“Correlation between NT- pro brain natriuretic peptide and myocardial dysfunction in children with septic shock –one year cross sectional Study”

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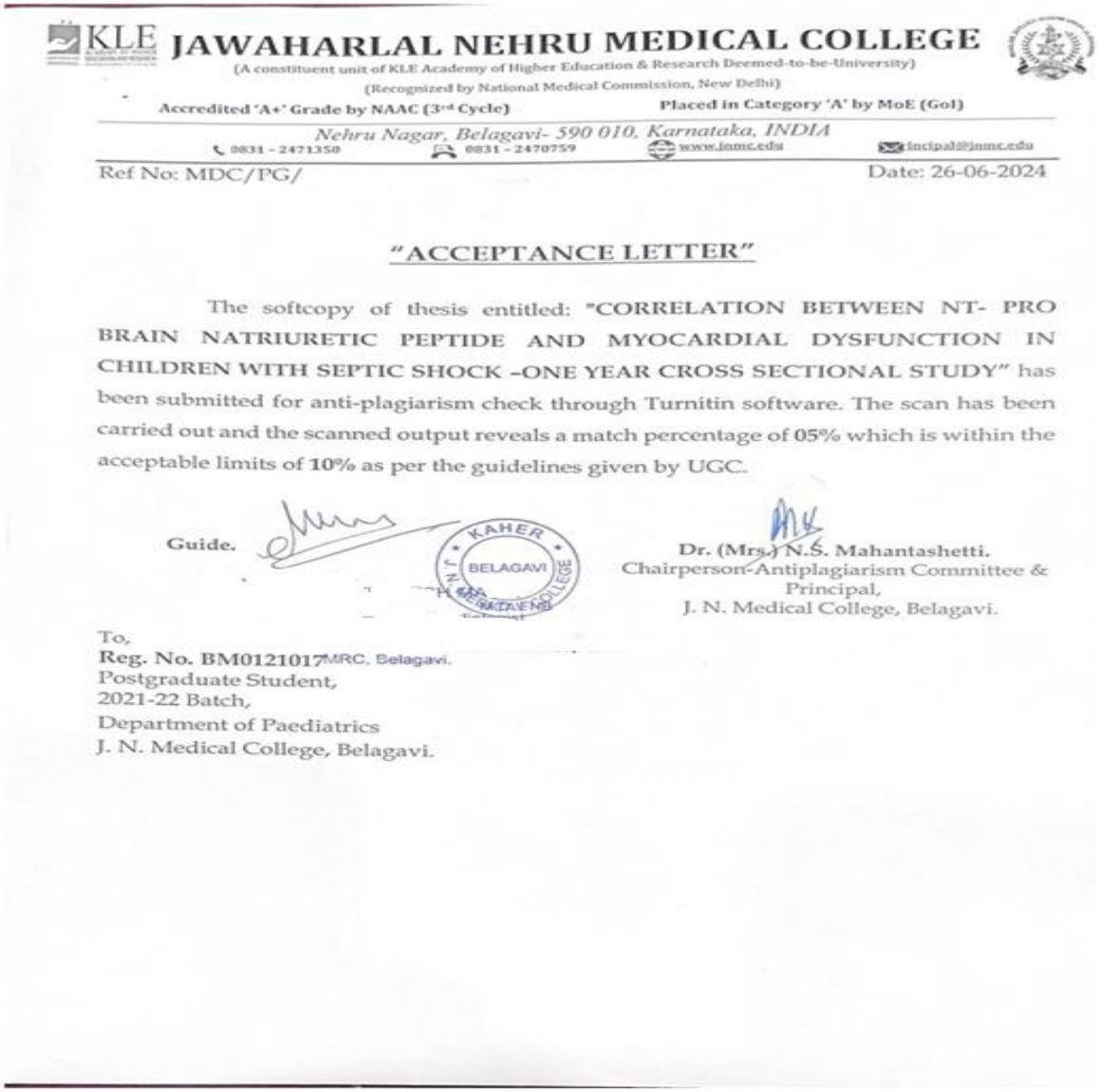

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Sub: Institutional Ethical Clearance for the study.

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ABSTRACT

Background:

Septic shock is a life-threatening condition characterized by systemic inflammation and cardiovascular dysfunction. N-terminal pro-B-type natriuretic peptide (NT-proBNP) has emerged as a potential biomarker for assessing myocardial dysfunction in critically ill patients. However, limited data are available on the correlation between NT-proBNP levels and myocardial dysfunction specifically in pediatric patients with septic shock.

Aim:

To assess the link between NT-proBNP and myocardial dysfunction, as well as between NT-proBNP and severity of disease in children with septic shock

Method:

NT-proBNP levels and the Pediatric Risk of Mortality (PRISM) score of 53 children with septic shock were evaluated at admission and 48 hours post-admission. Myocardial dysfunction (normal, mild, or severe) was evaluated using an echocardiography and severity of illness using the PRISM score. The relationship between NT-proBNP levels with cardiac dysfunction severity and sickness severity was investigated using Kurskal-Wallis test and Pearson's correlation coefficient respectively. R software version 4.2.2 was used for the analysis.

Result:

In our one-year cross-sectional study, we evaluated the correlation between NT-proBNP and PRISM score as well as NT-proBNP levels and myocardial dysfunction in 53 pediatric patients with septic shock. The study found a significant correlation between PRISM scores and NT-proBNP levels at both admission and after 48 hours, indicating that NT-proBNP

levels rise with increased severity of illness. The correlation coefficients were 0.60 at admission and 0.61 after 48 hours, with both p-values < 0.0001. The mean NT-proBNP levels were significantly higher in patients with severe myocardial dysfunction (28600 pg/mL at admission and 31200 pg/mL at 48 hours) compared to those with moderate (9350 pg/mL and 8418 pg/mL) or no dysfunction (1800 pg/mL and 1100 pg/mL). NT-proBNP levels >2000 pg/mL demonstrated high sensitivity (82%) and specificity (70%) for predicting myocardial dysfunction. The overall survival rate was 79%, with all deaths occurring in patients with severe myocardial dysfunction. These findings underscore NT-proBNP's role as a sensitive marker for myocardial dysfunction severity in pediatric septic shock.

Conclusion:

Our findings suggest that NT-proBNP levels may serve as a useful biomarker for assessing myocardial dysfunction severity and severity of illness in children with septic shock. Early identification and monitoring of NT-proBNP levels could aid in the timely recognition and management of cardiac involvement in septic shock, potentially improving patient outcome.

LIST OF ABBRIVATIONS

BNP	B - type natriuretic peptide
CK-MB	creatine kinase-MB
cTnI	troponin I
DIC	disseminated intravascular coagulation
EDTA	Ethylenediaminetetraacetic acid
IL-10	interleukin-10
MODS	multiorgan dysfunction syndrome
MRSA	multidrug-resistant bacterial strains (methicillin-resistant Staphylococcus)
NF-κB	nuclear factor kappa-B
NPV	negative predict vale
NT-proBNP	N-terminal proBNP
PICU	pediatric intensive care unit
POCUS	Point-of-Care Ultrasound
PPV	Positive predict value
SIMD	sepsis-induced myocardial dysfunction
SIMD	sepsis-induced myocardial dysfunction
SIRS	systemic inflammatory response syndrome
SOFA	Sequential (sepsis-related) Organ Failure Assessment
TNF-α	tumor necrosis factor-alpha
VRE	Vancomycin-resistant enterococci

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1. INTRODUCTION

Septic shock, a life-threatening condition resulting from a deregulated immune response to infection, continues to pose a significant global health challenge, particularly in the pediatric population. As per the global estimates, burden of the sepsis in children shows annual prevalence of 1.2 million cases. Fatality rates for sepsis and severe sepsis is reported to be 1-5% and 9-20% respectively[1,2]. Mortality rate as a result of septic shock is reported to be 45%[3] in india. Younger age, unclear vaccination status, healthcare-related infection, noncompliance with sepsis treatment bundles, multiple organ failure and underlying cardiovascular disease, may all be associated with an increased death risk. Among the many problems associated with septic shock, cardiac dysfunction stands out as a significant driver of illness and death in afflicted children.[4]

Septic shock initiates a complex cascade of events, involving systemic inflammation, microvascular dysfunction, and multiple organ failure[5]. Myocardial dysfunction, characterized by impaired cardiac contractility, ventricular dilatation, and compromised cardiac output, frequently emerges as a complication in children with septic shock. The incidence of myocardial dysfunction in this demographic is alarmingly high, with studies reporting an incidence ranging from 20% to 60%[6]. The variability in reported rates underscores the heterogeneity of patient populations, emphasizing the need for precise biomarkers to identify and monitor myocardial dysfunction in these cases.

The consequences of myocardial dysfunction due to septic shock in children are profound and directly linked to patient outcomes. Studies consistently reveal an increased mortality rate in those who develop myocardial dysfunction during the course of septic shock. It is present in over 40% of cases of sepsis[7], and its development can increase the mortality rate by up to 70%[8]. The intricate interplay between systemic inflammation, hemodynamic

instability, and compromised cardiac function creates a precarious scenario that contributes sigfenificantly to the mortality burden associated with pediatric septic shock.

NT-proBNP, a prohormone released by cardiac ventricles in response to amplified wall stress, has gained prominence as a marker for assessing cardiac function and diagnosing heart failure. Its utility extends beyond the realm of chronic cardiac conditions, as elevated NT-proBNP levels have been consistently observed in acute settings such as septic shock[9]. The importance of NT-proBNP lies in its sensitivity to cardiac stress and its role as a reliable marker for ventricular dysfunction. In the context of pediatric septic shock, where timely and accurate assessment is crucial, NT-proBNP emerges as a promising tool to identify and monitor myocardial dysfunction. Establishing a robust correlation between NT-proBNP levels and the severity of myocardial dysfunction can potentially serve as a prognostic indicator, enabling timely interventions to mitigate the risk of fatal outcomes[10].

Despite the recognized significance of NT-proBNP in adult septic shock patients, limited research has focused on its correlation with myocardial dysfunction in the pediatric population. The unique physiological characteristics of children, coupled with differences in the etiology and progression of septic shock, warrant a dedicated investigation into the role of NT-proBNP in this context. This research aims to bridge existing knowledge gaps and contribute to the refinement of clinical practices by elucidating the relation between NT-proBNP levels and the extent of myocardial dysfunction in children with septic shock.

This research holds profound implications for both clinical practice and academic advancement. By establishing a robust correlation between NT-proBNP and myocardial dysfunction in pediatric septic shock, clinicians can enhance their diagnostic and prognostic capabilities, allowing for more targeted therapeutic interventions. Furthermore, a deeper understanding of the molecular and physiological mechanisms involved in the relationship

between NT- pro BNP and myocardial dysfunction can pave the way for innovative treatment modalities and intervention strategies. The correlation between NT-proBNP and myocardial dysfunction in patients with septic shock addresses a critical gap in our understanding of this complex and life-threatening condition. Through meticulous investigation, this study aims to contribute valuable insights that may reshape the landscape of pediatric septic shock management, ultimately improving outcomes for these vulnerable patients.

2. REVIEW OF LITERATURE

Sepsis, sepsis syndromes, septic shock, and multiorgan system failure are critical conditions encountered in the pediatric intensive care unit (PICU) setting. Sepsis is a clinical syndrome that complicates severe infection and is characterized by systemic inflammation and widespread tissue injury. It is defined as a life-threatening organ dysfunction represented by an increase in the Sequential (sepsis-related) Organ Failure Assessment (SOFA) score, with septic shock being a subset of sepsis associated with profound circulatory, cellular, and metabolic abnormalities and a greater risk of mortality. Approximately 40% of patients with sepsis may develop septic shock, and mortality rates range from 40% to 75% in patients with multiorgan dysfunction syndrome (MODS). Table 1 shows the Definitions for Pediatric sepsis, severe sepsis, and septic shock as determined by the 2005 International Pediatric Sepsis Consensus Conference[11].

Table 1: Definition of sepsis in children

Term	Definitions
SIRS	•Meets at least two of the following requirements, one of which is temperature or WBC count
	• > 38.5 °C(Pyrexia) or < 36 °C (hypothermia)
	•Tachycardia or bradycardia which is age-dependent
	• require for mechanical ventilation or Tachypnea
	• > 10% immature neutrophils / Abnormal WBC count
Sepsis	**Confirmed or suspected infection and SIRS**
Severe sepsis	Respiratory dysfunction, or dysfunctions of two or more non-cardio respiratory organ system, **cardiovascular dysfunction and sepsis**
Septic shock	Defined as either hypotension, using vasoactive medications, or poor perfusion despite fluid resuscitation, **Sepsis and cardiovascular dysfunction**,

In this section, we discuss on Septic shock in children, which is severe illness that causes cardiovascular failure.

In 2016, the definitions for sepsis and septic shock in adults were revised, resulting in the publication of new criteria known as Sepsis-3. Under these criteria, sepsis is defined as organ Dysfunction caused by a dysregulated response to infection, while septic shock is identified as a subset of sepsis characterized by circulatory and cellular-metabolic dysfunction, which is associated with a higher risk of mortality[12].

In 2020, the Surviving Sepsis Campaign released guidelines for managing septic shock and sepsis-associated organ dysfunction in children. There is ongoing debate about whether the 'adult' definition of sepsis is applicable to children under five, and official updates to the 2005 pediatric sepsis definition are still awaited[13].

2.1. Epidemiology

The epidemiology of paediatric septic shock is a significant public health problem, with an estimated incidence of 1.2 million cases per year and a mortality rate ranging from 5% to 20% in developed countries[14]. A review of the incidence of Septic shock including severe sepsis among children admitted in hospital found that it ranges between 1-26%.[14] In developing countries, the burden of septic shock is particularly high , with the highest number of cases and deaths. Specialists emphasize that prevention, education, and coordination are key to reducing the burden of sepsis, especially in resource-limited settings[14,15] Several studies have reported a high prevalence of sepsis-induced myocardial dysfunction (SIMD) in pediatric patients with septic shock. SMID, a symptom of organ dysfunction in sepsis, is the primary cause of septic shock and is distinguished by myocardial systolic and diastolic dysfunction[16]. According to reports, septic shock patients might die at a rate of up to 38%[16]. The prevalence of SIMD in septic shock ranges from 71% to 23%, with diastolic dysfunction being more prevalent than systolic dysfunction. Myocardial dysfunction is associated with an increased requirement for inotropes and has been independently associated with mortality in

children with septic shock. The dysfunction is reversible in most cases, and the presence of myocardial dysfunction is associated with an increased requirement of vasopressors and mortality. Therefore, myocardial dysfunction is a clinically significant issue in the management of children with septic shock[6,17].

The epidemiology of pediatric septic shock in India is also of significant concern, with studies reporting high mortality rates. An Indian study from PGI, Chandigarh, reported a mortality rate of 65.8% in fluid-refractory septic shock[18]. Another study from Rohtak, Haryana, observed a mortality rate of 42% among children with sepsis, severe sepsis, and septic shock[19]. These findings highlight the substantial impact of septic shock on pediatric health in India. The overall prevalence of septic shock and severe sepsis among hospitalized children ranges from 1 to 26%, with fatality rates ranging from 5% in developed countries to higher rates in some circumstances.[14] Decreasing rate of mortality due to Sepsis in childhood is a global concern, particularly in developing nations like India, where the most cases and deaths are recorded[14]. A study evaluating 30 patients with septic shock in India found that myocardial dysfunction occurred frequently, with no significant effect on hospital length of stay but a mortality rate of 7%[17]. Another Indian study reported myocardial dysfunction in 71% of pediatric patients with septic shock, highlighting the commonality of this condition in this population[20]. The prevalence of left ventricular systolic and/or diastolic dysfunction was found to be 53% in a study of pediatric septic shock, indicating a high occurrence of myocardial dysfunction[17]. Additionally, a prospective observational study revealed that sepsis-induced myocardial dysfunction was associated with increased requirement of inotropes in the first 48 hours, emphasizing its clinical significance in the management of septic shock in children[6]. Therefore, the evidence from these studies suggests that myocardial dysfunction is a prevalent and clinically significant issue in the context of pediatric septic shock in India.

Immunosuppression, malignancy, starvation, invasive procedures, burns, major surgery, trauma, previous antibiotic therapy, an underlying genetic vulnerability and protracted hospitalization, all increase the risk of severe sepsis and septic shock[21,22]. In a large-scale research of various age groups and locales, diarrhoeal disease was the most prevalent underlying cause of sepsis, and lower respiratory infection was the most common underlying cause of sepsis-related mortality[22,23].

2.2. Aetiology

The aetiology of children with septic shock is commonly linked to severe infection leading to cardiovascular dysfunction and organ failure. The prevalence of severe sepsis and septic shock among children admitted in hospital ranges from 1 to 26%, with mortality rates ranging from 5% in developed countries to higher rates in certain settings[14]. Specific causes of septic shock in children can include bacterial, viral, or fungal infections, with factors such as age, underlying health conditions, and immune status influencing the risk and severity of the condition[24]. It's important to note that the aetiology of septic shock can vary across different populations and healthcare settings. The majority of sepsis patients, except for patients who are immune-compromised with neutropenia, have an infectious emphasis[22]. Sepsis was primarily caused by gram-positive bacteria prior to the use of antibiotics. Then Gram-negative bacteria become the primary pathogens causing septic shock. Septic shock and severe sepsis caused by gram-positive organisms have increased in recent years as the severely ill have used invasive treatments and vascular access more frequently. As a result, both gram-positive and gram-negative microbes are equally prone to cause septic shock in individuals. A meta-analysis study showed how bacterial strain and infection site affect mortality. In this investigation, association of gram-negative infections with increased fatality rates was reported. However, gram-positive infection with *Acinetobacter* or pneumonia with *Staphylococcus* resulted in a 40% mortality rate, with *Pseudomonal pneumonia* having the highest mortality rate of 70%.[25]

Vancomycin-resistant enterococci (VRE) and multidrug-resistant bacterial strains (methicillin-resistant Staphylococcus (MRSA) are responsible for the most Sepsis syndromes, with a current incidence of up to 25%; parasites and viruses cause substantially less occurrences, accounting for only 2% to 4%.[26] In one investigation, the most common infection location was reported to be the respiratory system (about 40%), followed by the bloodstream (19%)[21,22].

Myocardial dysfunction in children with septic shock can be attributed to sepsis-induced myocardial dysfunction (SIMD), which is a known consequence of severe sepsis and septic shock. The pathogenesis of this dysfunction is a result of an interplay of various factors, and the hemodynamic changes observed in children. These changes may differ from those in adults. The cause of sepsis-related cardiac dysfunction in children is not well understood, although it can be characterized as reversible intrinsic myocardial systolic and diastolic dysfunction[17,27,28].

