



## Journal Summary

# Journal watch

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## 1. Does childhood tuberculosis cause a decline in spirometry parameters?

Source: Lew YL, Tan AF, Yerkovich ST, Yeo TW, Chang AB, & Lowbridge CP. (2024). Pulmonary function outcomes after tuberculosis treatment in children: A systematic review and meta-analysis. *Archives of Disease in Childhood*, 109(3), 188–194. <https://doi.org/10.1136/archdischild-2023-326151>

Tuberculosis (TB) is a curable illness; however, even after clearing the infection, lung function impairments linked to post-tuberculosis lung disease (PTLD) may endure. While this is widely understood in adults, the degree and seriousness of PTLD in children are not thoroughly understood. Investigating this field is crucial due to the possible lasting effects of PTLD on children's lung health and growth.

This meta-analysis tries to answer some questions relating to the topic. The limited number of studies included highlights the global under-representation of childhood TB. Overall, the impact of pulmonary TB (PTB) on lung function showed a negative trend, indicating reduced lung function in both forced expiratory volume 1 (FEV1) and forced vital capacity (FVC) meta-analyses. These results are consistent with the current understanding of PTLD in adults, supporting the validity of the researchers' approach. However, high  $I^2$  (A high  $I^2$  value, generally considered to be above 50%, indicates that the studies in a meta-analysis are highly heterogeneous. This means that the observed differences between the studies are likely due to true differences between the studies rather than sampling error) values indicate significant heterogeneity between studies, a key limitation. This underscores a research gap in assessing the impact of childhood PTB on lung function outcomes, especially in high-prevalence areas.

Among the studies included, three examined primary diseases other than PTB, such as human immunodeficiency virus (HIV) coinfection and bronchiectasis, which were reasonable to include due to their relevance. One study focused on post-PTB health-related quality of life, reflecting recent shifts in evaluating PTLD. However, the timing of spirometry varied greatly among studies, making it difficult to determine its actual effect. A prospective cohort study of adult TB survivors showed a greater decline in FEV1 and FVC values three years after treatment completion compared to the 1<sup>st</sup> year post-treatment.

One study had a low-quality score, particularly due to the use of extrapolation in calculating spirometry z-scores for young children, potentially inflating effect sizes. The exclusion of this study led to a revised interpretation, indicating a large effect of childhood TB on FEV1. However, the removal of this study did not significantly alter the pooled effect size estimate for FVC. In addition, one study reported a more pronounced decline in FVC compared to FEV1 in HIV-infected individuals, suggesting HIV coinfection may contribute to observed heterogeneity.

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This is supported by another study indicating that early childhood respiratory infections have a greater effect on FVC than FEV1, suggesting HIV coinfection as a clinical factor contributing to the observed variability.

The implications of this study are significant for research, practice and policy. It advocates for the integration of regular pulmonary function tests into the follow-up care protocol for children with a history of TB, enabling early detection and intervention for PTLD. This approach could potentially improve long-term outcomes for children affected by TB and inform policy decisions regarding post-TB care guidelines.

## 2. Is a high-dose acetylsalicylic acid administration required with intravenous immunoglobulin therapy in the treatment of acute Kawasaki disease?

Source: Hayashi K, Miyakoshi C, Hoshino S, Kobayashi N, Nakajima R, Sagawa H, Hayashiya T, Suzuki A, Aota C, Nishijima S, Shimizu Y, Yamakawa M, & Tsuda E. (2024). Initial intravenous immunoglobulin therapy without aspirin for acute Kawasaki disease: A retrospective cohort study with a Bayesian inference. *BMJ Paediatrics Open*, 8(1), e002312. <https://doi.org/10.1136/bmjpo-2023-002312>

During the acute phase of Kawasaki disease (KD), there is a practice of simultaneously administering medium to high-dose (HD) aspirin acetylsalicylic acid (ASA) along with intravenous immunoglobulin (IVIG). Nevertheless, the effectiveness of ASA treatment in managing KD complications remains a subject of controversy.

