Volume 39 | Issue 1 | January - March 2024

Print ISSN 0975-5152

Karnataka Paediatric Journal

Official Publication of IAP Karnataka State Branch

IAP Karnataka State Branch

www.iap-kpj.org

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Karnataka Paediatric Journal (KPJ) is an open-access peer-reviewed journal committed to publishing high-quality articles in the field of Paediatrics. The journal is owned by the Indian Academy of Paediatrics Karnataka State Branch and published by the Scientific Scholar. Journal follows a double-blind review process with quarterly frequency.

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Editor:

Dr. Bhaskar Shenoy

Head, Department of Paediatrics,
Chief, Paediatric Infectious Diseases Division,
Manipal Hospital, 98, HAL Airport Road,
Bangalore – 560 017, India.
Email: editor2019kpj@gmail.com

Printed and Published by

Scientific Scholar
50 Woodgreen Drive,
Pittsford, New York, USA.
Email: publish@scientificscholar.com

Karnataka Paediatric Journal

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Volume 39 • Issue 1 • January-March 2024

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Karnataka Paediatric Journal

Editorial

The impact of war on children

Bhaskar Shenoy[1]

[1]Department of Paediatrics, Manipal Hospitals, Bengaluru, Karnataka, India.

***Corresponding author:**
Bhaskar Shenoy,
Department of Paediatrics,
Manipal Hospitals, Bengaluru,
Karnataka, India.

bshenoy@gmail.com

Received: 07 March 2024
Accepted: 07 March 2024
Published: 18 March 2024

DOI
10.25259/KPJ_6_2024

Quick Response Code:

In war, children suffer the most. Over 400 million children live in countries where there is war or other violent conflicts. According to United Nations Children's Fund (UNICEF), the estimated casualties of children during the past decade were: '2 million killed, 4–5 million disabled, 12 million left homeless, more than 1 million orphaned or separated from their parents and some 10 million psychologically traumatised.'

Often forced to flee their homes in search of safety, many remain displaced for extended periods or never return home. Some are orphaned or separated from parents and caregivers. Over half of all civilians killed by landmines and explosive remnants of war are children. Children are especially vulnerable to abuse, exploitation, and trafficking during emergencies and armed conflicts.

UNMET BASIC NEEDS DURING WARFARE

War disrupts the supply of necessities to children and their families, such as food, water, shelter, health services, and education. Lack of access to these basic needs may deprive children of their physical, social-emotional, and psychological development. In countries across Africa and the Middle East, over 2.5 million children are suffering from severe acute malnutrition. Economic sanctions, such as trade restrictions from the international community and organisations, may play a role in serious economic hardship and deterioration of infrastructure in armed conflict zones. This makes it extremely difficult for children to survive as they are usually at the most bottom level of socioeconomic status.

Inadequate safe drinking water, along with sufficient water for cooking and hygiene purposes, is making a bad situation worse. Hungry, thirsty, and weak, Gazans are becoming sick. It is reported that at least 90% of children under five are affected by at least one infectious disease.

War affects children in all the ways it affects adults, but also in different ways. First, children are dependent on the care, empathy, and attention of adults who love them. Their attachments are frequently disrupted in times of war due to the loss of parents, extreme preoccupation of parents in protecting and finding subsistence for the family, and emotional unavailability of depressed or distracted parents. The child may be in substitute care with someone who cares for them only slightly – relatives or an orphanage. A certain proportion of war-affected children lose all adult protection – 'unaccompanied children,' as they are known in refugee situations.

Second, impacts in childhood may adversely affect the life trajectory of children far more than adults. Consider children who lose the opportunity for education during war, children who are forced to move into refugee or displaced person camps, where they wait for years in miserable circumstances for normal life to resume, if it ever does. Consider a child disabled in war; they may, in addition to loss of a limb, sight, or cognitive capacity, lose the opportunity for schooling

and of a social life. A girl who is raped may be marginalised by her society and lose the opportunity for marriage. Long after the war has ended, these lives will never attain the potential they had before the impact of war.

Following are some of the impacts of war on children:

Death

Hundreds of thousands of children die of direct violence in war each year. They die as civilians caught in the violence of war, as combatants directly targeted, or in the course of ethnic cleansing.

Injury

Children suffer a range of war injuries. Certain weapons affect them particularly. A landmine explosion is more likely to kill or seriously injure a child than an adult. Thousands of children suffer landmine injuries each year.

Disability

Millions of children are disabled by war, many of whom have grossly inadequate access to rehabilitation services. A child may have to wait up to 10 years before having a prosthetic limb fitted. Children who survive landmine blasts rarely receive prostheses that are able to keep up with the continued growth of their limbs.

Illness

Conditions for maintenance of child health deteriorate in war – nutrition, water safety, sanitation, housing, and access to health services. There may be a loss of immunity to disease vectors with population movement. Refugee children are particularly vulnerable to the deadly combination of malnutrition and infectious illness. There is also an interruption of population immunisation programmes by war, which may be responsible for increases in child mortality.

Rape and prostitution for subsistence

These phenomena, which often occur in situations of war, ethnic cleansing, and refugee life, leave lasting physical impacts on sexually-transmitted diseases, including human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), psychological impacts, and changes in life trajectory.

Psychological suffering

Children are exposed to situations of terror and horror during the war – experiences that may leave enduring impacts on post-traumatic stress disorder. Severe losses and disruptions in their lives lead to high rates of depression and anxiety in war-affected children. These impacts may be prolonged by exposure to further privations and violence in refugee situations.

Moral and spiritual impacts

The experience of indifference from the surrounding world, or, worse still, malevolence, may cause children to suffer the loss of meaning in their construction of themselves in their world. They may have to change their moral structure and lie, steal, and sell sex to survive. They may have their moral structure forcibly dismantled and replaced in training to kill as part of a military force.

Social and cultural losses

Children may lose their community and its culture during the war, sometimes having it reconstituted in refugee situations.

NUTRITION CRISIS-RISING MALNUTRITION

As the conflict in Gaza enters its 20th week, an unprecedentedly rapid rise in malnutrition is threatening the lives of children and pregnant and breastfeeding women in the Gaza Strip. Amid ongoing hostilities following the October 7 attack on Israel, as UNICEF continues to call for an immediate humanitarian ceasefire and the safe return of all hostages, food and safe water are scarce in the Gaza Strip, and children are experiencing a sharp increase in malnutrition, according to a comprehensive new analysis released by the Global Nutrition Cluster, a group of United Nations (UN) and non-UN humanitarian organisations including UNICEF, the World Food Programme and the World Health Organization. Such a steep decline in a population's nutritional status in just three months is unprecedented globally.

The situation is particularly reported to be extreme in northern Gaza, which has been almost completely cut off from aid for weeks. Nutrition screenings conducted at shelters and health centres in the north in January found that one in six children under age 2 – 15.6% – are acutely malnourished. Of these, almost 3% suffer from severe wasting, the most life-threatening form of malnutrition, which puts children at highest risk of medical complications and death unless they receive urgent treatment. The total number of acutely malnourished children is expected to have risen even higher in the days and weeks since the screenings occurred. Similar screenings for children between the ages of 6 months and age 5 in southern Gaza, where aid has been more available, found that 5% of children under 2 are acutely malnourished – a clear indication that access to humanitarian aid is urgently needed and can help prevent the worst outcomes. An alarming lack of food, safe water, and health and nutrition services.

IMPACT ON PSYCHOLOGICAL DEVELOPMENT OF CHILDREN

Brain development

Early childhood experience accounts for a large part of human brain development. Neural connections for sensory ability, language, and cognitive function are all actively made during the 1st year for a child. The plasticity and malleability, which refer to the flexibility of the brain, are highest in the early brain development years. Therefore, the brain can be readily changed by the surrounding environments of children. In that sense, children in armed conflict zones may be more susceptible to mental problems such as anxiety and depression, as well as physiological problems in the immune system and central nervous systems.

Stress in early childhood can impede the brain development of children, which results in both physical and mental health problems. Healthy brain and physical development can be hampered by excessive or prolonged activation of stress response systems. Although both adrenaline and cortisol help prepare the body for coping with stressors, when they are used to prolonged and uncontrollable stress, this stress response system can lead to impairments in both mental and physical health.

Lack of basic resources may also impede child brain development. Childhood socioeconomic status influences neural development and affects cognitive ability and mental health through adult life. Especially, poverty is regarded to deteriorate cognitive capacity. Many studies have shown that poverty in early childhood can be harmful in that low-income families lack the time and financial resources to invest in promoting child development. This suggests that the serious deprivation of resources in armed conflict zones is extremely detrimental to the cognitive development of children during warfare.

REMEDIAL STRATEGIES

Action on this cluster of tragic phenomena is usually considered under two categories – how to mitigate some of the damage to children and how to heal children after they are damaged.

Making war less damaging to children (secondary prevention)

Implement international humanitarian law regarding the protection of children in war. The Geneva Conventions and the Convention on the Rights of the Child deal with the protection of war-affected children with regard to food, clothing, medicine, education, and family reunion. In addition, they are intended to protect children from ethnic cleansing and recruitment into the armed forces. However, compliance with these instruments is poor, especially when recruiting children into the armed forces is concerned.

Ensure that general economic sanctions against a country are never used again. Children and poor adults are those who suffer most from economic sanctions. The use of economic sanctions should be considered a war crime, just as is laying siege to a city to starve its population.

Ensure special consideration for children who are in flight from war zones and who live in camps for refugees and internally displaced people, especially children who are unaccompanied by adults. Special considerations need to be given for family reunions, systems of distribution of resources (sometimes to women rather than to men), the internal layout of camps (to prevent attacks on girls), the provision of facilities for education and play, and special help for child-headed families.

Institute measures to reduce sexual exploitation and gender-based violence against women and girls in war. These measures include training of soldiers, including peacekeeping forces; inclusion of relevant interventions in humanitarian responses to population emergencies in war; reporting and support systems for victims of rape in camps for refugees and internally displaced persons; the prosecution of rape as a war crime and making organised rape a crime against humanity.

Parties to a conflict must facilitate humanitarian assistance to ensure that the health infrastructure of children's lives is not destroyed. Perpetrators should be prosecuted for such actions as destroying clinics, schools, and hospitals – all of which are protected by international law. Where access to health services, such as immunisation, is hindered by the violent conflict, there should be humanitarian ceasefires to enable access.

Rehabilitating children affected by war (tertiary prevention)

During the immediate humanitarian response to victims of war and in the longer-term attempts to reconstruct health services after war, there are attempts by both local and international actors to care for children's needs for health care. Physical and psychological rehabilitation is instituted to varying degrees depending on the resources available. Sometimes, these are minimal or absent. There have been many efforts to help the psychological impacts of war on children. Few have been evaluated.

Some efforts at rehabilitation of war-affected children include social healing and moving toward education in the Culture of Peace. This is an approach to primary prevention of the recurrence of war.

IMPERATIVE TO END WAR

Although the many efforts to make war less damaging for children are important and should continue and be strengthened, this is a pathetically feeble response in light of the intensity and magnitude of the suffering involved. From a certain perspective, there is even something preposterous about an exclusive focus on making war more tolerable for children. We rail against approaching HIV/AIDS, tuberculosis, or malaria in this way. Poverty, on the other hand, like war, may be treated with the assumption that it will always be with us and is a fact of life. Judicial process: The World.

It is time for health professionals to define war as a serious global public health problem. The public health imperative is primary prevention – removing the vector of illness or making conditions unfavourable for the survival of the vector. If a peace system can be devised for an entity as large, diverse, and populous, it can be devised at a global level. It would be naive to suggest that this is easily achievable. But it would be cynical, in light of the suffering of the war-affected children of the world, to accept war as an inevitable part of the human condition. There are global networks, formal and informal, of health professionals who think in terms of eliminating war and who work to accomplish this.

Dr. Bhaskar Shenoy,
Editor in Chief,
Karnataka Paediatric Journal.

How to cite this article: Shenoy B. The impact of war on children. Karnataka Paediatr J. 2024;39:1-4. doi: 10.25259/KPJ_6_2024

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Karnataka Paediatric Journal

Review Article

Adenovirus infections in paediatrics: Understanding the symptoms, diagnosis and treatment

Pooja Doddikoppad[1], Bhaskar Shenoy[1]

[1]Department of Paediatrics, Manipal Hospitals, Bengaluru, Karnataka, India.

***Corresponding author:**
Pooja Doddikoppad,
Department of Paediatrics,
Manipal Hospitals, Bengaluru,
Karnataka, India.

pujanarendra86@gmail.com

Received: 05 June 2023
Accepted: 18 July 2023
EPub Ahead of Print: 13 December 2023
Published: 18 March 2024

DOI
10.25259/KPJ_38_2023

Quick Response Code:

ABSTRACT

Adenovirus infections in paediatrics present a significant health burden, causing various respiratory, gastrointestinal and ocular illnesses. Diagnosing adenovirus infections in pediatric patients can be challenging due to overlapping symptoms with other viral and bacterial infections. Molecular techniques, such as polymerase chain reaction, are highly sensitive and specific for adenovirus detection. Enhanced surveillance, accurate diagnosis, supportive management and preventive measures are crucial for reducing the morbidity and mortality associated with adenovirus infections in pediatric populations. Further research is needed to advance our understanding of adenovirus pathogenesis, develop effective antiviral therapies and improve vaccine strategies.

Keywords: Adenovirus, Symptoms, Diagnosis

INTRODUCTION

Adenoviruses are a common cause of respiratory, gastrointestinal, and ocular infections in paediatric populations. These viruses were first isolated from adenoid tissue.[1] They belong to the Adenoviridae family, which are small, non enveloped double stranded DNA viruses. They are responsible for a wide range of clinical manifestations, ranging from mild common cold-like symptoms to severe respiratory and systemic illnesses. This article aims to provide an overview of adenovirus infections in paediatrics, including their symptoms, diagnosis, and treatment options.

CHARACTERISTICS OF ADENOVIRUSES

Adenoviruses exhibit several distinctive features that set them apart from other viral pathogens. They possess an icosahedral capsid composed of 252 capsomeres, encapsulating their DNA genome. With a diameter of approximately 70–90 nanometres, these viruses are relatively large compared to other common viral pathogens. There are over 50 known serotypes of adenoviruses, classified into seven species (A–G), each exhibiting tropism for different host tissues and causing distinct clinical manifestations.[2]

EPIDEMIOLOGY

Transmission

Adenoviruses are highly contagious and can be transmitted through respiratory droplets, close personal contact, faecal-oral route, or contact with contaminated objects and surfaces (e.g.,

linens, pillows, and lockers,) or reactivation from a previous infection. The incidence of infection appears greatest.