2.3. Pathophysiology

The pathophysiology of septic shock in children involves a complex response to severe infection, leading to a dysregulated immune and inflammatory reaction. This response triggers the release of pro-inflammatory and anti-inflammatory mediators, activation of monocytes, macrophages, and neutrophils, and interaction with the endothelium, leading to microvascular injury, coagulation activation, and vascular dysfunction[26]. The process involves the diffuse activation of inflammatory and coagulation cascades, vasodilatation, vascular maldistribution, and defective oxygen and nutrient use at the cellular level. Septic shock is characterized by persistent hypotension and tissue hypoperfusion, leading to organ dysfunction and failure. The primary site of this response is the endothelium, which plays a central role in the pathophysiology of septic shock, causing both microvascular injury and coagulation activation. The in balance in oxygen supply and demand can lead to tissue

hypoperfusion, manifested by signs of end-organ damage. The pathogenesis of septic shock is not completely understood, but it is known to involve a complex response of cellular activation, triggering the release of a multitude of pro-inflammatory mediators (Figure 1).

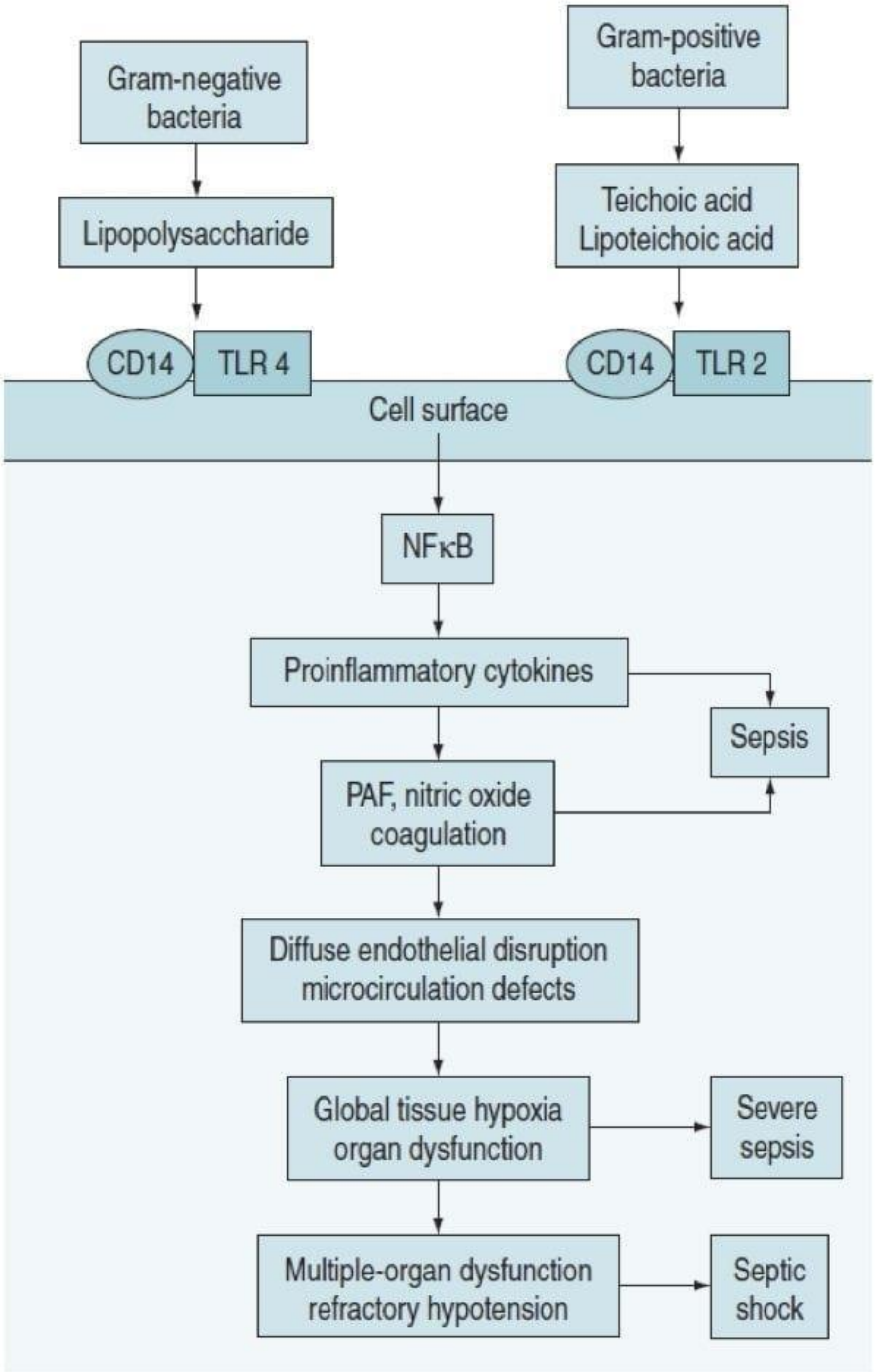

Figure 1: Pathophysiology of Septic shock

Research has shown that children with moderate-to-severe myocardial dysfunction associated with septic shock had greater plasma levels of inflammatory markers such as tumor necrosis factor-alpha (TNF-α) and interleukin-10 (IL-10)[17]. The activation of nuclear factor kappa-B (NF-κB), a key regulator of inflammatory responses, has been associated with myocardial dysfunction and mortality in children with septic shock[17]. The pathophysiology of sepsis-induced myocardial dysfunction (SIMD) involves a complex interplay of various factors, including the release of inflammatory mediators, changes in afterload , preload and myocardial contractility due to a dysregulated response to infection[6]. These findings suggest that the inflammatory response(Figure 2), characterized by the release of cytokines and the activation of NF-κB, contributes to the development of myocardial dysfunction in children with septic shock[6,17,27,28]. Another prominent hallmark of sepsis is microvascular thrombosis induced by impaired anticoagulant systems, often known as disseminated intravascular coagulation (DIC)[29]. Microvascular thrombus causes tissue hypo-perfusion as well as reduced oxygen delivery. Inflammatory cytokines produce vascular endothelium damage, resulting in barrier function loss, interstitial edema, reduced vasomotor tone and capillary leak,[30]. The inflammatory cytokines cause mitochondrial oxidative stress and malfunction[31](Figure 3).

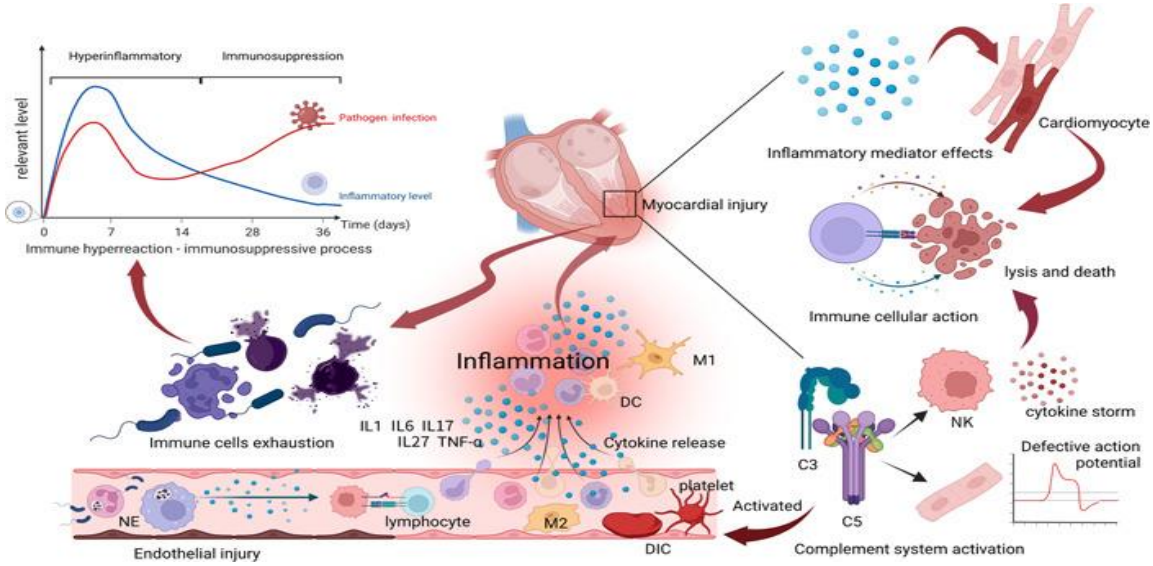

Figure 2: Myocardial dysfunction in sepsis mediated by immune response[32]

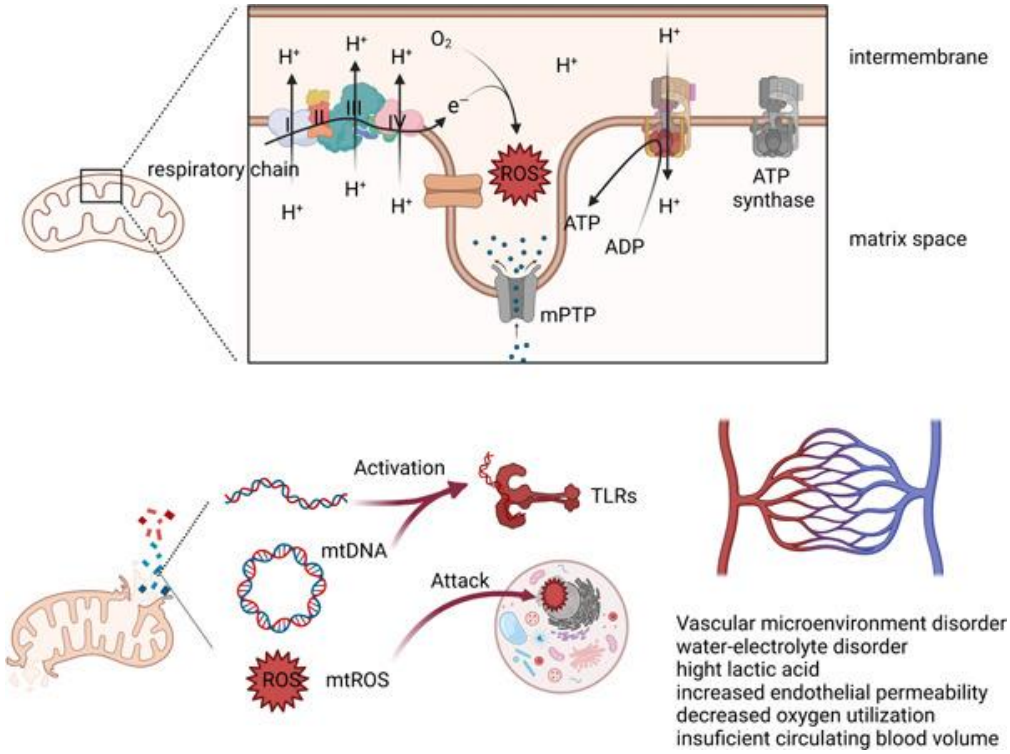

Figure 3: Mitochondrial oxidative stress[32]

2.4. Early diagnosis

Early diagnosis of myocardial dysfunction in children with septic shock is vital for timely intervention and improved outcomes. Given the severity of septic shock and its potential impact on cardiac function, here are some key considerations for early diagnosis:

2.4.1. Clinical Assessment

The clinical assessment of myocardial dysfunction in patients with septic shock typically involves a combination of clinical examination, laboratory tests, and echocardiography. Clinical examination may reveal signs of poor perfusion, such as cool extremities, delayed capillary refill, and altered mental status. Laboratory tests, including cardiac biomarkers such as troponin I and creatine kinase - MB, may be useful in identifying myocardial injury and dysfunction. Echocardiography is a important tool for the early detection of myocardial dysfunction in children with septic shock. Transthoracic echocardiography can evaluate

parameters such as left ventricular size and function, mitral valve inflow velocities, and myocardial performance index, which can effectively detect systolic and/or diastolic dysfunction in children with septic shock. Longitudinal studies have demonstrated the utility of echocardiographic measures in assessing myocardial dysfunction and its correlation with clinical outcomes in pediatric sepsis. Therefore, the clinical assessment of myocardial dysfunction in patient with septic shock involves a combination of clinical examination, laboratory tests, and echocardiography, with echocardiography being a valuable tool for early detection and monitoring of myocardial dysfunction in this population[6,20,33].

2.4.2. Hemodynamic monitoring

Effective hemodynamic monitoring can help identify cardiovascular instability early and choose targeted therapy timely[34]. Basic hemodynamics and advanced hemodynamics are the two groups of hemodynamics in sepsis. Basic hemodynamics include heart rate, systolic blood pressure, lactate level, mean arterial pressure, central venous pressure, and central venous oxygen saturation. Advanced hemodynamics include cardiac output, systemic vascular resistance, stroke volume, and stroke volume variation[35]. Hemodynamic monitoring can give values for recognizing the severity of myocardial dysfunction and guide the appropriate use of vasopressors and inotropic agents. Therefore, hemodynamic monitoring is an essential component of the management of septic shock in children with myocardial dysfunction.

2.4.3. Point-of-Care Ultrasound (POCUS)

Point-of-care ultrasonography (POCUS) enables quick assessment of cardiac function, fluid status, and obstructive physiology in patients with hemodynamic instability. POCUS can be combined with clinical assessment to help determine the cause of shock and guide the use of vasopressors or inotropes. Focused cardiac ultrasonography (FCU) facilitates the quick

evaluation of myocardial function. It can be particularly useful in identifying myocardial dysfunction in critically ill children with septic shock. Studies have shown that POCUS, including FCU, has a significant impact on medical and surgical management in the pediatric intensive care unit, making it a valuable tool for the assessment of myocardial dysfunction in this patient population[36].

2.4.4. Biomarkers

Biomarkers play a significant role in the assessment of myocardial dysfunction in children with septic shock. Studies have shown that cardiac biomarkers, such as troponin I (cTnI) and creatine kinase-MB (CK-MB), are associated with myocardial dysfunction in pediatric septic shock. Elevated cTnI and B - type natriuretic peptide (BNP) concentrations evaluated upon hospital admission have been linked to myocardial dysfunction among children with septic shock[17,37]. Additionally, longitudinal studies have demonstrated the utility of CK-MB in assessing myocardial dysfunction and its correlation with clinical outcomes in pediatric sepsis[20]. These biomarkers serve as valuable tools for identifying myocardial injury and dysfunction in children with septic shock, aiding in the early assessment and management of myocardial dysfunction in this population.

2.4.4.1. Brain natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP)

Brain natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP) are commonly employed as key indicators for clinical diagnosis of heart failure and cardiac dysfunction[9,38]. BNP was initially identified in 1988 after being isolated from pig brain. However, it was quickly discovered to originate primarily from the heart, indicating a cardiac hormone[39]. BNP is a member of the natriuretic peptide family, alongside ANP, CNP, and urodilatin, which share structural similarities. The natriuretic peptides share a biological structure consisting of a 17 amino acid ring and a disulfide bond between two cysteine molecules. The ventricular

myocardium produces and secretes the majority of BNP. Whereas ANP is kept in granules and released promptly after stimulation, BNP is only stored in small amounts, and the underlying mechanism for BNP secretion regulation involves fast gene expression with de novo peptide synthesis. BNP is synthesized as a Prehormone (pro BNP), which has 108 Amino Acids . In the circulation, it is broken in equal proportions to the physiologically active 32 amino acid BNP (C-terminal fragment) and 76 amino acid N-terminal fragment (NT-proBNP) which is biologically inactive. B-type natriuretic peptide (BNP) is a hormone primarily synthesized and secreted by the ventricular myocardium in response to mechanical stress, systemic ischemia, hypoxia, and neurohumoral factors. The synthesis and secretion of BNP are induced by myocyte stretch, which is a result of mechanical stress or pressure overload on the heart. Additionally, systemic ischemia and hypoxia, as well as neurohumoral factors, stimulate the secretion of BNP. The synthesis of BNP involves the translation of BNP mRNA into preproBNP, which is then converted to proBNP and subsequently cleaved into the biologically active BNP and the inactive N-terminal proBNP (NT-proBNP). These peptides are then secreted from the ventricles into the peripheral circulation(Figure 5).The synthesis and secretion of BNP are tightly regulated processes that play a crucial role in the maintenance of cardiovascular homeostasis. [9]The half-life of BNP is 20 minutes, while NT-proBNP has a half-life of 120 minutes[39].

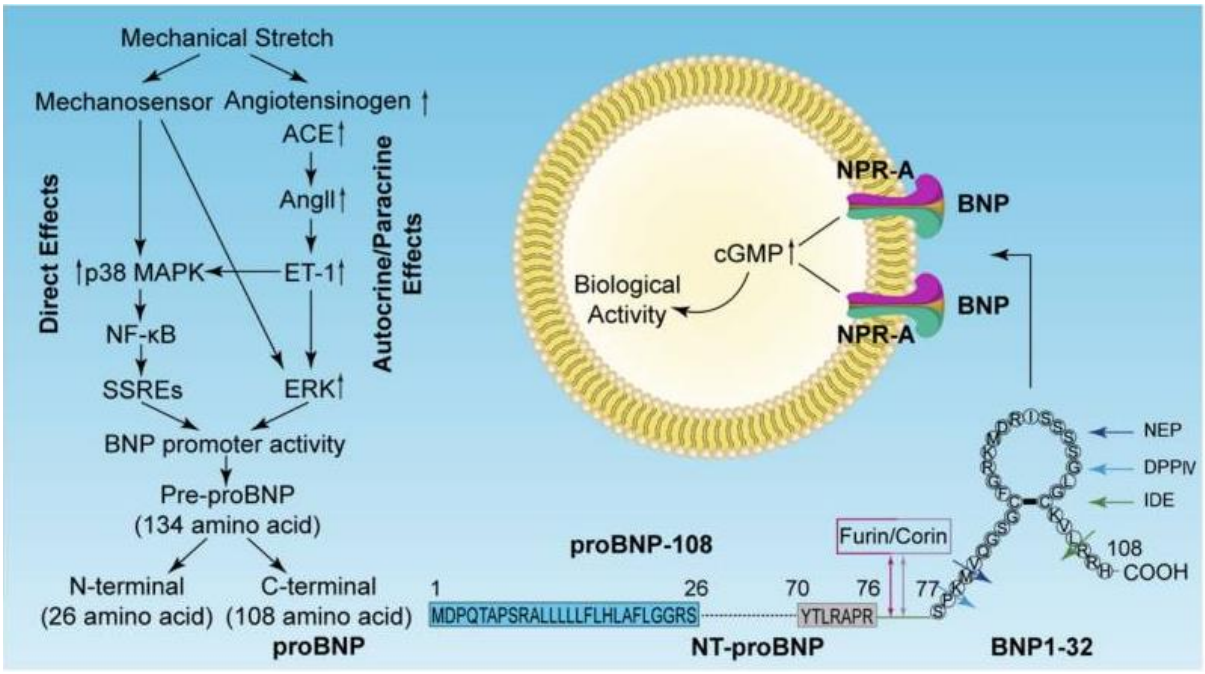

Figure 4: Synthesis of BNP and NT-proBNP[9]

Fully automated and commercially available assays can accurately assess BNP and NT-proBNP levels. Both markers tested at the point of care provide reliable results. BNP and NT -pro BNP plasma levels are measured in pg/mL or pmol/L. The conversion factor for BNP is 1 pg/ml = 0.289 pmol/l, while for NT-proBNP it is 1 pg/ml = 0.118 pmol/l. BNP is stable in whole blood at room temperature with EDTA for at least 24 hours, while NT-proBNP is stable for at least 72 hours without additives. BNP and NT-proBNP remain stable during freezing and thawing procedures[39].