HD-ASA exerts anti-inflammatory effects by inhibiting cyclooxygenase (COX)-2, while low-dose ASA inhibits COX-1 and has an antiplatelet effect. ASA is significantly less effective at inhibiting COX-2 than COX-1, resulting in different dosages required to achieve each effect. Previously, HD ASA was used for KD treatment due to its anti-inflammatory effects, but studies have not consistently shown its superiority over low-dose ASA in preventing coronary artery lesions (CALs). In this study, most non-HD group patients did not receive ASA initially, and the incidence of CALs was non-inferior to routine HD ASA administration.

A Bayesian analysis was conducted, indicating a posterior probability of HD ASA superiority of only 69.0%, even with a strongly favourable prior for HD treatment. Non-HD ASA treatment did not show inferiority in unresponsiveness to initial IVIG therapy compared to HD ASA, consistent with the previous studies. However, the duration of fever was shorter in the non-HD group, contradicting previous findings. Adverse events associated with ASA were similar between groups, but the study might have been underpowered to detect differences.

Limitations include the retrospective design and lack of standardisation in treatment protocols. The study excluded certain KD patients, potentially affecting generalizability.

Long-term outcomes were not assessed, and the sample size might have been insufficient for detecting differences in aneurysm regression. Despite these limitations, the study suggests reconsidering KD guidelines recommending ASA administration in the acute phase.

## 3. Does maternal influenza vaccination during pregnancy help the infant?

Source: Sahni LC, Olson SM, Halasa NB, Stewart LS, Michaels MG, Williams JV, Englund JA, Klein EJ, Staat MA, Schlaudecker EP, Selvarangan R, Schuster JE, Weinberg GA, Szilagyi PG, Boom JA, Patel MM, Muñoz FM, & New Vaccine Surveillance Network Collaborators (2024). Maternal vaccine effectiveness against influenza-associated hospitalisations and emergency department visits in infants. *JAMA Pediatrics*, 178(2), 176–184. <https://doi.org/10.1001/jamapediatrics.2023.5639>

In this extensive, multisite, multi-season and prospective-control study spanning the influenza seasons from 2016 to 2017 through 2019 to 2020, maternal influenza vaccination during pregnancy was linked to a reduction in the likelihood of infants under six months old experiencing medically attended influenza illness by one-third. The degree of effectiveness increased with the severity of infant disease, showing a 19% reduction in effectiveness against infant emergency department (ED) visits and a 39% reduction in effectiveness against infant hospitalisation. Similarly, the effectiveness was higher among infants born to mothers vaccinated later in pregnancy and was also more pronounced against influenza B and influenza A/H1N1 compared to influenza A/H3N2. However, estimates of effectiveness against infant ED visits for maternal vaccination during the first and second trimesters, as well as by influenza A subtype, were of small magnitude and did not reach statistical significance. It is worth noting that in our study, 54% of mothers of control infants received an influenza vaccine during pregnancy. Although this coverage is low, it aligns with national estimates and underscores the missed opportunity to shield mothers from influenza illness during pregnancy and safeguard their infants during the first six months of life when they are ineligible for vaccination. Finally, our effectiveness estimates are in line with previously published clinical trials and observational studies predating the 2009 H1N1 pandemic, indicating protection for infants born to mothers vaccinated during pregnancy.

This study has both strengths and limitations. The authors conducted prospective surveillance at various paediatric hospitals across diverse geographic and demographic settings throughout multiple influenza seasons, using sensitive molecular methods to detect influenza virus infection in infants. They ensured the accuracy of influenza vaccine receipt by objectively verifying it through immunisation information systems or provider data. However, the authors

faced challenges in obtaining verified information for some mothers, necessitating the inclusion of self-reported vaccination data when the timing of receipt during pregnancy was provided. In addition, they conducted an analysis to account for prior season vaccination to assess its impact on maternal vaccine effectiveness among infants born to mothers who received a vaccine intended for the previous season, potentially with antigenic mismatch, rather than the season experienced by the infant.

Unfortunately, the authors lacked information regarding maternal influenza virus infection during or after pregnancy. If infection occurred more frequently among unvaccinated pregnant individuals included in this assessment, they might have underestimated maternal effectiveness. Moreover, the authors did not collect data on influenza vaccination before conception or postpartum, which could confer some protection to infants and potentially influence the strength of the observed association.

