Child India

November 2021

Monthly e-Newsletter of Indian Academy of Pediatrics

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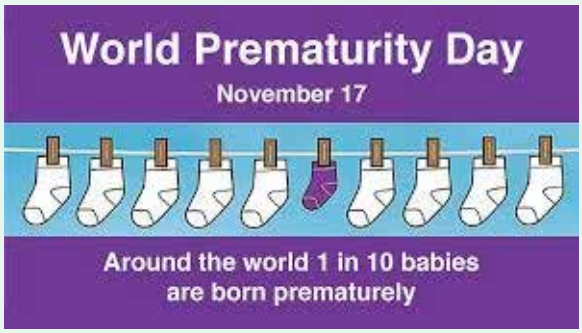
Editor's Note

Dear friends,

The November issue of Child India focuses on preterm babies.

World Prematurity Day on 17 November is one of the most important days in the year to raise awareness of the challenges and burden of preterm birth globally. The day was initiated by the European Foundation for the Care of Newborn Infants (EFCNI) and partnering European parent organisations in 2008. The international co founders LittleBigSouls (Africa), March of Dimes (USA) and National Premmie Foundation (Australia) joined the celebrations and made World Prematurity Day an intercontinental movement. Meanwhile, countless individuals and organisations from more than 100 countries join forces with activities, special events and commit to action to help address preterm birth and improve the situation of preterm babies and their families.



Purple is the official color for World Prematurity Day as it stands for sensitivity and exceptionality and the socksline has become a symbol for World Prematurity Day. The small pair of purple socks – framed by nine full-size baby socks – symbolises: 1 in 10 babies is born preterm worldwide.

The global theme for World Prematurity Day 2021 is: Zero Separation - Act now! Keep parents and babies born too soon together..

The campaign's goal is to raise awareness for the benefits of zero separation

of preterm and sick babies and their parents in the Neonatal Intensive Care Unit (NICU). Since the global spread of the Coronavirus and the introduction of measures against COVID-19, many parents struggled with the very restricted or even prohibited access to the neonatal intensive care units due to the pandemic. Experts after deliberations decided that.the separation of parents and babies had been decided on no current evidence and thus WHO developed this campaign with regards to the provision of newborn and maternal care in times of COVID-19. We need to support the campaign and provide statements and scientific data underlining the positive effect on long-term health outcomes of zero separation in NICUs.

November we also celebrate World Pneumonia Day. This year, World Pneumonia Day, on 12 November 2021, is held during COP 26 – the UN Climate Change Conference. Every Breath Counts is calling on governments with heavy burdens of pneumonia and air pollution to commit to reducing air pollution-related pneumonia deaths by 50 percent by 2030.

Keep contributing to child care.

Jai IAP!

Dr Jeeson C Unni
Editor-in-Chief

President's Address

Dear colleagues,

This month, while we celebrate World Prematurity Day, we must deliberate on ways to improve healthy survival of our preterm babies.

First of all we need to have systems in place, which is thus far lacking, to identify women at risk of preterm labor and support them to give birth in a health facility that can offer extra care when needed, such as support for adequate feeding with breast milk, continuous skin to skin contact, antibiotics, and antenatal corticosteroids.

Secondly, India needs to build upon the infrastructure facilities for improving neonatal survival outcomes at the same time strengthen the tertiary care services at medical colleges, creating secondary care special care neonatal units at district and sub-district health facilities and improving linkages. This is a huge task and needs innovative private-public partnership models, which can facilitate sharing the load taken on by public institutions that have limited capacity to deliver increasing demand for equitable services.

Thirdly, we need to evolve strategies for prevention of preterm birth – prevention of non-medically indicated late preterm birth; use of maternal progesterone supplementation; surgical closure of the cervix with cerclage; judicious use of fertility treatments; dedicated preterm birth prevention clinics, improved treatment of intra-uterine infection, improvements in maternal nutrition, lifestyle modifications to ameliorate maternal stress and widespread use of HPV vaccine – and thus prevent death and disability in large numbers of children.

Let us all pledge to work with our neonatology colleagues and neonatal nurses to optimise preterm care practices

Regards,

Piyush Gupta

National President, IAP 2021

Secretary's Message

Dear All,

Greetings!

"Dreams transform into thoughts and thoughts result in action."
- Dr. APJ Abdul Kalam.

It has been an eventful month at the IAP Child India in November 2021.

We have a very successfully conducted physical IAP Office Bearers Meeting 6th November 2021 and IAP Executive Board Meeting on 7th November 2021 at Hotel Taj Ganges, Varanasi, Uttar Pradesh. My heartfelt thanks to everyone for participating in this meeting. We also had the Periodic Virtual Review Meeting of CIAP staff on 3rd November 2021.

Also in this month, we conducted the Early Childhood Development (ECD) steering committee meeting on 16th November 2021. ECD is one of the precious and flagship programs of Indian Academy of Pediatrics.

We are happy to inform you that we have conducted the following Advance NRP ToT physically in October & November 2021:

1. Bangalore - 23rd & 24th October 21.

2. Guwahati - 30th & 31st October 21.

3. New Delhi - 13th & 14th November 21

Also, a total of 4 physical workshops of Advance NRP Programs has been conducted and 5 workshops are in pipeline in November 2021. About the Basic NRP total of 47 Basic IAP NRP FGM workshops have been Conducted and about 44 workshops are in pipeline in November 2021.

Mission School Uday is also one of the precious and flagship programs of Indian Academy of Pediatrics under the presidential action plan. We have conducted a total of 44 workshops and a total of 5446 pediatricians have been trained. Also, we have conducted 2 Virtual workshops of the CADE Module, 3 Workshops of Cure it Module, 2 IADVL Module, across India in November 2021.

We would like to inform you that, MOU of the National Tuberculosis Elimination Program (NTEP) was signed between the Central TB Division (CTD), Ministry of Health & Family Welfare Government of India and Indian Academy of Pediatrics.

Through this project, IAP essentially will train18,000 Pediatricians, on STCI through district-level CMEs and motivate them to be involved under the program. We have conducted 6 NTEP Programs to date and another 6 programs of NTEP in the pipeline.

Overall, the month of November 2021 has been very fruitful and focused on academic growth for their members and we look forward to having more such activities in the coming month.

Jai IAP!! Jai Hind!!

Sincere Regards,

Dr G V Basavaraja
Hon. Secretary General 2020 & 21

National EB meeting - 7th Nov 2021 - Varanasi

Follow up of the High risk newborn

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Introduction

Advances in perinatal intensive care have resulted in improved survival of extreme preterm and sick neonates. These neonatal intensive care unit (NICU) graduates are at risk of developmental disabilities, incidence of which increase with decreasing birth weight and gestation. A method of early detection and thereby early and appropriate intervention can modify these future disabilities.

Close monitoring of development together with coordination of treatment for any emerging problems is referred to as developmental follow-up.

Classification of Newborns as per Risk

Perinatal risk factors and course of neonatal illness define a group of neonates at increased risk of neurodevelopmental disability, classified as high, moderate, and mild risk. The type of follow-up provided is then based on severity. Risk factors are likely to be additive, with increased risk of adverse outcomes as number of risk factors increase.

Babies with moderate and high risk need to be followed up in a high risk clinic.

Clinical Outcomes of High risk Newborns

High risk Newborns may have Developmental Delay manifesting as delayed milestones, speech delay or academic underachievement; Motor deficits manifesting as delayed milestones, tone abnormality, cerebral palsy, or speech clarity issues; Sensorineural- vision and hearing abnormalities; Learning difficulties; Behaviour issues like ADHD, Autism and others.

Schedule for follow up: In India: Low Risk children are screened at 9m (months), 18m, 24m and 36 m visits with autism screen at 18m and 24 m. High Risk: 3.5-6m, 9m, 12m & 18m visits, every 6 m till 3 years and annually till 2 years after school entry. Autism screen is done at 18 m and 24 m. The high risk team consists of a multidisciplinary team.

Age used for follow up is calculated as corrected age. Corrected age is the sum of chrono-logic age in weeks minus the difference between gestational age at birth and 40 weeks of gestation. The correction is considered till 2 years of age.

Developmental Follow up

I) History: Evaluate for risk factors: Identify risk factors on history.

Assess the feeding, growth, sleep patterns, medical, social, economic and psychological background of the child and family. Elicit and attend to parents' concern regarding the child's development. Red Flags: A red flag means the child is not doing what 90% children can perform for the given age. These red flags are a quick guide for a busy pediatrician to simplify the task of early detection and referral but are not screening or diagnostic tools per se.

Table 1: Red flags: Motor and Fine motor (age in months)

Gross Motor:	Age	**Fine motor**	Age
No head control	4 ½ m	Persistent fisting	3 ½ m
No roll over	6 m	No holding rattle	4-5 m
No Sit without support	9 m	No transfer	5-6 m
No Walk	15 m	No pincer grasp	10-11 m
		Handedness	<18 m

Table 2 Red flags: Language and Social (age in months)

Receptive	Age	**Expressive**	Age	**Social**	Age
No turn sound	6 m	No vocalization	4 m	No social smile	3 m
No response name	9 m	No babble	12m	Hard to console	12 m
No simple commands follow	12 m	No gesture need	12 m		
Not locate or point 5objects	15 m	No bye or three words with meaning	15 m		

II) Cognitive follow up

A) Developmental screening Its purpose is to identify children who are in need of further evaluation. Screening tools can be parent report questionnaires or a directly administered tool. The Age Stage Questionnaire 3(ASQ- 3) is a parent report questionnaire validated against the Developmental Scale for Assessment of Indian Infants (DASII) and has the potential to be used in India after being translated into local languages if interviewer administration replaces parent-completion when required. Trivandrum Developmental Screening Chart (TDSC): It is a screening tool based on Bayley scale of Infant development- Baroda norms. It has two charts 0-3 years and 3-6 years. Items on the age line are administered. If the child fails item to the left of the line the child is referred for a more detailed evaluation. If a child fails a screening tool, he or she is referred for a detailed developmental assessment.