Several studies have consistently shown that BNP and NT-proBNP levels are related to gender, with greater values in women, as well as with age, with higher values in older people. The gender relationship assumed to be mediated by metabolic variations, whereas the association with age may represent preclinical structural and functional cardiac changes. Patients with impaired renal function had higher BNP and NT-proBNP levels, which correlate negatively with creatinine clearance levels. Worsening renal function appears to have a greater effect on NT-proBNP than BNP. Elevated BNP and NT-proBNP

concentrations may be caused by fluid overload, left ventricular hypertrophy or diastolic and systolic dysfunction in addition to decreased renal clearance.

2.5. Treatment

The treatment of septic shock in children with myocardial dysfunction typically involves a multifaceted approach, including the use of vasopressors, inotropic agents, and good supportive care. To prevent and treat SIMD, it's important to address the total host-pathogen interaction, as the inflammatory response to sepsis is systemic (not only the heart) (Figure 4). Surviving Sepsis Campaign guidelines are a valuable starting point for the management of septic shock, emphasizing the importance of early recognition and prompt intervention. Children have been found to show well response to inotropic and, at times, vasodilating agents, underscoring the significance of myocardial dysfunction in the management of septic shock in this population. The use of inotropic agents, along with good supportive care, is crucial to improve outcomes in children with septic shock and associated myocardial dysfunction. The management of septic shock is evolving, moving away from protocolized guidelines-based approaches toward a more nuanced understanding of the pathophysiological changes involved. As our understanding of the pathophysiology of septic shock and myocardial dysfunction continues to advance, the management strategies are also evolving to improve outcomes in this patient population[27,28,32]

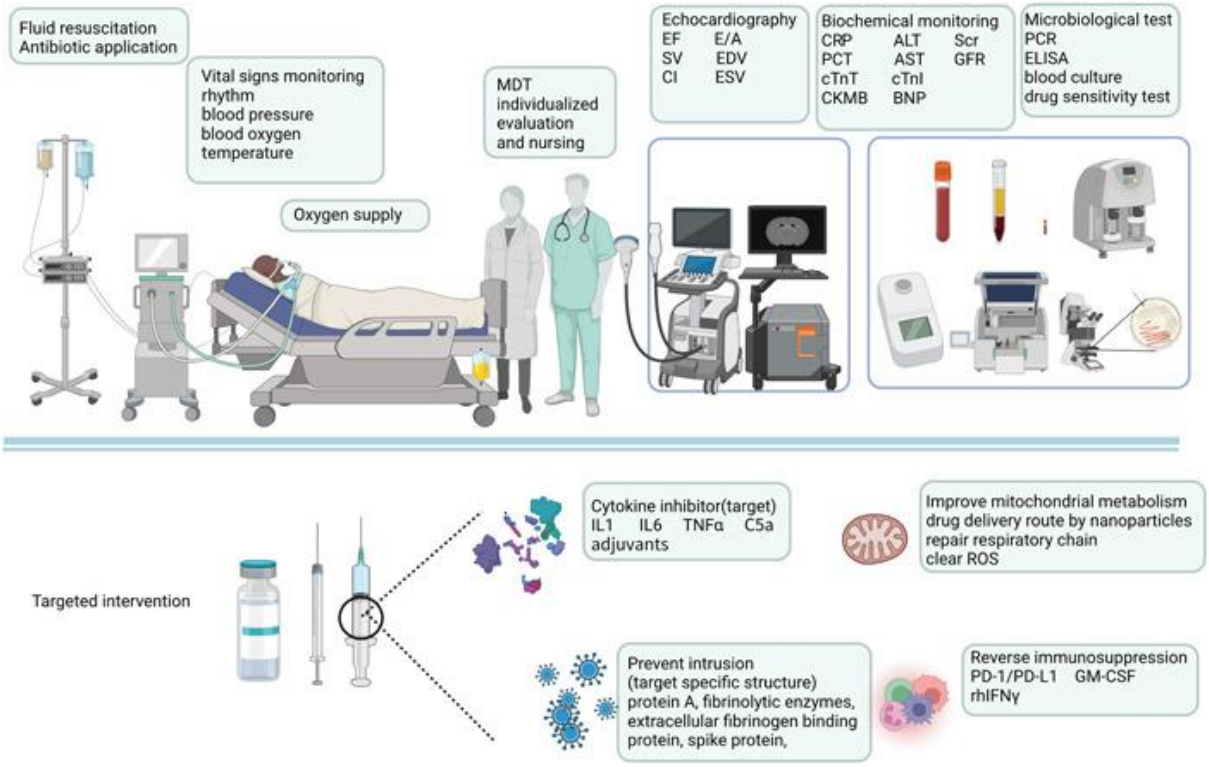

Figure 5: Treatment [32]

2.6. Association of NT-Pro BNP with cardiac dysfunction in children with septic shock

Several studies have demonstrated a correlation between B-type natriuretic peptide (BNP) levels and myocardial dysfunction in children with septic shock. Elevated NT-proBNP levels have been associated with cardiac dysfunction and poor clinical outcomes in pediatric septic patients[40,41]. Research has shown that NT-proBNP levels are elevated early in the disease course and are associated with cardiovascular dysfunction and worse outcomes in these patients[40]. Additionally, NT-proBNP levels have been found to be higher in patients with septic shock and myocardial dysfunction compared to those with preserved myocardial function, and they have been shown to correlate negatively with fractional shortening and positively with inotropic scores[40,42]. These findings support the utility of NT-proBNP as a biomarker for identifying and assessing myocardial dysfunction in children with septic shock.

The research paper "Early Elevated B-Type Natriuretic Peptide Levels are Associated with Cardiac Dysfunction and Poor Clinical Outcome in Pediatric Septic Patients" by Wu et al., 2015, investigated the association between B - type natriuretic peptide (BNP) levels, cardiac dysfunction, and clinical outcomes in pediatric septic patients. The study found that Brain natriuretic peptide levels were elevated initially in the disease course in pediatric septic patients and were associated with cardiovascular dysfunction and worse clinical outcomes. Specifically, elevated Brain natriuretic peptide levels were linked to the need for intensive care unit admission, mechanical ventilation, and inotropic support. While the association between elevated BNP levels and mortality was not statistically significant in this study, the findings indicated that elevated BNP levels were associated with increased morbidity in pediatric septic patients. The research suggests that BNP may serve as a valuable biomarker for identifying and assessing myocardial dysfunction in pediatric septic patients, and it may have implications for clinical management and outcomes in this patient population[40]. The study highlights the potential of BNP as an indicator of myocardial dysfunction and bad clinical outcomes in pediatric septic patients, providing valuable insights for the management of sepsis in this population.

The research paper "Diagnostic Accuracy of NT-ProBNP for Heart Failure with Sepsis in Patients Younger than 18 Years" investigated the potential of plasma NT-proBNP levels as a predictor of heart failure in pediatric patients with sepsis by Lin et al., 2016[10]. The study assessed NT – pro BNP levels in 211 pediatric sepsis patients and 126 healthy children. Patients were classified as having heart failure (HF) or non-heart failure (non-HF) and rated as having sepsis, severe sepsis, or septic shock. The study discovered that NT – pro BNP levels in sepsis patients were considerably greater than in healthy children, indicating the necessity to establish acceptable cut-off points for heart failure in pediatric sepsis. The study found that septic individuals with heart failure showed left ventricle systolic dysfunction, and

their NT-proBNP levels were considerably higher than those without. The study found the best plasma NT-ProBNP cut-off values for cardiac failure in various types of sepsis.This provided important clinical references for the heart failure diagnosis in pediatric patients with sepsis. The findings suggest that NT – pro BNP may predict mypcardial dysfunction in children with sepsis and can be a valuable tool for diagnosing and monitoring septic children for cardiac involvement.

The research paper "Clinical profile and outcome of septic shock in children admitted to a tertiary care referral hospital" by Kurade and Dhanawade (2016)[18] provides valuable insights into the clinical characteristics and outcomes of pediatric septic shock. The study was conducted in a tertiary care hospital and examined the case records of children aged 1 month to 18 years who had been diagnosed with septic shock. Out of 1035 admissions, 94 (9%) were found to have septic shock, with 53 (56.3%) being diagnosed with the condition. The mean age of the children with septic shock was 3 years, with the majority of cases (48.83%) occurring in infancy. The most common initial symptom was fever (62.79%), followed by disturbed mental status (30.23%). The pediatric SIRS criteria were met in 35 (81.3%) of cases. The study indicated that anemia, leucopenia, decompensated shock, and the necessity for mechanical ventilation were substantially linked with death ($p < 0.05$). Th e paper highlights the high mortality associated with septic shock in children and the importance of recognizing and managing the condition, especially in the presence of specific clinical and laboratory features. The findings from this research provide important insights into the clinical profile and outcomes of pediatric septic shock, emphasizing the need for early recognition and appropriate management to improve patient outcomes. The study's focus on specific clinical and laboratory parameters associated with mortality can help guide healthcare providers in identifying children at higher risk and implementing timely interventions to improve outcomes in this patient population.

The research paper "Association of NT-proBNP with clinical outcomes in children with systemic inflammatory response syndrome" by Mittelstaedt *et al.,* (2019) evaluated the impact of elevated N-terminal pro-brain type natriuretic peptide (NT-proBNP) levels in children with systemic inflammatory response syndrome (SIRS). The study found that severely elevated NT-proBNP levels were associated with increased morbidity in children with SIRS. Children with elevated NT-proBNP levels were more likely to require intensive care unit admission, mechanical ventilation, and inotropic support. While the relation between elevated NT-proBNP levels and mortality was not statistically significant in this study, the findings indicated that elevated NT-proBNP levels were linked to increased morbidity in children . The research suggests that NT-proBNP may serve as a valuable biomarker for identifying and assessing myocardial dysfunction in children with SIRS, and it may have implications for clinical management and outcomes in this patient population[43]. Further research in this area may help to elucidate the potential of NT-proBNP as a prognostic indicator and guide for therapeutic interventions in children with SIRS.

The paper "N-Terminal B Natriuretic Peptide as a Prognostic Marker in Sepsis-Induced Myocardial Dysfunction" by Kamal et al., (2022)[44] investigates the potential of N-terminal pro-brain natriuretic peptide (NT-proBNP) as a prognostic marker in sepsis-induced myocardial dysfunction[44]. The study aims to find the role of NT-proBNP in diagnosing sepsis-induced myocardial dysfunction (SIMD) and its association with clinical outcomes in pediatric patients. In this study, NT-pro BNP levels were found to be reliable predictors of cardiomyopathy across all patient groups. On the first day of admission, NT – pro BNP had a sensitivity of 75% and specificity of 70% at a cutoff level of >334 pg/ml. By the second day, the sensitivity was 65% and specificity increased to 80% with a cutoff level of >325 pg/ml. In subgroup analysis, pro - BNP showed 70% sensitivity and 90% specificity with a threshold of >334 pg/ml for predicting cardiomyopathy in the sepsis group. In the septic shock group, it

had 70% sensitivity and 80% specificity. Additionally, on the second day, pro - BNP was an excellent predictor of mortality in the septic shock group, achieving 100% sensitivity and specificity at a cutoff level of >350 pg/ml. The research provides insights into the diagnostic and prognostic utility of NT-proBNP in the context of sepsis-induced myocardial dysfunction, shedding light on its potential as a valuable biomarker for identifying and assessing cardiac involvement in septic patients.

3. AIMS AND OBJECTIVES

Primary objective:

To evaluate the Correlation between NT-proBNP and myocardial dysfunction in children with septic shock

Secondary Objective

To evaluate the correlation between NT-proBNP and severity of illness in children with septic shock

4. MATERIALS AND METHODS

Source of data:

Infants and children aged 29 days to 18 years with Septic Shock who were admitted to the PICU of the Department of Paediatrics at KLE's Dr Prabhakar Kore Hospital & Medical Research Centre in Belagavi, Karnataka.

Methods of Collection of Data:

A. STUDY DESIGN:

Cross sectional study

B. STUDY PERIOD:

One Year (January 2023- January 2024)

C. PLACE OF STUDY:

Department of Paediatrics at KLE's Dr Prabhakar Kore Hospital & Medical Research Centre in Belagavi, Karnataka

D. SAMPLE SIZE:

The sample size for the current study was calculated using following equation[45]

$$n = (\frac{Z_\alpha + Z_\beta}{C})^2 + 3$$

Where,

n= sample size

Z_{α}= score corresponding to the desired level of confidence (1.96 for a 95% confidence level)

Z_{β}= score corresponding to the desired power of the test (0.84 for 80% power)

C= The expected correlation coefficient = = $0.5 * In[\frac{(1+r)}{(1-r)}]$

Assuming the correlation between NT-proBNP and Myocardial Dysfunction in children with septic shock to be at least 0.4 the calculated sample size from above formula was 53 at 95% confidence interval and 80% power. Hence total 53 participants were included in the current study according to inclusion criteria.

E. SAMPLING TECHNIQUE

Purposive sampling was chosen for the current investigation because it involves the intentional selection of informants. It depends on their capacity to explain a given theme, concept, or phenomenon. Purposive sampling, as used in qualitative and mixed methods research, is an iterative process of selecting study subjects rather than beginning with a fixed sampling framework. The selection process includes finding themes, concepts, and indicators through observation and contemplation. Researchers frequently use a purposive sampling strategy to select informants based on their specific knowledge of, and/or experience with, the topic of empirical investigation.

F. INCLUSION CRITERIA

Infants and children aged 29 days to 18 years with septic shock and admitted in PICU at KLE's Dr Prabhakar Kore Hospital & Medical Research Centre were included in the study**.** All the patients who gave informed consent were considered in the current study. Septic shock was diagnosed on the basis of surviving sepsis campaign guidelines 2021[46].

G. EXCLUSION CRITERIA

Patients who were not willing to give consent, age >18 years, and receiving nesiritide (a recombinant form of human BNP) were excluded from the study. Patients with pre existing heart disease of any nature including repaired congenital heart defects and patients on circulatory assist devices (ECMO- extracorporeal membrane oxygenation) were excluded from the study.

H. METHODOLOGY

The study was a cross-sectional study conducted at KLE's Dr. Prabhakar Kore Hospital from January 2023 to January 2024. Following permission and clearance from the institutional ethics committee, patients who met the inclusion criteria were enrolled in the trial after providing informed consent (Annexure - 1) and explaining the study's design and aim in a language they understood.

The initial NT- pro BNP levels were obtained within 8H of admission to PICU. Subsequent measurement of NT- pro BNP levels was recorded at 48 H of admission. Severity of illness was determined clinically by PRISM III score (Annexure-2). It was calculated at the time of admission and at day two of admission. Myocardial dysfunction was evaluated by doing echocardiography within 24h of admission. Echocardiography results were interpreted by a paediatric cardiologist blinded to NT-Pro BNP levels. Demographic and clinical details of the children were collected using a semi-structured proforma that was developed for study (Annexure -3).

Total 53 patients were included in the current study. The socio-demographic information, clinical characteristics of patients and other required information were collected. Every piece of information was meticulously entered into an excel spread sheet and used for statistical analysis.

STATISTICAL ANALYSIS:

Continuous variables are represented as mean ± SD (standard deviation) whereas categorical variable are presented as frequency and percentages (n(%)).Continuous variables were compared using independent T-test/ or a Kruskal-Wallis test, and categorical variables were compared using a $\chi 2$ test or fisher's exact test to test association between attributes. P value < 0.05 was considered statistically significant. To identify the association between NT-pro BNP and Myocardial dysfunction, Pearson's or Spearman's rank correlation test was used. R version 4.2.2 statistical software was used for the statistical analyses. Microsoft word and Excel were used to generate graphs, tables etc.

5. RESULT

To evaluate the correlation between NT - proBNP and myocardial Dysfunction in children with septic shock and assess the relationship between severity of illness and NT-proBNP in septic shock children, a cross-sectional study was conducted on infants and children aged 29 days to 18 years with septic shock who were admitted to the PICU of the Department of Paediatrics at KLE's Dr Prabhakar Kore Hospital & Medical Research Centre in Belagavi, Karnataka between January 2023- January 2024. 53 patients according to inclusion criteria who provide informed consent to participate in the study were included in the study.

The study had 23(43%) female and 30(57%) male participants (Table 2). Distribution of patients based on gender is depicted in the following pie graph (Figure 6).

Table 2: Gender Distribution of study population (n=53)

Gender	Number of patients	Percent of patients (%)
Female	23	43
Male	30	57

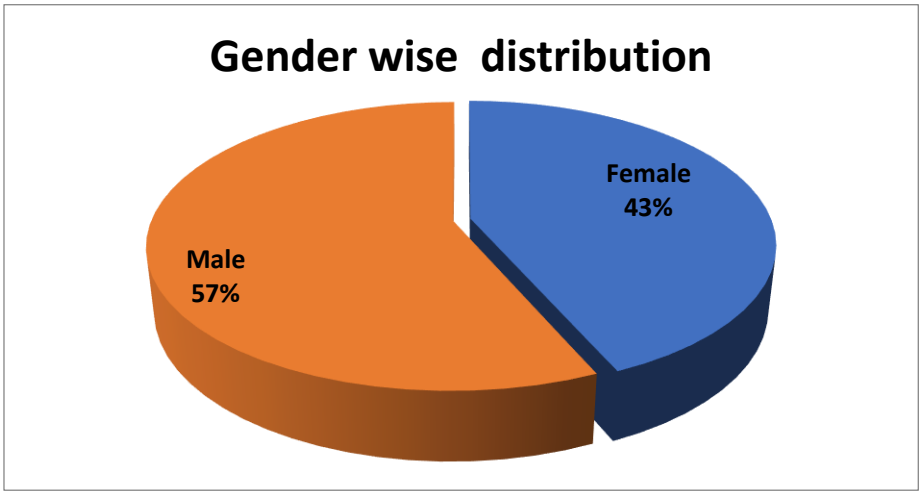

Figure 6: Pie chart showing distribution of gender

The mean age of the study population with standard deviation was calculated to be 7.65± 5.66 years with minimum age of 2 months and maximum age of 17 years (Figure 7). Table 3 show cases the mean value for age as well as age group wise distribution of 53 patients with septic shock. Over all 7(13.21%), 16(30.19%), 11(20.75%), 11(20.75%), and 8(15.09%) patients were belonged to the age groups of <1, 1-5, 6-10, 11-15 and >15 years respectively (Figure 8).