In lower socioeconomic groups and situations of crowding, there is a higher incidence of infection. Epidemic disease commonly occurs in military recruits. Outbreaks, especially of pharyngoconjunctival fever, have followed exposure at swimming pools, summer camps, and childcare centres and in health-care settings.[2]

Populations at risk

Adenoviruses can affect individuals of all ages, but young children are more susceptible, usually from age 6 months to 2 years of age, and can occur as well in 5–9-year-old children and immunocompromised individuals.

Seasonality: Adenoviral infections can occur throughout the year, but some serotypes exhibit seasonal patterns, with increased incidence during late winter and early spring.

CLASSIFICATION

Serotypes

Adenoviruses are classified into different serotypes based on their surface antigens. At present, there are seven species (A–G) of human adenoviruses and each species contains multiple serotypes. For example, species C includes serotypes C1–C5, and species D includes serotypes D1–D89. Serotypes within a species may share certain biological properties but can also cause distinct clinical manifestations. Adenoviruses in subgroups B and C, predominantly Group C, have the ability to cause latent infections in lymphoid cells.[2]

Here is a breakdown of the species and some notable types within each species:

- Species A: Includes types 12, 18, and 31, among others
- Species B: Includes types 3, 7, 11 and 14, among others
- Species C: Includes types 1, 2, 5 and 6, among others. Type 5 (HAdV-5) is the most extensively studied and commonly used in research
- Species D: Includes types 8, 9, 17, 19, and 37, among others. Type 8 (HAdV-8) is associated with epidemic keratoconjunctivitis (EKC)
- Species E: Includes types 4, 29, and 35, among others. Type 4 (HAdV-4) causes acute respiratory disease in military recruits
- Species F: Includes types 40 and 41, among others. These types are primarily associated with gastroenteritis, especially in children
- Species G: Includes types 52, 53 and 54, among others.

CLINICAL SIGNIFICANCE

Different adenovirus serotypes are associated with specific clinical syndromes. For instance, adenovirus serotype 1 through 7 and 21 is commonly associated with respiratory infections; types 8, 19, and 37 are most commonly associated with EKC, while serotypes 32, 40 and 41 are known to cause gastroenteritis. Disseminated adenovirus disease in immunocompromised children can be associated with several serotypes including 1–3, 5, 7, 11, 31, 34 and 35.[3]

CLINICAL MANIFESTATIONS

Adenovirus infections can cause a range of clinical manifestations, depending on the specific strain of the virus and the affected individual's immune system. The most common clinical manifestations of adenovirus infection include:

Adenoviruses commonly cause respiratory tract infections, leading to symptoms such as fever, sore throat, cough, nasal congestion, runny nose and sneezing. These symptoms are similar to those of the common cold or flu. Adenovirus is also known to cause bronchitis, laryngotracheobronchitis, pertussis-like syndrome, bronchiolitis, pneumonia, pleural effusions, necrotising pneumonia, and hyperlucent lung syndrome.

Adenoviral pneumonia is more serious in infants than older children often associated with lethargy, diarrhoea, and vomiting. On radiological examination, it reveals diffuse bilateral pulmonary infiltrates and is often associated with complications such as necrotising bronchitis, bronchiolitis and can be associated with long-term sequalae such as bronchiectasis and bronchiolitis obliterans. Pneumococcal vaccination has been associated with a reduction in the incidence of pneumonia in infants with adenovirus and other respiratory virus infections.[3]

Conjunctivitis

Adenovirus can cause acute follicular conjunctivitis without any long-term sequelae, also known as pink eye. This condition involves redness, irritation, and discharge in one or both eyes. The constellation of symptoms of conjunctivitis, fever, pharyngitis, and cervical or preauricular lymphadenopathy is called as adenoviral pharyngoconjunctival fever.

Gastrointestinal symptoms

It can cause gastroenteritis, resulting in symptoms such as diarrhoea, abdominal pain, nausea and vomiting. These gastrointestinal symptoms are more common in infants and young children. Adenoviruses can also be associated with mesenteric lymphadenitis, appendicitis and intussusception. Fulminant hepatic necrosis can occur in patients with disseminated adenoviral disease and in immunosuppressed patients.

Febrile illness

Adenovirus infections can lead to a febrile illness, characterised by a high fever (above 100.4°F or 38°C). Fever is a common symptom of many viral infections, including adenovirus and is also associated with febrile seizures.

Skin rash

Certain adenoviral infections can lead to a viral exanthem, which is a widespread rash on the skin. The rash is typically non-itchy and can appear in various patterns.

Enlarged lymph nodes

Adenoviral infections may cause swollen or tender lymph nodes, particularly in the neck region.

Pharyngitis and tonsillitis

Infections with adenoviruses can cause inflammation of the throat and tonsils, leading to symptoms such as sore throat, difficulty swallowing and swollen tonsils.

Otitis media

Adenoviral infections can sometimes result in middle ear infections, leading to symptoms such as ear pain, fluid drainage from the ear and temporary hearing loss.

Urinary tract infections

In children can result in acute haemorrhagic cystitis in both healthy and immunocompromised patients. The infection has been associated with nephritis, orchitis and haemolytic uremic syndrome. Children who have undergone bone marrow transplant are particularly at risk of developing haemorrhagic cystitis with systemic disease, leading to an increase in the incidence of mortality coinfection and morbidity.[4]

Adenoviruses can cause acute myocarditis and pericarditis associated with disseminated disease.

Skin infections

In rare cases, adenovirus can cause skin infections, resulting in symptoms such as a rash, blisters or ulcers. These skin manifestations are more commonly seen in immunocompromised individuals.

Neurologic manifestations

Although uncommon, adenovirus infections can occasionally affect the central nervous system, leading to symptoms such as headache, aseptic meningitis (inflammation of the membranes covering the brain and spinal cord) and encephalitis (inflammation of the brain), and transverse myelitis occurs rarely.

Adenovirus has been associated with infectious mononucleosis-like syndrome as well as Kawasaki disease-like syndrome.[3]

Good hygiene practices

Teach your child proper hand hygiene, including regular handwashing with soap and water for at least 20 seconds. Encourage them to cover their mouth and nose with a tissue or elbow when coughing or sneezing to prevent the spread of the virus.

Isolation and preventing spread

Adenoviruses are highly contagious, so it is important to keep infected children away from others, especially those who have weakened immune systems. Follow the guidance of your health-care provider regarding the duration of isolation and when it is safe for your child to return to school or day-care.

DIAGNOSIS

Clinical presentation plays an essential role in suspecting an adenoviral infection. Symptoms can vary depending on the site of infection and the serotype involved. Common clinical presentations include respiratory symptoms such as cough, sore throat and fever, as well as conjunctivitis, gastroenteritis and urinary tract infections. Epidemiological factors, such as exposure to affected individuals or outbreaks, also aid in suspecting an adenoviral infection.

Inflammatory markers

In contrast to other viral infections, adenoviral infections are associated with markedly elevated C-reactive protein.[5] Interleukin-6 concentration and erythrocyte sedimentation rate are associated with severity of adenoviral respiratory infections and are markedly elevated in children with severe fatal adenoviral infections.[6]

Viral culture

Viral culture involves inoculating patient samples, such as respiratory secretions, onto susceptible cell lines. Adenoviruses cause characteristic cytopathic effects in infected cells, allowing for their identification. However, viral culture is time-consuming, requiring several days to obtain results, and it may lack sensitivity compared to newer techniques.

Polymerase chain reaction (PCR)

It enables the detection and quantification of viral DNA/RNA in patient samples. Adenoviral PCR assays have been developed to target conserved regions of the viral genome,

ensuring broad coverage across different serotypes. PCR offers high sensitivity and specificity and can provide results within a few hours, making it an invaluable tool for rapid diagnosis.[7,8]

PCR is a highly sensitive and specific assay that can be used to detect adenovirus DNA from a variety of sterile specimens such as blood, cerebrospinal fluid and tissues. A positive result from upper respiratory tract or stool samples is more difficult to interpret as it may represent virus shedding rather than symptomatic infection. Therefore, PCR results must be interpreted in the context of the clinical findings of adenovirus disease.[9]

Serology

Serological testing plays a supportive role in diagnosing adenoviral infections. Serological assays detect specific antibodies (Immunoglobulin M and Immunoglobulin G) produced in response to adenovirus infection. Enzyme immunoassays and complement fixation assays measure adenovirus-specific anti-heron antibodies but do not provide information about the serotype. Detection of haemagglutination inhibition antibodies or neutralising antibodies is more sensitive and is serotype specific. A rise in antibody titres between acute and convalescent serum samples suggests a recent infection. Serology is particularly useful for epidemiological studies, determining the seroprevalence of adenovirus in a population and differentiating between primary and secondary infections.[10]

Antigen detection

Rapid antigen detection tests (RADTs) use monoclonal antibodies to detect viral antigens in patient samples, such as respiratory secretions or conjunctival swabs. RADTs are relatively quick, providing results within minutes to a few hours. However, they may have lower sensitivity compared to PCR and false negatives can occur, necessitating confirmation with other methods.

Next-generation sequencing (NGS)

NGS technologies have emerged as powerful tools for viral genome sequencing and characterisation. NGS enables the identification of adenovirus serotypes, the detection of novel or recombinant strains, and the analysis of viral genetic diversity. Whole-genome sequencing using NGS can provide valuable insights into adenovirus epidemiology, transmission patterns and drug resistance. However, NGS is still primarily used in research and surveillance settings due to its cost and technical complexity.

MANAGEMENT

It involves supportive care to alleviate symptoms and prevent complications. Here are some general guidelines for managing adenoviral infections

Rest and fluids

Adequate rest helps the body fight off the infection, while fluids prevent dehydration.

Fever control

Administer acetaminophen or ibuprofen to manage fever and alleviate discomfort.

Nasal congestion and cough

Use saline nasal drops or sprays to relieve nasal congestion. A cool-mist humidifier in the child's room can also help alleviate symptoms.

Eye infections

For conjunctivitis (pink eye), clean the eyes with warm water and use saline eye drops to relieve irritation. Avoid touching or rubbing the eyes and wash hands frequently to prevent spreading the infection.

Antiviral therapy

It is generally reserved for patients with severe adenovirus disease, the majority of whom are immunocompromised, Cidofovir is a commonly used antiviral agent with a major side effect of severe dose limiting nephrotoxicity and Fanconi type syndrome, the dose of 5 mg/kg once weekly for three weeks then every two weeks is being under trial. However, more guidelines and studies are needed for the management of adenoviral infections in children.[9]

Immunotherapy

There is an increased evidence regarding the use of pooled intravenous immunoglobulins in severe adenoviral infections in immunocompromised children.[10]

PREVENTION

Adenoviruses are non-enveloped viruses, being resistant to disinfection from alcohol and chlorhexidine that are known to cause increased mortality and morbidity in neonatal intensive care units and immunocompromised children.

Instruments contaminated with adenoviruses can be disinfected by immersion in a 1% solution of sodium hypochlorite for 10 min 22 or by steam autoclaving. Adenoviruses can persist on hands despite handwashing for 10 seconds; therefore, disposable gloves that are changed between contacts with patients should be used to help control institutional outbreaks.

The use of gowns and masks is recommended for tracheostomy care. Other measures to control adenovirus nosocomial infections are isolation and charting of ill patients.

Good hygiene practices

Proper hand hygiene, including regular handwashing with soap and water for at least 20 seconds. Encouraging them to cover their mouth and nose with a tissue or elbow when coughing or sneezing to prevent the spread of the virus.

Isolation and preventing spread

Adenoviruses are highly contagious, so it is important to keep infected children away from others, especially those who have weakened immune systems.

Emerging research and potential applications

Despite their pathogenic nature, adenoviruses have garnered interest in the field of gene therapy and vaccine development. Their ability to efficiently transduce mammalian cells and deliver foreign genes into the host genome has made them attractive vectors for gene therapy applications. Researchers have explored adenoviral vectors for various conditions, including cancer, genetic disorders and infectious diseases, utilising their ability to elicit robust immune responses.

Moreover, adenoviral vectors have played a pivotal role in the development of COVID-19 vaccines, including those by Oxford-AstraZeneca and Johnson and Johnson. These vaccines employ modified adenoviruses to deliver the genetic instructions to produce the spike protein of the SARS-CoV-2 virus, triggering an immune response and conferring protection against COVID-19.

CONCLUSION

Adenovirus infections in children can present with-respiratory, ocular, and gastrointestinal symptoms. Diagnosis often involves a combination of clinical evaluation and laboratory tests, considering the specific symptoms and medical history of the child. Effective treatment strategies include providing supportive care, including fever and pain relief, hydration, and good hygiene practices to prevent further transmission. However, in immunocompromised patients, various drugs, including cidofovir, ribavirin, ganciclovir, and vidarabine, have been employed to manage adenovirus infections. It's important to note that most of these medications are virostatic, they may lead to the development of drug resistance and carry significant risks of toxicities. The decision to use specific therapy for adenovirus infection in immunocompromised individuals should be carefully considered on a case-by-case basis.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

Patient consent not required as patient's identity is not disclosed or compromised.

Financial support and sponsorship

Nil.

Conflicts of interest

Bhaskar Shenoy is the member of the editorial board 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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How to cite this article: Doddikoppad P, Shenoy B. Adenovirus infections in paediatrics: Understanding the symptoms, diagnosis and treatment. Karnataka Paediatr J. 2024;39:5-9. doi: 10.25259/KPJ_38_2023

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Karnataka Paediatric Journal

Original Article

Study of bacteriological profile and its antibiogram in the newborn care unit of a rural tertiary care centre in India

Thageeru Mahesh Kumar[1], Srihari Alapati[1], Y. C. Beere Gowda[1], B. C. Balasunder[1]

[1]Department of Pediatrics, Sri Narasimha Raja District Hospital, Kolar, Karnataka, India.

***Corresponding author:**
Y. C. Beere Gowda,
Department of Pediatrics,
Sri Narasimha Raja District Hospital, Kolar, Karnataka, India.

beere999@gmail.com

Received: 20 May 2023
Accepted: 22 July 2023
EPub Ahead of Print: 15 September 2023
Published: 18 March 2024

DOI
10.25259/KPJ_35_2023

Quick Response Code:

ABSTRACT

Objectives: Neonatal sepsis is a serious medical condition that affects the newborn babies up to 28 days of postnatal life. Regular monitoring of the prevalent bacterial agents causing sepsis is essential for better patient management. The objective of the study was to determine the bacteriological profile and antibiotic susceptibility pattern of culture-positive neonatal sepsis in the newborn care unit of a rural tertiary care centre in India.