B) Developmental assessment: A developmental evaluation is an in-depth assessment used to create a profile of the child's strengths and weaknesses in all developmental areas. It is done if a child fails a developmental screen. Its results are used to plan intervention. They include 1. DASII- It is the Indian adaptation of the Bayley's scale for use in children between 0-2 ½ years. 2. Bayley Scale of Infant development (BSID) which can be used from 0- 3 ½ years. DQ <70 is delay.3. IQ tests: Wechsler Intelligence scale, Stanford Binet test are used above 2 ½ years and give a performance IQ and a verbal IQ.

III) Motor follow up: A motor evaluation needs to supplement a developmental screening tool because screening tools do not per se identify tone abnormalities.

1. In high risk babies discharged from the NICU, the General Movement (GM) assessment can be used to evaluate developing nervous system by observing spontaneous movement patterns of babies to predict a tone abnormality later diagnosed as cerebral palsy till 5 months of age. 2. In high risk developmental screening, the Amiel Tison can be used to detect tone abnormalities till one year of age. The Hammersmith Infant Neurological Examination

(HINE) can also be used between 2 to 24 months to identify children with early signs of CP.

III) Growth and Nutrition Follow up: Corrected age is used while monitoring growth.

IV) Neurosensory A) Vision screening for Retinopathy of Prematurity: This needs to be done for a baby with any one of the following: Birth weight ≤ 2000 grams or born at ≤ 34 weeks GA. Later annual examinations to look for strabismus, nystagmus, light reflex, tracking ability, and roving eye movements are recommended. B) Hearing Screening: First hearing screen needs to be done with OAE (Otoacoustic emissions) before discharge from hospital. If OAE is 'fail', it is repeated at 4 weeks /first immunization visit at 6 weeks. If it is 'fail' again, then ABR (Auditory Brainstem response) is done. A two-stage screen is 99% specific. All NICU babies need to undergo ABR as well as OAE because there is a high incidence of auditory neuropathy and auditory dyssynchrony in NICU babies.

V Behavioural issues follow up: With the high incidence of behavioural problems in the high risk newborn, follow up must probe for attention issues in social settings and its effect on learning. Administering a simple screen like the M-CHAT-R Follow -Up at 18 months and 24 months is recommended to screen for Autism.

Ideally follow up should continue till late adolescence as many cognitive, learning and behavioural problems more common in at risk newborn may only become apparent on longer follow up.

The ultimate aim of follow-up is to ensure early appropriate intervention before three years, keeping parents in the loop, to achieve better functional outcome for at risk neonates.

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Mother Own Milk (MOM): The Magic Bullet for Neonatal Intensive Care Unit (NICU) team?

Praveen Kumar
Dattatray Kulkarni
Srinivas Murki

Key points

- Mother own milk feeding is a cost-effective, life-saving intervention for premature infants
- Each neonatal centre should identify the enablers and barriers for MOM usage and identify effective, feasible and cost-effective interventions appropriate to own settings.
- Neonatal units should have structured policy of different maternal care practices where mother is an integral part for improving mother milk output and ensure full mother milk feeding until hospital discharge

Uniqueness of MOM composition

Increasing the MOM usage is the an evidence based intervention which requires mother's active participation in infant care. Mother own milk is gestation dependent, species specific and dynamic in relation to volume or composition1. We are still learning and discovering the different components and the uniqueness of mother milk on an everyday basis2,3. It is a complete nutritional package as it provides essential micronutrient (vitamins and minerals), developmental factors (growth factors ,cytokines and long chain polyunsaturated fatty acids) along with macronutrients (carbohydrates, protein and fats). It establishes the gut microbiome and modulates the developing immune system 4. Mother milk composition changes not only during different phases of lactation but even during a feeding and in different women. Preterm mother milk contain more proteins than term milk in the initial weeks after the birth with protein content decreasing each week to equalize to the mature milk5. The protein quality of the mother milk is different from bovine milk it is a whey predominant milk. The whey protein fraction is more easily digested and facilitate rapid gastric emptying. It contains lower concentrations of phenylalanine, tyrosine, and methionine and higher concentrations of taurine than the casein fraction and serves as a model for enteral and parenteral amino acid mixtures. The human milk oligosaccharides (HMO) in the mother milk ensure a softer stool consistency, non-pathogenic focal flora, and improved mineral absorption. HMO is bioactive carbohydrate polymers (also including glycoproteins) whose structure mimics specific bacterial antigen receptors and prevent bacterial attachment to the host mucosa. Some examples of human milk oligosaccharides (HMOs) include fucosylated glycans that specifically inhibit binding by Haemophilus influenza, Campylobacter jejuni, and some viral agents7. Mother milk lipid is an organised fat globule with bile salt stimulated lipases and is palmitate predominant. The fatty acids most abundant in mother milk are very long chain polyunsaturated fatty acids, arachidonic acid and docosa hexanoic acid compared t8. Fat content changes with maternal diet and even during a feed as hind milk has 3 times more fat than foremilk9. Mother milk is deficient in vitamin K but helps in establishing particular gut microbiome that produces less vitamin K 10.

Vitamin D content of mother milk is dependent on maternal stores and so either giving it on daily basis to mother or infant ensures adequacy of vitamin D11. Mother milk has less iron and hence supplementation since birth specially in preterm infants is adviced12. Though calcium and phosphorous concentration is less in mother milk, its better bioavailability ensures adequate bone mineral content in comparison to formula feed13. Mother milk is a rich source of carnitine which is needed for fatty acid oxidation. Mother milk contains plenty of bioactive factors which are missing in donor human milk 5, 14 (Table 1).

Table 1 : Bioactive factors of Mother's Milk

Type of factor	Effect of factor
A) Immunoglobulin	
Secretary IgA	Specific antigen directed anti-infective
IgG	antimicrobial
IgM	Complement activation
Lactoferrin	Immunomodulation, anti-infective, iron chelation, antiadhesive and intestinal growth
Lactadherin	Anti-inflammatory and Anti-viral
Lysozyme	Bactericidal, Immunomodulation
Gangliosides and glycoaminoglycans	Anti-infective
Cytokines	Proinflammatory, Anti-inflammatory, Epithelial barrier and Neutrophil recruitment
Macrophages	Anti-infective and T cell activation
Stem cells	Regeneration and repair
B) Enzymes	
Glutathione Peroxidase	Prevents lipid oxidation
Nucleotides	Enhance antibody response, gut flora formation
Glutamine	Intestinal cell fuel and immune response
Vitamin A,E and C	Antioxidant
Lipids	Anti-infective
PAF acetylhydrolase	Inhibit action of PAF
Mucin 1 and 4	Anti-infective
C) Hormones	
Adiponectin	Decrease BMI and Anti-inflammatory
Leptin	Regulate BMI and Appetite
Somatostatin	Regulate growth of gastric epithelium
Calcitonin	Development of enteric neurons
D) Growth factors	
VEGF	Angiogenesis and tissue repair
Insulin like growth factors	Luminal surveillance
Epidermal growth factors	Intestinal repair
Transforming growth factors	Epithelial cell growth, suppress lymphocyte growth
Erythropoietin	Erythropoisis and intestinal development

PAF: platelet activating factor, BMI: body mass index, VEGF; vascular endothelial growth factor

Benefits from mother milk : An evidence review

"Human milk" refers to a combination of mother's own milk and pasteurized human donor milk (DHM). Exclusive mother milk for all newborns, and in particular preterm infants, is recommended by the numerous professional organizations, including the American Academy of Pediatrics and World Health Organization.[15, 16]

In the following paragraphs, we shall discuss the studies reflecting the Mother milk benefits for morbidities in very low birth weight infants.

Neonatal Infections

Systematic review in 2004 in the Archive of childhood diseases, de Silva focused on three RCTs and six observational studies regarding relationship between nutrition, infection and mother milk in preterm VLBW infants and found that mother's milk has positive effect on onset of infections when compared to formula milk[17].

Late onset sepsis (LONS) : Ronnested et al in their large prospective study in ELBW infants observed significantly reduced risk of LONS by early enteral feeding with mother milk18. Schanler et al in a randomized trial of donor human milk versus preterm formula, a substitute for mothers' own milk, in the feeding of extremely premature infants had shown reduced risk of LONS19. Patel et al in their study on the impact of early human milk on sepsis and health-care costs in very low birth weight infants demonstrated reduced risk of LONS and improved the cost effectiveness.20. Furman Let al studied the effect of maternal milk on neonatal morbidity in very low birth weight infants and they found reduced risk of LONS in mother milk fed infants21

Necrotizing Enterocolitis (NEC): Two different meta analysis conducted by Boyd et al22 and Quigley23 et all suggest reduced incidence of NEC in infants fed with mother milk. Early mother milk feeding is associated with a lower risk of necrotizing enter colitis in very low birth weight infants. Schanler et al in his randomized controlled trial found reduced risk of NEC in the extremely premature infants who were given mother milk in comparsion with formula milk.19 ,27. The currently available evidence suggests that feeding preterm infants with artificial formula (rather than donor human milk when mothers own breast milk is not available) is associated with faster rates of growth, but with a near-doubling of the risk of developing necrotizing enterocolitis28.

Long Term Neurodevelopment

Smith et al observed better cognitive outcome at age of 6 to 8 years in VLBW infants who were breastfeed. Similarly Vohr and colleague's demonstrated beneficial effect of mother milk in ELBW infants at age 18 month29. O' conners et al showed best neurodevelopemental and motor outcomes in VLBW infants fed with fortified mother milk30. In contrast to this finding Lucas in his trial found no difference in neurological development31. However both studies suggest that mother milk may have independent effect on neurodevelopment of preterm infant, not only from the nutrient intakes.

Feed intolerance

Boyde et al in a meta analysis from RCTs indicated that feeding with formula milk, compared with donor human milk leads to higher rate of feed intolerance in preterm infants22. .Klingenberg et al in recent international survey observed that infants without access to donor milk frequently have delayed introduction enteral feeds until mother own milk is available. These data support beneficial effect of donor human milk in feeding tolerance.[32]

Metabolic Syndrome

Some long term studies suggest lower rates of metabolic syndrome and lower blood pressure, lower insulin resistance and low density lipoprotein in later life in mother milk fed preterm infants32. In the preterm infants, the type of feeding exposure in the early postnatal period may influence glucose, lipid and apolipoprotein metabolism, and affect markers of metabolic syndrome[34].

