight being important determinants of adverse neurodevelopmental outcomes, the risk factors identified include socio-economic status (AR: 41.4%), non-pregnant maternal weight (AR: 22.9%), maternal height (AR: 29.5%), severe anemia (AR: 34.5%) [11], pregnancy induced hypertension (OR: 4.09), maternal short stature (OR: 2.34) [12]. However, the epidemiology of the early stages of NDD, especially during the F-1000-D, is not available in India at Level I evidence. Secondly, as with the epidemiological studies in other countries in Asia, specific learning disability (SLD) is the most prevalent NDD in India as well. The normative data on the basic language, writing, and mathematical needs further validation in the context of SLD.

Recommendation I

There is a need for nationwide studies with representative sampling on epidemiology of babies with early NDD in the first thousand days in India.

Recommendation II

Specific learning disability (SLD) has been documented as the most common NDD in India after six years, and special efforts should be made to establish the epidemiology of infants and toddlers at risk for SLD, where ever measures are available.

B. Evidence-Based Practice in the Habilitation Process

The risk identification during pre-natal (conception and pregnancy) and perinatal period .

Research studies have suggested the following for risk identification during the prenatal and perinatal period; *i*) assisted conception (8.3% for birth defect) [13], *ii*) genetic tests like chromosomal aberrations (19-20%), monogenic disorders (1-25%), errors of metabolism (3-4%), *iii*) intrauterine infections (3-4%), *iv*) toxins (1%), *v*) HIE using modified Levene/Sarnat's score (14-31%) [14], *vi*) malnutrition [15], *vii*) pathological family functioning [16], *viii*) maternal TORCH infection [17], *ix*) neonatal hypoglycemia [18], *x*) significant neonatal jaundice [19], *xi*) tools like Hammersmith Neonatal Neurological Examination [20], Brazelton Neonatal Assessment Scale [21], perinatal risk factor stratification tool [22], Prechtl general movement assessment [23], *xii*) abnormal cranial ultrasound [24], and *xiii*) mother baby bonding assessment [25].

We used the following process of assigning a risk status to babies. The selection of a measure for identification of any form of risk in the F-1000-D was based on an acceptable clinical yield rate over multiple studies or

single well conducted study that established the diagnostic accuracy of at least a sensitivity of 70% and specificity of 80% [26]. **Table I** details the risk identification and tools for early detection during infancy and childhood.

C. Delivery Models for Habilitation Services in India

The service delivery models for habilitation process (HP) has not been specifically developed for India to provide the evidence-based screening and interventions discussed in the previous two sections. For an ideal HP services delivery model for baby at risk, in India, it should focus on a triadic approach, namely: *i*) focusing holistically on the various domains of the baby even if the risk is noted in only a domain, following an Individual Habilitation Plan (IHP); *ii*) Individualized family service plan (IFSP) which includes counseling and training in IHP, supporting the family to overcome the anxiety and grief about the risk factors and to have a watchful monitoring of the baby's development; *iii*) finally, linking the family with national and state programs for social and financial security with an individual social and financial security scheme (ISFS).

1. Review of delivery systems for habilitation process in India

A review of the available systems demonstrated that the Rashtriya Bal Swasthya Karyakram (RBSK) is the best fit for providing the Habilitation Services (HS) in India within the existing policies, programs and resources allocated at the national level (RBSK, 2013) with the addition of the 5th D- discernable risk factors. See **Table II**. However, for enhancing this ambitious and expanding initiative of the Government of India, seamless service provision between DEIC and the proposed Block Early Intervention Centers (BEIC), empowering the latter is required, with provision of social and financial security to the babies and families at risk [27] enabling access to habilitation services.

2. Enhanced Rashtriya Bal Swasthya Karyakram Model for Service Delivery of Habilitation Process With Block Early Intervention Centre (BEIC).

The rationale for developing the Enhanced Rashtriya Bal Swasthya Karyakram Model has been that self-referred, Community EIC and SNCU babies screened have been exponentially increasing ever since the provision of RBSK services (from 3,71,59,012 in 2014-2015 to 10,04,10,009 in 2019-2020) and more babies required transdisciplinary intervention during the same time (83,327 in 2014-2015 to 1,70,651 in 2019-2020). However, as part of the capacity building mandate of the RBSK, the post of a multipurpose developmental therapist has not been included, except as a pilot project in Kerala. Currently there are about 342 operational DEICs at the national level and there are 766 DEICs required to make it a pan-India program, which might happen in a phased manner. The approach to negate this widening gap has to be two-pronged, to facilitate the capacity building, to share the 4Ds/5Ds burden between DEIC and BEIC as well as to upgrade the functioning of BEIC in districts with paucity of health care-resources. It can be approximated that to make the DEICs functional in every district, around 800 developmental therapists (DTs) will be required at a minimum. In order to provide DTs at block levels in BEICs, the number required will be much more. Until the time the state universities take up the onus of creating graduate programs in Developmental Therapy, this gap in manpower can be met by short-term training of available manpower resources like Anganwadi Workers at CDCs/ DEICs. Further details on the infrastructure, human-resources for health and services provided at the DEIC can be obtained from the website *https://nhm.gov.in/images/pdf/programmes/RBSK/Operational_Guidelines/Operational-Guidelines-DEIC-RBSK.pdf*

3. Comparison of DEIC and BEIC for sharing of the 4Ds/ 5Ds: See **Web Table I.**

4. The organogram for the enhanced RBSK model for service delivery of habilitation process with BEIC (**Fig. 2**)

5. Advantages of the RBSK Model for Service Delivery of Habilitation Process with BEIC.

The early child development services, which includes the F-1000-D, has already materials that are being used during pregnancy and the first two years of life. It includes a booklet 'journey of first thousand days'; an android App 'Ayushman Bhava'; call centers that provide individualized counseling related to queries; the LaQshya program that promotes mother-friendly labour and a redesigned developed illustrative Mother and Child Protection Card to assists in developmental monitoring [28,29]. The screens and intervention available in the early child development services of RBSK can add to the evidence-based screening measures and interventions discussed earlier.

E. Preventive management in conception, pregnancy and perinatal period (PCPP)

Pre-conceptional counseling: Research studies as documented in previous section concludes that the single most important modifiable risk factor for neurodevelopmental outcome is Low birth weight baby, and the modifiable antenatal factors for LBW babies include *i*) Pre-pregnancy maternal weight, height *ii*) maternal nutrition *iii*) maternal infections. Hence, the preparation for prevention has to start much earlier with introduction of the concept of 'Pre-

Table I Early Detection of neurodevelopmental Disabilities During Infancy and Childhood

Risk situation and study	*Measure for risk*	*Accuracy*	*Age covered*
Preterm infant, 2020 [64]	Hammersmith infant neurological examination	Sn: 96%; Sp: 93%	At 12 mo corrected age (CP vs no CP)
Neonatal neuro abnormality, 2005 [65]	Amiel Tison neurological assessment	Sn: 92%; Sp: 46%	0-12 mo
Motor delay, 2014 [66]	CDC grading for head holding, sitting and standing	Unknown	0-12 mo
Developmental delay, 2014 [67]	Bayley infant neurodevelop mental screen	Sn: 75-86%; Sp: 75-86%	3-24 mo
Developmental delay, 2014[68]	Developmental observation card	Unknown	0-1 y
Developmental delay, 2013 [69]	Trivandrum developmental screening chart vs DDST	Sn: 84.6%; Sp: 90.8% NPV: 99.23%	0-6 y
Speech & Language Delay, 2016 [70]	Language evaluation scale Trivandrum vs REELS	Sn: 81%; Sp: 68%, NPV: 98%	0-6 y
Developmental delay, 2014 [71]	Denver developmental screening tool	Sn: 56-83%; Sp: 43-80%	0-6 y
Developmental delay, 2014 [72]	PEDS vs DPII and VSMS	Sn: 74-89; Sp: 70-80	0-8 y
Developmental delay, 2011 [73]	Ages and stages questionnaire vs DASII	Sn: 83%; Sp: 75.4%	1-66 mo/3-66 mo
Developmental delay, 1991 [74]	Baroda developmental screening tool	Sn: 66%; Sp: 77%	0-30 mo
Developmental delay, 2017 [75]	New Delhi-developmental screening questionnaire	Sn: 100%; Sp: 87%	9 mo and 18 mo
Developmental delay Pearson Clinicals [76]	Bayley scale of infant development-IV	Accuracy 82% for developmental delay	16 d- 42 mo
Developmental delay, 1997 [77]	Developmental assessment scale for Indian infants	Unknown	0-2 y
Developmental delay, 2007 [78]	Comm DEAL Developmental Assessment	Unknown	0-6 y
NDD, 2013 [79]	INCLEN- neurodevelopment screening tool	Test-retest reliability: 0.8 Inter-rater reliability: 0.8	6-12 y
ASD, 2014 [80]	INCLEN ASD vs DSM-IV-TR	Sn: 98%; Sp: 95%	2-9 y
ADHD, 2014 [81]	INCLEN ADHD vs Conners's parent rating scale	Sn: 87.7%; Sp: 97.2%	6-9 y
NMI, 2014 [82]	INCLEN NMI vs clinical assessment by experts	Sn: 75.4%; Sp: 86.8%	2-9 y
NMI, 2017 [83]	AIIMS modified INCLEN NMI vs expert clinical assessment	Sn: 90.4%; Sp: 95.5%	2-9 y
Epilepsy, 2014 [84]	INDT-EPI vs expert clinical assessment	Sn: 85.8%; Sp: 95.3%	2-9 y
Epilepsy, 2017 [85]	AIIMS modified INDT-EPI vs expert clinical assessment	Sn: 91.5% Sp: 88.6%	1 mo-18 y
ASD, 2019 [86]	AIIMS modified INDT-ASD against DSM-V	Sn: 98.4%; Sp: 91.7%	3-15 y
ADHD, 2020 [87]	AIIMS modified INDT-ADHD against DSMV	Sn: 100%; Sp: 90%	6-18 y
ASD, 2017 [88]	Childhood Autism Rating Scale - 2	Sn: 81.5%; Sp: 78.6%	2-6 y
	Indian scale for assessment of Autism	Sn: 93.3%; Sp: 97.4%	3-20 y
	Autism diagnostic interview - revised	Sn: 92%; Sp: 89%	Mental age > 2 y
ASD, 2023 [89]	Trivandrum autism behavioural checklist against CARS-2-ST	Sn: 96.29%; Sp: 81.57%	2-6 y
ADHD, 2016 [90]	NICHQ- Vanderbilt ADHD rating scale	Sn: 80%; Sp: 75%	6-12 y
SLD, 2017 [91]	NIMHANS SLD battery	Test retest reliability: 0.53	5-12 y
Cognition, 2021 [92]	Weschler's intelligence scale for children-IV	Internal consistency: 0.97 Test-retest: 0.93	6-16 y
Home and family pathology, 2009 [93]	Home screening questionnaire against HOME inventory	Sn: 83%; Sp: 82%	
Multiple disabilities Unknown	RBSK Tool- community based rehabilitation	Unknown	0 – 6 y

PEDS: Parental Evaluation of Developmental Status; DP-II: Developmental Profile-II; VSMS: Vineland Social Maturity Scale; DDST: Denver Developmental Screening Tool; REELS: Receptive Expressive Emergent Language Scale; DASII: Developmental Assessment of Indian Infants; CARS-2- ST: Childhood Autism Rating Scale- 2nd edition, standard version rating; Sn: Sensitivity; Sp: Specificity; PPV: Positive predictive value; NPV: Negative predictive value.

Table II Review of the Available Systems For the Habilitation Process

Scheme; Launch year	*Beneficiaries*	*Benefits*	*Habilitation/Rehabilitation Process*
Pradhan Mantri Surakshit Matritva Abhiyan (PMSMA); 2016	Pregnant women in 2nd and 3rd trimester	Health check-up, tests and required treatment on 9th of every month in all government hospitals across the country.	Habilitation process
Janani Suraksha Yojana	All pregnant women Below Poverty Line	Safe motherhood	Habilitation process
Navjaat Shishu Suraksha Karyakram (NSSK); 2009	Newborns	Basic newborn care, resuscitation, prevention of Hypothermia & Infection, early initiation of breast feeding	Habilitation process
Janani Shishu Suraksha Karyam (JSSK); 2011	Pregnant women & sick infants	Mother and baby treated within 48 hours. Medications, consumables, diagnostics, blood if required, free diet for 3 days during normal delivery/7 days for Cesarean. Similar entitlements for sick infants upto 1-year.	Habilitation process
Rashtriya Bal Swasthya Karyakram (RBSK); 2013	0-6 y (new-borns to young children)	Addressing the defects at birth, diseases, deficiencies & development delays, spanning 32 common health conditions	Habilitation & Rehabilitation process
Rashtriya Kishor Swasthya Karyakram (RKSK); 2014	10-19 y adolescents	Sexual & reproductive health, nutrition, injuries & violence, non-communicable diseases, mental health & substance misuse	Rehabilitation process

conception Counseling' aimed to reduce the risk of adverse health effects to the woman, fetus and neonate by addressing modifiable risk factors and by providing education about healthy pregnancy. The components would be as follows; *i*) Additional nutrition to pre-pubertal girls *ii*) Family life and life skill education for adolescents *iii*) Immunizations – Rubella, Hepatitis-B, HPV during early adolescence *iv*) Preconception folic acid intake *v*) Address body image/cosmetic concerns/ dental care. *vi*) Check-up – medical, ultrasound scan of abdomen and breast if indicated. *vii*) Screening for menstrual problems, Polycystic Ovary Disease, genito-urinary infections. *viii*) Screening for anxiety, depression, suicidal ideation *ix*) Newly-wed counseling – sexuality skills, understanding needs of self and partner and *x*) Self counseling for developing coping skills [30].

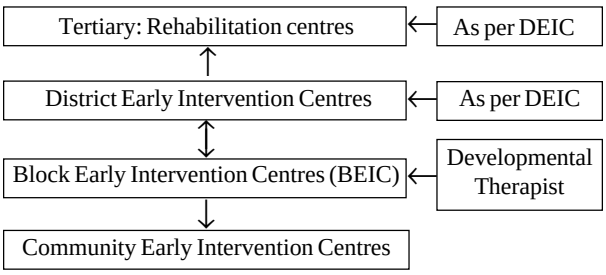

Fig. 2 The organogram for habilitation process based on the Enhanced Rashtriya Bal Swasthya Karyakram model of Block Early Intervention Centers (BEIC).

Joyful pregnancy: maternal stress and effect on baby: A systematic review and meta-analytical study suggests that prenatal stress may be associated with increased risk for ASD (pooled OR = 1.64) and ADHD (pooled OR = 1.72) [31]. Research studies also suggest that prenatal maternal stress maybe related to negative affect, surgency and self-regulatory capacities in the child [32]. UNICEF's vision for elevating parenting therefore includes promotion of parental mental health, emotional and social well-being, stress management and coping skills during pregnancy and early childhood as a part of the Nurturing Care Framework [33].

Recommendation III

Preconception counseling focusing on pre-pubertal girls' nutrition, family life education for adolescents and premarital and newly wed counseling for above 18 years, as part of focusing on first 1000 days (270+365+365 days).

E. Implementing best practices in the labor room and NICU to minimize brain injury

A large multi-center study conducted in 6 LMICs using WHO Essential Newborn Care Course found that after training, the rate of moderately or severely abnormal neurologic examinations at 7 days decreased from 8.0% before the intervention to 6.4% after (P = 0.01), even though there was no significant reduction in neonatal and perinatal mortality [34]. A study conducted in 14 teaching

hospitals in India also found that after training of personnel in NRP, there was a significant shift towards more rational resuscitation practices [35]. Apart from training of NICU staff in resuscitation and essential neonatal care, practices in the NICU should also include *i*) provision of optimal perinatal care, optimal nutrition and developmentally supportive care practices *ii*) optimized intensive care practices *iii*) promoting readiness of healthcare facilities iv) supporting the family and *v*) quality initiatives [36].

F. Early stimulation

As per WHO-ECD-Nurturing Care framework, early stimulation can be considered to be an integral part of Responsive care giving and promoting early learning [37]. Early stimulation refers to doing simple everyday activities with the baby, like talking, singing, reading and playing [38]. The CDC model early stimulation was developed based on the objective of stimulating the child through normal development channels, prevention of developmental delay, prevention of asymmetries and abnormalities, detection of transient tone abnormalities and minimization of persistent tone abnormalities. The module involves four major sensory modalities; *i*) visual stimulation *ii*) auditory stimulation *iii*) tactile stimulation *iv*) vestibular-kinesthetic stimulation [39].

The present guidelines are based on a seminal randomized controlled study involving 900 special care nursery graduates with "CDC model early stimulation" which showed significantly higher Bayley scores at one- and two-year of postnatal age compared to controls. The summary of the results showed that; *i*) as compared to 84.2 Bayley index (average of Mental Development Index and Psychomotor Development Index) for babies above 2500 grams, the babies below 1500 grams had 75.3 only, and *ii*) those babies below 1500 grams, who received stimulation had 83.8 Bayley index, which is almost same as 84.2 for normal birth weight babies, proving beyond doubt that early stimulation is effective. Multiple Regression Analysis for Bayley Score at two years showed that the most significant factor that decided better outcomes was provision of early stimulation [40].

Recommendation IV

Promote efforts to organize systematic training programs in Newborn Resuscitation Program, Lactation management, developmental follow-up and early stimulation for SNCU/ NICU graduates.

G. Very early risk stratification

A systematic review to predict adverse neonatal outcomes thorough antenatal risk scoring systems in India concluded that due to the low quality of such systems available in India, efforts should be directed towards development of the same using current evidence available [41]. As per the available practices and evidence (**Table II**), the neonatal risk stratification model and follow up protocol proposed by NNF and adopted by IAP as the part of consensus guideline in Early Childhood Development (ECD) would be extremely useful in planning for further interventions [42].

H. Early detection (ED)

Early detection of the 4Ds are an integral component of the Habilitation process and the steps for early detection and referral pathway are as follows:

Stage 1: Identification of concerns, acknowledge, listen and act.

Stage 2: General development monitoring at 4, 8, 12, 18, 24 and 30 months and medical assessment including checking hearing, vision, thyroid status.

Stage 3: Developmental screening using validated Indian tools in the first two years and at school entry and confirmation by a developmental pediatrician. Additionally screening for autism should be done at 18-24 months and again, at 3 years of age as per the existing IAP consensus guidelines on ASD [43].

Stage 4: Referral for specific assessments by a multidisciplinary team at DEIC/CDC as indicated by the disability suspected.

Stage 5: Discussion and intervention planning: Clear summary to parents, discuss assessment outcomes, counsel and follow up for comorbidity and growth and general health.

I. Relevant policies

Newborn Hearing Screening: As per IAP Guidelines, the first hearing screening should be conducted before the neonate's discharge from the hospital - if it 'fails', then it should be repeated after four weeks, or at first immunization visit. If it 'fails' again, then Auditory Brainstem Response (ABR) audiometry should be conducted. All babies with abnormal ABR should undergo detailed evaluation, hearing aid fitting and auditory rehabilitation, before six months of age [44,45].

Nurturing Care for Early Childhood Development: IAP-Task force recommended focusing on five essential components viz., *i*) good health, *ii*) adequate nutrition, *iii*) promotion of early childhood learning, *iv*) responsive caregiving, *v*) safety and security. UG/PG students also need to be exposed to hands-on-training at anganwadis, crèches, and in domestic setting [46].

Early Childhood Development: IAP consensus statement on Early Childhood Development suggest that interventions for ECD should begin from conception to adolescence, prioritized in first 3 years, inclusive and equitable for all, especially for high risk, vulnerable and marginalized families [47]. IAP Commitment to Nurturing Care for Early Childhood Development under National President 2021, is reflected in an exhaustive supplement that will go to over 30,000 members of the Academy and create awareness on the current status of national preparedness for implementing NC-ECD in India [48]. NNF commitment to Early Detection of Developmental Delay in India under National President 2021, is reflected in the DETECT training program successfully completed in all states of India and Nepal (NNF Today. Sep 2021; 2:9).

Recommendation V

Risk stratification of NICU graduates, newborn screening for congenital hypothyroidism and phenylketonuria and hearing screening, counseling parents for early stimulation and surveillance in the first two years as part of focusing on first 1000 days.

Recommendation VI

Screening for delays by trained AWWs/developmental nurse counsellors/developmental therapists/PHC doctors at CEIC/BEIC, using simple validated Indian screening tools at 4, 8, 12, 18 and 24 months.

Recommendation VII

Holistic assessment of 10 NDDs at CDCs/DEICs by multidisciplinary team members (developmental therapist/ development nurse counsellor, physiotherapist, occupational therapist, speech therapists, clinical psychologist) with developmental pediatrician/pediatrician as team leader.

Recommendation VIII

Confirmation of diagnosis by developmental pediatrician/ developmental neurologist/child psychiatrist using clinical/diagnostic tools at CDC/DEIC.

J. Early Intervention

Home-based intervention programs with parents as therapists have significant impact on outcome related to early childhood development [49]. The home environment of the child also needs to be assessed by the simple screening tool Home Screening Questionnaire (HSQ) that has been validated against the gold standard 'Home Observation for the Measurement of Environment (HOME)' inventory [50].

Optimal use of locally available Intervention Packages

It is important to have locally developed and validated screening tools and intervention packages. Randomized control studies have shown reasonable effectiveness and published for wider use [51]. Intervention tools can be indigenous and suited to the population being included. MKC's Trivandrum Developmental Screening and Intervention Package is one such example, where the Developmental Therapist-Pediatrician team introduces it to the mother at the center level using simple scientific and specific interventions to address delays/disabilities and the mother continues to do it at home and the child is monitored periodically at the center.

Individualized Care Plan (Bio-Psycho-Social model)

The steps are the following;

i) Initial SWOC (Strength-Weakness-Opportunities-Challenges) analysis on the family resources for supporting the child.

ii) Develop the Bio-Psycho-Social model for the child, the parents and the family/community in close proximity of the child.

iii) Plan intervention for each domain at each level targeting all three components of this model.

iv) Anticipatory guidance for development is to be provided to parents in order to promote optimal developmental outcomes [52].

The WHO-ICF (World Health Organization - International Classification of Functioning, Disability and Health) model can also be an extremely useful tool to formulate the Individualized Care Plan, taking into account not only the physical impairments of the child, but also the child's activities, participation, his environmental facilitators and barriers and his personal specificities [53]. Some intervention packages that may be used are listed in **Box I**.

Home-based vs Centre-based therapy: A program evaluation by Dixon et al in 2017 had concluded that participants made more significant progress in centre-based locations than home-based locations [54]. However, considering the skewed provider-recipient ratio in India, a low-intensity home- based approach utilizing the parent as the core therapist, assisted by the DT and allied therapists would be an effective approach, as demonstrated in a CDC, Kerala study in 2014 [55].

Family inclusiveness without stigma: Long-term parenting of children who have developmental disorders or mental

Box I Some Intervention Packages That May Be Used for Habilitation

1. CDC model early stimulation for at-risk babies [21].
2. CDC Grading based therapy for head holding, sitting and standing [36].
3. Developmental intervention package for babies < 1800g [37].
4. TDSC Items based therapy package among low birth weight babies [37].
5. Early Language intervention (0-3 y) for speech and language delay [38].
6. Clinic based, low intensity, early intervention for children with ASD [39].
7. Home based early intervention for Autism Spectrum Disorder [40].
8. NIMS Spectrum-CDRC Model Intervention for ASD [41].
9. Developmental diagnosis and use of home intervention package [42].
10. Organization of Clinical Child Development Services [44].
11. Child Development Aide (CDA) program [45].
12. Early intervention services to children with developmental delay [46].
13. Community Disability Intervention Program (*https://www.ubuntu-hub.org/*)
14. The ABAaNA early intervention programme.
15. Learning through Everyday Activitieswith Parents (LEAP-CP) [47].
16. Evidence-Based Interventions for Autism Spectrum Disorders [48].
17. Early Intervention and Prevention of Students with Specific Learning Disabilities [49].
18. Early Identification and Interventions for Children At - risk for Learning Disabilities [50].
19. Psychosocial Interventions for Students with ADHD [51].
20. Socio Communication Play and Educational Program Educating Parents on Direct and Interactive Teaching Techniques (SCoPEEDITT) [52].

health problems may place the parents at increased risk for poor physical and mental health [56]. Educating the family regarding the availability of various habilitation programs, social services and also to make sensible insurance policy decisions if available, are important especially in LMIC countries. Guidelines for Parents developed by IAP can be an extremely useful resource in this regard and can be provided to families of children diagnosed with delays and NDDs.

Apart from all these, already existing marital discord may worsen the socio-psychological family resource for caring a disabled child, especially so an autistic child. A practical way would be to use a Partner-Relationship Assessment Tool [57] that may highlight dissatisfaction in any of the domains of; *i*) Reality *ii*) Sexuality *iii*) Fantasy *iv*) Support *v*) Attitude *vi*) Personality *vii*) Conflict resolution. Family therapy is designed to help people within the family make sense of difficult situations, and help them work together to develop new ways of thinking about and managing these difficulties. Making a family plan at an early stage can avert various stressors especially among young eager parents [58].

Integrating and Coordinating Multidisciplinary Services: Families of children with NDDs, autism spectrum disorder (ASD) in particular, face long and complex process in navigating diagnosis and acquiring services for their children. The myriad presentations and severities of these conditions also means that a one-size-fits-all approach is not successful for all children. A transdisciplinary approach with the developmental pediatrician as the team leader, enables coordinated and coherent linkages between disciplines. Providing interdisciplinary education is essential to produce healthcare providers with the knowledge and skills required to optimally collaborate in working environments [59].

Recommendation IX

Provide parent guided low intensity multimodal therapies before 3 years as a centre-based or home-based or community-based rehabilitation services supported by a Developmental Pediatrician/ Physiatrist.

Setting-up of transition programs to school: The transition from early intervention programs to inclusive school settings and finally to college and to adult life represents a range of social challenges for children with developmental disabilities. Transitioning is an important and inevitable part of a child's life. Involvement and inclusiveness is another equally important domain necessary for a child to develop successfully. In a study in Australia, the challenges noted by parents included the school's lack of preparation for their child's particular developmental needs, especially in terms of the physical environment, while teachers reported challenges in meeting the needs of these children within the context and resources of the classroom [60]. The habilitation package therefore, should also include assessment of school readiness of children and pre-determined plans facilitating the smooth transition of children to schools.

K. Projected Effectiveness in the Context of IAP and NHP in India

Development of human resource to meet burden of at-risk, delay and NDDs in India

A good developmental surveillance program will depend

upon *i*) the degree of risk of developmental delay or discernable risk (example prevalence of low birth weight babies); *ii*) the burden of developmental delays in the community (2.5% in less than 3 years) [61] and *iii*) the burden of NDDs (9.2% in less than 6 years) [62]. The schedule of screening and follow up monitoring will differ according to level of risk, for eg. high-risk NICU graduates Vs low-risk post-natal babies [63]. To provide appropriate clinical habilitation service to this huge number of children, it is essential to concentrate on capacity building of manpower, building a team of developmental therapists (DT) or developmental nurse counselors (DNCs), well supported by developmental pediatricians wherever available.

Developmental Pediatricians and Developmental Nurse Counselor Team

Developmental Pediatrician (DP): In order to meet the need for qualified well trained developmental pediatricians, the IAP Neurodevelopmental Chapter initiated one year full-time Fellowship in Developmental and Behavioral Pediatrics at 15 accredited centres in India and each one of them is setting-up developmental pediatric units. This is in addition to the PG Diploma in Developmental Neurology Program of University of Kerala, conducted at CDC Kerala from 2004.

Developmental Therapists and Developmental Nurse Counselor (DNC): Developmental Therapists comprise a special team of graduates with two year full-time theoretical and practical training in clinical child development, certified by Government of Kerala. Kerala University of Health Sciences has already initiated the graduate program in Development Therapy. IAP Neurodevelopmental Chapter initiated one-year full-time Fellowship in Developmental Nurse Counselor Program for B.Sc. nursing graduates at NIMS-Spectrum-Child Development Research Centre, to be expanded to other accredited centers soon. The fellows in DNC and DTs are equipped to assist the pediatrician in the following roles; *i*) neurodevelopmental follow-up and early stimulation for NICU/SNCU graduates *ii*) early intervention for delays *iii*) assessment and intervention for 10 NDDs and *iv*) as a counsellor for parents of children with neurodevelopmental disorders/disabilities.

Allied therapists: The DT, being a multidisciplinary therapist, can be the nodal point of assessment and manage-ment in a BEIC. However, in a tertiary care centre, DEIC or CDC, a transdisciplinary assessment and management team is necessary, comprising the speech therapist, occupational therapist, physiotherapist, behavioral therapist with the pediatrician as the team leader and reference point.

Allied specialist medical professionals in the Habilitation Team

Role of pediatric neurologist: The developmental pediatrician should seek consultation from the pediatric neurologist in the following situations: *i*) Diagnostic dilemma *ii*) Features of neuroregression, neurometabolic or neurodegenerative disorders and global developmental delay, *iii*) Atypical regression in ASD and Attention-Deficit/Hyperactivity Disorder (ADHD), and *iv*) Pharmacological management.

Role of clinical geneticist: Services of a clinical geneticist available within the district or neighboring town or city should be sought in cases with *i*) dysmorphic features *ii*) global development delay *iii*) significant family history of genetic disorders and *iv*) on advice of pediatric neurologist.

Role of child psychologist: The child psychologist in the Habilitation team should play the following roles; *i*) Psychoeducational and behavioral assessment of the child *ii*) Provision of behavioral therapies, family therapies and counselling *iii*) Provision of remedial education along with the special educator and pre-school consultant

Role of child psychiatrist: The child psychiatrist should be consulted in case of *i*) management of maladaptive behaviors and aggression in children with NDDs *ii*) depression, anxiety and other psychiatric disorders *iii*) if psychotherapy is indicated.

Recommendation X

Developmental pediatrician to seek guidance when necessary of pediatric neurologist, geneticist, child psychiatrist, physiatrist, and other specialists, for special investigations and medications judiciously. Team leader to keep record of periodic follow-up assessment and feedback on emerging developmental status and the same to be shared with parents at regular intervals.

Recommendation XI

Need to promote ongoing academic programs in clinical child development which may be at graduate or post graduate level, or any other certificate program by NGOs or the Government under RBSK, for capacity building of community-based therapies.

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SUMMARY: SPECIFIC RECOMMENDATIONS

I There is a need for nationwide studies with representative sampling on epidemiology of babies with early NDD in the First 1000 days in India.

II SLD documented as the most common NDD in India after 6 years, and special efforts should be made to establish the epidemiology of infants and toddlers at risk for SLD, where ever measures are available.

III Preconception counseling focusing on pre-pubertal girls' nutrition, family life education for adolescents and premarital & newlywed counseling for above 18 years, as part of focusing on first 1000 days (270+365+365 days)

IV Promote efforts to organize systematic training programs in Newborn Resuscitation Program, Lactation management, developmental follow-up and early stimulation for SNCU/ NICU graduates.

V Risk stratification of NICU graduates, Newborn Screening for congenital hypothyroidism and phenylketonuria and hearing screening, counselling parents for early stimulation and surveillance in the first two years as part of focusing on first 1000 days.

VI Screening for delays by trained AWWs /developmental nurse counselors/developmental therapists/ PHC doctors at CEIC/BEIC, using simple validated Indian screening tools at 4, 8, 12, 18 and 24 months.

VII Holistic assessment of 10 NDDs at CDCs/DEICs by multidisciplinary team members (developmental therapist/ development nurse counselor, physiotherapist, occupational therapist, speech therapists, clinical psychologist) with developmental pediatrician/pediatrician as team leader.

VIII Confirmation of diagnosis by developmental pediatrician/developmental neurologist/child psychiatrist using clinical/diagnostic tools at CDC/ DEIC.

IX Provide parent guided low intensity multimodal therapies before 3 years as a center-based or home-based or community-based rehabilitation services supported by a Developmental Pediatrician/ Physiatrist.

X Developmental pediatrician to seek guidance, when necessary, of pediatric neurologist, geneticist, child psychiatrist, physiatrist, and other specialists, for special investigations and medications judiciously. Team leader to keep record of periodic follow-up assessment and feedback on emerging developmental status and the same to be shared with parents at regular intervals.

XI Need to promote ongoing academic programs in clinical child development namely PG diploma in Developmental Neurology (Kerala University), Fellowship in Developmental Pediatrics and Developmental Nurse Counsellor (IAP – NDP chapter) and B.Sc in Developmental Therapy (approved by Kerala University of Health Sciences) or any other certificate program by NGOs or the Government under RBSK, for capacity building of community based therapies.

Additional recommendations for Service Delivery of Habilitation Package:

XII Rashtriya Bal Swasthya Karyakram (RBSK) is the identified model for the Habilitation Services with an enhanced approach and collateral referral channels to other existing National Schemes, especially with the Pradhan Mantri Surakshit Matritva Abhiyan, Janani Shishu Suraksha Karyakram, Rashtriya Kishore Swasthya Karyakram to provide the full spectrum of care.

XIII Expanding beneficiaries of Rashtriya Bal Swasthya Karyakram (RBSK) and the fully functional District Early Intervention Centre (DIEC) available in 238 DIECs/766 (as on August 2022); it necessitates to enhance the RBSK by empowering the Block Early Intervention Centers (BEIC) to provide the clinical services sans medical services and certification.

NDD: neurodevelopmental delay; SLD: specific learning disability; SNCU: special neonatal care unit; NICU: neonatal intensive care unit; AWW: anganwadi worker; PHC: primary health care; CEIC: national ethics committee for clinical research; BEIC: Block Early Intervention Centres.

Web Table I District Early Intervention Center (DEIC) Vs Block Early Intervention Centres (BEIC)

Components	*District Early Intervention Center*	*Block Early Intervention Centres*
Ministry of support	Ministry of Health and Family Welfare (MOHFW)	Ministry of Health and Family Welfare/Women and Child Development
Mandate	Envisaged at the district level for 4D service provision & capacity building of staff posted at these centers	Definitive identification of at risk and early 4Ds and single allied health personal for transdisci -plinary service provision
Infrastructure	4000-5000 Sq.ft building with dedicated, standardized assessment & intervention rooms.	Not envisaged, needs planning
Human resources for health	Permanent and visiting medical and allied health specialist.	Developmental therapists (with multitasking skill): screening services, early stimulation and helping mother to be therapists
Service approach	Interdisciplinary	Transdisciplinary
Services provided	Cores service: Medical services, preventive health and immunization, general women and child services: nutritional and related to feeding of babies, neurological assessment, physiotherapy, occupational therapy, psychological services, cognitive development including play and socialization, testing for speech and language as well as vision and hearing Supplementary services: Certification	Cores service: General women and child services: nutritional and related to feeding of babies, neurological assessment, physiotherapy, occupational therapy, psychological services, cognitive development including play and socialization, testing for speech and language as well as vision and hearing Supplementary services: None
Outcome, documentation, referral & review	The 'DEIC Register' maintains the records of all outcomes. Monthly reports are captured through a chain comprising of DEIC manager, District Nodal Officer	The 'BEIC Register' maintains the records of all outcomes. Monthly reports are electronically/ manually sent through a chain comprising of BEIC manager to DEIC manager.