Material and Methods: The venous blood sample collected on the day of admission or on the 3rd day of admission for the neonates suspected to have sepsis with poor clinical improvement after a 2-day trial of empirical antibiotic therapy was subjected to culture and sensitivity pattern. Antibiotic susceptibility test was done using the Kirby-Bauer disc diffusion method. Data regarding the identified organism and its antibiotic sensitivity pattern from the blood samples of neonates were collected from the newborn care unit records.

Results: Out of 387 samples, culture positivity was 10.8%. Among culture positive isolates 57.14% are Gram-negative isolates and *Klebsiella* being the most common Gram-negative organism and 42.85% of Gram-positive isolates with *staphylococcus* predominance.

Conclusion: *Klebsiella* (40.4 %) followed by *Staphylococcus* (35.7%) are the most common bacterial pathogens identified in the rural newborn care centre in India. The routine empirical antibiotics in our unit cefotaxime and ampicillin are 100% resistant and need appropriate changes in the antibiotic policy by making piperacillin or cefoperazone and gentamicin as first-line empirical antibiotics.

Keywords: Antibiogram, *Klebsiella*, Neonatal sepsis, *Staphylococcus*

INTRODUCTION

Sepsis is a dysregulated host response to infection leading to life-threatening organ dysfunction.[1] The infection of the bloodstream in newborn babies younger than 28 days is referred to as neonatal sepsis. In developing and underdeveloped nations, it continues to be a significant factor in neonatal morbidity and mortality.[2] Blood cultures are an essential diagnostic tool for certain illnesses and antibiotic susceptibility patterns support therapeutic rationalisation. Prevalent bacterial agents and their antibiotic responsiveness usually vary with the geographical place and time.[3] Hence, regular monitoring of the prevalence of bacterial pathogens and their trend in antibiotic resistance patterns is essential to maintain the appropriate antibiotic policy and thereby better patient management. Therefore, the goal of the present study is to know the prevalent bacteria and their antibiotic resistance that lead to

neonatal sepsis in our unit which is a low-resourced hospital in a rural area.

MATERIAL AND METHODS

This was a retrospective study conducted in the special newborn care unit (SNCU) of Sri Narasimharaja District Hospital, Kolar, during the period from April 2021 to March 2023.

Aim

The aim of the study was to determine the bacteriological profile and antibiotic susceptibility pattern of culture-positive neonatal sepsis in the newborn care unit of a rural tertiary care centre in India.

Inclusion criteria

1. Neonates admitted with blood samples taken for sepsis with a positive bacterial culture were included in the study.

Exclusion criteria

The following criteria were excluded from the study:
1. Neonates admitted with health issues other than bacterial sepsis
2. Neonates with sterile blood culture.

Method

Neonates were suspected of sepsis based on clinical features such as lethargy, refusal to feed, temperature dysregulation, abdominal distension, convulsions, jaundice, rapid breathing and impaired consciousness. The blood sample was collected for culture along with routine first level investigations at the time of admission or on day 3 of inpatient care from the neonates with poor clinical improvement after a trial of 2 days of empirical antibiotic therapy with cefotaxime or ampicillin and amikacin as per the unit antibiotic policy. 1–2 mL of venous blood was collected in a brain heart infusion culture medium under strict aseptic precautions and the sample was subjected to culture and sensitivity pattern. Antibiotic susceptibility test was done using the Kirby-Bauer disc diffusion method, as per the Clinical and Laboratory Standards Institute guidelines (2014). Data regarding the identified organism and its antibiotic sensitivity pattern from the blood samples of neonates were collected from the newborn care unit records.

RESULTS

This study was conducted in an SNCU of a tertiary care low-resource setting hospital in a rural area. We collected 387 blood samples taken from inborn and outborn neonates admitted in our newborn care unit and those fit into our inclusion criteria, irrespective of gestational age and sex, with clinically suspected sepsis for blood culture and sensitivity and out of them, culture positivity was 10.8% with 42 samples tested positive for bacterial isolates. Out of which 57.14% are Gram-negative isolates and 42.85% of Gram-positive isolates. The most common organism identified was *Klebsiella* species in 17 among 42 samples which contribute to 40.4% followed by *Staphylococcus* species in 15 samples contributing 35.7% and all other prevalent organisms are <5% in the current sample [Table 1].

DISCUSSION

Neonatal sepsis is the second leading cause of infant mortality and India has the greatest frequency of the condition worldwide.[4] The prevalence of microorganisms varies depending on the environment, their ability to develop and how frequently they infect people. The common pathogens isolated from the blood of infants with septicaemic disease, their bacteriological proficiency and antimicrobial susceptibility pattern will give us a better idea of how it can be managed effectively to prevent mortality.

This is a retrospective and cross-sectional study analysis of all neonatal sepsis patients with positive bacterial blood cultures in tertiary care hospitals. This study is the first of its kind to be conducted in the SNCU of the district hospital in Kolar to establish an appropriate antibiotic policy.

It is important to determine the prevalence of the bacteria causing newborn sepsis and its antibiotic susceptibility for effective management. In our study, 57.14% of positive blood cultures were Gram-negative isolates which was similar to the study conducted by Londhe *et al*.[5] and 42.85% of Gram-positive isolates were found in our study in contrast to other similar studies conducted by Gupta *et al*.,[6] Sarangi *et al*.[7] and Parajuli *et al*.[8] Out of 42 samples, 17 were found to be *Klebsiella* species which contributes about 40.4% making it the most common species isolated among Gram-negative organisms in several studies such as in Gupta *et al*.,[6] Londhe *et al*.,[5] Muley *et al*.,[9] Pokhrel *et al*.,[10] Akter *et al*.,[11] Oyekale *et al*.[12] and Kumar *et al*.,[13] followed by *Staphylococcus* species in 15 samples contributing 35.7%which was similar to the study done by Londhe *et al*.,[5] Akter *et al*.,[11] Oyekale *et al*.[12] and Acheampong *et al*.[14] making it the predominant bacteria among Gram-positive isolates and all other prevalent organisms were <5% in the current sample.

The differences in culture positivity rates between studies may be caused by physical circulation, the style of study (retrospective vs. prospective) and whether the patient was on antibiotics before the blood sample being obtained for blood culture.[13] Based on the blood culture results, there is a low

Table 1: Prevalent bacteria in our SNCU.

Bacteria identified	No. of samples tested positive	Percentage
Klebsiella spp.	17	40.4
Staphylococcus spp.	15	35.7
Escherichia coli	2	4.7
Enterococcus	2	4.7
Citrobacter	2	4.7
Enterobacter	1	2.3
Acinetobacter	1	2.3
Streptococcus	1	2.3
Burkholderia	1	2.3

SNCU: Special newborn care unit

prevalence of sepsis positivity among the samples collected may be due to the inability of the laboratory setup to detect very small amounts of bacteria in the culture provided, the time taken between the collection of the sample and analysis of the sample and the medium used for their transport and growth.[14]

In our study, the antibiogram of Gram-negative organisms specifically that of *Klebsiella* was observed to be sensitive to Imipenem (77%), similar finding was seen in the study by Gupta *et al.*[6] and Akter *et al.*[11] followed by Gentamicin (75%) and Cotrimoxazole (75%) where sensitive to the bacteria. *Klebsiella* was found to be highly resistant to Ampicillin (100%), Cefotaxime (100%), Tigecycline (100%) and Cefuroxime (100%) [Table 2]. Similar resistance pattern has be observed in many studies such as in Akter *et al.*,[11] Oyekale *et al.*[12] and Acheampong *et al.*[14]

This shift in antimicrobial sensitivity patterns may be caused by the fact that microbes frequently develop resistance to antibiotics while retaining sensitivity to medicines that are administered infrequently. Antimicrobial sensitivity may also vary between studies and over time. This might result from the promiscuous use of antibiotics for both prophylaxis and the treatment of sick newborns, which has led to the emergence of resistant strains.[11]

Antibiogram of *Staphylococcus* in our study showed 100% of sensitivity to Vancomycin (100%) which was in concordance with the findings of previous studies, Gupta *et al.*,[6] Sarangi *et al.*,[7] Parajuli *et al.*[8] and Acheampong *et al.*[14] followed by Tigecycline (100%) similar to study by Sarangi *et al.*,[7] Teicoplanin (100%). They also show complete resistance to Oxacillin (100%) and Ceftriaxone (100%) [Table 3].

To avoid multidrug resistance, these medications can be used as empirical therapy, although they should be implemented with caution. Neonatal septicaemia's evolving microbial ecology is linked to considerable mortality as well as morbidity and long-term morbidity. Therefore, to guide the selection of empirical antibiotic therapy while awaiting the results of blood culture, regular periodical tracking of the neonatal sepsis-causing organisms and their patterns

Table 2: Antibiotic sensitivity pattern for *Klebsiella* species in our SNCU.

Antibiotic	Samples tested for sensitivity	*Klebsiella* (% s)	*Klebsiella* (% r)
Ciprofloxacin	15	33.3	66.6
Amikacin	14	57.1	42.8
Meropenem	14	64.2	35.7
Imipenem	13	77	23
Piperacillin and tazobactam	13	61.5	38.4
Amoxicillin and clavulanic acid	12	41.6	58.3
Gentamicin	12	75	25
Cotrimoxazole	12	75	25
Ampicillin	12	0	100
Cefepime	10	20	80
Cefotaxime	8	0	100
Ceftriaxone	7	14.2	85.7
Cefoperazone and sulbactam	7	71.4	28.5
Cefoxitin	6	0	100
Ertapenem	6	66.6	33.3
Colistin	4	25	75
Tigecycline	2	0	100
Cefuroxime	2	0	100

SNCU: Special newborn care unit, %s: Percentage of sensitivity, %r: Percentage of resistance

Table 3: Antibiotic sensitivity pattern for *Staphylococcus* species in our SNCU.

Antibiotic	Samples tested for sensitivity	*Staphylococcus* (% s)	*Staphylococcus* (% r)
Ciprofloxacin	15	46.6	53.3
Linezolid	15	93.3	6.6
Cotrimoxazole	15	46.6	53.4
Vancomycin	15	100	0
Erythromycin	14	35.7	64.2
Clindamycin	13	53.8	46.2
Gentamicin	13	92.3	7.6
Teicoplanin	12	100	0
Benzylpenicillin	12	8.3	91.6
Cefoxitin	11	27.3	72.7
Levofloxacin	10	40	60
Tetracycline	10	90	10
Oxacillin	9	0	100
Tigecycline	6	100	0
Ceftriaxone	1	0	100

SNCU: Special newborn care unit, %s: Percentage of sensitivity, %r: Percentage of resistance

of antibiotic susceptibility is required.[6] Our observation demonstrates that the issue of antibiotic resistance is a serious challenge for treating severe bacterial infections in newborns and poses a significant danger of antibiotic resistance. The use of antibiotics should be done wisely and with caution is a highly essential practice.[6,11]

CONCLUSION

In our study, the frequency of blood culture-positive sepsis was found to be 10.8% in which *Klebsiella* (40.4%) followed by *Staphylococcus* (35.7%) are the most common bacterial pathogens identified in the rural newborn care centre in India. The routine empirical antibiotics in our unit cefotaxime and ampicillin are 100% resistant and need appropriate changes in the antibiotic policy by making piperacillin or cefoperazone and gentamicin as first line empirical antibiotics.

Ethical approval

The research/study complied with the Helsinki Declaration of 1964.

Acknowledgment

I would like to thank my family and teachers for their constant support and guidance.

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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How to cite this article: Mahesh Kumar T, Alapati S, Beere Gowda Y, Balasunder B. Study of bacteriological profile and its antibiogram in the newborn care unit of a rural tertiary care centre in India. Karnataka Paediatr J. 2024;39:10-3. doi: 10.25259/KPJ_35_2023

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Karnataka Paediatric Journal

Original Article

Efficacy of the Ponseti method in the treatment of neglected idiopathic talipes equinovarus at a tertiary hospital in Nigeria

Wilson Ikpemhi Anetekhai[1], Omolade Ayoola Lasebikan[2], Joseph Asuquo[3], Chinenye Juliet Anetekhai[4], Best J Asuquo[5]

[1]Department of Orthopaedics, National Orthopaedic Hospital, Enugu, [2]Department of Orthopaedics, Institute of Orthopaedic and Plastic Surgery, National Orthopedic Hospital, Enugu, [3]Department of Orthopaedics and Traumatology, University of Calabar, Calabar, [4]Department of Nursing Sciences, University of Nigeria, Enugu, Nigeria, [5]Department of Community Medicine, University of Calabar Teaching Hospital, Calabar.

***Corresponding author:**
Joseph Asuquo,
Department of Orthopaedics and Traumatology, University of Calabar, Calabar, Nigeria.

itansuq@yahoo.com

Received: 05 January 2024
Accepted: 17 January 2024
Published: 18 March 2024

DOI
10.25259/KPJ_1_2024

Quick Response Code:

ABSTRACT

Objectives: Neglected clubfoot is common in our environment, for multifactorial reasons. It could cause pain and psychological distress to the patient and parents. We assessed the efficacy of the Ponseti method in the treatment of neglected clubfoot in a Nigerian Hospital.

Material and Methods: This was a 15-month prospective and interventional study. Patients at least one-year-old with untreated idiopathic talipes equino varus (ITEV) or inadequately nonoperatively treated ITEV were the study population. The number of castings required for correction, tenotomy rate, dorsiflexion angle before and after tenotomy, and abduction angle after treatment were obtained. The chi-square test of independence was used to test the relationship between categorical variables. Logistic regression was used to assess if the Pirani score at the presentation predicted a successful correction at the end of the study. The level of significance was set at $P < 0.05$.

Results: Forty-two children with 69 club feet were treated in this study. The mean age of presentation was 27.45 months (standard deviation [SD] = 19.22). The mean number of casting sessions required to achieve correction was 6.35 (SD = 1.95). The mean Pirani score at presentation was 4.27 (SD = 1.33) which reduced to 0.30 (SD = 0.35) after correction. The Pirani score at presentation had a positive correlation with the number of casts required for correction (r = 0.505, $P < 0.001$) but did not predict a successful correction after treatment. The success rate was 85.5%.

Conclusion: The Ponseti method of treatment showed a high success rate in the treatment of neglected ITEV.

Keywords: Neglected clubfoot, Ponseti technique, Efficacy, Tenotomy

INTRODUCTION

Congenital talipes equinovarus (CTEV), or idiopathic talipes equinovarus '*aka*' clubfoot, is the most common complex developmental foot and ankle deformity in children.[1] Children with CTEV commonly present at birth or shortly after that, as all newborns are screened for this deformity by the midwife, and any suspicions are reported appropriately for early review and management in developed nations.

