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VISUAL SNOW SYNDROME

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CONTENTS

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Congratulations to Our New Associate Editor

Recently *The Florida Pediatrician Journal* Editorial Board unanimously recommended Rani S. Gereige, MD, MPH, FAAP, to be elected as the journal's Associate Editor. Rani is well known to many pediatricians and pediatric specialists in Florida from his leadership roles in the FCAAP as well as the AAP to his role as the Director of Medical Education at Nicklaus Children's Hospital. In his capacity as a longstanding member of the journal Editorial Board, his expertise in multiple areas, including postgraduate medical education (he is an old hat at accreditation reviews), school health, primary care sports medicine, public health initiatives (note his master's degree in public health in maternal and child health from USF). Evidence-based medicine, pediatric oral health, pediatric sports medicine, and children with special health care needs have been invaluable to *The Florida Pediatrician Journal*. He is additionally an ex-pediatric chief resident and a graduate of the USF Leadership Institute, explaining his natural gravitation toward important leadership roles at local, state, and national levels.

Editorial work is not new for Rani. In addition to his many publications in peer-reviewed journals (27 at last count in PubMed), Rani is a member of the Editorial Board of *Pediatrics in Review* as Associate Editor for CME, and he serves as a manuscript reviewer for several other peer-reviewed journals. Rani currently holds the position of Clinical Professor, Department of Pediatrics, Florida International University Herbert Wertheim College of Medicine.

The members of *The Florida Pediatrician Journal* Editorial Board, its staff, and I look forward to working closely with Rani on our new journal initiatives, one of which is codifying a system of outside expert reviewers. This sounds simple enough, but it is far from being an easy task. Interestingly, the lead article in this issue of the journal concerning visual snow syndrome served as an additional catalyst for Rani and the Board's Editor Emeritus, Dr. Mobeen Rathore, to brainstorm enhancing our review processes with established experts outside the board at our last meeting. None of us were familiar enough with this fascinating condition to serve as an expert reviewer of the manuscript. This led to the Board's new requirement to ask manuscript authors to recommend expert reviewers (which we will vet) with their submissions and for a **call for expert reviewer volunteers**. If you are interested in reviewing 1-2 manuscripts per year for our journal, please contact me (michaeljmd156@gmail.com), Rani (rsgere@aol.com), or our journal Publication Coordinator, John Horne (publications@FCAAP.org). Please include your preferred area of expertise and a copy of your Curriculum Vitae.

Michael J. Muszynski, MD FAAP FPIDS
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Why We Should Remember that Everything Could be Tuberculosis

Submitted by Wendy Thanassi MD, MA; Senior Medical Director, Infectious Diseases, QIAGEN

Young adult author and YouTube guru John Green unfolds his nonfiction book Everything is Tuberculosis through the eyes of teenager Henry Reider. As the book progresses, we see the toll that tuberculosis (TB) takes on children, families, communities and nations. In the US, our clinicians and public health entities have done a remarkable job minimizing TB disease case numbers. Nonetheless, there are approximately 13 million people in the US with TB infection (TBI), and rates are on the rise.

Children are particularly vulnerable to acquiring TBI, and when it progresses to active TB disease (TBD) it manifests differently than in adults. Acquisition can occur when infants are held close to adult mouths, so for at least the first year, and concurrently with weaker immune systems, children can have disproportionately high exposures.

TB is tricky to recognize and to treat in children; the diagnosis starts with suspicion and identification of the infection. Families from medium and highly endemic countries confer higher than usual risk for TB exposure to children. These exposures can come from immediate or extended family members, community members such as caregivers and religious groups, and from travel to countries of origin.

Diagnostics for TB infection have advanced significantly over the past 20 years, after nearly 100 years of relying solely on the tuberculin skin test. Interferon-gamma release assays (IGRAs) are whole blood tests that precisely measure the amount of interferon gamma that is released after exposure to TB-specific antigens. The 2024 AAP guidelines now recommend the use of IGRAs for all ages. QuantiFERON-TB Gold Plus is one of the two IGRAs approved in the US, offering 94% sensitivity and 97% specificity for detecting latent infection (1).

If the TBI diagnosis is made in children, particular attention should be paid to the possibility of extrapulmonary (with or without concurrent pulmonary) TB disease. For this reason, chest radiography and sputum testing are not enough to rule out disseminated illness.

Treatment regimens vary from short courses of antibiotics to prevent progression, to multi-drug regimens that last many months – or even years. Mortality from active TB disease in the US is surprisingly high at over 5%, so implementing TB preventive therapy when a TBI diagnosis is made is a critical part of the care cascade.

For more information, Dr. Lindsay Cameron has a free on-demand educational session on pediatric tuberculosis. To operationalize the AAP's 2024 change, which extends IGRA use to children of all ages, QIAGEN offers a pediatric TB testing e-book that distills when to screen, which test to choose and how to counsel families. It also includes algorithms, downloadable slides, checklists, case vignettes and links to AAP/CDC information for physician or family education.

With pediatricians considering tuberculosis as a possible diagnosis, testing with QFT and treating infection with short-course antibiotics, we will all get closer to its elimination. Perhaps then best-selling books about children with TB will be a thing of the past.

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1. QuantiFERON-TB Gold Plus – world's leading tuberculosis blood test https://www.qiagen.com/tb-testing/what-is-quantiferon (Accessed December 12, 2025)

CASE REPORT

Visual Snow Syndrome: A Pediatric Case Report with Literature Review

James J. Burns, MD, MPH, FAAP[1]; Swetha Reddy Banswada, MD[2]; Anayah Sarkar, MD[3]

[1]Florida State University, College of Medicine; Nemours Children's Health

[2]Pediatric Resident, University of Florida, Pensacola

[3]Pediatrician, University of Florida, Pensacola

ABSTRACT

Visual snow syndrome is a benign but underdiagnosed debilitating neurological disorder characterized by a continuous visual disturbance that occupies the entire visual field. It is often described as many tiny flickering dots that resemble the noise of a detuned analog television. Individuals with "visual snow," as it has also come to be referred to, often experience symptoms like photophobia, tinnitus, migraines, and migraine auras, suggesting a possible relationship between visual snow and migraine disorders. Visual snow is considered its own clinical entity despite the association. We present a case involving a 15-year-old male with attention deficit hyperactivity disorder who presents with visual disturbances, auditory phenomena, and confusion for three days. The patient's symptoms are complex, involving both visual (static vision, blurred vision, seeing shapes and shadows) and auditory (ringing in his ears and hearing laughs) disturbances, as well as a report of disorientation and confusion. Pediatric cases of visual snow syndrome are relatively rare, mostly due to the complexity of diagnosing and the lack of treatment options. Pediatricians should be able to describe and analyze the clinical presentation, diagnosis, and management of the condition, with an emphasis on its impact on the child's vision and overall health. Treatment for visual snow syndrome is important for these individuals, perhaps even more so in young children and adolescents, for several reasons. There is the possible psychological effect of having such unusual and abnormal, undiagnosed visual percepts. Some adult patients with visual snow syndrome indicated their initial childhood reservation about confiding their symptoms to a friend or family member, fearing disbelief and even possible ridicule.

