

# The Epidemiology and Outcomes of Children Septic Shock in Developing Countries: A Literature Review

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## Abstract

Sepsis, a condition marked by an imbalanced immune response to infection, can lead to organ dysfunction, and potentially life-threatening consequences. Within the spectrum of sepsis, septic shock stands out as a severe manifestation with pronounced circulatory and cellular metabolism abnormalities, contributing to an elevated mortality rate. This literature review aims to provide an enhanced understanding of the epidemiology and outcomes of septic shock in children populations residing in developing countries. By synthesizing and expanding upon existing research in the field, this review seeks to offer a more comprehensive analysis of this critical healthcare issue.

Keywords: Epidemiology; Outcomes; Mortality; Sepsis; Septic Shock; Children

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## 1. Introduction

Septic shock is a subset of sepsis that exhibits severe circulatory and/or cellular metabolism abnormalities, resulting in a significantly higher mortality rate. The International Pediatric Sepsis Consensus Conference (IPSCC) in 2005 established standardized criteria for diagnosing and managing septic shock in children based on age-specific vital signs and physiological considerations [1]. Sepsis is a condition characterized by a potentially fatal dysfunction of organs due to an imbalanced immune response to infection. In order to detect septic shock, medical practitioners should observe signs in patients that suggest sepsis, systemic inflammatory response syndrome, and compromised tissue blood flow [2,3]. It should be emphasized that a significant proportion, ranging from five to 30%, of children diagnosed with sepsis ultimately progress to septic shock [4].

Studies have revealed that septic shock plays a substantial role in admissions to Pediatric Intensive Care Units (PICUs) and contributes to both morbidity and mortality rates in children [5]. Despite extensive efforts [6,7,8,9], severe sepsis and septic shock persist as the primary causes of infection-related deaths among children [10]. In 2013, it was estimated that more than 4 million children below the age of 5 died from infectious diseases worldwide, with a significant proportion of these fatalities attributed to the severe consequences of sepsis and septic shock [11].

Raising awareness about the burden of septic shock in children is crucial for developing targeted prevention and treatment strategies and optimizing healthcare resource allocation. This review provides a comprehensive overview of the epidemiology and outcomes of children septic shock, focusing on children

beyond the neonatal period. Examining the prevalence and outcomes aims to enhance understanding and guide evidence-based interventions for this urgent healthcare issue.

## **2. Epidemiology of Children Septic Shock in Developing Countries**

### **2.1. South Africa**

Septic shock is a significant children's disease that is both prevalent and severe. However, despite its importance and the efforts of various organizations, there is a lack of comprehensive epidemiological data on childhood sepsis at a global level. In Kenya, a hospital-based longitudinal study was conducted by Vekaria-Hirani et al. [12] at the Kenyatta National Hospital for two months. In this hospital-based longitudinal study, a total of 325 children were admitted, and 50 cases of septic shock were identified, resulting in a prevalence rate of 15.4%. The research provided valuable information about the demographic characteristics of the affected children. Among the cases of septic shock, the median age of the children was 4 months, and a significant percentage of them were neonates (25.6%) and infants (20.9%). Interestingly, no instances of septic shock were observed in children older than 60 months. In terms of gender distribution, the study population had a male-to-female ratio of approximately 1:1.8, indicating a slightly higher prevalence of septic shock among females. Since this study was the first of its kind on children septic shock in Kenya, it was not possible to compare the findings with any other local studies.

### **2.2. Indonesia**

In another study by Wati et al., the prevalence of sepsis and septic shock was examined in Denpasar, Bali, from January 2018 to December 2018 [13]. In this study, the prevalence of children experiencing sepsis between the ages of 0 to 18 years was 35.7% (10), and those experiencing septic shock were 60.7% (17). The infant age group had the highest percentage of septic shock diagnoses, which was 70.6%. In Indonesia, Ikatan Dokter Anak Indonesia (IDAI) implements guidelines for diagnosing sepsis by considering the presence of infection and signs of organ dysfunction. Organ dysfunction is evaluated using the Pediatric Logistic Organ Dysfunction-2 (PELOD-2) score. The diagnosis of sepsis is confirmed when the PELOD-2 score is  $\geq 11$  in type A hospitals or  $\geq 7$  in type B or C healthcare facilities. The pSOFA score was adjusted for the cardiovascular and renal systems, taking into account the PELOD-2 score [14]. Additionally, in this study, the evaluation of this score revealed that the dominance of patients with sepsis and septic shock was substantiated by an average pSOFA score of 5.94 (SD 2.79).

A similar investigation by Rusmawatiningsih and Nurnaningsih focused on septic shock prevalence and mortality in Yogyakarta, Indonesia by also evaluating PELOD scores [15]. Their study, conducted from November 2011 to June 2014, found that out of 239 patients, 136 were diagnosed with septic shock. The patients in the study had a median age of 16 months, with a majority of them being male (52.2%). The median initial PELOD scores observed were 22. It should be emphasized that the variation in PELOD-2 scores between studies may be influenced by discrepancies in the total sample size, as each study likely had different numbers of participants.

### **2.3. China**

A prospective, multicenter study conducted by Wang et al. in China aimed to investigate children sepsis in hospitalized children [16]. Among the 1,530 children meeting the sepsis criteria, 7.9% (121) were diagnosed with severe sepsis, and 2.1% (32) presented with septic shock. The age distribution of the patients revealed

that the majority, 55.7%, fell into the 1-month to less than 2 years age group. Furthermore, 24.3% were aged between 2 to 4 years, 10% between 5 to 7 years, and 10% between 8 to 14 years. Notably, approximately 80% (1,222) of the patients were under 5 years of age. Additionally, a higher preponderance of sepsis cases was observed in boys compared to girls across all age subgroups, with a ratio of approximately 2:1.