A neglected CTEV is thus defined as one that has not been treated before walking age or which has had an inadequate or inappropriate initial treatment (that is, a treatment that has

never resulted in correction, distinguishing it from cases of relapse) with deformity present at the time of walking.[2,3] African children are known to develop gross motor skills early compared to their Caucasian counterparts. Iloeje *et al*., in a study done in Southeast Nigeria, showed that children walk well alone at the age of 9–12 months, depending on the sex, as females walked earlier.[4] For this study, the walking age was set at 12 months. However, neglect is a problem in developing nations where ignorance, social stigma, poverty, and a lack of proper healthcare infrastructure militate against early presentation and treatment of children with CTEV.[2,5] These children often have pain, disability, callosities, rigidity, corns, ulcers, atrophy of the affected limb, and a poor psyche, especially in the much older ones who suffer from discrimination.[2,6]

The objective of the various treatment modalities that have evolved over time is to achieve a painless, supple, and plantigrade foot with good mobility without the need for orthoses. Treatment strategies that have been applied include extensive soft-tissue releases, external fixation, corrective osteotomies, triple arthrodesis, serial manipulation, and casting. Extensive surgical procedures are fraught with problems, including being of longer duration, resulting in a persistently painful and stiff foot in about half the cases on long-term follow-up and incomplete correction. The Ponseti method of serial manipulation and casting is preferable to the aforementioned treatment strategies, which produce morbidities that are almost always present in adulthood. Ponseti summarises it as follows: 'The successful non-operatively treated foot is much better than the successful surgically treated foot.' The Ponseti method of treatment has evolved to be the gold standard for the treatment of clubfoot in the past two decades.[1,2,7]

The literature abounds with studies on children who presented early, as Ponseti himself treated children six months and less with a successful correction in 90% of cases. The aim was to determine the success rate of the Ponseti method in the treatment of neglected CTEV and to relate the Pirani score(s) of the feet at presentation to the efficacy of the Ponseti method of treatment.

MATERIAL AND METHODS

The study was conducted at a regional tertiary Nigerian hospital located in the Southeast of Nigeria. Children attending the Clubfoot clinic of the hospital who met the inclusion criteria were recruited following documented informed consent. They were enrolled in the study after detailed consultation with their parents and/or guardians, highlighting the benefits and potential risks of the study and that prejudice shall not be given to their treatment should they decline consent at any time, even when previously enrolled. Fifteen-month prospective and interventional study (from June 1, 2018, to September 30, 2019) with recruitment of consecutive patients that fulfilled the inclusion criteria was adopted. The first 12 months were for recruitment and treatment, while the last three months were only for treatment of the children recruited on the 12th month of the study. The treatment lasted a maximum of 3 months. The efficacy of treatment was assessed at the removal of the last cast during the treatment period.

Forty-seven patients were recruited for the study. Five patients did not complete the treatment protocol as they were lost to follow-up at the time of the study. A total of 42 patients with 69 neglected feet completed the study.

Inclusion criteria

Children 1 year and above with untreated idiopathic CTEV and inadequately nonoperatively treated idiopathic CTEV patients a year and older with a minimum Pirani score of 1 were included in the study.

Exclusion criteria

Syndromic CTEV, secondary talipesequinovarus, for example, poliomyelitis, cerebral palsy, post burns, previous surgical intervention, those older than 16 years with idiopathic CTEV, and those that declined consent were excluded from the study.

A researcher designed pro forma was used to obtain patients' details. A goniometer (Plastic universal standard goniometer) was used to measure passive foot dorsiflexion and abduction angles.

The following parameters were documented during the study:

Outcome variables

Independent variables

1. Age at presentation, sex, and laterality (unilateral or bilateral)
2. Pirani score before the commencement of treatment
3. Number of manipulations and casting required for correction
4. Need for tenotomy
5. Degree of passive ankle dorsiflexion before and after treatment
6. Passive abduction angle at the end of casting.

Dependent variables (outcome measures)

Any patient who did not meet the following criterion was considered to have failed treatment; post-treatment Pirani score of 0 or 0.5, with or without percutaneous tendoachilles

tenotomy and/or anterior tibialis tendon transfer at the end of 3 months of treatment.

The success rate is defined below:

$$\text{Success rate}(\%) = \frac{\text{Number of feet with Pirani score} \leq 0.5 \text{ at the end of casting}}{\text{Total number of feet treated}} \times 100$$

The procedure was the standard Ponseti method of manipulation and casting in an outpatient setting.

An abduction angle of 30–60° was the goal; this was due to the relative difficulty in manipulating older children.

Percutaneous tendoachilles tenotomy was done if, at full correction of the cavus, adducts, and varus, the ankle dorsiflexion remained 10° or less or the talar head was covered completely, and the hindfoot score was still >1.

For patients older than 30 months with persistent heel varus and forefoot supination following correction of other deformities, an anterior tibialis tendon transfer to the middle of the lateral cuneiform was done in theatre. It was done as an isolated procedure or with Achilles tenotomy if more than 10° of dorsiflexion could not be achieved. At the end of the treatment and just before the commencement of bracing, the passive foot abduction and dorsiflexion angles were taken with a goniometer, and the number of manipulations and castings required to achieve these were noted.

Technique for angular measurements (passive dorsiflexion and abduction)

a. Measurement of passive dorsiflexion: With the child supine, the knee flexed to 45° and the subtalar joint held in neutral to avoid including pronation in the measurement, the ankle is dorsiflexed maximally by pushing through the head of the fifth metatarsal. The axis of rotation is the intersection of the midline of the fibula and the midline of the fifth metatarsal. The stationary arm is placed in line with the fibular head, while the moving arm aligns with the fifth metatarsal as it is fully dorsiflexed. This angle is read off the goniometer.
b. Measurement of passive foot abduction: With the child supine and the knee flexed to 45°, the foot is placed with the centre of the heel on the goniometer underneath it. The stationary limb of the goniometer is in line with the sagittal plane of the tibia. The examining index finger is placed over the medial malleolus to stabilise the leg, and the ipsilateral thumb is placed over the lateral aspect of the talar head. The forefoot is then maximally abducted with the contralateral hand while at the same time positioning the measurement limb of the goniometer on the axis of the second toe. The angle is read off the goniometer.

The procedure was judged to have failed if after serial manipulation and casting for a maximum of 3 months without percutaneous tendoachilles tenotomy and/or anterior tibialis tendon transfer to the lateral cuneiform, a plantigrade foot with a Pirani score of 0 or 0.5 was not achieved.

Appropriately sized foot abduction brace (Iowa brace, Clubfoot Solutions, Coralville, Iowa, USA) was worn on children at full correction. In unilateral cases, the brace was set at 60–70° of external rotation on the clubfoot side and 30–40° on the normal side. In bilateral cases, 70° of external rotation on both sides was set. The brace was worn as follows: Twenty-three hours a day bracing for children <4 years old for the first three months, then nap and nighttime bracing until age 4. For those older than four years, night and nap time bracing for at least one year was done.

The derived data were analysed with the IBM SPSS® version 20 software. Results were presented in texts, tables, figures, and charts. Data were presented as means and standard deviations (SDs) for continuous variables. Categorical variables were presented as frequencies and percentages. Logistic regression was used to assess if the Pirani score at the presentation predicted successful treatment. The level of significance was set at $P < 0.05$.

Ethical clearance was obtained from the Institutional Ethics and Research Committee.

RESULTS

The Ponseti protocol had a success rate of 85.5% in the treatment of neglected clubfoot in this study. At the end of the study, out of the 69 feet recruited, 59 had a Pirani score of 0 or 0.5. These were judged to be successfully corrected, while those who scored above 0.5 were classified as treatment failures.

Age and the Pirani score(s) at presentation did not predict a successful treatment. However, the likelihood of a successful treatment had an inverse relationship with the Pirani score at presentation, but this was not statistically significant [Table 1 for results of the binary logistic regression analysis].

The mean Pirani score at presentation was 4.27 (SD = 1.33), while the mean Pirani score at the end of manipulation and casting was 0.30 (SD = 0.35) [Figure 1].

Table 1: Effects of age and Pirani score at presentation on predicting successful treatment.

Variable	β	S.E	*P*-value	95% CI
Age	0.001	0.027	0.978	0.949–1.055
Pirani score at presentation	−0.485	0.305	0.112	0.338–1.120

S.E: Standard error, CI: Confidence interval, β:Probability of committing Type II error

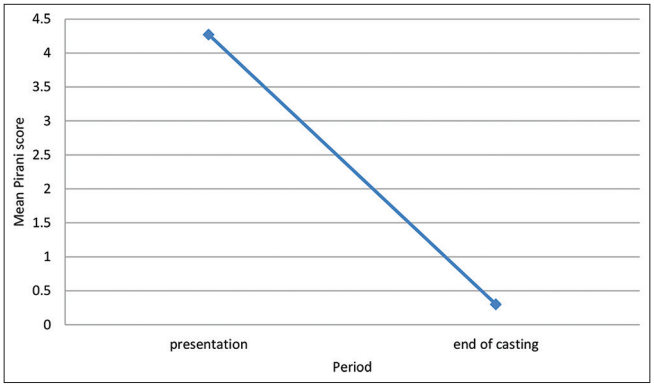

Figure 1: Line graph showing the change in the mean Pirani score at the end of casting.

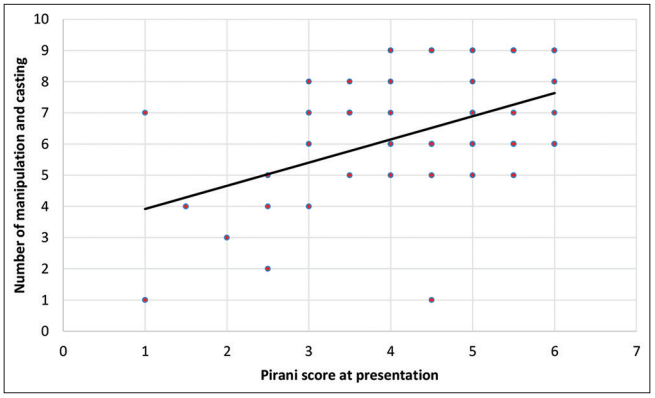

Figure 2: A scatter plot showing a strong positive correlation between Pirani scores at presentation and the number of manipulations and casting required to correct the deformity.

The mean number of manipulation and casting sessions required to achieve correction of the deformity was 6.35 (SD = 1.95). There was a statistically significant correlation between the Pirani score at presentation and the number of casting sessions required for correction; r = 0.505, $P < 0.001$ [Figure 2].

Approximately half of the feet in this study had a previous unsuccessful non-operative treatment [Figure 3].

Bilateral involvement was the most common mode of presentation. Fifteen children had unilateral pathology; the right foot was involved in eight of them. Both feet were involved in 27 children [Figure 4].

The male-to-female ratio was 3:1. The mean age of presentation was 27.45 months (SD = 19.22). The age range was 12–100 months. Most patients in the study presented in the 2nd and 3rd year of life (78.6%) [Table 2].

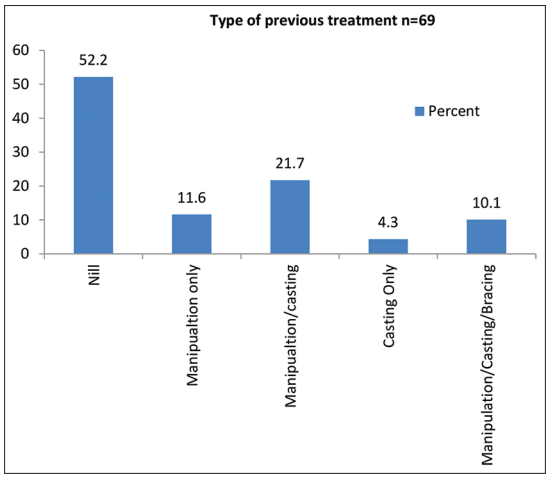

Figure 3: The percentage of the feet that had previous non-operative treatment.

DISCUSSION

The Ponseti method has been shown to be effective in the management of idiopathic CTEV. In this study, we are going to demonstrate that the Ponseti method is also efficacious in the treatment of neglected idiopathic CTEV.

The Ponseti method of treatment was successfully used to achieve the correction of neglected CTEV in 85.5% of the feet in this study. This is consistent with the works of Spiegel *et al.* and Adegbehingbe *et al.*, who successfully treated 86% and 78% of feet, respectively.[2,8] Qureshi and Warriach, Lourenço and Morcuende, Ayana *et al.* had lower success rates with the Ponseti protocol in neglected CTEV.[5,6,9] Although the mean Pirani scores and the age range in their studies were similar to findings in this study, the average number of manipulation and casting was higher (8–9), and they ended up with a much lower success rate as only two-thirds of the feet treated had successful correction. They may have had a considerable number of rigid clubfeet in their study population. These feet although did not attain full correction, but the deformity was attenuated to require minimal soft tissue and bony surgeries for full correction. However, Tindall *et al.*, Dargar *et al.*, El-Banna and Meguid, and Sinha *et al.* documented higher success rates using the Ponseti method in the treatment of neglected CTEV with values in the range of 92–100%.[10-13] The patients treated by El-Banna and Meguid were relatively younger (mean age of 16. 3 months), as well as those treated by Tindal *et al.* who had only 25% of their patients in the age range 18–48 months as part of a larger study of 75 patients (100 feet).[11,13] This relatively younger age group may explain their higher rate of success compared to our findings. Dargar *et al.* and Sinha *et al.* successfully treated 100% of their patients and had an age range of 1–10. For three years, their average Pirani scores at presentation (5 and 5.4, respectively) mirrored that of our study, but they did more sessions of manipulation and casting (9 and 12.8 sessions) in that order.[10,12] A study revealed that the higher the casting sessions the odds of ambulating with deformity reduces.[1]

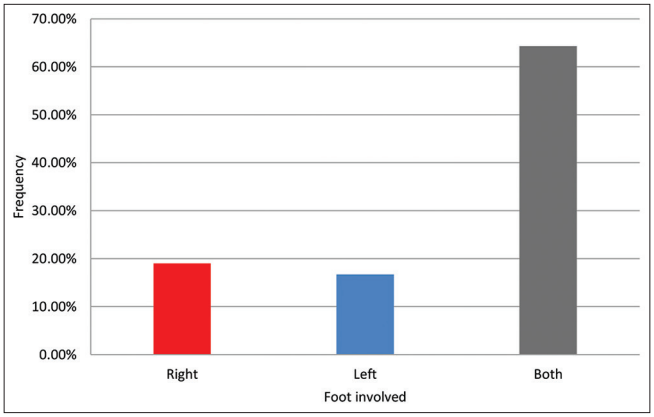

Figure 4: The distribution of the feet affected in the study.