CASE PRESENTATION

A 15-year-old male with a known history of attention deficit hyperactivity disorder (ADHD) presented to the emergency department with a 3-day history of visual disturbances, auditory phenomena, and confusion. The symptoms began suddenly during school and have since persisted. The patient described experiencing static vision, blurred vision, and seeing shapes on the floor and shadows on the walls, in addition to tinnitus (ringing in the ears). He also experienced confusion and disorientation, including a period of amnesia where he required assistance from his sister to remain oriented. The patient denied any recent head trauma, significant physical injury, or changes in his usual school and home routine. Notably, his initial eye pain and pressure resolved, but the visual disturbances and

tinnitus continued. He denied other symptoms, including headaches, dizziness, imbalance, fever, nausea, vomiting, or neck pain, and did not experience diplopia, nystagmus, or any recent trauma. The patient has a history of anxiety, with daily anxiety and occasional panic attacks, including one during school orientation. His family history is significant for bipolar disorder, anxiety, and post-traumatic stress disorder. He has no history of self-harm, suicidal ideation, or substance use. His developmental history includes a period of bullying from grades 3 to 8, but he has been socially well-adjusted since then and is in a stable relationship, though not sexually active. He has been on Aptensio XR® (methylphenidate hydrochloride extended-release) 60 mg daily for ADHD for several years with no recent dose changes or misuse.

Physical examination was unremarkable except for his perception of static images. Laboratory workup, including complete blood count, comprehensive metabolic panel, and a urine drug screen, was normal. Psychiatry consultation recommended a neurology and ophthalmology evaluation given the patient's stable psychiatric status. Pediatric neurology and ophthalmology consultations followed, and imaging studies (CT head, MRA brain, and MRI of the brain, face, neck, and orbits) were normal. No further neurological follow-up was necessary. Ophthalmology evaluation two months later revealed bilateral eye astigmatism, for which glasses were prescribed. The final diagnosis by ophthalmology was visual snow syndrome (VSS), and outpatient follow-up with ophthalmology was recommended.

DISCUSSION

VSS was first discovered and reported in the Transactions of the American Ophthalmological Society by Frank D. Carroll in 1944, and VSS was discovered to be its own medical condition separate from migraine/migraine aura in 1995 by Dr. Grant Liu.[1]

Patients with "visual snow" report continuous tiny dots in the entire visual field similar to the "noise" on the screen of an analog television.[2] As these patients frequently have migraine as a comorbidity, with ophthalmological, neurological, and radiological studies being normal, they are offered various diagnoses, including persistent migraine aura, post-hallucinogen flashback, or psychogenic disorder.[3] At this time, VSS is considered a separate clinical entity as it does not respond to migraine treatments.[3]

It is currently unknown how many patients suffer from visual snow worldwide. Adults with VSS may have reservations about confiding their symptoms, fearing disbelief, dismissal, and even ridicule.[4] Pediatric cases are often not reported. Available data tell us that there is possibly a higher prevalence of the disease in males and that the average age of affected people is relatively young.[5]

Thankfully, scientific understanding of VSS is growing. However, major challenges remain, including the subjective nature of the disease, its overlap with migraine, and the lack of quantifiable outcome measures, which are necessary for clinical trials. In this context, refined perceptual assessment, objective electrophysiological parameters, as well as advanced functional brain imaging studies, are promising tools in the investigative pipeline.[6]

Electrophysiological studies have revealed cortical hyperresponsivity in visual brain areas. Imaging studies have demonstrated microstructural and functional connectivity alterations in multiple cortical and thalamic regions, and in glutamatergic and serotonergic neurotransmission.[7]

The deficiency of knowledge on the basic biology of VSS has caused a general lack of effective treatment strategies for most affected people. Drugs like migraine preventives, antidepressants, or pain relievers have shown inconsistent results.[6-8] Lamotrigine has had some positive effects in some people but lacks robust evidence from clinical trials. Objective documentation of eye movement dysfunctions and advanced brain imaging studies are needed to determine the neural mechanisms underlying VSS. Two promising ophthalmologic therapeutic approaches have emerged, but larger studies are needed to confirm their efficacy. Chromatic tint therapy uses colored filters that help reduce the perception of visual snow, palinopsia, photopsia, and light sensitivity. Oculomotor-based therapy techniques targeting eye movement and saccadic tracking have been shown to reduce palinopsia and improve visual clarity.[8]

Psychiatric comorbidities seem to be quite common in VSS, especially affective disorders such as anxiety, up to 50%, and depression, up to 58%.[9] The larger concern is the debilitating nature of this chronic illness and the consequences on patients' coping and mental health. VSS patients showed high rates of anxiety and depression, depersonalization, fatigue, and poor sleep, which significantly impacted quality of life.[9,10]

CONCLUSION

VSS is a benign but significant disorder that can affect pediatric patients and can be associated easily with confounding comorbidities. Although its pathophysiology is not fully understood, recent advances in neuroimaging and electrophysiological studies have provided new insights. Despite the challenges in diagnosis and treatment, management strategies such as chromatic tint therapy and oculomotor-based interventions offer hope for improving the quality of life for affected individuals.[2] Pediatricians and healthcare providers should remain vigilant in identifying VSS and collaborate with neurologists, ophthalmologists, and psychiatrists to ensure a comprehensive and multidisciplinary approach to patient care. As psychiatric issues such as anxiety in our patient are already a concern, psychological support appears essential in medical management.

Author(s) Disclosure Statement: Authors report no conflicts of interest.

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QI RESEARCH

Safe Sleep Initiative: Promoting Newborn Safety in the Pediatric Emergency Department

Lisa M. Pace, MD; Todd Wylie, MD; Phyllis Hendry, MD; Jennifer Fishe, MD
University of Florida College of Medicine, Jacksonville

ABSTRACT

The "Safe Sleep Initiative" at the University of Florida Health Jacksonville aims to promote safe sleep practices for newborns in the pediatric emergency department through the utilization of educational surveys, informative videos, and visually engaging posters. This multifaceted approach seeks to educate parents, caregivers, and staff on the importance of safe sleep environments for infants. With the goal of video-interactive surveys, educational videos, and eye-catching posters, this initiative strives to increase awareness and adherence to safe sleep guidelines, ensuring the well-being of newborns in the pediatric emergency department setting and at home.

INTRODUCTION

Sleep-related infant mortality remains a significant public health concern in the United States. In 2020, approximately 3,389 infant deaths were attributed to sudden unexpected infant death (SUID), which encompasses sudden infant death syndrome (SIDS), accidental suffocation and strangulation in bed (ASSB), and other ill-defined causes. Among these, SIDS accounted for 41% of deaths, ASSB for 27%, and unknown causes for 32%.[1]

Despite longstanding recommendations from the American Academy of Pediatrics (AAP) advocating for safe sleep environments—including supine positioning, firm sl eep surfaces, and avoidance of soft bedding—adherence among caregivers remains suboptimal. Recent national survey data indicate that only 55% of infants are consistently placed in the supine sleep position, and nearly 40% of caregivers report engaging in bed-sharing practices.[2] These behaviors contribute to ongoing disparities in infant mortality rates and underscore the importance of clinician-driven education.

Healthcare providers are uniquely positioned to influence parental behaviors through anticipatory guidance and the consistent delivery of evidence-based recommendations. This manuscript examines current epidemiological trends in sleep-related infant deaths, evaluates the effectiveness of clinician-led educational interventions, and explores strategies to improve caregiver compliance. By strengthening provider communication and aligning clinical practice with public health messaging, clinicians can play a critical role in reducing preventable sleep-related infant mortality. The objective of this educational initiative was to raise awareness amongst clinicians and parents/caregivers of safe sleep practices.

METHODS

This prospective educational study was conducted in the pediatric emergency department (PED) at the University of Florida Health Jacksonville (UF Health) in Duval County, Florida, from July 2024 to July 2025. The project aimed to enhance safe sleep practices among caregivers of infants under one year of age and UF Health staff (attending physicians, resident physicians, nurses, and technicians) within the PED by implementing a multifaceted educational program.