While ongoing research is required to establish the most appropriate timing, health-care providers can offer influenza vaccination for those affordable, at any point during pregnancy to safeguard both the pregnant individual and the infant.

In conclusion, the evaluation revealed that maternal vaccination was linked to a decrease in the likelihood of influenza-related visits to the ED and hospitalisations in infants. The effectiveness of maternal vaccination was most pronounced among infants under three months old, those born to mothers vaccinated during the third trimester and in preventing influenza-related hospitalisations.

#### **4. Sildenafil may be useful in neonates with neonatal encephalopathy who had brain injury despite receiving therapeutic hypothermia.**

Source: Wintermark P, Lapointe A, Steinhorn R, Rampakakis E, Burhenne J, Meid AD, Bajraktari-Sylejmani G, Khairy M, Altit G, Adamo MT, Poccia A, Gilbert G, Saint-Martin C, Toffoli D, Vachon J, Hailu E, Colin P, & Haefeli WE. (2024). Feasibility and safety of sildenafil to repair brain injury secondary to birth asphyxia (SANE-01): A randomised, double-blind and placebo-controlled phase Ib clinical trial. *The Journal of Pediatrics*, 266, 113879. <https://doi.org/10.1016/j.jpeds.2023.113879>

Until now, infants with neonatal encephalopathy (NE) have typically received supportive care focused on maintaining homeostasis and preventing brain injury. This study marks the first randomised, double-blind and placebo-controlled clinical trial aimed at assessing the feasibility and safety of administering sildenafil orally to critically ill neonates with NE who develop brain injury despite therapeutic hypothermia (TH). In addition, the study aims to characterise the pharmacokinetics (PKs) of sildenafil in this specific

population. To mitigate risks, the researchers adopted a strategy of enrolling neonates with NE who exhibited brain injury confirmed by magnetic resonance imaging (MRI) despite undergoing TH, thus avoiding the exposure of all cooled neonates to sildenafil and instead selecting only those at highest risk. However, the need to await day-2 MRI confirmation of brain injury resulted in delayed initiation of the study medication until the 2<sup>nd</sup> or 3<sup>rd</sup> day of life. This approach aligns with preclinical research demonstrating the neuroprotective and neurorestorative effects of sildenafil, even when administered beyond the immediate aftermath of hypoxia-ischaemia. Furthermore, this design aimed to ensure that neonates with NE were in a hemodynamically stable condition, reducing the likelihood of hypotension on initiation of the sildenafil.

The study demonstrated that the treatment was both feasible and safe. Among the eight neonates, a slight decrease in blood pressure was observed in two of them after the first dose of sildenafil, but subsequent doses did not result in such effects. Only one infant required adjustment in blood pressure management. One neonate passed away after being transitioned to comfort care, a decision made by the parents due to their child's confirmed brain injury. This mortality event was determined to be unrelated to the study medication. Another neonate had elevated creatinine levels before starting the medication and received only one dose before meeting the study's discontinuation criteria. This increase in creatinine was attributed to underlying acute kidney injury secondary to NE rather than the study medication, as sildenafil is not known to be nephrotoxic. PK analysis of this patient confirmed that sildenafil did not accumulate in the body. Following an interim analysis of the first ten patients, which revealed adequate sildenafil concentrations during TH but a decrease in the days following TH completion, the data monitoring committee recommended halting the phase Ib trial and considering an open-label dose-escalation phase Ib trial.

In the study group, the newborn with increased levels of creatinine showed concentrations of sildenafil and N-desmethyl sildenafil that fell within the range observed in infants with normal kidney function. This indicates that a moderately raised creatinine level should not be used as a reason to discontinue treatment in these infants.