Table 2: The age categories and frequency of the subjects.

Age categories (months)	*N*	%
12–23	20	47.6
24–35	13	31.0
36–47	4	9.5
≥48	5	11.9

N: Frequency, %: Percentage frequency

The Pirani score(s) at the presentation did not predict a successful treatment. This finding may be the result of previous inappropriate or inadequate treatment(s) received by some of the patients (approximately half of the study population), weight-bearing contributing to stretching of the foot soft tissues, or the relative atrophy of the affected limbs, all resulting in a flexible foot. Furthermore, the Pirani score as an assessment tool for neglected CTEV commonly gives lower values. This limitation is occasioned by the obliteration of the medial and posterior creases with weight bearing and the decrease in the empty heel pad due to the usual loss of subcutaneous fat with growth, thus giving relatively lower scores with aging.[5,8]

At presentation, the mean Pirani score was slightly lower than the average Pirani score of the reviewed literature. This may likely be the effect of previous unsuccessful nonoperatively treated patients included in the study sample. These children had a milder deformity compared to their counterparts who had yet to receive any form of treatment as at the time of presentation. At the end of treatment, the mean Pirani score in this study was relatively higher compared to the post treatment Pirani score of 0.21 reported by an Indian study.[12] However, it was lower than the values recorded by studies from Egypt, Nepal and Pakistan which recorded 0.9, 2.1 (SD = 1.03) and 1.31 (SD = 0.43), respectively.[8,9,11]

The mean number of manipulation and casting sessions needed to achieve correction in this study was comparable to the findings reported by Nigerian, other African and Asian studies,[2,5,8,11,13] while some other studies reported relatively higher scores.[6,9,10,12] This may be accounted for by the slightly lower mean Pirani scores at presentation recorded in this study.

In this study, two patients with three affected feet (4.3%) required transfer of the anterior tibialis tendon (ATTT) to the lateral cuneiform to correct a dynamic forefoot supination noted at the end of serial manipulation and casting. El-Banna and Meguid performed ATTT in 24% of their patients, a value much higher in comparison to this study.[11] The upside of this finding is that all the procedures required to obtain correction in most of the patients were done outside of the operating room in this study.

Our study revealed that bilateral cases accounted for about two-thirds of the patients. This presentation was similar to another Nigerian study.[1] But different from what is recorded in the literature where bilateral cases accounted for about half of the patients.[2,5,14] The observed difference may have resulted from failure by parents/guardians to initiate or complete treatment (if at all it was sort for) due to double the financial cost of treatment materials when compared with unilateral cases. Furthermore, parents and caregivers of bilateral cases may have presented in higher proportion given more difficulty experienced by their children or wards during walking. This could also signify a changing demography of presentations.

In our study, there was male preponderance which was approximately equal to the global figure. The perceived slight increase in male patients with neglected clubfoot who presented to the hospital may have been due to the following reasons. First, a major factor may be the male preponderance in the global incidence of CTEV in general. In addition, many parents in our environment place more value on the cosmesis of their female children, which they believe will increase their chances at marriage, thereby presenting early to the hospital for care, thus reducing the prevalence of neglect in them and leaving mostly males to bear this burden. However, in some communities that hardly ever seek medical care for this deformity, late presentation may be the order of day generally, and since males enjoy higher enrolment rates into school, they may have presented on account of peer pressure. This male preponderance is also seen in the works done by Adegbehingbe *et al*., Qureshi and Warriach, El-Banna and Meguid, although to a lesser degree compared to this study, which led Adegbehingbe *et al*. to conclude that there was no gender bias in the presentation of neglected clubfoot cases in their series.[2,9,11]

The age range of children in this study was 12–100 months (8 years). This age bracket was similar to studies done by numerous researchers. The youngest child was one year old, in line with the inclusion criteria. Ayanna *et al*.,[5] Lourenco *et al*.,[6] Dargar *et al*.,[10] Spiegel *et al*.,[8] and Sinha *et al*.[12] all had a similar age range of 1–10 years.[5,6,8,10,12] Likewise, Adegbehingbe

et al. had 91.5% of their study group with an age range of 1–9 years; the oldest child in their work was 16 years.[2]

CONCLUSION

The Ponseti method can be used for the treatment of neglected idiopathic congenital talipes equinovarus deformity with a high success rate. Therefore, it is recommended as the first line of treatment for neglected CTEV.

The age of the children and their Pirani scores at presentation did not predict the likelihood of a successfully corrected neglected idiopathic CTEV using the Ponseti method.

Ethical approval

The Institutional Review Board has waived the ethical approval for this study.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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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How to cite this article: Anetekhai WI, Lasebikan OA, Asuquo J, Anetekhai CJ, Asuquo BJ. Efficacy of the Ponseti method in the treatment of neglected idiopathic talipes equinovarus at a tertiary hospital in Nigeria. Karnataka Paediatr J. 2024;39:14-9. doi: 10.25259/KPJ_1_2024

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Karnataka Paediatric Journal

Case Series

Acute leukoencephalopathy with restricted diffusion – Case Series

Badiginchala Naga Jyothi[1], C. P. Ravi Kumar[1], Ravindra B. Kamble[2], Shanthi Manivannan[1]

[1]Department of Paediatric Neurology, Aster CMI Hospital, [2]Department of Neuroradiology, Aster RV, Bengaluru, Karnataka, India.

***Corresponding author:**
C. P. Ravi Kumar,
Department of Paediatric Neurology, Aster CMI Hospital, Bengaluru, Karnataka, India.

cpravikumar@gmail.com

Received: 12 December 2023
Accepted: 14 January 2024
Published: 18 March 2024

DOI
10.25259/KPJ_59_2023

Quick Response Code:

ABSTRACT

Acute leukoencephalopathy with restricted diffusion (ALERD) is a clinicopathological diagnosis that is characterized by severe encephalopathy and seizures with extensive areas of restricted diffusion in cerebral parenchyma. Case 1: Apparently healthy 13-month-old male child presented with acute febrile encephalopathy with a flurry of seizures with raised intracranial pressure. Investigations were consistent with multiorgan dysfunction along with severe metabolic acidosis, ketosis, and hyperammonemia. Initial magnetic resonance imaging (MRI) Brain was normal. However subsequent MRI brain suggested features of diffuse ALERD. With immunotherapy and supportive management, he improved and was discharged without sequelae. Case 2: A 9-month-old male child who was premorbidly normal presented with fever, status epilepticus, and encephalopathy. MRI Brain was suggestive of central sparing ALERD. He was discharged with sequelae with the advice of rehabilitation. Unfortunately, he got succumbed due to aspiration. Case 3: A 10-day-old neonate presented with the refusal of feeds, multiple seizures, and encephalopathy. MRI Brain revealed central sparing ALERD. Improved with immunotherapy and was developmentally normal at five months of age. ALERD is a clinic-radiological syndrome characterized by acute encephalopathy with restricted areas of diffusion in subcortical white matter on MRI. Reported two categories are Diffuse and Central sparing ALERD. Diffuse ALERD has severe manifestations. However, Case 1 had a good outcome, suggesting a variable prognosis. Central sparing ALERD is a milder form, but when basal ganglia are involved, it may have a worsened outcome, as seen in Case 2. Case 3 had central sparing ALERD, and had a good prognosis as described in literature. This study highlights the varied signs and symptoms of ALERD, including neonatal age of onset. Diagnosis is based on the restricted diffusion in white matter on diffusion-weighted imaging and the apparent diffusion coefficient in MRI of the brain. MRI may be normal in the initial course; hence, it's important to repeat if strongly suspected. Prompt immunotherapy and supportive care are emphasised.

Keywords: Acute leukoencephalopathy with restricted diffusion, Apparent diffusion coefficient, Diffusion-weighted imaging, Immunotherapy

INTRODUCTION

Acute leukoencephalopathy with restricted diffusion (ALERD) is a clinical-radiological diagnosis that is characterised by severe encephalopathy and seizures with extensive areas of restricted diffusion in the bilateral cerebral parenchyma on magnetic resonance imaging (MRI).

ALERD is one of the infection-associated encephalopathy disorders reported in children.[1] According to the distribution of brain lesions, there are two varieties of ALERD: Diffuse ALERD with diffuse areas of restricted diffusion on MRI and central sparing ALERD, also known as Acute Encephalopathy with Biphasic Seizures and Late Reduced Diffusion.

Here, we report 3 cases with ALERD and review of literature on the same.

CASE SERIES

Case 1

A 13-month-old child who was previously healthy and developmentally normal child was admitted to another hospital with a history of fever for five days. He had status epilepticus on day 4 of illness, followed by encephalopathy. MRI Brain was normal on day 4 of illness. Despite being on two anti-seizure medications, he continued to have seizures. He had features of raised intracranial pressure. He was referred to our hospital for further management. At the time of presentation, he had an episode of hypoglycemia with high ammonia (650 μ/dL), severe metabolic acidosis, substantially increased lactate, and encephalopathy. He had Multiorgan dysfunction involving the central nervous system (CNS), cardiac dysfunction, Acute liver failure with coagulopathy, and bone marrow suppression involving two cell lines. He was intubated due to shallow respiratory efforts, and hemodynamics were stabilised. Neuroprotective measures were taken, and titrated the Antiseizure medications accordingly. He was transfused with packed red blood cells and 2 pints of Fresh frozen plasma. He remained encephalopathic for the next 3–4 days and responded gradually. Repeat MRI brain on day 8 of illness showed a diffuse ALERD picture [Figure 1]. Blood culture, cerebrospinal fluid (CSF) analysis, culture, and meningoencephalitis panel were negative. EEG showed diffuse slowing with delta activity. Metabolic workup revealed a possibility of mitochondrial disease; however, it was dismissed after genetic workup. Gradually, he responded to the given treatment, and his sensorium improved. He was discharged on day 20 of illness with no neurological deficits.

Case 2

A 9-month-old child was admitted to an elsewhere hospital with a history of fever on and off for 3–4 days multiple episodes of generalized tonic-clonic seizure with encephalopathy. He was treated with IV antibiotics, multiple Antiseizure medications, and neuroprotective measures. MRI Brain was normal on day 3 of illness. CSF analysis and meningoencephalitis panel were normal. In view of Persistent encephalopathy, he was referred to our hospital on day 8 of illness. On arrival, he was encephalopathic and had poor respiratory efforts. Hence, he was intubated and continued on ventilatory support. Relevant blood investigations were normal, except positivity for Dengue immunoglobulin M. Repeat MRI brain showed a picture of Central sparing ALERD [Figure 1]. He remained seizure-free for four days and again developed multiple episodes of focal seizures. Gradually, he was weaned off from ventilatory support after stabilization. He showed a very slow recovery with significant cortico-visual impairment and weak swallowing. Hence, he was discharged with an NG tube for feeds and with early intervention therapies. The very next day, he was presented with status epilepticus with cyanosis. Managed accordingly and discharged after three days. Unfortunately, after one week, he presented to the emergency room with sudden unresponsiveness, cessation of breathing, and cyanosis. Despite the best resuscitatory measures, he could not be revived!

Case 3

A 10-days-old neonate, born to a non-consanguineous couple, 2nd issue, with no significant antenatal and perinatal history, with a birth weight of 3 kg, was brought with complaints of refusal to feeds, which was followed by four episodes of right focal tonic-clonic seizures and encephalopathy. He was loaded with phenobarbitone and Levetiracetam. Basic blood investigations were within normal range. The Sepsis screen was negative. CSF analysis, culture, and Meningoencephalitis Panel, including enterovirus, were negative. He was treated empirically with antibiotics. MRI brain revealed central sparing ALERD. Blood Tandem mass spectrometry (TMS)was negative. He improved gradually and was discharged on day 17 of life with Levetiracetam. During follow-up, at five months of age, development was age-appropriate with no focal neurological deficits. The repeat MRI brain was normal [Figure 1].

DISCUSSION

ALERD is a clinicopathological syndrome characterized by acute encephalopathy with restricted areas of diffusion in subcortical white matter on MRI.[1] Infectious ALERD develops after infections, while toxic ALERD occurs on exposure to poisons, drug abuse, and cranial radiation, as described by Kamate.[1]

There are two different categories of brain lesions, namely Diffuse ALERD and Central sparing ALERD, based on their distribution.

Diffuse ALERD is a severe manifestation characterised by rapid deterioration of consciousness with shock and multiorgan dysfunction, leading to Coma. It's associated with a guarded prognosis and can be associated with mortality. Neurosequelae are in the form of cognitive impairment, epilepsy, and behavioral problems. Case 1 had diffuse ALERD and presented with refractory status epilepticus, Coma, shock, Multiorgan dysfunction syndrome, had a malignant clinical course, and was discharged without neurological sequelae. This shows the variable prognosis of ALERD.

Central sparing ALERD is a relatively milder form. These patients have a biphasic clinical course. Onset is frequently characterised by fever status epilepticus followed by improved sensorium. Coma is rare, and a variable degree

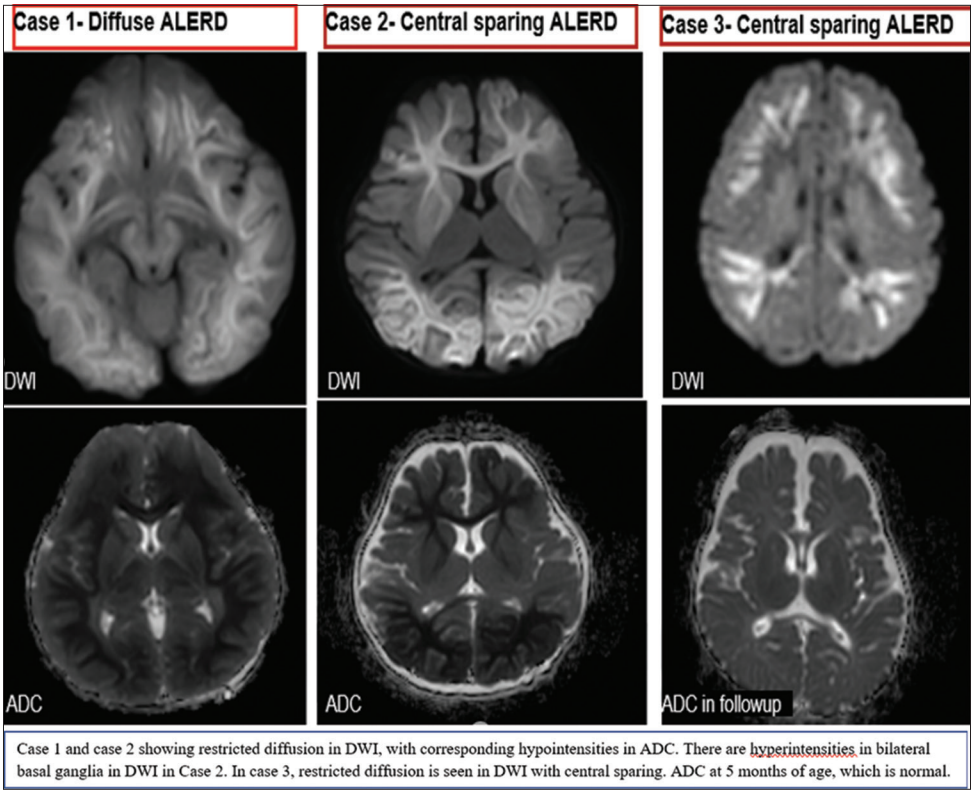

Figure 1: ALERD: Acute leukoencephalopathy with restricted diffusion. DWI: Diffusion-weighted imaging, ADC: Apparent diffusion coefficient.

of cognitive impairment is noticed. Two of our cases had central sparing ALERD. 2nd case presented with shock, status epilepticus, and biphasic seizures. He was discharged with neurological sequelae in the form of dystonia and dysphagia. He succumbed after two weeks of discharge due to breakthrough seizures and cardiorespiratory arrest. A possibility of aspiration or sudden unexplained death in epilepsy was considered. Despite the central sparing type of ALERD, this child had neurological sequelae and died. This can be explained by the involvement of bilateral basal ganglia, which is a predictor of poor prognosis[2,3] also the delay in initiation of diagnosis-specific treatment (Steroids and IVIG started on day 8 of illness). This prompts the importance of early management in the case of ALERD.