Intervention Components

1. Visual Educational Materials: Posters illustrating the AAP's safe sleep recommendations—placing infants on their backs, in a crib, and without soft bedding—were displayed prominently in PED examination rooms and waiting areas. Each poster included a Quick Response (QR) code linking to additional resources on safe sleep practices. All resources were provided in both English and Spanish.
2. Informational Postcards: Caregivers received postcards containing QR codes that directed them to videos demonstrating safe sleep environments and presenting statistics specific to SIDS in Duval County. These materials aimed to provide accessible and localized information to caregivers. All resources were provided in both English and Spanish.
3. Educational Video: An evidence-based educational video was utilized from the National Institutes of Health and made available to both caregivers and PED staff. The footage covered key aspects of safe sleep practices, including the importance of placing infants on their backs to sleep, using a firm sleep surface, and avoiding bed-sharing. The video was accessible via QR codes on the posters and postcards for staff and families.

Participants

The study included two primary participant groups:

1. Caregivers - Individuals who were the primary caregivers of infants under one year of age presenting to the PED during the study period.
2. PED staff - Attending physicians, resident physicians, nurses, and technicians involved in the care of infants in the PED.

Data Collection

Both caregivers and PED staff were invited to complete pre-intervention surveys assessing their baseline knowledge and attitudes regarding safe sleep practices. Each group was shown posters, provided with postcards with safe sleep resources, and watched the National Institutes of Health NIH approved educational video demonstrating safe sleep practices. Participants then completed post-intervention surveys to evaluate changes in knowledge and comprehension. Surveys included multiple-choice questions covering topics such as recommended sleep positions, appropriate sleep environments, and awareness of SIDS risk factors.

Data Analysis

We performed descriptive statistics, including frequencies, means, and medians, as appropriate, for survey responses and demographics of respondents. We compared before and after responses for each group (i.e., caregiver or PED staff) using the student's t-test.

Ethical Considerations

The study protocol was reviewed and approved by the University of Florida - Jacksonville Institutional Review Board as exempt human subjects research (UF IRB registration #ET00042844). Participation was voluntary, and informed consent was obtained from all participants prior to enrollment. Data confidentiality and participant anonymity were maintained throughout the study.

This multifaceted educational approach aimed to reinforce safe sleep practices among caregivers and healthcare providers, thereby contributing to the reduction of sleep-related infant deaths in Duval County.

RESULTS

Demographics

A total of 20 caregivers of infants under 12 months of age and 60 pediatric emergency medicine faculty members, including residents, attending physicians, nurses, and technicians, participated in the study. Further demographic data, such as age, ethnicity, race, and gender, were not obtained during this study.

Caregiver Knowledge and Understanding

Pre-intervention surveys indicated that 95% of caregivers correctly identified the supine position as the safest for infant sleep. Post-intervention, this remained at 95%. Awareness of the importance of a firm sleep surface rose from 75% to 85% ($P = 0.4350$). Although not statistically significant, it is valuable to note that 10% of caregivers who previously practiced co-sleeping reported an increased awareness that co-sleeping should be avoided. Furthermore, post-intervention, an additional 10% of caregivers recognized

the importance of using a firm mattress for infant sleep, and a further 5% acknowledged that the crib should be free of other items, such as toys, pillows, or loose bedding.

While future behavioral intentions were not surveyed during this study, many caregivers self-expressed that they knew someone who had a child affected by SIDS and that they felt the interventions were necessary. Additionally, caregivers mentioned that the educational video was helpful and that the QR code-linked resources were easy to access.

Faculty Knowledge and Confidence

Among faculty, knowledge of the AAP safe sleep guidelines, there was a statistically significant improvement in PED staff knowledge regarding the association between overheating and the risk of SIDS. As seen in the table below, there was a 28.4% increase in correct responses post-intervention ($p < 0.001$). Among all PED staff, there was 100% accuracy when identifying that infants should not have pillows in the crib, should not co-sleep with another individual, and should not use blankets or comforters. Analysis of parent and caregiver survey data further revealed that all respondents correctly understood that infants should be placed on their backs to sleep, may sleep in the same room as an adult, and should sleep in a separate crib.

Knowledge regarding the protective role of pacifier use in reducing the risk of SIDS was limited among both PED staff and caregivers. Only 55% of faculty and 60% of caregivers answered correctly on the pre-intervention survey.

Engagement with Educational Materials

After implementing posters, postcards, and educational videos, PED staff reported that they felt the information was easy to distribute to caregivers. Feedback was overall positive, and users found the materials helpful in understanding and implementing safe sleep practices.

Summary

The implementation of visual aids, educational videos, and QR code-linked resources in the pediatric emergency department significantly enhanced both caregiver and faculty knowledge and confidence regarding safe sleep practices. The intervention also positively influenced caregivers, suggesting that such multifaceted educational approaches can be effective in promoting safe sleep environments for infants.

DISCUSSION

The reviewed interventions demonstrate that targeted education, whether through digital platforms, community engagement, or hospital initiatives, can significantly improve adherence to safe sleep practices. Hospital-led projects underscore the importance of institutional commitment to safe sleep education, though identifying the most impactful components remains a challenge.[4]

As demonstrated in Table 1, there was a statistically significant improvement in PED staff knowledge regarding the association between overheating and the risk of SIDS. Specifically, there was a 28.4% increase in correct responses post-intervention ($p < 0.001$). Additionally, all PED staff participants accurately identified that infants should not have pillows in the crib, should not co-sleep with another individual, and should not use blankets or comforters—practices aligned with current safe sleep recommendations. Analysis of parent and caregiver survey data (Table 2) further revealed that all respondents correctly understood that infants should be placed on their backs to sleep, may sleep in the same room as an adult, and should sleep in a separate crib.

Question (Reference Answer)	Pre	Post	P Value
Babies should be placed to sleep on their back (YES)	59/60	55/55	P = 0.3335
When the baby is sleeping, there should be a pillow in the crib for them to rest their head on (NO)	60/60	55/55	Not applicable
At night, the baby can sleep in the same room as a parent or another adult (YES)	46/60	43/55	P = 0.8485
The baby should sleep in the same bed as the parent or with someone else (NO)	60/60	55/55	Not applicable
The mattress in the crib should be firm (YES)	58/60	55/55	P = 0.1695
It is okay to have a stuffed animal in the crib with the baby (NO)	57/60	54/55	P = 0.3510
Heavy blanket, comforter, or bedspreads should be in the crib with the baby (NO)	60/60	55/55	Not applicable
It is beneficial to give the baby a pacifier when putting them down for sleep (YES)	33/60	31/55	P = 0.8890
Being too warm is a risk factor for SIDS (YES)	43/60	55/55	P < 0.0001

Table 1: Pediatric Emergency Department Staff Survey

Question (Reference answer)	Pre	Post	P Value
Babies should be placed to sleep on their back (YES)	19/20	19/20	Not applicable
Does the baby sleep in the same room as you or another adult? (YES)	20/20	20/20	Not applicable
Does your baby sleep in a crib? (YES)	17/20	17/20	Not applicable
If yes, to Question 3: Is the mattress in the crib firm? (YES)	15/20*	17/20*	P = 0.4350
If yes, to Question 3: Is there anything else in the crib with the baby? (NO)	16/20**	17/20**	P = 0.6812
Does your baby sleep in the same bed with you or someone else? (NO)	15/20	17/20	P = 0.4350
Do you give your baby a pacifier to sleep? (YES)	12/20	11/20	P = 0.7521

Table 2: Caregiver Survey

*** Counted non-answers as NOT YES***
****Counted non-answers as NOT NO***

Although the findings were not statistically significant, it is noteworthy that 10% of caregivers who previously practiced co-sleeping reported an increased awareness that co-sleeping should be avoided. Furthermore, after receiving educational materials, an additional 10% of caregivers recognized the importance of using a firm mattress for infant sleep, and a further 5% acknowledged that the crib should be free of other items, such as toys, pillows, or loose bedding.