Joint Statement on Comprehensive Education for Adolescents and Young People to Support Their Healthy Development and Wellbeing: Adolescent Health Academy, Indian Academy of Pediatrics, Federation of Obstetric and Gynecological Societies of India, Indian Association of Preventive and Social Medicine, and Indian Public Health Association

Sukanta Chatterjee,[1*] Upendra Kinjawadekar,[2] HD Pai,[3] AM Kadri,[4] Sanghamitra Ghosh,[5] Vineet Saxena,[6] GV Basavaraja,[7] V Chandra-Mouli,[8] Rajesh Mehta,[8] Geeta Patil,[9] RN Sharma,[10] Madhuri Patel,[11] Supriya Jaiswal,[12] Purushottam Giri,[13] Kaushik Mitra[14]

[1]Chairperson 2023, Adolescent Health Academy (AHA), Indian Academy of Pediatrics (IAP), Agra, Uttar Pradesh; [2]President 2023, Indian Academy of Pediatrics, Mumbai, Maharashtra; [3]President, Federation of Obstetric and Gynecological Societies of India (FOGSI), New Delhi; [4]President, Indian Association of Preventive and Social Medicine (IAPSM), Badnapur, Maharashtra; [5]President, Indian Public Health Association, Kolkata, West Bengal; [6] Honorary Secretary General (2022, 2023), Indian Academy of Pediatrics, Mumbai, Maharashtra; [7]President 2024, Indian Academy of Pediatrics, Mumbai, Maharashtra; [8]Independent Experts, Geneva and New Delhi; [9]Chairperson Elect 2023, Adolescent Health Academy (AHA), Indian Academy of Pediatrics (IAP), Agra, Uttar Pradesh; [10]Secretary. Adolescent Health Academy (AHA), Indian Academy of Pediatrics (IAP), Agra, Uttar Pradesh; [11]Honorary General Secretary, FOGSI. New Delhi; [12]Chairperson, Adolescent Health Committee, FOGSI, New Delhi; [13]Secretary General, IAPSM, Badnapur, Maharashtra; [14]Secretary General, Indian Public Health Association, Kolkata, West Bengal.

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PREAMBLE

We, the national professional associations as advocates and contributors to health and development of the people in India, coming together for promoting realization of the opportunity of demographic dividend presented by the biggest cohort of adolescents and young people in the contemporary history of India; recalling the commitments made by India to the framework of the Sustainable Development Goals (SDG) [1], in particular those relating to health and well-being, education and gender equality; Recalling the National Education Policy 2020 that seeks to align with the national commitment under SDG4 to "ensure inclusive and equitable quality education and promote lifelong learning opportunities for all by 2030"; Reaffirming the rights and principles enshrined in the constitution of India that relate to health and wellbeing of people as well as country's commitment to the International Convention on the Rights of the Child, the Convention on the Elimination of all Forms of Discrimination Against Women, and others; Reaffirming the right of every human being to the highest attainable status of health, including sexual and reproductive health, and the right to education; Convinced that adolescents and young people are heterogonous groups, but as a combined force and a demographic dividend, are indispensable for the national economic and social development and represent a great potential as change agents to transform the society; Recognizing that crises like the coronavirus disease-19 (COVID-19) pandemic, conflicts, natural disasters, and other situations increase the vulnerability of adolescents' and young people's and limit their access to quality education and health services including information on sexual and reproductive health, mental wellbeing etc.; Acknowledging that it is essential to strengthen the capacity of adolescents and young people by providing them with age-appropriate, scientific and culturally-appropriate information, skills and services to make informed choices, adopt healthy behaviors, to overcome gender inequalities, be safe from coercion, exploitation and all types of violence, and to lead healthy and fulfilling lives to realize their full potential; Acknowledging also the high cost of not doing this in terms of immediate adverse implications on health and wellbeing of adolescents and young people, disengagement within family and education system as well as potential social disharmony in the long term.

Proclaim our collective commitment to work with the whole society towards holistic healthy development and wellbeing of adolescents and young people of our country; where all adolescents and young people possess the

Correspondence to: Dr. Sukanta Chatterjee, 889A, Lake Town, Kolkata, West Bengal 700089.
sukantachatterjee@hotmail.com

knowledge, skills, attitudes,and values they need to transition to adulthood, maintain healthy and respectful relationships with others, and be prepared to become active, empowered, and responsible citizens and help the country to realize full potential of national social and economic development.

CONTEXT

Public health issues and challenges in adolescence

India has a young population and there are about 378 million young people (10-24 years) including 250 million adolescents (10-19 years) [2]. They are generally perceived to be healthy but there are several public health issues that are common in this age in India:

Triple burden of nutritional disorders: Undernutrition, overnutrition and micronutrient deficiencies (like anemia) are common among girls and boys during adolescence [3].

Menstrual health and needs: A large number of adolescent girls and young women have inadequate knowledge about menstrual health [4]. Many girls lack access to adequate facilities for menstrual hygiene and with the associated social stigma this may lead to school absenteeism and increased dropout.

Substance use: There is a significant use of tobacco, alcohol and illegal substances among adolescents and young people that is detrimental to their health, education and social outcomes [3].

Mental health issues: Stress, anxiety, depression, self-harm and suicides are common among adolescents and young people but under reported [5]. There was an upsurge in these conditions during the COVID-19 pandemic and prolonged lockdown periods. Suicides have increasingly been reported among students from coaching institutes for competitive examinations in a city in northern India.

Risks of internet use: The internet and social media present, both, a great potential for adolescent and young people's development, and a significant exposure to new risks and dangers. Excessive and overuse of internet interferes with sleep, formal learning in schools and colleges, and presents challenges to mental wellbeing. Exposure to inappropriate, incorrect and harmful content like violence and explicit sexuality are associated with deleterious effects on their wellbeing and development. There is also an increased risk of cyber bullying, cyber-stalking, and exposure to online sexual predators [6].

Early sexual experimentation: Consequent to social-cultural changes, the opportunities for sexual experimentation and engagement have increased. Early sexual debut is more likely to be unsafe leading to unintended pregnancy and sexually transmitted infections [3].

Early marriage and unintended pregnancies: Child marriages (under 18 years age among girls) are progressively decreasing in India. Nevertheless, early marriage is associated with lesser use of modern contraception and higher fertility [3]. Adolescent pregnancies are associated with higher health risks for the mothers and their infants. Maternal mortality is the leading cause of death among adolescents and young women [7]. Early marriage and pregnancy also contribute to school dropout and disruption in social and economic activities.

High unmet need for contraception: Adolescents have higher unmet needs of family planning as well as for modern contraceptive methods compared to older age groups [3].

Social norms and gender-based violence: Gender-based violence (GBV) including harassment and sexual violence, physical and psychological violence are present in our society and are often reinforced by gender norms that justify these.

Limited access to timely and relevant information and quality sexual and reproductive health (SRH) services: Lack of access to timely and scientific information on sexuality and reproductive health, and responsive services for adolescents and young people, especially girls, increases the risk of unintended adolescent pregnancy, unsafe abortion, human immune deficiency virus (HIV), and other sexually transmitted infections (STIs). Poor information and awareness also lead to a lack of self-confidence in understanding sexuality and managing related situations and to decreased utilization of the required services.

Limited societal awareness, cultural barriers and dialogue: Parents, teachers and other members of society often have limited awareness of SRH needs of adolescents and their concerns. In addition, cultural barriers and social stigma related to sexuality prevents a healthy dialogue with the adolescents, especially girls, before, and around puberty.

Society's reaction and response to adolescent behavior: Recent media coverage that gained public attention demonstrates a lop-sided response to the adolescent sexual curiosity that manifested as finding of contraceptives in the bags of school students in a metro city [8]. The reaction adopted by local authorities points out to inadequate awareness of adolescent sexuality and deep social and cultural overlay in managing the situation.

Restrictive legal and policy framework: There is a need for ensuring consistency and coherence across multiple existing government policies and laws that affect adolescents and young people so that the barriers to provision of information and services to adolescents (legally minors). It is required to strike a balance between the ethical and human rights for adolescents to seek sexual and reproductive health education and services and the need for parental consent, as well as the provisions of child protection laws like Protection of Children Against Sexual Offences (POCSO) Act.

Opportunities

Given India's young and dynamic population, investing in health and education will ensure economic and social empowerment of young people and will help in realizing the demographic dividend leading to rapid economic growth for the country.

Global International Technical Guidance on Sexuality Education (UNESCO, UNAIDS, WHO and partners), 2018, provides an evidence-based framework for a holistic and comprehensive education covering the common health risks faced by Indian adolescents mentioned above [9]. The technical guidance informs that the evidence shows that it is possible to implement effective education and information programs for SRH that are aligned with the laws, policies, values, and culture of a country. Such programs lead to improved knowledge, acquisition of appropriate skills and attitudes about reproduction and social relationships, as well as a reduction in risk of pregnancy, STIs, HIV and GBV.

In India, there are presently several significant opportunities for provision of information, and knowledge, and develop skills and attitude among adolescents and young people towards realizing the demographic dividend for national development.

Box 1 enlists the public health issues and challenges in adolescence.

- Triple burden of nutritional disorders
- Menstrual health and needs
- Substance use
- Mental health issues
- Risks of internet use
- Early sexual experimentation
- Early marriage and unintended pregnancies
- High unmet need for contraception
- Social norms and gender-based violence
- Limited access to timely and relevant information and quality SRH services
- Limited societal awareness, cultural barriers and dialogue
- Society's reaction and response
- Restrictive legal and policy framework.

Adolescent Education Program (AEP): The government of India is implementing the revised adolescence education program developed by National Council of Educational Research and Training (NCERT) through state AIDS control societies in coordination with the State Councils of Educational Research and Training (SCERTs) for adolescents both inside and outside formal schools, since 2013. The aim is to empower adolescent learners to acquire knowledge of their needs and concerns related to the period of adolescence and develop life skills that enable them to practice informed and responsible behaviors [10]. However, the scale up has been slow-only an estimated 25% schools are implementing AEP and some states are not implementing it at all.

Rashtriya Kishor Swasthya Karyakram (RKSK, National Adolescent Health Program): Government of India is presently implementing this national program under National Health Mission (NHM) since 2014 with the objectives to promote healthy lifestyle, reproductive and sexual health, nutritional status, substance misuse prevention, violence free living, and mental and emotional wellbeing [11]. This builds upon the previous phase of national adolescent health program (RCH-II ARSH strategy) implemented during 2005-2014 that also emphasized provision of appropriate information to adolescents in health services and in schools.

National Education Policy 2020: This policy provides another huge opportunity with expanding school enrolment and educational opportunities with modern pedagogy, full equity and inclusion, and emphasis on character-building of children including creativity and critical thinking, life skills, ethical and human values, all of which contributes to the wider goal of national building [12].

School Health and Wellness Program (SHWP): Ministries of Health and Education have jointly launched the intensified school health program through health and wellness school initiative. This proposes curriculum-based participatory learning process by trained school teachers in collaboration with trained health workers and peer educators in the schools [13].

Digital technology expansion: Access to mobile devices, internet connectivity and usage rates are growing rapidly in India. The information and communication technology has tremendous potential to reach young people, especially those who are hardest to reach. However, a careful approach is required to minimize multiple risks of

unsupervised and excessive use of screen-based activities. A young population, combined with increasing rates of internet connectivity and use in India, could be a decisive advantage in promoting awareness, self-respect and esteem, health, wellbeing, and effective behaviors for respectful treatment of self and othersas well as self- care. The technology also provides an opportunity for rapidly engaging with parents, families, teachers, other gatekeepers and stakeholders to ensure a supportive and safe environment for the growing adolescents and young people.

Call to Action

We, the related national professional associations, strongly recommend immediate actions by all actors to support large scale programs for information, education and services towards healthy development of all adolescents and young people, everywhere in our country.

- We commit ourselves and call upon other stakeholders to support and facilitate, without delay, the following actions to ensure that all adolescents and young people, in schools, colleges and other educational institutes like coaching centers, as well as those outside the educational institutes, receive all the age-appropriate, scientific and evidence-based information. Harmonization of multi-sectoral policies and strategies to protect the health and education rights of all adolescent girls and boys, and young women and men.
- Education system to implement comprehensive information and education programs and addressing the cognitive, emotional, physical and social aspects of health and wellbeing of adolescents and young people in variety of educational institutions, starting from 5 years of age. Such a system should provide age-appropriate scientific information and necessary skills to understand their responsibilities to remain healthy, and to be able to develop respectful social relationships, realize positive or negative consequences of their choices for their own well-being and that of others.
- Health system to collaborate with education system in providing information and skills, especially related to sexual and reproductive health with the aim of promoting holistic healthy development and wellbeing of adolescents and to provide acceptable and accessible health services through facility-based and community-oriented adolescent-friendly health approaches.
- Whole society to come together to provide safe and supportive environment for providing ample opportunities to all adolescents and young people to acquire necessary information, skills, attitudes and values as well appropriate services, in school or out-of-school, for maintaining good health including sexual and reproductive health and overall wellbeing, and prevent h nder norms that can be detrimental to the health and well-being of adolescent girls and boys and young people.

Our collectively aim is to equip them with the correct knowledge, skills, attitudes, and values that will enable them to live life and thrive with good health, well-being and dignity.

RECOMMENDED STRATEGIES

Engage all actors and beneficiaries: Increase awareness and engagement of all relevant stakeholders, gatekeepers and beneficiaries – including adolescents and young people, parents and families, community, government functionaries, political and religious leaders, teachers, civilsociety organizations, technical and financial partners, and international organizations.

Ensure collaboration: Ensure strengthened collaboration and synergy of action between different sectors (e.g. education, health, social welfare, child protection, finance, justice and media) at all levels, in particular between education and health departments.

Intergenerational dialogue: Promote through formal and informal programs, an ongoing dialogue among adolescents, young people, parents-families and teachers on overall health and wellbeing; sustain efforts to increase the comfort level of adolescents, parents and teachers to discuss issues related to sexuality, reproduction, social relationships, gender etc. and facilitate use of appropriate education and health services.

Reduce social stigma around adolescent sexuality: Take collective actions to reduce social and cultural stigma, deconstruct taboos and stereotypicbeliefs; examine andre-engineer social andgender norms that can be detrimental to the health and well-being of adolescent girls and boys and young people.

Scale up implementation of comprehensive education and information programs with good quality in schools: Education and health departments to scale up effective implementation of existing programs like Adolescence Education Program (AEP), RKSK, School Health and Wellness Program (SHWP) and ensure that formal and non-formal educationincludes comprehensive, scientifically accurate, age-appropriate, and culturally sensitive curricula from early childhood to higher education, that are easily accessible to children, adolescents and young

people, girls and boys alike in and out of school settings, everywhere. While undertaking this, keep an ongoing dialogue and collaboration with all the staff members of educational institutes and parents to ensure their comfort and capabilities.

Capacity building and training of teachers: Strengthen the training programs for teachers through pre-service and in-service settings to build their capacity to comfortably deliver quality comprehensive health education and information programs using participatory and learner-centered pedagogical approaches, as well as develop and disseminate appropriate teaching materials and guidance tools to support this function and for continued engagement with parents.

Linking with adolescent health services: Health department must strengthen provision of adolescent friendly health services including SRH services as per the RKSK and collaborate with the education sector for improving the quality and coverage of school health services under SHWP. Such linkage would provide appropriate and effective referral services from educational institutions to health services.

Strengthen monitoring and evaluation: The government should strengthen the monitoring and evaluation systems for effective monitoring of the performance of health and education systems through collection and analysis of good quality, disaggregated data to inform the decision-making process and program management. Invest in documentation and research to understand the situation and keep abreast of the evolving needs of adolescents and young people. The recommended strategies are summarized in **Box 2**.

Action Now

We reach out to policy makers and all relevant stakeholders across the society for collectively developing and sustaining a public movement for provision of comprehensive health education for children, adolescents and young people to support their healthy development and wellbeing with a sense of urgency so that India realizes the demographic dividend in her progress towards becoming a developed economy and a prosperous and peaceful society.

Box 2 Recommended Strategies

- Engage all actors and beneficiaries.
- Ensure collaboration.
- Intergenerational dialogue.
- Reduce social stigma around adolescent sexuality.
- Scale up implementation of comprehensive education and information programs with good quality in schools.
- Capacity building and training of teachers.
- Linking with adolescent health services.
- Strengthen monitoring and evaluation.

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INVITED COMMENTARY

Why Parental Education may be the Key to Raising the Digital Natives?

Anjali Varma,[1*] Annapurna Sudarsanam[2]

[1]Associate Professor, Department of Psychiatry and Behavioral Medicine, Virginia Tech Carilion School of Medicine, and Director Mental Health Clinic, Salem VA Health Care System Salem, Virginia 24153, USA.
[2]Consultant Pediatric Neurologist, Birmingham Children's Hospital, United Kingdom.
[*]anjali.varma@va.gov

We are living in a rapidly changing world. We belong to a generation that is witnessing a sea change in lifestyles courtesy economic empowerment, exposure to world culture through travel and media and most importantly technological advancements. These have challenged and threatened traditional ways of living, family life and the upbringing of children.

The first two years of life are a period of intense neural development by way of rapidly expanding synaptogenesis and pruning of neural pathways. It lays the foundation for neural networks which in turn form the basis for future learning, language development, memory, social and emotional development. These processes are refined by the exposures and interactions in those crucial initial periods of life among other things.

Smart phones made their debut in the 2000s and are now embedded in the daily lives of our children. The portable nature of these devices has meant that they have now entered every living space including the dining room, the bedrooms, the cars etc. They are being used as "virtual pacifiers" or "electronic babysitters" to keep children occupied during typical daily routines [1,2]. Their interactive nature makes them more appealing than the relatively passive television. Children are interacting with and immersed in cyberspace where they learn, entertain themselves and play. Television and smart devices do not offer the same experiences as traditional practices do and the effects of these changes on the developing child especially in the first few years are still widely unknown.

Flashing lights, quick edits and auditory cuts, ability to flip through video content whilst overstimulating the developing brain, keep the infant engaged. These are way different to the reality of everyday life which the toddler then finds underwhelming and boring and therefore struggles to keep engaged and maintain focus. Chen et al [3] showed children who had more screen time had a higher reward orientation and weaker fronto-striatal connectivity. Their study showed screen time influences dorsal striatum connectivity and provides neural and behavioral evidence for the negative impact of daily screen use on developing children.

The time spent on the media is time lost from engaging in positive interaction with family, enriching activities like reading and physical play. Parents often allow use of digital media for the perceived educational value. Evidence from research does not appear to support a positive impact of educational programming on the very young age group (under-2 years) who find it more difficult to learn information from a video compared to the same information being taught in a live presentation by a human. In their meta-analysis looking at the association between screen use and child language skills, Magidan et al emphasize that when young children are exposed to screens, it interferes with their engagement in verbal dyadic exchanges that have been shown to promote communication and language acquisition [4]. There is research to support the notion that increased quantity of screen use is linked with delayed language acquisition in children less than 2 years of age [5].

Much is known and published about how our teenagers are being negatively impacted by excessive screen time both in terms of their physical and mental health. Obesity and increased incidence of myopia has been linked to early screen exposure. Sleep-wake cycle disruption of kids due to late night screen exposure is also well known [6,7].

The American Academy of Pediatrics (AAP) as well as the Indian Academy of Pediatrics (IAP) recommend keeping "children under two" as "screen-free" as possible due to potential adverse effects on early brain development. However, there is very little parental and even professional awareness of this [8,9]. As more research and expert opinion regarding the profound negative impact of digital exposure is being published and is being brought to public awareness, parents are struggling to limit screen time and access to the smartphones with their older kids (age 6-12 years) and teens who have been exposed and

'addicted' to the dopamine release from the likes, comments and shares as well as consistent self-doubt in the absence of these. As we try to reclaim the childhood of our next generation and want kids to be kids a little longer, the key is early awareness and education of parents to limit screen time in early childhood.

In the current issue of *Indian Pediatrics*, Gupta et al [10] report an open labeled randomized controlled trial with a focused parental education and anticipatory guidance for limiting screen time in early childhood during immunization visit for 120 healthy 9-10-month-old infants. The study is simple yet carefully crafted where consenting primary caregivers in the education group received education in multiple formats including in person, face to face active counseling, printed take home educational material that was reinforced telephonically monthly for 6 months targeting reduction of screen time. The control group received routine counseling on general health measures such as nutrition, immunization and general safety measures. Development, behavior scoring and anthropometry were recorded after six months of intervention, again during routine immunization visit and screen time data was collected from parents along with interim medical and psychosocial history. Primary outcome measures revealed that 3% (2/60) children in the education group had screen time > 1 hour/day as compared to 53% (32/60) ($P < 0.001$) in the control group. The median interquartile range for total screen duration in the education group was 35 (30, 49) min/day in comparison to 75 (50, 90) min/day in the control group. Children in the educational group had a significant change in developmental domains of fine motor and adaptive skills. No behavioral issues were noted in either group and there were no differences in anthropometric parameters.

This is one of the first studies that focuses specifically on infants less than one year of age and their parents in the Indian setting. The results of this study by Gupta et al are consistent with some of the recent studies cited in a recent meta-analysis on interventions to reduce sedentary behavior in 0-5-year-olds where interventions lasting more than 6 months in home, preschool and community settings are likely to be most effective in reducing screen time [11].

These results are interesting as they highlight the use of the immunization visits as a 'golden opportunity' to target the parent audience to focused education and guidance regarding the need to limit screen exposure for children under 2 years age. An intervention like the one cited in the study is quite resource intensive. However, the value of such an early intervention like the one detailed in this study may be the key to preventing an epidemic of developmental and behavioral problems in our children and youth. If such interventions can be incorporated as standard of care and pursued on a long-term basis during all pediatric annual well visits, we may be able to save our society from what we are experiencing today in terms of childhood obesity, early onset of myopia, lack of social connectivity, increased prevalence of emotional dysregulation, depression, suicide, anxiety and self-harm among children and youth which is only the tip of the iceberg as we see it. It is our responsibility as the adults in the society to preserve the childhood of our next generation and hence a call for action for legislative reforms, rules from school authorities as well as consistent rules from not only parents but also caregivers, teachers, in addition to pediatricians and child psychiatrists that convey the same message that the devil lies in the screen.

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ORIGINAL ARTICLE

Parental Education for Limiting Screen Time in Early Childhood: A Randomized Controlled Trial

Yashika Poonia, Sumaira Khalil, Pinky Meena, Dheeraj Shah, Piyush Gupta

Department of Pediatrics, University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi.

ABSTRACT

Objective: To assess the impact of focused parental education on limiting screen time in early childhood.

Methods: An open label randomized controlled trial was conducted in a tertiary care hospital in Delhi wherein 120 healthy children aged 9-10 months of age, born at term gestation and appropriate for gestational age (birth weight ≥ 2500 g), attending the immunization clinic reporting for measles-rubella (MR) vaccination were enrolled. Primary caregivers were randomized to either receive 30 minutes of in-person active counselling with pre-designed content including a printed pamphlet targeted at reduction of screen time (Educational group, n = 60) or to receive routine in-person counseling on general health measures (Control group, n = 60). All caregivers were followed up. Primary caregivers in both groups were reinforced telephonically every month for 6 months. At the end of six months, we assessed the proportion of children with screen-time > 1 hour/day and the median duration of screen-time (minutes / day). We also compared both groups in terms of changes in pre-post intervention developmental and behavioral scores (measured with Ages and Stages questionnaires).

Results: After 6 months of follow-up, 3% (2/60) children in the Educational group had screen time > 1 hour/day as compared to 53% (32/60) (P < 0.001) in the Control group. Median (IQR) for total screen duration in the Educational group was 35 (30,49) minutes/day compared to 75 (50,90) minutes/day in the Control group (P < 0.001). Children in the Educational group were also observed to have a significant change in behavioral score and fine motor and adaptive skills as compared to controls.

Conclusion: Parental education starting in infancy is a promising intervention to reduce screen exposure in children; it may also have a positive impact on their developmental and behavioral skills.

Keywords: *Behavior, Development, Digital Media, Infants, Smartphone, Television*

INTRODUCTION

Children are exposed to screen-based devices from early childhood [1]. In a recent study from urban Delhi, 99.7% children were exposed to screen-based media by 18 months of age; with nearly 90% viewing the screen for more than an hour a day [2]. Excessive screen exposure reportedly leads to delay in gross and fine motor development and impairment in expressive language development [3]; and may also affect attentional capacity, problem solving, and behavioral development. Parental screen habits and attitudes influence a child's screen-time significantly, as children tend to imitate what they see in their surroundings [1].

A multitude of interventions have been found to be effective in reducing screen time in children [4-9]. Early childhood interventions in the form of responsive parenting [9], reducing the number of screens within the home [5], reducing screen access to kids [8], and condi-tioning children to physical activity [4] are reported to be effective interventions. However, there is paucity of specific studies on the impact of parental counseling targeting a reduction in screen-time in the first 2 years of life, especially in the Indian context.

We hypothesized that an intervention starting within the first year of life in the form of parental education and early anticipatory guidance can limit screen-time in the initial two years of life. Screentime reduction may also have a positive impact on the development and behavior of the child. We conducted this study to assess the impact of focused parental education on limiting screen time in early childhood and improvement in behavior and development.

METHODS

We conducted this open label randomized controlled trial (RCT) in a medical college affiliated teaching hospital between January, 2021 and August, 2022. A written

Correspondence to: Dr. Piyush Gupta, Professor, Department of Pediatrics, University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi-110095.
prof.piyush.gupta@gmail.com
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informed consent was obtained from caregivers of all participants and an ethical clearance was obtained from the Institutional Ethics Committee prior to commencing the study.

Healthy children between 9-10 months of age, born at term gestation and appropriate for gestational age (birth weight > 2500 grams) reporting to the immunization clinic for measles-rubella (MR) vaccination were approached for inclusion. Infants with weight-for-age and weight-for-length < - 2SD (as per WHO growth standards), congenital malformations, developmental delay, chronic or acute systemic illness, cerebral palsy, syndromic disorder, and visual or hearing impairment were excluded. Children and caregivers not having access to screen media (television, smartphone, tablet, laptop, computer, and video game device) were also excluded.

At enrolment, anthropometry of all children was recorded and interpreted as per standard procedures [10-12]. Details regarding the primary caregiver, their educational qualifications, socioeconomic status as per modified Kuppuswamy scale [13], and primary rearing environment were recorded. Household ownership of television, handheld devices like smartphones, tablets, laptops, and personal computers was also ascertained. Frequency of screen viewing practices of their child (days/week), time (minutes) that their child spent on viewing the screen during the past week (specifying the days) were also recorded. Child's age at first exposure to screen devices was ascertained and the primary caregiver's screen-time (frequency and duration in a week) were also documented. Parental modelling for screen viewing was ascertained at the time of enrolment by asking the primary caregiver about perception of their own and their child's screen viewing habits; and involvement in activities like watching/using screen device during meal time, for entertainment and academic activities. We also assessed the developmental scores using the age-appropriate Ages and Stages Questionnaire (ASQ3) [14] and behavioral scores using the Ages and Stages Questionnaire: Social-Emotional-2 (ASQ:SE2) questionnaire [15] at enrolment. The Hindi versions of these questionnaires have been validated in Indian settings by AIIMS, New Delhi. The ASQ3 questionnaire was used to address competence behaviors, whereas, ASQ:SE2 questionnaire was used to assess both competence and problem behaviour. Low scores using the ASQ:SE2 questionnaire are indicative of normal behavior, and higher scores indicate behavioral problems. High scores on ASQ3 questionnaire are rated better as compared to low scores.

Children were randomized using block randomization of varying blocks into two groups: Educational group and Control group. The random number sequence was generated by a third person not related to the study. Allocation was concealed by the sealed envelope technique. Both participants and investigators were aware of the intervention being done or otherwise.

Parents in the Educational group received 30 minutes of in-person active counseling with pre-designed content targeted at reduction of screen time in a language (English/Hindi) the caregivers could understand. During the session, they were guided to incorporate age-appropriate responsive parenting skills, increase interactive play of the infant, limit screen exposure, and modify parental media habits. The content was delivered as a one-to-one structured talk, and a printed pamphlet with these instructions was also handed over to the primary caregiver at the end of the session. The same was also reinforced telephonically on monthly basis (5 sessions) till the end of the study i.e., for 6 months from enrolment.

Primary caregivers in the Control group received routine counselling regarding nutrition, immunization, and general safety measures. They were informed about the screen use guidelines [16] for infants and young children if asked for. They were also contacted telephonically every month and reminded about general health care and safety measures and about filling the screen time data form for the child. They did not receive any active counselling regarding reducing/modifying screen-time of their children. In both groups, the primary caregivers were instructed to maintain a weekly screen chart in a prescribed format.

Development, behavior scoring, and anthropometry were recorded after 6 months of intervention (conducted at 15-18 months of age during routine immunization visit). The screen-time data sheets filled by the parents were collected. Any significant health related events during follow up duration were noted (illness requiring hospital admissions, family issues impacting development). They were then guided regarding further screen time limitation of their child.

The primary outcome measures included *a*) proportion of children with screen-time >1 hour/day; and *b*) median duration of screen-time (minutes/day). Secondary outcome measures were *a*) change in developmental scores and *b*) proportion of children with problematic behavioral scores.

A previous study reported that 88.7% of children were viewing screen for > 1 h/day by the age of 15-18 months [2]. Aiming for a 25% relative reduction in this proportion, we needed to study 54 intervention and 54 control group participants to be able to reject the null hypothesis with power of 0.8 and Type I error of 0.05. Assuming a 10%

dropout, we included 60 participants in each group.

Statistical analysis: Data were analyzed using IBM SPSS Statistics version 20.0. For normally distributed data, continuous variables between the two groups were compared using Student *t*-test and for data that were not normally distributed, Mann-Whitney *U* test was used. Proportions of young children with screen-time > 1 hour/day, and problematic behavior in the two groups were compared using chi-square test. Changes in developmental and behavioral scores (between baseline and 6 months after intervention) were compared by paired t test. In case of lost to follow up, censoring was done at the last available observation. Intention to treat analysis was used for all primary outcomes. *P* value < 0.05 was considered significant.

RESULTS

Out of 128 children who were approached; 120 children, median (IQR) age 9 (9,10) months; 53% (*n* = 56) boys, were finally enrolled. The flow of participants is depicted in **Fig. 1**. Most of the participants belonged to the urban middle class (90%); mother was identified as the primary caregiver in 95% families. Almost all parents were literate with a third of them being graduates. In most homes, the father was employed (98%) and the mother was a home maker (86%). The mean (SD) weight-for-age (*z*-score) (WFAZ), mean (SD) length/height-for-age (*z*-score) (HFAZ)), and mean (SD) weight-for-length/height (*z*-score) (WFHZ) of enrolled children were -0.8 (0.5), -0.9 (5.2) and -0.9 (0.6), respectively. Baseline socio-demographic characteristics between the two groups were comparable (data not shown).

Smartphone was universally present in all households; in 115 (96%) families, both parents owned a separate smartphone. Television and computer or laptop or tablet were owned by 71 (59%) and 28 (23%) families, respectively. The median (IQR) age at the first exposure to a smartphone was 6 (6,7) months, starting as early as from 3 months of age. The frequency and duration of watching the phone screen were comparable in the two groups. However, the frequency and duration of watching television was significantly higher in children of the Educational Group (**Table I**).

Comparing the screen use practices in the primary caregivers between the groups, the frequency of watching screens of all devices was comparable. However, the duration of use of mobile phones was significantly more in caregivers of the Educational group as compared to the

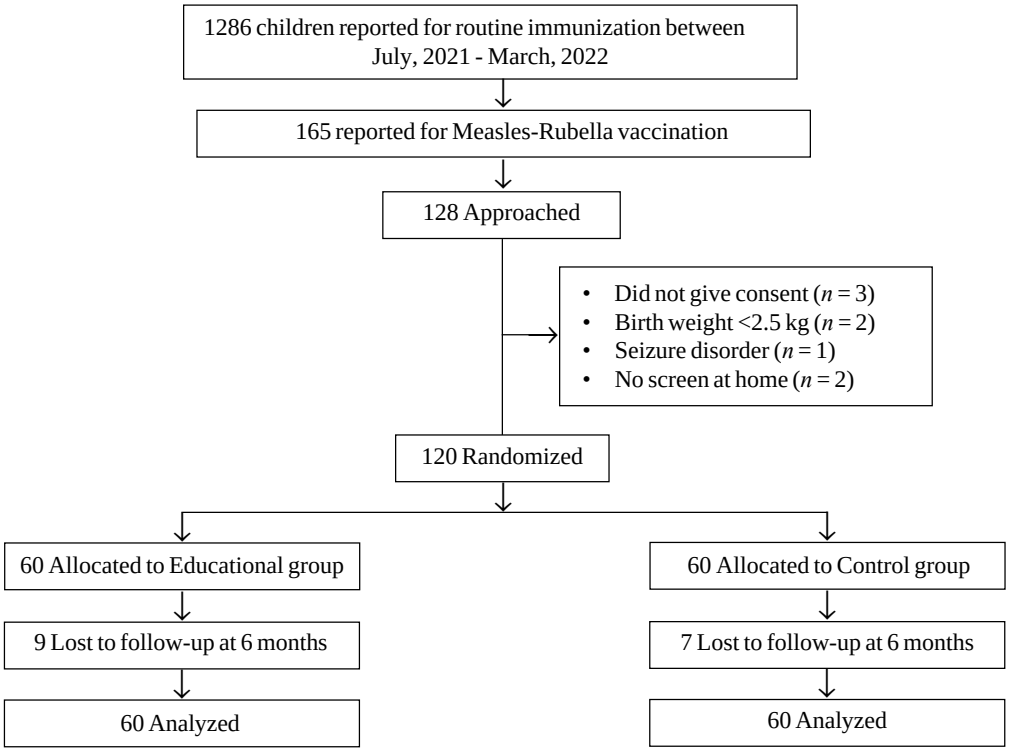

Fig.1 Study flow chart showing enrolment of participants

Table I Baseline Screen Use Practices in Caregivers and Children Enrolled in the Study

Parents	*Educational group (n = 60)*	*Control group (n = 60)*
Mobile device exposure frequency duration (days/week)	7 (7, 7)	7 (7, 7)
Television exposure frequency (days/week)	6 (0, 7)	2 (0, 5)
Duration of mobile devices exposure (minutes/day)[a]	120 (60, 120)	60 (60, 120)
Duration of television exposure (minutes/day)	30 (0, 90)	30 (0, 60)
Children		
Mobile device exposure frequency duration (days/week)	7 (7, 7)	7 (5, 7)
Television exposure frequency (days/week)[b]	2 (0, 7)	0 (0, 6.5)
Duration of mobile devices exposure (minutes/day)	30 (15, 30)	30 (15, 30)
Duration of television exposure (minutes/day)[b]	10 (0, 30)	0 (0, 20)

Values expressed as median (IQR); [a]P = 0.05; [b]P < 0.05.

Control group. More than half (n = 61) of the caregivers were concerned quite a bit about the time they spend on screen; while only 40% (n = 48) restricted screen exposure of their children. Most of the caregivers were watching screens with their child while eating dinner (108/120,90%).

After 6 months of follow up, only 3% (n = 2) children in the Educational group had screen time > 1 h/day as compared to 53% (n = 32, P < 0.001) in the Control group. Median (IQR) duration of screen time after 6 months reduced significantly in the Educational group to 35 min/day (30, 49), while the reduction in the Control group was 75 (50, 90) min/day (**Table II)**.

After 6 months of intervention, children in the Educational group had a significant change in developmental domains of fine motor and adaptive skills. Change in pre-post intervention behavioral score was also significantly higher in the Educational group (**Table III**). There were no behavioral issues with any of the kids in both groups, either at baseline or at end point. No difference was noted for the anthropometric parameters between the groups at the end of the study (data not shown).