Case 3 had a stormy course in NICU with biphasic seizures, discharged without sequelae. During follow-up at five months of age, his development was age-appropriate and with normal MRI findings. This showed a favourable prognosis as described in the literature—a first-ever reported case of ALERD in the neonatal age group, according to the best of our knowledge.

As described in the literature, central sparing ALERD is in the common form in our case reports.[2,3]

In a cohort of Japan study, which included 44 patients, the causative pathogens isolated were human herpesvirus-6, adenovirus, rotavirus, influenza virus, Mycoplasma pneumoniae, Enterovirus type Coxsackievirus A6, Escherichia coli O157:H7, and Streptococcus pneumonia.[4] In our case reports, no organism was isolated in two, and one had dengue infection. The absence of etiological organisms can be explained by the hypothesis put forward by Okumura *et al.*[5] that the pathophysiology doesn't require direct CNS infection.

All 3 cases presented with prolonged multiple seizures and status epilepticus. One of the pathophysiological mechanisms for prolonged seizures and poor outcomes in people with ALERD has been identified as excitotoxic injury caused by excessive glutamine release.[6]

MRI is usually normal at the initial presentation, and once the disease progresses, it shows restricted diffusion in diffusion-weighted imaging (DWI) sequences. The changes in conventional sequences like T1 weighted, T2 weighted, and fluid-attenuated inversion recovery are very subtle to diagnose ALERD and are frequently missed. Signal alterations are more prominent on DWI sequences with substantially restricted diffusion (or hyperintensities) and edematous changes throughout the cortical and subcortical areas that show hypointensities in apparent diffusion coefficient (ADC) maps, which is diagnostic of ALERD.[1]

Case 1 and case 2 had normal initial MRI findings, where a repeat MRI was performed in view of persistent encephalopathy, which revealed a picture of ALERD. This would prompt the importance of repeat MRI if a high suspicion were made, as postulated by Kamate.[1]

In cases of ALERD, dextromethorphan, an antagonist of the N-methyl-D-aspartate receptor, and cyclosporine A, an apoptosis inhibitor, have been used.[7] However, a large cohort of studies are required.

All the 3 cases were treated with a pulse dose of methylprednisolone. Cases 1 and 2 required IV Immunoglobulins in view of poor progress.

CONCLUSION

- This study highlights the varied signs and symptoms of ALERD, including neonatal age of onset.
- Diagnosis is based on the finding of restricted diffusion in white matter and/or cortex on DWI and ADC in MRI of the brain. MRI may be normal in the initial 3–4 days, and hence, it is important to repeat MRI if ALERD is a strong suspect in a given case.
- Prompt immunotherapy and supportive care are emphasised. Diffuse ALERD has a poor prognosis as compared to the central-sparing type of ALERD. However, it's variable.

Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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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How to cite this article: Jyothi BN, Kumar CP, Kamble RB, Manivannan S. Acute leukoencephalopathy with restricted diffusion – Case Series. Karnataka Paediatr J. 2024;39:20-3. doi: 10.25259/KPJ_59_2023

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Karnataka Paediatric Journal

Case Series

Childhood lupus emergency presentation: Is early treatment justified: A case series

Rajendra Raghunath Khadke[1], Abhijit Venkatesh Joshi[1], Ganesh Laxmikantrao Kulkarni[1], Manish Ganesh Kulkarni[1]

[1]Department of Paediatrics, Varad Medical Foundation, Aurangabad, Maharashtra, India.

***Corresponding author:**
Abhijit Venkatesh Joshi, Department of Paediatrics, Chiranjeev Children's Hospital and Critical Care Center, Aurangabad, Maharashtra, India.

joshiabhijit71@yahoo.com

Received: 10 August 2023
Accepted: 27 August 2023
EPub Ahead of Print: 04 November 2023
Published: 18 March 2024

DOI
10.25259/KPJ_48_2023

Quick Response Code:

ABSTRACT

Juvenile systemic lupus erythematosus is a multisystem disorder of autoimmune aetiology and is diagnosed on the basis of criteria such as the constitutional symptoms, various symptoms, and signs related to multi-system involvement and supporting laboratory investigations. It is sometimes very challenging when we come across some JSLE cases with an atypical presentation or as a catastrophe. We have discussed a few atypical cases of systemic lupus erythematosus here. Definitive diagnostic tests such as the anti-nuclear antibody with a high negative predictive value and other diagnostic tests would take time and it is worth starting treatment rather than waiting for the investigations in some cases. This case report study is to sensitise the treating paediatrician to use clinical acumen to plan meticulously the management of JSLE cases.

Keywords: Haemolytic anaemia, Autoimmune, Lupus vasculitis, Central nervous system, Retinal artery occlusion

INTRODUCTION

The diagnosis of systemic lupus erythematosus (SLE) becomes challenging due to the lack of definite pathognomonic features or tests. We have compiled clinical data of four interesting cases of childhood SLE which posed a diagnostic challenge. These cases had variable clinical presentations and a stormy course. The clinical data compiled includes the clinical presentation and diagnostic workup of these cases. This includes one case of unilateral central retinal artery occlusion, a case of autoimmune thrombocytopenia with haemolytic anaemia (Evan's syndrome), a case of autoimmune haemolytic anaemia (AIHA), and a case of neuropsychiatric systemic lupus erythematosus (NPSLE). These cases posed problems for the diagnosis due to their stormy course and atypical presentation. A rapid treatment plan changed the outcome and prevented the deterioration of all patients. A delay in the diagnosis and urgent treatment would seriously jeopardize the outcome of all these cases.

We applied the European League Against Rheumatism/American College of Rheumatology 2019 criteria for SLE diagnosis with a positive anti-nuclear antibody (ANA) as the entry criterion and other criteria for fulfilling the diagnosis [Figure 1].[1]

CASE SERIES

Case 1

A 16-year-old girl had symptoms in the form of polymenorrhagia and extreme weakness and a history of hair loss over 4 months. She presented with severe anaemia in cardiac failure and

compatible blood of the same ABO and Rh type could not be arranged due to mismatch. She presented with non-scarring patchy alopecia, malar rash, and a rash over the neck with photosensitivity. Investigations revealed severe anaemia of macrocytic red cells, elevated indirect bilirubin level, a strong positive direct Coombs test, positive indirect Coombs test, and an elevated reticulocyte count pointing to AIHA. With a high index of suspicion for SLE, pending ANA report, she was treated with methylprednisolone in high doses followed by a maintenance dose of oral steroids and hydroxychloroquine. She recovered from severe anaemia without a blood transfusion. She showed a positive ANA by immunofluorescence. A positive double-stranded DNA antibody (anti-dsDNA) was also added to the diagnosis.

Case 2

A 12-year-old female presented to the emergency room needing mechanical ventilator support for breathlessness and parenteral fluids and inotropes for circulatory shock. She had a history of prolonged and heavy menstrual bleeding and severe weakness over 1 and ½ months. She presented with a characteristic malar rash over the face and a macular rash over the limbs. She had severe anaemia, leukopenia, and severe thrombocytopenia, with elevated reticulocyte count and a strong positive direct Coombs test. Her chest radiograph showed bilateral pulmonary infiltrates. Along with supportive care, she needed packed red blood cells, platelets transfusion, and steroids given initially in high doses. With a high index for suspicion of SLE with vasculitis, a further workup showed a positive ANA by IF, positive anti-dsDNA, low serum complement levels, and positive anti-SM antibody. She also had significant proteinuria and her planned kidney biopsy revealed class 3 nephritis. Cyclophosphamide was started for the induction remission and she was put on low-dose steroids and hydroxychloroquine with advice to have a regular follow-up.

Entry criterion
Antinuclear antibodies (ANA) at a titer of ≥1:80 on HEp-2 cells or an equivalent positive test (ever)

↓

If absent, do not classify as SLE
If present, apply additive criteria

↓

Additive criteria
Do not count a criterion if there is a more likely explanation than SLE.
Occurrence of a criterion on at least one occasion is sufficient.
SLE classification requires at least one clinical criterion and ≥10 points.
Criteria need not occur simultaneously.
Within each domain, only the highest weighted criterion is counted toward the total score§.

Clinical domains and criteria	Weight	Immunology domains and criteria	Weight
Constitutional		***Antiphospholipid antibodies***	
Fever	2	Anti-cardiolipin antibodies OR	
Hematologic		Anti-β2GP1 antibodies OR	
Leukopenia	3	Lupus anticoagulant	2
Thrombocytopenia	4	***Complement proteins***	
Autoimmune hemolysis	4	Low C3 OR low C4	3
Neuropsychiatric		Low C3 AND low C4	4
Delirium	2	***SLE-specific antibodies***	
Psychosis	3	Anti-dsDNA antibody* OR	
Seizure	5	Anti-Smith antibody	6
Mucocutaneous			
Non-scarring alopecia	2		
Oral ulcers	2		
Subacute cutaneous OR discoid lupus	4		
Acute cutaneous lupus	6		
Serosal			
Pleural or pericardial effusion	5		
Acute pericarditis	6		
Musculoskeletal			
Joint involvement	6		
Renal			
Proteinuria >0.5g/24h	4		
Renal biopsy Class II or V lupus nephritis	8		
Renal biopsy Class III or IV lupus nephritis	10		

Total score:

↓

Classify as Systemic Lupus Erythematosus with a score of 10 or more if entry criterion fulfilled.

Figure 1: Adapted from 2019 European League Against Rheumatism/ American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus. SLE: Systemic lupus erythematosus, C3: Complement 3, C4: Complement 4, *: Anti-double-stranded DNA (deoxyribonucleic acid) antibodies.

Case 3

A 10-year-old boy was referred with pain in the digits and feet with peeling of skin over palms over 1 month followed by sudden dimness of vision in the left eye. He also had a fever over 4–5 days which was not attributed to any infective aetiology. His general examination showed hypertension. His left eye fundus showed macular oedema, haemorrhages around the disc, tortuous blood vessels, and cherry red spots [Figure 2]. On investigations, he had anaemia, raised C-reactive protein, and significant proteinuria. His coagulation profile including prothrombin time, activated partial thromboplastin time protein-C activity, protein-S activity, and antithrombin 3 was normal. By keeping the possibility of inflammatory multisystem disease with probable vasculitis, ANA by IF was done and turned positive, with a positive dsDNA antibody, low complement C3 and C4, and a high urinary protein to creatinine ratio. He was put on steroids, antihypertensive drugs, and acetylsalicylate. His kidney biopsy was planned later which showed class 2 nephritis. Cyclophosphamide was started as induction remission. There was a slight improvement in vision in the form of perception of light but his vision could not recover despite the continuation of treatment.

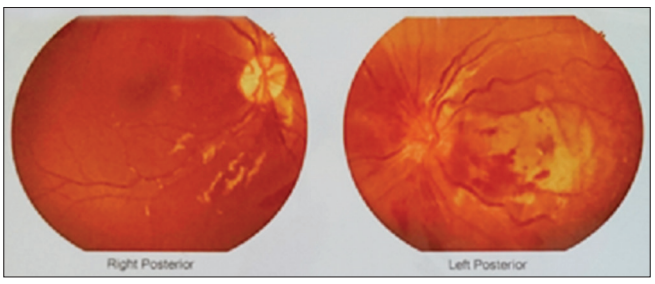

Figure 2: Fundus Right eye: Normal, Left eye: tortuous blood vessels, hemorrhages around the disc, macular edema, cherry red spots, optic neuritis with retinitis with sub-foveal serous fluid.

Case 4

A 7-year-old girl presented to another hospital for a high intermittent fever for 2 months and was hospitalised for convulsions. She had generalised lymphadenopathy, and oral ulcers on clinical examination. Her investigations showed bicytopenia in the form of anaemia and thrombocytopenia. Cerebrospinal fluid had leukocytosis and computed tomography (CT) brain was reported normal. She was treated for tuberculous meningitis though specific tests for bacteriological confirmation were negative. She recovered partially from the illness but landed with us in status epilepticus with a fever. She needed mechanical ventilator support for respiratory failure and encephalopathy. She had hypertension and developed a macular rash over the body and had hepato-splenomegaly. The bicytopenia persisted and the repeat CT scan brain was normal. In v/o persistent fever, pancytopenia, and clinical picture s/o a non-infective aetiology, the possibility of lupus is kept in mind after a normal bone marrow examination. She was treated empirically for neurogenic lupus with steroids, and cyclophosphamide, pending the reports. Her ANA and anti-SM antibodies turned positive. She recovered and was seizure free and with an intact neurological status.