Table 3: **Distribution of patients based on age group**

Age, (Years)	Mean	Standard deviation
	7.56	5.66
Age group	Number of patients	Percentage of patients (%)
<1 year	7	13.21
1-5 years	16	30.19
6-10 years	11	20.75
11-15 years	11	20.75
>15 years	8	15.09

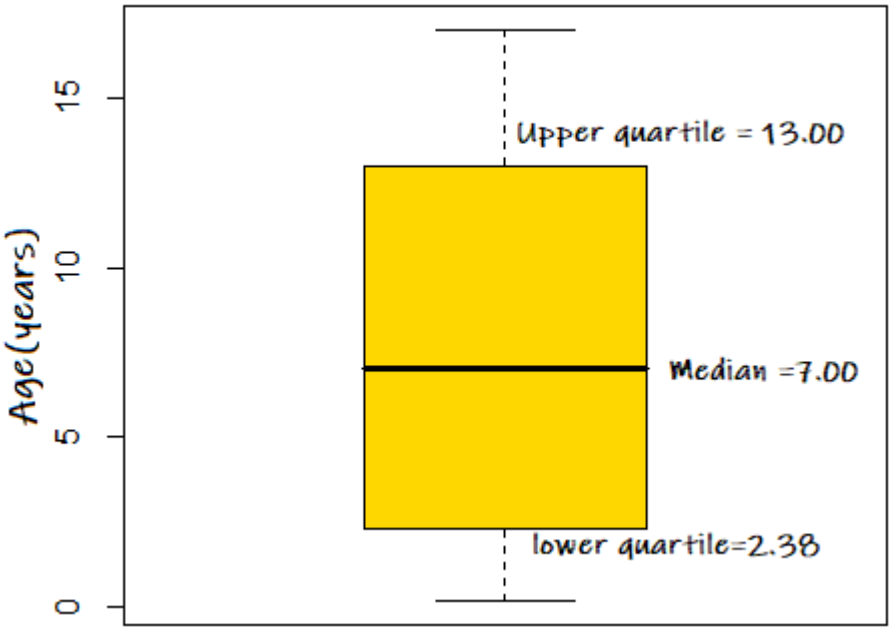

Figure 7: box plot showing Age distribution

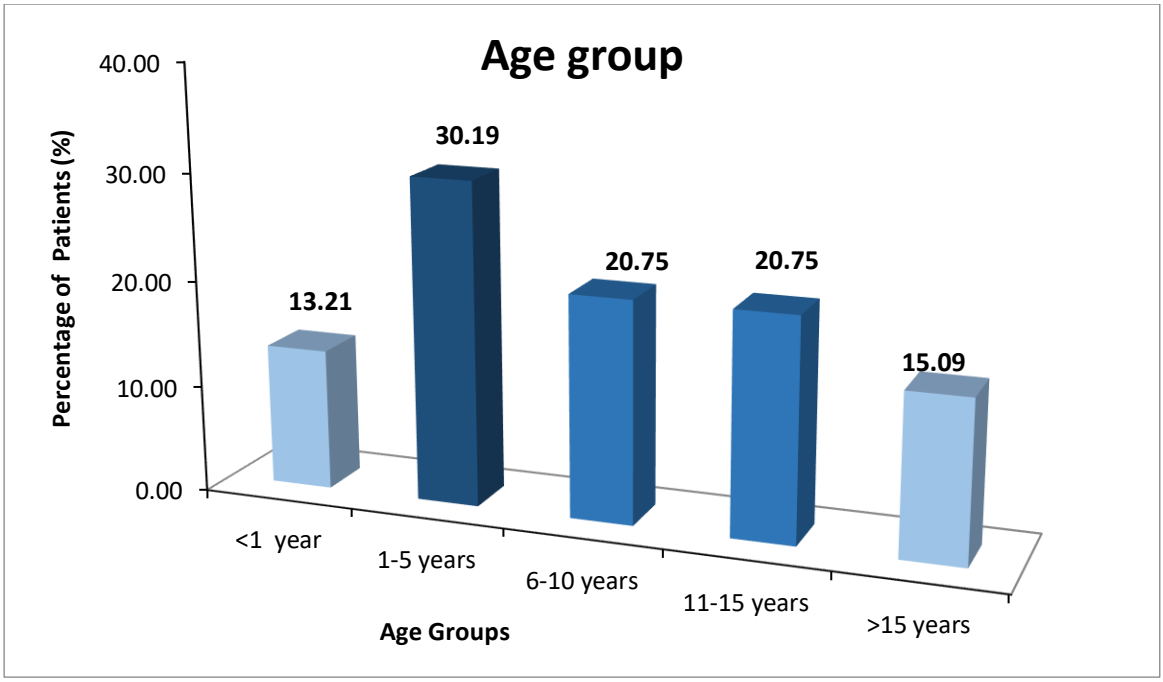

Figure 8: Bar graph for Distribution of patients based on age groups

PRISM score of patients at the time of Admission and After 48 hours were estimated and is tabulated in Table 4. Mean PRISM score at the time of admission and after 48 hours were 13.73±8.02 and 12.65±10.04 respectively. Graphical representation of distribution of PRISM score at the time of admission and after 48 hours is shown in Figure 9.

Table 4: Range of PRISM score

PRISM Score	Mean ± SD	Minimum-maximum
Admission	13.73±8.02	4.00-34.00
After 48 hours	12.65±10.04	2.00-38.00

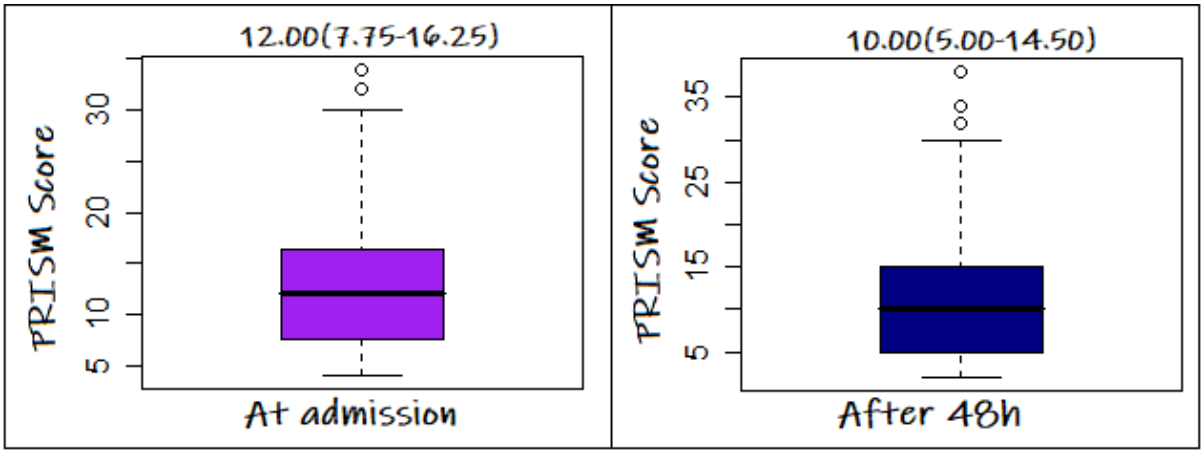

Figure 9: Box plot Distribution of PRISM score

Based on ECHO, myocardial dysfunction was divided into no, mild &moderate and severe dysfunction. Distribution of the patients based on severity of myocardial distribution is detailed in Table 5. It was found that 19(35.85%), 16(30.19%) and 18(33.96%) patients had no, mild & moderate and severe myocardial dysfunction respectively (Figure 10).

Table 5: Distribution of patients based on severity of myocardial dysfunction

Myocardial dysfunction	Number of patients	Percentage of patients
No dysfunction	19	35.85
Mild & Moderate dysfunction	16	30.19
Severe dysfunction	18	33.96

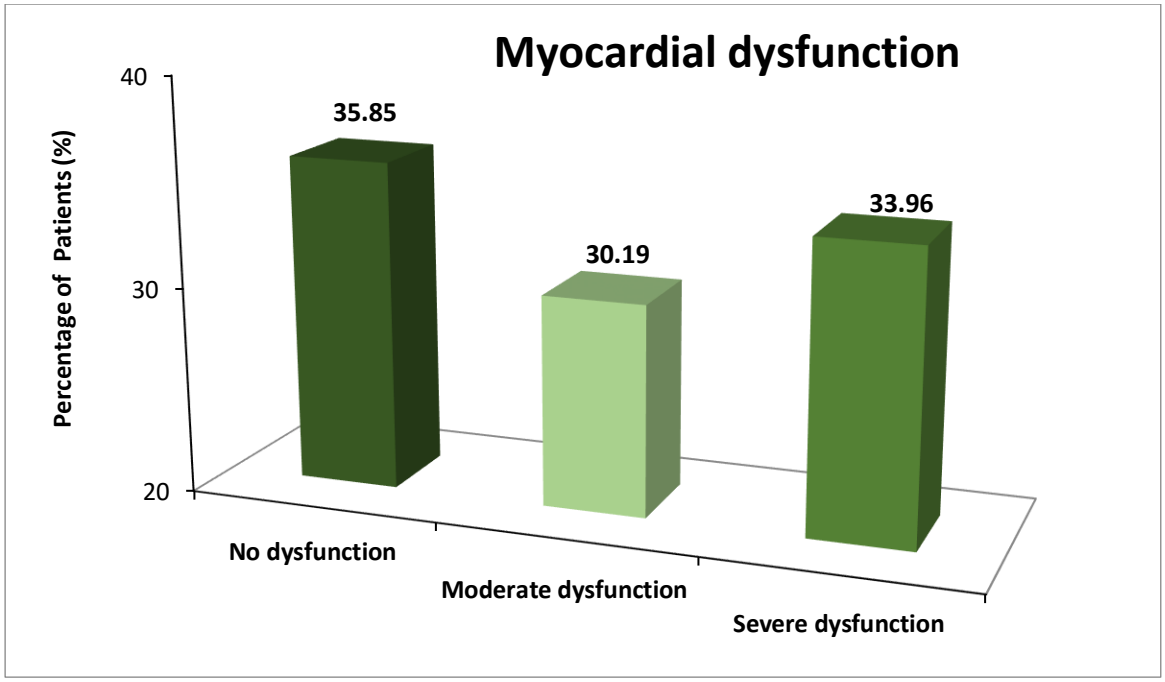

Figure 10: Bar graph showing distribution of patients based on type of myocardial dysfunction

Mean LVEF (left ventricular ejection fraction with myocardial dysfunction) of study population was 45.19±14.00% with minimum and maximum values of 20% and 60% respectively. Distribution of LVEF in the study population is shown in Figure 11.

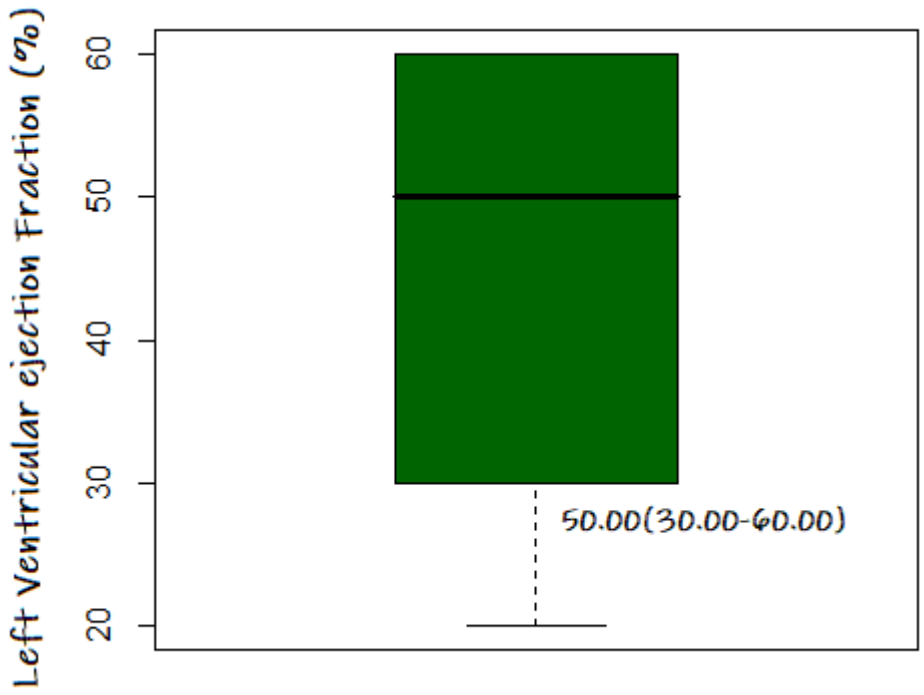

Figure 11: Distribution of Left ventricular ejection fraction presented in box plot

NT-proBNP values of patients at the time of admission and after 48 hours were measured and are shown in Table 6. 13993±12775 pg/mL and 14086±13346 pg/mL respectively were the mean (±SD) values of NT-proBNP at the time of admission and after 48 hours. Pictorial representation of distribution of NT-proBNP levels of patients at the time of admission and after 48 hours is shown in Figure 12 and 13 respectively.

Table 6: Distribution of NT-proBNP

NT-proBNP	Mean ± SD (pg/mL)	Minimum-maximum
Admission	13993±12775	52-36000
After 48 hours	14086±13346	480-37200

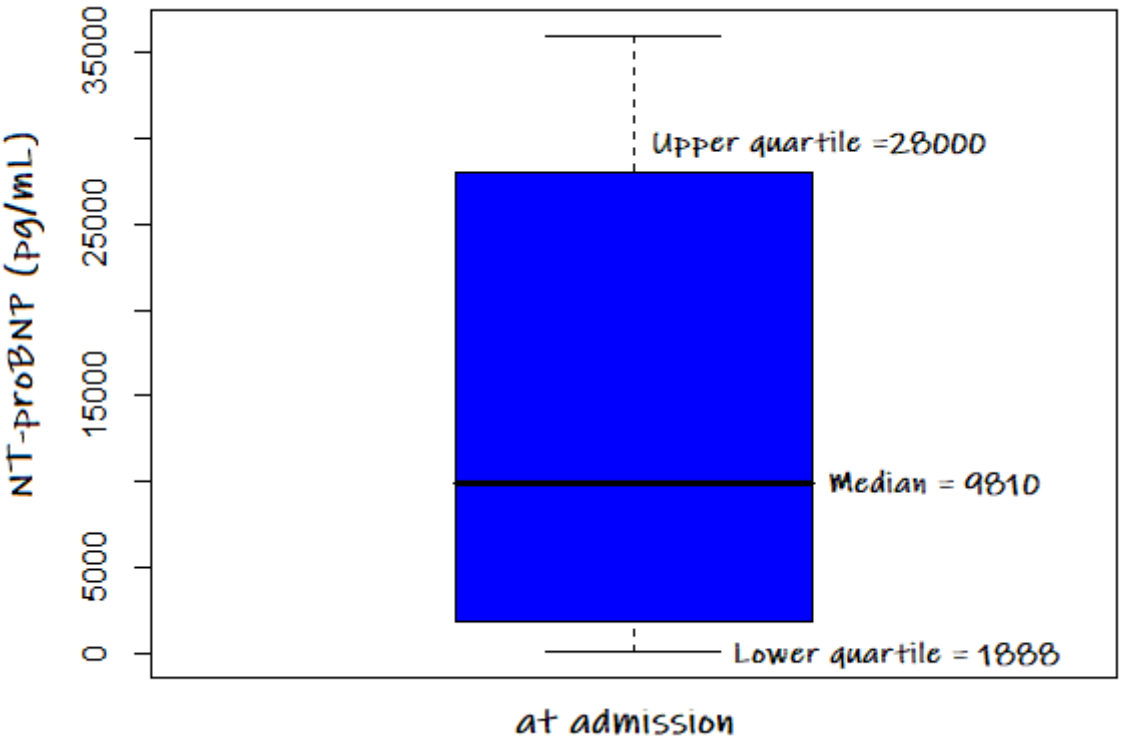

Figure 12: Box plot showing distribution of NT-proBNP level at the time of admission

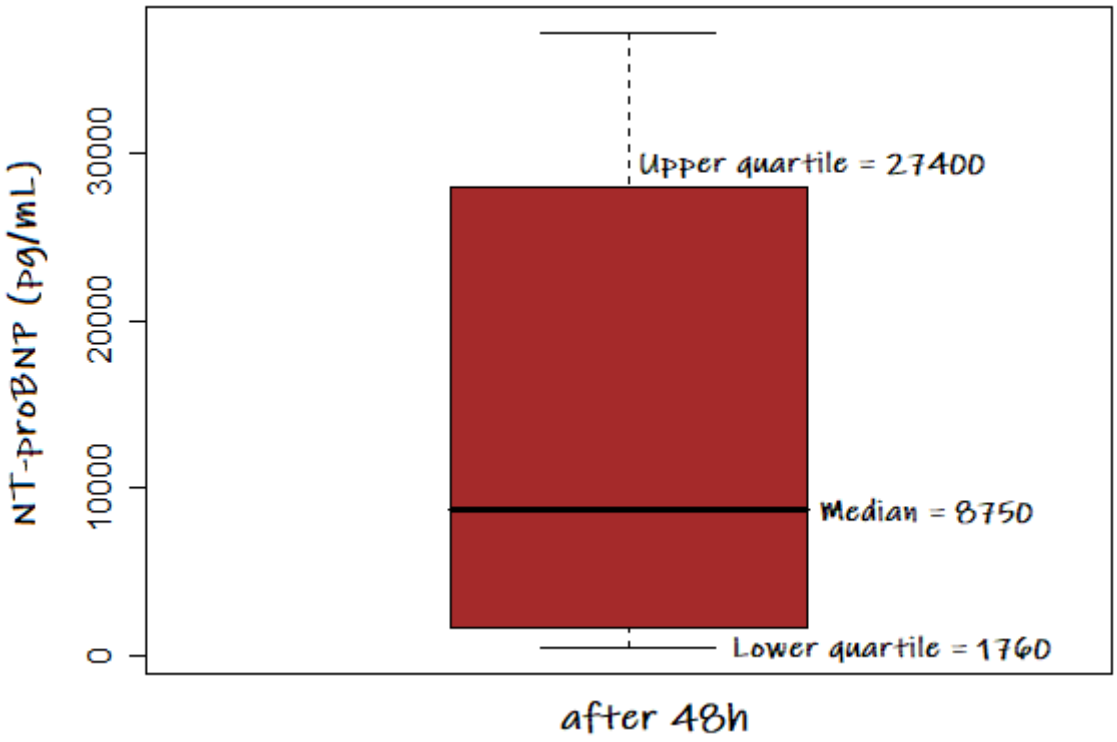

Figure 13: Distribution of NT-proBNP level after 48h presented in box plot

Minimum PICU stay by patient was 2 days where as maximum was 14 days. The mean PICU stay of study population was 5.39±1.94. Distribution of PICU days of study population with median and quartile values are shown in Figure 14.