DISCUSSION

In this RCT, we ascertained the efficacy of parental education for reducing screen-time in infancy. The screen-time of children decreased significantly in the Educational group with significant improvement in behavioral and developmental scores after 6 months of intervention.

Indian Academy of Pediatrics (IAP) formulated recommendations for limiting screen-time in Indian infants, children, and adolescents, and recommended that children below 24 months of age should not be exposed to any type of screen and screen should not be used as a measure to calm the child or to feed [17]. Parents should avoid watching screens while with the child and they should be more involved in physical activity and age-appropriate activities. In our study, the median (IQR) age at the first exposure to mobile phones was 6 (6,7) months starting as early as 3 months for smartphones and video-calls which was similar to that reported by Meena et al [2]. Madigan et al [3] in a longitudinal cohort study including 2441 mothers and children, reported that higher levels of screen time at 24 and 36 months were significantly associated with poorer performance on developmental screening tests at 36 months (β - 0.06; 95% CI -0.10 to -0.01) and 60 months (β - 0.08; 95% CI -0.13 to -0.02), respectively. Therefore, we included infants hypothesizing that early childhood intervention with in first year of life would lead to limitation of screen time and positively impact their development.

In a systematic review [18], behavior change tech-

Table II Duration of Screen Exposure in the Two Groups After 6 Months Intervention

Parameters	*Educational group (n = 60)*	*Control group (n = 60)*	*P value*
Total screen duration (minutes/day)	35 (30, 49)	75 (50, 90)	< 0.001
Duration of mobile device exposure (minutes/day)	22 (20, 30)	46 (30, 60)	< 0.001
Duration of television exposure (minutes/day)	13 (0, 30)	30 (0, 30)	< 0.001

Values in median (IQR).

Table III Change in the Behavioral and Developmental Scores Following Intervention (*n*=120)

	Educational group			*Control group*			*Mean Difference*	*P value*
	Baseline	*Follow-up*	*Change*	*Baseline*	*Follow-up*	*Change*	*(95% CI)*	
Behavioural Score ASQ:SE2	32 (8.5)	26 (7.3)	7 (7)	30 (11.5)	28 (9)	2.3 (8)	4.3 (1.4-7.1)	0.004
ASQ3 Language	56.4 (3.3)	56 (2.3)	0.08 (3.2)	56 (3.2)	56 (3)	0.25 (3.6)	-0.167 (-1.4-1.0)	0.777
ASQ3 Gross motor	57 (3.5)	59 (2.1)	1.4 (3.4)	57 (3)	57 (3)	0.08 (3.5)	1.33 (0.07-2.5)	0.061
ASQ3 Fine motor	56.2 (4)	56.4 (3)	0.17 (3)	57 (3)	56 (2)	-1.0 (3)	1.16 (0.06-2.2)	0.041
ASQ3 Personal social	57 (3)	56.8 (2.7)	0.25 (3)	56 (3)	55 3)	-1.08 (3)	1.3 (0.24-2.4)	0.152
ASQ3 Adaptive	56 (2.5)	57 (2.7)	0.5 (3)	56 (3)	56 (3)	-0.33 (3.03)	0.83 (-0.2-1.92)	0.019

Values in mean (SD). ASQ3: Ages and Stages Questionnaire3, ASQ:SE2: Ages and Stages Questionnaire: Socio-emotional, ASQ-SE2 low score indicates normal behaviour and higher score is suggestive of behavioural problem, ASQ3 high score is better as compared to low.

niques, like "behavior substitution", "information about social and environmental consequences", "demonstration of the behavior", "behavioral practice/rehearsal" and "goal setting (behavior)" are reported to be most promising in reducing screen exposure. Parental education intervention is one such effective intervention [19]. A parental education intervention in our study led to a significant reduction in the proportion of infants with daily screen time > 1 hour and duration of screen-time after 6 months of follow up. Lin et al [20] conducted a cluster randomized controlled trial with the aim to investigate the effect of a parental educational program on screen use among preschoolers and reported a significant reduction in screen time (effect size: 0.83, $P < 0.001$), improved sleep quality (effect size: 0.57, $P = 0.01$) and attention score (effect size: 0.77, $P = 0.02$) for psychosocial adaptation in children in the experimental group. Similar results were reported by Dennison et al [21] and Fitzgibbon et al [22].

Intervention Nurses Start Infants Growing on Healthy Trajectories (INSIGHT) trial [9], conducted an RCT in 2018 where primiparous mother-newborn dyads ($n = 279$) were randomized and responsive parenting was trained to the Educational group by nurses at 3, 16, 28, and 40 weeks to minimize screen exposure. They concluded that from infancy to early childhood, responsive parenting reduced screen time and television exposure, but did not increase the frequency or amount of interactive play. A recent systematic review specifically targeting children aged under six years found that interventions lasting greater than six months and conducted in a community, home, or pre-school setting were most effective at reducing screen time [23]. Similar observations were seen in our study, re-emphasizing the positive impact of parental education intervention on reducing screen exposure starting as early as neonates to less than 1 year of age.

Excessive screen exposure is found to be significantly associated with delayed motor skills, cognitive and language development [24,25]. Screen exposure in infancy is found to be positively associated with self-regulatory problems later [26]. In our study, development scores for fine motor and adaptive skills were better in the Educational group as compared to the Control group, while there was no difference in gross motor, personal social, and language skills. Also, behavioral scores were found to be better in the Educational group as compared to the Control group. Xie et al [27] observed that preschoolers with screen time of more than 60 minutes tend to have significantly more behavioral problems (total problem: 35.84 vs 32.76, $P = 0.024$; externalizing: 11.54 vs 9.08, $P = 0.016$). Similarly, Christakis et al [28] reported that an increase in the number of hours that a child watched television at the age of 1 year predicted a 28% increase in attention problems when the child reaches age seven. In our study, children enrolled were less than 1 year of age, as maximum brain development occurs in the first 2 years of life. Therefore, promoting age-appropriate responsive parenting, with parental education and early anticipatory guidance within the first year of life can prevent behavioral and developmental problems due to early screen exposure.

An RCT conducted in the past reported greater reductions in targeted sedentary behavior ($P < 0.001$), children's BMI ($P < 0.05$), and energy intake ($P < 0.05$) in the Intervention group compared to the Control group [29]. In our study, no difference in the anthropometric parameters were seen between the Educational group and the Control group. This difference could be attributed to the shorter period of follow-up in our study as compared to the above study where monitoring was done for 2 years.

The study had some limitations. This was an open labelled study where blinding could not be done and only one face to face interactive session was conducted with the primary caregivers. Since data collection relied on parental reports, there was a risk of recall and social desirability biases which also could be a limitation of the study. Children were followed only for 6 months, which might be

WHAT THIS STUDY ADDS?

- Early childhood intervention in the form of parental counseling is an effective intervention in reducing screen-time duration in children aged below 18 months.

too short a period to assess development and behaviour, therefore studies with longer follow-ups must be conducted in the future. The screen-time duration and frequency was noted as provided by the caregiver and was not supervised due to logistic constraints involved in collecting such data. The content of media use was not assessed which also is an essential factor. The Hawthorne effect in the Control group could also be a confounding factor.

We conclude that early childhood intervention starting within the first year of life in the form of parental education and early anticipatory guidance can limit screen time in the initial 2 years. Reduction of screen time may have a positive impact on the behavioral and developmental scores of the child. Guidelines regarding screen time must be inculcated by the pediatricians in their daily practice on every well baby visit. Primary caregivers can also be counseled at Anganwadi centers regarding reducing screen exposure and their harmful effects. Educational interventions must be started at an early age to promote the reduction of screen exposure and more age-appropriate activities to enhance the holistic development of children.

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ORIGINAL ARTICLE

Profile of Childhood Cancers From Hospital-Based Cancer Registries in India, 2012-19

Gauri Kapoor,[1] Ramandeep Singh Arora,[2] Venkatraman Radhakrishnan,[3] Anita Nath,[4] Payal Malhotra,[1] Sunu Lazar Cyriac,[5] Gangadharan VP,[6] Sadashivudu G,[7] Thilagavathi Ramamoorthy,[4] Sudarshan KL,[4] Prashant Mathur[4]

[1]Department of Pediatric Hematology Oncology, Rajiv Gandhi Cancer Institute and Research Centre, Delhi.
[2]Department of Pediatric Oncology, Max Super Speciality Hospital, New Delhi.
[3]Department of Medical Oncology, Adyar Cancer Institute, Chennai, Tamil Nadu.
[4]ICMR - National Centre for Disease Informatics and Research, Indian Council of Medical Research, Bengaluru, Karnataka.
[5]Department of Medical Oncology and Hematology, Amala Institute of Medical Sciences, Thrissur, Kerala.
[6]Department of Medical and Pediatric Oncology, Lakeshore Hospital, Kochi, Kerala.
[7]Department of Medical Oncology, Nizam's Institute of Medical Sciences, Hyderabad, Telangana.

ABSTRACT

Objective: To describe the clinical pattern of childhood and adolescent cancers across India using hospital-based data in the National Cancer Registry Program.

Methods: Records of 60720 cancer cases in the 0-19 year age group for the period 2012-2019 from 96 hospital-based cancer registries were reviewed. Childhood cancers were classified based on the International Classification of Childhood Cancer (ICCC). Descriptive analysis was used to examine the distribution of cancer by five-year age groups, sex and ICCC diagnostic groups and subgroups. Data were analysed using IBM SPSS software and visualised using R software.

Results: 3.2% and 4.6% of all cancer cases in India were among children in the 0-14 year and 0-19 year age groups respectively. The male-to-female ratio for all cancers was 1.72 for 0-14 years and 1.73 for 0-19 years. The four leading groups of cancers among 0-14 year olds were leukemia (40%), lymphoma (12%), central nervous system tumor (11%) and bone cancer (8%). The four leading cancers among the 0-19 year age group were leukemia (36%), lymphoma (12%), bone (11%) and central nervous system tumor (10%).

Conclusion: Cancers in the 0-14 and 0-19 age groups accounted for a considerable proportion of all cancers with significant male preponderance. Such information helps to fine-tune research and planning strategies.

Keywords: *Adolescent, Cancer, Child, India, Registries*

INTRODUCTION

Strategies to control cancer start with understanding the occurrence of cancer and its distribution. Knowing how many patients develop, are treated for, and ultimately survive cancer is vital data for evidence-based resource allocation. Cancer registries collect accurate and complete cancer data that can be used for cancer control and epidemiological research, public health program planning, and patient care improvement. In childhood cancer, such information helps to understand disease etiology, improve access to care, plan investments in service delivery, advocate for resource allocation, and measure the quality of different health system components involved [1]. Ultimately, all of these activities reduce the burden of cancer.

Data from the National Cancer Registry Programme (NCRP), established by the Indian Council of Medical Research (ICMR) in 1981, is generated through a network of 38 Population-Based Cancer Registries (PBCRs) and 246 Hospital-Based Cancer Registries (HBCRs). The recent NCRP report of 96 HBCRs has captured data on the topography (site), clinical staging, histology, site of pediatric cancers and treatment details [2].

In India, previous publications on the distribution of childhood cancer in India have been restricted to particular geographical regions [3,4] and have generally excluded adolescents with cancer. Globally, there is a relative lack of representation on registry-level information on childhood

Correspondence to: Dr. Prashant Mathur, National Centre for Disease Informatics and Research, Indian Council of Medical Research, Bengaluru, Karnataka.
director-ncdir@icmr.gov.in
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and adolescent cancer from low and middle-income countries (LMIC), which account for more than 80% of the burden of children with cancer [5]. The present paper offers an opportunity to address this gap and describes the clinical pattern of childhood and adolescent cancers across India using hospital-based data in the NCRP.

METHODS

The present study was a descriptive cross-sectional analysis based on eight-year data (2012 to 2019) on childhood cancers from 96 HBCRs [2]. These HBCRs are located in specialised oncology centres /general or multi-speciality hospitals (public and private) covering urban and rural areas of the country. Data collection was done using a standardized common core form consisting of patient identifying and socio-demographic information, details of diagnosis, clinical extent of disease, and broad type of treatment.

Topography (site) was coded according to the International Classification of Diseases-10th Revision (ICD-10) and morphology by the International Classification of Diseases for Oncology, 3rd edition (ICD-O-3) [6,7]. Only tumors with malignant behaviour were reported.

Childhood cancers were defined as cancers in two broad categories: 0-14 and 0-19 years that were classified based on the International Classification of Childhood Cancer (ICCC), 3rd edition [8].

Statistical analysis: Descriptive analysis was used to examine the distribution of cancer by five-year age groups, sex and ICCC diagnostic groups and subgroups. Data were analyzed using SPSS software (Version 27.0; IBM Corp, Armonk, NY, USA) and visualized using R software.

RESULTS

Among the 1332207 cancer cases in all sites that were registered at 96 HBCRs during 2012-19, 3.2% (42527) were among children in the 0-14 year age group, 1.4% (18193) were adolescents in the 15-19 year age group, and the cancers in the combined group (0-19 year) constituted 4.6 % of all cases (**Table I**). The male-to-female ratio was 1.72 in the 0-14 and 1.73 in the 0-19 age groups.

The four leading groups of cancers among 0-14 years were leukemia (40%), lymphoma (12%), central nervous system (CNS) tumor (11%) and bone cancer (8%) (**Fig. 1**). The distribution among boys and girls was broadly similar, except that the proportion of lymphoma was higher in boys (15%) than in girls (7%).

The four leading cancers among the 0-19 year age group were leukemia (36%), lymphoma (12%), bone (11%), CNS (10%) and soft tissue cancers (7%), as seen in **Fig.1**. Lymphomas were more common among males than females (15% vs 8%). However, the reverse was observed for carcinomas (5% vs 7%) and germ cells (2% vs 4%).

Leukemias constituted the most prominent group across all ages, constituting half of all cancers in the 0-4 year (42.1%) and the 5-9 year age group (42.5%), as described in **Table II**. This was followed by lymphomas (12.3%) that had the most significant proportion in the 5-9 year age group (15.7%), of which Hodgkin lymphoma was the most typical (7.9%). Malignant bone tumors (10.7%) were the third largest group overall and the second most common cancer group in the 10-14 year (16.0%) and 15-19 year age group (17.9%), mainly constituted by osteosarcoma and Ewing sarcoma. Rhabdomyosarcoma, retinoblastoma, Wilm's tumor and neuroblastoma were all seen primarily in the 0-4 year age group. CNS tumors had an overall proportion of 9.6% in the 0-19 year age group, with the highest proportion between 5-9 years, and the most significant pathological type was primitive neuroectodermal tumors (PNET).

DISCUSSION

Based on NCRP data, the present study analyzed 60720 cancer cases (0-19 years) from 96 HBCRs, over eight years. With a younger population pyramid, it is not

Table I Childhood Cancers Relative to Cancers Across All Ages: Data from 96 Hospital-Based Cancer Registries, India, 2012-2019

Age (y)	*Boys (n = 705395)*		*Girls (n = 626812)*		*Total (n = 1332207)*	
	n	*% of all cancers*	*n*	*% of all cancers*	*n*	*% of all cancers*
0-4	9320	1.3	5764	0.9	15084	1.1
5-9	8883	1.3	4728	0.8	13611	1.0
10-14	8668	1.2	5164	0.8	13832	1.0
15-19	11589	1.6	6604	1.1	18193	1.4
0-14	26871	3.8	15656	2.5	42527	3.2
0-19	38460	5.5	22260	3.6	60720	4.6

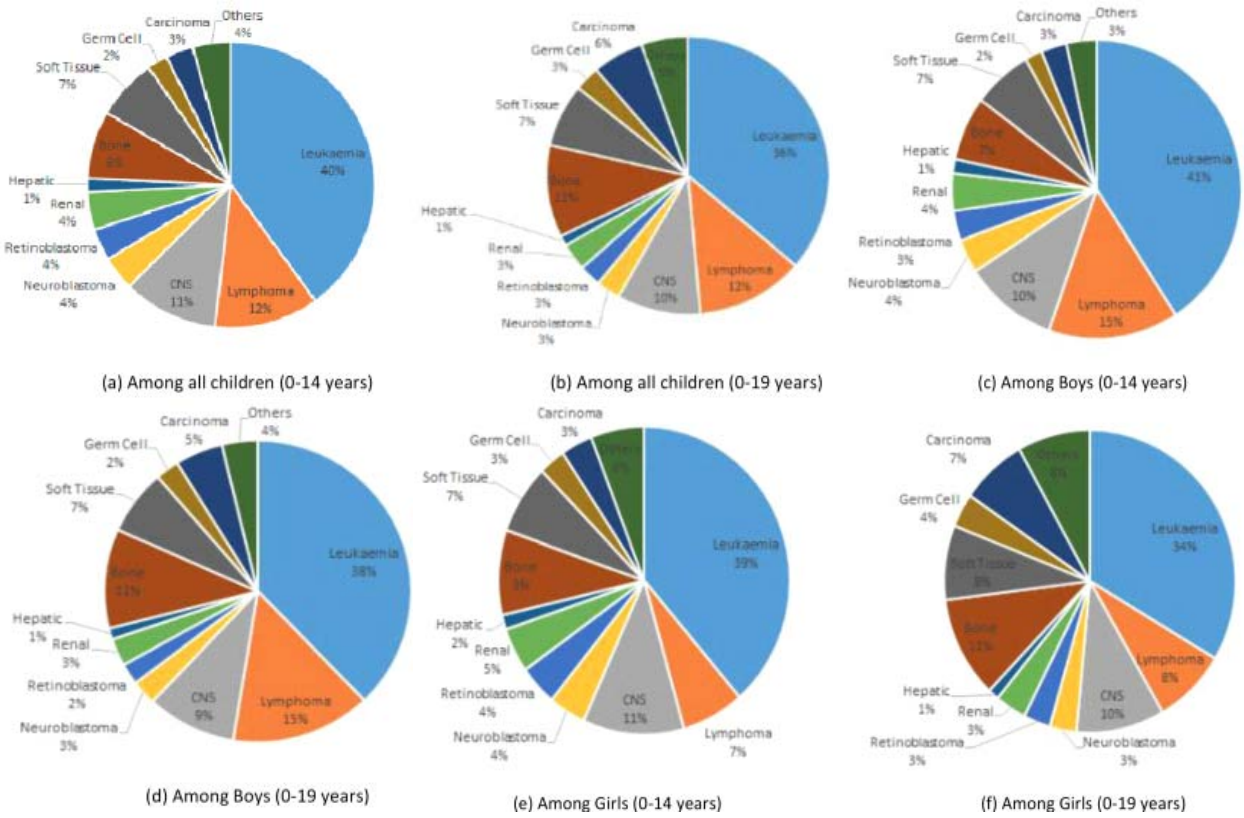

Fig. 1 Relative contribution of the 12 diagnostic groups of childhood cancer in (0-14) and (0-19) years.

surprising that children 0-14 and adolescents 0-19 years of age represent 3.2% and 4.6% of the total cancers reported at hospitals. In contrast, this proportion is 1-2% in countries with high human development index [9].

Leukemias comprised nearly half of all cancers in the 0-14 and 0-19 age groups, which is in accordance with findings from other studies [10,11]. Lymphoid leukemia, including acute lymphoblastic leukemia (ALL), comprised most leukemia types. Similar to the high male-to-female ratio of cancer cases observed in our study, sex disparity in cancer registration has previously been described in LMICs, especially those with low female education rates, wherein girls with cancer often go undiagnosed [12]. The higher sex differential in India could be ascribed to social determinants such as gender discrimination and skewed sex ratio due to male birth preferences that outnumber female births in India [13]. The proportion of leukemias and bone cancer in the 0-14 and the 0-19 year age group was higher than population-based data from India in the IICC paper by Steliarova-Foucher et al in which reported proportions of leukemia were 38.4% and 34.1% and for bone cancer, 5.6% and 7.6% in the 0-14 and 0-19 year age groups respectively, which could be accounted for by differences in the hospital referral practices [14]. Furthermore, the proportional distribution of CNS tumors reported internationally (17-26%) is remarkably higher than that observed in the present analysis (11% in 0-14 and 10 % in 0-19 age group). One explanation for this wide gap is that CNS tumors are possibly treated in neurosurgical centres in multi-speciality (general) hospitals rather than dedicated cancer centres in India. Another explanation could be that currently, the NCRP only registers "malignant" (defined as World Health Organization Grade 3 and 4) CNS tumors.

The proportion of Non-Hodgkin lymphomas (NHL) increased with rising age groups in our analysis, supporting evidence that NHL increases steadily with age and more so in males, which may result from innate sex differences in susceptibility and HIV [15]. The higher proportion of malignant bone tumors in girls is probably due to earlier skeletal maturity. The data from the Indian HBCRs not only gives us valuable information on the distribution of cancer in children and adolescents but also supplements the PBCRs, allowing estimates of incidence and longitudinal trends. Cancers in the 0-19 age group accounted for a considerable proportion of all cancers, with significant male preponderance.

Table II Number and Proportion of Specific Types of Cancers (ICCC-3 Classification) by 5 Year Age Groups, India, 2012-2019

	0-4y		*5-9y*		*10-14y*		*15-19y*		*Total (0-14y)*		*Total (0-19y)*	
Cancer classification	n	%	n	%	n	%	n	%	n	%	n	%
Leukemia	6354	42.1	5790	42.5	4843	35.0	4963	27.3	16987	39.9	21950	36.1
Lymphoid leukemia	4871	32.3	4227	31.1	3037	22.0	2649	14.6	12135	28.5	14784	24.3
Acute non-lymphocytic leukemia	897	5.9	950	7.0	1132	8.2	1249	6.9	2979	7.0	4228	7.0
Chronic myeloid leukemia	54	0.4	133	1.0	279	2.0	539	3.0	466	1.1	1005	1.7
Other specified leukemia	55	0.4	29	0.2	24	0.2	38	0.2	108	0.3	146	0.2
Unspecified leukemia	477	3.2	451	3.3	371	2.7	488	2.7	1299	3.1	1787	2.9
Lymphomas and reticuloendothelial neoplasm	762	5.1	2134	15.7	2089	15.1	2502	13.8	4985	11.7	7487	12.3
Hodgkin lymphoma	170	1.1	1070	7.9	943	6.8	1163	6.4	2183	5.1	3346	5.5
Non-Hodgkin lymphoma	315	2.1	673	4.9	869	6.3	1132	6.2	1857	4.4	2989	4.9
Burkitt's lymphoma	140	0.9	273	2.0	138	1.0	69	0.4	551	1.3	620	1.0
Miscellaneous lymphoreticular neoplasms	108	0.7	35	0.3	33	0.2	31	0.2	176	0.4	207	0.3
Unspecified lymphomas	29	0.2	83	0.6	106	0.8	107	0.6	218	0.5	325	0.5
Central Nervous System and miscellaneous intracranial and intraspinal neoplasms	1047	6.9	1907	14.0	1604	11.6	1249	6.9	4558	10.7	5807	9.6
Ependymoma	233	1.5	262	1.9	173	1.3	122	0.7	668	1.6	790	1.3
Astrocytoma	138	0.9	369	2.7	461	3.3	512	2.8	968	2.3	1480	2.4
Primitive neuroectodermal tumors	434	2.9	706	5.2	562	4.1	271	1.5	1702	4.0	1973	3.2
Other gliomas	131	0.9	424	3.1	293	2.1	244	1.3	848	2.0	1092	1.8
Other specified intracranial and intraspinal neoplasms	42	0.3	39	0.3	51	0.4	52	0.3	132	0.3	184	0.3
Unspecified intracranial and intraspinal neoplasms	69	0.5	107	0.8	64	0.5	48	0.3	240	0.6	288	0.5
Sympathetic Nervous System tumors	1139	7.6	407	3.0	116	0.8	72	0.4	1662	3.9	1734	2.9
Neuroblastoma and ganglioneuroblastoma	1128	7.5	395	2.9	100	0.7	45	0.2	1623	3.8	1668	2.7
Other SNS tumors	11	0.1	12	0.1	16	0.1	27	0.1	39	0.1	66	0.1
Retinoblastoma	1284	8.5	219	1.6	29	0.2	3	<0.1	1532	3.6	1535	2.5
Renal tumors	1279	8.5	435	3.2	103	0.7	74	0.4	1817	4.3	1891	3.1
Wilm's tumor, rhabdoid and clear cell sarcoma	1260	8.4	410	3.0	73	0.5	24	0.1	1743	4.1	1767	2.9
Renal carcinoma	19	0.1	25	0.2	30	0.2	50	0.3	74	0.2	124	0.2
Hepatic tumors	475	3.1	108	0.8	64	0.5	80	0.4	647	1.5	727	1.2
Hepatoblastoma	425	2.8	77	0.6	26	0.2	3	<0.1	528	1.2	531	0.9
Hepatic carcinoma	29	0.2	24	0.2	36	0.3	70	0.4	89	0.2	159	0.3

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0-4y			*5-9y*		*10-14y*		*15-19y*		*Total (0-14y)*		*Total (0-19y)*	
Unspecified malignant hepatic tumors	21	0.1	7	0.1	2	< 0.1	7	< 0.1	30	0.1	37	0.1
Malignant bone tumors	216	1.4	822	6.0	2212	16.0	3253	17.9	3250	7.6	6503	10.7
Osteosarcoma	24	0.2	314	2.3	1285	9.3	2120	11.7	1623	3.8	3743	6.2
Chondrosarcoma	2	0.0	7	0.1	43	0.3	86	0.5	52	0.1	138	0.2
Ewing sarcoma	140	0.9	453	3.3	757	5.5	804	4.4	1350	3.2	2154	3.5
Other specified malignant bone tumors	24	0.2	13	0.1	41	0.3	123	0.7	78	0.2	201	0.3
Unspecified malignant bone tumors	26	0.2	35	0.3	86	0.6	120	0.7	147	0.3	267	0.4
Soft-tissue sarcomas	1059	7.0	839	6.2	1022	7.4	1532	8.4	2920	6.9	4452	7.3
Rhabdomyosarcoma and embryonal sarcomas	650	4.3	398	2.9	272	2.0	267	1.5	1320	3.1	1587	2.6
Fibrosarcoma, neurofibrosarcoma and other fibromatous neoplasms	51	0.3	44	0.3	75	0.5	138	0.8	170	0.4	308	0.5
Kaposis sarcoma	0	0.0	0	0.0	3	< 0.1	3	< 0.1	3	< 0.1	6	< 0.1
Other specified soft tissue sarcoma	257	1.7	297	2.2	512	3.7	814	4.5	1066	2.5	1880	3.1
Unspecified soft tissue sarcoma	101	0.7	100	0.7	160	1.2	310	1.7	361	0.8	671	1.1
Germ-cell trophoblastic and other gonadal neoplasms	528	3.5	150	1.1	299	2.2	779	4.3	977	2.3	1756	2.9
Intracranial and intraspinal GC tumors	23	0.2	28	0.2	60	0.4	53	0.3	111	0.3	164	0.3
Other and unspecified non-gonadal GC tumors	232	1.5	20	0.1	33	0.2	119	0.7	285	0.7	404	0.7
Gonadal germ cell tumors	264	1.8	89	0.7	179	1.3	503	2.8	532	1.3	1035	1.7
Gonadal carcinomas	5	< 0.1	5	< 0.1	15	0.1	65	0.4	25	0.1	90	0.1
Other and unspecified gonadal tumors	4	0.0	8	0.1	12	0.1	39	0.2	24	0.1	63	0.1
Carcinoma and other malignant epithelial neoplasms	211	1.4	331	2.4	774	5.6	2251	12.4	1316	3.1	3567	5.9
Adrenocortical carcinoma	26	0.2	17	0.1	13	0.1	10	0.1	56	0.1	66	0.1
Thyroid carcinoma	3	< 0.1	8	0.1	33	0.2	159	0.9	44	0.1	203	0.3
Nasopharyngeal carcinoma	0	0.0	26	0.2	181	1.3	323	1.8	207	0.5	530	0.9
Malignant melanoma	11	0.1	9	0.1	7	0.1	31	0.2	27	0.1	58	0.1
Skin carcinoma	8	0.1	27	0.2	27	0.2	63	0.3	62	0.1	125	0.2
Other and unspecified carcinoma	163	1.1	244	1.8	513	3.7	1665	9.2	920	2.2	2585	4.3
Other and unspecified malignant neoplasms	389	2.6	180	1.3	188	1.4	383	2.1	757	1.8	1140	1.9
Other specified malignant tumors	22	0.1	13	0.1	16	0.1	30	0.2	51	0.1	81	0.1
Other unspecified malignant tumors	708	4.7	456	3.4	661	4.8	1406	7.7	1825	4.3	3231	5.3
Total	15085	100.0	13611	100.0	13832	100.0	18194	100.0	42528	100.0	60722	100.0

WHAT THIS STUDY ADDS?

- Descriptive profile of 60,720 childhood cancer cases (0-19 years) in India from 96 hospitals between 2012-2019.

One of the main limitations of the present analysis was that cancer incidence rates could not be calculated since the data used was hospital-based. However, there is a wide belief that HBCRs could provide population-based statistics for childhood cancers since these are primarily treated at highly specialised hospitals. Therefore, it is vital to strengthen the HBCRs to obtain robust data which may be achieved by increasing the number of HBCRs (as has been steadily happening) and ensuring that data capture in each hospital is not limited to one department. By providing patient registration from all relevant departments within the hospital, including pathology and radiology, the case ascertainment can be close to complete.

Future efforts should include strengthening the existing childhood component of the HBCRs. A robust childhood cancer policy would augment better allocation of resources for the overall growth and survival of children.

Ethics clearance: Institutional Ethics Committee, ICMR-NCDIR; No.NCDIR/IEC/2017/5, dated March 1, 2017.
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ORIGINAL ARTICLE

Early Predictors of Ventilator Associated Pneumonia in Preterm Neonates Admitted in a Special Newborn Care Unit

Simran Pahwa,[1] Amanpreet Sethi,[1] Gurmeet Kaur,[1] Shashi Kant Dhir,[1] Neerja Jindal,[2] Seema Rai,[1] Sakshi Jindal[1]

[1]Department of Pediatrics, Guru Gobind Singh Medical College, Faridkot, Punjab.
[2]Department of Microbiology, Guru Gobind Singh Medical College, Faridkot, Punjab.

ABSTRACT

Objective: To determine the utility of microscopic examination and culture of endotracheal aspirate (ETA) in the early diagnosis of ventilator-associated pneumonia (VAP) in preterm neonates.

Methods: We enrolled 80 consecutive neonates (both inborn and out-born) with gestational age of < 37 weeks admitted in Special Newborn Care Unit (SNCU) and requiring mechanical ventilation (MV) for ≥ 48 hours. The diagnosis of VAP was made using the criteria laid down by the Centers for Disease Control (CDC).

Results: 47 preterm neonates (58.5%) developed VAP; the overall incidence was 74.7/1000 ventilator-days. The mean (SD) time (hours) to ETA culture was less as compared to diagnosis based on CDC criteria [108.9 (8.00 hrs) vs 132.4 (53.24); *P = 0.004*] with sensitivity and specificity of 80.8% and 72.7%, respectively. Outborn delivery was the single most important risk factor for VAP. Multidrug resistant (MDR) *Klebsiella pneumoniae* (63.9%) was the most prevalent organism.

Conclusions: We noticed a very high incidence of VAP among preterm neonates in SNCU. ETA culture can aid in early diagnosis.

Keywords: *Culture, Endotracheal tube, Klebsiella, Special newborn care units*

INTRODUCTION

Excessive and unsupervised use of mechanical ventilation in preterm neonates can predispose to complications like volutrauma leading to chronic lung disease, ventilator associated pneumonia (VAP), air leaks, and subglottic stenosis etc [1]. VAP is defined as hospital acquired pneumonia, developing in patients after 48 hours of initiation of mechanical ventilation (MV) [2]. It is one of the most common nosocomial infections associated with high morbidity, mortality, and medical cost [3]. The incidence of VAP varies greatly from 2.7 to 10.9 episodes per 1000 ventilator days in high income countries and up to 37.2 per 1000 ventilator days in low-and middle-income countries [4,5].

There is paucity of data regarding the early predictors of VAP among preterm neonates from tertiary level special newborn care units (SNCU) in India. The time taken to reach a microbiological diagnosis in suspected VAP is of crucial importance. We could find only one study from India which showed a high sensitivity and specificity of endotracheal aspirate (ETA) microscopy and culture in the early diagnosis of VAP in near term and term neonates [6]. In the current study, we aimed to determine the early predictors of VAP by examining the ETA microscopy, culture and endotracheal tube (ET) tip culture among ventilated preterm neonates in an SNCU. We also determined the incidence, risk factors, causative microbial agents, and outcome of VAP in these neonates.

Correspondence to: Dr Amanpreet Sethi, Assistant Professor, Department of Pediatrics (Neonatology), Guru Gobind Singh Medical College, Faridkot, Punjab 151 203.
sethi.amanpreet702@gmail.com
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METHODS

In this prospective observational study, we included all consecutive neonates (inborn and out-born) with a gestational age of < 37 weeks, who required MV for ≥ 48 hours and admitted in our 12-bedded tertiary level SNCU. The study period was from August 2019 to August 2020. Informed consent was obtained from parents/guardians. All preterm neonates with suspected or diagnosed pneumonia at the time of initiation of MV, major congenital birth anomalies (including antenatally detected critical cyanotic congenital heart disease), pulmonary hemorrhage, outborn neonates intubated at admission and with a

previous history of MV were excluded. Analysis of our unit's previous years admission data, revealed that there were 1000 new admissions in the SNCU out of which 40% were preterm neonates. Assuming that 20% of these would require MV, we decided to enrol a convenient sample of 80 eligible consecutive neonates over a period of 12 months.

Neonates who needed ventilatory support were intubated by orotracheal route in the labor room or NICU. One set of sterile/autoclaved ventilator circuit with heated humidification system was used till extubation. We used open method for suctioning of secretions. The endotracheal (ET) tube was changed only if blocked or displaced for each patient.We continuously recorded vitals and ventilator settings every two hourly in a pre-designed proforma. The clinical diagnosis of VAP was made on the basis of Centers for Disease control (CDC), USA criteria [7]. As per unit's protocol, we extubated the preterm neonates when all of the following criteria were met: *a*) Adequate spontaneous efforts, *b*) hemodynamically stable with no inotropes, *c*) FiO_2 requirement was less than 30% to maintain sPO_2 between 90-95%, *d*) requirement of peak inspiratory pressure (PIP) and peak end expiratory pressure (PEEP) was less than 15 cm and 5 cm of H_2O respectively.

Samples of ETA were collected by open suction after 48 hours of MV, under aseptic precautions. ET tip sample was sent for cultures per standard protocol at first ET replacement or during extubation, whichever was earlier. The samples of endotracheal aspirate (ETA) and ET tip underwent qualitative culture microscopic analysis and quantitative culture within one hour of collection. A smear was prepared from ETA for gram staining. Culture (conventional and BACTEC) was done on blood and MacConkey agar and antibiotic sensitivity was done using Muller Hinton agar.

Statistical analysis: We compared quantitative variables between the VAP and non-VAP groups using Student t-test and Mann Whitney U test. For comparing categorical data, Chi square (X^2) test and Fisher's exact test was used. Sensitivity, specificity, positive (PPV) and negative predictive values (NPV) for ETA microscopy and culture were also calculated. For risk factor analysis, both univariate and multivariate logistic regression analyses were included. A probability value (*P* value) less than 0.05 was considered statistically significant. All statistical calculations were done using Statistical Package for the Social Science 21 version (SPSS Inc.).