That being said, septic shock is a significant and prevalent disease among children, with varying prevalence rates across different regions. The reported prevalence rates in the studies ranged from 15.4% in Kenya to 60.7% in Bali, Indonesia, demonstrating an age-based vulnerability to septic shock. Consistently, the studies identified younger age groups, such as neonates and infants, as having a higher percentage of septic shock cases. The implementation of standardized guidelines and scoring systems for diagnosing sepsis, such as PELOD-2 and pSOFA, can facilitate accurate identification and assessment of sepsis and septic shock in Indonesia.

However, establishing the baseline prevalence of sepsis and septic shock is hindered by the limited availability of comprehensive epidemiological data in low- and middle-income countries (LMICs). A review of the literature spanning from 1980 to 2008 indicated a lack of studies examining the incidence, prevalence, mortality, or case fatality rates of sepsis in developing nations [17]. This highlights the pressing necessity for increased research efforts and data collection in LMICs to improve our comprehension of the burden posed by sepsis and septic shock in these regions.

### 3. Outcomes

Global mortality rates from septic shock continue to be significant and are affected by the timely identification and initiation of goal-directed treatment [8,2]. Furthermore, mortality rates remain notably high within the first 72 hours of sepsis and septic shock onset, primarily due to the hyper-inflammatory phase (cytokine storm) of the immune response [18]. Various factors have been linked to unfavorable outcomes, such as low arterial systolic blood pressure and pH, disseminated intravascular coagulation, and the degree of multi-organ failure [19].

#### 3.1. South Africa

In the Kenya-based study, a total of 50 children diagnosed with septic shock were examined, revealing that 56% (28) exhibited low blood pressure [12]. However, due to incomplete documentation of other clinical signs from another facility, comprehensive data analysis was limited. Despite the limited data, the available information indicates a considerable mortality rate of 70% (35) within 72 hours of admission, with a median time of 14 hours. Infants had the highest case fatality rate, reaching 82.6%. Furthermore, it was found that the absence of mechanical ventilation and the presence of hypotension upon admission were associated with an elevated risk of mortality.

#### 3.2. Indonesia

The study conducted in Yogyakarta highlighted a significant mortality rate of 88.2% among patients with septic shock admitted to the Pediatric Intensive Care Unit (PICU) [13]. This finding was based on a comprehensive analysis of individual medical records. Intriguingly, the observed mortality rate surpassed the predictions made based on signs such as liver enlargement in 60% (48) patients, lung rales in 36.25% (29) patients, gallop sound in 2.5% (2) patients, and increased jugular venous pressure in 1.25% (1) patient. These data were also documented in the medical records. Notably, the observed mortality rate was significantly higher compared to data from developed countries, where lower rates ranging from 20-30% were typically

reported. Additionally, the study identified multiple organ dysfunction syndrome (MODS) of more than 3 and fluid overload (FO) as predictors of mortality.

Another study conducted in Bali examined the distribution of outcomes in the Pediatric Intensive Care Unit (PICU) based on diagnoses. It revealed that 30.0% of cases with sepsis resulted in death [15]. Among these cases, septic shock was the most prevalent diagnosis, with a mortality rate of 47.1%. Furthermore, an analysis of outcomes based on organ involvement demonstrated that 58.3% of cases exhibited the involvement of three organs, ultimately leading to fatal outcomes.

These studies highlight the use of different clinical parameters to analyze patient outcomes. It is worth noting that in developing countries, the common findings of variation in parameters contribute to the limited data available in developing countries regarding mortality rates and specific contributing factors in children.

### 3.3. China

The study revealed an overall case fatality rate of 3.5% for sepsis cases, with a particularly high mortality rate of 34.6% observed in severe sepsis and septic shock cases [16]. It is noteworthy that more than 70% of these deaths occurred within the first 72 hours after admission. The authors emphasized that the elevated mortality rate among Chinese children with septic shock was not attributable to pre-existing medical conditions that could increase susceptibility to complicated infections, as the majority of the children were previously healthy. Instead, the high mortality rate was linked to delays in diagnosis and hospital admission, typically occurring by the third day of illness, as well as delays in treatment and non-adherence to international guidelines for severe sepsis and septic shock management. However, a consistent conclusion across all studies is that sepsis imposes a significant burden and is associated with a high mortality rate in children.

## 4. Conclusion

In conclusion, the studies conducted in some developing countries, South Africa, Indonesia, and China provide valuable insights into the outcomes of septic shock in children. These studies consistently report high mortality rates, particularly within the initial 72 hours after admission. Factors such as delayed diagnosis and treatment, along with the presence of multiple organ dysfunction, contribute to the poorer outcomes observed in these cases.

The findings underscore the critical importance of early recognition and prompt initiation of appropriate treatment in improving outcomes and reducing mortality rates. Timely interventions can help mitigate the impact of septic shock on vital organs and improve patient survival. Further research and efforts are needed to enhance our understanding of septic shock in children, particularly in developing countries, where limited epidemiological data exists. By addressing the challenges associated with timely diagnosis and treatment, healthcare professionals can strive to improve outcomes and alleviate the burden of septic shock in children's populations.

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