Knowledge regarding the protective role of pacifier use in reducing the risk of SIDS was limited among both PED staff and caregivers. Only 55% of faculty and 60% of caregivers correctly identified pacifier use as a protective factor when placing an infant to sleep, as indicated by responses on the pre-intervention survey. This data suggests an area where further education may be warranted.

Per the AAP guidelines, a pacifier should be offered at nap time and bedtime to reduce the risk of SIDS.[7] While the exact mechanism remains unclear, hypotheses suggest that pacifier use may promote airway patency, enhance autonomic control, or increase arousability during sleep.[5,6] These findings support the inclusion of pacifier use in safe sleep education initiatives aimed at reducing SIDS incidence. For breastfed infants, pacifier introduction should be delayed until breastfeeding is well established, typically around 3 to 4 weeks of age.[7] Caregivers should not force pacifier use if the infant refuses it, and if the pacifier falls out during sleep, it does not need to be replaced.[7] To ensure safety, pacifiers should not be attached to the infant with cords or clips, and they should be kept clean and replaced regularly.[7]

Safe sleep education is typically introduced to caregivers shortly after birth and prior to discharge from the newborn nursery. Responses from the pre-intervention surveys suggested that families did receive this information and did implement many meaningful safe sleep practices once they had returned home. Examples of this include knowing that babies should be placed on their backs to sleep, crib mattresses should be firm, and cribs should be empty without blankets, comforters, or stuffed animals. Given the high levels of stress and information overload experienced by families during the immediate postpartum period, the retention and application of safe sleep practices may be limited at that time. Therefore, reinforcing this education in the pediatric emergency department—when families are more settled and receptive—serves as a critical opportunity to enhance understanding and adherence to safe sleep guidelines.

Despite these successes, barriers persist. Cultural norms, misinformation, and socioeconomic constraints can hinder the adoption of safe sleep practices.[3,4] For instance, some caregivers may prioritize traditional practices or lack access to safe sleep environments. Therefore, interventions must be culturally sensitive and address the specific needs of diverse populations. Additionally, ongoing support and reinforcement of safe sleep messages are crucial to sustain behavior change.[3,4]

The results of our educational initiative in the pediatric emergency department at the University of Florida Health Jacksonville demonstrate promising improvements in staff knowledge and caregiver receptivity to safe sleep practices for infants. Staff showed a statistically significant increase in correct responses regarding the association between overheating and the risk of SIDS. Caregivers responded positively to the delivered educational materials, including QR-code links and videos, indicating that hospital-based reinforcement of safe-sleep messaging is feasible even in a busy emergency-department context.

Several factors limit the scope and generalizability of our findings. First, the caregiver cohort consisted of only 20 participants, and the staff cohort consisted of 60 participants, yielding small sample sizes that reduce statistical power. Second, this study was conducted in a single institution within one geographic region and health-system context, which may limit the applicability of results to other settings, populations, or institutional cultures. Third, because baseline knowledge among caregivers was already high for some items (e.g., 95% correctly identified supine positioning pre-intervention), a ceiling effect may have limited the measurable improvement. Finally, we did not collect detailed demographic or contextual information (e.g., caregiver socioeconomic status, ethnicity, or home

sleep environment), limiting our ability to explore subgroup differences or contextual moderators of the intervention effect.

Given these limitations, future research should aim to engage larger sample sizes across multiple institutions, potentially include longitudinal follow-up assessing actual sleep practices and infant safety outcomes, and incorporate detailed demographic and contextual data.

CONCLUSION

Promoting safe sleep practices among caregivers of infants under one year requires a multifaceted approach. Community-based programs and hospital-led initiatives each play a vital role in educating caregivers and reducing the risk of sleep-related infant deaths. To enhance the effectiveness of these interventions, future efforts should focus on cultural competence, accessibility, and continuous engagement with caregivers. By addressing the diverse factors influencing caregiver behavior, we can work towards ensuring safer sleep environments for all infants.

Conflict of Interest Disclosures (includes financial disclosures): All authors have no conflicts of interest to disclose.

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REVIEW ARTICLE

Autism Spectrum Disorder (ASD) and Its Comorbidities: Diagnosing and Management for Primary Care Providers

Ruchita Kachru, MD[1]; Mary Valletta, MD[1]; Bilal Khodr, MD[1]; David Matsibekker, MD[1]; Sanjeev Tuli, MD[2]

[1]Department of Pediatrics, University of Florida, Gainesville, FL

[2]Department of Pediatrics, University of Texas Medical Branch, Galveston, TX

INTRODUCTION

Autism Spectrum Disorder (ASD) is a complex and lifelong neurodevelopmental condition that affects individuals in varied and often profound ways. Characterized by impairments in social communication and restricted, repetitive behaviors, ASD is frequently accompanied by a range of comorbid conditions that exacerbate its impact on individuals and families. The increasing prevalence of ASD, along with the growing recognition of its comorbidities, underscores the need for primary care providers (PCPs) to take a more active role in diagnosing and managing the disorder.

Recent studies indicate that the prevalence of ASD has risen dramatically, with the Centers for Disease Control and Prevention (CDC) estimating that 1 in 36 children in the United States have ASD, according to 2020 data from the Autism and Developmental Disabilities Monitoring (ADDM) Network.[1] This represents an increase from previous estimates, reflecting not only a true rise in cases but also improved awareness, better screening, and expanded access to diagnostic services. The male-to-female ratio for ASD remains approximately 3.7 to 1, with boys being more frequently diagnosed than girls.[2,3]

Recent data also show a shift in the racial and ethnic distribution of ASD diagnoses. Historically underserved communities, particularly Asian Pacific Islander populations, have seen higher rates of ASD diagnoses in part due to improved screening practices and greater access to healthcare services. However, significant regional disparities in access to care remain, particularly in rural areas. For instance, a 2026 analysis by Twelve Oaks Psychiatry of Florida Department of Health licensure data found that 18 of Florida's 67 counties have no psychiatrist.[4] This shortage of specialists places additional pressure on primary care providers to manage both the primary disorder and its comorbidities.

In addition to the core symptoms of ASD, comorbid conditions such as attention-deficit/hyperactivity disorder (ADHD), anxiety, epilepsy, and learning disabilities are highly prevalent and can significantly affect the quality of life of individuals with ASD. Understanding these comorbidities, along with current diagnostic and therapeutic strategies, is essential for PCPs to provide comprehensive care to these patients.

UNDERSTANDING ASD

ASD is a neurodevelopmental disorder that impacts communication, social interaction, and behavior. It manifests on a continuum, with individuals exhibiting a broad range of severity in symptoms. The diagnosis of ASD is based on the criteria in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). These criteria emphasize two primary domains:

1. Persistent deficits in social communication and social interaction: Difficulty with verbal and nonverbal communication, challenges in initiating and maintaining conversations, and an inability to engage in reciprocal social interactions.
2. Restricted, repetitive patterns of behavior, interests, or activities: Repetitive movements, rigid adherence to routines, intense focus on specific interests, and sensory sensitivities.

The presentation of ASD can vary widely among individuals, making diagnosis challenging. In some cases, ASD may present in a highly visible manner, such as when a child avoids eye contact or exhibits repetitive behaviors. In others, symptoms may be subtle and harder to identify, making early diagnosis and intervention critical.