RESULTS

Out of 193 mechanically ventilated preterm neonates, 122 were ventilated for more than 48 hours. Of these, six families refused consent, and 36 were excluded (congenital anomalies 9; congenital pneumonia 14; congenital heart disease 6; and, pulmonary hemorrhage 7), and 80 were finally enrolled. 47 (58.5%) neonates developed VAP with an overall incidence of 74.7/1000 ventilator-

Table I Factors Associated With Ventilator-associated Pneumonia

Factors	*VAP group (n = 47)*	*Non-VAP group (n = 33)*	*Odds ratio (95% CI)*	*P value*
Gestational age (< 32 weeks)	15 (31.9)	9 (27.3)	1.25 (0.47-3.34)	0.656
Birth Weight (< 1500 grams)	20 (42.6)	10 (30.3)	1.71 (0.67-4.37)	0.265
Female sex	16 (34.0)	14 (42.4)	0.70 (0.28-1.75)	0.446
Leaking for more than 24 hours	15 (31.9)	11 (33.3)	0.94 (0.36-2.42)	0.894
Vaginal delivery	33 (70.2)	15 (45.5)	2.83 (1.12-7.15)	0.037
Outborn delivery	25 (53.2)	5 (15.1)	6.32 (2.09-19.32)	0.001
Need of resuscitation at birth	14 (29.8)	11 (33.3)	0.85 (0.33-2.21)	0.736
Need for PRBC transfusion	36 (76.6)	16 (48.5)	3.47 (1.33-9.08)	0.009
Opiate therapy	6 (12.8)	10 (30.3)	0.34 (0.11-1.05)	0.087
Invasive procedure (PICC line/UVC)	34 (72.3)	8 (24.2)	8.17 (2.94-22.68)	0.001
Duration of mechanical ventilation in days[a]	9.87 (4.37)	5.00 (1.56)	-	< 0.001
Duration of NICU stay in days[b]	12 (8-15.5)	8 (5-10)	-	< 0.005
No. of ET changes (≥ 2)	37 (78.7)	6 (18.2)	16.65 (5.39-51.39)	< 0.001
ET suctions per day (≥ 3)	12 (25.5)	1(3.0)	10.97 (1.35-89.19)	0.011
Duration of MV (days) (≥ 7)	32 (68.1)	3 (9.1)	21.33 (5.61-81.14)	< 0.001

Values expressed as n(%), [a]mean (SD) or [b]median (IQR). VAP: Ventilator acquired pneumonia; PICC: Peripheral inserted central catheter; UVC: Umbilical venous catheter; ET: Endotracheal tube; MV: Mechanical ventilation; PRBC: Packed red blood cell transfusion; 95% CI: 95% Confidence Interval.

days. The mean gestational age (weeks) in the VAP and non-VAP group was comparable [32.2 (2.9) vs 32.9 (2.6); $P = 0.25$]. The mean (SD) birth weight (g) was less in the VAP group compared to the non-VAP group but the difference was statistically non-significant [1567.2 (469.8) vs 1714.5 (498.1); $P = 0.18$]. There was no significant difference between the rate of mortality between the two groups (57.4% in VAP group vs 63.6% in non-VAP group; $P = 0.72$). The various causes of mortality are compared in **Table II**.

On univariate analysis, delivery through vaginal route, out-born delivery, greater need of blood transfusion, use of invasive procedures (peripherally inserted central catheter and umbilical venous catheter), a greater number of ET changes and suctioning per day, longer duration of MV and NICU stay were significantly associated with the development of VAP as shown in **Table I**. On multivariate analysis, only out-born delivery, as a risk factor was independently associated with the development of VAP (Odds Ratio:13.77; 95% CI: 2.257-84.134; $P = 0.004$).

The mean (SD) time to diagnosis of VAP by ETA microscopy and culture was 57.79 (4.43) and 108.9 (8.0) hours, respectively, which were significantly shorter ($P < 0.001$ and $P = 0.004$, respectively) than time to clinical diagnosis by CDC criteria at 132.4 (53.2) hours. We also found that ETA microscopy was positive in 59.5% neonates of VAP group and 12.1% neonates of non-VAP group. ETA culture was positive in 80.9% neonates of VAP group and 27.3% neonates of Non-VAP group. The sensitivity, specificity, PPV and NPV of ETA microscopy in our study was 59.5%, 87.8%, 87.5% and 60.4%, respectively; whereas for ETA culture, it was 80.8%, 72.7%, 84.4% and 72.7%, respectively. In ETA culture, gram negative organisms like *Klebsiella pneumoniae* (63.9%) and *Citrobacter freundii* (10.7%) were the most predominant. Among the isolated organisms, the antibiotic resistance was very high with 33 out of 38 (86.8%) being multidrug resistant and showing sensitivity to polymyxin group of antibiotics only. The most common cause of mortality in both the groups was sepsis (55.5% vs 52.4%). The pathogens detected in blood culture were *Klebsiella pneumoniae* (5 in VAP group; 3 in Non-VAP group), *Candida albicans* (4 in VAP group, 2 in Non-VAP group), Methicillin resistant *Staphylococcus aureus* (3 in VAP group), Methicillin resistant coagulase negative *Staphylococcus aureus* (3 in Non-VAP group).

DISCUSSION

The incidence of VAP in other studies ranges from 13.2-57.1% and 7.1 to 70.3 per 1000 ventilator days [8-10]. This variation may be due to difference in diagnostic criteria used for defining VAP and the level of asepsis maintained at various centers. We assume that important factors contributing to a higher incidence of VAP in our study could be limited resources such as low nurse to patient ratio and low hand hygiene compliance based on the previous study's data from our unit [11]. Previous authors [5,8,9] also did not find any difference between the VAP and the non-VAP groups with respect to mortality. Our study population comprised of sick preterm neonates with a mean gestational age of around 32 weeks, so the rate of mortality was very high in both the groups. The reasons of mortality in both the groups were causes other than VAP.

Previous authors did not find any difference in the demographic profile between the two groups [10,12]. In our study, the outborn neonates could possibly be at greater risk of VAP as compared to those who were inborn because of severity of sickness; issues related to transportation such as thermoregulation; level of asepsis maintained during delivery, particularly home delivery and type of antibiotics received before reporting to us. However, Afjeh et al [13] did not find any difference between the two groups with respect to place of delivery.

In a recent study, the mean (SD) time of result of ETA microscopy and culture was 55.7 (4.3) h and 108.3 (19.7) h, respectively [7]. The clinical diagnosis was made much later using CDC criteria [7]. In the study conducted by Gupta et al the sensitivity, specificity, PPV and NPV of ETA culture was 75%, 90%, 84% and 83.7% respectively [6].

Table II Causes of Mortality in Preterm Neonates Receiving Mechanical Ventilation

Cause	*VAP group (n = 47)*	*Non-VAP group (n = 33)*	*P value*
Hypoxic ischemic encephalopathy	4 (14.8%)	3 (14.3%)	0.958
Extreme prematurity	3 (11.1%)	4 (19.0%)	0.439
Respiratory distress syndrome.	5 (18.6%)	3 (14.3%)	0.696
Early onset sepsis	9 (33.3%)	6 (28.6%)	0.724
Late onset sepsis	6 (22.2%)	5 (23.8%)	0.897
Total	27 (57.4%)	21 (63.6%)	0.724

Values in n (%). VAP: Ventilator-associated pneumonia

WHAT THIS STUDY ADDS?

- We noticed a very high incidence of VAP (74.7/1000 ventilator days) among ventilated preterm neonates along with very high incidence of multidrug resistant bugs.
- ET aspiration culture and microscopy provides an opportunity for early diagnosis of VAP as compared to CDC clinical criteria.

We could not collect data on human related factors like percentage of hand hygiene compliance before and after ET suctioning, and percentage of health care staff wearing sterile gloves while suctioning and intubation. This could have affected the incidence of VAP in our neonates.

In our unit with a high incidence of VAP among ventilated preterm neonates, ET aspiration culture and microscopy provided an opportunity for early diagnosis of VAP.

Ethics clearance: Institutional ethics committee, Guru Gobind Singh Medical College, Faridkot, Punjab; No. BFUHS/2K19p-TH/893 dated May 29, 2019.
Contributors: SP: Conceptualized and designed the study, analyzed data and drafted the manuscript; AS: Conceptualized and designed the study, supervised data collection and drafted the manuscript; GK: Conceptualized and designed the study and supervised the sample collection and manuscript; SKD: Supervised data and samples collection and provided inputs for writing the manuscript; NJ: Supervised sample collection and analysis of samples in the microbiology department; SR: assisted in sample collection, data analysis, and writing of manuscript; SJ: Assisted in sample collection, data analysis, and writing of manuscript. All authors approved the final version of manuscript, and are accountable for all aspects related to the study.
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ORIGINAL ARTICLE

Pulmonary Artery Hypertension in Transfusion-Dependent Thalassemia

Vineeta Gupta,[1] Vishnu Vijayakumar,[1] Priyanka Aggarwal,[1] Ishan Kumar,[2] Vikas Agrawal[3]

[1]Division of Pediatric Hematology Oncology, Department pf Pediatrics,Institute of Medical Sciences, Banaras Hindu University (BHU), Varanasi, Uttar Pradesh.
[2]Department of Radiodiagnosis, Institute of Medical Sciences, BHU, Varanasi, Uttar Pradesh.
[3]Department of Cardiology, Institute of Medical Sciences, BHU, Varanasi, Uttar Pradesh.

ABSTRACT

Objective: Patients with transfusion-dependent thalassemia (TDT) are at risk of developing pulmonary artery hypertension (PAH) due to chronic hemolysis, iron overload, hypercoagulability and splenectomy. The objective of the study was to assess the prevalence and predictors of PAH in patients with TDT.

Methods: Patients aged 6-18 years with TDT were included. 2D-echocardiography was done to measure the pulmonary artery systolic pressure (PASP) and left ventricular ejection fraction (LVEF). T2* MRI was done to evaluate cardiac iron overload. N-terminal-pro brain natriuretic peptide (NT-pro BNP) level was also assessed.

Results: Out of 60 participants, PAH was noted in 19 (31.6%). Mean (SD) age of the patients with PAH and without PAH was 12.2 (3.8) and 9.6 (3.5) years, respectively ($P = 0.016$). Five of 19 patients with PAH (26.3%) had undergone splenectomy as against 5 of 41 patients without PAH (12.2%) ($P = 0.17$). Years since splenectomy was higher in the PAH group. Mean (SD) NT-Pro BNP levels were also higher in patients with PAH [63.80 (25.89) vs 41.97 (23.95), $P = 0.01$]. Significantly higher number of patients with PAH had cardiac T2* value of < 10 ms ($P = 0.04$). Age (OR 4.11; 95% CI 1.46-8.77), years since splenectomy (OR 3.24; 95% CI 1.30-7.86), NT-Pro BNP levels (OR 4.43; 95% CI 2.14-9.60) and cardiac T2* MRI (OR 2.46; 95% CI 2.18-6.90) values were predictors of PAH in patients with TDT.

Conclusion: PAH was observed in 31.6 % of patients, with older age and years since splenectomy being important risk factors. NT-Pro BNP can be used as screening test for detecting PAH.

Keywords: *Chronic hemolysis, Iron overload, Pulmonary hypertension, Thalassemia*

INTRODUCTION

The development of pulmonary artery hypertension (PAH) in thalassemia is thought to be multifactorial with chronic hemolysis, iron overload due to transfusion therapy, hypercoagulability and changes to circulating red cells due to splenectomy being some of the implicated factors [1].

Pulmonary arterial hypertension is defined as a resting mean pulmonary artery pressure of 25 mm Hg or above [2]. Echocardiography is often employed as a screening tool to identify patients at high risk for PAH. The present study was carried out to find out the prevalence and predictors of PAH in children with transfusion-dependent thalassemia (TDT). We also correlated PAH with age, gender, number of years of transfusion, serum ferritin, platelet count, splenectomy, serum N-terminal Pro-brain natriuretic peptide (BNP) levels, left ventricular ejection fraction (LVEF) and T2* values of cardiac MRI.

Correspondence to: Prof. Vineeta Gupta, Division of Pediatric Hematology Oncology, Department of Pediatrics, Institute of Medical Sciences, Banaras Hindu University, Varanasi.
vineetaguptabhu@gmail.com
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METHODS

The study was conducted in the Division of Pediatric Hematology Oncology, Department of Pediatrics, in collaboration with Departments of Cardiology and Radiodiagnosis and Imaging of a tertiary care university hospital, over a period of 24 months (October 2019-November 2021). Children aged 6 to 18 years with thalassemia, receiving regular blood transfusion, and those who had received at least 20 transfusions till the date of enrollment, were considered eligible for inclusion in this study. Patients with pre-existing cardiac or pulmonary disease were excluded. This study was approved by the Institutional Ethics Committee. A written informed consent was taken from the parents/guardians. Assent was obtained from older children after explaining the study protocol.

The socio-demographic profile of the participants was noted from the records maintained in the thalassemia unit. Nutritional status of the participants was assessed by measuring height for age, weight for age and body mass index (BMI) using the Indian academy of Pediatrics (IAP) 2015 growth charts as reference [3]. Patients with BMI less than 3rd centile were classified as underweight.

All participants underwent a thorough clinical examination including respiratory and cardiac examination. At enrolment, complete blood count (CBC), renal function test (RFT), liver function test (LFT), serum ferritin and electrocardiogram (ECG), cardiac T2*MRI and serum N-terminal-Pro Brain Natriuretic Peptide (NT-pro BNP) were assessed. 2-D echocardiogram (ACUSON CV70 cardiovascular system, Philips) was used for the assessment of left ventricular ejection fraction (LVEF) and pulmonary artery systolic pressure (PASP). PAH was defined as resting mean pulmonary artery pressure of 25 mm Hg or above. LVEF was measured by modified Simpson's method (biplane method of disks) as recommended by the American Society of Echocardiography [4]. For measuring PASP, transthoracic echocardiography was done.

Cardiac iron load was estimated by T2* magnetic resonance imaging (MRI) using a 1.5 Tesla system (Siemens Avanto) with an actively shielded whole body superconducting magnet. Cardiac imaging was performed using body matrix coil and prospective ECG triggering. A short breath hold coaching session was performed for each patient prior to the scan. Quantitative T2* relaxation maps (MapIt, Siemens Healthcare) were obtained in a single 10 mm mid ventricular short axis view and four chambered view using a single breath hold gradient echo sequence with eight TEs (time to echo) (2.4-16 ms). The addition of a four chambered sequence added less than 1 minute to the overall scan time. Adequate breath hold was achieved in all the patients. MRI of all patients was done by a single technician and analyzed by a single radiologist. The grading of cardiac iron overload based on T2* MRI value was done as: normal (> 20 ms), mild (15-20 ms), moderate (10-14 ms), severe (< 10 ms) [5].

Venous samples were collected in the morning of the doppler echocardiographic examination, centrifuged and stored at -80^{0}C till analysis. Serum ferritin levels were measured by chemiluminescent immunoassay method (Architect Ferritin reagent kit, Abbott) as per manufacturer's instructions. Serum NT-Pro-BNP levels were measured using stored sera by ELISA technique (Wuhan Fine Biotech Co. Ltd).

RESULTS

Majority of the patients were in the age-group 6-10 years (46.7%) followed by 11-15 years (38.3%) and > 15 years (15%) with mean (SD) age of 10.68 (3.91) years. The male to female ratio was 3:1. Thirty nine patients (65.0%) were homozygous beta thalassemia whereas the remaining (35%) were compound heterozygous thalassemia (HbEβ and HbSβ). The characteristics of the study population has been presented in **Table I**. Four patients (6.7%) with BMI less than 3rd centile were classified as underweight. All patients were receiving oral chelation with deferasirox (20-40mg/kg/day) in once daily dose with good compliance. Only two patients were on dual chelators with deferasirox and deferiprone. No patient was receiving deferioxamine. Four patients had mild elevation of hepatic transaminases which normalized on decreasing the dose of deferasirox.

Of the 60 patients, 19 (31.6%) had PAH. The mean (SD) PASP in the groups with and without PAH was 32.2 (5.8) *versus* 17.7 (5.0) respectively ($P < 0.001$). In the patients with PAH, 12 (63.1%) had homozygous beta-thalassemia and 7 (36.9%) had compound heterozygous thalassemia whereas of the 41 patients without PAH, 27 (65.8%) had homozygous beta thalassemia and 14 (34.2%) had compound heterozygous thalassemia ($P = 0.75$). Five of 19 (26.3%) patients with PAH had undergone a splenectomy as against 5 of 41 patients (12.2%)

Table I Characteristics of the Study Participants

Parameters	*Number n (%)*
Age (y)	
6-10	28 (46.7)
11-15	23 (38.3)
> 15	9 (15.0)
Gender	
Male	46 (76.7)
Female	14 (23.3)
Religion	
Hindu	45 (75.0)
Muslim	15 (25.0)
Type of thalassemia	
Homozygous beta thalassemia	39 (65.0)
Compound heterozygous thalassemia	21 (35.0)
Weight for age	
≥ 3rd centile	58 (96.7)
< 3rd centile	2 (3.3)
Height for age	
≥ 3rd centile	45 (75.0)
< 3rd centile	15 (25.0)
Body mass index (BMI)	
Normal	56 (93.3)
Underweight	4 (6.7)

without PAH (P = 0.17). Out of the 10 patients who had been splenectomized, 5 developed PAH (50%), whereas out of the remaining 50 patients who had not been splenectomized, 14 (28%) developed PAH (P = 0.17). On comparison of the clinical characteristics of the patients with and without PAH, age and years since splenectomy were significantly different between the two groups (**Table II**). Patients with PAH were significantly older compared to patients without PAH, P = 0.016. There was no significant difference in the LVEF between the groups. However, the mean (SD) NT-Pro-BNP level (pg/mL) was significantly higher in the patients with PAH compared to patients without PAH [63.80 (25.89) vs 41.97 (23.95), P = 0.01]. On comparing the cardiac T*MRI value between the two groups, a significantly higher number of patients with PAH had T2* MRI value of < 10 msec.

DISCUSSION

Pulmonary artery hypertension in patients with thalassemia or other hemoglobinopathies is not uncommon. In vast majority of the cases, it remains underdiagnosed due to subtle and overlapping symptoms with chronic anemia. Transthoracic echocardiography is widely used for diagnosis but may not give accurate results. Tricuspid jet velocity (TRV), which is the flow of retrograde blood across the tricuspid valve during systole estimates the right ventricular pressure and correlates with pulmonary artery pressure (PAP). However, PAP may be underestimated by echocardiography due to insufficient doppler envelope or eccentric tricuspid regurgitation jet. Situations of high cardiac output, as in chronic hemolytic anemias may require direct measurement by right heart catheterization to confirm PAH. As cardiac catheterization is an invasive procedure, echocardiography is still accepted as a screening tool for PAH despite its shortcomings [6].

In our study, PAH was observed in 31.6% of patients with thalassemia who were receiving regular blood transfusion. The mean age of the patients with PAH was significantly higher than those without PAH. Another study on adult patients with thalassemia major observed PAH in 18.5% patients but evidence of clinical disease was seen in 3.7% patients only [7]. Two other studies in patients with HbSβ and HbEβ, have reported the incidence of PAH as 27% and 37.3% respectively [6,8]. However, both the studies were carried out in older patients where the mean age was around 31 to 34 years. We did not find any study carried out exclusively in children as the present study. Our patient cohort was much younger compared to the other two studies. One of the studies included young patients but had older patients also (age 2-24 years). The incidence of PAH was found to be very high. Twenty eight of the 33 patients (age 2-24 years) had high pulmonary systolic pressure. Age had a significant correlation with PAH and was >30 mm Hg in all the patients who were more than 10 years old [9].

Splenectomy has been found to have an association with PAH. In our cohort, 26.3% of the patients with PAH had undergone splenectomy as against 12.2% of the patients without PAH. This was similar to another study, where 32 of the 61 splenectomized patients (52.5%) developed PAH [6]. More than half of these patients (53%) were in their second decade showing that increasing age is a risk factor for development of PAH. Other risk factors for PAH have been identified as female sex, HbEβ thalassemia, years since splenectomy, thrombocytosis and high serum ferritin levels [10]. In the present study, we did not find association of PAH with these parameters except

Table II Clinical and Laboratory Profile of Transfusion-dependent Thalassemia Patients With and Without Pulmonary Artery Hypertension (PAH)

Parameters	*With PAH (n = 19)*	*Without PAH (n = 41)*	*P value*
Age (y)	12.2 (3.8)	9.6 (3.5)	0.02
Male gender[a]	14 (73.7)	32 (78.1)	0.71
Body mass index (kg/m^2)	16.3 (1.2)	16.0 (1.9)	0.61
Years of transfusion	9.1 (4.70	7 (4.5)	0.11
Years since splenectomy	4.8 (2.1)	3.5 (1.8)	0.01
Hemoglobin (g/dL)	7.9 (1)	7.5 (1.4)	0.68
Platelets (lacs/mm^3)	3.0 (1.6)	2.9 (1.7)	0.48
Serum ferritin (ng/mL)	2308.9 (1394.2)	2265.7 (1526.6)	0.49
Left ventricular ejection fraction (%)	61.8 (5.1)	62.6 (4.5)	0.47
N-terminal Pro B type Natriuretic peptide (pg/mL)	63.8 (25.9)	41.97 (23.9)	0.01
Cardiac T*MRI > 10 ms[a]	14 (73.7)	38 (92.7)	0.04

Values expressed as mean (SD) or [a]n (%)

WHAT THIS STUDY ADDS?

- N-terminal pro brain natriuretic peptide (NT-pro BNP) can be used as a screening test for detecting pulmonary artery hypertension in transfusion-dependent thalassemia.

years since splenectomy. Significant association was found with NT-Pro-BNP levels which were higher in the patients with PAH. Similar observation was made in one other study also where NT-Pro-BNP level was elevated in patients with HbSβ thalassemia [11]. Cardiac biomarkers especially troponin are important diagnostic tools in the workup of the patients with cardiovascular disease. The main stimulus for the increased synthesis and secretion of NT-Pro-BNP is myocardial wall stress. In patients with TDT, chronic hemolysis and cardiac iron overload may have caused the increased levels of NT-Pro-BNP [12]. We also observed that significantly higher number of patients with PAH had T2*cardiac MRI value of <10 ms. This finding is also consistent with cardiac iron overload. We could not find any other study which had made such an observation.

Although majority of the studies have reported varying incidence of PAH in thalassemia, there are a few studies which have observed that PAH did not develop in well transfused patients with thalassemia [13,14]. The strength of our study is that we have studied a relatively less studied aspect of management of TDT. However, the limitation is the cross-sectional nature of the study. It would be worthwhile to follow up the patients and observe the development of PAH in a longitudinal study. The other limitation was that PAH was measured by 2D echocardiography and not by cardiac catheterization which gives more accurate results.

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ORIGINAL ARTICLE

Psychological Distress During COVID-19 Pandemic in School-age Children of Health Care Professionals

Priya Sharma, Lakhan Poswal, Ritvika Jyani, Rajendra Chandel

Department of Pediatrics, Rabindranath Tagore Medical College, Udaipur, Rajasthan 313001.

ABSTRACT

Background: COVID-19 pandemic had a profound impact on the psychosocial well-being of societies across nations.

Methods: This prospective interventional study assessed the psychological distress in children, aged 6-19 years, whose parents were health care professionals. Parents were interviewed with a set of questionnaires based on signs of psychological distress given in the UNICEF and Childline's manual "Psychosocial Support for Children during COVID-19". Reassessment with same questionnaire was done after 15 days of intervention in the form of counseling and use of toolkits provided in the manual.

Results: The mean (SD) score was highest in children whose both parents were healthcare professionals. A significant reduction in psychological distress was seen after parents were provided with knowledge about UNICEF and Childline's manual ($P < 0.001$).

Conclusion: Counseling activities and toolkits provided in the manual were effective in reduction of psychological distress in children during COVID-19 pandemic.

Keywords: *Child, Counseling, SARS CoV-2, Stress*

INTRODUCTION

Corona Virus Disease 2019 (COVID-19) was particularly stressful for health care professionals (HCPs) as well as their children. Being keen observers of people and environments, children notice, absorb and react to the stress in their caregivers and community members, which unavoidably affect their wellbeing [1]. Additional stressors faced by frontline workers (including doctors and nurses) were stigmatization towards working with COVID-19 patients, physical strain of protective equipment, higher demands in work setting etc [2]. Children of single parent and frontline workers also face unique problems [3]. In the times of paramount stress and uncertainty, a secure family environment which the parents can provide is a strong protective factor [4]. The aim of the study was to understand the implications of COVID-19 pandemic on mental health and psychosocial well-being of children of health care professionals.

METHODS

This prospective interventional study was conducted on health care professionals (doctors and nurses) having children in the age-group of 6-19 years for recognition of signs of psychological distress in their children during COVID-19 pandemic.

Sample size was calculated by using formula: $n = (Z_{\alpha}+Z_{1-\beta})^2P(1-P)/E^2$, based on a study from India [5], 139 or more measurements/surveys were needed to have a confidence level of 95% so that the real value was within 5% of the measured/surveyed value. HCPs having children in age group of 6-19 years, who gave written informed consent, were included in the study. They were interviewed with a set of self-made questionnaires based upon the signs of psychological distress needing specialized help as specified in the manual published by UNICEF and Childline "Psychosocial Support for Children during COVID-19, A Manual for Parents and Caregivers" [1]. For each sign parents were advised to give a score of 0, 1 or 2, where 0 indicated that given sign was not at all present in child, 1 that given sign was present but specialized help from a trained professional was not required, 2 that sign was present and specialized help from a trained professional was required. Academic performance of the child was compared to the previous years' performances. All parents were given knowledge about UNICEF and Childline's manual. Parents were counseled regarding emotional needs of children, how to help children to deal with stressful events and how to talk to them about COVID-19 based on the manual. Softcopies/hardcopies of

Correspondence to: Dr Ritvika Jyani, Department of Pediatrics, RNT Medical College, Udaipur, Rajasthan.
jyani.ritvika@gmail.com
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manual were provided to the parents as per their requirement. Parents were advised to follow the tips and to use separate toolkits given in the manual for children aged 6-10 years and 11-19 years [1]. A repeat reminder was given after 7 days telephonically. After a period of 15 days parents were again interviewed with same set of questionnaire and assessment was done regarding any improvement in psychosocial wellbeing of children based upon decrease in total score of children. The children still having signs of psychological distress needing specialized help were kept under follow up with a child psychologist.

Statistical Analysis: The data were compiled on MS excel sheet and was analysed by SPSS version 20. Paired *t*-test was applied to compare score of children before and after counseling. *P*-value less than 0.05 was considered statistically significant.

RESULTS

A total of 211 children's parents whose one or both parents were HCPs were included. The number of children in the two age-groups and their gender distribution were comparable. There were 55 males and 54 females in the age-group 6-10 years, and 53 males and 49 females in 11-19-year age-groups. The informant was the mother in 128 cases and the father in 83 cases. 127 fathers were HCPs and 84 belonged to other professions. Among mothers 147 were HCPs, 34 belonged to other professions and 29 mothers were homemakers. All of these HCPs belonged to upper socioeconomic class according to the modified Kuppuswamy scale.

The children aged 6-10 years reported an increase in screen time (76%), decline in academic performance (51.4%), difficulty in sleeping (40.3%), decreased interest in playing (39.4%), withdrawn/aggressive behaviour (32.1%), afraid to be left alone (30.2%), new fears (28.4%), being sad/crying more than usual (26.6%), clinging/dependent behaviour (22.9%), pain in stomach/headache without physical reason (14.6%) and nightmares (10%) as depicted in **Table I**. The mean (standard deviation, SD) psychological distress score in this age-group before and after counseling was 4.4 (3.9) and 2.7 (2.4) respectively. There was 39.58% reduction in the psychological distress score after counseling ($P < 0.001$).

The children aged 11-19 years reported an increase in screen time (79.4%), decline in academic performance (58.8%), decreased interest in playing (48%), new fears (37.2%), difficulty in sleeping (31.3%), being sad/crying more than usual (20.6%), withdrawn/aggressive behaviour (19.6%), pain in stomach/headache without physical reason (18.6%), fear/afraid to be left alone (11.8%), nightmares (9%) and clinging/dependent behaviour (4.9%) as shown in **Table II**. The mean (SD) psychological distress score in this age-group before and after counseling was 4.1 (3.4) and 2.4 (2.1) respectively. There was a 42% reduction in score after counseling ($P < 0.001$).

Common reasons stated for decline in academic performance were closure of schools, lack of monitoring and evaluation of students. The mean psychological distress score before counseling weas slightly higher in children whose both mother and father were HCPs (4.8) as compared to those with only mother as a HCP (4.5), with only father as a HCP and mother in another profession (3.7), with only father as a HCP and mother homemaker (3.1).

Table I Change in Signs of Psychological Distress Before and After Counseling and Use of Toolkits in Age group 6-10 Years

Symptoms	*Before counseling*			*After counseling*		
	0	*1*	*2*	*0*	*1*	*2*
Difficulty in sleeping	65 (59.6)	35 (32.1)	9 (8)	73 (66.9)	33 (30.2)	3 (2.7)
Nightmares	98 (89.9)	11 (10)	0	108 (99)	1 (0.9)	0
Withdrawn/aggressive behavior	74 (67.8)	31 (28.4)	4 (3)	93 (85.3)	16 (14.6)	0
Pain in stomach/headache without physical reason	93 (85.3)	14 (12.8)	2 (1.8)	95 (87.1)	14 (12.8)	0
Afraid to be left alone	76 (69.7)	31 (28.4)	2 (1.8)	84 (77)	25 (22.9)	0
Clinging/dependent behavior	84 (77)	25 (22.9)	0	92 (84.4)	17 (15.5)	0
New fears	78 (71.5)	24 (22)	7 (6.4)	86 (78.8)	23 (21.1)	0
Decreased interest in playing	66 (60.5)	35 (32.1)	8 (7.3)	95 (87.1)	13 (11.9)	1 (0.9)
Being sad or crying more than usual	80 (73.3)	28 (25.6)	1 (0.9)	97 (88.9)	12 (11)	0
Decline in academic performance	53 (48.6)	43 (39.4)	13 (11.9)	58 (53.2)	42 (38.5)	9 (8.2)
Increase in screen time	26 (23.8)	53 (51.9)	30 (29.4)	43 (39.4)	60 (55)	6 (5.5)

Values expressed as n (%)

Table II Change in Signs of Psychological Distress Before and After Counseling and Use of Toolkits in Age group 11-19 Years

Symptoms	*Before counseling*			*After counseling*		
	0	*1*	*2*	*0*	*1*	*2*
Difficulty in sleeping	70 (68.6)	25 (24)	7 (6.8)	84 (82.3)	16 (15.7)	2 (1.9)
Nightmares	92 (90)	10 (9.8)	0	101 (99)	1 (0.9)	0
Withdrawn/Aggressive behavior	82 (80)	18 (17.6)	2 (1.9)	94 (92)	8 (7.8)	0
Pain in stomach/headache without physical reason	83 (81)	17 (16.6)	2 (1.9)	94 (92)	8 (7.8)	0
Afraid to be left alone	90 (88.2)	10 (9.8)	2 (1.9)	95 (93)	7 (6.8)	0
Clinging/dependent behavior	97 (95)	3 (2.9)	2 (1.9)	98 (96)	4 (3.9)	0
New fears	64 (62.7)	33 (32.3)	5 (4.9)	77 (75.4)	22 (21.5)	3 (2.9)
Decreased interest in playing	53 (51)	41 (40)	8 (7.8)	83 (81.3)	18 (17.6)	2 (1.9)
Being sad or crying more than usual	81 (79)	18 (17.6)	3 (2.9)	93 (91.1)	9 (8.8)	0
Decline in academic performance	42 (41)	47 (46)	13 (12.7)	50 (49)	45 (44.1)	7 (6.8)
Increase in screen time	21 (20)	48 (47)	33 (32.3)	29(28.4)	61 (59.8)	12 (11.7)

Values expressed as n (%)

A reduction in score after counseling was 39% when both parents were HCPs ($P < 0.001$), 38% when father was a HCP and mother in another profession ($P < 0.001$), 51% when father was a HCP and mother was homemaker ($P < 0.001$), 43% when mother was a HCP and father was in another profession ($P < 0.001$) (**Table III**).

DISCUSSION

An increase in signs of psychological distress amongst children was observed during COVID-19 pandemic by many parents. Children whose both parents were HCPs had more signs of psychological distress as compared to those whose only one parent was a HCP. There was a decrease in the time devoted by HCPs to their children during the pandemic as admitted by most of them either due increased working hours or the fear of transmitting COVID-19 to their children. An increase in screen time was one of the most commonly reported symptoms. It was attributed to a lack of outdoor activities and excessive use of electronic media for academic purposes. Knowledge and use of toolkits provided by UNICEF and Childline helped parents to manage the time they spent with their children, provided alternatives to outdoor play during home confinement, and even provided guidance on methods to reduce stress and anxiety in children.

In our study an increase in screen time was the most commonly reported symptom in both age-groups (77.7%) similar to that reported by Pasi et al [6]. We reported a decline in academic performance in about 55% of children. Bansal et al [7] reported remote learning was perceived to be stressful for child by 75.4% of parents. In the study conducted by Kecojevic et al [8], majority of students reported experiencing academic difficulties since the start of pandemic. Ability to focus on academic work (73.5%) and difficulties with online learning (58.6%) were the most commonly cited issues related to academics. Decline in academic performance observed in this study was less as compared to studies in general population probably because of higher socioeconomic and educational status of the parents who were HCPs. Decreased interest in playing (45.4%) and difficulty in sleeping (36%) were higher than the systematic review and meta-analysis conducted by Panda et al [9]. They found that 35.2% and 21.3% of children had boredom and sleep disturbances. Sleep disturbances were reported in 41.8% of children by Bansal et al [7] which was similar to our study. Sleep disturbances, decreased interest in playing were more in children of HCPs because of factors like less time spent with children, fear of contact with parents and shifting of children to relative's home during the pandemic. Manifestations of new fears mostly related to COVID-19 (33%) were higher in children of HCPs. It was higher compared to that reported by Panda et al (22.5%) in general population [9]. It was probably due to more chances of exposure to COVID-19 because of occupational exposure of parents. In our study 26% of children were reported to have withdrawn/aggressive behaviour, 23.6% children were reported to be being sad or crying more than usual, 21.3% children were afraid to be left alone. These findings are similar to those reported by Duan et al (22.8%) [10] and Shah et al (25.2%) [11]. Parents reported that their children were having pain in stomach/headache without any physical reason (16.5%), clinging or dependent behaviour (14.2%), and nightmares (9.9%). Various physical symptoms reported by Bansal et al during

WHAT THIS STUDY ADDS?

- Simple tips and toolkits are effective in promoting psychosocial well-being of children.

Table III Psychological Distress Scores Before and After Counseling of Parents

Groups of children	*Score before counseling*	*Score after counseling*	*% reduction in score*
Age 6-10 y	4.4 (3.9)	2.7 (2.4)	39.58 (26.36)
Age 11-19 y	4.1 (3.4)	2.4 (2.1)	42 (29.62)
Age 6-19 y	4.3 (3.7)	2.5 (2.3)	40 (27.97)
Both parent HCPs	4.8 (3.76)	2.92 (2.21)	39 (23.16)
Father HCP and mother in another profession	3.7 (4.0)	2.26 (2.31)	38 (22.37)
Father HCP and mother homemaker	3.1 (3.23)	1.52 (1.9)	51.1 (35.16)
Mother HCP and father in another profession	4.52 (3.63)	2.53 (2.33)	43 (30.34)

Values expressed as mean (SD). HCP: Health care professional

COVID-19 period related to stress due to remote learning were headache (34.8%), decreased appetite (16.7%) [7].