Psychological and Relational Aspect

Mothers of premature infants frequently have sense of guilt and defeat for not able to carry pregnancy to term. For the the relief of mothers, free access to wards, touching and feeding of infants by the mothers is essential. Breastfeeding and provision of expressed breast milk creates great emotional involvement and sense of gratification. In this case breastfeeding can be considered a part of NIDCAP or a mother centric care.35

Key concepts in Lactation and Clinical Implication of Lactation Sufficiency

New research suggested that lactiferous sinuses are nonexistent and most glandular

Table 2 : Relevant Summary of Lactation Stages

Stage	I	II	III
Definition	Secretary initiation	Secretary activation	Galactopoisis
Time	Mid pregnancy	48 to 72 hours	9 days after postpartum approximately
Control	Endocrine	Endocrine	Autocrine (local)
Key features of control	Progesterone –high Prolactin	Progesterone-decline abruptly Prolactin & cortisol –increase Insulin & thyroxin-supporting role	FIL : feedback inhibitor of lactation High FIL –less milk Low FIL-more milk Oxytocin-milk letting down
End result	Glandular secretion	Transitonal Milk is coming in (mother feels milk coming in)	Volume coming in of mature milk (proportional to expression or emptying by mother)
Associated clinical condition	Mostly unaffected	Cesarean section, preterm birth, hypothyroidism & glucose metabolism related conditions like high BMI,diabetes mellitus; higher infant birth weight	Mother-infant separation Less number of expressions Anatomical factors

tissue is near to the nipple along with lactiferous duct branching which are variable38. So these anatomical things have implication for expression by manual methods. Understanding lactation staging (table 2) and risk factors for lactation failure (Table 3) is utmost important for lactation management.

Various Barriers to Mothers Own Milk

Mothers of preterm infants face multiple problems in breastfeeding; there is a reduction milk supply as result of inadequate mammary gland development38. Lacto genesis II (milk let down) is delayed following cesarean section and with complicated pregnancies like preeclampsia which are particularly common among VLBW mothers39 . Mother-infant dyad separation often begins immediately after birth leading to less frequent skin to skin contact and reduced milk production in preterm birth. Because of the immaturity, preterm infants are unable to suck directly at breast. Preterm mothers rely on breast pumping or hand expression of milk. All these factors result in reduction in own mother's milk in preterm mother-infant dyads. Prospective observational studies indicate that both maternal and fetal stress during labor; during the delivery (e.g. urgent caesarean section or long duration of Labor in vaginal delivery) are associated with delayed onset of lactation 42. Sisk et al 43and Hurst et al44 observed that lack of motivation support hinders ability to frequently pump breast milk .Insufficient availability of lactation expert in NICU and inadequate supply of hospital grade pumps can also lead to less human milk consumption in preterm infants. The early initiation of frequent and complete milk expression has been found to be a key factor for adequate milk supply by the mothers. For effective counseling and timely maternal support during entire lactation period, understanding of nursing and medical staff about their lactation knowledge and the various factors affecting usage of MOM milk in preterm infants are listed below 45

Table 3
Factors affecting Mother's Own Milk usage in Neonatal Intensive Care Unit

1	Inadequate expression facility like electronic breast pumps, feeding room in hospital
2	Mother involvement in infant care practices like kangaroo mother care, nutritive sucking and oro-motor stimulation by mother
3	Maternal feelings of vulnerability and lack of confidence
4	Infants' immature feeding behaviors
5	Lack of commitment or desire to breastfeeding prior to the birth
6	Personal choice
7	Bottle feeding
8	Ability of father or other family members to participate in feedings
9	Avoidance of embarrassment of feeding in public
10	Ease of pumping and storing breast milk
11	Maternal lack of confidence
12	Parental need to quantify intake
13	Lack of informational and emotional support

Evidence based Enablers for mother's Own Milk usage

Nyqvist et al47 and Meier et al48 summarized evidence based practices to support mother milk use.

A) Education for staff and family : Education regarding importance of mother milk, assisting mothers in hand expression, pumping and assessment of latch have shown to improve milk production

B) Early initiation: Early hand expression on breast and pumping of milk increases its production .Parker et al in their study noticed greater milk volume in mothers who initiated expression in < 1 hour after birth compared to those between 1 to 6 hours

C) Continuations : Frequent pumping and or hand expression leads to greater milk volume over time . Many hospital advise mothers to pump at least 8 times per day

D) Acuna-Muga et al noticed that mothers produced greater milk volume when pumping after performing skin to skin contact (SSC). Peer counselors program, assistance with breast pump, acquisition, transportation and support group can improve MOM production with time 49

E) Nipple shields have shown to improve milk transfer for preterm infant while breast feeding

F) Donor human milk (DHM) availability in the form of milk banking increases use of MOM in preference to formula milk

Research suggested that sharing the information on the mother milk will influence the mother's decision for choosing the best milk for their infant and educating the mother on the need for milk expression resulted in better initiation of lactation54,55.

Quite a good number of quality collaborative and improvements projects suggest that primary change drivers that worked in their units are lactation protocols, lactation nurse, pump availability and comprehensive nutritional programme for mother milk feeding56, 57.

Met analysis by the mekonnen et al in 2019 consisting of 8 RCT with 5 being from India involving the preterm and low birth weight neonates show that kangaroo mother care intervention group had initiated mother milk feeding 2.6 days earlier compared to conventional care group58. Cochrane database systemic review consisting of the 46 trials with 3850 mother-infant healthy dyad suggested skin to skin care for early breastfeeding59.

The infant care practices focusing on infants' oral motor skills are non-nutritive sucking and oro-motor stimulation require mother participation. There is very limited evidence on these interventions needed for maintaining sucking skills needed for breastfeeding in preterm infants. Meta-analysis consisting of 12 trials with

746 preterm infant show the significant effect on quicker transition from gavages feeding to full oral breastfeeding at the breast with no effect on rates of breastfeeding or full mother milk at the time of discharge but the trials included in the meta-analysis were small sized and methodologically weaker emphasizing that future studies to demonstrate the effect of non nutritive sucking on the mother milk feeding60. Chocrane review of the 19 randomized trial with 823 mother infant dyads had shown the effect of oro-motor stimulation on transition of gavages feeding to full oral feeding with no effect on the mother milk feeding but trials were of significant bias with poor methodology61. Oro-motor stimulation in neonates is not a standard routine preterm care practice. Presently it is a growing area of interest for neonatal teams to develop a protocol for improving oral skills in preterm infants. Most of the neonatal units of India practices non-nutritive sucking to enhance oral motor function but they lack regular practice of oromotor stimulation62.

Mother-infant proximity during the early postpartum period impact the mother-infant dyad interaction which is essential in regulation of mother milk production and milk supply. Mother infant dyad staying together likely results in predominantly mother milk feeding63-65. The Ministry of Health and Family Welfare (MOHFW), Government of India, through its National Health Mission (NHM), had included the family participatory care for small and sick neonate66. Including the family-centered supportive care as the standard model like in many high-income countries, India had became the first among low- and middle-income countries to have introduced a national policy to integrate family-centered care in neonatal units67.

Best healthcare practices of lactation for preterm mothers in neonatal unit

- Education of the nurses, mothers, resident doctors, lactations consultants, lactation nurse, obstetricians and neonatologist in neonatal unit
- Expression of milk: initiation and maintenance of lactation
- Mother –infant bonding promotion

Education about mother milk

For education of mothers, counseling and educating them on the importance of MOM and the expression of milk. The maternal awareness and participation helps in improving early initiation of lactation. Continued verbal education, daily counseling at admission and during daily clinical round; education leaflet for the mothers are steps to be taken by neonatal team. Graphical charts mentioning the mother milk usages in the NICU leads to improved feedback from neonatal team and mothers. For sustaining effect in neonatal hospitals, workshops on benefits of Breast milk and techniques of milk expression (manual and use of electronic pumps), quiz programs on mother milk for resident doctors, all NICU nurses, lactation nurses and consultants in the hospital, counseling of mothers and family to involve in milk expression and baby care practices daily and at admission, discussion of MOM feedings on daily clinical rounds should be done.

Lactation initiation and sustenance

For ensuring milk expression by the mother, NICU team should have a dedicated lactation nurse for NICU and she should target each mother for milk expression on day 1, more number of milk expressions till first week. All the mothers should have access to electronic pumps from hospital facility to augment the milk expressions. The document or pictorial information to the mother regarding the expression techniques should be given to mother on the birth of the baby.

Mother and Infant bonding

Under this neonatal unit should target for increasing the duration of skin to skin contact, increase maternal visits to the NICU and time

spent by mother at the baby bedside, involvement of mother in baby care activities, early and increased time of non-nutritive sucking on empty breast (after milk expression) and initiation of breastfeeding with nipple shield after attainment of gestation of 32 week or earlier. Neonatal unit should have standard operating procedures of non nutritive sucking, oro-motor stimulation, early initiation of breastfeeding and skin to skin contact.

Future directions

- Each neonatal unit should measure mother milk usage. Amount of mother own milk feeding received during critical periods of neonatal stay (day 1-14 and 1-28 post birth) as well as throughout the hospital stay , and at discharge are true measurements of MOM intake and best quality indicators of neonatal care .
- Establishment and management of Lactation Management Centers in public health facilities for safe human milk for the admitted new-born, especially those who are sick, preterm, low birth weight.
- Use of Human milk analyzer for measuring the energy, fat, carbohydrate and protein content in mother milk guiding clinicians to do fortification for the actual macronutrient content of the milk.