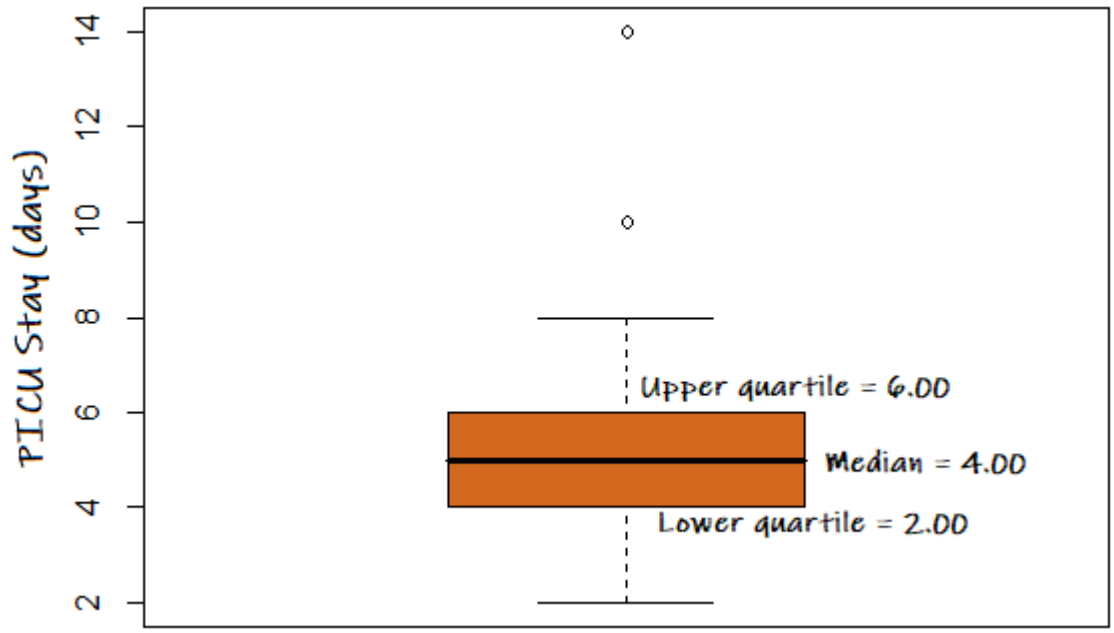

Figure 14: Box plot presenting distribution of PICU stay of patients

Survival of the patients is tabulated in Table 7. Out of 53 patients in the current study, 42(79%) patients survived where as 11 (21%) patients died (Figure 15).

Table 7: Distribution of the patients based on mortality

Outcome	Number of patients	Percentage of patients (%)
Survival	42	79
Death	11	21

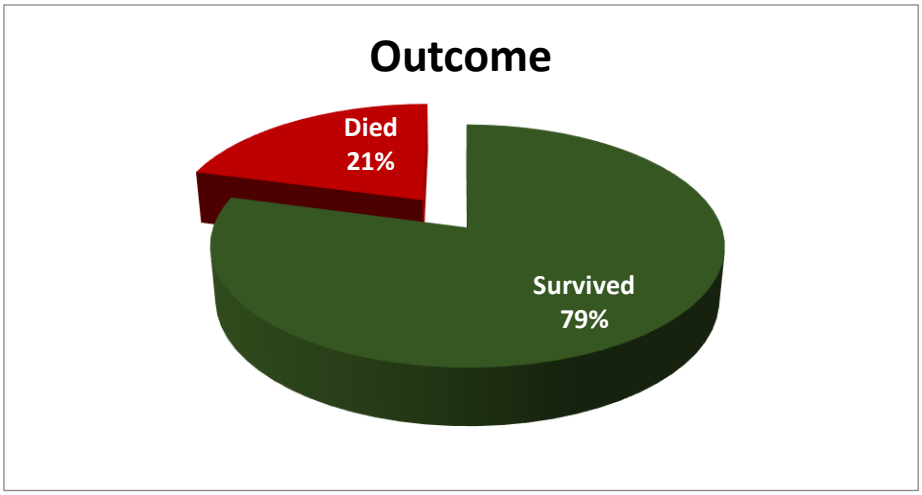

Figure 15: Distribution of patients based on outcome

Association of survival of patients and age and age group was assessed in the current study. Table 8 compares the mean age of survived and died patients, it found the mean age of patients who survived are significantly higher (8.71±5.45 years) than that of died patients (3.17±4.30 years).

Table 8: Distribution of patients based on age and survival

Outcome	Age (years) Mean ±SD
Survived	8.71±5.45
Died	3.17±4.30

Distribution of patients based on age group with respect to survival and death is shown in Table 9. It was found that significantly high number of patients (73%) in death group was in the

age group below 5 years and only 36% of patients below 5 years survived. Figure 16 shows the distribution of survived and died patients based on age groups.

Table 9: Distribution of patients based on age group and outcome

Age group	Survival (n=42)	Death (n=11)
<1 year, n (%)	3(7.14)	4(36.36)
1-5 years, n (%)	12(28.57)	4(36.36)
6-10 years, n (%)	10(23.81)	1(9.09)
11-15 years, n (%)	10(23.81)	1(9.09)
>15 years, n (%)	7(16.67)	1(9.09)

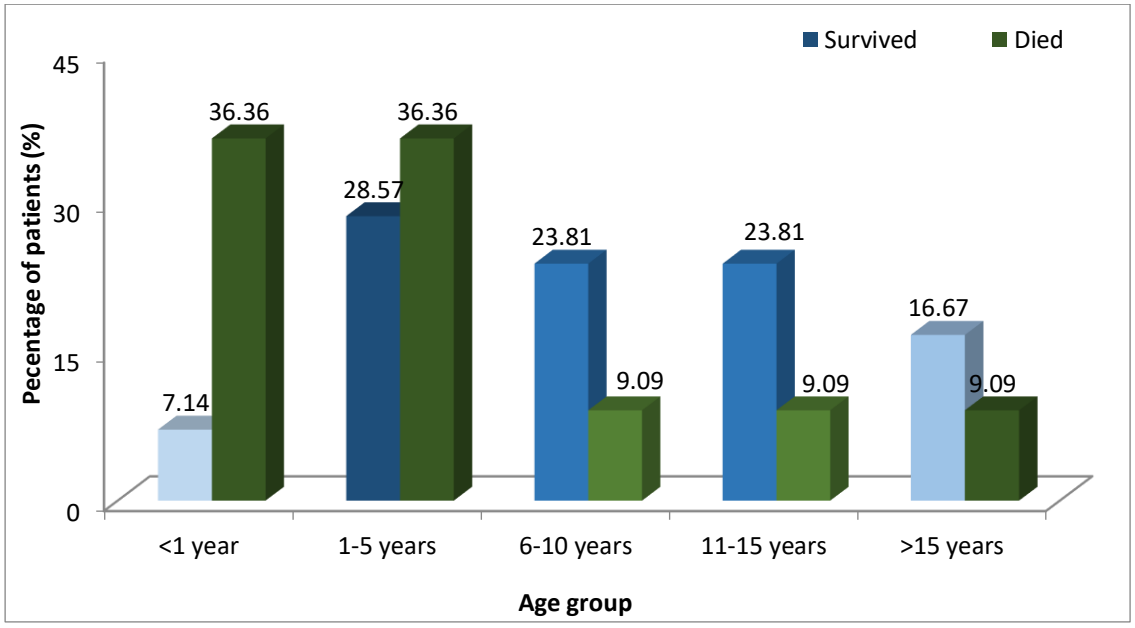

Figure 16: Column graph to show distribution based on age group and outcome

Distribution of male and female patients based on survival and death did not show any statistical difference (Table 10). Among the survival group of 42 patients there were 19(45.23%) female and 23(54.77%) male.

Table 10: Distribution of patients based on gender and outcome

Gender	Survival (n=42)	Death (n=11)
Female, n (%)	19(45.23)	4(36.36)
Male, n (%)	23(54.77)	7(63.64)

The association of PRISM score during admission and after 48 hours was evaluated for the study population. Significantly higher (P value <0.0001) PRISM score for both during admission and after 48 H was recorded for death when compared to survival (Table 11) and Table 12). The PRISM score for death at admission and after 48h was recorded as 8.33±4.63 and respectively. Whereas the PRISM scores for survival at admission and after 48h was recorded as 10.50±4.13 and 30.80±4.54. Graphical representations of the distribution of PRISM value at two different timings for survival and death are shown in Figure 16 and Figure 17.

Table 11: Association between PRISM Score at admission and outcome of patients

Outcome	PRISM Score at admission Mean ±SD	P value*
Survival	10.50±4.13	**<0.0001**
Death	27.4±5.42	

*statistically significant if p value <0.05 for t-test

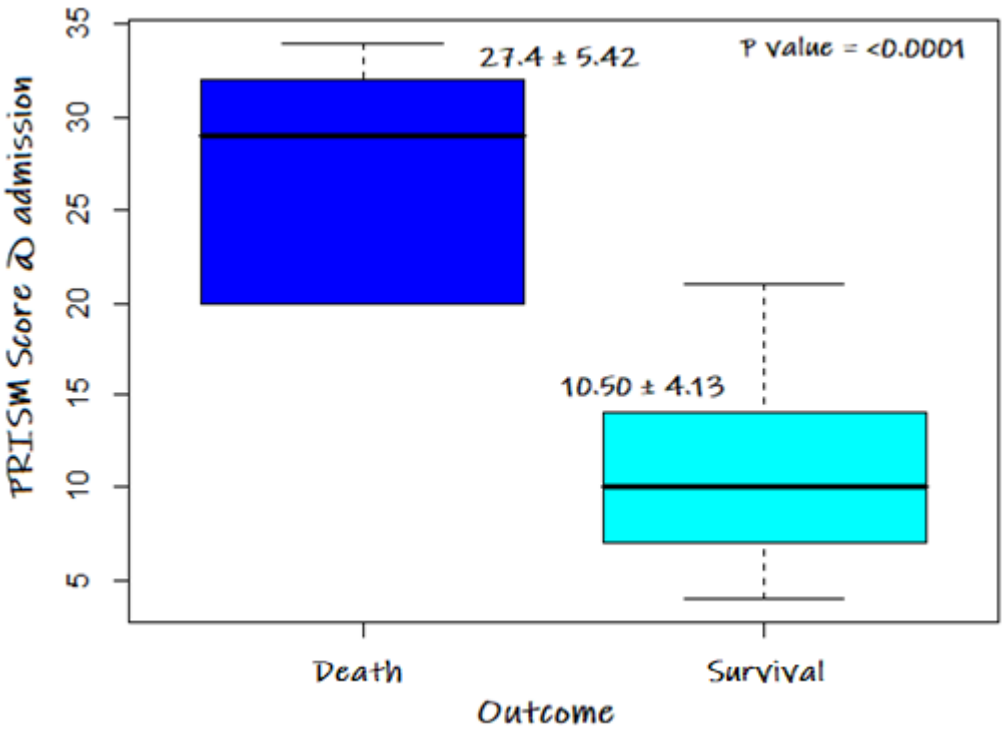

Figure 17: whisker plots show casing the association between PRISM Score at admission and outcome of patients

Table 12: Association between PRISM Score after 48h and outcome of patients

Outcome	PRISM Score after 48h Mean ±SD	P value*
Survival	8.33±4.63	**<0.0001**
Death	30.80±4.54	

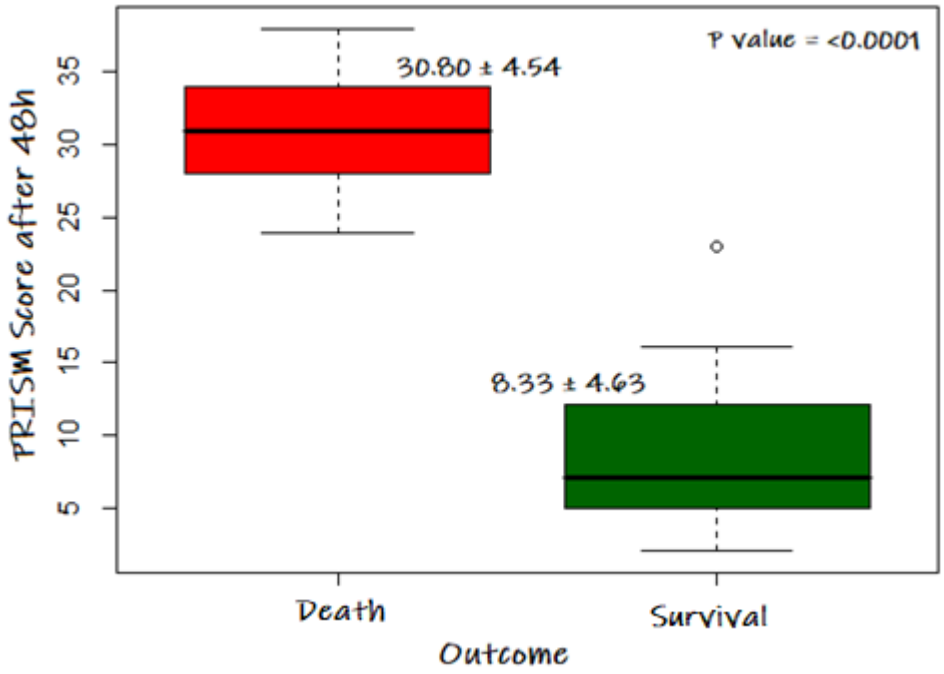

Figure 18: Box plot showing association between PRISM Score after 48h and out come

Association of NT-proBNP levels at admission and the outcome of the study (survival and death) were determined (Table 13). Significantly higher levels of NT-proBNP at admission was recorded for Death (29550 (28600 -33909) pg/mL) when compared for survival (6408(1800-16700) pg/mL) .Comparative box plots in Figure 19 present the distribution of NT-proBNP levels for death and survival.

Table 13: Association between NT- proBNP at admission and outcome of patients

Outcome	NT-proBNP at admission (pg/mL) Median(Q1-Q3)	P value*
Survival	6408(1800-16700)	**<0.0001**
Death	29550 (28600 -33909)	

*statistically significant if p value <0.05 for wilcoxon test

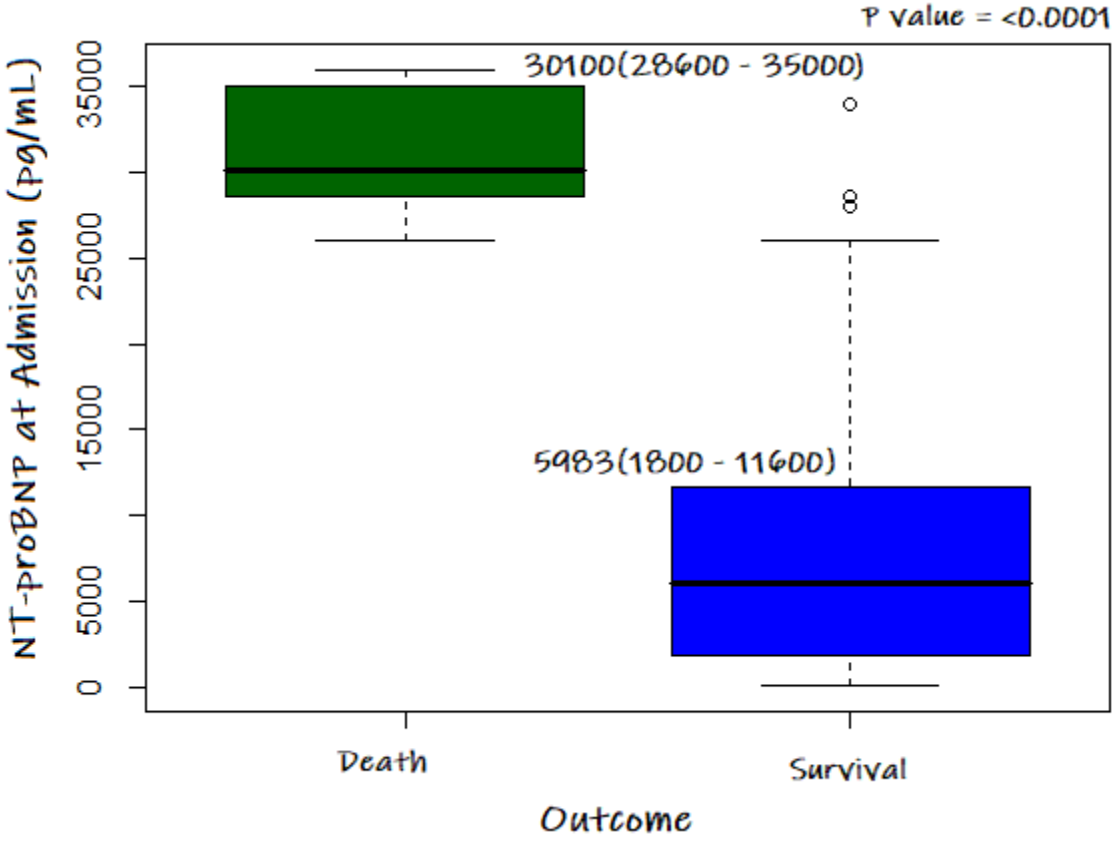

Figure 19: Association of NT-proBNP at admission and survival (box plot)

The relation between NT-proBNP levels after 48 hours and the study's outcome (survival or death) was determined (Table 14). NT - pro BNP levels were significantly greater after 48 hours for death (33100 (31400 -34875) pg/mL) than for survival (6867(1618-18625) pg/mL). Figure 20 shows comparative box plots of NT-proBNP levels at 48h for death and survival.

Table 14: Association between NT- proBNP after 48h and survival of patients

Outcome	NT-proBNP after 48h (pg/mL) Median(Q1-Q3)	P value*
Survived	6867(1618-18625)	**<0.0001**
Died	33100 (31400 -34875)	

*statistically significant if p value <0.05 for wilcoxon test

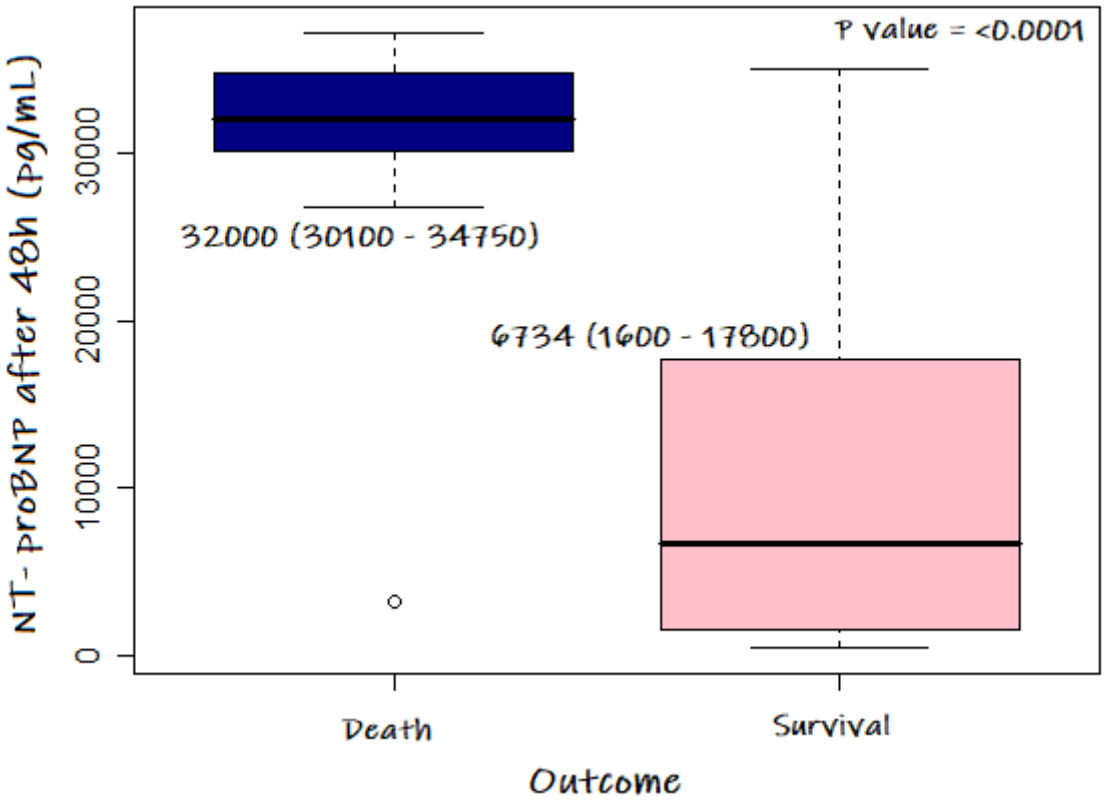

Figure 20: Box plots of NT-proBNP levels at 48h for death and survival.