We did not measure the time devoted by parents to children and also the pre-COVID psychological distress for comparison. Our study had a scope for recall bias and there was a lack of direct contact with children. Although, there is evidence to show that parental practices and coping measures can affect children's post-disaster mental health [12], we could not find any study assessing the impact of counseling of parents on the psychological distress in children during the pandemic.

We found counseling of parents and toolkits provided in UNICEF and Childline's manual were effective tools for reducing the psychological distress in children.

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ORIGINAL ARTICLE

Procalcitonin as Point-of-Care Testing Modality for the Diagnosis of Pneumonia in Children With Influenza-like Illness

Susanna Hernández-Bou, Victoria Trenchs, Cristina Guirado, Ignacio Castrillón, Carles Luaces

Pediatric Emergency Department, Hospital Sant Joan de Déu Barcelona, Passeig Sant Joan de Déu, 2, 08950 Esplugues de Llobregat, Barcelona, Spain.

ABSTRACT

Objective: To evaluate the usefulness of procalcitonin (PCT) as a point-of-care testing to screen for radiographic pneumonia among children with influenza-like illness (ILI) and prolonged fever.

Methods: A prospective cohort study conducted at the pediatric emergency department of a tertiary hospital. Point-of-care testing for PCT was determined for 185 children aged 3 months to < 18 years with ILI and fever lasting > 4 days seen during the flu season in 2020. A chest radiograph (CXR) was performed for patients with PCT > 0.5 ng/mL.

Results: PCT value was > 0.5 ng/mL in 46 (24.9%) patients; a CXR was ordered in all cases except one and 14 (31.1%) of them had radiographic pneumonia (all had a PCT value > 0.7 ng/mL). Among the 139 (75.1%) patients with a PCT value ≤ 0.5 ng/mL, 137 (98.6%) were managed in the outpatient with symptomatic treatment; the remaining two cases warranted a CXR which was unremarkable in both. At evolution, no radiographic pneumonia was diagnosted in any of them.

Conclusion: PCT is a useful tool for point-of-care testing in patients with ILI and fever > 4 days to guide the indication for CXR to rule out radiographic pneumonia and helps in avoiding unnecessary radiation exposure.

Keywords: *Chest, Emergency, Influenza, Pneumonia, Radiograph*

INTRODUCTION

Every year, influenza exerts enormous pressure on pediatric emergency departments [1]. Although most children recover in a few days, some of them develop complications, with bacterial pneumonia being the most common secondary respiratory affliction [2]. A chest radiograph (CXR) is frequently indicated for children with influenza-like illness (ILI) and prolonged fever to rule out underlying pneumonia, even in patients without indicative clinical signs or symptoms. We performed a retrospective study including 179 children aged 3 months to 18 years with ILI and prolonged fever, normal oxygen saturation, and normal lung auscultation who underwent a CXR to rule out pneumonia. Findings from our study indicated that the prevalence of radiographic pneumonia was 19.6% and that none of the clinical factors analyzed proved useful in predicting it [3]. Because only patients who underwent a CXR were included in the study, the actual prevalence of pneumonia in this population is expected to be even lower. In line with our findings, two meta-analyses examining clinical predictors of pneumonia in children observed that no single sign or symptom was highly accurate for the identification of radiographic pneumonia [4,5]. A more recent systematic review by Rees, et al [6] reported that specificity in predicting pneumonia was improved when several individual clinical factors were combined; however, sensitivity was lower. Because of the limited utility of clinical factors, some authors have evaluated the usefulness of several biomarkers, especially C-reactive protein and procalcitonin (PCT), to distinguish viral from bacterial pneumonia, with controversial results [7-18]. Although some studies showed that PCT was more useful than C-reactive protein and interleukin-6 levels or white blood cell counts [8,10,11,13,15-17], the predictive role of PCT for childhood radiographic pneumonia remains ambiguous. The objective of the study was to determine the usefulness of point-of-care PCT testing in identifying children with ILI and fever >4 days at increased risk of radiographic pneumonia.

Correspondence to: Dr. Victoria Trenchs, Pediatric Emergency Department, Hospital Sant Joan de Déu Barcelona, Passeig Sant Joan de Déu 2, 08940 Esplugues de Llobregat (Barcelona), Spain. *victoria.trenchs@sjd.es*
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METHODS

A prospective observational cohort study was conducted in the emergency department of a 275-bedded tertiary care

pediatric hospital. The hospital is a reference center for an area encompassing 1.8 million inhabitants and it receives about 105,000 visits a year.

Children aged 3 months to 18 years of age with ILI (clinical suspicion and/or microbiological confirmation), a fever lasting > 4 days and normal lung auscultation, seen during the 8 weeks of the 2020 flu season, were included.

Children who were not well-appearing, hypoxemic (hemoglobin saturation <93% with FiO_2 21%), those currently receiving antibiotics, those with another source of fever upon physical examination warranting antibiotic prescription, those with chronic medical diseases, and/or those for which informed consent was not obtained were excluded.

Prior approval was obtained from the institutional Research Ethics Committee (PIC-166-18). Signed informed consent forms were obtained from the parents or legal guardians of all participants. Adapted information was given, and assent was also obtained from participants aged ≥ 12 years as applicable.

The definitions used in the study included the following:

Influenza-like illness: Abrupt onset of fever (axillary temperature ≥38ºC) and other general symptoms such as fatigue, muscle aches and/or headache, associated with signs or symptoms of acute respiratory infection (coughing, odynophagia, nasal flare, shortness of breath, tachypnea/dyspnea, grunting, etc) [19].

Not well-appearing: Appearance of every eligible participant was systematically evaluated using the Pediatric Assessment Triangle [20]; children were considered not well-appearing if this was abnormal.

Radiographic pneumonia: Radiologist reporting definite or equivocal "consolidation", "infiltrate", and/or "pneumonia" on the CXR. This definition was considered because patients with these radiological findings are usually treated with antibiotics for suspected bacterial etiology [21]. During the study period, the CXRs performed in the emergency department were systematically interpreted by a pediatric radiologist as part of routine clinical care within 24-48 hours after they were taken.

Before the study, all the physicians and nurses involved were informed about the study's design and conduct. Accordingly, an algorithm was designed; consent was obtained and all patients included underwent point-of-care PCT testing. Children with a PCT value of ≤0.5 ng/mL were discharged with advice of symptomatic treatment at home. In those with a PCT value of >0.5 ng/mL, a CXR was indicated; when the CXR was considered normal, the attending physician decided the subsequent management (**Fig 1)**. We established this PCT cut off value because it is the classical level used to differentiate between viral and bacterial infections.

PCT was tested using the commercially available, CE marked, kits (Thermo Scientific BRAHMS PCT direct, Berlin, Germany). All testing was performed by trained nurses using a 20 µL finger prick capillary blood sample. Results were available within 20 minutes to the attending physician, with values ranging from 0.1 to 10 µg/L. Quality was checked by making regular use of a Thermo Scientific BRAHMS PCT direct control.

Anonymized data were collected using standardized case report forms. The data collected included patient demographics, fever characteristics, diagnostic test for influenza, PCT result, indication and CXR findings, any complementary tests performed and antibiotics prescribed. Follow-up data of children managed as outpatients without performing CXR were recorded.

Statistical analysis: The data analysis was conducted using the SPSS software Version 25.0 for Windows. Descriptive statistics were reported as absolute frequencies or rates for categorical variables and as median (interquartile range, IQR; 25th to 75th percentile) for continuous variables. The Kolmogorov-Smirnov test was used for the data distribution. Statistical comparisons were made using Pearson Chi-square test or Fisher exact test for categorical variables and Student *t* test or the Mann-Whitney U test for continuous variables. *P*-values < 0.05 were considered statistically significant.

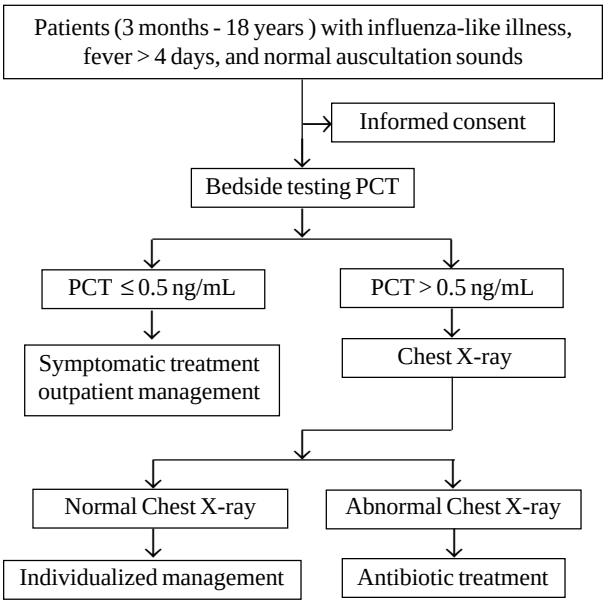

Fig. 1 Study protocol

RESULTS

One hundred and eighty-five cases were included. Demographic and clinical characteristics are reported in **Table I**. PCT > 0.5 ng/mL (range 0.5-10) was observed in 46 (24.9%) patients; a CXR was ordered in all cases except one (97.8%). The attending pediatrician diagnosed radiographic pneumonia and prescribed antibiotic treatment in 23 (51.1%) patients. However, the radiologist reported radiographic pneumonia in only 14 patients (31.1%; 95% CI 19.5-45.7%); all were found to have PCT ≥ 0.7 ng/mL (9 had a PCT value ≥ 1 ng/mL). The concordance rate for CXR interpretation between emergency pediatrician and radiologist was 75.5% (34 of 45) with a moderate agreement (Kappa 0.515, $P < 0.001$); all except one discordant case were false-positive interpretations. Among the 22 (48.9%) children with PCT > 0.5 ng/mL and a normal CXR, one or more additional complementary tests were performed in 8 (36.4%) cases; two were diagnosed with a urinary tract infection and one with an adenovirus infection. All 22 children were managed as outpatients.

Regarding the 139 (75.1%) patients with a PCT ≤ 0.5 ng/mL, outpatient management with symptomatic treatment was indicated in 137 (98.6%). The remaining two patients underwent a CXR, both were reported as unremarkable. Fifteen (10.8%) children were re-evaluated due to the same febrile process, none were diagnosed with pneumonia, and all were discharged home.

Therefore, the prevalence of radiographic pneumonia in the entire sample was 7.6% and a PCT cut-off of > 0.5 ng/mL showed a sensitivity of 100%, a specificity of 81.3%, a positive predictive value (PPV) of 30.4%, and a negative predictive value (NPV) of 100%.

DISCUSSION

The results of our study suggest that point-of-care testing for PCT could be a useful tool in the emergency department to guide the performance of a CXR to rule out radiographic pneumonia in patients presenting with ILI and prolonged fever, with a sensitivity and NPV of 100%. In our study, less than 8% patients were diagnosed with radiographic pneumonia, emphasizing the importance of properly selecting these patients.

To the best of our knowledge, this is the first study specifically evaluating the utility of point-of-care testing for PCT to identify patients with ILI and prolonged fever who are at increased risk of radiographic pneumonia. Previously, Khan et al [14] compared the accuracy of PCT with C-reactive protein for the early diagnosis of bacterial pneumonia in 92 children. PCT showed better diagnostic accuracy (sensitivity 83%, specificity 72%) at the cut-off point of ≥ 1 ng/mL. In our series, five (35.7%) patients with pneumonia would have been underdiagnosed with their higher proposed PCT cut-off; this difference can be explained because they included only admitted children with severe bacterial pneumonia, who are expected to have higher PCT values, whereas most of our patients had uncomplicated pneumonia and were managed as outpatients. Nevertheless, in our study all patients with radiographic pneumonia had a PCT value of ≥ 0.7 ng/mL. So, if we use this cut-off point, we will probably better select patients; the percentage of patients at low risk would grow to 80% and the PPV would also be higher (37.8%). In this vein, Lipsett et al [22] have just developed and validated a novel score, a clinical tool utilizing several signs and symptoms to determine a child's risk of radiographic pneumonia. They conclude that the use of the score is superior to clinician judgment with a prevalence of 6%, 22% and 63% for the low, moderate, and high-risk category, respectively. They propose observation without CXR or antibiotic use for children in the low-risk group, empirical antibiotic treatment without CXR for children in the high-risk group, and CXR for those in moderate-risk group. Interestingly, if we apply their proposed score, most of our patients (up to 86%) would be classified as moderate-risk**,** so a CXR would be recommended. This percentage is clearly higher than ours, where CXR would be only recommended in 24.9% of patients. So, the incorporation of this biomarker could substantially improve the clinical risk stratification for radiographic pneumonia in these patients.

In our study, 3 out of every 4 patients had a low-risk based on PCT value; they were safely managed with symptomatic treatment, avoiding unnecessary radiation exposure. The identification of those patients at low risk will also prevent the overuse of antibiotics that sometimes accompanies CXR interpretation [23]. In our study, the interobserver agreement was moderate, and in all but one case of discordance the pediatrician over-diagnosed radio-

Table I Demographic and Clinical Characteristics of Participants (*n*=185)

Characteristics	*Value*
Age (years)[a]	3.3 (1.7-4.9)
Female sex	93 (50.3)
Fever[a]	
Duration (days)[a]	5 (5-6)
Maximum temperature (ºC)[a]	39.5 (39-39.8)
Diagnostic testing for influenza	64 (34.6)
Global positive	48 (75)
Positive for influenza A	36 (75)
Positive for influenza B	12 (25)

Values in n (%) or [a]median (IQR)

WHAT THIS STUDY ADDS?

- Procalcitonin is a useful biomarker for guiding the performance of a chest radiograph to rule out pneumonia in children with influenza-like illness and prolonged fever.

graphic pneumonia and therefore prescribed unnecessary antibiotic treatment. Although these discrepancies could be attributed mainly to the difficulty clinicians have with CXR interpretations [23,24], knowing that the patient has a PCT value associated with bacterial infection may have also influenced the pediatrician's attitude. Accordingly, several studies showed that pre-antibiotic plan based on the clinical impression was the strongest predictor of antibiotic prescription, regardless of CXR results [21,25].

This study had several limitations. First, it focused on children with mild illness, so the results may not be generalized to all patients with suspected pneumonia, especially to those children with moderate to severe pneumonia. Further studies are needed that include a more heterogenous population. Second, CXR was used as the gold standard for pneumonia diagnosis and radiographic pneumonia was defined as per the radiologist's report. Recent evidence has showcased the limitations of CXR, which include high inter-observer variability, an inability to distinguish viral from bacterial pneumonia, and radiation exposure. We used CXR as the reference standard, in line with similar studies performed in emergency department settings, in which a CXR is usually still ordered when pneumonia is suspected. Lastly, because a CXR was only ordered for those patients considered to have a pre-established high-risk PCT value, we could not accurately determine its diagnostic utility. Nevertheless, no patients with a low-risk PCT value were diagnosed with pneumonia at evolution, so we could assume that the prevalence of radiographic pneumonia among these children was probably non-existent or very low.

Procalcitonin can be used to avoid unnecessary radiation exposure in children with ILI and prolonged fever. If the present results are confirmed by further studies in the general pediatric population, the introduction of point-of-care PCT testing, which can be performed quickly in the emergency department, may improve the management of children with suspected pneumonia in pediatric clinical practice.

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Contributors: SHB: Conceptualized and designed the study, analyzed, and interpreted data, and drafted the initial manuscript; VT: Conceptualized and designed the study, was involved in obtaining ethics approval, analyzed, and interpreted data and revised the manuscript; CG, IC: Conceptualized the study, enrolled patients and did data collection; CL: Conceptualized the study and provided critical review of the original and subsequent manuscript drafts. All authors approved the final manuscript as submitted.
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ORIGINAL ARTICLE

Congenital Diaphragmatic Hernia at a Non-ECMO Center in Jordan

Montaha Al-Iede,[1] Eman Badran,[2] Raed Al-Taher,[3] Iyad Al-Ammouri,[4] Omar Ashour,[5] Tara Ghazi,[5] Mahmoud Abu Zahra,[6] Abdulrahman Alhanbali,[5,7] Hebah Qutishat,[8] Enas Al-Zayadneh,[1] Manar Al-Lawama[2,9]

[1]Department of Pediatrics, Division of Respiratory Medicine, School of Medicine, The University of Jordan, Amman, Jordan.
[2]Department of Pediatrics, Division of Neonatology, School of Medicine, The University of Jordan, Amman, Jordan.
[3]Department of General Surgery, Division of Pediatric Surgery, School of Medicine, The University of Jordan, Amman, Jordan.
[4]Department of Pediatrics, Division of Cardiology, School of Medicine, The University of Jordan, Amman, Jordan.
[5]School of Medicine, The University of Jordan, Amman, Jordan.
[6]Pediatric Pulmonary Fellow, Division of Respiratory and Sleep Medicine, The Children's Hospital at Montefiore, Albert Einstein College of Medicine, USA.
[7]University of Texas Medical Branch, Department of Pediatrics, Texas, USA.
[8]Neonatal Fellow, Division of Neonatology, Cook Country Health and Hospital System, Chicago, IL.
[9]Department of Clinical Sciences, Yarmouk University, Irbid, Jordan.

ABSTRACT

Objectives: We studied the clinical characteristics and outcomes of neonates with congenital diaphragmatic hernia (CDH) admitted to a non-extracorporeal membrane oxygenation (ECMO) center.

Methods: A retrospective chart review of neonates with CDH admitted to a University Hospital, in Amman, Jordan, between 2005 and 2019. Demographic characteristics and their management details were extracted and factors associated with survival were analyzed.

Results: A total of 28 neonates born with CDH were included; their survival rate was 39.3%. Onset of respiratory distress, pre-operative ventilation, and length of hospitalization were significantly associated with mortality. Survival after surgery was significantly associated with a higher gestational age and a longer hospital stay.

Conclusion: Our study showed a high mortality rate for CDH patients. Decreasing the health inequity and improved clinical interventions could improve outcomes.

Keywords*: Pulmonary hypertension, Survival rate, Ventilation*

INTRODUCTION

Congenital diaphragmatic hernia (CDH) is a structural defect in the diaphragm leading to herniation of abdominal organs into the chest cavity [1]. Pulmonary hypoplasia and persistent pulmonary hypertension (PPHN) are direct complications associated with CDH [2]. Mortality and survival rates related to CDH demonstrate large disparities between different centers in different countries. For example, the survival rate for a single center in India was 84.3% [3], while in Saudi Arabia it was 62% [4]. One possible explanation for this discrepancy is the difference in capabilities between centers in different countries [4].

Correspondance to: Dr. Montaha Al-lede, School of Medicine, The University of Jordan, Department of Pediatrics, Division of Respiratory Medicine, Jordan University Hospital, Amman-Jordan 11942.
montaha95@yahoo.com
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Currently, gentle ventilation with permissive hypercapnia is considered the cornerstone in managing these children [5]. Extra-corporeal membrane oxygenation (ECMO) is considered a mainstay rescue measure used in severe CDH [6]. Sildenafil, inhaled nitric oxide (iNO) and magnesium sulfate ($MgSO_4$) are being increasingly used as a measure of controlling PPHN associated with CDH [1]. We studied the characteristics of babies with CDH managed at our center over 15 years to investigate the factors affecting their outcome.

METHODS

This study was conducted at a tertiary care hospital in Amman, Jordan. Both ECMO and iNO are not available in our hospital. Additionally, high-frequency oscillatory ventilation (HFOV) is also not always available.

In this retrospective study, we analyzed the electronic medical charts of 28 neonates diagnosed with CDH in our

hospital between January, 2005 and January, 2019. Patients who presented beyond the neonatal period (> 28 days) were excluded. Neonates who were antenatally diagnosed and were distressed at birth were intubated according to the guidelines [7]. Prior to the introduction of HFOV in our hospital in 2014, conventional ventilation was done via assisted ventilation mode. Since 2014, HFOV became the first choice of ventilation for newborns with CDH, except in some mild cases. We also administered surfactant within two hours of birth in term infants with CDH, to possibly help in improving gas exchange related to reduced lung compliance, despite the lack of robust evidence of its use. Pre-and post-ductal saturations and echocardiogram were used to detect PPHN. Treatment for PPHN was initiated if pre-ductal saturation was less than 85% [8]. In severe cases, where a high ventilation settings were required, the permissive hypercarbia principle was applied. Echocardiography was performed within 12 hours after birth. Dobutamine was started in all patients with pulmonary hypertension. Sedation was achieved by fentanyl with a starting dose of 1 µg/kg. Enteral sildenafil was started at a dose of 1-2 mg/kg every 6 hours. Total parenteral nutrition was started immediately after birth via umbilical venous line.

Surgical repair was done after physiologic stabilization; this was evident by low to moderate ventilator setting, and oxygen saturation within the targeted ranges on < 40% FiO2. An open surgical approach was used and after surgery, extubation was planned as soon as possible. Oral feeding was started shortly with expressed breast milk if available or with formula appropriate for the infant's birth weight.

The collected variables included: demographic and clinical data, time of diagnosis (antenatal or postnatal diagnosis), associated structural cardiac abnormalities, presence of lung hypoplasia which was diagnosed using the routine antenatal ultrasound and post-natal chest-*X*-ray, sepsis, presence of PPHN which was diagnosed by a pediatric cardiologist after performing an echocardiogram, treatment of pulmonary hypertension including use of sildenafil and/or magnesium sulfate, need of surfactant and/or HFOV, use of antireflux medications, operative and postoperative course, and outcome. Patient outcome was defined as either being dead or alive regardless of whether or not surgical treatment was received.

Statistical analysis: This analysis was performed using IBM SPSS Statistics for Windows, version 23. Categorical associations were evaluated using the Chi-square test, while associations involving continuous data were assessed using Student *t*-test. Multivariate logistic regression analysis was used to detect predictors of mortality.

RESULTS

We reviewed 28 (14 females) medical records of live births known to have CDH. Patient characteristics are summarized in **Table I**. Of our sample, only less than half (12; 42.9%) babies were diagnosed antenatally. The antenatal diagnosis did not show a significant change in survivability ($P = 0.253$) (**Table I**).

The hernia was left-sided in 22 (78.6%) babies. The herniated content was bowel in 18 (64.3%) babies. CDH was associated with lung hypoplasia in 16 (57.1%) patients and with PPHN in 16 (57.1%) patients. No significant association was found between lung hypoplasia, having PPHN, or getting sepsis (which was defined as a positive blood culture) and survivability (**Table I**). A

Table I Demographic Characteristics of the Study Population (*n* = 28)

Characteristics	*Value*
Male sex	14 (50)
Gestational age (weeks)[a]	37.46 (1.03)
Gestational age	
< 37 weeks	4 (14.3)
37 weeks	13 (46.4)
38 weeks	6 (21.4)
39 weeks	4 (14.3)
40 weeks	1 (3.6)
Birth weight (kg)[a]	2.85 (0.50)
Birth weight < 2.5 kg	4 (14.8)
Apgar score[a]	
1 min	6.09 (1.77)
5 min	7.68 (1.96)
Antenatal diagnosis	12 (42.9)
Left sided hernia	22 (78.6)

Values expressed as n (%) or [a]mean (SD)

Table II Management and Outcome of Congenital Diaphragmatic Hernia (*n* = 28)

Variables	*Value*
Duration of surgery (hours)	1.50 (1)
Duration of postoperative ventilation (days)	6.50 (6)
Postoperative sildenafil use[a]	6 (40.0)
Length of hospitalization (days)	16.50 (13)
Duration of oxygen therapy prior to discharge (days)	7.50 (10)
Age at discharge (days)[c]	25.0 (13.5)
Weight at discharge (kg)[b,c]	3.05 (0.49)
Death[a,c]	4 (26.7)

Values are median (interquartile range), [a]n (%) or [b]mean(SD). [c]Outcomes with surgery

WHAT THIS STUDY ADDS?

- Data on congenital diaphragmatic herniais is presented from a tertiary care center in Jordan.

total of 11 (39.3%) babies survived. **Table II** provides the characteristics of babies who underwent surgical intervention.

Upon comparing survivors with non-survivors, significant differences were found in having surgery done ($P < 0.001$), usage of reflux medicationsx ($P = 0.02$), and usage of inotropes ($P = 0.002$) as seen in **Table III**. The survivors and non-survivors, differed significantly with respect to the age at discharge (days) [25.36 (14.44) *versus* 8.29 (9.49); $P = 0.001$] and length of hospitalization (days) [21.45 (12.45) vs 6.84 (7.94); $P = 0.001$].

DISCUSSION

This is a single tertiary center study with an overall mortality rate in CDA of 60.7%. This is considered higher than the reported mortality rate from the International Clearinghouse for Birth Defects Surveillance and Research from 36 countries (37.7%) [9] but comparable to reports from Brazil (63·7%), and Iran (58.4%) [10,11]. This could be attributed to health inequities and limited resouces [4]. The overall median length of hospitalization was short (15 days), when compared to what was reported in different studies ranging from 31 to 39 days [12,13]. This is largely due to early mortality associated with CDH in our center, as more time spent at the hospital was associated with higher numbers of survivors.

Table III Comparison of Characterstics Between Survivors and Non-Survivors With Congenital Diaphragmatic Hernia

Variables	*Odds ratio*	*P value*
Male sex	2.5 (2.52-11.92)	0.220
Left sided hernia	0.23 (0.03-1.59)	0.174
Structural heart disease	0.58 (0.41-0.80)	0.505
Lung hypoplasia	0.23 (0.05-1.19)	0.121
Pulmonary hypertension	0.24 (0.05-1.19)	0.121
Sepsis	0.92 (0.12-6.82)	0.999
Antenatal diagnosis	0.33 (0.06-1.71)	0.253
Being sedated	0.09 (0.01-1)	0.047
Being intubated	0.35 (0.21-0.59)	0.146
Using blood products	0.86 (0.15-4.81)	0.999
Using surfactant	0.16 (0.02-0.95)	0.054
Using HFOV	0.14 (0.015-1.38)	0.099
Using inotropes	0.03 (0.003-0.35)	0.002
Using reflux medicines	8.1 (1.41-47.01)	0.020
Sildenafil	0.16 (0.03-0.84)	0.051
Magnesium sulphate	3.2 (1.54-6.61)	-
Having surgery done	0.26 (0.11-0.62)	< 0.001
Postoperative sildenafil	0.50 (0.22-1.11)	0.055

Early intubation of antenatally diagnosed neonates is an essential step in management of CDA [14]. In our study, a total of 26 neonates needed early intubation while only two cases were managed by non-invasive mechanical ventilation. The use of non-invasive neurally-adjusted ventilator assist has been reported to be effective when used in the postoperative period [15]. In our case, the two neonates were managed by non-invasive positive pressure ventilation pre and post-operatively with both patients surviving to discharge, possibly due to smaller defect size with less pulmonary effect reflected by their minimal need for oxygen.

The delayed surgical intervention used by us is supported by recent literature, which states that surgery should be undertaken after stabilizing the infant [16]. All patients managed with magnesium sulfate died, which raises a question on its effectiveness; although magnesium sulfate has been reported to be useful [17].

Previous literature supports the use of inotropes to help with the survival of CDH patients [19]. However, the use of inotropes was not found to improve survival rates in our study. HFOV is a widely used ventilation approach in infants with respiratory distress. In our study, no significant association was found between the outcome of CDH patients and the use of HFOV. There is still a controversy regarding the benefit of HVOF in such patients, and a study reported no significant difference in the mortality between conventional ventilation and HFOV [5].

Our study is a retrospective, single-center study which may limit its generalizability. However, this series shows the current status of CDH in this region. Adoption of iNO and other evidence-based management options may further improve the outcomes of CDH.

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ERRATUM

Retrospective Open Access Article

The article "Pediatrics in Artificial Intelligence Era: A Systematic Review on Challenges, Opportunities, and Explainability" written by Yashaswini Balla, Santosh Tirunagari, David Windridge, was originally published electronically on the publisher's internet portal *https://link.springer.com/article/10.1007/s13312-023-2936-8* on 24 July, 2023 without open access. With the author(s)' decision to opt for Open Choice the copyright of the article changed to © The Author(s) and the article is forthwith distributed under a Creative Commons Attribution 4.0 International License *https://creativecommons.org/licenses/by/4.0/*, which permits use, duplication, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, and indicate if changes were made.

RESEARCH LETTER

Prevalence and Predictors of Effective Face Mask Usage Among Children During the COVID-19 Pandemic

ABSTRACT

A total of 320 children, aged 1 to 14 years were observed to ascertain the prevalence of face mask usage and the factors affecting the same. 67% of children used face masks, but only 25% of them used them correctly. Factors such as age, type of school, socioeconomic status, maternal education, history of allergic diseases, COVID vaccination status of the parents, and having a sibling were significantly associated with the use of face masks. Age-appropriate targeted health interventions should be implemented to improve proper mask usage.

Keywords: *Coronavirus, Mask etiquette, Pediatric, Prevention, SARS-CoV-2*

The COVID-19 pandemic has brought about unprecedented challenges worldwide, affecting nearly every aspect of daily life. One of the most critical measures taken to curb the spread of the virus has been the widespread use of face masks. The commonly used face masks are surgical mask, respirators, such as N95, FFP2, or the equivalent and cloth-based face masks. While mask usage has been extensively studied in adults, there is limited research on the adoption, effectiveness, and adherence to mask-wearing among children [1]. Children represent a vulnerable population, and understanding the factors that influence mask etiquette in this group is crucial for the development of effective public health strategies regarding optimal mask usage in children.

Multiple studies have assessed the impact of mask-wearing in reducing COVID-19 transmission in adults, emphasizing its importance in mitigating the spread of the virus [2,3]. However, given the physiological, cognitive, and behavioural differences between children and adults, it is essential to investigate mask usage and etiquette specifically among children [4].

Children can tolerate and adapt to mask usage with appropriate guidance and support from parents, teachers, and caregivers [5]. It is important to understand the age-related variations in mask acceptance and compliance and the role of cultural, socio-economic, and psychological factors in shaping children's mask-wearing behaviours [6]. This study was conducted with the aim of identifying the pattern of mask usage and the determinants of mask etiquette among children.

This hospital-based, cross-sectional study was conducted in a tertiary care hospital in South India between August 2021 to October 2021 after obtaining ethical clearance. All children aged 1 to 14 years attending the pediatric out-patient department (OPD) were included in the study after obtaining informed consent from legal guardians. The study involved only the general pediatrics OPD and not the speciality clinics. Children with congenital cyanotic heart diseases, chronic lung diseases like cystic fibrosis, chronic kidney disease and neuro-developmental disorders were excluded from the study. The sociodemographic details were documented. The children were observed for 15 minutes in the OPD waiting area and in the consultation rooms by the study team and the different parameters related to mask use were documented and analysed. Appropriate mask use was defined as a child following all of the following while using a mask *a*) the child must wear a mask, *b*) the mask must cover mouth and nose, *c*) the child should not touch the mask and in case it is essential to touch the mask, hand hygiene should be observed, and *d*) the mask should be held in appropriate position without slipping.

Statistical analysis was done using 'stata' software. Descriptive statistics were calculated. Chi-square test was done to find out the association between categorical variables and the mask usage. *P* value less than 0.05 was considered as statistically significant.

A total of 320 children were included in the study. Out of them, 144 (45%) were males and 176 (55%) were females. The mean (SD) age of presentation was 6.3 (4.008) years. 209 (66%) of patients belonged to lower-middle and 111 belonged to upper-middle (34%) socio-economic status as per modified Kuppuswamy scale-2021. Out of all 320 children, 45 (14%) had fever and 85 (27%) had respiratory symptoms as the presenting complaints. 213 (66.6%) of children wore a mask whereas 107 (33.4%) did not wear it at all. Only 78 (24.5%) children used it appropriately. Types of masks used were cloth mask, surgical mask and N95 mask in 195 (91.5%), 11(5.2%) and 7 (3.3%) respectively. Using appropriate-sized mask, keeping the mask in correct position (i.e., covering both mouth and nose), and removing the mask during observation was seen in 190 (89.2%), 156 (73.2%)

and 79 (37.1%) children respectively. The median (interquartile range, IQR) number of times each child touched the mask was 2 (0, 5). **Table I** and **Table II** represent the factors affecting mask usage and appropriate mask usage respectively. These results underscore the need for targeted interventions to promote mask adoption and proper use among children. This includes creating health awareness among parents, practical demonstration of the correct method of using masks and teaching them about the do's and don'ts of mask etiquette at schools.

There was a significant association between mask usage and appropriate mask-wearing with increasing age among children. The ability to tolerate and adapt to mask usage improves with age due to the development of cognitive and motor skills and the support provided by parents, teachers, and caregivers [7]. Public health initiatives should take these age-related differences into account while planning targeted interventions.

There was a significant difference in mask usage and appropriate mask-wearing between children attending private schools and those attending government schools or not attending any school. This discrepancy could be attributed to the socio-economic factors. Private schools may have greater resources for promoting and monitoring mask-wearing practices among their students [8]. Moreover, parents of children attending private schools may have higher levels of education and awareness regarding the importance of masks in mitigating the spread of COVID-19, thus influencing their children's behaviour [9].

Mask usage was higher among those with allergic diseases as these children might be more inclined to use masks for protection against potential allergens or irritants and may also have prior experience of using masks [10]. Mask usage was more among children of parents who had better compliance with COVID vaccination. This emphasizes that awareness among parents is directly related to the health promoting behaviour of children. The children who have siblings were found to have a significantly higher rate of mask usage compared to those who were single children. It highlights the influence of siblings on developing good habits among kids.

This study has few limitations. It's a single centre study and it reveals the mask etiquette of children belonging to a particular geographic area. A certain degree of observer bias is inevitable. The size of the masks was not standardised as they were sourced by the parents themselves.

Only a small proportion of children were found to wear mask appropriately. The effective mask usage is influenced by numerous factors including age of children, type of school, and maternal education. Lack of clear guidelines from authorities regarding mask usage in children leading to confusion among parents could have influenced the mask usage among children. The findings suggest that targeted interventions, considering age, socio-

Table I Factors Affecting Prevalence of Mask Usage

Factor	*Not using a mask (n = 107)*	*Using a mask (n = 213)*	*P value*
Age (y)[a]	2.7 (2.5)	8.1 (3.3)	< 0.001
Age categories			
1-5 years	90 (84.1)	59 (27.7)	< 0.001
6-11 years	17 (15.9)	108 (50.7)	
12-14 years	0	46 (21.6)	
Male gender	46 (43.0)	98 (46.0)	0.64
Locality			
Urban	52 (48.6)	106 (49.8)	0.91
Rural	55 (51.4)	107 (50.2)	
School			
No	80 (74.8)	33 (15.5)	< 0.001
Public	14 (13.1)	66 (31.0)	
Private	13 (12.1)	114 (53.5)	
History of allergic diseases[b]	6 (5.6)	33 (15.5)	0.011
Past history of covid in family			
Nil	86 (81.9)	188 (88.3)	0.36
Child	1 (1)	2 (0.9)	
Child and parent	1 (1)	1 (0.5)	
Parent	17 (16.2)	20 (9.4)	
Parent and siblings	0	2 (0.9)	
COVID vaccination status of parents			
Nil	19 (17.8)	17 (8.0%)	0.040
1 dose	23 (21.5)	53 (24.9%)	
2 dose	65 (60.7)	143 (67.1%)	
Maternal education			
Illiterate	8 (7.5)	35 (16.4)	0.037
Primary school	4 (3.8)	9 (4.2)	
Middle school	13 (12.3)	19 (8.9)	
High school	22 (20.8)	47 (22.1)	
Intermediate/diploma	24 (22.6)	37 (17.4)	
Graduate	20 (18.9)	54 (25.4)	
Professional	15 (14.2)	12 (5.6)	
Socioeconomic status			
Upper	7 (6.5)	7 (3.3)	0.047
Upper middle	32 (29.9)	70 (32.9)	
Lower middle	45 (42.1)	62 (29.1)	
Upper lower	20 (18.7)	64 (30.0)	
Lower	3 (2.8)	10 (4.7)	
Having siblings	64 (59.8)	173 (81.2)	< 0.001
Fever	15 (14.0)	30 (14.1)	1.00
Respiratory complaints	27 (25.2)	58 (27.2)	0.79

Data are presented as n (%) or [a]mean (SD). [b]Bronchial asthma, allergic rhinitis, atopic dermatitis.

