JOURNAL OF INTERNATIONAL CRISIS AND RISK COMMUNICATION RESEARCH
ISSN: 2576-0017
2026, VOL 9, NO 4

Recognizing And Managing Sepsis In Children‘S Emergency Care: A Systematic Review

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Abstract

Background:
Sepsis is a clinical condition arising from an abnormal host response to severe infection. However, the definition of sepsis in children remains a challenge. Childhood sepsis is a major health challenge and a leading cause of mortality and morbidity that requires correct and prompt diagnosis and treatment.
Aim:
To assess the diagnosis and treatment of sepsis among children by reviewing the previous original research conducted on this subject.
Methods:
An exploration of scientific databases was performed to obtain relevant articles; this exploration procedure was performed using several related terms. The selection of articles was based on definite criteria.
Results:
A total of eight studies met the inclusion criteria and were included in this review.
Conclusion:
Diagnosis of sepsis in children is difficult, and there is a delay in the provision of treatment, which can lead to unfavorable outcomes. Additionally, there is insufficient adoption of diagnostic criteria and treatment guidelines, and these two elements contribute to the hard diagnosis and suboptimal treatment provision.

Keywords: Sepsis, Diagnosis, Management, Children.

Introduction:

Sepsis can be defined as a clinical condition arising from an abnormal host response to severe infection [1]. Based on the 2016 third international consensus on sepsis, it was defined as a syndrome characterized by an uncontrolled response of the organism to an infectious trigger, and it is considered a life-threatening condition [2, 3]. It is a common reason for individuals to admit to the emergency department [4]. Defining children's sepsis remains a challenge due to the variations and differences in consensus opinions on the applicability and relevance of

criteria to children [5]. Childhood sepsis is a major health challenge and a leading cause of mortality and morbidity, although the presence of standardized therapeutic protocols and widespread immunization efforts [5].

Sepsis incidence is considerably age-dependent throughout life, with the greatest rate discovered in preterm neonates, followed by neonates, infants, and children [6]. Severe sepsis represents more than 8% of all admissions to pediatric intensive care units (PICUs) and results in more than 4.5 million deaths of children globally and annually [7-9]. Septic shock is the most severe manifestation and can be defined as a subset of sepsis that presents considerable cellular, circulatory, and metabolic abnormalities. It is characterized by a drop in blood pressure leading to reduced tissue perfusion and shock-induced hypoxia. This condition leads to an elevated mortality compared to sepsis alone [10].

Conventionally, the diagnosis and treatment of sepsis have been restricted to the emergency department (ED) or hospital settings [1]. However, sepsis often presents a wide variety of manifestations that can resemble varied medical conditions, highlighting the urgent need for more effective and precise diagnosis methods [4].

Early and immediate provision of antimicrobial treatment is a crucial step for improving the outcomes of patients with sepsis and septic shock [11]. Other treatment interventions include vasoactive agents, vascular access and fluid resuscitation, corticosteroids, respiratory support, metabolites and electrolytes provision, and blood transfusion. Such interventions are provided based on the condition and the requirements of each sepsis patient [1].

Children's sepsis carries a potential global burden on the health of children, with outcomes for children dependent on timely recognition and management; therefore, early diagnosis and treatment are important for a good prognosis [12]. Most children with sepsis seek support in emergency care settings on first presentation [12]. However, there was no previous systematic review conducted to report the recognition and treatment of sepsis in children, and the available literature consists of reviews focusing on guidelines or other topics. So, this systematic review was performed to assess the diagnosis and treatment of sepsis among children by reviewing the previous original research reported on this subject.

Method and Search strategy:

The PRISMA guidance **[13]** was followed to write this systematic review. Searching through electronic databases was done to obtain the related articles; such databases included PubMed, Science Direct, Google Scholar, and Scopus. The searching process was limited to the articles published in the recent ten years from 2017 till now. Several terms were used as keywords for the searching process, including "Sepsis, Diagnosis, Recognition, Treatment, Management, Therapy, Children, Pediatrics, ED, and Emergency Care." All the produced titles were reviewed precisely to avoid missing potential studies.