This phase Ib study was primarily focused on assessing safety rather than efficacy. However, the researchers examined neuroimaging findings and 18-month outcome data to evaluate long-term safety and to ensure that there were no adverse effects on long-term outcomes that would hinder further investigation. This study marks the first attempt to address the repair of damaged neonatal brains. Both groups of infants exhibited similar brain injuries on the 2<sup>nd</sup> day, with comparable Apparent Diffusion Coefficient (ADC) and Lactate/N-acetyl aspartate (Lac/NAA) ratios. However,

infants receiving sildenafil showed higher levels of cardiac troponin and creatinine, which are recognised as risk factors for more severe brain injury. Despite these risk factors, measures such as ADC, Fractional Anisotropy (FA) and Lac/NAA ratios did not show significant differences over time between the groups. Encouragingly, 71% of infants treated with sildenafil exhibited partial recovery of their injuries, fewer cystic lesions and less brain volume loss, as evidenced by quantitative assessments of the Deep Grey Matter (DGM) area progressing over time.

In contrast, infants treated with TH and given a placebo showed no signs of recovery. Traditional neuroimaging techniques used to assess the early success of TH, such as diffusion-weighted imaging, diffusion-tensor imaging and spectroscopy, may not adequately detect brain repair in the immediate postnatal period. In preclinical models of NE, sildenafil has been shown to reduce the extent of brain injury and improve myelination. Therefore, monitoring brain growth and myelination over time, processes that occur during the 1<sup>st</sup> months or years of life and can be affected by NE may offer an alternative approach to tracking potential repair processes in injured neonatal brains.

All neonates included in this study had significant brain injury at the outset. Therefore, it was anticipated that they would experience poorer neurodevelopmental outcomes compared to a general population of neonates with NE treated with TH. The combined outcome of death or survival with severe neurodevelopmental impairment at 18 months did not differ between the groups.

The ideal dose of sildenafil that maximises effectiveness while minimising adverse effects has yet to be determined for neonates with NE. Animal studies have indicated that the highest dose is most effective for recovering from brain injury. Although the maximum safe dose of sildenafil has been established for treating Persistent pulmonary hypertension of the newborn (PPHN) in neonates, it remains uncertain if the same dose is safe for neonates with NE undergoing TH, who are at risk of hypotension due to myocardial dysfunction and PPHN. Considering the reduced clearance of compounds metabolised by cytochrome 3A4 in adult patients and healthy volunteers with hypothermia, the researchers opted for a conservative sildenafil dose to prevent excessive exposure. However, whether a higher dose provides additional benefits to the brain and cardiopulmonary hemodynamics of these neonates needs further clarification.

The primary limitation of this study is its small sample size due to its phase Ib design in a high-risk population of neonates. Larger studies involving more neonates are necessary to confirm safety and eliminate potential adverse effects. Phase II and III trials with a larger participant pool are also required to establish the potential efficacy of sildenafil in the context of NE. Another limitation is the under-

representation of placebo-exposed neonates with NE in this study; nevertheless, they were representative of the extensive research on clinical management and neuroimaging of neonates with NE and brain injury despite TH. Although imaging is typically reported after TH completion, day-2 MRIs have been demonstrated to be reflective of later post-TH MRIs and equally predictive of long-term outcomes.

In summary, enteral administration of sildenafil to critically ill neonates with moderate and severe NE developing brain injury despite TH was found to be both feasible and safe. Sildenafil was effectively absorbed during TH and was well tolerated. Dose-escalation studies are now warranted to determine the optimal sildenafil dose before large-scale randomised, double-blind and placebo-controlled phase II and III clinical trials can be conducted to assess the neuroprotective/neurorestorative potential of sildenafil in the context of NE.

### **5. Maternal hyperemesis gravidarum and increased risk of respiratory morbidity in offspring's early childhood.!!**

Source: Hazan G, Sheiner E, Golan-Tripto I, Goldbart A, Sergienko R, & Wainstock T. (2024). The impact of maternal hyperemesis gravidarum on early childhood respiratory morbidity. *Pediatric Pulmonology*, 59(3), 707–714. <https://doi.org/10.1002/ppul.26817>

This study delves into how maternal hyperemesis gravidarum (HG) during pregnancy might influence respiratory issues in early childhood, considering that lung development can be affected by maternal nutrition during gestation.