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Neuro Protective Strategies in Preterm

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More and more preterm infants are surviving in tertiary care centres in India. These infants must complete neurogenesis and cortical organization outside their protected intrauterine environment. Advances in neonatal critical care have resulted in dramatic decrease in mortality shifting focus from survival to quality of survival to these at risk infants which in turn is linked to their neurological integrity. Preterm brain injury remains a great challenge in neonatal medicine and these children now constitute the majority of children with cerebral palsy. Of the approximately, 90% of VLBW infants who survive, major motor deficits (e.g., cerebral palsy) occurs in 5-10% of them, while 25-50% of infants suffer from cognitive, behavioural, attentional, and socialization defects. Notably, therefore, cognitive deficits without major motor deficits are now the dominant neurodevelopmental sequelae in the survivors of early preterm birth.1

Preterm brain injury:

The predominant form of brain injury in premature infants consists of:

1. **Germinal matrix-intraventricular haemorrhage (GM-IVH):** Especially with periventricular hemorrhagic infarction (PVHI) and posthemorrhagic hydrocephalus (PHH).
2. **Periventricular leukomalacia (PVL):** PVL literally meaning softening of white matter refers to injury to cerebral white matter, generally more severe in deep than superficial white matter. It consists of two major components, focal necrosis deep in the white matter with loss of all cellular elements, and a more diffuse component in central cerebral white matter, with injury to premyelinating oligodendrocytes (pre-OLs) and a marked astrocytosis and microgliosis. The focal necrotic lesions may be macroscopic in size and evolve to cysts, readily visualized on cranial ultrasound or MRI scans. This severe lesion occurs in less than 5% of VLBW infants in modern neonatal intensive care units. Much more commonly, the focal necrotic lesions are microscopic in size and evolve to small glial scars, not easily seen on neuroimaging and accompanying neuronal/axonal abnormalities. In Indian study, incident of PVL of all forms as detected by ultrasound was 32.5 % in VLBW babies of tertiary care centre, out of which 93.5 % were of persistent flare and only 6.5 % were localized cystic PVL.2 The spectrum of neuropathology of brain injuries in extremely preterm infants has changed over time, from acute periventricular lesions to subclinical injury of both grey and white matter and particularly diffuse white matter injury (DWMI). Because the neuronal/axonal abnormalities principally accompany PVL, which was previously under – recognized, a new term "encephalopathy of prematurity" has been coined by Volpe.1 Neuroimaging studies indicate that PVL in its various forms is by far the most common, occurring in 50% or more of VLBW.3 In addition, as focal brain lesions become less common, diffuse injury to

both grey and white matter is now the primary focus for improving neurologic outcomes in survivors.

Neuroprotective Strategies- Prenatal

- **Prevention of preterm birth:** Prevention of preterm birth is most effective method of reducing the incidence of IVH and PVL. It comprises of identification of women at risk of premature delivery, use of tocolytics, treatment of maternal infections and patient education.
- **In Utero Transport:** Premature deliveries should be conducted at tertiary care centre. In utero transport of selected high-risk pregnancies is preferred despite the ability to provide safe, effective transport of ill neonates over long distances as the incidence of grades III/IV IVH has been found to be higher in transported infants compared with maternal transports and inborn babies.[4]
- **Optimal management of labor and delivery:** Prolonged labor and breech delivery could lead to impairment of cerebral autoregulation increasing the risk of IVH. Cesarean section has been found to reduce the frequency of IVH in one study5, but not in all and more data is needed to define the specific circumstances warranting abdominal delivery. Mode of delivery has also not found to be of importance in occurrence of PVL.
- **Pharmacological interventions:**
- **Antenatal steroids:** It is single most effective antenatal pharmacological intervention for prevention of IVH and PVL. A complete course results in 40% reduction in severe IVH in VLBW infants, while an incomplete course is partially protective.6 The data regarding safety of repeat course of antenatal steroids is lacking.
- **Magnesium sulphate:** Fetal and newborn brain is more susceptible to damage from glutamate release. Magnesium sulphate can prevent post hypoxic brain injury by blocking glutamate receptors and reducing the excess release of glutamate in the calcium channel, consequently, reduce the risk of brain injury in the perinatal period. A meta analysis of five RCT's on antenatal magnesium sulphate therapy has found that when given to women at risk of preterm birth it substantially reduced the risk of cerebral palsy (RR 0.68; 95% CI 0.54 to 0.87; five trials; 6145 infants). There was also a significant reduction in the rate of substantial gross motor dysfunction (RR 0.61; 95% CI 0.44 to 0.85; four trials; 5980 infants).7 American College of Obstetricians and Gynecologists (ACOG 2010), Society of Obstetricians and Gynaecologists of Canada (SOGC 2011) and Australian National Clinical Practice Guidelines (2010) recommend the use of magnesium sulphate for fetal neuroprotection.[8]
- **Phenobarbitone:** Prophylactic maternal phenobarbital neither prevent intaventricular hemorrhage in preterm nor protect them from neurological disability in childhood and in fact may lead to increased maternal sedation, hence should not be used.9
- **Vit K:** Not useful for prevention of IVH.10

Neuroprotective Strategies - Postnatal

- **Cord Clamping:** Delaying cord clamping more than 30 seconds provides additional placental blood to the preterm baby. Recent meta analysis proves that delaying cord clamping by 30-120 seconds is associated with lesser need for transfusion, better circulatory stability, less intraventricular haemorrhage (all grades) and lower risk for necrotising enterocolitis11. A recent study also documented that DCC was associated with a reduction in the composite outcome of severe neurological injury (IVH grade >3 with or without persistent periventricular echogenicity) or mortality in extreme preterm neonates12 . However, long term outcome of this benefit is unclear.

- **Neonatal Resuscitation:** The aim is to establish adequate ventilation promptly, avoid hypoxemia as well as hyperoxemia, two alterations that result in pressure passive circulation.
- **Avoid fluctuation of Cerebral Blood Flow:** Care must be taken to avoid rapid and sharp fluctuations in blood pressure and cerebral blood flow like avoiding rapid fluid boluses and hyperosmolar solutions like sodium bicarbonate, gentle handling and minimal tracheal suctioning.2
- **Neonatal Care Practices:** NICU characteristics, independent of patient level risk factors, accounted for 31% of the variation in the incidence of IVH. NICUs with high patient volume and high neonatologist/staff ratio had lower rates of severe IVH13. Minimal handling and stimulation protocols and Newborn Individualized Developmental Care and Assessment Program (NIDCAP) is a humane way of caring for preterm babies and has been found to reduce NICU stay and improves neurodevelopmental outcome14 in many studies although a recent meta analysis did not find any evidence that NIDCAP improves long-term neurodevelopmental or short-term medical outcomes.15 Skin to skin contact has also been found to accelerate brain maturation in healthy preterm infants.16 There is mounting evidence that repeated stress especially during early period of development has long lasting effect on central nervous system. Exposure to stressors in NICU has been found to be associated with the regional alteration in brain structure and functions that may potentially adversely affect neurodevelopment.17 Nesting, Kangaroo mother care, soft music therapy, gentle oil massage, swaddling, and cuddling the baby helps in decreasing the stress to the baby.
- **Ventilation and Surfactant Protocol:** Early use of nasal CPAP (ENCPAP) can help in avoiding intubation and mechanical ventilation. Infants treated successfully with early NCPAP has been found to be at lesser risk of developing severe IVH.18 Mechanical ventilation plays a role in predicting severe IVH. Both the time at which ventilation was initiated and the duration of ventilation are important determinants of severe IVH. The risk for severe IVH in infants who were never intubated in delivery room or during the first 3 days of life is miniscule.19 Also, there is no clear evidence that elective HFOV offers important advantages over conventional ventilation when used as the initial ventilation strategy to treat preterm infants with acute pulmonary dysfunction.20,21 Early surfactant has been found to reduce the incidence of IVH.22 A new mode of surfactant administration without intubation - less invasive surfactant administration (LISA) has been found to have significantly higher survival rates and significantly less intraventricular hemorrhage (IVH), severe IVH and cystic periventricular leukomalacia.23
- **Hypocarbia:** Episodes of hypocarbia have been implicated as a risk factor for PVL, possibly mediated through reduction in cerebral blood flow. Series of studies have found association between hypocarbia and periventricular leukomalacia with $PaCO_2$ values ranging from 15- 35 mm of Hg.24 Shankaran et al calculated the cumulative exposure to $PaCO_2$ <35 mm of Hg during first 7 days of life and its impact on PVL. They demonstrated that cumulative exposure to hypocarbia was independently related to risk of periventricular leukomalacia in low birth weight infants.25 In light of available evidence and the lack of any advantage being suggested for hypocarbia, it is recommend strongly to avoid hypocarbia (especially $PaCO_2$ < 25 mm Hg) which arises as a result of inadequate monitoring of the effects of mechanical ventilation.

- **Permissive hypercapnia:** Hypercapnia may influence the development of IVH by causing vasodilation of cerebral resistance arterioles, increasing CBF, and by impairing intact cerebral autoregulation. It has been found that maximum PaCO2 during the first 72 h of life is a dose-dependent predictor for severe IVH in VLBW infants.26 Further, hypercapnia may abolish or impair cerebral autoregulation, causing the cerebral vasculature to be at risk for ischemia or hyperperfusion during fluctuations of blood pressure. Meta analysis also could not demonstrate any significant overall benefit of a permissive hypercapnia/ minimal ventilation strategy which targeted hypercapnia compared to a routine ventilation strategy aiming for normocapnia.27 Hence, ventilator strategies which target higher levels of PaCO2 of > 55 mmHg are not recommended.
- **Aggressive Nutrition:** Most critical developmental period of brain growth and function occurs during the third trimester of pregnancy and the first 2 years of postnatal life and the provision of adequate nutrition during this period is important. There is accumulating evidence that malnutrition during this period of vulnerability alters the growth of the developing brain and may have permanent negative developmental consequences. Several studies have demonstrated the safety of the early provision of higher levels of protein and energy intake without adverse clinical sequelae. Recently, "early aggressive" parenteral and enteral nutrition has been advocated to prevent nutritional deficits.28-31 Provision of energy and protein intakes in first week of life independently contribute to the neurodevelopmental outcome in the ELBW infants. Increased first-week protein and energy intakes are associated with higher Mental Development Index scores and lower likelihood of length growth restrictions at 18 months in extremely low birth weight infants. An increase in first-week energy intake of 42 kJ (10 kcal)/kg per day was independently associated with an 5-point increase in MDI, and an increase in first-week protein intake of 1 g/kg per day was independently associated with an 8-point increase in MDI.32 A clear association between early enteral intake and neurodevelopmental outcome has also been demonstrated in larger preterm infants. Better neurodevelopment outcome has been found when preterm infants are fed with higher protein and calorie in hospital and in post discharge period.33,34
- **Pharmacological Intervention:**

  Caffeine: Caffeine therapy for apnea of prematurity (CAP trial) has been found to improves the rate of survival without neurodevelopmental disability at 18 to 21 months and reduced the incidence of cerebral palsy and cognitive delay in VLBW babies.35 Long term neurodevelopment outcome data at age 11 years has found improved visuomotor, visuoperceptual, and visuospatial abilities without any adverse effect on general intelligence, attention, and behavior confirming long-term safety of caffeine in very low birth weight neonates36

- **Doxapram:** The use of doxapram has been associated with alarming rise in blood pressure and even at low doses, hence should not be used during the first few days of life.37
- **Indomethacin:** Cochrane meta analysis of 19 eligible trials has concluded that prophylactic indomethacin reduced the incidence of sever intraventricular hemorrhage. However, there is no evidence of effect on mortality or neurodevelopment.38 It is interesting to speculate on why indomethacin noticeably reduces lesions of the periventricular white matter (haemorrhagic or ischaemic), yet this is not associated with improved outcome later on. Indomethacin may possibly induce cerebral ischaemia as a result of its prostaglandin inhibition, and the obvious beneficial effects may be negated by adverse effects elsewhere.