It was found that there was a significant difference in the distribution of patients' outcome based on the severity of myocardial dysfunction. No patients had death with no or moderate dysfunction. It was seen that all those died had a severe dysfunction (Table 15). Among survived 19(45.24%), 16(38.09%) and 7(16.67%) had no, Mild & moderate and severe myocardial dysfunction respectively (Figure 21).

Table 15: Association between outcome and type of myocardial dysfunction

Outcome	Myocardial dysfunction			P value
	No	Mild & Moderate	Severe	
Survival, n (%)	19(45.24)	16(38.09)	7(16.67)	**0.000002**
Death, n (%)	0(0.00)	0(0.00)	11(100)	

*statistically significant if p value <0.05

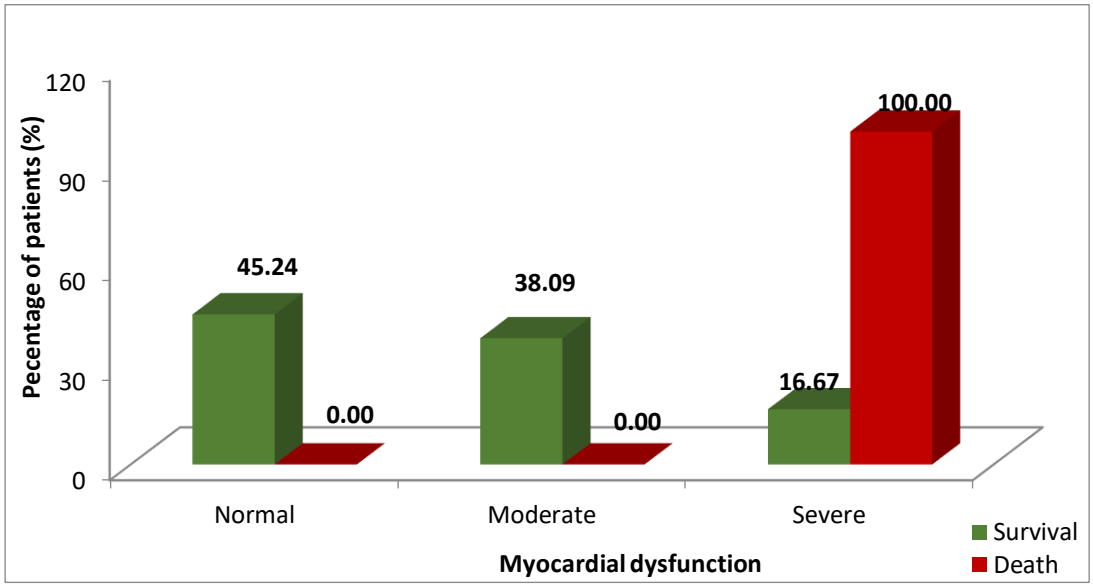

Figure 21: Association between myocardial dysfunction severity and survival

NT-ProBNP levels at admission and after 48 hours were evaluated for the types of myocardial dysfunction (Table 16). NT- proBNP levels for severe myocardial dysfunction was significantly higher when compared to mild & moderate and no myocardial dysfunction. NT-pro BNP in both the cases was found to rise with increasing severity of dysfunction from no dysfunction to severe dysfunction. NT-proBNP values for different myocardial dysfunctions are tabulated in Table 16. Comparative distributions of NT-proBNP at admission and after 48h for different myocardial dysfunction are shown in Figure 22 and 23.

Table 16: Association between NT-proBNP and myocardial dysfunction

NT-ProBNP	Myocardial dysfunction			P value *
	No	Mild &Moderate	Severe	
At admission (pg/mL)	1800(940-2650)	9350(5187-10775)	28600(28000-34000)	<0.0001
After 48H (pg/mL)	1100(900-2345)	8418(4420-9305)	31200(29200-34500)	<0.0001

*statistically significant if p value <0.05 for Kruskal Wallis test

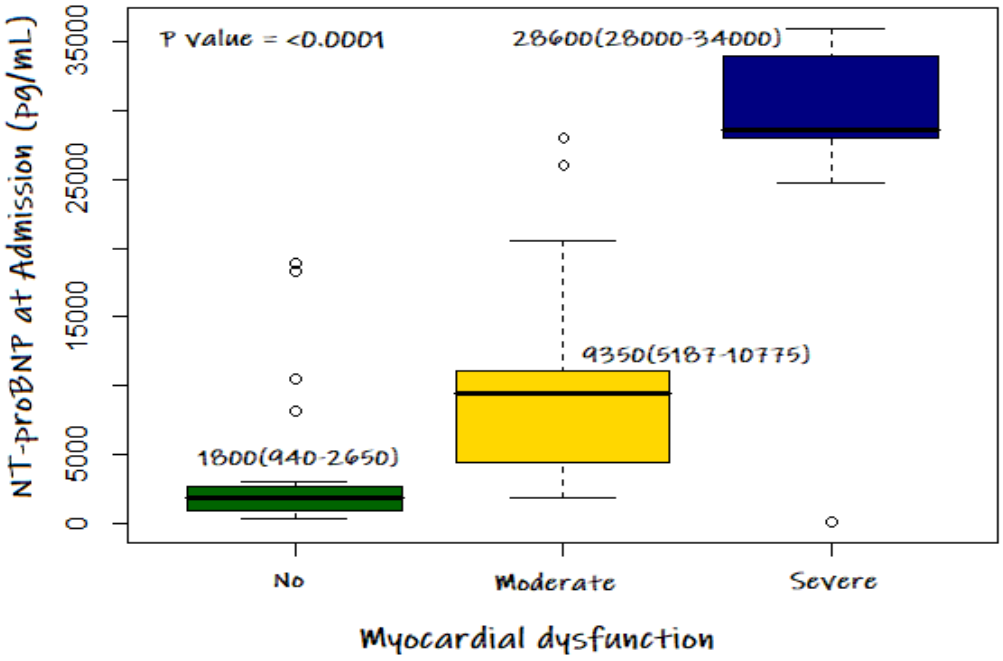

Figure 22: Box plots showing association between NT-proBNP levels at admission and myocardial dysfunction

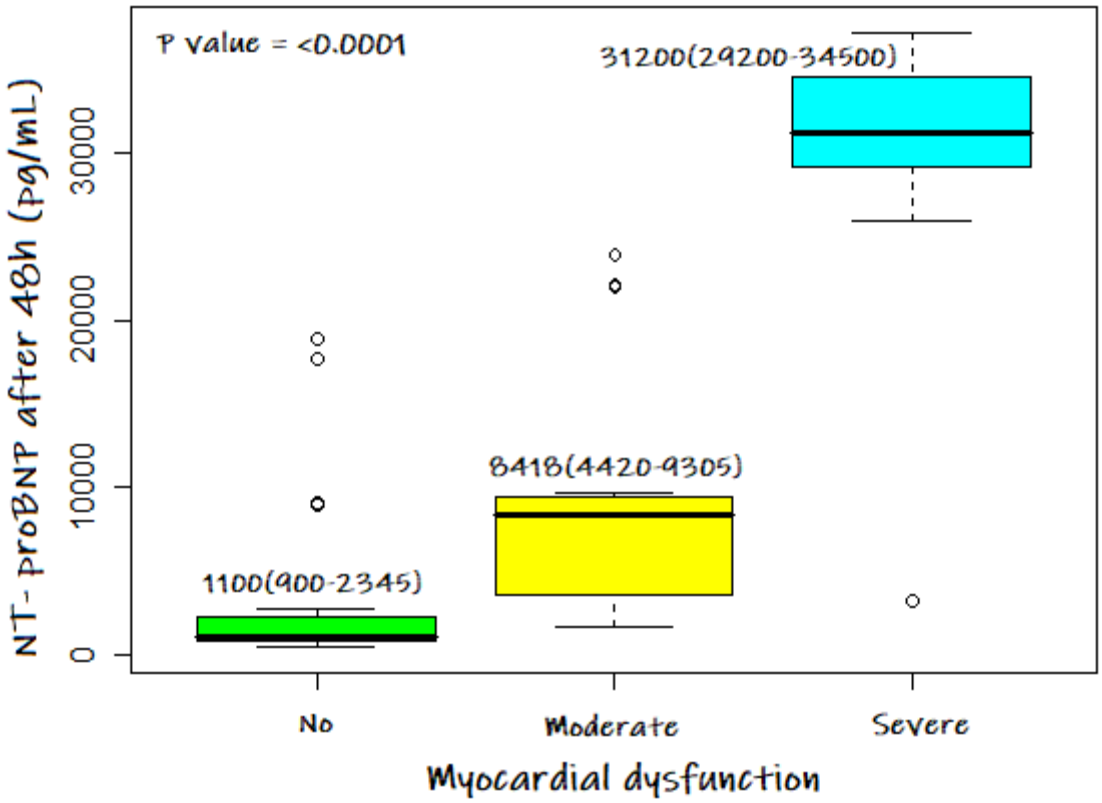

Figure 23: Box plot showing association between NT-proBNP after 48H and myocardial dysfunction

Correlation of NT-proBNP and PRISM score was carried out using Pearson's correlation test to know the Association of NT-proBNP levels and Severity of illness. Correlation between PRISM sore and NT-proBNP levels at admission and after 48hours was studied. During both the stages, study showed a significant correlation between NT –pro BNP and PRISM score indicating rise in NT-proBNP with increased serverity of illness (Figure 24 and 25). Correlation coefficient (R) values for data at admission and after 48 hours were found to be 0.60 and 0.61 respectively with p value <0.0001.

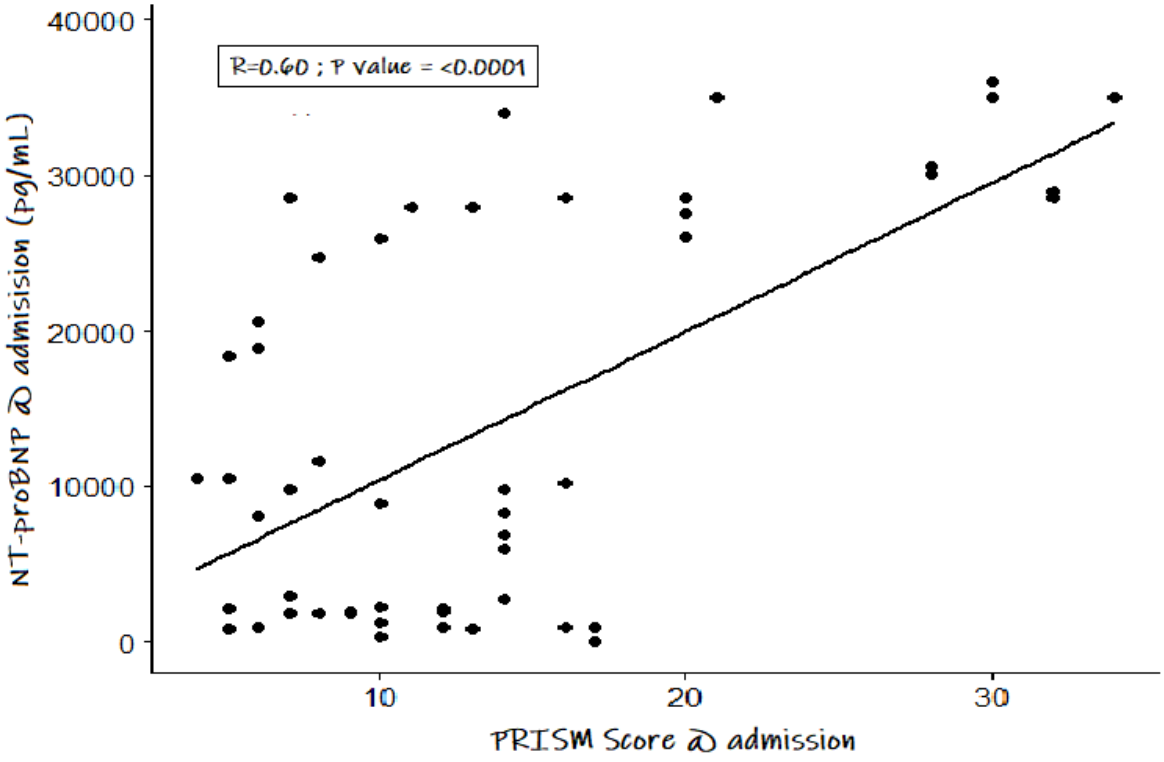

Figure 24: Scatter plot showing correlation between PRISM score and NT-proBNP levels at admission

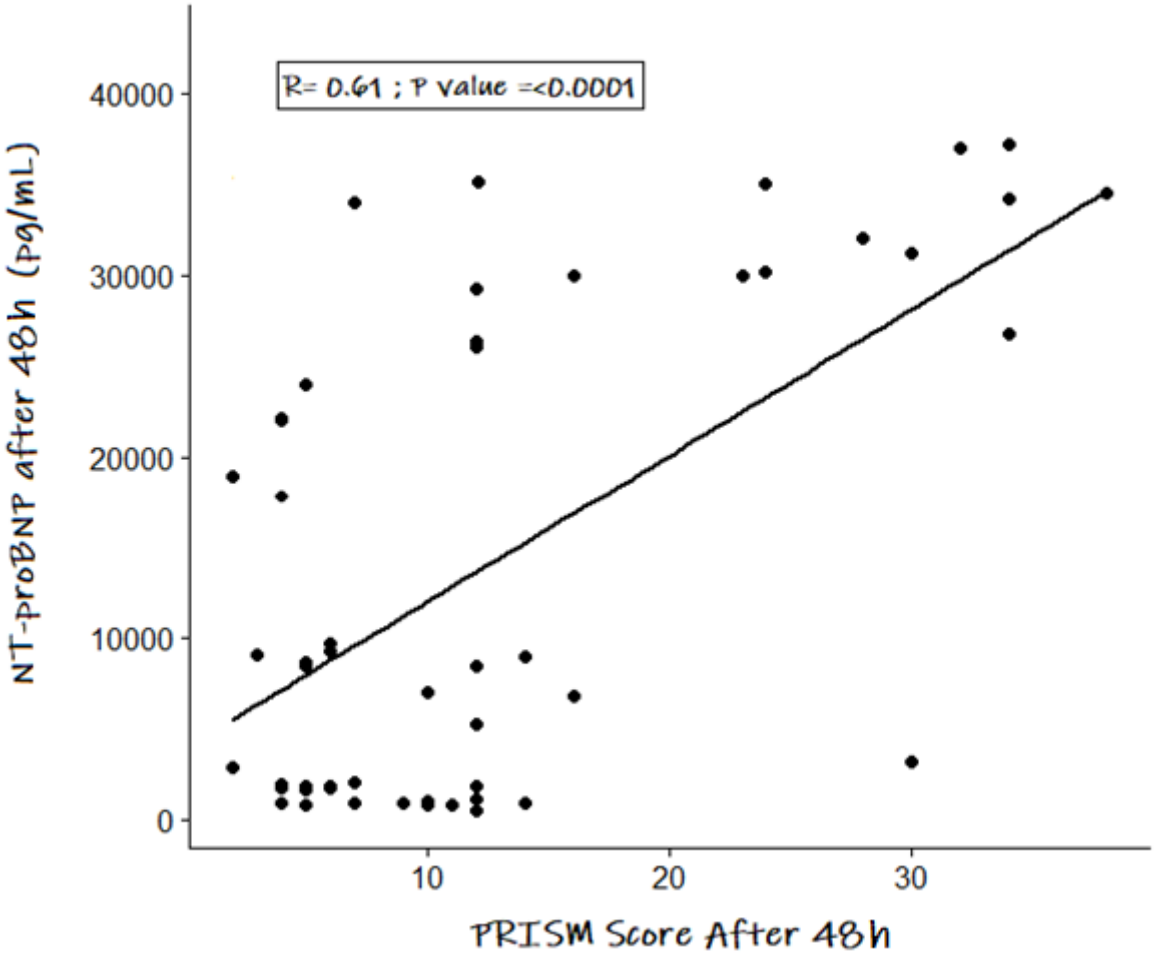

Figure 25: Scatter plot showing correlation between PRISM score and NT-proBNP levels after 48h

The Table 17 presents the statistics summary for the relationship between NT-proBNP levels and myocardial dysfunction in 53 children. NT-proBNP levels are used to assess cardiac function. Levels above 2000 pg/mL are considered raised, and levels below 2000 pg/ml are considered normal. Raised NT-proBNP Levels (>2000 pg/mL) was found in 27 children who had cardiac dysfunction and 6 children who did not have cardiac dysfunction. Normal NT-proBNP Levels (<2000 pg/mL) was found in 6 children who had cardiac dysfunction and 14 children did not have cardiac dysfunction. Prediction of myocardial dysfunction based on NT-proBNP levels has high accuracy with sensitivity of 82% and specificity of 70%. This indicates that NT-proBNP levels >2000 pg/mL correctly identified 82% of the children with cardiac dysfunction (27 out of 33 children

with cardiac dysfunction had raised NT-proBNP levels) and NT-proBNP levels <2000 pg/mL correctly identified 70% of the children without cardiac dysfunction (14 out of 20 children without cardiac dysfunction had normal NT-proBNP levels). Positive predict value (PPV) was 81% and negative predict vale (NPV) of 70%. This indicates among the children with raised NT-proBNP levels, 81% actually had cardiac dysfunction (27 out of 33). Among the children with normal NT-proBNP levels, 70% did not have cardiac dysfunction (14 out of 20).