Eligibility criteria:

The findings were examined to exclude duplicate articles to reduce the number of studies; this step was followed by checking the publication date to exclude studies published more than ten years ago. Also, articles that focused on the adult population and didn't report children and/or the pediatric population in the title and/or object were excluded. Furthermore, studies conducted on children in the emergency department (ED) were considered eligible, whereas those conducted on children from other settings were excluded. All study designs were eligible except for the articles that didn't report the study design. The remaining findings were considered as eligible in case of being original research, written in the English language, available for full-text, and providing clear data without overlapping. The description of the eligibility is displayed in figure 1.

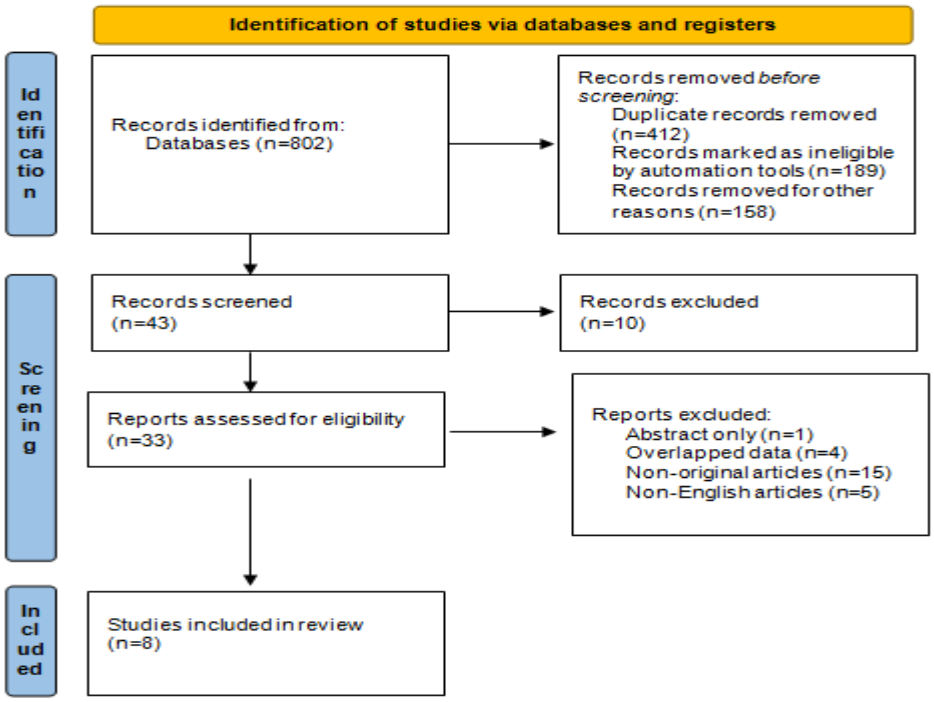

Fig 1: Planning of Eligible criteria

Data review and analysis:

The first step in this stage was reviewing each abstract of each included article to determine the main data of interest required for extraction. Then the full text article was reviewed, and data were extracted using a pre-designed Excel sheet. After the extraction of the data from all articles, the data was revised and then transferred to a pre-designed table for summarization.

Results:

A total of eight articles met the criteria and were included [14-21] (Table 1). The included studies were published between 2018 and 2024. The most common study design was retrospective of six studies [14, 16, 17, 19-21], except for two studies; one study was prospective [15], and one was cross-sectional [18].

The total number of children was 23111 subjects, and the age of included children was heterogeneous, as some studies included children with ages ranging from days to years, some studies reported the age range, others reported the mean age, and other studies reported the median age.

The reported and studied objectives among the included studies were various and they included delayed treatment and risk of mortality [14], sepsis caused by infectious diarrhea [15], timing of antibiotic therapy in sepsis cases [16, 21], treatment in sepsis [17], management of shock [18], treatment of sepsis and septic shock among those with and without chronic diseases [19], and treatment of sepsis and concordance with guidelines [20].