Using a retrospective cohort design, data from all single-term deliveries at Soroka University Medical Centre between 1991 and 2021 were examined, excluding cases of preterm birth, perinatal mortality, multiple gestations and infants with congenital anomalies. The primary focus was on hospitalisations for respiratory conditions such as pneumonia, acute bronchiolitis, asthma or wheezing among offspring.

The findings revealed that out of 232,476 deliveries, 3227 (1.4%) mothers were diagnosed with HG. Offspring born to mothers with HG showed elevated rates of respiratory problems such as asthma, acute bronchiolitis and pneumonia. Further analysis, adjusting for various factors, demonstrated a relationship between the risk of asthma and pneumonia and the child's age.

Strengths of the study include its large sample size encompassing a wide timeframe, allowing for robust statistical analysis and increased generalizability. In addition, the use of a retrospective cohort design provides insights into long-term outcomes, and the exclusion criteria ensure a more homogeneous study population. Furthermore, the study adjusted for potential confounding factors and focused on objective outcome measures, enhancing the reliability of the findings.

However, limitations include the retrospective nature of the



design, which may introduce recall bias or missing data. Despite adjustments, residual confounding from unmeasured variables could still affect the results. In addition, findings from a single medical centre may not fully represent other populations, limiting generalizability. Lack of detailed clinical data and the inability to establish causality are also noteworthy limitations.

Future research directions stemming from this study could include prospective cohort studies to validate the observed associations and explore potential causality between maternal HG and respiratory morbidity in offspring. Longitudinal studies tracking respiratory health outcomes from infancy through childhood could provide further insight into the temporal relationship between maternal HG and respiratory issues.

In addition, mechanistic studies investigating the underlying pathways linking maternal HG with altered foetal lung development and respiratory morbidity could enhance understanding. Exploring the role of specific nutritional deficiencies or metabolic changes associated with HG in lung development and function may be warranted.

Furthermore, interventional studies focusing on improving maternal nutrition during pregnancy, particularly in women with HG, could assess whether interventions aimed at optimising maternal nutritional status mitigate the risk of respiratory morbidity in offspring. Such interventions might include dietary supplementation or nutritional counselling.

In conclusion, this research highlights a potential association between maternal HG during pregnancy and an increased likelihood of respiratory issues in early childhood. It underscores the importance of maternal nutritional status during pregnancy in influencing lung development and subsequently impacting the respiratory health of offspring.

## 6. Adjunctive Therapies in severe acute asthma are highly variable even in the USA PICUs...

Source: Rogerson CM, Hogan AH, Waldo B, White BR, Carroll CL, & Shein SL. (2024). Wide institutional variability in the treatment of paediatric critical asthma: A multicentre retrospective study. *Pediatric Critical Care Medicine: A Journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies*, 25(1), 37–46. <https://doi.org/10.1097/PCC.0000000000003347>

Children with acute severe asthma, unresponsive to initial treatments such as systemic corticosteroids and inhaled beta-agonists, often require additional therapies. The absence of national guidelines governing asthma treatments in paediatric intensive care units (PICUs) prompted the researchers to investigate the variability among institutions in utilising supplementary asthma treatments and their relationship with length of stay (LOS) and PICU utilisation.

This multicentre retrospective cohort study was conducted in several cities across the USA, utilising administrative data from the Paediatric Health Information Systems (PHISs) database. It included all inpatients aged 2–18 years admitted to a PHIS hospital between 2013 and 2021 with a diagnostic code for asthma.

The analysis covered 213,506 inpatient encounters for asthma, with 29,026 patient encounters receiving care in a PICU across 39 institutions. Significant variation was observed among institutions regarding both the quantity (ranging from 0.6 to 2.5, median: 1.7) and types (aminophylline, ipratropium, magnesium, epinephrine and terbutaline) of adjunctive asthma therapies used per encounter ( $P < 0.01$ ). Median hospital LOS varied between 1 (interquartile range: 1, 3) and 4 (3, 6) days across centres, with the proportion of asthma admissions leading to PICU admission ranging widely from 5.2% to 47.3%. Notably, the average number of adjunctive therapies per institution did not significantly correlate with hospital LOS ( $P = 0.81$ ) or the percentage of encounters resulting in PICU admission ( $P = 0.47$ ).