- **Early rhEPO:** rhEPO originally, used for anemia of prematurity, also found to have neuroprotective effects like, anti-apoptosis, anti-inflammation, anti-neurotoxicity, promotion of neural regeneration, protection of white matter from injury and protection of brain from edema. In a total of 18 trials, EPO was used as neuroprotective agent in preterm babies in different dosage schedule, and has been found it to be a safe. A recent trial has shown that high-dose Epo treatment is positively correlated with both cognitive and motor scores, modest improvement of neurodevelopment outcome.39 Increase in cumulative erythropoietin exposure is also associated with improved mental development index.40 Thus, EPO has the potential of acting as neuroprotective agent in preterms however, optimum dose and route of administration still needs to be defined, before it can be recommended for use.
- **Phenobarbitone:** Postnatal administration of phenobarbital cannot be recommended as prophylaxis to prevent IVH in preterm infants and is associated with increased risk of mechanical ventilation.41
- **Vitamin E:** Evidence does not support the routine use of vitamin E supplementation in preterm infants as its use though has been associated with reduced the risk of intracranial hemorrhage but there is increase risk of sepsis.42
- **Ethamsylate:** Ethamsylate reduce bleeding time and blood loss from wounds, and increases platelet aggregation mediated by a thromboxane A2. Though, few studies has documented the reduction the incidence of intraventricular haemorrhage, but the meta-analysis showed no reductions in mortality or neurodevelopmental impairment. Hence, its routine use as a therapy for improving mortality or neurodevelopmental outcome is not recommended.43
- **Inhaled Nitric Oxide (iNO):** Endogenously produced nitric oxide in the brain regulates local blood flow and offer neuroprotection. Inhaled NO therapy may led to modulation of circulating neutrophil, monocytes and platelets as they pass through lungs. iNO down regulates the lung derived cytokines and oxidant stress which may lead to brain injury.44 Although iNO-mediated decreases in chronic lung disease and severe intraventricular hemorrhage/periventricular leukomalacia may contribute to improved neurodevelopmental outcomes, iNO may also have an independent neuroprotective effect. Due to conflicting clinical evidence, there is uncertainty about the impact of iNO on long-term outcomes for premature infants. Routine use of iNO in moderately ill infants weighing >1000 g decreased the risk of cerebral palsy.45 One additional report, found significant improvement in neurodevelopmental outcomes at two years of age for moderately ill infants.46 However, recent meta-analysis concludes that iNO as rescue therapy for the very ill preterm infant does not appear to be effective and early routine use of iNO in preterm infants with respiratory disease does not affect serious brain injury or improve survival without BPD.47,48 NIH Consensus Development Conference also stated that 'the available evidence does not support the use of iNO in early routine, early rescue or later rescue regimens in the care of premature infants <34 weeks' gestation'.49 Though iNO is safe in tertiary care settings, additional studies addressing the long term neurodevelopment outcome, are required before it can be recommended in preterm infants.
- **Postnatal steroids:** Postnatal corticosteroid is a potentially neurotoxic drug especially when given in high dose or when used in the first 96 hours of life. Follow up studies of postnatal steroids used in bronchopulmonay dysplasia have shown that its use in preterms is associated with reduction in cortical gray matter, impaired brain development and

worse neurological outcome.50,51 There is increasing evidence that its exposure impairs memory and increases the risk of cerebral palsy.52 The mechanism by which it causes cerebral palsy is unknown, but may increase the risk of PVL.23 Many studies on postnatal steroids in the treatment of neonatal lung disease have been published since 1972 and have been subjected to a number of meta-analyses. Barrington reviewed the results of follow-up studies in babies enrolled into RCT of corticosteroids used to treat chronic lung disease and showed that the risk of cerebral palsy among surviving followed-up infants was doubled compared with control infants. He concluded that ''the single most effective intervention which could currently be introduced for improving neurodevelopmental outcomes of extremely low birth weight infants would be to immediately abandon the use of postnatal steroids for chronic lung disease''.53 American Academy of Pediatrics and the Canadian Paediatric Society also recommend that postnatal use of systemic dexamethasone for the prevention or treatment of chronic lung disease should be limited to carefully designed randomised double-masked controlled trials and outside the context of a randomised, controlled trial, the use of corticosteroids should be limited to exceptional clinical circumstances for example an infant on maximal ventilatory and oxygen support.54 A similar European guideline by Halliday recommended that ''neonatal steroids should be avoided if at all possible'', although allowing that ''steroids might be indicated for very ill ventilator-dependent infants'' and parental consent should be obtained before their use.55

Summary

Advances in perinatal care have significantly improved the survival of extremely preterm babies across the globe including India. Better understanding of neuropathology and sophisticated imaging modalities have shown that diffuse white matter injury and gray matter abnormalities are more common that previous thought of. The real challenge in NICU now a days is to protect the brain of these preterms so as to improve their neurodevelopment outcome. Antenatal steroids and antenatal magnesium sulphate have established its role in reducing the preterm brain injury. Postnatal practices of delayed cord clamping, minimal stimulation, following care practices that reduce the physiological and emotional stress in the acute neonatal period. NIDCAP, aggressive nutritional care, early use of NCPAP, early use of surfactant and caffeine therapy have the potential to improve the neurodevelopment outcome of these preterm infants. Avoidance of hypocarbia, hypercapnia and postnatal steroids are important in protecting the brain of these fragile infants. More studies are needed to prove the role of rhEPO and iNO in preterm neuroprotection. In future, to help us further improve neurologic morbidity in these infants, clinical practice should build upon excellent research focused on premature brain injury.

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Respiratory distress syndrome in preterm babies: The frequently asked questions

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What is Respiratory distress syndrome (RDS)?

Respiratory distress syndrome (RDS), previously known as hyaline membrane disease (HMD), is the leading cause of morbidity and mortality in preterm babies. It presents within hours after birth, most often immediately after birth. It is caused by primary surfactant deficiency combined with structural immaturity of the lung. The mandatory criteria for the diagnosis of RDS are respiratory distress appearing within the first 24 h of life, with complete, sustained, and prompt response to surfactant or lung recruitment or both; additional non-mandatory criteria are lung imaging supporting the diagnosis.

What is neonatal acute respiratory distress syndrome (NARDS)?

Acute onset respiratory distress with presence of diffuse, bilateral, irregular opacities, infiltrates, or complete opacification of the lungs, which are not fully explained by the conditions representing the exclusion criteria (Exclusion criteria are; RDS, TTN, or congenital anomalies involving the lungs). NARDS occurs in babies who have functional surfactant and developmentally normal lungs prior to NARDS onset. NARDS is characterized by an increased surfactant catabolism leading to a qualitative and quantitative surfactant injury, lung tissue inflammation and endothelial/epithelial damage. Surfactant replacement will be less efficacious in NARDS.

What is surfactant?

Surfactants are surface active materials lining the inner alveolar margins produced by type 2 alveolar cells. It appears by 24 weeks of gestation with a quantitative and qualitative increase with increasing gestational age. It decreases the surface tension in alveoli and thus preventing the alveolar collapse. It is composed of 90% lipids and 10% proteins. Surfactant is stored in lamellar bodies of type 2 alveolar cells. These lamellar bodies are secreted by exocytosis into the alveolar lining fluid, where the surfactant forms a meshwork of tubular myelin. Full term infants are estimated to have an alveolar storage pool of approximately 100 mg/kg of surfactant, while preterm infants have an estimated 4–5 mg/kg at birth.

How common is the disease?

1% of all neonates develop RDS. Incidence is almost 100% at 26 weeks or less. With increasing gestational age the incidence decrease approximately 30% at 30 weeks, 3% at 36 weeks and 0.1% among term babies.

What is the cause of RDS?

Surfactant deficiency is the main cause of RDS. In babies <30-32 weeks the structural immaturity of the lung also contributes to the disease. In the absence of an adequate amount of mature pulmonary surfactant, babies with RDS will progressively develop atelectasis and abnormalities of lung function. The alveoli tend

to collapse at end-expiration, resulting in a low functional residual capacity and impaired gas exchange. Widespread and repeated atelectasis eventually damages the respiratory epithelium, causing a cytokine-mediated inflammatory response. As pulmonary edema develops as a result of the inflammatory response, increasing amounts of protein-rich fluid from the vascular space to leak into the alveoli, which further inactivate surfactant. Thus RDS can cause hypoxemia through alveolar collapse, diffusion abnormality, ventilation-perfusion mismatch, intrapulmonary shunting, or a combination of these mechanisms.

Surfactant deficiency → Alveolar atelectasis (↓FRC → Impaired gas exchange) → Respiratory epithelium and vascular epithelium damage → Inflammatory response → leakage of protein rich fluid to alveolar space → hyaline membrane formation

What is the natural history of RDS?

In untreated RDS, the symptoms will progressively worsen over 48 to 72 hours towards respiratory failure, and the baby may become lethargic and apneic. The endogenous surfactant production commences from 2–3 days of age and heralds clinical recovery from respiratory distress. By reducing surface tension, surfactant allows the alveoli to re-expand with inspiration. Clinically, the functional residual capacity improves and the work of breathing decreases markedly due to the decreased airway resistance and improved lung compliance. Babies usually recover from the disease by 5-7 days, usually heralded by diuresis on day 3-4 of life.