Consequently, the results and findings of the studies were heterogeneous due to the variations in the subjects and objects; therefore, the findings are presented as follows:

Regarding guidelines followed for diagnosis and management, only a few studies reported guidelines, and one study reported diagnosing sepsis cases based on local criteria in Australia [16]. Two studies reported diagnosis and/or classification of sepsis severity based on the IPSCC definitions [17, 21]. One study reported that sepsis diagnosis was according to the Children‘s Hospital Association‘s IPSO [19]. Regarding treatment guidelines, one study reported using the criteria of the 2012 Surviving Sepsis Campaign (SSC) [17], and another study reported ACCM pediatric sepsis guidelines [20].

Also, regarding diagnosis, one study revealed no combination of common signs in those with sepsis or severe sepsis, whereas the diagnosis of septic shock was mostly confirmed by a

combination of some symptoms [17]. Another study revealed that diagnosis of septic shock on admission occurred among 81.2% of cases, and severe sepsis was the cause of septic shock among 53.1% [18]. One study revealed that there was no variation in the mode of recognition of suspected sepsis or septic shock among children with and without chronic diseases (P=0.2) [19].

Regarding timing and delay of treatment, one study revealed that the large majority of patients (98.2%) received antibiotics at less than 330 minutes (5.5 hours) and this category of patients reported lower 3-day mortality rate (0.5%) compared to those who received antibiotics (1.2%) and similarly for 30-day mortality (0.9% Vs 2%, respectively). Additionally, receiving treatment after 330 minutes was associated with higher odds for mortality at three days (OR 3.44) and 30 days (OR 3.63) [14]. Another study determined a delay of treatment provision at more than 60 minutes (one hour) and reported that most patients received delayed therapy (76%). The factors that contributed to delayed treatment provision included high patient load, long waiting periods, difficult intravenous access, delayed prescribing, insufficient staffing, and difficulty distinguishing between a viral infection and a serious bacterial infection [16]. The third study revealed a higher mortality rate among those who received antibiotics within one hour from sepsis recognition (P=0.009) and more organ dysfunction, longer time on a vasoactive infusion, and longer LOS (P< 0.05) compared to those who received antibiotics after one hour [21].

One study reported variations in time till the provision of therapy, between patients with sepsis and septic shock; the median time to therapy including antibiotic and fluid administration among those with sepsis and severe sepsis was 3 hours, whereas that for patients with septic shock was 2hours and 2.5 hours for antibiotic and fluid, and it was longer for vasoactive drugs reaching to six hours. Regarding outcomes, the length of hospital stay was considerably longer for sepsis and severe sepsis compared to septic shock (P<0.001), whereas the in-hospital mortality rate was higher for septic shock compared to sepsis and severe sepsis (P<0.001) [17]. Also, another study revealed variation in time spent till provision of antibiotics to children; this variation was related to the presence and absence of chronic diseases, where those with chronic diseases received therapy earlier compared to those without chronic disease, but with no significant variation (P=0.1). Also, receiving antibiotics wasn't varied between those with and without a catheter (P=0.06). However, the time to first intravenous fluid for those with chronic disease was considerably longer compared to those without chronic diseases (P=0.01) [19].

One study focused on the management of septic shock reported provision of oxygen therapy for most cases, vascular filling was required by almost all patients, and it was done mainly via the peripheral vein. Saline was the main fluid used for filling. Inotropes were used for only two cases, using either dobutamine or adrenaline. The used antibiotics included quinolones and aminoglycosides. The mortality rate was 50%, and it was related to the presence of fever on admission [18].

Another study reported the use of broad-spectrum antibiotics, which were provided to patients within 60 minutes of sepsis recognition in the majority of cases. There 70% of the patients had hypotension, and more than one-half of them experienced hypotension resolution without vasoactives before 60 minutes, but 21% of those experienced resolution required vasoactives in the first 24 hours. Receiving care in concordance with guidelines resulted in lower LOS; however, adjusted analysis revealed no association between guideline-concordant care and LOS [20].

Regarding markers, it was found that both CRP and PCT levels were considerably higher for patients who required antibiotic treatment for sepsis (P<0.001). Also, younger children significantly tended to stay compared to those who were discharged from the ED (P=0.007). Therefore, the multiple regression analysis revealed that those factors, including age (OR 0.6), increased CRP (OR 1.4), and higher PCR levels were predictors for increased admission rate and requirement of emergent treatment [15].

