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Newer **R**esearch and recommendations **I**n **C**hild **H**ealth

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Dear fellow IAPans,

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Newer **R**esearch and recommendations **I**n **C**hild **H**ealth-aims to bring you the abstracts of some of the breakthrough developments in pediatrics, carefully selected from reputed journals published worldwide.

Expert commentaries will evaluate the importance and relevance of the article and discuss its application in Indian settings. nRICH will cover all the different subspecialities of pediatrics from neonatology, gastroenterology, hematology, adolescent medicine, allergy and immunology, to urology, neurology,vaccinology etc. Each issue will begin with a concise abstract and will represent the main points and ideas found in the originals. It will then be followed by the thoughtful and erudite commentary of Indian experts from various subspecialties who will give an insight on way to read and analyze these articles.

I'm sure students, practitioners and all those interested in knowing about the latest research and recommendations in child health will be immensely benefitted by this endeavor which will be published online on every Monday.

Happy reading!

Upendra Kinjawadekar
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A comparative study of IL-6, CRP, NT-proBNP levels in post-COVID multisystem inflammatory syndrome in children (MISC) and Kawasaki disease patient.

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BASED ON ARTICLE

Ganguly M, Nandi A, Banerjee P, Gupta P, Sarkar SD, Basu S, Pal P. A comparative study of IL-6, CRP, NT-proBNP levels in post-COVID multisystem inflammatory syndrome in children (MISC) and Kawasaki disease patients. Int J Rheum Dis. 2021;00:1–5.

ABSTRACT

Background: Multisystem inflammatory syndrome (MIS-C) in children is a new hyperinflammatory complication of Covid-19 infection recognized during the Covid pandemic globally. It predominantly affects previously healthy children and adolescents with majority requiring hospitalization in pediatric intensive care. Whether it falls in the same spectrum as Kawasaki disease or represents a separate entity following Covid-19 infection is still debatable (1). Differentiating MIS-C from Kawasaki disease, in the beginning, is crucial for initiating appropriate therapeutic measures. However, the clinical features of both conditions overlap significantly, posing a challenge in differentiating them at the bedside.

Methods: This analytical comparative study was conducted Institute of Child Health, Kolkata, India during July 2020-December 2020 over a period of 6 months. The comparison was done with a group of Kawasaki disease patients in which 30% had coronary artery abnormalities seen from Jan 2017 to June 2018.

Results: In this study, mean IL-6 value in Kawasaki disease was 83.22 pg/mL and in MIS-C 199.91 pg/mL, which was not found to be statistically significant ($P = 0.322 > 0.05$).However, mean NT-proBNP (914.91 pg/mL) with CRP level (96.32 mg/L) in Kawasaki disease was significantly lower ($P < 0.05$ for both cases) than that in MIS-C (9141.16 pg/mL and 145.66 mg/L respectively). ROC analysis showed NT-proBNP has the best sensitivity and specificity in predicting MIS-C.

Conclusion: NT-proBNP and CRP are significantly higher among MIS-C patients; ROC analysis shows levels >935.7 pg/mL and >99.55 mg/L, respectively might act as a guide to differentiate between them.

COMMENTARY

MIS-C is a potentially life-threatening condition initially reported in the United Kingdom in 2020. Subsequently, many cases were reported from different regions across the globe. The clinical features of MIS-C closely mimic Kawasaki disease, and it is still unknown whether it's a spectrum of Kawasaki

disease or is a distinct entity resulting from exposure to the Covid-19 infection. However, the manifestations in both conditions originate from an aberrant hyperinflammatory response. Inflammatory parameters like Interleukin-6 (IL-6), C-reactive protein (CRP) and N-terminal Prohormone of Brain Natriuretic peptide (NT-ProBNP), a marker of cardiac damage are elevated during the acute stage of Kawasaki disease and MIS-C. In this study, the authors have compared the serum level of CRP, IL6, and NT-ProBNP between patients of MIS-C, diagnosed over six months, and Kawasaki disease diagnosed over 18 months (Jan 2017-June 2018). A significant difference in serum concentration of CRP, NT-Pro BNP was noted between the groups. However, the IL-6 concentration between the groups was non-significant. Additionally, the authors carried out receiver operating curve (ROC) analysis for the aforesaid parameters for the predicament of MIS-C in children. NT-ProBNP was found to be sensitive and specific for differentiating MIS-C from Kawasaki disease. The authors also carried out correlation analysis between cardiac involvement and NT-ProBNP concentration. However, no correlation was evident between these parameters.

NT-ProBNP as a biomarker for MIS-C vis-à-vis Kawasaki disease:
NT-ProBNP is a surrogate marker of myocardial damage in Kawasaki disease as well as in MIS-C. In this study, the mean NT-proBNP in MIS-C has been documented to be significantly higher than in Kawasaki disease. Additionally, an NT-proBNP level of more than 937.5pg/ml has been illustrated as a predictor of MIS-C.

It is believed that the myocardial involvement in Kawasaki disease is universal. Hence the role of NT-proBNP has been extensively evaluated in Kawasaki disease. NT-proBNP value between 629-1300pg/ml has a sensitivity of 70-79% and specificity of 58 -77% in diagnosing Kawasaki disease (2,3). A study from India has also documented that a cut-off level of 1025pg/ml has a sensitivity of 88% and a specificity of 96% for diagnosing KD (4). Hence, using an isolated biomarker like NTproBNP to predict MIS-C is problematic in this context.

Furthermore, although the authors have depicted ROC curve analysis, and calculated the optimum cut-off value using Youden's J Index for NT-ProBNP, CRP, and IL-6, information on area under the curve (AUC), 95% confidence interval, and 'P' value are missing. Similarly, the authors have illustrated CRP 99.5mg/L has sensitivity of 59.1% and a specificity of 73.61% for prediction of MIS-C. However, it would have been more informative if the ROC analysis had been carried out by combining both parameters (CRP and NT-Pro BNP). Likewise,no correlation between NT-ProBNP concentration and cardiac involvement in MIS-C (R-value of 0.0314, P value of .915) was documented by the authors in this paper. However, this might be attributed to the non-availability of NT-ProBNP parameter of eighteen patients (25%) with MIS-C.

Limitation of the study: This is a single-centre comparative study involving 71 MIS-C cases, and in 25% patients data of NT-ProBNP is unavailable. Hence, extrapolation of this outcome, in general, is open to questions.

Conclusion: Diagnosing MIS-C using isolated biomarkers is still challenging. Combining multiple biomarkers with an appropriate sample size is necessary for differentiating MIS-C from Kawasaki disease. Future prospective studies across various regions in India may throw more light on the value of these inflammatory parameters in differentiating the two conditions. This is more important in the context of a positive Covid antibody in the major sections of the population either due to a past infection or vaccination with the Covid-19 vaccine.

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