Table 17: Prediction of Myocardial dysfunction based on NT-proBNP level

NT-ProBNP levels	**Cardiac Dysfunction**	**No Cardiac Dysfunction**	**Total**
Raised (>2000 pg/mL)	27	6	33
Normal (<2000 pg/mL)	6	14	20
Total	33	20	53

6. DISCUSSION

In pediatric patients, sepsis presents with a complex array of hemodynamic responses, including myocardial and vasomotor dysfunction or a combination of both. Younger children experience alterations in cardiac function, while older children tend to exhibit changes in peripheral vascular tone. Due to the varied nature of these cardiac and vasomotor dysfunction, appropriate identification and management of myocardial dysfunction in pediatric sepsis is challenging[40]. Brain natruretic peptide (BNP) is a prohormone secreted by cardiomyocytes and has been observed to increase in patients with myocardial dysfunction. Elevated plasma levels of BNP is associated with unfavorable prognosis in patients with severe sepsis and septic shock[47]. Despite this, less difference has been made between sepsis and septic shock in many studies, which often focus on biomarkers. Sepsis is particularly difficult to detect, requiring many scoring systems, whereas septic shock, identified by unstable vital signs and higher mortality, can be immediately recognized through the patient's clinical status[46].

In emergency settings, finding predictive factors for in-hospital mortality due to septic shock is critical for improving patient survival rates and optimizing the use of limited medical resources. The NT-proBNP is measured in patients with unstable vital signs to detect left ventricular dysfunction and has shown potential as a predictor of sepsis[48]. Therefore the current study titled "Correlation between NT- pro brain natriuretic peptide and myocardial dysfunction in children with septic shock –one year cross sectional Study" was carried out at KLEH Dr. Prabhakar Kore Hospital, Belgaum, Karnataka from January 2023 to January 2024 to evaluate the correlation between NT-proBNP and myocardial Dysfunction in children with septic shock and to evaluate the relation between NT-proBNP and severity of illness in children with septic shock.

The current study included 53 paediatric patients with septic shock, ranging between 29 days and 18 years, who met the inclusion criteria. The gender distribution showed a male predominance, with 57% of the participants being male and 43% female. This finding is consistent with other published studies, which have also reported a high prevalence of sepsis and septic shock in males compared to females. Hermon *et al.*[49] reported that 53% of their sepsis patients were male, while John *et al.*[50] found an even higher proportion of males, with 73.2% of their 220 patients being male and only 26.8% female. Similarly, Zaher *et al.*[51] documented a 60% male prevalence among their septic patients. Hartman *et al.*[52] and Prout et al.[53] also reported male predominance, with 55% and 54.2% male prevalence, respectively.

Mean age of children with septic shock in the current study was 7.65±5.66 years with maximum patients in the age group of 1-5 years (30.19%). This demographic distribution reflects the vulnerability of younger children to severe infections and adverse outcomes, consistent with reports from Hermon *et al.*[49] and the World Health Organization (WHO)[54]. Hermon *et al.* reported that over 70% of septic shock cases were observed in children under the age of six, emphasizing the susceptibility of younger age groups to this condition[49]. Similarly, the WHO highlights that children under five years old account for nearly half of all estimated sepsis cases globally[54]. In our study, the mortality rate was notably high at 20.7%, with younger children, particularly those under 5 years old, exhibiting a significantly higher mortality rate compared to older children. The mean age of survivors was significantly higher than that of non-survivors, suggesting that age is a critical factor in the prognosis of pediatric septic shock. This observation underscores the heightened vulnerability of younger children to severe outcomes in pediatric septic shock. The relation between age and mortality in paediatric septic shock has been well-documented in various epidemiological studies, including those conducted in India. Studies from India report alarmingly high mortality rates among children with septic shock. For instance, studies from PGI Chandigarh and Rohtak,

Haryana, reported mortality rates of 65.8% and 42%, respectively, underscoring the severe impact of septic shock on pediatric health in this region[18,19]. Globally, the incidence of severe sepsis and septic shock among children admitted in hospital varies significantly, with mortality rates ranging from 5% in developed countries to much higher rates in resource-limited settings[14]. Addressing sepsis-related mortality in childhood is a formidable global challenge, particularly in developing countries like India, where the burden of cases and deaths is disproportionately high[14]. The heightened mortality risk observed in younger children can be attributed to several factors, including their immature immune systems, atypical clinical presentations, and the challenges associated with proper fluid management in this age group. Azevedo *et al.* emphasize that younger children, especially those with underlying conditions like cancer, face particularly increased mortality rates in the context of septic shock.[55]

The Pediatric Risk of Mortality (PRISM) score is a widely used tool to predict mortality in pediatric patients, including those with septic shock. The PRISM score was developed from the Physiologic Stability Index (PSI) to reduce the number of physiologic variables required for pediatric ICU (PICU) mortality risk assessment[56]. In our study the PRISM scores, both at admission and after 48 hours, were significantly higher in patients who did not survive, indicating that higher PRISM scores correlate with increased mortality risk. This finding is in line with previous studies that have utilized PRISM scores to predict outcomes in critically ill paediatric patients. Higher PRISM scores are associated with an increase in mortality. For example, the proportion of deaths increases gradually with higher scores, reaching 66.7% among children with a score of > 30[57].The PRISM score has been shown to have good predictive value in assessing the probability of mortality in relation to children admitted to a PICU[56,58–60].

The significant correlation between PRISM scores and NT-proBNP levels at both time points further underscores the utility of NT-proBNP as a marker for illness severity. The correlation coefficients (R) of 0.60 and 0.61 for NT - proBNP levels at admission and after 48 hours, respectively, reflect a strong relationship between elevated NT-proBNP levels and higher PRISM scores. There are no studies highlighting the direct association of NT-proBNP levels and higher PRISM scores so far. However In their study, Liu and colleagues found that blood NT-proBNP levels and PRISM III score were considerably greater in the death group than in the survival group, and these indicators still had some predictive value for 28-day mortality and children prognosis.[61] According to Liu et al., the high-risk group had significantly higher blood NT-proBNP levels and mortality rates compared to the low- and non-risk groups ($P<0.01$, respectively). The ROC curve study revealed an area under the curve of 0.705 ($P<0.001$, sensitivity = 0.643, specificity = 0.692)[61].

MYocardial dysfunction is a critical complication in pediatric septic shock, significantly impacting patient outcomes and mortality. In our study, myocardial dysfunction was prevalent, with 30.19% of patients experiencing moderate dysfunction and 33.96% severe dysfunction. The association between myocardial dysfunction severity and survival was stark: all patients who succumbed to septic shock had severe myocardial dysfunction, while those with no or moderate dysfunction had better survival rates. Our findings align with previous research highlighting the prevalence and clinical significance of myocardial dysfunction in pediatric septic shock, particularly in the context of studies conducted in India. For instance, studies have reported myocardial dysfunction rates ranging from 53% to as high as 71% among pediatric patients with septic shock.[17,20] The clinical implications of myocardial dysfunction in pediatric septic shock are profound. It has been associated with increased requirements for inotropic support and vasopressors, reflecting its impact on hemodynamic stability and management complexity[6]. Furthermore, myocardial dysfunction

has been independently linked to higher mortality rates in children with septic shock, highlighting its critical role in predicting outcomes and guiding therapeutic interventions.

The present study found that NT-proBNP levels were significantly higher in patients with severe myocardial dysfunction compared to those with mild & moderate or no dysfunction. At admission, the NT-proBNP levels for severe dysfunction were markedly elevated (28600 pg/mL) compared to mild & moderate (9350 pg/mL) and no dysfunction (1800 pg/mL). This pattern persisted after 48 hours, with levels for severe dysfunction (31200 pg/mL) remaining significantly higher than those for mild & moderate (8418 pg/mL) and no dysfunction (1100 pg/mL). This highlights the significance of NT-proBNP as a sensitive biomarker for assessing the severity of myocardial dysfunction in pediatric septic shock. Our findings reveal that NT-proBNP levels were markedly elevated in patients with severe myocardial dysfunction compared to those with moderate or no dysfunction. These results are consistent with previous research demonstrating a clear association between elevated NT-proBNP levels and myocardial dysfunction in pediatric septic patients. Studies have consistently shown that NT-proBNP levels correlate with the severity of cardiovascular dysfunction and serve as a prognostic indicator for adverse clinical outcomes in these patients [40,42]. Lin et al., reported that the median plasma NT-proBNP levels were significantly higher in patients with moderate (3472.15 ng/L) and severe (4236.23 ng/L) heart failure compared to those with mild heart failure (1348.22 ng/L)[10]. Elevated NT-proBNP levels have been linked to increased requirements for inotropes and vasopressors, as well as worse clinical outcomes, underscoring its utility in guiding therapeutic interventions and predicting patient prognosis[40,43]. The findings from Wu *et al.* emphasize the early elevation of BNP levels in pediatric septic patients, associating it with cardiovascular dysfunction and poorer clinical outcomes, although the direct mortality association was not statistically significant in their study[40]. Moreover, Lin et al. (2016) demonstrated the diagnostic accuracy of NT-proBNP in

identifying heart failure in pediatric sepsis, highlighting its potential as a diagnostic tool in clinical practice[61]. These studies collectively support NT-proBNP as a valuable biomarker for assessing myocardial dysfunction and guiding clinical management in pediatric septic shock. The high prevalence of myocardial dysfunction in pediatric septic shock, as indicated by previous studies conducted in India and globally, further emphasizes the clinical relevance of NT – pro BNP assessment in this patient population[17,20].

In addition to its diagnostic utility, NT-proBNP levels may aid in stratification of risk and treatment decision-making. Kamal *et al.* (2022) investigated NT-proBNP as a prognostic marker specifically in myocardial dysfunction induced by sepsis, revealing its potential to predict cardiomyopathy and mortality in pediatric patients with septic shock[44]. This underscores the broader implications of NT-proBNP in predicting not only the severity of myocardial dysfunction but also clinical outcomes crucial for optimizing patient care. In our study we found significantly high level of NTproBNP for death than for survival. A meta-analysis estimated that an NT-proBNP cutoff of 4000 pg/mL had the greatest discrimination for predicting short-term mortality in patients with sepsis, with a sensitivity of 0.728 and specificity of 0.789[62]. Choi and Lee used the area under the receiver operating characteristic (AUROC) curve to evaluate the efficacy of NT-proBNP as a predictor of in-hospital mortality. The AUROC curve was 0.648 and the cut-off value for NT-proBNP was >2591pg/mL (69% sensitivity, 55% specificity)[48]. Given its role in early identification and prognostication, NT-proBNP holds promise as a biomarker that could potentially enhance the management and outcomes of pediatric septic shock by facilitating timely interventions and targeted therapies.

Plasma NT – pro BNP levels are widely recognized as a biomarker for heart failure[63–67]. In children up to 14 years, the threshold is 500 ng/L[68]. Elevated NT-proBNP levels also correlate with both systolic and diastolic dysfunction[69–72]. However, the established cut-off

points for diagnosing heart failure in septic patients may differ due to the unique pathophysiological processes involved in sepsis[73]. Our study demonstrated that NT-proBNP levels >2000 pg/mL had a high sensitivity (82%) and specificity (70%) for predicting myocardial dysfunction. The positive predictive value (PPV) of 81% and negative predictive value (NPV) of 70% indicate that NT-proBNP is a reliable biomarker for identifying children with and without myocardial dysfunction. This aligns with previous research suggesting that elevated NT-proBNP levels are indicative of cardiac stress and dysfunction in critically ill patients. For instance, Lin *et al.*[10] reported that the NT-proBNP cut-off value for heart failure in septic shock patients (1525 ng/L) was significantly higher than in those with severe sepsis (1368 ng/L), indicating that septic shock has a more substantial impact on NT-proBNP levels due to the release of inflammatory factors during septic shock. Kamal *et al.*[44] also highlighted the diagnostic utility of NT-proBNP, showing that NT-proBNP levels were significant predictors of cardiomyopathy across different groups with varying sensitivities and specificities depending on the cut-off levels and timing of measurement. On the first day of admission, NT-proBNP levels >334 pg/mL had 75% sensitivity and 70% specificity, while on the second day, levels >325 pg/mL showed 65% sensitivity and 80% specificity. In a subgroup analysis, NT-proBNP levels >334 pg/mL had 70% sensitivity and 90% specificity for predicting cardiomyopathy in the sepsis group, and levels >357 pg/mL had 70% sensitivity and 80% specificity in the septic shock group. Notably, NT-proBNP levels >350 pg/mL on the second day were excellent predictors of mortality in the septic shock group, with 100% sensitivity and specificity.

These findings collectively emphasize the clinical relevance of NT-proBNP as a biomarker for myocardial dysfunction in septic shock. Elevated NT-proBNP levels not only reflect cardiac stress and dysfunction but also provide critical prognostic information that can guide therapeutic interventions and improve patient outcomes. Given the variability in cut-off

points and their implications, further research is warranted to standardize NT-proBNP thresholds specifically for septic shock and to understand the underlying mechanisms linking NT-proBNP with inflammatory factors in septic conditions preferably using a randomised Control trial .

c

7. CONCLUSION

This one-year cross-sectional study investigated the correlation between NT-proBNP levels and myocardial dysfunction in children with septic shock, as well as the association between NT-proBNP levels and the severity of illness. NT-proBNP levels were significantly elevated in children with septic shock who had severe myocardial dysfunction compared to those with moderate or no dysfunction. NT-proBNP levels at admission and after 48 hours were strong indicators of the severity of myocardial dysfunction. There was a significant positive correlation between NT-proBNP levels and PRISM scores at both admission and after 48 hours, suggesting that higher NT-proBNP levels are associated with greater severity of illness. NT-proBNP levels >2000 pg/mL demonstrated high sensitivity (82%) and specificity (70%) in predicting myocardial dysfunction. The positive predictive value (PPV) of 81% and negative predictive value (NPV) of 70% further confirmed NT-proBNP as a reliable marker for identifying cardiac dysfunction in pediatric patients with septic shock. Younger children, especially those under 5 years old, had a significantly higher mortality rate. The mean age of survivors was significantly higher than that of non-survivors, indicating that younger age is a risk factor for poor outcomes in septic shock. All non-survivors in the study had severe myocardial dysfunction, highlighting the critical impact of severe cardiac dysfunction on mortality in pediatric septic shock.

In conclusion, NT-proBNP is a valuable biomarker for assessing myocardial dysfunction and predicting the severity of illness in children with septic shock. Its significant correlation with PRISM scores and its predictive accuracy underscore its potential role in guiding clinical decisions and improving patient management. Early identification and intervention in cases of elevated NT-proBNP can help optimize outcomes and reduce mortality in this vulnerable

population. Further research with larger sample sizes is recommended to confirm these findings and refine the clinical application of NT-proBNP in pediatric septic shock. Research with larger cohorts is warranted to validate these findings and refine the use of NT-proBNP in clinical practice. The study underscores the need for timely and accurate assessment of NT-proBNP levels to improve prognostic accuracy and patient outcomes in pediatric septic shock.

8. SUMMARY

A cross-sectional study was conducted to evaluate the correlation between NT-proBNP levels and myocardial dysfunction in children with septic shock and to assess the severity of illness. The study included 53 Patients aged 29 days to 18 years, admitted to the PICU at KLE's Dr. Prabhakar Kore Hospital in Belagavi, Karnataka, from January 2023 to January 2024. The key findings of the study are summarised below

1. **Demographics**

i. The study included 53 pediatric patients with septic shock

ii. Participants' ages ranged from 2 months to 17 years, with a mean age of 7.65 years

iii. There was a male predominance, with 57% male and 43% female participants.

2. **PRISM Scores and Outcomes**

i. The mean PRISM score at admission was 13.73±8.02, and after 48 hours, it was 12.65±10.04

ii. Higher PRISM scores were significantly associated with non-survival, indicating increased mortality risk with higher illness severity

3. **Myocardial Dysfunction**

i. Myocardial dysfunction was categorized as no dysfunction (35.85%),

mild & moderate dysfunction (30.19%), and severe dysfunction (33.96%).

ii. Severe myocardial dysfunction was significantly associated with non-survival; all patients who died had severe dysfunction.

4. **NT-proBNP Levels**

   i. NT – pro BNP levels were measured at admission and after 48 hours.

   ii. At admission, the mean NT-proBNP level was 13993±12775 pg/mL , and after 48 hours, it was 14086±13346 pg/mL

   iii. NT-proBNP levels were significantly higher in patients with severe myocardial dysfunction compared to those with moderate or no dysfunction.

5. **Survival Analysis**

   i. The overall survival rate was 79%, with 42 survivors and 11 non-survivors.

   ii. Survivors had a significantly higher mean age (8.71±5.45 years) compared to non-survivors (3.17±4.30 years).

   iii. Younger children (especially those under 5 years) had a higher mortality rate.

6. **Correlation between NT-proBNP and PRISM Scores**

A significant positive correlation was found between NT-proBNP levels and PRISM scores both at admission and after 48 hours (correlation coefficients of 0.60 and 0.61, respectively).

7. **Predictive Accuracy of NT-proBNP**

   i. NT-proBNP levels showed a high positive predictive value (81%) and a reasonable negative predictive value (70%) for myocardial dysfunction.

   ii. Significantly higher levels of NT-proBNP at admission was recorded for death (29550 (28600 -33909) pg/mL) when compared for survival 6408(1800-16700) pg/mL) .

   iii. NT-proBNP levels were significantly greater after 48 hours for death (33100 (31400 -34875) pg/mL) than for survival (6867(1618-18625) pg/mL).

   iv. NT-proBNP levels were significantly greater in non-survivors both at admission and after 48 hours, indicating its potential as a prognostic marker.

These key findings demonstrate the utility of NT – pro BNP as a biomarker for detecting myocardial dysfunction and assessing the severity of illness in children with septic shock. The results suggest that early identification of elevated NT-proBNP levels can guide clinical decisions and potentially improve patient outcomes.

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10. Annexure

ANNEXURE I – INFORMED CONSENT

KAHERs JNMC
BELAGAVI
INFORMED CONSENT FORM

Correlation between nt-pro brain natriuretic peptide and myocardial dysfunction in children with septic shock A ONE YEAR CROSS SECTIONAL STUDY

Name of Student/Principal Investigator: **REG NO –BM0121017**

Name of Guide/Co Investigators: **GUIDE(PROFESSOR)**

Objective:

1. To evaluate correlation between NT-proBNP with myocardial dysfunction in children with septic shock
2. To evaluate the correlation between NT-pro BNP with severity of illness in children with septic shock

You are hereby requested to involve yourself and your baby in the above said research to be conducted at KLE's Dr Prabhakar kore Hospital and Medical Research Centre , Belgaum by me.

Introduction:

Participation of your child will help us to know if NT-pro BNP levels correlate with degree of myocardial dysfunction and they could potentially be used to guide therapy. You are free to discontinue the participation in the study at any time for any reasons and you will not be paid any reimbursement for participation in the research. Hence involving your child in the study is your voluntary decision

Explanation of procedure:

The initial NT –pro BNP levels will be obtained within 8 hrs of admission to PICU. subsequent measurement of NT-pro BNP will be obtained at 48 hrs of admission. Cardiac status will be evaluated by doing echocardiography with in 24 hrs of admission

Withdrawal from participation in the study: Participation in this study is voluntary. You will be free to decide whether to participate in this study or continue participation once enrolled. In case you decide to withdraw your participation, you are free to do so. However, please convey the decision to the principal investigator.