The authors conclude that, even in a country like the USA, the utilisation of adjunctive therapies for acute severe asthma displays significant variation among major children's hospitals and is not linked to hospital LOS or PICU admission rates. This wide variance underscores the need for standardising care through evidence-based guidelines to enhance outcomes, mitigate adverse effects and reduce hospital costs.

The significance of this study extends beyond high-income countries and holds particular relevance in low- and middle-income countries (LMICs) like Bharat. In LMICs, where healthcare resources may be scarce and access to specialised care such as PICUs can be challenging, understanding the variability in asthma treatment practices becomes even more crucial.

Given the burden of asthma in LMICs and the potential for severe cases like acute asthma to arise, optimising treatment strategies becomes paramount. By identifying patterns of adjunctive therapy use and their impact on outcomes such as LOS and PICU utilisation, this study offers valuable insights that can guide clinical practice in Bharat and similar settings.

Furthermore, the findings emphasise the importance of developing context-specific guidelines tailored to the resources and healthcare infrastructure available in LMICs. Standardising care based on evidence-based practices can help optimise outcomes, alleviate the burden on healthcare systems and enhance the quality of asthma management for children in Bharat and other LMICs.

## 7. Anti-seizure medications can be safely discontinued in certain cases of hypoxic-ischaemic encephalopathy-induced neonatal seizures.

Source: Jagadish S, Czech TM, Zimmerman MB, & Glykys J. (2024). Epilepsy incidence and developmental outcomes after early discontinuation of anti-seizure medication in neonatal hypoxic-ischaemic encephalopathy. *Pediatric Neurology*, 153, 48–55. Advanced online publication. <https://doi.org/10.1016/j.pediatrneurol.2024.01.009>

Neonatal seizures occur in approximately one to three out of every 1000 live births among term infants. The leading cause of these seizures is neonatal hypoxic-ischaemic encephalopathy (HIE), responsible for around 38% of cases. Survivors of HIE often face neurodevelopmental challenges such as cerebral palsy, learning disabilities and epilepsy. Swift identification and management of neonatal seizures are vital to preventing further brain damage and long-term developmental issues. However, the optimal duration for administering anti-seizure medication (ASM) after initial seizure control remains unclear.

Phenobarbital is the most commonly used ASM for neonatal seizures, but there's considerable variation in how long it's continued after seizures stop. Concerns about seizure recurrence lead some practitioners to extend ASM treatment for months, though clinical practice varies widely. Recently, there has been a shift toward shorter treatment durations. Neonatal seizures and their treatment both carry risks. Animal studies indicate that seizures in neonates can hinder neurogenesis and impact behaviour, seizure susceptibility and brain development. Likewise, treating neonatal seizures with medications like phenobarbital can have adverse effects, including reduced brain growth and neuronal cell death.

While recent studies and recommendations from the International League Against Epilepsy's Neonatal Task Force suggest that shorter treatment durations pose no significant risk of seizure recurrence, there is still insufficient data to establish evidence-based guidelines for treatment duration based on neonatal health status.

In this study, the authors conducted a retrospective chart review at their institution to investigate whether discontinuing ASM early in neonates with HIE-induced seizures correlates with a higher likelihood of postnatal epilepsy and impaired developmental outcomes at 3, 6 and 12 months of age.

The authors conducted a single institution retrospective observational cohort study, a review of medical records for all neonates admitted to their neonatal intensive care unit (NICU) between January 2008 and February 2021, diagnosed with HIE, treated with therapeutic hypothermia and experienced seizures. The patient cohort was identified from their database. Among 215 neonates diagnosed with HIE and treated with therapeutic hypothermia during this period, 146 were excluded (21 neonatal deaths and 125 without seizure development, constituting 58%). Thus, a total of 69 neonates who developed seizures met the study

criteria. These neonates were divided into two groups based on whether ASM was continued at discharge ( $n = 41$ , 59%) or discontinued before discharge ( $n = 28$ , 41%).