Table II Factors Affecting Appropriate Mask Usage

Factor	*Inappropriate mask use (n = 242)*	*Appropriate mask use (n = 78)*
Age (y)[a,b]	5.6 (3.9)	8.4 (3.5)
Age categories		
1-5 y	126 (52.1)	23 (29.5)
6-11 y	88 (36.4)	37 (47.4)
12-14 y	28 (11.5)	18 (23.1)
Male gender	107 (44.2)	37 (47.4)
Urban residence	118 (48.8)	40 (51.3)
School[b]		
No	102 (42.1)	11 (14.1)
Public	54 (22.3)	26 (33.3)
Private	86 (35.5)	41 (52.6)
History of allergic diseases	26 (10.7)	13 (16.7)
Past history of covid in family		
Child	2 (0.8)	1 (1.3)
Child and parent	2 (0.8)	0
Parent	29 (12.1)	8 (10.3)
Parent and siblings	1 (0.4)	1 (1.3)
Covid vaccination status of parents		
1 dose	60 (24.8)	16 (20.5)
2 doses	152 (62.8)	56 (71.8)
Maternal education[c]		
Illiterate	27 (11.2)	16 (20.5)
Primary school	9 (3.7)	4 (5.1)
Middle school	30 (12.4)	2 (2.6)
High school	52 (21.6)	17 (21.8)
Intermediate/diploma	51 (21.2)	10 (12.8)
Graduate	48 (19.9)	26 (33.3)
Professional	24 (10.0)	3 (3.8)
Socioeconomic status		
Upper	12 (5.0)	2 (2.6)
Upper middle	74 (30.6)	28 (35.9)
Lower middle	88 (36.4)	19 (24.4)
Upper lower	59 (24.4)	25 (32.1
Lower	9 (3.7)	4 (5.1)
Siblings	180 (74.4)	57 (73.1)
Fever	37 (15.3)	8 (10.3)
Respiratory complaints	64 (26.4)	21 (26.9)

Data are presented as n (%) or [a]mean (SD). [b]P<0.001; [c]P<0.01

economic factors, and specific health conditions, are essential in improving mask etiquette in this vulnerable population. Mask usage in children has significant implications even beyond the COVID-19 pandemic era due to the ongoing outbreaks of viral respiratory illnesses that continue to happen throughout the year. Further research should explore other potential determinants of mask-wearing behaviours in children in order to develop an evidence-based mask usage guideline for children.

Ethics clearance: Institutional Ethical committee No. AIIMS/MG/IEC/2022-23/143.
Contributors: DS and TAB: Designed the study. DS, SB and AMB: Data collection. YM, DS, TAB: Statistical analysis. DS, SM, AMB, YM: Review of literature and drafted the initial version of the manuscript, TAB: Critical review of manuscript. All authors approved the final version of the manuscript. TAB will act as guarantor of the paper.
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Diptirekha Satapathy,[1] Thirunavukkarasu Arun Babu,[1*] Sandhya Bommidi, [1]Yamini Marimuthu,[2] Appikatla Madhu Bhavana[1]
[1]Department of Pediatrics, All India Institute of Medical Sciences (AIIMS), Mangalagiri, Andhra Pradesh.
[2]Department of Community and Family Medicine, AIIMS, Mangalagiri, Andhra Pradesh.
**babuarun@yahoo.com*

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UPDATE

The 5th Edition of the World Health Organization (WHO) Classification of Hematolymphoid Tumors: What's New in Pediatrics?

Debabrata Mohapatra,[1] Rachna Seth,[1] Saumyaranjan Mallick[2]

[1]Division of Pediatric Oncology, Department of Pediatrics, All India Institute of Medical Sciences (AIIMS), New Delhi.
[2]Department of Pathology, AIIMS, New Delhi.

ABSTRACT

The World Health Organization (WHO) has revised the classification of hematolymphoid tumors (WHO-HAEM5) in August 2022 to incorporate certain recent changes in understanding of disease biology. This article highlights the important changes, with particular reference to those most relevant to children.

Keywords: *Blood, Cancer, Classification, Leukemia, Lymphoma.*

The 5th edition of the World Health Organization (WHO) classification of hematolymphoid tumors (WHO-HAEM5) was released in August 2022 [1] that now replaces the previously updated 4th edition (WHO-HAEM4) published in 2017 [2]. There have been changes in the definition, nomenclature and sub-categorization of certain subtypes of acute leukemias, lymphomas and myeloid neoplasms. In this article we highlight the salient changes in the recent WHO-HAEM5 those are of utmost interest to pediatricians while drawing its differences from the older version.

Lymphoid neoplasms

The lymphoid neoplasms have been categorized into two groups: B-cell and T/NK-cell which have been further grouped based on the maturation stage, phenotypic character, histomorphological features, clinical information, and cytogenetic/molecular genetic findings. **Table I** highlights these changes from the WHO-HAEM4 version [3].

1. Tumour-like lesions with B-cell predominance

This group includes five distinct entities with B-lymphocytic proliferations, which do not meet sufficient criteria for lymphoma. They lack clonality and immunophenotypic characters of lymphoma. This includes Castleman disease, now classified into three distinct entities: unicentric Castleman disease, idiopathic multicentric Castleman disease, and KSHV/HHV8-associated multicentric Castleman disease based on clinical and immuno-morphological criteria. This group also includes reactive B-cell-rich lymphoid proliferations and IgG4-related disease those were previously not included.

Correspondence to: Dr. Rachna Seth,
Professor and Incharge, Division of Pediatric Oncology,
Department of Pediatrics, All India Institute of Medical Sciences, New Delhi.
drrachnaseth1967@gmail.com

2. Precursor B-cell neoplasms

Like the previous versions, lymphoblastic leukemia and lymphomas are classified as the same entity. However, WHO-HAEM5 focuses more on molecular alterations than cytogenetic aberrations in naming ALL with recurrent genetic aberrations in view of more molecular testing in diagnosing leukemia, e.g. B-ALL with ETV6::RUNX1 fusion, instead of t(12;21). B-ALL with high hyperdiploidy, defined as having 51-64 chromosomes, will be used instead of B-ALL with hyperdiploidy to highlight their prognostic difference [4].

Some entities, which have been newly included are: B-ALL with BCR::ABL1-like features, B-ALL with ETV6::RUNX1-like features and B-ALL with TCF3: :HLF fusion. Novel recurrent mutations have been clubbed as "B-ALL with other defined genetic abnormalities" and includes B-ALL with DUX4, MEF2D, ZNF384 or NUTM1 rearrangements, IG::MYC fusion, and PAX5alt or PAX5 p.P80R abnormalities.

3. Mature B-cell neoplasms

From being a subtype of marginal zone lymphoma 'pediatric Nodal Marginal Zone lymphoma (pNMZL)' is made a separate entity like pediatric-type follicular

Table I Changes in Classification of Pediatric Lymphoid Neoplasms in 5th Edition of WHO Classification 2022

4th Edition of WHO Classification 2017	*5th Edition of WHO classification 2022*
Tumour-like lesions with B-cell predominance	
Not previously included	Reactive B-cell-rich lymphoid proliferations that can mimic lymphoma
Not previously included	IgG4-related disease
Not previously included	Unicentric Castleman disease
Not previously included	Idiopathic multicentric Castleman disease
Multicentric Castleman disease	KSHV/HHV8-associated multicentric Castleman disease
Precursor B-cell neoplasms	
B-lymphoblastic leukemia/ lymphoma with hyperdiploidy	B-lymphoblastic leukemia/ lymphoma with high hyperdiploidy
Nomenclature focuses on cytogenetic alterations	B-lymphoblastic leukemia/ lymphoma with recurrent genetic aberrations nomenclature focuses on the molecular events
Not previously included	B-lymphoblastic leukemia/ lymphoma with TCF3::HLF fusion
Not previously included	B-lymphoblastic leukemia/ lymphoma with ETV6::RUNX1-likefeatures
Mature B-cell neoplasms	
Same	Pediatric marginal zone lymphoma
Same	Pediatric type follicular lymphoma
High-grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements	Diffuse large B-cell lymphoma/ high grade B-cell lymphoma with MYC and BCL2 rearrangements
Burkitt-like lymphoma with 11q aberration	High-grade B-cell lymphoma with 11q aberrations
Not previously included, encompassing primary diffuse large B-cell lymphoma of the CNS in revised 4th edition (plus primary large B-cell lymphoma of the vitreo-retina and primary large B-cell lymphoma of the testis)	Primary large B-cell lymphoma of immune-privileged sites
Lymphoid proliferations and lymphomas associated with immune deficiency and dysregulation	
Not previously included, encompassing non-destructive post-transplant lymphoproliferative disorders, among others	Hyperplasia arising in immune deficiency/dysregulation
Not previously included, encompassing polymorphic post-transplant lymphoproliferative disorders, other iatrogenic immunodeficiency-associated lymphoproliferative disorders, among others	Polymorphic lymphoproliferative disorders arising in immunedeficiency/ dysregulation
Not previously included, encompassing monomorphic post-transplant lymphoproliferative disorders, classic Hodgkin lymphoma post-transplant lymphoproliferative disorders, lymphomas associated with HIV infection,among others	Lymphomas arising in immune deficiency/ dysregulation
Lymphoproliferative diseases associated with primary immune disorders	Inborn error of immunity-associated lymphoid proliferations and lymphomas
Tumour-like lesions with T-cell predominance	
Not previously included	Kikuchi-Fujimoto disease
Not previously included	Indolent T-lymphoblastic proliferation
Not previously included	Autoimmune lymphoproliferative syndrome
EBV-positive NK/T-cell lymphomas	
Not previously included	EBV-positive nodal T- and NK-cell lymphoma
Extranodal NK/T-cell lymphoma, nasal-type	Extranodal NK/T-cell lymphoma
EBV-positive T- and NK-cell lymphoid proliferations and lymphomas of childhood	
Same	Severe mosquito bite allergy
Hydroa vacciniforme-like lymphoproliferative disorder	Hydroa vacciniforme lymphoproliferative disorder
Chronic active EBV infection of T- and NK-cell type, systemic form	Systemic chronic active EBV disease
Same	Systemic EBV-positive T-cell lymphoma of childhood

lymphoma, due to its more indolent behavior than their adult counter parts.

High-grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements (previously double/triple-hit lymphoma) has been merged into the entity 'diffuse large B-cell lymphoma (DLBL)/ high-grade B-cell lymphoma with MYC and BCL2 rearrangements' because of similar gene expression profiles despite variable morphologies. Burkitt-like lymphoma with 11q aberration is renamed as 'high-grade B-cell lymphoma with 11q aberration' as their mutational spectrum and genomic imbalances are closer to diffuse large B-cell lymphoma-germinal centre B-cell like (DLBCL-GCB) type despite morphological similarity to Burkitt lymphoma.

Primary DLBCL of the vitreo-retina and testis, that were previously included among diffuse large B-cell lymphoma, not otherwise specified (DLBCL, NOS), and primary central nervous system lymphoma (PCNSL) are clubbed together as large B-cell lymphomas (LBCL) of immune-privileged sites due to similar pathogenesis from evasion of immune surveillance in sanctuary sites.

\The classification identifies two distinct types of Burkitt lymphoma (BL) in pediatrics depending on the EBV status and mutational profile. 'EBV-negative BL' has more mutations in the genes encoding transcription factor TCF3, the repressor ID3 or TP53, while 'EBV positive BL' harbours more mutations in noncoding sequences close to transcription start site and an enrichment of FOXO1 and GNA13. Their prognostic differences are not known.

4. Lymphoid proliferations and lymphomas associated with immune deficiency and dysregulation

This group includes lymphoproliferations and lymphomas arising in post-transplant and immunodeficient patients. It is being understood that polychemotherapy also causes immunosuppression, as does the immune-dysregulation by newer modalities like immunotherapies, chimeric antigen receptor T-cell (CAR-T) therapy and checkpoint inhibitors. Hence, the term "immune deficiency/dysregulation" (IDD) is introduced in place of 'immunodeficiency'.

The classification describes three-part nomenclature for these entities: 1) histological diagnosis, 2) viral association and 3) immune deficiency/dysregulation setting; for example: "polymorphic lymphoproliferative disorder, EBV related, post-renal transplant".

5. Hodgkin lymphoma

Though nodular lymphocyte predominant Hodgkin lymphoma (NLPHL) may be more accurately called "nodular lymphocyte predominant B-cell lymphoma" owing to its biological differences from Hodgkin lymphoma, WHO-HAEM5 does not strictly separate it out from HL so as not to interfere with ongoing trials, but it acknowledges that this term will be adopted in future [5].

6. Tumour-like lesions with T-cell predominance

Analogous to classification of B-cell neoplasms, this entity includes three separate entities: indolent T-lymphoblastic proliferation (ITLP), Kikuchi-Fujimoto disease (KFD), and autoimmune lymphoproliferative syndrome (ALPS). Despite growing as clusters or confluent sheets of lymphoid cells with TdT expression, ITLP can be distinguished from T-lymphoma by absence of monoclonal TCR gene rearrangement and preserved nodal architecture. Kikuchi-Fujimoto disease (KFD) presents as cervical lymphadenopathy in young women that shows infiltrate of CD 123+ plasmacytoid dendritic cells with significant apoptosis. Autoimmune lymphoproliferative syndrome (ALPS) presents as non-destructive infiltration of CD4-/CD8-T cells in nodal and extra-nodal sites in young patients, characterized by defective FAS-mediated apoptosis and auto-immunity.

Classification of most of the precursor T-cell neoplasms and mature T-cell and NK-cell neoplasms have mostly remained unchanged or have minor changes that are of no relevance to pediatric population.

7. EBV-positive NK/ T-cell lymphomas (ENKTL)

Though relatively uncommon in childhood the nasal type NK/ T-cell lymphoma is also found in other extranodal sites like skin, salivary gland, testis, and gastrointestinal tract. Hence, the term "nasal-type" is dropped from extranodal NK/ T-cell lymphoma, nasal-type. Nodal EBV-positive T and NK-cell lymphoma is recognized as a separate entity as it presents with nodal mass with or without extranodal involvement and lacks the coagulative necrosis, angioinvasion and genetic landscape of ENKTL.

8. EBV-positive T- and NK-cell lymphoid proliferations and lymphomas of childhood

Chronic active EBV diseases (CAEBVD) are EBV-associated lymphoid proliferations and lymphomas that occur mostly in Asian and native American children [6]. These rare T- and NK-cell disorders have a variable spectrum from localized severe mosquito bite allergy and hydroa vacciniforme lymphoproliferative disorder (HVLPD) to systemic CAEBVD and EBV-positive T-cell lymphoma of childhood. HVLPD is further identified to have a classic cutaneous form and a systemic form resembling CAEBVD. Due to its aggressive systemic

nature the benign sounding "chronic active EBV infection, systemic form" is renamed as "systemic CAEBVD".

Myeloid neoplasms

The WHO-HAEM5 classification categorizes myeloid proliferations and neoplasms into the following nine sub-categories: *a*). Myeloid precursor lesions (new), *b*). Myeloproliferative neoplasms (MPNs), *c*). Mastocytosis, *d*). Myelodysplastic neoplasms (MDNs, previously known as myelodysplastic syndrome, MDS), *e*). MDN/MPNs, *f*). Acute myeloid leukemia (AML), *g*). Secondary myeloid neoplasms (new), h). Myeloid/lymphoid neoplasms with eosinophilia and defining gene rearrangement, *i*). Acute leukemias of mixed or ambiguous lineage (MPAL/ALAL). **Table II** depicts the salient changes in classification [7].

1. Acute myeloid leukemia (AML)

WHO-HAEM5 separates 'AML with defining genetic abnormalities' from 'AML defined by differentiation (the

Table II Changes in Classification of Pediatric Myeloid Neoplasms in 5th Edition of WHO Classification 2022

4th Edition of WHO classification 2017	*5th Edition of WHO classification 2022*
Myeloproliferative neoplasms	
CML phases: chronic, accelerated and blast phases	CML phases consolidated into chronic and blast phases, with emphasis on risk features in chronic phase
JMML is categorized under myeloproliferative neoplasms/ MDS	JMML is categorized under myeloproliferative neoplasms
Myelodysplastic neoplasms	
Myelodysplastic syndrome	Myelodysplastic neoplasms
Refractory cytopenia of childhood (RCC)	MDS with low blasts (MDS-LB)
MDS with excess blasts	MDS with increased blasts (MDS-IB)
Acute myeloid leukemia	
Previously AML defined by differentiation was included under AML NOS	The separation of AML with defining genetic abnormalities from AML defined by differentiation
AML "with myelodysplasia-related changes" (AML/MDS)	AML-MR replaces the former term AML "with myelodysplasia-related changes", and its diagnostic criteria are updated.
Previously except for CBF AML and APML rest types required atleast 20% blasts for diagnosis	AML with BCR::ABL1 and AML with CEBPA mutation are the only disease types with a defined genetic abnormality that require atleast 20% blasts for diagnosis
Secondary myeloid neoplasms	
Replaces therapy related AML/MDS	Myeloid neoplasms (MDS, MDS/MPN, and AML) post cytotoxic therapy (MN-pCT)
No explicit characterization or separate subdivisions	Myeloid neoplasms associated with germline predisposition grouped into three subtypes 1. Myeloid neoplasms with germline predisposition without a preexisting platelet disorder or organ dysfunction (e.g., Li-Fraumeni syndrome) 2. Myeloid neoplasms with germline predisposition with preexisting platelet disorder (e.g., Familial platelet disorders) 3. Myeloid neoplasms with germline predisposition with potential organ dysfunction (e.g., IBMFS, RASopathies, Down syndrome)
Acute leukemias of mixed or ambiguous lineage	
Previously they were defined based on immunophenotyping only	A framework for a molecular classification is laid byseparating ALAL/MPAL with defining genetic abnormalities from those that are defined based on immunophenotyping only.
Histiocytic/dendritic cell neoplasms	
These groups were described separately	Histiocytic/dendritic cell neoplasms are described with myeloid neoplasms
Previously not included	ALK-positive histiocytosis is described as a new addition

FAB subtypes)' to prevent inclusion of the latter group under a single entity AML-NOS. The "no blast cut-of" has been expanded to all 'AML with defining genetic abnormalities' except for AML with BCR::ABL1 fusion (to distinguish from CML), CEBPA mutation and 'myelodysplasia-related AML (AML-MR)'. AML-MR is the new term instead of AML "with myelodysplasia-related changes" for AML types with cytogenetic and molecular abnormalities associated with MDS and requires ≥20% blast cut-off.

2. Myeloproliferative neoplasms (MPN)

As the triphasic natural history of CML is uncommon in the imatinib era and as the focus has shifted from naming accelerated phase (AP) to emphasis on high-risk features associated with progression to blast phase (BP), AP is omitted in the classification keeping the previous cut-off of 20% for BP. Due to absence of typical dysplasia and presence of more proliferative mutations in the pathogenesis of juvenile myelomonocytic leukemia (JMML), it is now classified under MPN rather than MDS/MPN [8].

3. Myelodysplastic neoplasms (MDNs)

To highlight its malignant nature, MDS has been renamed as 'myelodysplastic neoplasms' parallel to MPN. MDS with defining genetic abnormalities have been separated. Due to different mutational landscape, childhood MDS remains distinct from adults and includes mostly two groups of anomalies. MDS with monosomy 7, 7q-, or complex karyotype behave aggressively requiring transplant, while cases with trisomy 8 or normal karyotype can have an indolent course. Childhood MDS with low blasts (cMDS-LB) and with increased blasts (cMDS-IB) replace the terms refractory cytopenia of childhood (RCC) and MDS with excess blasts (MDS-EB) respectively with acquired cytogenetic abnormalities and RAS-pathway mutations being more common in cMDS-IB [9].

4. Secondary myeloid neoplasms

This group includes myeloid neoplasms developing "post-cytotoxic therapy" or "associated with germline predisposition" [10]. Myeloid neoplasms post-cytotoxic therapy (MN-pCT) is the new term for therapy-related AML. Exposure to methotrexate has been excluded as a cause of MN-pCT. Myeloid neoplasms arising in the setting of inherited marrow failure syndromes, Down syndrome, and RASopathies are discussed under "myeloid neoplasms with germline predisposition".

5. Acute leukemia of mixed or ambiguous lineage (MPAL/ALAL)

ALAL/MPAL are split into two groups: 'ALAL with defining genetic abnormalities' and 'ALAL, immunophenotypically defined'[11]. Two new defining genetic alterations are ZNF384 rearrangement, found in ~50% of pediatric B/myeloid MPAL and BCL11B rearrangement, found in acute undifferentiated leukaemia (AUL) and ~20-30% of T/myeloid MPAL and ~20-30% of ETP-ALL.

6. Histiocytic/dendritic cell neoplasms

Due to common myeloid lineage, dendritic and histiocytic neoplasms like Langerhans cell histiocytosis, indeterminate dendritic cell tumour, interdigitating dendritic cell sarcoma, juvenile xanthogranuloma, Rosai-Dorfman-Disease (RDD), Erdheim-Chester disease, and histiocytic sarcoma are included here. A new indolent entity anaplastic lymphoma kinase (ALK)-positive histiocytosis, with translocation KIF5B::ALK has been characterized in infants, with involvement of liver, spleen and/or bone marrow.

Implications

This new classification has systematically described entities under the particular group of diseases from benign to aggressive ones and sub-classifies them into subtypes based on their biology and genomics rather than simple histo-morphology. Non-malignant entities (e.g. Kikuchi-Fujimoto disease, IgG4 related disease etc.) mimicking lymphoma have been described and given space in the classification, to remove the ambiguity regarding their clinical behaviours and origin. Changes more relevant to pediatric population are: nomenclature of ALL subtypes, pNMZL as a separate entity, classification of JMML as pure MPN and recognition of secondary myeloid neoplasms as a separate umbrella category.

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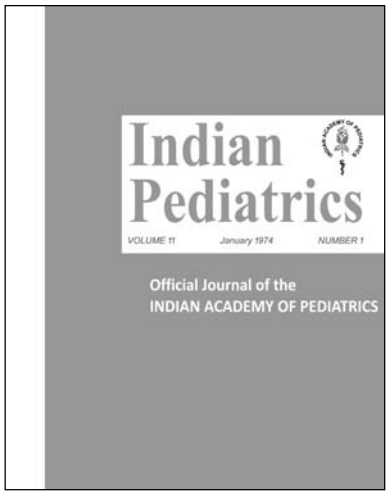
Evolution in Diagnostics of Intellectual Developmental Disorders

Shantasree Ghosh, Jaya Shankar Kaushik
Department of Pediatrics, All India Institute of Medical Sciences, Guwahati, Assam 781101

The January 1974 issue of *Indian Pediatrics* reported an article describing the etiology of mental retardation in 303 cases [1]. There is also another article published alongside where the authors have narrated clinical details of five cases of leucodystrophies as a cause of mental retardation [2]. This article provides a platform to discuss the evolution of diagnostics in children with mental retardation/intellectual disability.



The term mental retardation being socially harmful and scientifically not relevant has been replaced with the term "intellectual disability" in early 2000s [3]. International Classification of Diseases (ICD-11) uses the term "disorders of intellectual development". Since the deficit in cognitive capacity begins in the developmental period, it is more appropriate to use the term "intellectual developmental disorder." Hence DSM-5 has replaced the term mental retardation with intellectual disability (intellectual developmental disorder).

Intellectual disability (ID) is a heterogeneous group of disorders with a wide range of causes. It is a lifelong debilitating condition affecting between 2% and 3% of children and adults globally [4]. ID may be subdivided into two major categories – syndromic, characterized by specific clinical features associated with certain radiological, metabolic, or biological characteristics (for example, Down's syndrome), and non-syndromic, in which the cognitive impairment represents the only manifestation of the disease (most common being single gene defects).

The etiology of ID could range from infectious, traumatic, toxic/metabolic, genetic and acquired pathology [5]. Given the etiological heterogeneity, the diagnostic evaluation of ID is a challenge for the treating physicians. Over the last few decades, the diagnostic approach has taken a considerable leap from clinical diagnosis to the current genetic workup practice. There is an emerging era of genomics and genetic testing that has revolutionized the evaluation of children with ID/IDD. The current guidelines for the clinical evaluation of genetic causes are based on frequencies of single gene defects and the yield of diagnostic tools [6]. Genomic copy number variations (CNVs) constitute a well-established aetiological subgroup of ID. The most common diagnoses in ID are trisomy 21 (Down syndrome), 22q11 deletion syndrome (DiGeorge syndrome), and Fragile X syndrome (caused by a CGG expansion in FMR1).

Correspondence to: Dr. Jaya Shankar Kaushik, Additional Professor, Department of Pediatrics, All India Institute of Medical Sciences, Guwahati, Assam 781101.
jayashankarkaushik@gmail.com

THE PAST

In the study by Joshua GE, [1] etiology of 303 mentally retarded children under 12 years of age was performed, where they found 47% of the cases to be of genetic origin, 33% were due to acquired factors, and 20% both genetic and acquired factors were responsible. Their diagnosis was mainly based on clinical evaluation and biochemical parameters. The hereditary causes included Inborn Errors of Metabolism (22%) with sphingolipid error of 14.5% and congenital anomalies of 9.6%. Out of the acquired factors, post-encephalitic and post-meningitic sequelae formed 19% of the total. Other causes included birth trauma, close consanguinity, degenerative brain disease, and miscellaneous conditions like amyotonia congenita Syndrome, Idiopathic hypoglycemia, and hypothyroidism.

In another article published in the same issue of Indian Pediatrics, Joshua et al. [2] reported five cases of leukodystrophy (2 cases each of late infantile metachromatic leucodystrophy and Krabbe's Leukodystrophy and 1 case of Pelizaeus Merzbacher's type of leukodystrophy). Their diagnosis was based on the brain biopsy and quantitative

and qualitative estimation of sphingolipids, cerebrosides, sulfatide, cerebrosulphotransferase and ganglioside of the brain. It is commendable that authors have attempted to delineate the etiology of mental retardation in children in an era where neuroimaging and genetic testing were still developing. This speaks of the clinical acumen of the pediatricians of those eras who, with the sole help of clinical evaluation and limited biochemical tests, were able to arrive at the most probable genetic diagnosis.

THE PRESENT

'Intellectual Disability' (ID) is defined as a group of developmental conditions characterized by significant impairment of cognitive functions, associated with learning limitations, adaptive behaviour, and skills. There has been a considerable revolution in the diagnostics of intellectual disability in the last 50 years. There have been significant advances in the cytogenetic testing for ID from Karyotyping and FISH to chromosomal microarray [7]. Karyotyping can identify aneuploidies, such as Down's (trisomy 21) and Edwards (trisomy 18), and large structural re-arrangements, such as insertions, deletions, and duplications. Fluorescence *in situ* hybridization (FISH) can be used to detect structural abnormalities and numerical changes in chromosomes [8]. Chromosomal microarray can identify causative copy number variations (CNVs) in ID [9]. Most of the disorders with CNVs have additional clinical features like facial dysmorphism, congenital anomalies, and autistic features, along with intellectual disability.

Monogenic forms of ID due to mutations in X-linked and autosomal genes are being increasingly identified in syndromic and nonsyndromic forms of ID. Now, we can confirm the clinical diagnosis of a few syndromic causes of X-linked mental retardation, including Fragile X syndrome, MECP2 duplication syndrome and Pelizaeus Merzbacher disease. Fragile X syndrome is the most important single gene disorder responsible for 0.5 - 1.2% cases of ID [10] .

The introduction of next-generation sequencing (NGS) in this 21st century has revolutionized help in identifying autosomal de novo mutations in 16-55% of patients with ID, and biallelic mutations are seen in autosomal recessive ID in 25% of the cases [11]. An era of biochemical diagnosis for Inborn Errors of metabolism has been replaced with a genetic diagnosis with the introduction of NGS. In this context, it is noteworthy to mention the effort to identify treatable causes of ID through Treatable Intellectual Disability Endeavour (TIDE) [12]. TIDE was established to improve outcomes for children with rare diseases by way of enhanced diagnosis and treatment. It is a two-tiered protocol. The first tier includes readily available biochemical tests of urine and blood with the potential to identify 52 of 81 treatable IDs [12]. The 2nd tier aims at identifying the remaining 29 causes and involves a targeted workup, including single metabolite or primary molecular analysis.

Clinical diagnoses of acquired etiology like perinatal asphyxia and post-meningitic sequelae are often supported by neuroimaging. MRI Brain is often used to diagnose structural brain malformations like porencephaly, schizencephaly, lissencephaly, and heterotopias. Many genetic conditions of ID have few signature neuroimaging findings. Similarly, few patterns of findings on neuroimaging can help arrive at the diagnosis of leukodystrophy, and this now obviates the need for pathological diagnosis through brain biopsy.

THE FUTURE

Rapid advances in genetics and neuroimaging has revolutionized the dignosis and management of children with ID. A combined approach of next-generation sequencing and functional, electrophysiological, and bioinformatics analysis will help to identify new ways to understand the causes of ID and interpret novel ID-causing genes. This approach offers new targets for ID therapy and increases the efficiency of diagnosis. The most recent functional advancements and new gene editing techniques involving the use of CRISPR–Cas9 allow for targeted editing of DNA *in vitro* and more effective mammalian and human tissue-derived disease models. CRISPR–Cas9 technology will possibly help to cure diseases that have no treatment option, such as trinucleotide repeat expansion diseases causing neurological disorders [13]

Novel tools including gene-specific functional tests, animal models, and quantitative facial phenotyping might help improve the treatment and outcome of patients with ID. [14]. Preimplantation genetic diagnosis (PIGD) can help determine genetic defects in embryos (in vitro fertilization) before implantation in the uterus [15]. This technique has promise in preventing the incidence of intellectual disability or other serious genetic conditions among high-risk couples who have children with ID.

With the pace of technological advances, the future has many things in store. The emergence of virtual reality (VR) technology is an advancement in computer-aided rehabilitation. Through a human-computer interface, users can experience practical training that is otherwise difficult to be presented in words and images [16]. In this era of mobile applications, HikePal is a game-inspired app to motivate adult individuals with intellectual disabilities to do physical activity outdoors. CapacitaBOT, another educational mobile application based on a chatbot, allows

people with intellectual disabilities to work and train their social skills.

Genetic investigations, including whole exome and whole genome sequencing are readily available to clinicians. Moreover, with government-funded and private medical insurance policies, more patients can afford these investigations, and cost is no longer a limiting factor. Every technological advance has flaws, especially when the genetic reports do not correlate with clinical thoughts. This again reminds us of an era 50 years ago when we had astute clinicians who made clinical diagnoses with the support of limited biochemical tests.

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ERRATUM

Please note the following correction in the Author's Reply to the Correspondence titled "Do pain and physiological stress occur during MIST?" published in Indian Pediatr. 2023;60:1043. The name of the authors of the reply should be "Swati Manerkar,* Jayashree Mondkar, Department of Neonatology, Lokmanya Tilak Municipal Medical College, and General Hospital, Mumbai, Maharashtra.**drswatimanerkar@gmail.com*" in place of "Sriparna Basu, Department of Neonatology, AIIMS, Rishikesh, Uttarakhand. *sriparna.neonat@aiimsrishikesh.edu.in*" Appropriate corrections have already been done in the web version at *https://www. indianpediatrics.net/dec2023/1043.pdf* on December 19, 2023.

ANCA-Associated Vasculitis With Predominant Kidney Involvement in COVID era: A Case Series

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has been discovered to be exceptionally proficient at triggering autoimmunity; multiple novel onset autoimmune illnesses such as autoimmune hemolytic anemia, Guillain–Barré syndrome, and idiopathic thrombocytopenic purpura were reported in association with SARS-Co-V-2 infection [1]. Anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis, is one such autoimmune condition, characterised by small vessel involvement and paucity of immune complex deposition; kidney injury results due to the glomerular injury caused by these circulating ANCAs. While most of these autoimmune phenomena were reported more frequently in adults, multisystem inflammatory syndrome in children (MIS-C) was a form which was reported in the pediatric age-group. ANCA-associated vasculitis (AAV) as a post-infectious complication of COVID-19 infection has been reported in only a handful of cases [2-4].

This case series describes three previously healthy adolescents who had an asymptomatic COVID-19 infection followed by new-onset AAV. All three adolescents presented with hypertensive emergency, pulmonary hemorrhage and rapidly progressive acute kidney injury (AKI), following COVID-19 infection. Treatment included steroids, immunomodulators, hemo-dialysis and plasmapheresis. One of the three succumbed to pulmonary hemorrhage while the other two survived, one of whom has remained dialysis-dependent. This case series is one among the rare instances of AAV in children and adds to the growing evidence that COVID-19 causes autoimmunity, an aspect the general pediatrician must anticipate when faced with similar cases.

All the three patients had an asymptomatic COVID infection following which they developed rapidly progressive renal failure. The time duration between the infection and onset of symptoms was 6 weeks in patient 1, 8 weeks in patient 2 and not known for patient 3 as there was no symptomatic index case in the family. All children had AKI at presentation. While patient 2 and patient 3 presented with hypertensive emergency, patient 1 had a history of hemoptysis; chest radiographs of all the patients revealed bilateral diffuse alveolar opacities possibly secondary to diffuse alveolar hemorrhage. All patients were severely anemic with leucocytosis, had raised ESR levels and raised COVID antibody titres. Kidney biopsy showed pauci-immune crescentic glomerulo-nephritis (**Fig. 1**). Hemodialysis was required in two children in view of rising serum creatinine and oliguria. One child needed mechanical ventilation in view of respiratory failure secondary to diffuse alveolar hemorr-hage. Immunomodulation was used in all children with patient 1 receiving pulse methylprednisolone (MPS) followed by intravenous (IV) cyclophosphamide (15 mg/kg once in two weeks for 6 doses), patient 2 received pulse MPS, cyclophosphamide and underwent plasmapheresis while patient 3 received pulse MPS followed by IV rituximab. Patient 2 died due to massive pulmonary hemorrhage while the others had a hospital stay of about one-month duration. Patient 1 remained dialysis-dependent at one year follow-up while patient 3 was lost to follow up.

AAV is extremely rare in children. Its pathogenesis includes an initial insult that generates an aberrant pathogenic autoimmune response, followed by an active injury phase mediated predominantly by neutrophils, and a response to the injury which involves monocytes, macrophages, and T-lymphocytes. Mild injury can result in complete resolution, while severe injury can result in scarring with residual dysfunction, including necrotizing glomerular injury and countless acute lesions occurring in multiple organs. The antibodies include antibodies against myeloperoxidase (MPO) and proteinase 3 (PR3). Renal involvement is more commonly seen in MPO positive AAV (perinuclear-ANCA) suggestive of microscopic polyangitis (MPA). In 2022, American college of Rheumatology/European Alliance of Association for Rheumatology published criteria for MPA. In the criteria, a maximum score of +6 is given for p-ANCA positivity and a score of +3 is given for paucimmune crescentric glomerulonephritis. Other parameters include, lung fibrosis (+3), sinonasal symptoms (-3), c-ANCA positive (-1) and eosinophil count $>1\times10^9$/l (-4) [5]. A total score of 5 and above is considered diagnostic of MPA. All our patients had score above 5. **Table I** depicts the features of the three cases.