How do we clinically suspect RDS?

Any preterm baby developing respiratory distress within 6 hrs of birth should be suspected to have RDS unless until proven otherwise. An audible grunt is an important sign as it indicates the baby has a low functional residual capacity and it breathing against a partially closed glottis.

How do we clinically assess the severity of RDS?

Usually Silverman Anderson Score (SAS) is used to objectively assess the severity of RDS. Score <3 indicates mild disease, Score 4-6 indicated moderate disease and score >7 indicates severe disease.

We should document the SAS score every 3-6 hrs. This helps us in objectively assessing the progression of RDS.

What is the role of chest x-ray in the management of RDS and what are the x-ray findings in RDS?

For initial management of RDS x-ray chest is not required for starting intervention for RDS such as, CPAP and surfactant. Any premature baby <34 weeks with respiratory distress should be started on positive pressure support and surfactant can be given without getting the x-ray chest done. However whenever there is doubt about the diagnosis of RDS, x-ray chest should be done. Chest x-ray also confirms our clinical diagnosis and helps us in grading the severity of RDS.

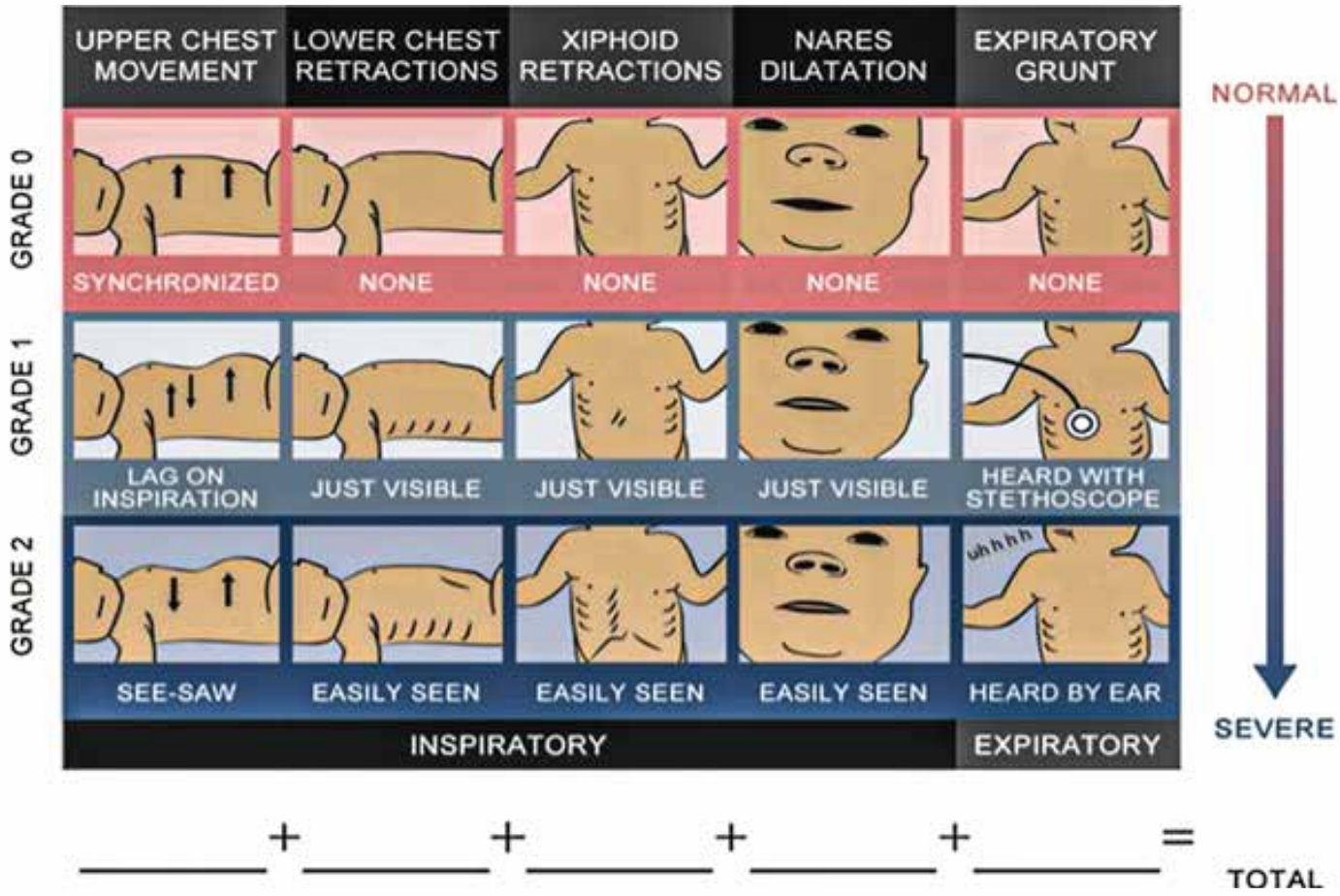
Chest x-ray findings pathognomic of RDS include homogenous lung disease with diffuse atelectasis, classically described as having a ground-glass reticulo-granular appearance with air bronchograms, as well as low lung volumes. The air tissue interface formed between micro-alveolar collapse in the background with the air-filled larger airways in the foreground creates the classic appearance of air bronchograms. We can grade the severity of RDS on the basis of X-ray findings.

Grade 1: Symmetrical reticulogranular pattern.

Grade2: Presence of air bronchogram.

Grade3: Blurry diaphragm and heart.

Grade 4: White out lungs.


UPPER CHEST MOVEMENT
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SYNCHRONIZED
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NONE
NONE
NONE
GRADE 1
LAG ON INSPIRATION
JUST VISIBLE
JUST VISIBLE
JUST VISIBLE
HEARD WITH STETHOSCOPE
GRADE 2
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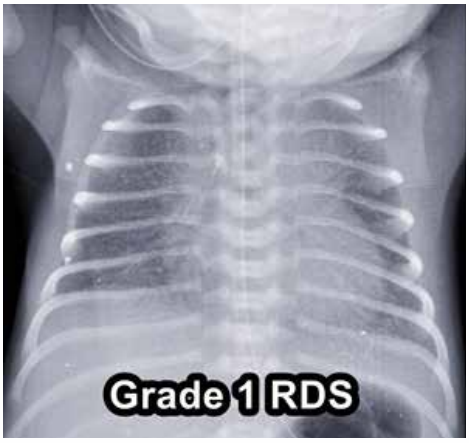
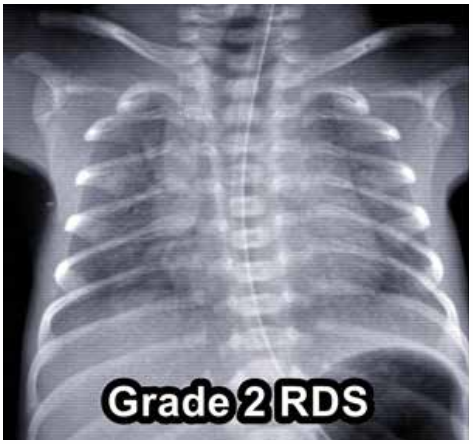
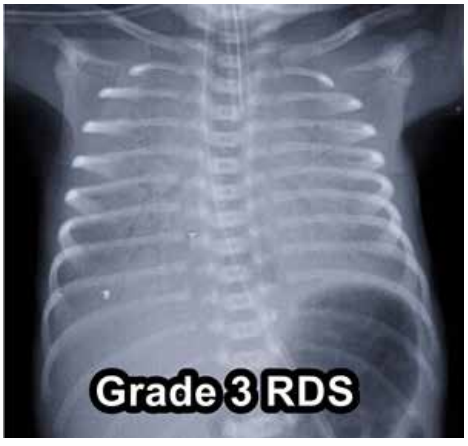
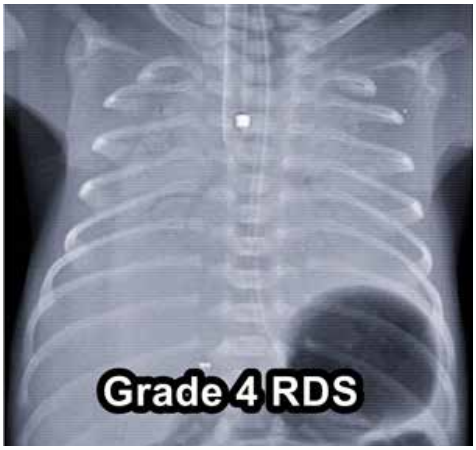

Grade 1 RDS


Grade 2 RDS


Grade 3 RDS


Grade 4 RDS

What is the role of lung USG in the management of RDS?

The use of ultrasound as a point of care tool is increasingly being used in NICUs for a variety of purposes. There are many studies to show the usefulness of lung USG for the diagnosis of RDS in preterm babies. It is very helpful in differentiating RDS from TTNB and congenital pneumonia. The lung ultrasound has some benefits including lower exposure to radiation, easy to perform at bedside, can be repeated several times a day, and has a low cost. But the availability of a good lung ultrasound machine with an appropriate high resolution and a microlinear probe is a problem. It is an evolving modality in the management of RDS. It also requires special training in performing lung USG. Last but not the least, the lung ultrasound has very high accuracy and reliability in diagnosing pulmonary disease

What is the role of blood gas analysis in the management of RDS?

Blood gas analysis has become an integral part of management of any sick neonate. Apart from traditional parameters like pH, PaO2, PaCO2 and Base excess, the modern blood gas machines give us many more parameters like; electrolytes, lactate, BUN, creatinine, sugar etc. Pulse oximeter is good to detect hypoxemia but it cannot detect acidosis and hypercapnia. Values of pH and PaCO2 are helpful in titrating the respiratory support of a baby with RDS.

How do we assess the severity of the RDS on the basis of oxygen and pressure requirement for a baby with RDS on CPAP of ventilation?

For a baby with RDS on CPAP or ventilation the severity of the RDS can be assessed by estimating the requirement of FiO2 and airway pressure (MAP or CPAP). Oxygen index is a useful index to assess the severity. Oxygen index requires invasive sampling, thus non-invasive index Oxygen Saturation Index (OSI) can be used.