Table 1: Summary of the extracted data

Author and Publication year	Study design	Population characteristics	Item reported	Results and main findings
Lane et al 2024 [14]	Retrospective cohort	-N=19515 with sepsis -Age: 2-12 Y	Delayed treatment & risk of mortality	*Patients who received an antibiotic in<330 minutes (98.2%) had sepsis-attributable 3-day mortality of 0.5% (93 patients) and 30-day mortality of 0.9% (163 patients). *Patients who received antibiotics at 330 minutes or later (1.8%) had 3-day sepsis-attributable mortality of 1.2% (4 patients), 30-day mortality of 2.0% (7 patients). *Receiving after 330 minutes was linked with increased adjusted odds of mortality at both 3 days (OR 3.44; P= 0.02) and 30 days (OR 3.63; P=0.002) compared with those who received antibiotics within 330 minutes.
Lee et al 2024 [15]	Prospective	-N=105 with acute bacterial colitis and suspected sepsis -Age: mean±SD =3.75±3.52 Y	Suspected sepsis caused by acute infectious diarrhea	*CRP and PCT levels were significantly higher at admission (P< 0.001) and in the antibiotic treatment groups (P<0.001). *The mean age of admitted patients was significantly younger than that of children discharged from the ED (P=0.007). *Multiple regression analysis revealed that three parameters were associated with an increased rate of admission, including age (OR 0.635; P<0.001), increased CRP OR 1.404; P=0.025), and PCT levels (OR 1).
Mwanza et al 2023 [16]	Retrospective	-N=144 febrile children -Age: 3.9-37 M	Timing of antibiotics in febrile cases meeting sepsis criteria	*There 26% met local sepsis criteria and 74% had no sepsis. *Delay (>60 min) occurred in 26 (76%) children. *Reported reasons contributing to delay included high patient load, long waiting times, difficult intravenous access, delayed prescribing, inadequate staffing, and difficulty distinguishing between a viral infection and a serious bacterial infection.
Medeiros et al 2022 [17]	Retrospective, observational	-N= 399 children met criteria for sepsis -Age: The median age was	Treatment of sepsis in ED	*The prevalence of sepsis, severe sepsis, and septic shock was 292 (73.2%), 97 (24.3%), and 10 (2.5%), respectively, based on the 2005 IPSCC definitions. * There was no combination of common clinical signs in patients with sepsis or severe sepsis.

		*21.5 months for sepsis children. *12 months for children with severe sepsis *20.5 months for septic shock children		*The diagnosis of septic shock was mostly confirmed by a combination of tachycardia, tachypnea, altered level of consciousness, and abnormal perfusion. * The treatment was based on the criteria of the 2012 Surviving Sepsis Campaign (SSC). *The median time to antibiotic and fluid administration was 3 hours in patients with sepsis and severe sepsis. *In patients with septic shock, the median times to administer antibiotics, fluid, and vasoactive drugs were 2 hours, 2.5 hours, and 6 hours, respectively. * The median length of hospital stay of those with sepsis, severe sepsis, and septic shock was 3 days, 4 days, and 1 day (P<0.001), respectively. *In-hospital mortality rate among those with sepsis (1.4%), severe sepsis (1%), and septic shock (70%) was significantly varied (P<0.001).
Zohoun et al 2021 [18]	Cross-sectional	-N= 2411 children admitted to ED *Shock=64 (2.6%) children -Age: median=29.5 M	Management of shock	*Diagnosis of shock was made on admission in 81.2% of cases. *Severe sepsis was the cause of septic shock among 53.1%. *Oxygen therapy was provided to 84.4%, vascular filling was required by 63 patients, and was done mainly via peripheral vein (95.3%). *Saline was the main fluid used for filling (53.1%). *Inotropes were used for two cases, one required dobutamine and one required adrenaline. *The used antibiotics included quinolones (17.1%) and aminoglycosides (11%) *Mortality was 50%, related to the presence of fever on admission.
Hegamyer et al 2021 [19]	Retrospective	-N= 312 children with sepsis or septic shock in children with and without chronic diseases	Treatment of sepsis and septic shock among children with and without chronic disease	*Sepsis diagnosis was based on the Children's Hospital Association's IPSO. Median time to antibiotics in those with chronic disease was 41.9 min versus 43.0 min in those without chronic disease (P= 0.181).