Acute kidney injury (AKI) is seen in 20-30% of children developing severe COVID-19 infection or MIS-C [6,7]. A meta-analysis of 11 studies showed AKI developing in 20% of children with MIS-C; about 15%

required renal replacement therapy (RRT) and 4% children succumbed [6]. Another analysis showed the incidence of AKI as 30% in COVID-19 positive children with 0.56% requiring RRT and a mortality of 2.5% [7]. Besides AKI, glomerular involvement can also be seen following COVID-19 infection. A case report from Korea identified crescentic immune complex glomerulonephritis in an eleven-year-old boy after COVID-19 infection. The patient responded to steroids and cyclophosphamide [8]. Another case study reported two patients aged 13 years and 16 years, respectively, who developed severe, rapidly progressive glomerulonephritis and end-stage renal disease after COVID-19. Renal biopsy revealed immunoglobulin A (IgA) nephropathy with crescentic GN, acute tubular injury, and focal medium-artery vasculitis [9]. Other renal complications reported in children post COVID-19 include mesangioproliferative GN and tubulointerstitial nephritis [10], which have been shown to respond to immunosuppressive therapy.

Genetic, environmental and viral triggers for autoimmune illnesses like AAV have been documented. Of the viral illnesses, SARS-COV-2 infection can trigger autoimmune diseases in some patients and though the exact etiology of autoimmune disorders is yet unclear, there is evolving evidence that there is a role for both genetic predisposition and environmental factors [1]. Molecular mimicry and hyperinflammation brought on by immune system overstimulation appear to be the possible mechanisms of autoimmunity in COVID-19 and may cause emergence of previously undetectable autoantibodies. Activating platelets and neutrophil extracellular traps (NETs), which are involved in a number of autoimmune illnesses, has also been demonstrated to activate complement in COVID-19.

In our case series, all children showed significantly high antibody titres for COVID-19 with pauci-immune crescentic glomerulonephritis. Hence, in these cases, SARS-CoV-2 infection being the trigger, or an exacerbating factor of vasculitis is suspected.

There are limited studies in pediatric population which mention ANCA-vasculitis following COVID infection. A study by Powell et al showed MPO positivity in a child diagnosed after COVID-19 infection [3]. A systematic review done by Bryant et al has shown a total of only four pediatric patients with AAV with COVID infection since 2019. An interesting point to note is that while most of the patients with AAV have been shown to respond to standard

Table I Baseline characteristics, laboratory findings, treatment received and outcome of patients

Characteristics	*Patient 1*	*Patient 2*	*Patient 3*
Age of presentation (years)	14	10	12
Gender	Female	Male	Female
Hemoglobin (g/dL)	6.6	4.1	4.6
ESR (mm/h)	54	85	>140
CRP (mg/L)	< 1.0	51.8	38
Ferritin (ng/mL)	230	641.02	83.15
Serum creatinine on presentation (mg/dL)	2.57	2.61	1.61
COVID-19 antibody titers (IU/mL)	1188.5	433	1124.5
p-ANCA (MPO) (Non-reactive < 20 RU/mL)	188	198.11	32.6
Anti GBMantibodies	Negative	Negative	Not done
Renal biopsy			
Light microscopy	Pauci-immune crescentic glomerulonephritis with 20-25% chronicity	Pauci-immune crescentic glomerulonephritis	Pauci-immune crescentic glomerulonephritis
Immunofluorescence	No immune deposits	No immune deposits	No immune deposits
ACR Score for MPA	9	9	9
Modality of treatment	Methylprednisolone Cyclophosphamide Hemodialysis	Methylprednisolone Rituximab Hemodialysis	Methylprednisolone Cyclophosphamide Plasmapharesis
Outcome	Dialysis-dependent	Expired	Lost to follow up

ACR: American College of Rheumatology, CRP: C-reactive protein, COVID-19: Coronavirus disease, ESR: Erythrocyte sedimentation rate, GBM: Glomerular basement membrane, MPA: Microscopic polyangiitis, MPO: Myeloperoxidase, p-ANCA: Perinuclear anti-neutrophil cytoplasmic antibody

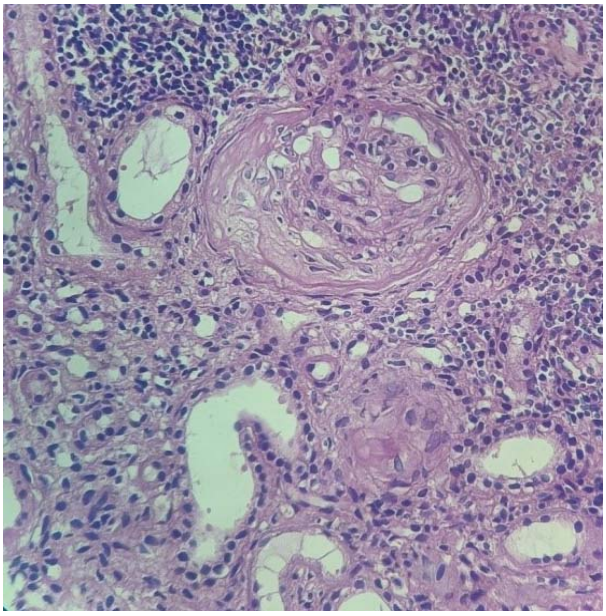

Fig. 1 Light microscopy H and E stain: Kidney biopsy of patient with ANCA associated vasculitis showing crescents in the glomerulus with no immune deposits on immunofluorescence and neutrophilic infiltration and severe tubular injury.

treatment [11], two of our patients did not respond to the standard treatment. Though the association/causality with COVID-19 infection is unknown, considering the high morbidity and mortality observed in this series, it may be prudent to build a concerted nationwide database to explore further and shed more light into this possible association and the interplay of other influential factors.

Madhura Fadnis,[1] Vrushali Kore,[2] Bhakti Sarangi,[3*] Jitendra Oswal,[4] Ajay Walimbe[3]

[1]Pediatric Nephrologist, Department of Pediatrics, Bharati Vidyapeeth Medical College and Hospital, Pune, Maharashtra

[2]Department of Pediatrics, Bharati Vidyapeeth Medical College and Hospital, Pune Maharashtra

[3]Pediatric Intensivist, Department of Pediatrics, Bharati Vidyapeeth Medical College and Hospital, Pune, Maharashtra.

[4]Department of Rheumatology, Bharati Vidyapeeth Medical College and Hospital, Pune, Maharashtra.

**dr.bhaktisarangi@gmail.com*

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Cerebral Venous Sinus Thrombosis in Children With SARS-COV-2-infection

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection causes self-limiting respiratory illness in children; however, post-infectious inflammation leads to morbidity and mortality [1]. Central nervous system (CNS) manifestations during acute infection as well as due to post-infectious immune stimulation are well known. In critically ill adults with comorbidities, thrombotic events (venous and arterial) have been reported [2-4]. Cerebral venous sinus thrombosis (CVST) in association with SARS-CoV-2 is rarely described in children [3,5-7] . We report four

patients with CVST associated with SARS-CoV-2 infection managed between March, 2020 and July, 2021 who responded to anti-coagulation and recovered without sequelae.

SARS-CoV-2 rarely causes severe pneumonia. Multi-systemic-inflammatory syndrome in Children (MIS-C), a post-infectious immune mediated inflammation, contributes to increased morbidity and mortality in pediatric age group [1]. Childhood neurological manifestations are seizure, encephalopathy, Guillain-Barré syndrome (GBS), stroke, demyelination etc.

Four children with suspected SARS-CoV-2 infection presented with neurological symptoms. Headache with vomiting (n = 4) and fever with altered mental status (n = 3) were the chief presenting symptoms. One patient had papilledema but none had focal neurological deficits. Acute SARS-CoV-2 infection was detected in three children (SARS-CoV-2 PCR positive in 2, SARS-CoV-2 PCR positive family members in 1; positive SARS-Cov2 immunoglobulin G (IgG) antibodies in 1). Radiograph of the chest, high resolution computed tomography (HRCT) thorax and 2D-echocardiography were normal in all. Three patients had multiple CVST (predominantly posterior) while one had single superior sagittal sinus thrombosis with venous infarction. All had no previous thrombotic events. **Table I** highlights the laboratory profile of these cases. Three of them had mild anemia. Mean D-dimer was 877 ng/dL while ESR, CRP, sickling test, vitamin B12, serum homocysteine, lupus anticoagulant and anti-phospholipid antibodies were unremarkable. Both girls had absent anti-nuclear anti-bodies (ANA) and perinuclear anti-neutrophil cyto-plasmic antibodies (p-ANCA) titres. On follow-up, three patients were investigated and had normal inherited

Table I Summary of Patients Presenting With CVST With SARS-CoV-2 Infection in Follow-Up duration of 2 years

Age (y) Sex	*Presenting features*	*Evidence of SARS-CoV-2*	*MR Brain & MR Venogram*	*Investigations*	*Treatment duration*	*Follow up MRI & MR Venograms*
14 y, Male	Headache, fever, malaise	SARS-CoV-2 PCR +	Left sigmiod and transverse sinus thrombosis	Hb: 15.2g/dL, WBC: 16130/ mm^3 Platelet count: 3.13 lac/mm^3 Vitamin B12 : 353 pg/mL CRP: 4.6 mg/dL Serum homocysteine: 11 µmol/mL d-Dimer: 1567 ng/mL Anti-phospholipid IgG: 0.5 ng/dL Lupus anti-coagulant: Negative	4 months	Recanalization of affected venous sinuses.
15 y, Female	Headache, fever, ence-phalopathy	SARS COV2 PCR +	Post sagittal; left- transverse and sigmiod and internal jugular vein thrombosis	Hb :9.8 g/dL, WBC:4600/ mm^3 Platelet count:1.24 lac/mm^3 Vitamin B12 > 2000 pg/mL CRP: 26.5 mg/dL;d-Dimer: 884 ng/mL Serum homocysteine:10.8 µmol/L Anti-phospholipid IgG:1.50 ng/dL Lupus anticoagulant: Negative TFT: normal	6 months	Recanalization of affected venous sinuses
16 y, Male	Fever, headache, lethargy	Contact with SARS-CoV-2 PCR positive person in family	Anterior sagittal sinus thrombosis with bilateral anterior frontal lobe DWI changes	Hb: 8 g/dlWBC: 5300/mm^3 Platelet count: 4.2 lac/mm^3 Vitamin B12: 786 pg/mL ESR: 29; CRP: 6.8 mg/dL d-Dimer: 505 ng/mL Serum homocysteine 18 µmol/mL Anti-phospholipid IgG: 1.2 ng/dL Lupus anti-coagulant: Negative	6 months	Recanalization of affected venous sinuses with gliotic changes
14 y, Female	Headache, vomiting	Covid Anti-bodies IgG +	Tiny DWI right centrum semiovale, right transverse, sigmoid and right internal jugular vein thrombosis	Hb: 9.2 g/dL WBC: 8000/mm^3 Platelet count: 4.05/mm^3 Vitamin B12: 856 pg/mL CRP: 4.2 mg/dL d-dimer: 556 ng/mL Serum homocysteine: 17.18 µmol/mL Anti-phospholipid IgG:1.3 ng/dL Lupus anti-coagulant: Negative	3 months	Recanalization of affected venous sinuses

CRP: C-reactive protein; DWI: diffusion-weighted imaging; Hb: hemoglobin; WBC: white blood cells

thrombophilia profile (protein C, protein S; anti-thrombin 3; MTHFR and factor V Leiden mutations). All received low molecular weight heparin (LMWH) for 2 weeks followed by 3-6 months of oral anticoagulation with re-canalization of sinuses on magnetic resonance venography (MRV) was documented 2-6 months from diagnosis. All recovered without any motor/cognitive deficit or recurrence at follow up of two years.

MIS-C results in multi-organ involvement and 5% of them have been reported to develop life threatening CNS involvement viz. severe encephalopathy, acute ischemic or hemorrhagic stroke, ADEM, GBS etc. [8]. Childhood CVST is rare with incidence of 0.67 cases per 100,000 per year. Risk factors are young age (neonates and infants), local extra and intra-cranial infections, dehydration and inherited thrombo-philia. In 35 childhood CVST reported from India [9], risk factors were head and neck infections (42.9%) and inherited thrombophilia (11.6%).

SARS-CoV-2 infection is an emerging trigger for CVST. Few case series of adult CVST associated with SARS-CoV-2 have reported comorbidities, multi-factorial etiology and variable mortality [2-4]. However, only five childhood CVST cases in association with SARS-CoV-2 infection have been published till date [3,5-7]. Three were adolescent boys (15 years, 12 years and 17 years) and one had obesity and hypertension. They had an insidious onset of drowsiness, headache, vomiting and focal neurological deficit with multiple CVST. Pro-coagulation work up was normal. They improved with anti-coagulation and had no morbidity later. Two younger children (boy aged 7 weeks and girl aged 31 months) had concurrent risk factors (homozygous MTHFR677C > T mutation and tubercular meningitis, respectively) with significant morbidity [5]. Unlike previously reported cases, none of our patients had focal neurological deficits at presentation, possibly due to early diagnosis. Mild anemia (n=3), direct Coombs test positive without hemolysis (n=1), obesity (n=2), metabolic syndrome (n=1) were concurrent risk factors. One child only had SARS-CoV-2 antibodies without MIS-C with CVST, a combination not previously reported.

In SARS-CoV-2 infection, the theories postulated for hyper-coagulation include [10]: virus invades endothelial cells via ACE-2 receptors leading to their internalization and engulfment; causing unopposed ACE-1 activity and excessive production of angiotensin-II inducing thrombosis [4]; damage of vascular endothelial cells by disruption of intercellular junctions, loss of basal membrane contacts etc. leading to dysregulation of hemostasis and vascular permeability; virus induced oxidative stress results in chronic reactive endothelitis which releases vWF multimers; immune response to virus causes activation of CD8+ T cells and inflammatory molecules likes tumor necrosis factor (TNF) alpha or interleukin-6 (IL6) resulting in autoimmune prothrombotic state; and, intracellular virus initiates formation of capillary micro-thrombi leading to disseminated intravascular coagulation (DIC).

CVST associated with SARS-CoV-2 infection is rare in children. A high index of suspicion in a child with subtle neurological manifestations and appropriate radiological investigations yields accurate diagnosis and prompt management with good outcome.

Abhijeet Botre,[1*] Ambrish Mishra,[2] Sarita Verma,[3] Madhumati Otiv[4]

[1]Department of Pediatric Neurology, KEM Hospital, Pune, Maharashtra.*
[2]Department of Pediatrics, KEM Hospital, Pune,Maharashtra.
[3]Department of Pediatric Hemato-Oncology, KEM Hospital, Pune, Maharashtra.
[4]Department of Pediatric Critical Care, KEM Hospital, Pune, Maharashtra.
**drabhijeetbotre@gmail.com*

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Dyslipidemia Amongst the Overweight and Obese Children in Jharkhand: More Questions Than Answers!

We read with great interest the article by Sinha et al [1]. Though the study is a novel one, there remain a few queries to enhance our understanding of the paper. We understand that though the prevalence of tribals in the state is significant, but being a hospital-based study, does AIIMS, Deoghar, primarily serve tribals? This is particularly relevant as the tribal status of the children recruited in the study has not been presented. Moreover, a hospital-based enrolment of subjects, as was done in this study, is not reflective of the true prevalence; rather a community- or school-based study would have been more appropriate. Further, a clarification on the process of case selection is necessary for a clearer understanding.

We are also inquisitive as to why children as young as two years were included as overweight; obesity and dyslipidemia are phenomena which have significance in older children. Obesity onset in children younger than 5 years is endogenous or monogenic in nature rather than exogenic. Hence, rationality of screening such young children needs to be clearly stated. The exclusion criteria could have been broader with addition of children with hypothyroidism, nephrotic syndrome, steroid or immunomodulator use, familial dyslipidemias, acute pancreatitis etc. which would have made the results more meaningful.

Dyslipidemia was defined as per a study on adults with fasting lipid profiles being measured with a 10-hour fasting requirement [2]. Could the authors explain how this fasting protocol was managed for outpatient patients, especially for younger children? The authors could have defined dyslipidemia using the normative data published in children [3-5]. Similarly, the use of World Health Organization (WHO) growth charts for defining overweight and obesity may be inaccurate, especially because the Indian Academy of Pediatrics (IAP) growth charts using body mass index (BMI) cut-offs are available and more appropriate for Indian children.

The paper calculates the sample size based on the prevalence from a study conducted by ElmaoÃgullari et al [6]. We are curious as to why the sample size was not determined using prevalence data from a similar geographical region or population, especially when many studies from India are also available. In the article it is mentioned that samples were collected for fasting blood sugar and HbA1c estimation but the results of the same were completely omitted. Table I provides data on overweight and obesity among babies at birth. We request clarification on how these conditions were defined at birth and how they differed from those in children less than 5 years of age. There also seems to be a discrepancy between the data in Table I and the text regarding the number of children with abnormal triglyceride (TG) and high density lipoprotein (HDL) levels which needs to be corrected.

Muralidhar Subhiksha, Joseph John*
All India Institute of Medical Sciences, Bhubaneswar, Odisha.
**ped_joseph@aiimsbhubaneswar.edu.in*

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AUTHORS' REPLY

We are thankful to the readers for their interest in the article [1]. AIIMS Deoghar plays a crucial role in catering to the health-care needs of a significant portion of the tribal

population in Jharkhand, particularly in the Santhal Pragana region. AIIMS Deoghar is an institution of national significance established by the Ministry of Health and Family Welfare. This hospital caters to the needs of all individuals without discrimination based on caste, religion, or any other criteria.

Regarding the tribal status and the background of the children, our recruitment efforts aimed to include children from tribal areas without being selective based on their specific origins. However, we acknowledge that gathering information on the tribal status of the patients would have been a valuable addition, potentially yielding a more dependable set of results.

For a prevalence study, the most optimal approach typically involves community or school-based research, often requiring an extended duration. However, given the constraints of this short-term studentship project under ICMR, our investigation was conducted within the confines of our hospital.

In accordance with the guidelines from the Indian Academy of Pediatrics (IAP) and the American Academy of Pediatrics (AAP), the classification for overweight and obesity varies for children under 2 years and those between 2 to18 years of age. We concur with the understanding that obesity onset in children under 5 years is more likely to be attributed to endogenous or monogenic factors rather than solely influenced by exogenous factors. In our study, we set specific exclusion criteria, which entailed excluding children with obesity who had comorbidities and unstable vitals [1].

As per the 2023 guidelines of the American Academy of Pediatrics (AAP), dyslipidemia in obese children is defined by specific cut-off values, including a total cholesterol level exceeding 200 mg/dL, low-density lipoprotein (LDL) cholesterol surpassing 130 mg/dL, triglyceride levels exceeding 130 mg/dL, and a high-density lipoprotein cholesterol level (HDL-C) lower than 40 mg/dL. It is important to note that before the year 2023, there were no established guidelines for dyslipidemia cut-offs among obese children. In our study, we used cut-off values for all parameters that were more than those provided by the AAP. If we had adopted the AAP's cut-off values, our reported prevalence of dyslipidemia would likely have been higher. Additionally, for the fasting samples, we ensured a fasting period of eight to twelve hours before conducting the tests on the subsequent day [2].

Adopting the IAP chart is a viable option for our situation, it's good to consider the recommendations and guidance provided by the IAP. The lack of existing literature on the prevalence of dyslipidemia among obese Indian children prompted us to undertake this study. All the participants had normal fasting blood glucose and HbA1c levels. This sentence has been mentioned in 3rd paragraph of result section.

Table I includes information on the age of onset of obesity, which has been gathered by history taking. In this context, neonatal adiposity at birth is regarded as the initiation of obesity at birth [3]. Infants born with low birth weight (<2500 g) and high birth weight (>4000 g) exhibit an elevated risk of obesity compared to those with birth weights ranging between 2500 and 4000 g. Children who underwent swift weight gain from birth to age 2 y demonstrated an increased likelihood, up to 3.6 times, of developing overweight or obesity during childhood or adulthood. The association was particularly robust in relation to childhood obesity and overweight, emphasizing the significance of rapid infant weight gain as a contributing factor [2,4,5].

Our objective is to highlight that the commencement of exogenous obesity can occur either at birth or within the first five years of life. It is important to emphasize that obesity in children under five years old may not always a endogenous origin. The total no of children with abnormal TG were sixty five and the number of children with abnormal HDL were eighty six.

Sarthak Das
Department of Pediatrics,
All India Institute of Medical Sciences,
Deoghar,
Jharkhand.
sarthak.ped@aiimsdeoghar.edu.in

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CLIPPINGS: MEDICAL EDUCATION

Mobile technologies to support workplace-based assessment for entrustment decisions: Guidelines for programs and educators: AMEE Guide No. 154 (*Med Teach. 2023;45:1203-13*)

Entrustable professional activities (EPAs) are a set of activities which tell us about the ability of the learner to perform a clinical task truly independently. Assessment of these EPAs have become pivotal in the clinical assessment of a trainee. The authors, in this AMEE guide have described various methods, *viz*., brief direct observations, longitudinal monitoring, individual discussions, and product evaluation for workplace-based assessment (WPBA), along with the challenges being faced during the WPBA. They have explained in detail how mobile technology-based assessment can be used effectively in EPAs and other types of WPBA. Four types of assessments, *viz.* Provisional self-assessment, Supervisor assessment, Simultaneous self- and supervisor assessment, and Learner-initiated direct access and assessment have been described. They have described the points which should be considered before, during or after choosing the type of mobile technologies for such assessment. They have also covered the implementation barriers being faced in the mobile technology-based assessment.

Successful implementation of a rater training program for medical students to evaluate simulated pediatric emergencies (*GMS J Med Educ. 2023;40:Doc47*)

Simulation-based training in pediatric emergencies is one of the currently preferred methods of teaching learning. Astute observation and evaluation of the team performance for the debriefing process is the cornerstone of any simulation-based training. In the current study, the authors have described the development, evaluation, and successful implementation of a rater training program for medical students to assess guideline adherence, teamwork and team communication. Five medical students were systematically trained for assessing the videos for adequate teamwork using Performance Evaluation Checklist for Pulseless Ventricular Tachycardia (PEC-PVT) and Teamwork Emergency Assessment Measure (TEAM). Basic theoretical knowledge was also provided to the students and a rater training handbook was also developed to improve the evaluation by the raters. During the study, 16 videos from the three sessions were evaluated by a pair of medical students and principal investigator. They reported that 10 out of 15 pairs of the evaluation did show that the inter-rater reliability was moderate to high between the beginner medical students and the experts. The current study concludes that beginner medical students if adequately and systematically trained, could also evaluate the clinical skills, teamwork and intra-team communication skills in complex simulated scenarios thus adding to the bench strength of the assessors.

The art of the consult call: improving communication through shared mental models. (*MedEdPORTAL. 2023;19:11347*)

The physician-to-physician communication and consultation regarding a patient is an integral part of multidisciplinary and holistic patient management. Formal standardized training in this aspect of patient care is yet to be established. In the current study, fifteen pairs of junior and senior learners were paired together. The junior learner went through the clinical case and consulted the senior learner on phone who in turn assessed the quality of the information given by the junior learner. Checklist based on Kessler's 5C consultation model having five core components which should be considered when contacting another physician , viz contact, communicate, core question, collaborate, and close the loop was used during this study. The learners were also asked to communicate with their partners using a paired artistic activity. This activity was followed by a facilitator led debriefing session and explanation of the core elements of the model. Post intervention similar exercise was repeated. Of the fifteen pairs who completed both the pre- and post-intervention evaluations, learners completed a mean of 51% of core consult call components pre-intervention as compared to a mean of 84% post-intervention, which was found to be statistically significant ($P < 0.001$; 95% CI 19.9 - 46.1). The students also gave a positive feedback about the exercise. They concluded that the inter-physician complex communication skills can be made better by using a validated model for consultation calls.

Using insights from cognitive science for the teaching of clinical skills: AMEE Guide No. 155 (*Med Teach. 2023;45:1214-23*)

Clinical skill acquisition requires active integration between the declarative knowledge (knowing what) and the procedural knowledge (knows how). In the current guide, the authors have explained how the procedural skills are widely learnt using the mastery learning (learning and mastering one step after the another) and deliberate practice (selecting best actions and improving their own actions based upon them under teacher's supervision). Clinical skills may decay if there is either loss of knowledge or procedural skills and both require periodic honing. Retention of the learned clinical skills is of equal importance as the acquisition. The authors have described various cognitive science evidence-based practices which can be used to retain the clinical skills. Spacing (distribution of the learning sessions with longer time intervals between sessions), testing (both theory and skill of the participants at different times), feedback (guided feedback during study/training sessions and after tests), interleaving (integrate all different aspects in a single training session) etc. have been explained with examples as few of these techniques. They have also recommended that the skill level identification of each learner at the beginning of skill teaching is an important step to decide the appropriate mixing of knowledge and procedural components of the skill teaching. The authors describe how it is possible to integrate these strategies into the clinical skill training. The health educators should integrate the cognitive science strategies with their current approaches for teaching clinical skills.

Shashi Kant Dhir
Professor and Head, Department of Pediatrics
Guru Gobind Singh Medical College, Faridkot, Punjab 151203.
drshashikantdhir@gmail.com

Congenital Syphilis: Addressing a Missed Opportunity

Morbidity and Mortality Weekly Report (MMWR) by Centers for Disease Control (CDC) reported a ten times surge in cases of congenital syphilis over a decade between 2012 to 2022. The CDC recommends antenatal testing for syphilis at first antenatal visit. If not possible, then it should be done as soon as the pregnancy is identified. For those at high risk of contracting syphilis during pregnancy, and those not screened earlier, screening for syphilis is recommended at 28 weeks of gestation and at delivery.

Missed opportunity of testing and treatment of syphilis during antenatal period was considered to be the major reason for this surge. With the objective of specifically looking into this, the cases were assessed under six possible risk factors. These included no documented testing or non-timely testing, late identification of seroconversion, no or non-documented treatment, inadequate treatment, clinical evidence of congenital syphilis despite documented adequate maternal treatment, and insufficient data. Timely testing was defined as testing completed ≥30 days before delivery; late identified cases were those which were diagnosed within 30 days before delivery; while those who received adequately dosed and spaced penicillin-based treatment ≥30 days before delivery were defined as adequately treated. Further on, those patients who were diagnosed as congenital syphilis despite adequate and timely treatment were also categorized accordingly. A 31% increase in cases of congenital syphilis was observed in 2022 from 2021, with an overall increase in primary and secondary syphilis among women of child bearing age; 88% of which was attributed to lack of timely testing and adequate treatment during antenatal period. Additionally, a shortage of benzathine penicillin was a contributary factor for inadequate treatment. Despite the major limitation of the study being inconsistent data, missed opportunity for antenatal diagnosis and treatment of syphilis is a major cause for this surge. (*McDonald R, O'Callaghan K, Torrone E, et al. Vital Signs: Missed Opportunities for Congenital Syphilis – United States, 2022. MMR Morb Motal Wkly Rep. ePub: November 7, 2023*)

Rajasthan: Congratulations for the First Digitized Child Health Services!

Rajasthan will soon be able to have the status of the first state in India to have complete digitization of child health under the Reproductive and Child Health (RCH) Program. This has been possible as a result of the initiatives taken by Rajasthan National Health Mission in collaboration with Johns Hopkins Program for International Education in Gynecology and Obstetrics.

The system will be able to track maternal and child health, starting from antenatal registries. The system will be managed by the Auxiliary Nurse Midwives (ANMs) using mobile phone devices. 'Thursday' of each week will be observed as the safe motherhood day when pregnant women will be investigated near their residences. Rajasthan is also one of the states to show the fastest decline in maternal mortality rates over the last decade owing to its effective RCH services. This initiative will further help to strengthen the maternal and child health by digital tracking of their health providing real-time monitoring. (*The Hindu. August 17, 2023*)

Even Veggie Foods can be Junk

Plant-based foods including vegetarian and vegan diets are gaining popularity globally due to their potential health benefits like blood cholesterol and sugar lowering effects based on years of scientific research. Also, harmful environmental effects of animal rearing like green-house effect and water conservation are motivating millennials to follow animal protecting life style practices.

Balanced natural plant-based diets, which include fruits, dairy products, non-starchy foods, nuts, plant proteins etc. are considered a great option. However, there is a need to realize that several plant-based foods can be categorized as 'junk'. Some of the examples include processed breakfast cereals, pre-packaged instant foods, energy bars, packaged fruit-drinks and dairy products and many more. The products are rich in calories, sugars, salts and other preservatives. They have been proven to be associated with increased risk of high blood sugars, cholesterol, obesity, and some cancers. These ultra-processed foods also lack the essential minerals and vitamins. Therefore, one should take care to avoid ultra-processed, carbohydrate-rich plant foods which tend to have a filling effect. With awareness about the right plant-based foods while avoiding junks, we can have a new living style, that is quite consistent with the age-old culture and traditions. (*Medical News Today; August 22, 2023*)

Updated Target Regimen Profiles for Tuberculosis

Target regimen profiles (TRP) aim to focus and develop optimal regimens, rather than focus on individual drugs, for the treatment of tuberculosis. With an increase in prevalence of drug-resistant tuberculosis, and development of facilities to identify these, especially nucleic acid amplification test (NAAT), World Health Organization (WHO) focused on TRPs in the year 2016 and intensified it in 2022. Scientific TRP Development Group (STG) was formed with the aim to develop targeted regimens for rifampicin-sensitive (RS), rifampicin-resistant (RR) and pan-resistant (PR) tuberculosis. The document discussed minimal (lowest acceptable) and optimal (most favourable) targets across thirteen characteristics, viz, target population; populations of special interest; drug–drug interaction and metabolism; forgiveness of the regimen; number of component drugs; dosage form, dosing frequency and route of administration; shelf life; efficacy; safety; duration of regimens; indication and need for drug sensitivity testing (DST); pro-pensity to develop resistance and the pill burden. While developing the TRPs, adjustment or cross-cutting was needed among the 13 characteristics, to get the best possible regimen. The various aspects that needed trade-off

were DST, duration of treatment, treatment adherence, treatment strategies, post-treatment lung disease, equitable access and cost effectiveness.

A document was prepared and published in the public domain in February 2023 and the stakeholders were invited to provide feedback. Out of fifty-eight respondents, fifty were in agreement while eight made some suggestions. These suggestions were further discussed and amendments were made in the document. The amendment also emphasized addition of at least one drug from a completely new class within the respective chapters and incorporation of dispersible tablets in place of syrups for pediatric patients so as to have a better drug stability without the need for cold chain. (*World Health Organization. Target regimen profiles for tuberculosis treatment, 2023 update. November 2, 2023*)

Prerna Batra
Director-Professor,
Department of Pediatrics,
University College of Medical Sciences, Delhi.
drprernabatra@yahoo.com

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SIMULUS - 9

9th Annual Conference of PediSTARS on Healthcare Simulation

Theme: PURSUE PERFECTION THROUGH SIMULATION

PediSTARS INDIA

Host by

Bharati Vidyapeeth University Medical College & Hospital, Pune in association with PediSTARS

Preconference workshops: 31st August 2024 **Main Conference:** 1st September 2024

FDP (Faculty Development Program): 02nd & 03rd September 2024

Venue: Ground Floor Auditorium, Bharati Vidyapeeth University Medical College, Pune

Event/ Workshop		Early Bird Registration (till 30th April 2024)	from 1st May to 31st Jul 2024	SPOT Registration (01st August 2024 onwards)
Simulus – 9 Conference	PediSTARS non-members	3000	4000	4500
	PediSTARS members	2500	3500	4000
	Nurses/Allied Health Care Professionals, Students (MBBS/Interns/PG Students)	1200	1800	2500
STEP Workshop (Pediatric Simulation)	(Max. 40 participants)	3000	3500	SPOT Registration is not applicable
NeoSIM Workshop (Neonate Simulation)	(Max. 40 participants)	3000	3500	
SNAP Workshop (Nursing Simulation)	(Max. 40 participants)	2000	2500	
SimWars Workshop (Max. Group 8 and 4 members per group)		1000/participant	1200/participant	
Competency Based Skills Trainer Course for Medical Faculty Workshop (CBME) (Max. 40 participants)		5000	6000	
FDP (Faculty Development Program) **Workshop** (Max. 40 participants)	PediSTARS Doctor member	18000	23000	
	Non- PediSTARS Doctor member	20000	25000	
	Nurses	10000	12500	

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Email id: simulus09@gmail.com

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INSTRUCTIONS FOR AUTHORS

Indian Pediatrics is the official peer-reviewed journal of the Indian Academy of Pediatrics. It is being published every month since 1964 and endeavours to showcase the latest advances and research in child health, policy, and advocacy. The journal gives priority to reports of outstanding clinical work, as well as important contributions related to common and topical problems related to neonates, children and adolescents, especially those relevant to developing countries. The journal is indexed in PubMed, Current Contents/Clinical Medicine, Science Citation Index Expanded, Medline, Embase, Scopus, UGC-CARE List, Journal Citation Reports/Science Edition, Indian Science Abstracts, Psych Line and DERMLINE. The Journal follows International Committee of Medical Journal Editors (ICMJE) recommendations for the conduct, reporting, editing and publication of scholarly work in medical journals. *Indian Pediatrics* is also a member journal of Committee on Publication Ethics (COPE). The Impact factor (2022) of *Indian Pediatrics* is 2.3. The journal website consistently receives around 1.8 million hits per month.

Indian Pediatrics is also available online at *www.indianpediatrics.net* (free full text access) and at *www.springer.com/medicine/pediatrics/journal/13312* (International edition). The online edition of *Indian Pediatrics* is the journal of record and contains access to all articles published in print as well as includes certain content available only on web (Web Figures, Web Tables). The journal does not charge any article processing fee and is available at no cost to all readers.

MANUSCRIPT SUBMISSION

When preparing a manuscript for Pediatrics, authors must first determine the manuscript type and then prepare the manuscript according to the specific instructions below. Indian Pediatrics utilizes the online manuscript management and processing system of Editorial Manager for online submission of manuscripts. Please login directly to the site *https://www.editorialmanager.com/inpe*. You will need to register (first visit only) and upload your manuscript following the instructions given on the screen. Please ensure you provide all relevant editable source files at every submission and revision. For your manuscript text please always submit in common word processing formats such as .docx. All manuscripts must be accompanied by a signed Copyright Transfer Form. Available from: *https://indianpediatrics.net/AnnexureI.pdf*.

CRITERIA FOR ACCEPTANCE

Manuscripts submitted are judged on the basis of originality, clinical relevance, robust methodology, scientific merit, ethical standards and sound conclusions. The articles should be submitted as per the instructions for authors (vide infra). All submitted articles conforming to ICMJE guidelines [1] undergo a double blinded peer review process. Manuscripts that do not adhere to journal guidelines or ICMJE guidelines are sent back to the authors without initiating the peer-review process. After completion of the review process and on acceptance of the manuscript, the final version of the article undergoes modifications as per the journal's style to suit the language and style of *Indian Pediatrics,* following which it will be sent to the corresponding author for approval.