DIAGNOSTIC CRITERIA AND DSM-5 CHANGES

The DSM-5 consolidated several disorders from the DSM-IV, including Asperger's Syndrome, Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS), and Childhood Disintegrative Disorder, under the umbrella of ASD. The DSM-5 also introduced new guidance on the role of sensory processing issues, which are common but often overlooked in clinical practice.

While the DSM-5 provides a standardized diagnostic framework, the heterogeneity of ASD means that no single clinical presentation fits all individuals. Children with ASD may exhibit a wide range of intellectual and language abilities, from nonverbal children with profound intellectual disabilities to high-functioning individuals with above-average intelligence.[5]

Screening Domain	Tool(s)
Developmental screening	M-CHAT, ASQ, SCQ, SWYC
Anxiety screening	SCARED, GAD-7
Depression screening	PHQ-9
Suicide risk screening	CSRS, ASQ
Internalizing/Externalizing behavior	PSC-17
Aggression screening	MOAS

Table 1: Common behavioral and mental health screeners used in primary care pediatrics

Footnotes (Abbreviations):
- *M-CHAT = Modified Checklist for Autism in Toddlers*
- *ASQ (developmental) = Ages & Stages Questionnaires*
- *ASQ (suicide) = Ask Suicide-Screening Questions*
- *SCQ = Social Communication Questionnaire*
- *SWYC = Survey of Well-being of Young Children*
- *SCARED = Screen for Child Anxiety Related Emotional Disorders*
- *GAD-7 = Generalized Anxiety Disorder, 7-item scale*
- *PHQ-9 = Patient Health Questionnaire, 9-item scale*
- *CSRS = Columbia Suicide Severity Rating Scale (often written as C-SSRS)*
- *PSC-17 = Pediatric Symptom Checklist–17*
- *MOAS = Modified Overt Aggression Scale*

COMORBIDITIES IN AUTISM SPECTRUM DISORDER

Comorbidities are defined as conditions that exist simultaneously with ASD, and they can significantly complicate diagnosis and treatment. The Swedish twin study, which interviewed 9-year-old twins born between 1992 and 2001, found that 50% of children with ASD had four or more co-occurring psychiatric disorders.[6] A more recent cohort study involving 42,564 children with ASD found that 74% of these children had at least one comorbidity, and 50% had more than four coexisting conditions.[7] The most common comorbidities in children with ASD in the analysis included:

- Developmental coordination disorders: 87-88%
- Sensory processing disorder: 70-90%
- Sleep-wake problems: 36-50%
- ADHD: 28-46%
- Anxiety: 30-39%
- Intellectual disabilities: 26-41%
- Motor problems: 19-64%
- Feeding and eating disorders: 20-46%
- Disruptive behavior: 21-36%
- Depressive disorders: 15-21%
- Specific learning disorders: 8-20%
- Seizure disorders (epilepsy): 20-30%

Each of these comorbidities poses unique challenges and requires specific management strategies. Notably, children with ASD experience a higher burden of medical and psychiatric comorbidities compared to their neurotypical peers. This necessitates regular screening (Table 1) and individualized treatment plans.[8]

COMMON COMORBIDITIES IN ASD AND CURRENT MANAGEMENT

1. Attention-Deficit/Hyperactivity Disorder

ADHD is one of the most common comorbidities in ASD, affecting up to 50% of children with ASD. Symptoms of ADHD, such as inattention, hyperactivity, and impulsivity, overlap with ASD symptoms but are treated differently. Accurate diagnosis requires a comprehensive assessment, including behavior observation across multiple settings and a psychoeducational evaluation.

- Medication management: Stimulant medications (e.g., methylphenidate) are often effective but may have heightened side effects in children with ASD. Non-stimulant medications, such as alpha-2 adrenergic agonists (e.g., guanfacine and clonidine), are alternative treatments.
- Additional management: Behavioral interventions, including parent management training and cognitive-behavioral therapy (CBT), can help address symptoms of ADHD.

2. Anxiety and Depression

Anxiety and depression are common among individuals with ASD but are often underdiagnosed due to the overlap with ASD symptoms. Children with ASD may have difficulty articulating their feelings of anxiety, which can manifest as irritability, withdrawal, or increased repetitive behaviors.

- Anxiety: Cognitive-behavioral therapy (CBT) is effective for children with ASD. Medications such as selective serotonin reuptake inhibitors (SSRIs) are also used, although caution is needed due to the potential for side effects. Escitalopram is currently approved by the U.S. Food and Drug Administration (FDA) for use in children with anxiety aged 7 years and older.
- Depression: Depression is more difficult to detect in children with ASD, but screening tools like the Patient Health Questionnaire (PHQ-9) and the Columbia Suicide Severity Rating Scale can aid in diagnosis. SSRIs, such as fluoxetine and sertraline, may be prescribed, starting at the lowest dose and titrated slowly.

3. Epilepsy

Seizures are common in individuals with ASD, affecting about 20-30% of children with the disorder. Seizures tend to present in early childhood or adolescence and are more common in those with intellectual disabilities or nonverbal communication. If seizures are suspected, an electroencephalogram should be performed. Genetic testing may provide additional insights into potential underlying syndromes.

- Treatment: Antiepileptic drugs (AEDs) are used to manage seizures. Lamotrigine is often preferred due to its favorable side-effect profile, though other AEDs may be necessary based on seizure type.

4. Learning Disabilities

Learning disabilities are present in a significant portion of individuals with ASD. These include difficulties in reading, writing, math, and executive functioning. Psychoeducational evaluations are essential to identify specific learning challenges and develop

appropriate educational plans.

- Educational Support: Individualized Education Plans (IEPs) or Section 504 Plans are used to provide accommodations in school settings, including modified curricula, extended testing time, or behavioral interventions.
- Therapeutic Interventions: Speech therapy, occupational therapy, and other related services can support children in developing functional skills.

5. Sleep Disorders

Sleep problems are prevalent in children with ASD, including difficulties with sleep onset, sleep maintenance, and early awakening. These issues can exacerbate behavioral problems and affect daytime functioning.

- Behavioral Interventions: Establishing a consistent bedtime routine and limiting stimulating activities before bed can improve sleep hygiene.
- Pharmacological Interventions: Melatonin, a hormone that regulates the sleep-wake cycle, is frequently used to address sleep disturbances in children with ASD.

A MULTIDISCIPLINARY, INDIVIDUALIZED MODEL

Managing ASD requires a holistic approach that integrates medical, behavioral, educational, and psychological interventions. Regular follow-up and routine screenings for comorbid conditions are essential. Given the complexity of ASD and its comorbidities, PCPs should work closely with specialists in pediatric neurology, psychiatry, psychology, and occupational therapy to provide comprehensive care. In addition, parents and caregivers must be actively involved in the treatment process, as they play a crucial role in the implementation of interventions.[9]

CONCLUSION

Autism Spectrum Disorder is a complex, multifaceted condition that requires early diagnosis and ongoing, individualized treatment. With the rising prevalence of ASD and its associated comorbidities, primary care providers must be prepared to recognize and manage these challenges. By adopting a comprehensive, team-based approach, PCPs can significantly improve outcomes for individuals with ASD, enhancing their quality of life and supporting their families.