DISCUSSION

This case study report again highlighted that though AIHA as the initial presentation of underlying SLE is extremely rare,[2] a high index of suspicion for SLE as the cause is worthy [Table 1].[3] In both our cases of AIHA, the first was referred to us in cardiac failure with severe anaemia, and cross matching with compatible blood was not possible in view of positive direct agglutination test. This led us to search for the cause and yielded positive ANA and anti-DNA antibodies. The second case was with prolonged bleeding with thrombocytopenia and presented with pulmonary haemorrhage. This guided us to think of vasculitis as the cause. The lupus anticoagulant was negative and negative anti-CL antibodies ruled out antiphospholipid antibody syndrome. This was treated as SLE with severe thrombocytopenia causing pulmonary haemorrhage. A thorough work-up in AIHA will aid in the detection of underlying secondary conditions. The response rate to steroids in AIHA is reported to be around 80%.[4]

Unilateral branch retinal artery occlusion (BRAO), though as the sole presentation of retinopathy is extremely rare in SLE, the only ophthalmological evaluation will not reveal the cause and other evidence for SLE has to be looked for. The child in our case had other features of SLE in addition to BRAO, such as macular rash, hypertension with proteinuria, and joint symptoms. This confirmed the diagnosis of SLE; the treatment was directed to SLE as a whole in the form of immunotherapy and only optical manoeuvres could not resolve the symptoms even if the main symptoms were in the retina.[5]

Only 25% of Juvenile-onset systemic lupus erythematosus patients present as NPSLE. The incidence of seizures at the initial presentation is only 25%.[4,5] With clinical features of NPSLE very variable and non-specific in children, the diagnosis is at times challenging and poses under-recognition and subsequent high rates of complications.[6,7]

CONCLUSION

These clinical scenarios show a series of difficult, at risk SLE cases with variable presentation posing a difficulty for the

Table 1: Application of EULAR/ACR criteria for classification of SLE.

ACR criteria	Case 1	Case 2	Case 3	Case 4
ANA	1:1000	1:3200	1:320	2.23 index
Constitutional symptoms	Present	Present	Present	Present
Muco-cutaneous	Hair loss	Malar rash/ photosensitivity	Absent	Rash/oral ulcers
Musculo-skeletal	Absent	Absent	Arthralgia	Absent
Neuropsychiatric	Absent	Absent	Headache Multiple hemorrhagic infarcts brain	Status epilepticus
Hematological	Immune hemolytic anemia	Immune hemolytic anemia/ thrombocytopenia	Immune hemolytic anemia	Leukopenia/ thrombocytopenia
Serositis (pleural/ pericardial)	Absent	Pleural effusion/ascites	Pleuro-pulmonic pathology	Absent
Immunological	Low serum C3 and C4	Low serum C3 and C4, positive ds-DNA and Sm antigen	Low serum C3 and C4, positive anti-ds-DNA	Absent
Renal	Absent	Class 2 nephritis	Class 2 nephritis	Hypertension Proteinuria

ACR: American college of Rheumatology, ANA: Anti-nuclear antibody, C3 and C4-complement 3 and 4, ds-DNA: Double stranded DNA, Sm: Smith, EULAR: European league against rheumatism, SLE: Systemic lupus erythematosus.

clinician to diagnose and manage with limited resources. A high clinical acumen and a high index of suspicion for SLE in these cases underlie the success with the help of an urgent treatment plan pending the investigation results. This study emphasises the need to put lupus high as the differential in such as haematological, neurological, and ophthalmological emergencies presenting to the emergency room.

The idea behind this article is to sensitise the clinicians involved to become aware of the different clinical spectrums with which SLE can present.

Ethical approval

The research/study complied with the Helsinki Declaration of 1964.

Declaration of patient consent

Patient consent is not required as patient identity is not disclosed or compromised.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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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How to cite this article: Khadke RR, Joshi AV, Kulkarni GL, Kulkarni MG. Childhood lupus emergency presentation: Is early treatment justified: A case series. Karnataka Paediatr J. 2024;39:24-7. doi: 10.25259/KPJ_48_2023

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Karnataka Paediatric Journal

Case Report

Wilson's disease presenting with transient pancytopenia – An uncommon presentation of rare disease

Arundhathi Shankaralingappa[1], Thirunavukkarasu Arun Babu[2]

Departments of [1]Pathology, and [2]Pediatrics, All India Institute of Medical Sciences (AIIMS), Mangalagiri, Andhra Pradesh, India.

***Corresponding author:**
Thirunavukkarasu Arun Babu,
Department of Pediatrics,
All India Institute of Medical Sciences (AIIMS), Mangalagiri,
Andhra Pradesh, India.

babuarun@yahoo.com

Received: 11 June 2023
Accepted: 30 July 2023
EPub Ahead of Print: 15 September 2023
Published: 18 March 2024

DOI
10.25259/KPJ_40_2023

Quick Response Code:

ABSTRACT

Wilson's disease (WD) is an inherited autosomal recessive disorder of copper metabolism, characterised by an excess accumulation of free copper in the liver, brain, and eyes. Patients with WD commonly present with hepatic or neurological symptoms, whereas pancytopenia is an unusual initial presentation of this disease. We are presenting the case of an 8-year-old boy with WD who presented with pancytopenia.

Keywords: Wilson's disease, Autosomal recessive, Pancytopenia, Kayser–Fleischer rings

INTRODUCTION

Wilson's disease (WD) is an inherited autosomal recessive disorder of copper metabolism, characterised by excess accumulation of free copper in the liver, brain, eyes, and other tissues. Its diagnosis is based on typical clinical features such as Kayser–Fleischer (KF) rings, neurological symptoms and/or low serum ceruloplasmin levels.[1] Patients with WD commonly present with hepatic or neurological symptoms, and early detection and management have favourable results.[2] Pancytopenia is an unusual initial presentation of this disease, and when present, it diverts the usual diagnostic algorithm, thus delaying the treatment.[3] Here, we describe an 8-year-old boy with WD who initially presented with pancytopenia.

CASE REPORT

An 8 years and 1-month-old boy presented with fever for 4 days. His history revealed that when the boy was 6 years old, he developed fever followed by jaundice for 10 days. During that time, platelet count had dropped to 73,000/μL of blood. The doctors had advised a bone marrow study, but the parents had refused. Three months back, the child developed fever again and the platelet count at that time was 82,000/μL of blood. There was a history of transfusion (one unit packed red cell and one unit platelet) almost a year back. On clinical examination, the boy was conscious and oriented. He had bilateral cataracts and small hypopigmented spots over his upper chest and back suggestive of tinea versicolor. He had short stubby fingers and firm swelling of the right testis. The liver was palpable and 3.5 cm below the right costal margin in the mid-clavicular line with the liver span being 9.5 cm. The spleen was also palpable and 2 cm below the left costal margin. A complete haemogram showed mild anaemia (haemoglobin – 9 g/dL), leukopenia (total leukcocyte count – 3240/μL of blood), and thrombocytopenia (platelet count – 100,000/μL of blood). The absolute

neutrophil count was 1070/μL of blood. Peripheral smear was reported as pancytopenia. Red blood cell indices and serum iron panel were normal (Serum ferritin – 102 μg/L, serum iron – 52 μg/dL, total iron binding capacity – 320 μg/dL, transferrin saturation – 32%, mean corpuscular volume – 82.7 fl, mean corpuscular hemoglobin concentration – 34.7 g/dL, mean corpuscular haemoglobin – 28.7 pg and red cell distribution width – 15%). Prothrombin time was normal (21.8 s), whereas activated partial thromboplastin time was prolonged (66.6 s). Liver function test revealed normal bilirubin and mild elevation of alanine aminotransferase (40 U/L) and aspartate aminotransferase (58 U/L) with a marked increase in alkaline phosphatase (529 U/L). Total serum protein and albumin were reduced. Ultrasound of the abdomen revealed altered liver echotexture with a 10.6 cm liver span and mild splenomegaly with no ascites. Upper gastrointestinal (GI) endoscopy revealed no varies. Slit-lamp examination revealed bilateral sunflower cataract with KF ring. Serology for human immunodeficiency virus, hepatitis B and C was negative. Serum ceruloplasmin was low, <9.7 mg/dL (normal 18–50 mg/dL) and 24 h urinary copper level was 114.09 mcg/dL (normal 20–50 μg/24 h). Factor VIII and IX assay was normal. Bone marrow aspiration was also normal. Genetic testing detected pathogenic variants in the ATP7B gene (c.2131G>T in Exon 8 with homozygosity) confirming the diagnosis of WD. Thrombocytopenia and leukopenia normalised as the fever settled. However, our diagnosis of WD was delayed due to the atypical presenting feature of pancytopenia.

DISCUSSION

WD (Syn: Hepatolenticular degeneration) is an inherited autosomal recessive disorder characterised by a defect in cellular copper transport, with an approximate prevalence of 1 in 30,000 live births. It results from a mutation in the ATP7B gene located on chromosome 13.[4] Patients with WD commonly present with hepatic or neurological manifestations. Diagnosis is based on considering the clinical and biochemical parameters. KF rings are identified in 50–60% of patients with hepatic involvement.[1] No extra tests are needed for the diagnosis of WD if KF rings are present and serum ceruloplasmin levels are low. In 85% of patients, serum ceruloplasmin levels are below the normal range. However, in the absence of KF rings, a low ceruloplasmin level is not diagnostic for WD, as it may be below the normal range in severely malnourished individuals and carriers of the WD gene. The utility of urinary copper is limited in clinical practice.[1]

Pancytopenia is the simultaneous occurrence of anaemia, leukopenia, and thrombocytopenia. Anaemia, infections and bleeding are the cardinal features of pancytopenia. There are many causes for pancytopenia, such as megaloblastic anaemia, hypersplenism, malaria, leukaemia, aplastic anaemia and autoimmune disorders, and rare causes including WD, Kala-azar, HIV, and alcoholism.[5]

Treatment with penicillamine, a copper chelator resulting in copper deficiency, has been documented to result in cytopenias.[6] However, our case presented with pancytopenia as the initial symptom, which is rare in WD. The pancytopenia was transient in our case, ruling out the possibility of hypersplenism being the sole contributor. The pancytopenia could possibly be due to a viral infection along with associated transient hypersplenism. The child presented with pancytopenia whenever he had a fever, which led to misguidance in arriving at a diagnosis.'

CONCLUSION

This unusual presentation may misguide the clinician and delay the treatment, worsening the condition. Thus, we are presenting this case so that we can shed some light on this rare presentation of WD, which is known to occur rarely. The patient we are presenting had past episodes of fever, followed by jaundice and pancytopenia. The cause of pancytopenia could be a viral fever causing transient bone marrow suppression. This presentation could have been the reason for missing the workup for WD in the first instance, thus resulting in a delay in diagnosis and treatment. WD should be suspected in cases of unexplained pancytopenia, which could be a rare initial presentation.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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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How to cite this article: Shankaralingappa A, Arun Babu T. Wilson's disease presenting with transient pancytopenia – An uncommon presentation of rare disease. Karnataka Paediatr J. 2024;39:28-30. doi: 10.25259/KPJ_40_2023

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Karnataka Paediatric Journal

Case Report

Parotid gland abscess in an underweight infant: A comprehensive analysis

M. S. Vishak[1], Tejaswi Mishra[1], Kalaiarasi Raja[1]

[1]Department of Otorhinolaryngology, Jawaharlal Institute of Post Graduate Medical Education and Research, Puducherry, India.

***Corresponding author:**
M. S. Vishak,
Department of Otorhinolaryngology, Jawaharlal Institute of Post Graduate Medical Education and Research, Puducherry, India.

jrvishak94@gmail.com

Received: 15 September 2023
Accepted: 08 October 2023
EPub Ahead of Print: 04 November 2023
Published: 18 March 2024

DOI
10.25259/KPJ_50_2023

Quick Response Code:

ABSTRACT

We report a case of a 7-month-old underweight male infant who developed a unilateral parotid abscess due to *Staphylococcus aureus* infection and was managed with surgical intervention. An acute parotid abscess is uncommon in paediatric patients but can occur in neonates and premature infants with certain risk factors. Parotitis, the most common inflammatory condition of the parotid gland, usually responds well to medical management but can occasionally progress to a parotid abscess. Conservative management with hydration, oral hygiene, and antibiotics is recommended, but if the disease worsens, suppurative parotitis or parotid abscess can develop. *S. aureus* and anaerobic bacteria are the most common pathogens, with streptococci and candida also reported. Ductal stones are rare in children and parotid abscesses are usually non-obstructive. Differential diagnosis should consider other conditions such as trauma, lymphadenitis, and neoplasia. Computed tomography scans are preferred for complications or suspected neoplastic lesions. Incision and drainage in paediatric patients can have good outcomes, but there is a risk of facial nerve damage.

Keywords: Parotid abscess, Underweight, Infant, Newborn, Parotitis, Abscess, Drainage

INTRODUCTION

An acute parotid abscess is an uncommon occurrence in paediatric patients and it usually occurs in neonates and premature infants with risk factors such as prematurity, low birth weight, dehydration, prolonged orogastric feeding, immunosuppression, and parotid duct anomalies. Common cause includes infections such as viral, bacterial, and rarely fungal, autoimmune conditions, ductal calculi, or stenosis.[1,2] Acute parotitis, which is the most common inflammatory condition of the parotid gland, seldom sporadically turns into a parotid abscess. Unilateral disease is more commonly reported. Common organisms isolated are *Staphylococcus aureus*, *Streptococcus pyogenes,* and anaerobes.[3,4] The role of ultrasound is crucial in distinguishing inflammatory changes from the collection of pus thus directing the management plan. Here, we report a case of a 7-month-old underweight male infant who developed a unilateral parotid abscess due to *S. aureus* infection and was managed with surgical intervention.

CASE REPORT

A 7-month-old male infant, developmentally normal for his age, immunised till date, underweight [Table 1], presented to paediatric emergency with chief complaints of swelling in the right cheek for the past 7 days and fever for 3 days subsided with paracetamol, not associated with chills and rigors.

The swelling was diffuse, insidious in onset, and gradually progressed over 7 days to a size of ~4 × 4 cm at the time of presentation with warmth and tenderness over the swelling. There was no history of recent fever/upper respiratory tract infection, poor feeding or poor activity. There was no history of contact with tuberculosis. The child had papular lesions all over the body and was diagnosed with a case of scabies after a dermatology consultation which was managed with 5% permethrin ointment. General and systemic examination was normal and blood investigations were done for the infant [Table 2].

Ultrasonography of the right parotid appeared heterogeneous with a 2.3 × 2.1 cm heterogenous hypoechoic area with minimal internal echoes. The blood culture taken at the time of presentation was sterile. The patient was started on intravenous antibiotics (cloxacillin and clindamycin) and intravenous fluids. Incision and drainage were done [Figure 1] and ~15 mL pus was drained and sent for exudate culture, Genexpert, and acid-fast bacilli smear. *S. aureus* was isolated in pus culture which was sensitive to clindamycin, oxacillin, a combination of trimethoprim and sulfamethoxazole, tetracycline and erythromycin, and cloxacillin and clindamycin which were continued as per sensitivity report. In Genexpert, no mycobacteria were detected. Daily cleaning and dressing were done and the patient was discharged.