Oxygenation index (OI): MAP X FiO2 X 100 / PaO2

Oxygen saturation index (OSI): MAP X FiO2 X 100 / SpO2

These indices are very helpful in assessing the progression of the disease and also in assessing the efficacy of the intervention done.

What is the triple therapy for RDS?

The combination of the three main interventions used for management of RDS is known as "Triple therapy for RDS". These are antenatal steroid, CPAP and early rescue surfactant. If these three interventions are used appropriately the need for ventilation can be avoided in majority of the babies with RDS. Antenatal steroid boosts surfactant production, early CPAP conserves surfactant and if these are not enough, early rescue surfactant can be given to supplement the missing surfactant. Rescue surfactant should be given as soon as possible; within 2 hours of life.

How do you manage a preterm baby with respiratory distress in labour room?

Preterm babies with RDS will usually try to breathe during transition at birth, although they may subsequently struggle to maintain adequate alveolar aeration. "Supporting transition" rather than "resuscitation" is therefore preferred term in RDS labour room management, and infants should be allowed to gently transition. Delayed "physiological" clamping after lung aeration should be practiced. Umbilical cord milking may be an alternative to delayed cord clamping in emergency situations.

Spontaneously breathing babies should be started on CPAP in delivery room (DR-CPAP) as soon as possible. Stimulation of the infant during stabilization helps these babies to establish regular respiration and adequate FRC. CPAP should be started at 6 cm of water in the labour room. "T" piece device is a preferred way

of delivering the DR-CPAP. Delivery room CPAP decreases the need for ventilation and surfactant by 50%. Immediate wrapping in a polythene bag under a radiant warmer is indicated for babies <32 weeks or babies with <1.5 kg birth weight. SpO2 should be measured at the right wrist by pulse oximetry and it should be >80% by 5 minutes of life. These babies should be immediately transferred to NICU in a pre-warmed transport incubator. CPAP should be administered by "T" piece device during transport. An early, uninterrupted and optimally delivered CPAP is the mantra of RDS management.

What is the golden hour management of a preterm baby with RDS in NICU?

By the end of one hour of NICU admission the preterm baby with RDS should have received the initial treatment. The treatment within one hour of admission includes; starting the CPAP, adjusting the CPAP, placing umbilical venous line, sending the initial investigation, starting the parenteral nutrition, starting the caffeine, starting the antibiotics (if indicated) and giving surfactant if FiO2 requirement is more than 30-40%.

How do you optimize the CPAP therapy for RDS?

In NICU CPAP should be started at 5 cm of water and 50% of FiO2. The CPAP pressure to be increased till child is comfortable and has minimal chest retraction. CPAP can be safely increased till 8 cm of water. After adjusting the pressure FiO2 can be adjusted. Target SpO2 should be 91-95%. Chest x-ray should be done ½ hour after starting CPAP.

What is the indication of surfactant therapy?

Surfactant should be given in delivery room to a <28-30 weeks gestational age baby if the baby requires intubation for resuscitation. Baby should not be intubated in delivery room only for giving surfactant. In NICU early rescue surfactant should be given by INSURE (Intubate give Surfactant Extubate) technique as early as possible, but before 2 hours of life if a baby requires >30% of FiO2 and CPAP of at least 6 cm of water. For intubated baby the surfactant should be given, if FiO2 requirement is >30%. A second and occasionally a third dose of surfactant should be given, if there is ongoing evidence of RDS such as persistent high oxygen requirement (>30-40%) and other problems have been excluded (e.g. pneumonia, PDA, air-leaks) . Repeat dose can be administered after 6-8 hours of the previous dose.

Most of the head-to-head trials show that surfactants have similar efficacy when used in similar doses. However, there is a survival advantage when 200 mg/kg of Curosurf is compared with 100 mg/kg of Survanta or 100 mg/kg Curosurf to treat RDS. Recommended dose of Alveofact is lesser (50mg/kg), but experience in our country with this surfactant is limited.

Brand	Type of surfactant	Phospho -lipid per ml	Recommended dose	Available vial size	Price per 100mg
Curosurf (Poractant alfa)	Porcine lung lipid extract (extracted from material derived from minced pig lung)	80mg /ml	100-200 mg/kg (1.25-2.5ml/kg)	1.5m, 3ml	Rs 7037
Survanta (Beractant)	Modified bovine lung lipid extract (extracted from minced cow lung with additional DPPC, palmitic acid and tripalmitin)	25 mg /ml	100 mg/kg (4ml/kg)	4ml, 8ml	Rs 7040
Neosurf (BLES)	Bovine lung lipid extract (extracted from cow lung lavage fluid)	27 mg/ml	135mg/kg (5ml/kg)	3ml, 5 ml	Rs 7038
Alveofact (Bovactant)	Bovine lung lipid extract (extracted from cow lung lavage fluid)	42 mg/ml	50mg/kg (1.2ml/kg)	1.2ml	Rs7508

What are the criteria for CPAP failure?

There is no consensus about the criteria of failure of CPAP in management of preterm baby with RDS. In our country the general agreement about the CPAP failure criteria is; worsening respiratory distress (as indicated by Silverman scoring) and/or hypoxemia (PaO_2 <50mmHg) and/or hypercarbia ($PaCO_2$ >60 mmHg) despite CPAP pressure of 7-8 cm H_2O and FiO_2 of 0.8. Apart from this, if the baby has major apnea (episode of apnea requiring bag and mask ventilation) or frequent apnea/bradycardia (>2–3 episodes per hour) are considered as CPAP failure.

Can we use High flow nasal canula (HFNC) oxygen therapy as a primary mode of respiratory support in a baby with RDS?

When used as a primary mode of respiratory support for RDS, HFNC was found to have higher failure rates compared to CPAP. However, most neonates could be rescued using CPAP and there was no increase in need for MV or surfactant administration. Thus, HFNC can be used as a primary mode of respiratory support in RDS, especially in low risk babies. Babies with gestational age >32 weeks, birth weight >1.5 kg, no need of PPV in delivery room, with appropriate antenatal steroid cover and mother having no evidence of chorioamnionitis are considered as low risk babies. These babies can be started on HFNC as a primary mode for RDS treatment.

What are the indications of nasal ventilation (nasal intermittent positive pressure ventilation [NIPPV]) in RDS and what are the advantages over CPAP?

In the meta-analysis, when used for RDS, NIPPV compared to CPAP, NIPPV use results in a reduced risk of treatment failures, decreased need for invasive mechanical ventilation, decreased incidence of air leaks and decreased mortality. The NIPPV can be used as a primary mode of ventilation, when there is high risk for CPAP failure. The high risk factors associated with increased incidence of CPAP failure are; no or inadequate antenatal steroid administration, gestational age <28 wks, history of PPV in delivery room and increased severity of RDS ($A\text{-}aDO_2$ >180 mmHg in 1st ABG, severe RDS in initial Chest X-ray, Downe's score >7 at starting or even at 2 hrs of CPAP, FiO_2 > 50% after 2 hrs of CPAP). NIPPV also can be used in post extubation period.

What are the indications of invasive mechanical ventilation in RDS?

Failure of CPAP or NIPPV is the indication to intubate the baby and start on invasive mechanical ventilation. The criteria for NIPPV failure are; significant acidosis (blood gas pH <7.25), hypercarbia ($PaCO_2$ >60 mm Hg), major apnea(episode of apnea requiring bag and mask ventilation), frequent apnea/ bradycardia (>2–3 episodes per hour) not responding to caffeine therapy and frequent desaturation <90% >3 episodes per hour not responding to increased ventilator settings.

What is the best invasive ventilation strategy for RDS?

Volume targeted ventilation (VTV) is the best invasive ventilation strategy in premature baby with RDS. VTV enables us to ventilate with less variable tidal volumes and real-time weaning of pressure as lung compliance improves. VTV compared with time-cycled pressure targeted ventilation results in less time on the ventilator, fewer air leaks and less BPD. An initial set tidal volume of about 5 mL/kg and an estimated maximum PIP according to observation of chest movement may need to be adjusted according to the baby's own respiratory efforts and gas exchange assessment.

Do we need to give antibiotics for RDS treatment?

There is no role of routine antibiotics for a preterm baby with RDS. If there are risk factors

present for early onset sepsis, antibiotics should be started.

What are the complications associated with RDS?

The complications associated with preterm baby with RDS can be divided as early, late and chronic complications. The early complications within first week are; pneumothorax, intra-ventricular haemorrhage, patent ductus arteriosus and healthcare associated infections. The late complications are; healthcare associated infections (septicaemia, ventilator associated pneumonia), under nutrition, retinopathy of prematurity and chronic lung disease. The chronic complications are related to lungs (hyper-reactive airway disease) and neurological system (motor deficit, cognitive deficit, impaired hearing and impaired vision).

How do we prevent RDS in premature babies?

The most important is to prevent preterm births. The second most important is to give antenatal steroid, it decreases the RDS incidence by 34%.

How do we decrease the severity of RDS in premature babies?

Most important is the in-utero transfer to a tertiary care perinatal center of an imminent preterm delivery. Second most important is to give antenatal steroid for imminent preterm delivery; it decreases the severity of RDS. Third most important intervention is early (delivery room CPAP), uninterrupted (CPAP during transport) and optimal application of CPAP in NICU.

Suggested readings:

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Kangaroo Mother Care - Zero Separation, ACT NOW!

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Why care of low birth weight infants is crucial?

Every year, approximately 20 million babies, 15% of all births, are born low birth weight. Over 70% of all newborn deaths occur in this vulnerable group. Interventions to reduce mortality in low birth weight infants is crucial if the countries have to attain the sustainable development goal of reducing neonatal mortality to less than 12 per 1000 live births by 2030.

Kangaroo Mother Care

Among the various interventions to improve survival among low-birth-weight infants, Kangaroo Mother Care (KMC) is among the most effective (40% mortality reduction). KMC involves keeping the baby in skin-to-skin contact on her chest continuously (until the baby no longer wants to stay in that position) and feeding the baby only with her breast milk. KMC not only helps the baby survive reducing problems such as hypothermia and hypoglycemia but also promotes growth and long-term neurodevelopment. Currently, KMC is recommended by WHO for all LBW babies to be initiated in health facilities when the babies are clinically stable.