The authors observed that discontinuing ASM at discharge was not associated with a higher risk of postneonatal epilepsy by 12 months of age. However, patients in whom ASM was continued demonstrated poorer developmental outcomes at 12 months compared to those in whom ASM was discontinued. Their findings suggest that early discontinuation of ASM before discharge is not linked to an increased risk of postneonatal epilepsy or developmental delay up to the age of 12 months in neonates with HIE and acute symptomatic seizures. The authors recommend that providers consider EEG background, duration of seizure activity and brain magnetic resonance imaging findings when deciding to discontinue ASM before discharge from the NICU, aiming to minimise unnecessary exposure to potentially neurotoxic ASM.

By providing some evidence supporting the safe discontinuation of ASM in certain cases of HIE-induced neonatal seizures, this study offers valuable insights that can inform clinical practice and improve outcomes for neonates in Bharat and similar settings.

### **8. Multisystem inflammatory syndrome in children may not have long-term cardiac sequelae.**

Source: Karagözlü S, Ramoğlu MG, Bayram Ö, Bakhtiyarzada J, Aydın A, Yılmaz MM, Murt B, Özkan Eİnceli HB, Gurbanov A, Şükriye Y, Demir B, Özdemir H, Çiftçi E, Kendirli T, Uçar T, Fitoz ÖS, & Tutar E. (2024). Cardiovascular manifestations and cardiac magnetic resonance follow-up of multisystem inflammatory syndrome in children. *Cardiology in the Young*, 34(2), 291–300. <https://doi.org/10.1017/S1047951123001348>

This research aimed to assess the cardiovascular issues and monitoring of multisystem inflammatory syndrome in children (MIS-C) and to establish a connection between echocardiographic and cardiac magnetic resonance imaging findings.

Forty-four children diagnosed with MIS-C and cardiac involvement were part of this observational descriptive study. MIS-C diagnosis followed the criteria set by the Centres for Disease Control and Prevention. Clinical, laboratory, electrocardiographic and echocardiographic findings were evaluated at diagnosis and during follow-up.

Left ventricular systolic dysfunction, valvulitis and pericardial effusion were common echocardiographic findings on admission. Cardiac magnetic resonance was performed on 28 cases. Higher levels of N-terminal pro-B-type natriuretic peptide were associated with the need for inotropic support and paediatric intensive care unit admission. One-year follow-up imaging was conducted for all cases

with abnormal initial cardiac magnetic resonance findings. The study included 44 patients (56.8% male) mean age of  $8.5 \pm 4.8$  years. High-sensitivity cardiac troponin T showed a significant positive correlation with N-terminal pro-B-type natriuretic peptide. Most cases had electrocardiographic (77%) and echocardiographic (70%) abnormalities. Left ventricular systolic dysfunction and pericardial effusion were common on admission. Some cases showed cardiac magnetic resonance findings suggestive of myocardial inflammation and pericardial effusion.

Follow-up cardiac magnetic resonance scans showed normalisation in all cases. Despite the limited number of cases with cardiac magnetic resonance findings, it was observed that even those with normal echocardiograms could have abnormal cardiac magnetic resonance findings, such as fibrosis and oedema. Thus, cardiac magnetic resonance might be useful, particularly for evaluating patients interested in sports participation.

Most cardiac abnormalities resolved, indicating that while myocardial involvement may occur during acute disease, MIS-C typically does not cause significant damage during one year of follow-up. Cardiac magnetic resonance is valuable for assessing myocardial involvement in MIS-C cases.

The study's main limitation was its relatively small sample size, and technical difficulties prevented cardiac magnetic resonance in some cases due to patient refusal or concerns about sedation. One case with late gadolinium enhancement on cardiac magnetic resonance at 18 months was excluded

from statistical analyses, which focused on initial cardiac magnetic resonance findings.

#### **Ethical approval**

The Institutional Review Board approval is not required.

#### **Declaration of patient consent**

Patient' consent was not required as there are no patients in this study.

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Nil.

#### **Conflicts of interest**

Vikram Sakleshpur Kumar is one of the State Advisory Members of the journal.

#### **Use of artificial intelligence (AI)-assisted technology for manuscript preparation**

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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