Review process

All manuscripts undergo an initial review by the Editorial Board. Some manuscripts may be rejected at this stage. The usual reasons for rejection at this stage are insufficient originality, serious scientific or presentation flaws, major ethical issues, absence of a message, article not related to children or adolescents, not submitted in desired format, not of interest to majority of readers, or not in accordance with the current priorities of the journal. Decision on such papers is communicated to authors usually within two weeks. Rest of the manuscripts undergo a very stringent double blinded peer review process. Reviewers having sufficient experience on the subject are sent the submitted articles for peer review in a 'masked fashion'. Manuscripts are reviewed while maintaining the authors' confidentiality. Authors should take care not to disclose their own and their institution's identity in the text of the 'blinded manuscript.' The peer reviewer identity is also kept confidential. The time from submission to first decision may vary from 1 week to 6 weeks (average 7.6 days) depending on the availability of reviewers, and timely response from them.

CATEGORIES OF ARTICLES

Unsolicited manuscripts are published in the following categories: original research (research papers, research briefs, research letters), clinical material (clinical case letters, clinico-pathological conference, images), guidelines or recommendations or position paper, review articles (narrative reviews, systematic reviews and meta-analysis, drug review, perspectives), special articles, and correspondence.

The journal also solicits articles under the headings of editorial commentaries, ethisection, beyond borders, book reviews and journal club to provide the readers insights on various issues related to child health from reputed experts. We also regularly publish announcements related to academic courses, scientific conferences and job openings for the readers and pediatric specialists.

Original Research

Manuscripts reporting original research may be submitted as Research Paper, Research Brief or Research Letter.

Research Paper

The submission should report research relevant to clinical pediatrics including randomized clinical trials, other intervention studies, studies of screening and diagnostic tests, analytical cohort and case-control studies, systematic reviews and cost-effectiveness analyses. Descriptive studies, surveys, case records/series, pilot interventional studies, and secondary analyses of data are usually not preferred for this section. Each manuscript should be accompanied with a 4-point abstract (Objective, Methods, Results, and Conclusions) in not more than 250 words. The methods should try to include the study design, participants, intervention and outcome variables of the study. The main text of the manuscript should be arranged in sections on Introduction, Methods, Results and Discussion. The authors should take care to avoid use of sub-headings in the Results or Discussion section. However, Methods section should always include a sub-heading of 'Statistical analysis'. The key messages from the study should be provided as one or two bulleted points at the end of the manuscript in a box under the heading: 'What this Study Adds?'. The number of tables and figures should be limited to a maximum of four and two, respectively. Additional tables and figures, subject to clearance by editorial review process, may be made available only at the journal website, as web table or web figure. The text should contain no more than 2500 words (excluding title page, abstract, tables, figures, acknowledgments, key messages and references) and up to 25 recent references.

Research Brief

Descriptive observational studies, and epidemiological assessments are published as Research Briefs. Knowledge, attitude, practice (KAP) studies surveys are generally not preferred. Some of the manuscripts submitted as 'Research Papers' may also be considered for publication under this section at the discretion of editors. A structured abstract using the following sub-headings: Objective, Methods, Results, and Conclusions, should be provided with a word count not exceeding 150 words. The text should contain no more than 1800 words, up to 2 tables, 1 figure and up to 15 recent references. The text should be arranged in order of Introduction, Methods, Results and Discussion. Also include a box entitled 'What this Study Adds?' highlighting the main result of the study.

The distinction between Research Brief and Research Paper is purely the journal's prerogative and does not reflect on the originality of the research submitted. The manuscripts will be finally published under the heading of Original Articles.

Research Letter

Research Letters reporting original research should not exceed 1000 words of text and up to 10 references. They may have no more than five authors. An unstructured abstract of up to 50 words reporting the key findings should also be included. Letters must not duplicate other material published, submitted or planned to be submitted for publication. Although unstructured, the text should follow the general sequence of introduction, methods, results and discussion.

Clinical Case Letter

Clinical cases highlighting some unusual or new but 'clinically relevant' aspects of a condition are published as Clinical Case Letters. Such reports should highlight some novel aspect regarding etiopathogenesis, diagnosis or management of a condition that adds to the existing body of knowledge. Rarity of the reported condition alone will not be a criterion for acceptance. Solitary cases are generally not preferred. Genetic syndromes not reporting novel mutations explaining pathophysiology and/or genotype-phenotype correlation may not be considered for publication. Minor or clinically insignificant variations of rare but well-known disorders are also not preferred. The text should not exceed 800 words and should be in running text with unlabelled paragraphs sequentially containing introduction, clinical description, and discussion. Include a maximum of 6 references. Only one very relevant figure (image) is allowed. Only color photographs should be submitted; black-and-white images will not be entertained. Color images will be published only in the web-version of the journal; for print version, these will be converted to black and white (For details, see below under Figures and Illustrations). Authors primarily reporting some visual clinical observation may consider submitting to the Images section instead of this section. A maximum of four authors are permitted. Whenever there is a clinical image, patient's written consent (or that of the next of kin) to publication must be obtained, and the same must be affirmed/stated on the Title page of the manuscript. The editorial board may ask for such a consent form at any time during the manuscript review process.

Images

Only clinical photographs with/without accompanying skiagrams or pathological images are considered for publication. Images of radiographs/histopathology slides alone (without accompanying clinical photograph) are not considered for this section. Image should clearly identify the condition and have the classical characteristics of the clinical condition. Clinical photograph of conditions that are very common, extremely rare, where diagnosis is obvious (e.g., penile agenesis), or where diagnosis is not possible on images alone would not be considered. A short text of about 300 words should be provided in two paragraphs; first paragraph having description of condition, and second paragraph discussing differential diagnosis and management. No references are needed. See guidelines for preparing and submitting Figures/images (*vide infra*). A maximum of three authors are permitted. The authors should ensure that images of similar nature have not been published earlier in *Indian Pediatrics*. Authors must obtain a signed informed consent from the parent/legal guardian, and the same must be stated on the Title page. The informed consent documents should also be attached as a supplementary material while submitting the manuscript.

Reviews

The journal encourages submission of review articles addressing recent advances/controversies. These may be submitted as either Review Papers, Drug Review, Update or Perspective. Please note that as a routine, all review papers submitted to *Indian Pediatrics* undergo a plagiarism check, and the articles are promptly sent back for revision or rejected depending on the extent of similarity with the published literature.

Review Paper

State-of-the-art review articles with, critical assessments of literature are published. Generally, review articles solicited. The authors may consult the Editor-in-Chief before submitting such articles, as similar reviews may already be in submission. Generally, a review article on a subject already published in *Indian Pediatrics* in last five years is not accepted. The typical length for review articles is 2500-3000 words (excluding tables, figures, and references). An abstract of around 200 words with the following sections: *Context* (describing the clinical question or issue and its importance in clinical practice or public heath), *Evidence acquisition* (describing the data sources used, including the search strategies, years searched, and other sources), *Results* (major findings of the review with the greatest emphasis laid on the findings based on highest quality evidence), and *Conclusions* (emphasize how clinicians should apply current knowledge) is needed. The number of references should be limited to 35. Authors should take care to avoid excessive self-citation. The number of authors should be limited to five.

Systematic Review and Meta-Analysis

The methods section for these manuscripts should be divided in to the following sub-headings:

- *Search eligibility*: Mention the inclusion criteria (in the PICOT format; patient, intervention, comparison, outcome, time) and exclusion criteria.
- *Search strategy*: This should mention the time frame of the literature search, the names of the databases, and the search strategy. The names of the databases are to be mentioned, giving full details of search terms and strategy may be additionally provided as a web table. It should show the syntaxes used in database searches in a tabulated manner with column headings: Name of Database; Search strategy; Results (no. of articles obtained).
- *Data extraction*: Here authors should mention where the data obtained in the databases was exported and thereafter, what kind of data extraction form was used to extract data of the eligible articles (after removing duplicates), giving the few relevant headings of the form e.g. *i*) study information, including geographic location, survey years, research design, sample size, percentage of respondents among eligible participants, and number of institutions included; *ii*) characteristics of participants, including mean age, gender, specialties; and *iii*) outcomes.
- *Quality assessment*: The methodology for quality assessment is to be mentioned here, clearly describing the scoring criteria.
- *Statistical analysis*: The statistical analyses carried out should be mentioned, including heterogeneity, estimate of effect, sensitivity and subgroup analysis.
- The results section should describe the included studies giving the PRISMA flow diagram showing the number of studies excluded and the reasons. A table is to be given showing the characteristics of the included studies, mentioning the author with the citation, country, year, number of participants in the study, and other important parameters as per the purpose of the review.
- The quality assessment of each included study needs to be elaborately depicted in a tabulated manner or in the form of a figure, mentioning the scores against each

criterion. This quality assessment table/figure is to be provided by authors as a web fig. or web table.

- It is desirable that meta-analyses is depicted as 1-2 Forest plot figures. The Forest plot is to be labelled completely and it should show the name of the author, with citation, year, *n* and either RR or OR or MD or HR (with 95% CI) against each weighted horizontal bar, with the weights being mentioned for each bar. The heterogeneity with *P* value also needs to be shown in the figure.
- Additional sensitivity analysis, sub-group analysis, or publication bias Funnel plot, if done by authors, may be provided as a web figure or web table.

Drug Review

Indian Pediatrics publishes state of the art reviews on drugs/agents meant for therapeutic or prophylactic use in children. It is expected that the authors have sufficient credible experience in the related field. The following guidelines should be adhered to when preparing a drug review:

- Drug should be recently developed and should be available commercially (in India) for use in human subjects. Reviews related to agents under research and development, are generally not accepted.
- Drug should preferably belong to a new class of drugs or having substantial difference in properties and not just an addition to the existing drugs having many similar properties/actions in that class/group of compounds.
- The drug should have the potential to be used on a large scale for pediatric conditions. Drugs primarily catering to other medical fields (e.g. adult medicine, dermatology) are not preferred.
- The drug and related review should have the potential to influence practice, policy and research related issues.
- The review should be a systematic, critical assessment of the literature and not just an elaboration of the information already provided by pharmaceutical companies.

Update

Short write-ups on recent modifications or revisions of standard guidelines, classifications or recommendations issued by global organizations on topics of interest to pediatricians are published in this section. The word limit is 1000 words, author limit is three, and a maximum of two brief tables and 10 references are allowed. An unstructured abstract of up to 50 words should also be included. It is preferable that only the most relevant changes from the previous version are provided in a tabular form. The manuscript should preferably include an 'introduction' detailing the current status of the disease/guideline and the need for the revision, important changes in the new version, and the implications of the changes. Avoid reproducing large parts of the guidelines/recommendations in the manuscript. Only the significant changes should be detailed.

Perspective

Articles should cover challenging and controversial topics of current interest in pediatric health care and the intersection between medicine and society. Though the articles are usually solicited, we welcome submissions and proposals from researchers and opinion-makers, provided they have sufficient credible experience and recognition on the subject for giving opinions. The number of authors should usually be limited to three. The word limit is about 2000 words and may include one figure and one table. It should be accompanied with an unstructured abstract of up to 150 words. The views should be supported by appropriate evidence and references. Number of references should be limited to a maximum of 25. Some of the manuscripts submitted as 'Review Articles' may also be considered for publication under this section after editing, at the discretion of editors. Articles pertaining to medical education will also be considered in this section.

Clinical Practice Guidelines/Recommendations

In order to streamline the diagnosis, management and prevention of various childhood problems, *Indian Pediatrics* periodically publishes guidelines and recommendations formulated by various Chapters and Task Forces constituted by Indian Academy of Pediatrics (IAP) or a similar National Association/ Society. The eight desirable attributes of practice guidelines are validity, reliability and reproducibility, clinical applicability, flexibility, clarity, documentation, development by a multidisciplinary process, and plans for review. In order to maintain uniformity of reporting and improve readability and applicability of these practice guidelines, the following 10-point policy should be followed:

1. The Guideline/Recommendation should have been formalized through a consultative meeting/ conference/workshop having a National representation approved by Indian Academy of Pediatrics (IAP) or a similar society. The guidelines emerging out of one such meeting should be preferably presented in a single paper.
2. The date(s) and place of such meeting should be

clearly mentioned in the Introduction. The names of the chairperson, convener and participants should be listed as 'Annexure' at the end of the draft.

3. All the authors of the guidelines should fulfil the authorship criteria as per ICMJE. All other people who have contributed to the development of guidelines, including the members of the committee framing the guidelines, should be listed in an annexure as contributors. The whole committee should not be the author of a guideline, unless all the members fulfil the ICMJE authorship criteria; it is preferable to have a writing committee of 6-8 members for the purpose.
4. The final guidelines should be cleared by the related Society/Chapter. A letter to this effect should be enclosed. All guidelines of IAP should be routed through the concerned chapter, and should be approved by the Executive Board of IAP. The corresponding author must obtain permission from all members of the committee/expert group to act in this capacity.
5. The manuscript should consist of an Abstract (250-300 words), Text (3000-4000 words), and References (up to 50). The number of figures and tables should be limited to two and four respectively.
6. Abstract should be structured as Justification, Process, Objectives, and Recommendations.
7. Text should be arranged under the following headings: Introduction, Aims and Objectives, and Recommendations. A concluding paragraph should be provided.
    a) *Introduction*: Justify the need of formulating the guidelines/recommendations in a brief paragraph followed by the process of arriving at the guidelines/recommendations. Describe the methods used to search the literature, and criteria used to grade the quality of evidence.
    b) *Objectives*: Should clearly state (in doable terms, using action verbs) the terms of reference of the consultative meeting/conference/workshop. List 2-3 main objectives only.
    c) *Text*: The main text of the Guidelines/ Recommendations should be mentioned under the same terms of reference as per aims and objectives outlined earlier. Preferably, provide level of evidence for each major recommendation.
    d) The Recommendations should not provide 'Review of literature' or 'What is already known'. Background material on the concerned subject will not be published.
    e) If guidelines are adapted from statement of some other society or from earlier recommendations, only changes need to be highlighted (preferably in a tabular form) without repeating the detailed guidelines. However, if there is a pressing need to repeat the recommendations, it should be done after taking permission from the parent society/ journal (as applicable) clearly mentioning and citing the source.
8. State, whether or not there is a plan to review these guidelines and an expiration date for this version of the guideline.
9. Any competing interest, including funding support, should be declared.
10. We encourage the authors to attach an AGREE (Appraisal of Guidelines Research & Evaluation) checklist for reporting clinical practice guidelines (*www.equator-network.org/wp-content/uploads/2016/03/AGREE-Reporting-Checklist.pdf*).

Authors should note that the words/phrases like 'recommended', 'strongly recommended', 'mandated', 'should be done', 'should be considered' have different connotations. Such terms should be clarified in the context of the guidelines, either in the Introduction section or as a Box in the beginning of the article.

Clinicopathological Conference (CPC)

Clinicopathological conference, a method of case-based teaching, is frequently used in institutions and primarily consists of a logical, narrowing of the differential diagnosis in a patient. The journal publishes CPCs, provided they fulfil the following criteria:

- At least three different departments are involved in the CPC, with each providing significant contribution to the discussion.
- The case represents a problem likely to be seen in the routine pediatric settings in India. They patient may later-on be diagnosed with a rare condition, but the initial presentation should be mimicking a common condition.
- An unstructured abstract of up to 100 words, and 3-5 keywords should be provided.
- The write-up should have the following headings: *i*) Clinical Protocol; *ii*) Pathology Protocol; *iii*) Open Forum; *iv*) Discussion; and *v*) References.
- The discussants' names should not be provided in the manuscript and should be the referred to as Pediatrician 1, Pediatrician 2…; Pediatric surgeon 1,

Pediatric surgeon 2,…; Neurologist 1, Neurologist 2,… and so on. The names of these persons may be listed at the end of manuscript as participants.

- The typical word count for this section is 2500-3000 words with upto 15 references. Up to three persons from the primary department and one person from each of the associated department may be included as the author of the manuscript.
- Up to two tables and two figures are permitted in this section.
- The full discussion held in the CPC need not be presented verbatim. Questions and answer dealing with the same aspect should be clubbed together.

Correspondence

Letters commenting upon recent articles in *Indian Pediatrics* are welcome. Such letters should be received within three months of the article's publication. Letters commenting on 'Invited or Special Articles', 'Case Reports' and 'Correspondence', are generally not preferred. At the Editorial Board's discretion, the letter may be sent to the authors for reply and the letter alone or letter and reply together may be published after appropriate review. Letters may also relate to other topics of interest to pediatricians, or useful clinical observations. The manuscript must have a title that should be different from the title of the paper it intends to comment upon. Letters should not have more than 500 words, and 5 most recent references. The text need not be divided into sections. The number of authors should not exceed two, including the authors' reply in response to a letter commenting upon an article published in *Indian Pediatrics*. In the latter case, inclusion of only one of the authors (of the article in question) is permissible along with the corresponding author. Names of additional persons who have helped in drafting the letter can be mentioned in the acknowledgment section.

Ethisection

Ethics in patient care and research is being increasingly recognized as an integral aspect of medical profession. However, there remains considerable variation in the interpretation, acceptance and integration of ethical principles into day-to-day clinical practice. This section presents deliberations of situations that illustrate challenging ethical considerations in patient care, research or administration. The aim is to stimulate reflection using illustrative cases to understand the varied ethical perspectives, dilemmas faced and provide a balanced view point.

The article should be structured as a brief introduction, an illustrative case(s) followed by an analysis of the ethical issues involved through two or three commentaries, outcome of the case and a concluding paragraph providing a balanced ethical viewpoint. The case should highlight an ethical dilemma encountered in clinical practice, research or administrative set up. Some examples of cases that can be studied include issues related to inclusion of children from low- and middle-income countries (LMICs) as participants in funded clinical trials, triage in disasters, pediatric organ donation and transplantation, teenage pregnancy, prenatal counseling in genetic syndromes, disclosure of medical information to parents, etc. The case should be presented as a situational narrative in about 300-400 words. The privacy and confidentiality of the patient(s) must be maintained. The case is to be followed by a commentary of about 1200-1500 words by 2-3 authors who should be from different specialties/ disciplines/with different administrative roles; a legal perspective should be preferably included. The article may present only one viewpoint or present an argument between two different perspectives which may be valid in different situations. The commentary is followed by a brief description of the outcome of the case, and the learning points from the case. The total word count should not exceed 2000 words with a maximum of 10 references. A total of 5 authors is permitted. An unstructured abstract of about 200 words with a brief case summary and the ethical issue as a question should be included with 3-5 keywords.

This section will normally include articles by invitation. However, unsolicited articles are occasionally considered. The authors can contact the editor about the suitability of their ethical dilemma by sending an email to the editorial office of *Indian Pediatrics*. Prospective authors are encouraged to avoid topics that have already been covered in previous issues under this heading.

Beyond Borders

This section aims at featuring ideas from around the world that can inspire and guide efforts to create uniformity in healthcare standards globally. A perspective of about 1800 words is invited from public health experts to highlight the concerns in healthcare of children outside India attributed to region-specific problems like war, climate change, migrant population, cultural practices, and poverty. This section explores not only the barriers in healthcare but also provides promising solutions to help decrease the inequity in health.

The article should include a brief introduction which describes the origin of the problem (500 words) which is followed by a situational analysis highlighting the challenges and barriers contributing to the problem and the possible way forward (1000 words), and should end with a

concluding paragraph of about 300 words. A maximum of 3 authors are permitted for this section. An unstructured abstract of about 200 words with 3-5 keywords, highlighting the region-specific problem, challenges and prospective solutions should be provided.

Child Health Technology

This section highlights innovations, inventions, pioneering research, or technological advancements in child health, that is likely to shape the future of child health. The aim is to apprise the readers about the technological breakthroughs in diagnosis and treatment of various clinical conditions. This section includes a commentary of about 1200 words describing the technological advancement, progress made in India including its availability and accessibility, implications for patients and the roadmap ahead.

Table 1 provides a snapshot of format and requirements for manuscripts submitted to *Indian Pediatrics* in various categories.

PREPARING THE MANUSCRIPT

For reporting research, the authors are expected to comply with the "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (ICMJE Recommendations) prepared by the International Committee of Medical Journal Editors" (ICMJE) (*www.icmje.org*) [1]. Additionally, authors need to adhere to the standard recommended reporting guidelines depending on the study design of the submitted article (*www.equator-network.org*).

Manuscripts not fulfilling the technical requirements shall be returned to the authors without initiating the peer-review process. A summary of technical requirements for preparing the manuscript is provided below:

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- Double-space throughout, in the sequence including title page, abstract, blinded manuscript, key messages, references, figure legends and tables. Start each of these sections (in same order) on a new page, numbered consecutively in the upper right hand corner.
- Use 12-point font size (Times New Roman or Garamond) and leave margins of 1.75 cm (0.7 inch) on all sides. The whole manuscript should be formatted in 'portrait' layout.
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- Use non-proprietary names of drugs, devices and other products. Proprietary names, if given, should not have a superscript © or TM or R; just capitalize the first word. This should be be followed by name of manufacturer in round parenthesis.
- There should not be any discrepancy in names and sequence of authors, and the corresponding author details, as submitted in the title page and as uploaded in the online manuscript management system.
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- All submitted manuscripts should be accompanied by a signed statement by all authors regarding authorship criteria, responsibility, financial disclosure and acknow-ledgement, as per a standard format (Available from: *https://indianpediatrics.net/AnnexureI.pdf*). The signatures should be in the sequence of authorship of the manuscript. The statement with original signatures is to be uploaded as a scanned file. Scanned signatures pasted on the copyright transfer form are not acceptable; authors may sign and upload separate forms if all authors are unable to sign on one form.

Title Page: At the beginning, mention the category (i.e. Research Paper, Research Brief, etc.) for which the article is being submitted. The page should contain (*i*) the title of the article: which should be concise but informative; the type of study may be added in title after a colon; (*ii*) a short running title of not more than 40 characters; (*iii*) first name and surname (both are essential) of each author with the highest academic degree(s) and designation at the time when the work was done; initials will not be accepted for surnames. For example; 'Vidya K': here, 'K' will be considered as the Initial and 'Vidya' will be indexed as Last name; (*iv*) details of the contribution of each author; (*v*) name of department(s) and institution(s) to which the work should be attributed (This should mention the institution of affiliation at the time of conduct of the study, not your current affiliation); (*vi*) disclaimers, if any; (*vii*) name, address and e-mail of the corresponding author, (*viii*) source(s) of support in the form of grants, equipment, drugs or all of these; (*ix*) declaration on competing interests; (*x*) Status of ethical clearance for the study along with name of Ethics Committee clearing the research study, and the date and number of the clearance from the committee; (*xi*) Clinical trial registration number in cases of clinical trials; and (*xii*) word count (not including

Table 1. Requirements of Manuscripts Submitted to Indian Pediatrics

Material	*Abstract*	*Word Count*	*No. of authors*	*No. of references*	*No. of tables*	*No. of figures/ images*
Research paper	Structured, 4-point (Objectives, Methods, Results, Conclusions), 250 words; 3-5 keywords	2500	-	25	4	2
Research Brief	Structured, 4-point (Objectives, Methods, Results, Conclusions) 150 words; 3-5 keywords	1800	-	15	2	1
Research Letter	Unstructured; 50 words; 3-5 keywords	1000	5	10	1	1
Clinical Case Letter	Unstructured; 50 words; 3-5 keywords	800	4	6	1	1
Clinicopathological conference	Unstructured; 100 words; 3-5 keywords	2500-3000	3 (primary dept) + 1 each from associated dept.	15	2	2
Images	-	300	3	0	0	1
Review Article*/ Systematic Review	Structured;4-point (Context, Evidence acquisition, Results, Conclusions); 300 words; 3-5 keywords	3000	5	35	4	2
Drug Review	-	500	2	6	1	-
Position Paper/ Recommendations/ Guidelines	Structured; 4-point (Justification, Process, Objectives, and Recommendations); 250-300 words	4000	- 2	35-50	4	
Perspective/ Special Article	Unstructured; 150 words	2000 1	3	25	1	
Ethisection*	Unstructured; 200 words	2000	5	10	-	-
Update	Unstructured; 50 words	1000	3	10	2	1
Beyond Borders*	Unstructured; 200 words	1800	3	15	-	-
Child Health Technology*	Unstructured; 150 words	1200	3	10	-	-
Correspondence	-	500	2	5	-	-

**Generally solicited by editorial board members. Interested experts may contact the Editor-in-Chief by emailing at jiap@iapindia.org before submitting a manuscript in this section to avoid rejection.*

abstract, tables, figures, acknowledgments, key messages and references). A statement regarding ethical clearance and trial registration (if done) should also be provided in the methods section of the manuscript, without including any identifying details (Ethics committee name, Trial registration number etc.)

Authorship Criteria: All persons designated as authors should qualify for authorship. The journal endorses the ICMJE requirements for authorship, which is based on the following four criteria: *(i)* Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND (*ii*) Drafting the work or revising it critically for important intellectual content; AND (*iii*) Final approval of the version to be published; AND (*iv*) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Conditions (*i*), (*ii*) (*iii*) and (*iv*) must all be met, for all authors, individually.

One of the authors shall act as corresponding author of the paper and he/she should take the responsibility of co-ordinating the work as a whole, from its inception to published article. All authors must give signed consent to publication. Available from: *https://indianpediatrics.net/AnnexureI.pdf*. The name of the designated author who should be approached for access to raw data should also be stated in the contributors' details, along with e-mail (if different from the corresponding author).

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Change in Authorship: The authorship list and author order should be determined before submitting to *Indian Pediatrics*. Any requests to add, remove, or reorder author names must be e-mailed to the Editorial Office from the corresponding author of the accepted manuscript and must be justified with a sound reason. Confirmation e-mails from all authors (individually) that they agree with the modification is mandatory.

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Competing Interests: Competing interest for a manuscript exists when the author has ties to activities that could inappropriately influence his or her judgment, whether or not judgment is in fact affected. Financial relationships with industry, for example, through employment, consultancies, stock ownership, honoraria, grant, expert testimony, either directly or through immediate family, are usually considered to be the most important competing interests. If competing interest exists, the author(s) must disclose them while submitting the manuscript.

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Abstract and Keywords: A structured abstract is to be sent in case of Research Paper (250 words), Review (300 words), Research Brief (150 words) and Guidelines (300 words). Unstructured abstract is required for Perspective (150 words), Clinicopathological Conference (100 words), Update (50 words), Research letters (50 words), Ethisection (200 words), Beyond Borders (200 words) and Child Health Technology (150 words). For brevity, parts of the abstract may be written as phrases rather than complete sentences [2]. No abbreviations should be used in the abstract.

Three to five key words to facilitate indexing should be provided in alphabetical order below the abstract. Terms from the Medical Subject Headings (MESH) list of *National Library of Medicine* should preferably be used. Do not repeat words already included in the title.

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Introduction: The introduction must clearly justify and state the question that the author(s) tried to answer in the study [2]. It may be necessary to briefly review the relevant literature. Cite only those references that are essential to justify the proposed study.

Methods: The methods section should describe, in logical sequence, how the study was designed (e.g. how randomization was done), carried out (e.g. how subjects were chosen or excluded, ethical considerations, accurate details of materials used, exact drug dosage and form of treatment) and data were analyzed (e.g. an estimate of the power of the study, exact test used for statistical analysis) [3]. For standard methods, appropriate references are sufficient, but if standard methods are modified these should be clearly brought out. Authors should provide complete details of any new methods or apparatus used. Commercial names of the drugs/equipment may be used once at first mention, with the initial letter capitalized and manufacturer's name in parentheses. Subsequently the scientific/non-propriety name is to be used throughout. © or TM in superscript after the propriety name is not required.

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Trial registration: We strongly recommend that all authors register their clinical trials involving human subjects in the Clinical Trials Registry of India at *www.ctri.in*, hosted by the Indian Council of Medical Research. Preference will be accorded to registered clinical trials. Registration in following trial registries is also acceptable: *http://www.actr.org.au; http://www. clinicaltrials.gov; http://isrctn.org; http://www.trial register.nl/trialreg/index.asp; and http://www.umin. ac.jp/ctr.* The trial registration status and number should be mentioned on title page in all interventional studies.

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Statistics: Describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to verify the reported results [4]. When possible, quantify findings and present them with appropriate indicators of measurement error or uncertainty (such as confidence intervals). Provide actual *P* values, rather than stating as just < 0.05 or > 0.05. References for statistical methods should be to standard works when possible (with pages stated) rather than to papers in which the methods were originally reported. Specify any general use computer programs used. Define statistical terms, abbreviations, and most symbols. The relevant guidelines may be consulted for appropriate reporting.

Results: This section should include only relevant, representative data and not all information collected during the study. Major findings should be presented clearly and concisely [5]. It may also be useful to mention what the study did not find. Write units along with data at all places in the manuscript. Journal uses the format "mean (SD), median (IQR)" rather than "mean ± SD, median ± IQR" for reporting summary measures. Text, tables, and illustrations should be used judiciously. Avoid repeating in the text the data depicted in the tables or illustrations; emphasize or summarize only important observations. Restrict tables and figures to those needed to explain the argument of the paper. Cite the tables sequentially in the text, and provide each table on a new page after the reference section. Do not insert figures or tables in the main text of the manuscript. Avoid the terms mutation and polymorphism, instead use sequence variant, sequence variation, alteration or allelic variation. Similarly, use SNV (single nucleotide variation) instead of SNP (single nucleotide polymorphism).

Units of measurement: Measurements of length, height, weight, and volume should be reported in metric units, i.e. meter (m), gram (g), or liter (L) or their decimal multiples. *P* value to be expressed upto three decimal places. All other values to be reported up to two decimal places.

Table 2 Details of Reporting Guidelines for Different Study Designs

Study Design	*Guideline/Statement*
Randomized controlled trial	CONsolidated Standards Of Reporting Trials (CONSORT) Statement *https://www.equator-network.org/reporting-guidelines/consort/*
Diagnostic/ Prognostic studies	STAndards for Reporting of Diagnostic accuracy (STARD), *https://www.equator-network.org/reporting-guidelines/stard/*
Observational studies	STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) *https://www.equator-network.org/reporting-guidelines/strobe/*
Systematic reviews/ Meta-analyses of RCT	Preferred Reporting Items for Systematicreviews and Meta-Analyses (PRISMA) *https://www.equator-network.org/reporting-guidelines/prisma/*
Meta-analyses of observational studies	Meta-analysis Of Observational Studiesin Epidemiology (MOOSE), *https://www.equator-network.org/reporting-guidelines/meta-analysis-of-observational-studies-in-epidemiology-a-proposal-for-reporting-meta-analysis-of-observational-studies-in-epidemiology-moose-group/*
Qualitative Studies	Standards or Reporting Qualitative Research (SRQR) *https://www.equator-network.org/reporting-guidelines/srqr/*
Quality Improvement Studies	*Standards for Quality Improvement Reporting Excellence (SQUIRE) https://www.equator-network.org/reporting-guidelines/squire/*

Milliliter or deciliter should be expressed as mL or dL and not ml or dl. Red blood cell, white blood cell and platelet counts are to be expressed as $\times 10^{12}$/L, $\times 10^{9}$/L and $\times 10^{9}$/L, respectively. Temperatures should be given in degrees Celsius. Blood pressures should be given in millimeters of mercury (mmHg). All hematological and clinical chemistry measurements should be reported in terms of the International System of Units (SI).

Abbreviations and symbols: Use only standard abbreviations. Avoid abbreviations in the title and abstract, unless pertinent. The expanded form of the abbreviation should precede its first use in the text, unless it is a standard unit of measurement. Year, month, week, day, hour, minute and second should be abbreviated as y, mo, wk, d, h, min, and s, respectively in tables and figures, but not in text.

Discussion: Ordinarily it should not be more than one-fourth of the total length of the manuscript. Do not attempt a detailed review of literature [6]. This section should include (unheaded paragraphs in the order specified): (*i*) a summary of the major findings, (*ii*) limitations of the study, (*iii*) their relationship to other similar studies, and (*iv*) generalizability of the findings, and implications for practice/policy/research. Conclusions should be linked to the goals of the study. Avoid unqualified statements and conclusions not completely supported by the data. Authors should also refrain from making statements on economic benefits and costs unless their manuscript includes economic data and analyses.

References: Authors need to be accurate in citing and quoting references [7]. References should be numbered consecutively in the order in which they are first mentioned in the text. Identify references in text, tables, and legends by Arabic numerals in square brackets. References cited only in tables or in legends to figures should be numbered in accordance with the sequence established by the first identification in the text of the particular table or figure. Use the style of the examples below. The titles of journals should be abbreviated according to the style used in PubMed. Do not use unpublished observations and personal communications as references. References to papers accepted but not yet published should be designated as "in press"; authors should obtain written permission to cite such papers as well as verification that they have been accepted for publication. Do not cite foreign language references unless a certified English version is also available. The references must be verified by the author against the original documents. The Uniform Requirements style (the Vancouver style) is based largely on an American National Standards Institute (ANSI) standard style adapted by the NLM for its databases. Please take care that citations are not directly copied and pasted from websites; remove the hyperlinks from the same. If the web version of a journal has been consulted instead of the print version, the same should be listed in the list of references. Avoid including any reference to the studies published in predatory journals [8]. Ensure that all hyperlinks have been removed from references. The manuscript may be returned to authors for re-typing, in case this is detected during the final page-setting. There is no need to provide location of the publisher for books and reports in references.

Article in journals: List all authors when six or less. When seven or more, list only first three and add et al.

Kaur K, Khalil S, Singh NP, Dewan P, Gupta P, Shah D. Antibiotic susceptibility, carrier state and predictors of outcome of Staphylococcus aureus infections in hospitalized children. Indian Pediatr. 2023;60:49-53.

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Personal author (book)

Gupta P, Joshi P, Dewan P. Essential Pediatric Nursing, 5th ed. Jaypee Brothers Medical Publishers; 2022.

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Khilnani P, Singhal N. Respiratory failure. *In*: Choudhury P, Bagga A, Chugh K, Ramji S, Gupta P, editors. Principles of Pediatric and Neonatal Emergencies. 3rd ed. Jaypee Brothers; 2011.p.74-83.

Conference paper

Das G, Seth R, Jain V, Jana M, Gupta AK, Meena J. Sarcopenic obesity in childhood acute lymphoblastic leukemia survivors: More here than meets the eye. Pediatric Hematology Oncology Journal. 2022:7:S1-2. *https://doi.org/10.1016/j.phoj.2022.10.234*

Newspaper article

City sees no respite from swine flu, 8 new cases reported. Hindustan Times 2015 Mar 08; New Delhi:p. 8 (col 4).

Dictionary and similar references

Stedman's Medical Dictionary. 26th ed. Baltimore: Williams & Wilkins;1995. Apraxia; p.119-20.

Material published early on website but not yet published in print

Mandlecha TH, Mundada SM, Gire PK, et al. Effect of oral zinc supplementation on serum bilirubin levels in term neonates with hyperbilirubinemia undergoing phototherapy: A double-blind randomized controlled trial. Indian Pediatr. 2023 Sep 11:S097475591600569. Epub ahead of print.

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Equator Network. CONSORT 2010 Statement: Updated Guidelines for Reporting Parallel Group Randomised Trials. Accessed November 26, 2023. Available from: *https://www.equator-network.org/reporting-guidelines/consort/*

Electronic material

Neonatal Resuscitation Program (NRP) Training Aids [on CD-ROM]. National Neonatology Forum, New Delhi, 2006.Hemodynamics III: the ups and downs of hemodynamics [computer program]. Version 2.2. Orlando (FL): Computerized Educational Systems;1993.

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REFERENCES

1. International Committee of Medical Journal Editors. Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (Updated December 2019).use 23 version. Available from: *http://www.icmje.org/icmje-recommendations.pdf.* Accessed December 27, 2019.
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