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ORIGINAL RESEARCH

Predictors of Length of Stay and Early Cardiac Outcomes in Pediatric Patients with Multisystem Inflammatory Syndrome: A Retrospective Cohort Study (2020-2022)

Alfredo Pacheco Aponte, MD; Buse Baykoca Arslan, MD; Richard Ulangca, MD; Amelia B. Thompson, MD, MPH; Jennifer Armstrong, APRN; Caitlin Crosley, PharmD; Jonathan Chan, MD, MBA, MHA; Shani Cunningham, DO; Carolina Echeverri, MD; Kimberly Fenton, MD; Jennifer Held, RN; Kelvin Lee, MD; Alberto Marante, MD; Amy Painter, APRN; Bhavya Trivedi, MD; Fatma Levent, MD

AdventHealth for Children, Orlando, FL

ABSTRACT

Background

Multisystem inflammatory syndrome in children (MIS-C) is a severe, delayed hyperinflammatory condition occurring after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Organ involvement includes cardiac complications such as myocardial dysfunction and elevated troponin levels. While acute outcomes are now well described, there is less data available regarding long-term prognosis. This study aims to identify predictors of hospital length of stay (LOS) and cardiac recovery in pediatric MIS-C patients admitted to AdventHealth for Children between July 2020 and March 2022.

Methods

This retrospective cohort study examined clinical and laboratory data from 105 pediatric patients diagnosed with MIS-C at our institution. Inclusion criteria were based on the Centers for Disease Control and Prevention (CDC) definition of MIS-C. Data included demographics, vaccination status, comorbidities, ejection fraction (EF), troponin levels, and acute cardiac complications. Key outcomes were hospital LOS and EF. Statistical analyses were performed using R version 4.1, with continuous variables analyzed via Pearson correlation and group comparisons using t-tests or ANOVA.

Results

There was no statistically significant difference in LOS or EF when comparing males to females. Increasing age demonstrated a moderate inverse relationship with discharge EF, suggesting that older children tended to have slightly lower EFs on follow-up. The presence of myocarditis moderately correlated with increased LOS ($r=.29$, $p<.05$. Age inversely correlated with EF ($r=-.32$, $p<.001$)

Conclusions

Our study reinforces the importance of routine outpatient cardiology follow-up, as recommended by current guidelines, and particularly for older patients and those with myocarditis. Limitations of this study include its retrospective design, small sample size, and reliance on clinical documentation for outcome assessment.

INTRODUCTION

MIS-C is a severe, hyperinflammatory condition occurring 2–6 weeks after SARS-CoV-2 infection in children and adolescents under 21 years of age. MIS-C is characterized by fever, laboratory evidence of inflammation, clinically severe illness requiring hospitalization, and multisystem organ involvement. Diagnosis requires the exclusion of alternative plausible causes and confirmation of SARS-CoV-2 infection, either by polymerase chain reaction (PCR), serologic, or antigen testing, or SARS-CoV-2 exposure within the preceding four weeks.[1]

In a study by Messiah et al., when comparing long-term complications of coronavirus disease 2019 (COVID-19) among a diverse sample of children, they found that females were almost twice as likely to report long-term symptoms versus males, and a substantial proportion of ethnically diverse children from low-resource backgrounds with severe COVID-19 reported long-term impacts.[2]

Organ involvement can be broad and severe, with cardiac complications such as myocardial dysfunction, coronary artery dilatation, aneurysm, and elevated troponins being among the most concerning. Other common manifestations include mucocutaneous signs (rash, mucositis, and conjunctivitis), gastrointestinal symptoms (abdominal pain, vomiting, and diarrhea), hematologic abnormalities (thrombocytopenia and neutropenia), and circulatory shock.

In the acute period, the mortality rate of MIS-C has been estimated to be approximately 1–2%.[3] Kavurt et al.[4] found that the most common echocardiographic findings in MIS-C patients are ventricular dysfunction associated with a myocarditis-like condition, pericardial effusion, mitral regurgitation, and rare coronary artery involvement in the acute phase of the disease. However, in their study, ventricular systolic function recovered during hospitalization, but left ventricular diastolic dysfunction persisted in the reduced left ventricular EF group. Similarly, a meta-analysis by Zhao et al. found no significant differences in troponin levels between MIS-C and COVID-19 patients with severe or non-severe MIS-C, as well as between MIS-C patients with and without coronary artery abnormalities.[5]

While acute outcomes are better understood, there is a paucity of literature regarding long-term prognosis.[6,7] This retrospective study evaluates predictors of LOS and cardiac function at discharge in pediatric patients diagnosed with MIS-C at our institution, with a particular focus on cardiovascular and pulmonary sequelae. By contributing to the growing body of follow-up data, we aim to define the recovery trajectory better and support evidence-based management of this novel pediatric inflammatory condition.

METHODS

This retrospective cohort study examined clinical, laboratory, and testing data from all pediatric patients diagnosed with multisystem MIS-C at AdventHealth for Children between July 2020 and March 2022. Inclusion criteria followed the CDC's case definition for MIS-C—fever, multisystem organ involvement, laboratory evidence of inflammation, and confirmed (by PCR, serology, or antigen test) or SARS-CoV-2 exposure within the preceding four weeks (CDC, 2020). Exclusion criteria included patients older than 21 years, those negative for SARS-CoV-2 infection (as determined by PCR, serology, or antigen test), and individuals with an alternative diagnosis. Electronic health records were queried to identify 105 patients meeting these criteria; all had a documented deceased status of "alive," indicating zero in-hospital mortality in this cohort. Subject selection is summarized in Figure 1.

Demographic data (age in years, sex, and self- or parent-reported race/ethnicity) and clinical variables were obtained from the electronic medical record. ICD-10 code M35.8 was used to identify MIS-C diagnosis in the chart. COVID-19 infection status was coded as positive or negative based on PCR or serology testing results; vaccination status was recorded as vaccinated or unvaccinated. We captured binary indicators for acute cardiac complications (myocarditis, cardiogenic shock, coronary artery aneurysm, first-degree atrioventricular block) and underlying comorbidities (obesity; chronic respiratory failure; congenital heart block; abnormal blood chemistry; cardiovascular, lung, or immunosuppressive conditions).

Key outcomes included hospital LOS and left ventricular EF% as measured by transthoracic echocardiography. We recorded troponin levels, reported initially as "Negative," "<X," or as a numeric value—as a continuous variable by assigning "Negative" = 0 ng/mL and "<X" = X/2 ng/mL, as per established methods for censored laboratory data.[8]

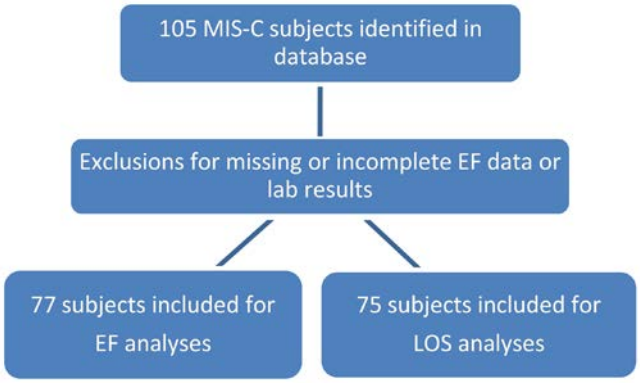

Figure 1: Subject selection Flow Diagram.

Variable	N	Mean (± SD)	Median (IQR)	Range
AGE	105	12.51 (± 4.87)	13 (8-16)	4 - 24
Length of Stay (In days)	105	6.75 (± 3.78)	6 (4-8)	1 - 25

Table 1: Demographics table.

All analyses were conducted in R version 4.1.[9] Continuous variables are presented as mean ± SD and median (interquartile range) (Table 1); categorical variables are presented as counts and percentages.[10] Bivariate associations were explored using Pearson correlations for continuous measures and independent-samples of t-tests or one-way ANOVA for group comparisons.[11]

To identify independent predictors of EF and LOS (days), we performed hierarchical linear regression with block entry: first, demographics (age, sex, and race); then, COVID-19 variables (infection status and vaccination); followed by troponin and acute cardiac complications; and finally, comorbidities. Logistic regression models evaluated odds of myocarditis, and receiver operating characteristic (ROC) curves quantified model discrimination.[12] Statistical significance was set at two-tailed $p < .05$ throughout.