Possible benefits from participating in the study: You will/will not have nor get any benefits by participating in this study. The data gathered will help the population at large.

Possible risks from participating in the study: There are no risks involved in participating in this study.

Privacy and confidentiality: The information collected from you will be coded, to prevent any person from identifying you. Your identity will never be revealed. The data collected from you will be kept confidential and only processed or aggregated data will be used for publication.

Financial incentives: You will not receive any payment for participating in this study.

Authorization for publication of aggregated data: Results obtained after processing of the aggregated data will be published for scientific purposes and or presented to scientific groups. However, your identity will never be revealed.

Questions: In case of any questions with regard to this study, you are free to contact:

REG NO BM0121017

If you have any question or complaints with regard to your right as study participant you may contact Dr Harsha Hegde, Chairperson, Ethical committee of JNMC, 0831-2473777 Extension 4052.

Legal rights: By signing this consent form, we are not waving any of your legal rights.

CONSENT STATEMENT

I am making a voluntary decision to participate in the study Correlation between nt-pro brain natriuretic peptide and myocardial dysfunction in children with septic shock A ONE YEAR CROSS SECTIONAL STUDY

"My signature below indicates that I have decided to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

Name of the child:

Age of the child:

Signature or left thumb impression of the child:

(if more than 12 years)

Verbal consent from child:

(7 to 12 years)

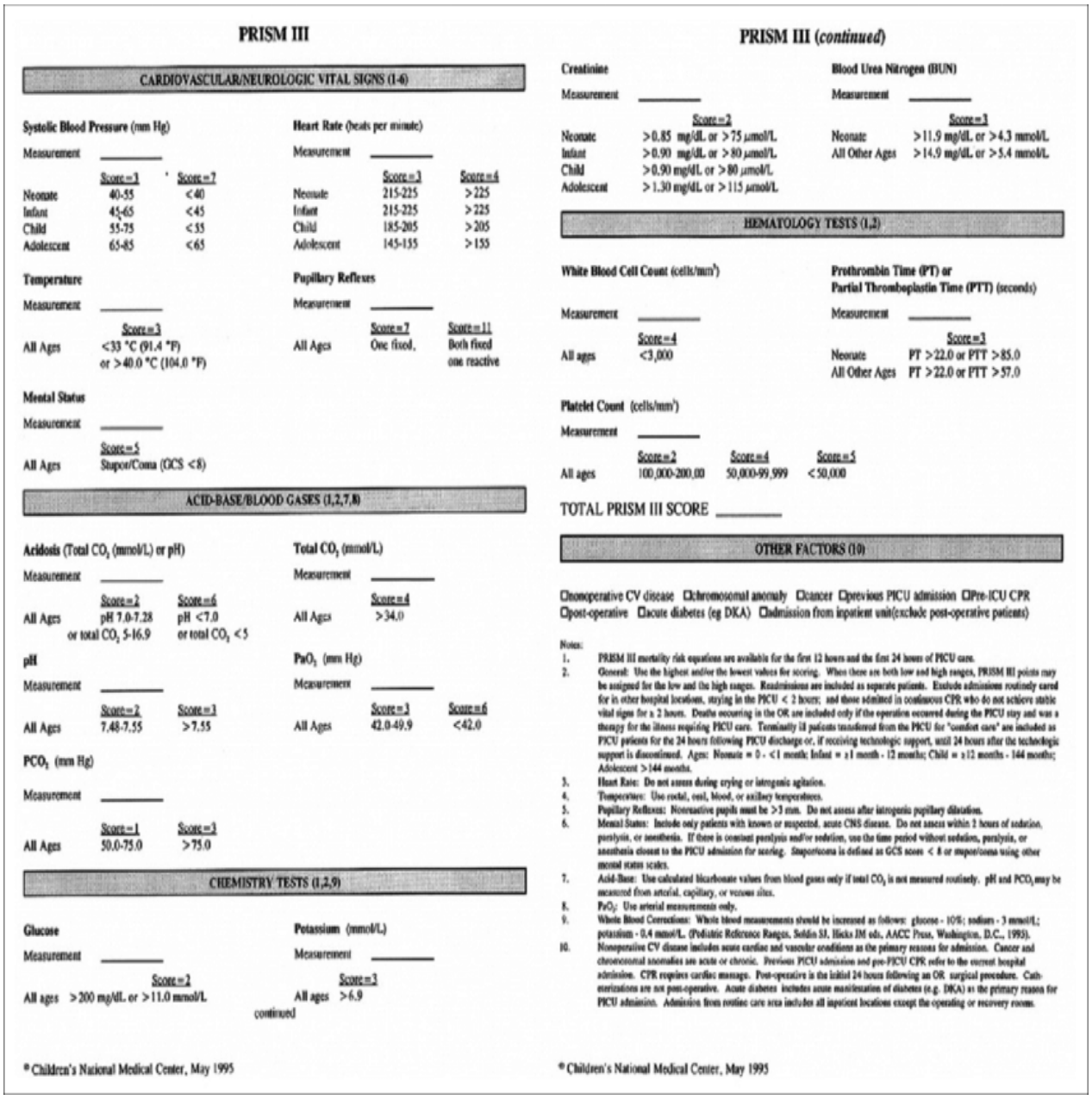
Name of the parent:

Signature or left thumb impression of the parent:

Name of the investigator:

Signature of the investigator:

ANNEXURE II – PRISM SCORE



PRISM III

CARDIOVASCULAR/NEUROLOGIC VITAL SIGNS (1-6)

Systolic Blood Pressure (mm Hg)

Measurement _____

	Score = 1	Score = 7
Neonate	40-55	<40
Infant	45-65	<45
Child	55-75	<55
Adolescent	65-85	<65

Heart Rate (beats per minute)

Measurement _____

	Score = 3	Score = 4
Neonate	215-225	>225
Infant	215-225	>225
Child	185-205	>205
Adolescent	145-155	>155

Temperature

Measurement _____

	Score = 3
All Ages	<33 °C (91.4 °F) or >40.0 °C (104.0 °F)

Pupillary Reflexes

Measurement _____

	Score = 7	Score = 11
All Ages	One fixed,	Both fixed one reactive

Mental Status

Measurement _____

	Score = 5
All Ages	Stupor/Coma (GCS <8)

ACID-BASE/BLOOD GASES (1,2,7,8)

Acidosis (Total CO_2 (mmol/L) or pH)

Measurement _____

	Score = 2	Score = 6
All Ages	pH 7.0-7.28 or total CO_2 5-16.9	pH <7.0 or total CO_2 <5

Total CO_2 (mmol/L)

Measurement _____

	Score = 4
All Ages	>34.0

pH

Measurement _____

	Score = 2	Score = 1
All Ages	7.48-7.55	>7.55

PaO_2 (mm Hg)

Measurement _____

	Score = 3	Score = 6
All Ages	42.0-49.9	<42.0

PCO_2 (mm Hg)

Measurement _____

	Score = 1	Score = 3
All Ages	50.0-75.0	>75.0

CHEMISTRY TESTS (1,2,9)

Glucose

Measurement _____

	Score = 2
All ages	>200 mg/dL or >11.0 mmol/L

Potassium (mmol/L)

Measurement _____

	Score = 3
All ages	>6.9

continued

* Children's National Medical Center, May 1995

PRISM III (*continued*)

Creatinine

Measurement _____

	Score = 2
Neonate	>0.85 mg/dL or >75 µmol/L
Infant	>0.90 mg/dL or >80 µmol/L
Child	>0.90 mg/dL or >80 µmol/L
Adolescent	>1.30 mg/dL or >115 µmol/L

Blood Urea Nitrogen (BUN)

Measurement _____

	Score = 3
Neonate	>11.9 mg/dL or >4.3 mmol/L
All Other Ages	>14.9 mg/dL or >5.4 mmol/L

HEMATOLOGY TESTS (1,2)

White Blood Cell Count (cells/mm³)

Measurement _____

	Score = 4
All ages	<3,000

Prothrombin Time (PT) or Partial Thromboplastin Time (PTT) (seconds)

Measurement _____

	Score = 3
Neonate	PT >22.0 or PTT >85.0
All Other Ages	PT >22.0 or PTT >57.0

Platelet Count (cells/mm³)

Measurement _____

	Score = 2	Score = 4	Score = 5
All ages	100,000-200,00	50,000-99,999	<50,000

TOTAL PRISM III SCORE _____

OTHER FACTORS (10)

☐nonoperative CV disease ☐chromosomal anomaly ☐cancer ☐previous PICU admission ☐Pre-ICU CPR ☐post-operative ☐acute diabetes (eg DKA) ☐admission from inpatient unit(exclude post-operative patients)

Notes:

1. PRISM III mortality risk equations are available for the first 12 hours and the first 24 hours of PICU care.
2. General: Use the highest and/or the lowest values for scoring. When there are both low and high ranges, PRISM III points may be assigned for the low and the high ranges. Readmissions are included as separate patients. Exclude admissions routinely cared for in other hospital locations, staying in the PICU < 2 hours; and those admitted in continuous CPR who do not achieve stable vital signs for ≥ 2 hours. Deaths occurring in the OR are included only if the operation occurred during the PICU stay and was a therapy for the illness requiring PICU care. Terminally ill patients transferred from the PICU for "comfort care" are included as PICU patients for the 24 hours following PICU discharge or, if receiving technologic support, until 24 hours after the technologic support is discontinued. Ages: Neonate = 0 - <1 month; Infant = ≥1 month - 12 months; Child = ≥12 months - 144 months; Adolescent >144 months.
3. Heart Rate: Do not assess during crying or iatrogenic agitation.
4. Temperature: Use rectal, oral, blood, or axillary temperatures.
5. Pupillary Reflexes: Nonreactive pupils must be >3 mm. Do not assess after iatrogenic pupillary dilatation.
6. Mental Status: Include only patients with known or suspected, acute CNS disease. Do not assess within 2 hours of sedation, paralysis, or anesthesia. If there is constant paralysis and/or sedation, use the time period without sedation, paralysis, or anesthesia closest to the PICU admission for scoring. Stupor/coma is defined as GCS score < 8 or stupor/coma using other mental status scales.
7. Acid-Base: Use calculated bicarbonate values from blood gases only if total CO_2 is not measured routinely. pH and PCO_2 may be measured from arterial, capillary, or venous sites.
8. PaO_2: Use arterial measurements only.
9. Whole Blood Corrections: Whole blood measurements should be increased as follows: glucose - 10%; sodium - 3 mmol/L; potassium - 0.4 mmol/L. (Pediatric Reference Ranges, Seldin SJ, Hicks JM eds, AACC Press, Washington, D.C., 1995).
10. Nonoperative CV disease includes acute cardiac and vascular conditions as the primary reasons for admission. Cancer and chromosomal anomalies are acute or chronic. Previous PICU admission and pre-PICU CPR refer to the current hospital admission. CPR requires cardiac massage. Post-operative is the initial 24 hours following an OR surgical procedure. Catheterizations are not post-operative. Acute diabetes includes acute manifestation of diabetes (e.g. DKA) as the primary reason for PICU admission. Admission from routine care area includes all inpatient locations except the operating or recovery rooms.

* Children's National Medical Center, May 1995

ANNEXURE III- PERFORMA

CASE NO:

NAME:

AGE/SEX:

FATHER NAME:

MOTHER NAME:

PHONE NUMBER:

IP NO.:

DATE OF BIRTH

DATE OF ADMISSION

ADDRESS:

COMPLAINTS AT PRESENTATION:

CLINICAL EXAMINATION ON ADMISSION

Past history:

Family history:

Personal history:

INVESTIGATIONS

	At the time of admission	48 hours of admission	Score
Systolic BP			
Heart rate			
Temperature			
GCS			
Pupillary reaction			
Ph			
PO2			
PCO2			
Blood glucose			
Potassium			
Creatinine			
Blood urea			
WBC			
Platelet			
PT/APTT			

CULTURE REPORT

HSCRP

FIRST SAMPLE NT PRO BNP LEVELS(DATE&TIME)

SECOND SAMPLE NT PRO BNP LEVELS(DATE&TIME-)

2D ECHO REPORT FINDINGS

DYSFUNCTION

LVEF

LVDd

LVSd

Fractional shortening

Treatment given

Final outcome

Number of days of PICU stay

COMMENTS

ANNEXURE IV- MASTER CHART

S. NO	AGE	GENDER	DATE OF ADMISSION	PRISM SCORE AT ADMISSION	PRISM SCORE AT 48 HOURS	ECHO REPORT	LVEF	NT PRO BNP ON ADMISSION (pg/ml)	NT PRO BNP AT 48 HOURS (pg/ml)	PICU STAY	OUTCOME
1	15 years	female	27/12/2022	17	12	severe LV systolic dysfunction	25%	52	35000	7 days	Survived
2	17 year	male	1//01/23	16	10	normal ventricular function	60%	900	800	4 days	Survived
3	13 Years	male	01-04-2023	13	4	normal ventricular function	60%	860	920	5 days	Survived
4	10 year	female	02-08-2023	17	12	normal ventricular function	60%	980	1100	6 days	Survived
5	11 months	male	22/02/2023	20	24	severe LV systolic dysfunction	20%	28600	30200	2 days	Death
6	2 year 6 month	female	26/01/2023	10	4	mild LV dysfunction	40%	26000	22000	7 days	Survived
7	5 years	Male	02-05-2023	9	4	mild LV dysfunction	40%	1912	1700	5 days	Survived
8	1 year 5 months	male	02-06-2023	12	6	normal ventricular function	60%	1923	1800	4 days	Survived
9	9 year	Male	02-10-2023	14	7	mil LV dysfunction	40%	2800	1982	5 days	Survived
10	7year	female	02-12-2023	7	2	normal ventricular function	60%	3000	2800	6 days	Survived
11	15 years	female	18/02/2023	21	23	severe RV AND LV DYSFUNCTION	25%	35000	30000	3 days	AMA
12	15 years	male	20/02/2023	5	2	normal ventricular function	60%	18400	18900	5 days	Survived
13	13 yaer	female	24/02/2023	5	3	normal ventricular function	60%	10480	9040	5 days	Survived
14	2 year	Male	19/03/2023	20	24	severe LV systolic dysfunction	30%	26052	35000	6 days	Death
15	7 year	female	20/03/2023	6	4	normal ventricular function	60%	18900	17800	4 days	Survived
16	16 year	female	23/03/2023	12	6	mild LV dysfunction	45%	2109	1670	10 days	Survived
17	5 years	Male	22/03/2023	6	3	normal ventricular function	60%	8068	9000	4 days	Survived
18	14 years	female	23/03/2023	32	34	severe LV dysfunction	30%	29000	26800	5 days	Death
19	12 yaer	male	26/03/2023	11	5	mild systolic dysfunction	50%	28000	24000	5 days	Survived
20	9 months	Male	19/04/2023	8	5	normal ventricular function	60%	1800	1600	5 days	Survived
21	6 yaer	female	21/04/2023	9	9	normal LV function	60%	1800	900	6 days	Survived
22	7 months	female	26/04/2023	28	28	severe myocardial systolic dysfunction	30%	30100	32000	2days	Death
23	10 year	Male	28/04/2023	13	12	severe systolic dysfunction	30%	28000	26000	4 days	Survived
24	12 year	female	05-01-2023	7	7	Severe LV systolic dysfunction	25%	28600	34000	6 days	Survived

25	16 yaer	male	05-08-2023	6	5	normal ventricular function	60%	900	800	4 days	Survived
26	13 Years	male	19/05/2023	5	7	normal ventricular function	60%	860	900	4 days	Survived
27	1 year 1 month	Male	21/05/2023	32	30	severe LV dysfunction	25%	28,600	3200	3 days	Expired
28	6 year	Male	23/05/2023	7	5	mild LV dysfunction	45%	1816	1780	4 days	Survived
29	16 year	female	18/05/2023	14	16	severe LV dysfunction	30%	34000	30000	6 days	Survived
30	13 years	Male	06-09-2023	4	5	moderate lv dysfunction	50%	10500	8400	6 days	Survived
31	3 years	Male	18/06/2023	20	34	severe myocardial dysfunction	30%	27600	342000	5 days	Death
32	13 yaer	Male	23/06/2023	10	10	normal ventricular function	60%	1280	980	5days	Survived
33	4 years	male	12/07/2023	6	4	Moderate LV dysfunction	50%	20600	22100	6 days	Survived
34	16 year	female	14/07/2023	10	12	normal ventricular dysfunction	60%	2300	1800	4 days	Survived
35	16 year	male	18/07/2023	7	5	mild LV systolic dysfunction	45%	9800	8600	8 days	Survived
36	5 years	Male	08-06-2023	8	6	mild LV systolic dysfunction	50%	11,600	9620	5 days	Survived
37	5 years	female	14/09/2023	5	4	normal ventricular function	60%	2200	1890	5 days	Survived
38	7 year	female	14/09/2023	8	12	Severe LV dysfunction	30%	24800	26400	8 days	Survived
39	2 months	male	26/09/2023	16	12	Severe LV dysfunction	30%	28600	29200	4 days	Survived
40	3 years	female	10-10-2023	10	6	mild systolic LV dysfunction	50%	8900	9200	14 days	Survived
41	4 years	female	18/10/2023	14	10	mild systolic LV dysfunction	50%	9820	7000	7 days	Survived
42	2 year 6 months	male	14/10/2023	34	38	severe LV dysfunction	30%	35000	34500	4 days	Death
43	7 year	male	12-12-2023	16	14	moderate LV dysfunction	45%	10190	8900	8 days	Survived
44	1 year 2 months	female	13/12/2023	12	11	normal ventricular function	60%	980	800	6 days	Survived
45	1 year 8 month	female	16/12/2023	30	32	severe myocardial dysfunction	25%	35000	37000	4 days	Death
46	2 year	male	28/12/2023	14	12	mild LV dysfunction	50%	5,983	5233	6 days	Survived
47	7 year	male	01-01-2024	28	30	severe myocardial dysfunction	25%	30636	31200	5 days	Death
48	10 MONTHS	male	01-03-2024	14	12	MILD LV dysfunction	50%	8238	8435	6 days	Survived
49	16 year	female	01-10-2024	10	12	Normal LV function	60%	300	480	7 dyas	Survived
50	2 year	female	01-12-2024	14	16	moderate LV dysfunction	45%	6833	6734	6 days	Survived
51	5 month	male	13/01/2024	30	34	severe LV dysfunction	25%	36,000	37,200	4 days	Death
52	8 year	male	15/1/2024	12	14	Normal LV dysfunction	60%	980	900	5 days	Survived
53	5 years	female	16/01/2024	14	12	normal ventricular function	60%	1200	1400	6 days	Survived