Table 1: Anthropometric data of the infant.

Measure	Patient	Interpretation	Comments
Weight	7.5 kg on admission	0–1z	Severe underweight
Height	62 cm	0–1z	Normal
Head circumference	43 cm		

Table 2: Blood investigations.

Haemoglobin	9 g/dL
Total leukocyte count	28,610/mm^3
Differential leukocyte count	Neutrophil-49%, Lymphocytes-44%
Platelet count	4.03 lacs/mm^3
Mean corpuscular volume	69
Mean corpuscular haemoglobin	19.9
Haematocrit	32.9
Sodium	137 mmol/dL
Potassium	4.73 mmol/dL
Serum albumin	3.57 g/dL

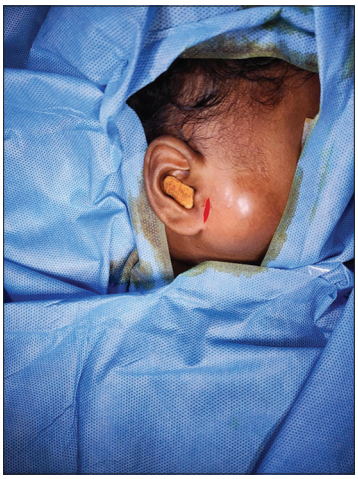

Figure 1: 7-month-old male infant with the right parotid swelling with incision given for abscess drainage.

DISCUSSION

Acute parotitis is the most common inflammatory condition of the parotid gland and usually responds well to medical management but seldom sporadically evolves into a parotid abscess.[5] Parotid abscess is more common among elderly or immune-compromised patients, but their presentation in immune-competent healthy children and adults is well documented in clinical practice.[3]

Parotitis should be conservatively managed with adequate hydration, good oral hygiene, and antibiotics if indicated.[6] However, if treatment is inadequate and/or the disease progresses, suppurative parotitis or parotid abscess can develop with serious complications.[7] Various bacteria cause suppuration of the parotid gland, with *S. aureus* and anaerobic bacteria being the most common pathogens reported and streptococci encountered, as well.[3,4] Furthermore, there is a case report of candida as a causative organism.[8] Although tuberculosis is endemic in India but is rarely the causative organism. A recent study showed a possibility of 13-valent pneumococcal conjugate vaccine-derived parotitis in an infant.[2]

Ductal stones are rare in children and parotid abscess formation is in most cases of non-obstructive origin.[1]

Furthermore, a differential diagnosis which includes, trauma, lymphadenitis, hemangioma, adenoma, lipoma, parotid gland duct anomalies, intraglandular abscess, and neoplasia should be kept in mind.[8]

Ultrasonography is the basic radiological investigation of salivary gland swellings and should be the initial imaging modality. Computed tomography scans were preferred over ultrasonography where complications or a neoplastic lesion in a deep location or bone infiltration are suspected.[6,9]

Management of parotid abscess includes pus drainage and appropriate antibiotic therapy.[6] Drainage of the pus within the gland can be done either by needle aspiration or incision and drainage of pus. Most paediatric incisions and drainage do not have a complication and show good outcomes while rarer complications, of which most frequently being facial

nerve damage can occur in paediatric patients hence making aspiration or exclusive medical therapy generally preferable to incision and drainage.[5]

CONCLUSION

Although uncommon in children, parotid abscess should be considered as a differential for parotid swellings. Early diagnosis, appropriate antibiotics, and surgical drainage are key for good outcomes. This report adds to the limited literature on parotid abscesses in infants.

Ethical approval

The research/study complied with the Helsinki Declaration of 1964.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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

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How to cite this article: Vishak MS, Mishra T, Raja K. Parotid gland abscess in an underweight infant: A comprehensive analysis. Karnataka Paediatr J. 2024;39:31-3. doi: 10.25259/KPJ_50_2023

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Karnataka Paediatric Journal

Case Report

The mandibular distraction osteogenesis; the key dental technique to success in a neonate with Pierre Robin's sequence – A case report

H. A. Venkatesh[1], H. V. Shubha[1], Krishna Shama Rao[1], Swathi Venkatesh[2]

[1]Department of Neonatology, Manipal Hospital, [2]Department of Paediatrics, Ramaiah Hospital, Bengaluru, Karnataka, India.

***Corresponding author:**
H. A. Venkatesh,
Department of Neonatology,
Manipal Hospital, Bengaluru,
Karnataka, India.

venkatveena46@gmail.com

Received: 16 December 2023
Accepted: 04 February 2024
Published: 18 March 2024

DOI
10.25259/KPJ_61_2023

Quick Response Code:

ABSTRACT

A 15-day female neonate term small for gestational age with Pierre Robin Sequence was presented with respiratory distress, requiring respiratory care. The mandibular distraction surgery was performed for micrognathia and progressive respiratory distress. Gradually, she improved and was discharged home on gastrostomy tube feeding. This case underscores the importance of dentistry in the neonatal management of complicated Pierre Robin Sequence successfully.

Keywords: Neonate, Pierre robin sequence, Mandibular distraction osteogenesis, Dentistry

INTRODUCTION

Pierre Robin's sequence is a congenital malformation seen in neonates causing respiratory morbidity. Many milder forms need a prone position and do well gradually. The severe forms may need a novel technique called mandibular distraction osteogenesis for the growth of the mandible, as it was used in our index case as a ray of hope.

CASE REPORT

A term small for gestational age born to a non-consanguineous couple was presented with dysmorphic features such as a small chin, retrognathia and cleft palate [Figure 1]. She required resuscitation – delivery room continuous positive airway pressure (CPAP) and required ventilation for progressive respiratory failure. She was continued on the respiratory support and could not be weaned. Her upper airway was evaluated using bronchoscopy and demonstrated severe laryngomalacia needing aryepiglottoplasty. She continued to be on the respiratory support and in the prone position with no improvement in the respiratory condition. The maxillofacial surgeon opined the benefit of performing mandibular distraction osteogenesis (MDO) procedures. The computed tomography (CT) imaging of the mandible was performed before the procedure [Figure 2]. Post-procedure, the screw distraction of 1 mm/day for one week and then 2 mm up–39 mm over a period of 20 days. Gradually, she improved and could be weaned from the ventilator to CPAP and then to room air. The mandibular distractor was kept *in situ* for three months [Figure 3] until the repeat CT mandible showed adequate density of the bone [Figure 4].

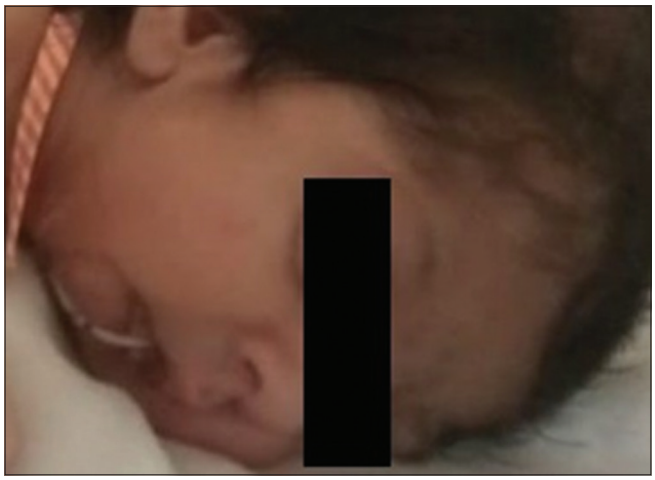

Figure 1: The neonate with micrognathia and retrognathia.

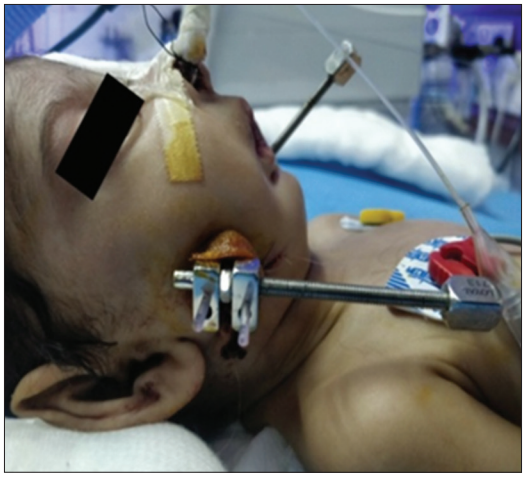

Figure 2: Micrognathia with mandible distraction device fixed.

The feeding management included gastrostomy tube feeding in the initial phase and gradually started enteral feeds. The follow-up clinic demonstrated adequate growth and development. At around eight months of age, she underwent cleft palate closure.

DISCUSSION

The retro positioning of the tongue and hypoplasia of the mandible is an abnormality that causes airway obstruction in Robin's syndrome and was first described in 1934.[1] The severe airway obstruction happens in around 23% of neonates, with Robin's sequence requiring surgical intervention. In around 40–70% of cases, the airway obstruction is relieved by nursing the baby prone.[2-4] The nasopharyngeal airway relieves obstruction in some cases until the mandible grows.[5,6] Our index case had stridor secondary to severe laryngomalacia requiring CPAP and later needed aryepiglottoplasty.

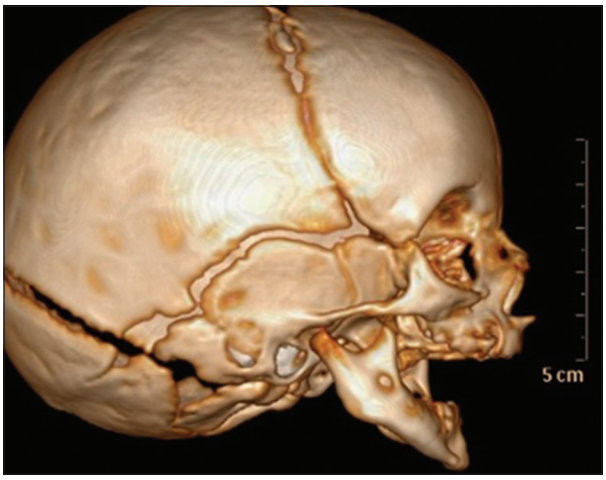

Figure 3: The computed tomography scan of head and neck showing small and retro mandible before the device placement.

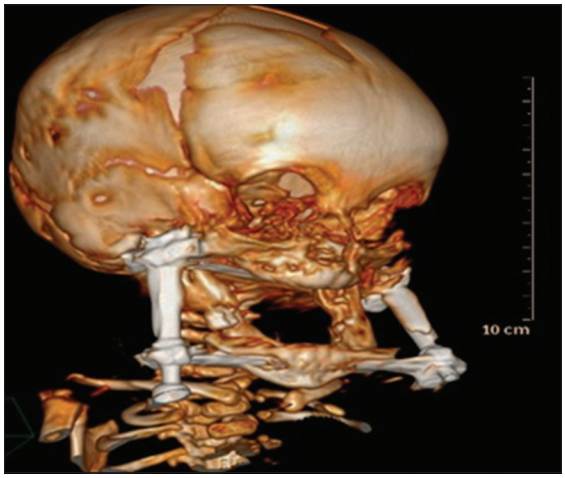

Figure 4: Computed tomography scan of head and neck showing the lengthening of mandible after a period of device placement.

The prone nursing, nasopharyngeal airway, CPAP and aryepiglottoplasty did not relieve airway obstruction. The tracheostomy would be the historical treatment of such neonates. The mortality and morbidity, the difficulties in taking care, the long time required for decannulation and its impact on language and speech have limited this procedure and, hence, not been considered.

The MDO gained importance recently in the management of airway obstruction. Initially, this procedure was performed in patients failing tracheostomy and or tongue lip adhesion.[7,8] This technique lengthens the mandible, bringing the tongue forward and addressing both micrognathia and glossoptosis in relieving airway obstruction. This has become a promising therapy in most of the centres. The procedure requires a specialised person trained in the technique and is performed

in phases. The device placement and osteotomy followed by the active distraction of 1–2 mm/day until 35–40 mm is achieved. Once the distraction was completed, the device was left for 4–6 weeks for the consolidation of regenerated bone.

In the index case, the MDO procedure was performed on day 90 after performing the CT head and neck to know the mandibular size, and later, gradually she was weaned from the ventilator to CPAP after two weeks of the procedure. Here the distraction device with the two screws was attached to the mandible after the incision and its separation. The screw was turned 1 mm every day for one week and 2 mm later for 20 days till around 40 mm, and then the device was kept for another four weeks without any distraction. The turning of the screw after the surgery will further separate the bone. The device was later left *in situ* for four weeks without screwing. The procedure, though safe, can be associated with complications, including damage to inferior alveolar nerves, infections, failure of distraction and the dislodgment of the device. In our case, none of the complications arose. There are different devices used in the mandibular distraction procedure – the external and the internal. The external device fixation was performed in our case. Post-MDO, her oxygenation improved. She was weaned gradually from CPAP to room air. The feeding gastrostomy was inserted as she did not tolerate the tube feeding and was discharged home on gastrostomy tube feeding for a couple of months. And was removed once the oral feed was established. The follow-up CT of the head and neck demonstrated the grown-up chin, and the device was removed. Currently, she is on full oral feeds with adequate weight and demonstrating normal milestones.

CONCLUSION

This case underscores the importance of dentistry in the neonatal management of complicated Pierre Robin Sequence successfully.

Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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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How to cite this article: Venkatesh HA, Shubha HV, Rao KS, Venkatesh S. The mandibular distraction osteogenesis; the key dental technique to success in a neonate with Pierre Robin's sequence – A case report. Karnataka Paediatr J. 2024;39:34-6. doi: 10.25259/KPJ_61_2023

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Karnataka Paediatric Journal

Journal Summary

Journal watch

Vikram Sakleshpur Kumar[1]

[1]Department of Pediatrics, Subbaiah Medical College, Shivamogga, Karnataka, India.

***Corresponding author:**
Vikram Sakleshpur Kumar, Department of Pediatrics, Subbaiah Medical College, Shivamogga, Karnataka, India.

vikramskumar@yahoo.co.in

Received: 29 February 2024
Accepted: 04 March 2024
Published: 18 March 2024

DOI
10.25259/KPJ_5_2024

Quick Response Code:

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 1st 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.

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 2nd or 3rd 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 2nd 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 1st 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 ± 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.

Financial support and sponsorship

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.

How to cite this article: Kumar VS. Journal watch. Karnataka Paediatr J. 2024;39:37-43. doi: 10.25259/KPJ_5_2024