This study was designed to answer the following:

- Is there a significant difference in hospital LOS between male and female MIS-C patients?
- Is there a significant difference in left ventricular EF at discharge between male and female MIS-C patients?
- What are the pairwise correlations among key demographic, laboratory, and clinical variables (age, LOS, EF, troponin, COVID-19 status, complications, comorbidities) in this MIS-C cohort?
- To what extent do demographics (age, sex, race) and COVID-19 variables (infection, vaccination) explain variance in discharge EF?
- To what extent do demographics, COVID-19 variables, EF, troponin, and acute cardiac complications predict log-transformed LOS?
- Do age and peak troponin levels independently predict the odds of developing myocarditis during hospitalization for MIS-C?
- Does peak troponin mediate the relationship between patient age and discharge EF?
- Does peak troponin moderate (i.e., alter) the strength of the age–EF association?
- How well do combined demographic and clinical predictors discriminate via area under the curve (AUC) between patients with EF < 55 % and those with EF ≥ 55 %?
- How well do these predictors discriminate between patients with prolonged LOS (> median) and shorter stays?

RESULTS

An independent-samples t-test was conducted to compare hospital LOS in days between male and female patients. Male patients (n = 66) had a mean LOS of 6.52 ± 3.24 days, whereas female patients (n = 39) had a mean LOS of 7.15 ± 4.57 days. The difference was not statistically significant, $t(103) = -0.84$, $p = .405$, Cohen's $d = 0.23$, indicating no appreciable gender effect on LOS. (Table 2)

Similarly, left ventricular EF was compared between genders. Male patients (n = 66) demonstrated a mean EF of 65.93 ± 6.70 %,

and female patients (n = 39) demonstrated a mean EF of 64.91 ± 5.91 %. This difference also did not reach significance, t (103) = 0.79, p = .433, Cohen's d = 0.20. (Table 2).

Pearson correlations among all numeric predictors—including demographic variables, clinical measures, binary complications, and comorbidities—are shown in Table 3. Overall, pairwise correlation exceeded r = .35, indicating minimal multicollinearity for subsequent regression models.

Age demonstrated a moderate inverse relationship with discharge ejection fraction (EF; r = –.32), suggesting that older children in our cohort tended to have slightly lower EF values on follow-up. Age also correlated positively with myocarditis (r = .35) and modestly with hospital LOS (r = .22).

Myocarditis was moderately associated with LOS (r = .29), indicating longer admissions for those with acute myocardial inflammation.

Troponin (TROPONIN_NUM) showed negligible correlations with EF (r = –.07) and LOS (r = .01), indicating that quantitative peak troponin levels were not strongly linked to these outcomes in our sample group. COVID-19 positivity and vaccination status were independent of clinical severity measures (all r < 0.12). Underlying comorbidities, such as obesity, chronic lung disease, and cardiovascular disease, exhibited only weak intercorrelations (all r < 0.20), which alleviated concerns about collinearity in multivariable analyses.

Outcome	Male (M ± SD)	Female (M ± SD)	t	df	p	Cohen's d
LOS (days)	6.52 (± 3.24)	7.15 (± 4.57)	–0.84	103	.405	0.23
EF (%)	65.93 (± 6.70)	64.91 (± 5.91)	0.79	103	.433	0.20

Table 2: Gender differences in LOS and EF
Note: LOS: Length of stay; EF: Left Ventricular Ejection Fraction.

Predictor	B	SE	p-value	95% CI
Intercept	1.635	0.716	.025	[0.208, 3.062]
Sex (Male vs. Female)	–0.006	0.117	.962	[–0.240, 0.228]
Race (ref = White)				
• Black or African American	0.044	0.191	.821	[–0.338, 0.425]
• Chinese	–0.727	0.556	.195	[–1.834, 0.381]
• Decline to Answer	–0.168	0.262	.522	[–0.691, 0.354]
• Other	–0.210	0.191	.279	[–0.597, 0.178]
• Unspecified	–0.197	0.201	.333	[–0.598, 0.203]
Age (years)	0.018	0.017	.296	[–0.015, 0.051]
COVID-19 Positive vs. Negative	0.087	0.190	.651	[–0.293, 0.468]
COVID-19 Vaccinated vs. Unvaccinated	–0.222	0.274	.423	[–0.768, 0.323]
EF (%)	–0.007	0.005	.195	[–0.017, 0.003]
Troponin (ng/mL)	0.016	0.014	.258	[–0.011, 0.044]
Myocarditis (yes vs no)	0.210	0.188	.272	[–0.164, 0.585]
Cardiogenic Shock (yes vs no)	0.200	0.193	.309	[–0.186, 0.586]
Coronary Artery Aneurysm (yes vs no)	–0.032	0.226	.886	[–0.483, 0.419]
First-degree AV Block (yes vs no)	0.043	0.302	.888	[–0.560, 0.645]

Table 3: Hierarchical regression results for the final LOS model

A hierarchical linear regression was conducted to examine predictors of left ventricular EF% among pediatric MIS-C patients (n = 77 complete cases). The final model, selected for its parsimony and significant R^2 gain, included demographics (age, sex, and race) and COVID-19 variables (infection status and vaccination) that were entered simultaneously. This model accounted for 21.1% of variance in EF, R2 = .211, F (6,70) = 2.28, p = .025, representing a significant improvement over demographics alone, ΔR2 = .024, FΔ (2,70) = 2.49, p = .09. Within this model, age emerged as the only statistically significant predictor: each additional year of age was associated with a 0.58% decrease in EF, B = –0.58, SE = 0.15, t (70) = –3.87, p < .001, 95% CI [–0.88, –0.28]. Neither sex nor any race category differed significantly from the reference group (White), and COVID-19 positivity and vaccination status were not significant predictors (all p > .05).

Subsequent blocks, which added acute cardiac complications and comorbidities, did not yield significant increases in explained variance (p > .10), confirming the final model's balance of explanatory power and parsimony. Therefore, we report final model results as the final EF model.

A hierarchical linear regression analysis was also performed to identify predictors of hospital LOS among MIS-C patients with complete data (n = 75 complete cases) for all variables. Only 75 cases (out of 105) were identified with complete data available. Demographic factors (age, sex, race), COVID-19 status, left ventricular EF%, troponin levels, and acute cardiac complications (myocarditis, cardiogenic shock, coronary artery aneurysm, first-degree atrioventricular block) were entered as a single block. This model explained 29.2% of the variance in LOS, $R^2 = 0.292$, F (10, 64) = 2.17, p = 0.061, representing the most significant increase in explanatory power over earlier blocks ($\Delta R^2 = 0.112$, p = 0.061). Although the overall block did not approach conventional significance, it was retained for its substantive contribution to explaining variance.

Within the final model, no individual predictors reached statistical significance (all p > .05), although the direction of effects suggested that longer LOS was modestly associated with lower EF and the presence of myocarditis or shock. The subsequent addition of underlying comorbidities did not further improve the model fit ($\Delta R^2 = .022$, p = .425), affirming the final model as the most parsimonious, which captured the key drivers of LOS variation. (Table 3).