Benefits of KMC

Though it is promoted as an effective, safe and cost effective alternative to conventional care in resource-limited countries to improve survival, the positive effects of KMC extend well beyond the neonatal period. (Table 1)

Table 1: Benefits of Kangaroo Mother Care

Benefits in the neonatal period • Improved survival • Temperature regulation – reduced hypothermia • Physiologic stability – heart rate, oxygenation • Reduced nosocomial sepsis • Pain reduction • Sleep organization • Improved growth • Improved breastfeeding
Benefits to the mother • Increased confidence, satisfaction • Better bonding • Empowerment • Better milk production • Early discharge • Lower stress • Lower post partum depression
Benefits in infancy and childhood • Growth • Neurodevelopment Increased IQ Better executive functions • Physiologic Organization • Lower stress • Better parent- infant interaction • Lower admission rate

Cochrane meta-analysis

Recent Cochrane meta-analysis concluded that compared with conventional neonatal care, KMC was found to reduce mortality at discharge or at 40 to 41 weeks 'postmenstrual age and at latest follow-up, severe infection/sepsis, nosocomial infection/sepsis, hypothermia, severe illness, and lower respiratory tract disease. Moreover, KMC increased weight, length, and head circumference gain, breastfeeding at discharge or at 40 to 41 weeks' postmenstrual age and at one to three months' follow-up, mother satisfaction with method of infant care, some measures of maternal-infant attachment, and home environment

Immediate Kangaroo Mother Care

Unfortunately, the infants who are most likely to die in the first few days of life may not be eligible for KMC as per the current recommendation. Most newborn deaths occur in the first 3 days of life, when most babies <2000g would not be considered stable. Thus, the 40% mortality impact of KMC seen in the KMC studies would only be in survivors until this time. There is a critical knowledge gap regarding the effect of initiating continuous KMC immediately after birth on survival.

WHO coordinated a large multicentric-multicountry clinical trial that recruited 3211 low birth weight infants between 1.0 and 1.8 kg and their mothers in 5 hospitals with neonatal intensive care units in Ghana, India, Malawi, Nigeria and Tanzania from December 2017 to January 2020. In this trial, LBW babies in the immediate KMC group were initiated with KMC with either the mother or a surrogate (till the mother was able to do KMC) immediately after birth irrespective of stabilisation. Mothers were able to provide about 17 hours of KMC per day to their sick small newborn in the first few days of life in the intensive care unit. Results of this study published in the New England Journal of Medicine showed that starting KMC early before waiting for the LBW baby to stabilise reduced the mortality by 25%. The intervention provided to 27 babies saved one additional life. Thus, starting KMC immediately after birth has the potential to save up to 150,000 more lives each year, compared to the current recommendation of starting it only once a baby is stable.

Immediate KMC reduces neonatal mortality by 25% lower, hypothermia by 35% and clinically suspected sepsis by 18%.

A small baby receiving Immediate KMC in India
Courtesy: Safdurjung Hospital, India

Mother - Newborn ICU – A Paradigm shift in the concept of intensive care for the small newborn

For the mother or the surrogate to be available 24/7 for their LBW in the ICU requires the conversion of the ICU to Mother-Newborn ICU. This is a paradigm shift in neonatal care of the small and sick newborn. The Mother-Newborn ICU staff should be able to provide care for not only the LBW baby but also care for the mother. The M-NICU has all facilities for the basic needs of the mother such as an area to warm food and eat, a toilet and a shower.

As the mother is continuously in close contact with her baby, she is able to help the nurses monitor her baby. The presence of the

mother continuously in the neonatal intensive care unit provides more opportunities for breastfeeding, reduces handling by health care providers.

One should not lose sight of the fact that the immediate KMC intervention cannot be provided in isolation. The infants in this weight category of <1.8 kg are very small and sick and a minimum package of high quality care focusing on warmth, infection prevention and provision of respiratory support is vital.

What next ?

This study was tweeted as a candidate for the most important neonatal trail in the 21st century. The study has the potential to bring about a paradigm shift in how the small and sick newborns are cared for immediately after birth, laying the path for zero separation of the LBW baby from his/her mother. This trial has been the basis for the World Prematurity Day theme

"Zero separation - ACT NOW! Keep parents and babies born too soon together."

WHO is considering this intervention in the upcoming update of guidelines for care of low birth weight babies. If recommended, neonatal health stakeholders around the world will have to consider how this can rapidly scaled up. Neonatal, obstetric, midwifery and nursing professionals will need to embrace this paradigm shift in care of small babies. Governments globally will have to consider how to re-model current NICUs to M-NICUs and build M-NICUs when new facilities are constructed.

For centuries, the medical profession has separated mother from her small or sick newborn. The results of the study highlights that restoring the mother to her rightful place at the centre of her baby's universe has profound benefits in improving the survival of the small newborn.

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WHO Immediate KMC Study Group, Immediate "Kangaroo Mother Care" and Survival of Infants with Low Birth Weight. N Engl J Med. 2021 May 27;384(21):2028-2038. doi: 10.1056/NEJMoa2026486. PMID: 34038632; PMCID: PMC8108485.

https://www.efcni.org/activities/campaigns/wpd/

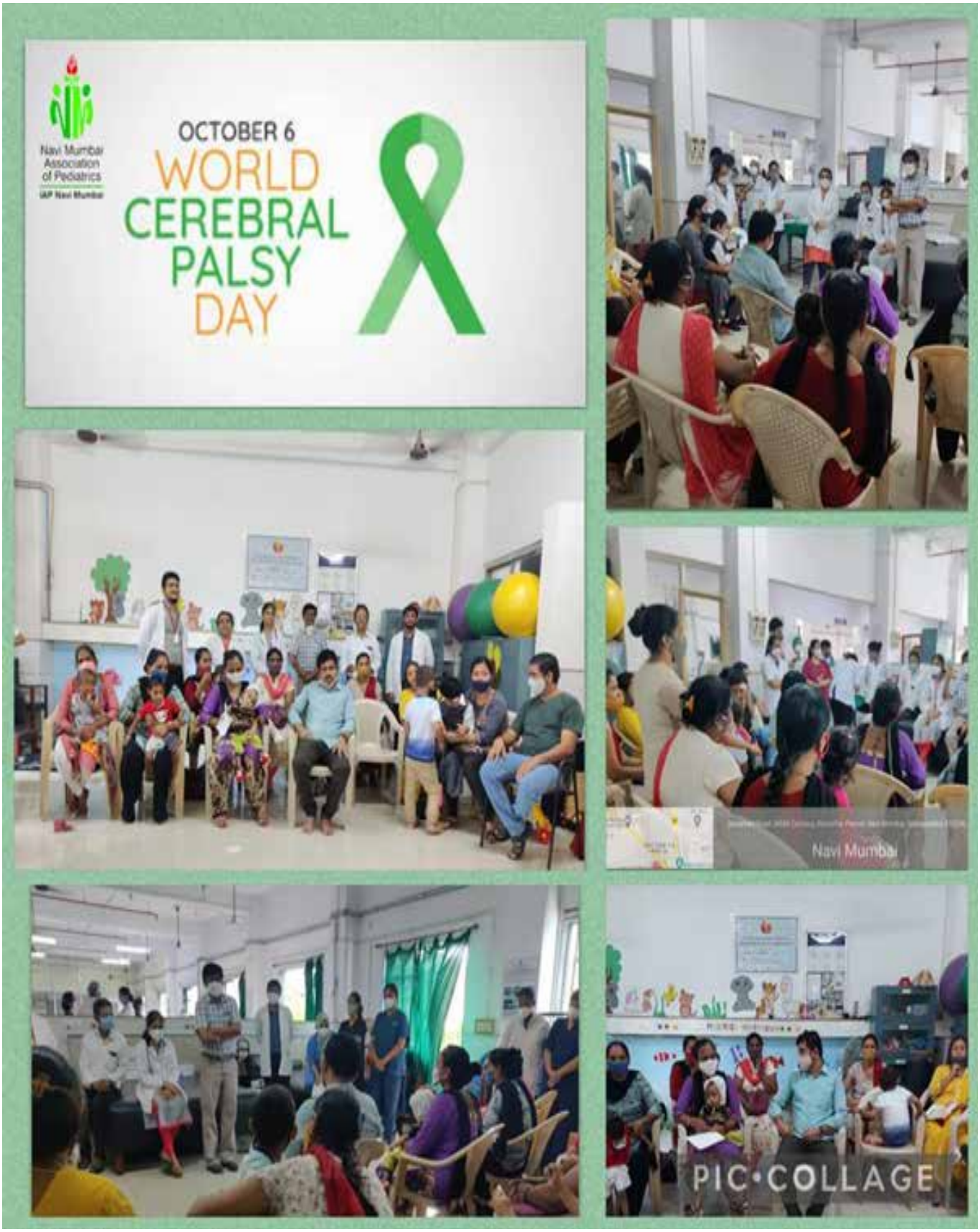
IAP Navi Mumbai

IAP Navi Mumbai

NMAP participated as Finalist in the Maharashtra level Quiz on Rational Antibiotics for practicing Pediatricians organized by IAP Pune.

IAP Navi Mumbai

IAP Navi Mumbai



IAP Kerala

IAP PG Quiz Kozhikode Division - organised by IAP Thrissur

Presidential Action Plan - Pediatric Trauma mangement

Presidential Action Plan - Suicide Prevention - IAP Trivandrum

National Nutritional week IAP Trivandrum

IAP Kerala

Antibiotic awareness week -
IAP Kozhikode

PED Heart conference -
IAP Pariyaram

Antibiotic awareness week -
IAP Thalassery

Pediatric Critical Care Nursing workshop -IAP Kannur

IAP Kerala

Antibiotic awareness week -
IAP Thrissur

Free medical camp
IAP Kasargode

National nutrition week -
IAP Vadakara

Presidential Action Plan - Pediatric Aerosol therapy in Asthma- IAP Kozhikode

IAP Jalandhar

"CAHCW" CELEBRATION REPORT

IAP Jalandhar

DAUGHTER'S DAY CELEBRATION REPORT

IAP Jalandhar

"Teenage Day" Celebration Report