A binomial logistic regression was performed to assess whether age and troponin level predicted the odds of developing myocarditis during MIS-C hospitalization (n = 93 complete cases with identified troponin levels). Age was a significant predictor: each additional year increased odds of myocarditis by 21.5% (OR = 1.215, 95% CI unavailable; p = .004). On the other hand, troponin level was not associated with myocarditis (OR = 0.999, p = .873). (Table 4)

A mediation analysis was conducted to examine whether troponin level mediated the relationship between age and left ventricular EF%. Age was significantly associated with EF, B = –0.482, SE = 0.137, and p = .001. Controlling for troponin, age remained a significant predictor of EF, B = –0.477, SE = 0.139, p = .001. The Sobel test indicated a non-significant indirect effect of age on EF via troponin, z = –0.24, p = .809. As a result, there was no evidence that troponin impacted the effect of age on EF; the direct pathway from age to EF was robust, and the indirect path through troponin was null.

Additionally, a moderation analysis assessed whether troponin moderated the association between age and EF. In terms of the main effect of age, it was found that older age is associated with lower EF, B = –0.457, SE = 0.142, t = –3.22, p = .002. Although the model accounted for 13.4% of the variance in EF, troponin did not moderate the effect of age on EF; age remained the sole significant predictor of EF. These results indicate that while age consistently predicts EF in pediatric MIS-C, troponin neither mediates nor moderates this relationship.

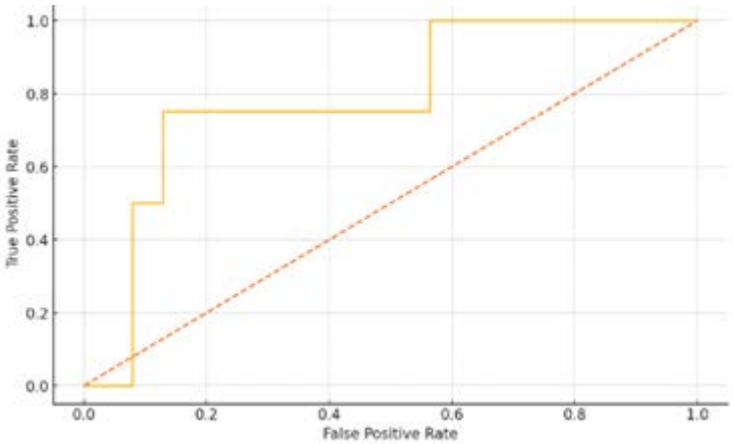

Figure 2: Receiver Operating Characteristic (ROC) Curve for Predicting Reduced Ejection Fraction (<55%) in MIS-C Patients. The model includes age, sex, race, COVID-19 status, and vaccination status. Area under the curve (AUC) = 0.67, indicating modest discrimination.

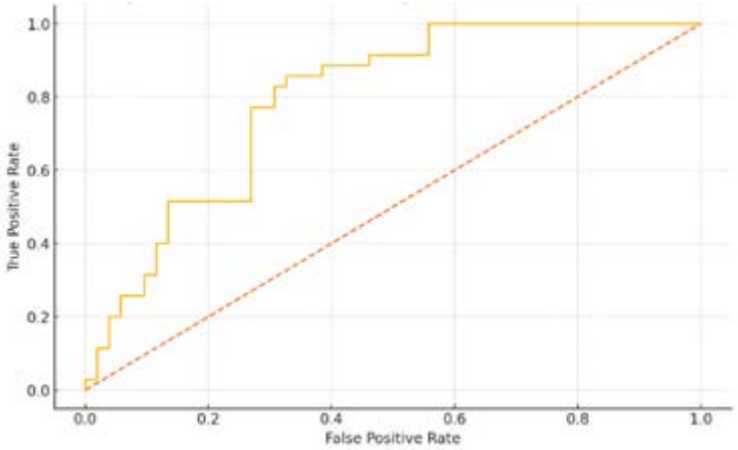

Figure 3: ROC Curve for Predicting Prolonged Hospital Stay (>6 days) in MIS-C Patients. The model incorporates EF, troponin, acute cardiac complications, and demographic/ COVID-19 predictors. AUC = 0.72, reflecting acceptable discrimination.

Finally, ROC curves were generated to evaluate the discriminative ability of our final logistic models for two clinically relevant outcomes: reduced ejection fraction (EF < 55%) and prolonged hospital stay (> 6 days). For the EF model, which included age, sex, race, COVID-19 status, and vaccination status, the area under the ROC curve (AUC) was 0.67 (Figure 2), indicating modest discrimination between patients with and without reduced EF.

Predictor	B	SE	OR	95% CI for OR	p-value
Intercept	–4.082	1.027	0.017	—	<.001
Age (years)	0.194	0.067	1.215	—	.004
Troponin (ng/mL)	–0.001	0.006	0.999	—	.873

Table 4: Simple logistic regression predicting myocarditis (age and troponin)
Note. OR = odds ratio. CI for OR could not be estimated due to data separation at extremes.

For the prolonged LOS model, which included ejection fraction, troponin, and acute cardiac complications in addition to demographic and COVID-19 predictors, the AUC improved to 0.72 (Figure 3), reflecting acceptable discrimination in identifying patients at risk for more extended hospitalization. These findings suggest that while the demographic/COVID-19 predictors alone are of limited utility for flagging reduced EF (AUC = .67), incorporating clinical severity markers enhances the model's ability to predict extended LOS (AUC = .72). An AUC of 0.67 for EF prediction indicates modest discrimination, meaning the model has limited ability to distinguish patients with reduced EF (<55%) from those with normal EF. In contrast, the LOS model's AUC of 0.72 reflects acceptable discrimination, suggesting that incorporating clinical severity markers improves prediction of prolonged hospitalization.

DISCUSSION

The findings of this study provide important insights into the predictors of hospital LOS and left ventricular EF in pediatric patients. The lack of significant gender differences in LOS and EF suggests that these outcomes are not influenced by gender in this population.

The moderate inverse association between age and EF and the positive association between age and myocarditis highlight the importance of age as a predictor of these outcomes. The hierarchical linear regression models further support the significance of age in predicting EF, with each additional year associated with a decrease in EF.

Although the hierarchical regression model for LOS approached significance, the lack of significant individual predictors suggests that other factors not included in the model may be influencing LOS. The direction of effects indicates that longer LOS is associated with lower EF, and the presence of myocarditis or cardiogenic shock warrants further investigation.

The logistic regression analysis identified age as a significant predictor of myocarditis, while troponin levels were not significant. The inability to estimate confidence intervals due to data separation highlights the need for larger sample sizes or alternative statistical methods in future studies. The mediation and moderation analyses did not find evidence that troponin mediates or moderates the relationship between age and EF. These findings suggest that troponin levels do not influence the relationship between age and EF.

The ROC curve analysis demonstrated modest to acceptable discrimination for predicting reduced EF and prolonged LOS, respectively. These results underscore the potential utility of clinical severity markers in predicting extended hospitalization. Overall, the findings of this study suggest the potential contribution to the understanding of the predictors of LOS and EF in pediatric patients. However, these findings must be interpreted cautiously, given the small sample size. Also, we were able to evaluate the patients six months after the initial illness, even if some have been lost to follow-up. Of the ones we were able to evaluate, all had excellent outcomes.

Future work could explore additional biomarkers or imaging techniques to optimize further these predictive algorithms, including larger sample sizes and investigating additional factors that may influence these early and long-term outcomes.

CONCLUSION

This retrospective review suggests that age and EF might be some of the key indicators of LOS as predictors of early outcomes in patients with MIS-C and reinforces the importance of routine outpatient follow-up, as recommended by current guidelines. It raises the question of whether prolonged surveillance is necessary for all patients, particularly those with complete resolution of echocardiogram findings. As more patients transition into post-acute care, understanding long-term outcomes is critical for informing follow-up practices and healthcare resource allocation. Larger multicenter studies are needed to evaluate these variables further and to design follow-up protocols.[13-17]

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