		-Age:0-20 Y		*Time to first intravenous fluid in those with chronic disease was 22 min versus 12 min in those without (P=0.010). *Those with an indwelling line/catheter (n=40) received intravenous fluid slower than those without (n=272), with no significant difference in time to antibiotic administration by indwelling catheter status (p=0.06). *There were no significant differences in the mode of identification of suspected sepsis or septic shock between those with versus without chronic disease (P=0.2).
Greenwald et al 2021 [20]	Retrospective observational	-N= 90 children with severe sepsis -Age: 9.8 Y	Treatment of sepsis & concordance with guidelines	*24% received guideline-concordant care as described in the ACCM Pediatric Sepsis guidelines. *Broad-spectrum antibiotics were provided within 60 minutes of recognition in the majority of cases. * There were 63 patients with hypotension, and 39 (62%) had hypotension resolve without vasoactives before 60 minutes. *21% of those with initially resolved hypotension went on to require vasoactives in the first 24 hours. *Children receiving concordant care had a median hospital LOS of 95.3 hours (50.9–163.8 hours), whereas in nonconcordant care, the LOS was 88.3 hours (57.3–193.2 hours). *In adjusted analysis, guideline-concordant care was not associated with hospital LOS (incident rate ratio, 0.99 [0.64–1.52]).
Creedon et al 2018 [21]	Retrospective	-N=135 children -Age: ≤18 Y	Timing of antibiotic administration	*Diagnosis of sepsis was based on IPSCC. * Among the 42 (31%) with antibiotics within one hour of the criteria for sepsis, there was higher mortality (P = 0.009), more organ dysfunction, longer time on a vasoactive infusion, and increased intensive care unit and hospital lengths of stay (all P < 0.05) compared to those who received antibiotics after one hour.

CPR; C-reactive protein, PCT; Procalcitonin, ED; Emergency department, OR; Odd ratio, IPSCC; International Pediatric Sepsis Consensus Conference, IPSO; Improving Pediatric Sepsis Outcomes, LOS; Length of stay, ACCM; American college of critical care medicine.

Discussion:

The accurate characterization and diagnosis of sepsis in children remains challenging despite the sepsis-3 concept of suspected or confirmed infection with organ dysfunction, which is theoretically applicable to children and neonates [22]. Additionally, the outcomes of children's sepsis are affected by the time of recognition and treatment [1]. Therefore, there is a lack of original studies focusing on the diagnosis and management of sepsis in children, and there has been no previous systematic review conducted on this subject. Therefore, this systematic review was established in an attempt to fill the gap in the literature regarding this topic.

In 2005, the IPSCC proposed criteria for sepsis due to the need for a sensitive definition for sepsis to facilitate early recognition; these criteria are still widely used [23]. This involves characterizing sepsis as suspected or confirmed infection in the presence of systemic inflammatory response syndrome (SIRS), which can be identified by abnormal physiological signs such as tachypnea, tachycardia, and fever [23]. The sepsis criteria were updated in 2016 in the form of the sepsis-3 criteria [24]. Regarding treatment, the SSC has focused on standardizing the recognition and management of sepsis in children [12].

In the current analysis, we found that a few studies reported the adoption of standardized criteria and guidelines for the diagnosis and management of sepsis. Only four studies reported following definite criteria [16, 17, 19, 21]; however, only two studies followed the IPSCC definitions [17, 21], whereas one study adopted the Children‘s Hospital Association‘s IPSO [19] and the fourth study adopted local criteria. Additionally, regarding treatment, only two studies reported following treatment guidelines and bundles; one study followed the SSC [17], and the other adopted ACCM [20].

Such findings reveal that the diagnosis and management of sepsis in ED in different regions and countries don't follow the standardized criteria and guidelines, and this may lead to missed diagnosis and inappropriate treatment, which consequently leads to poor prognosis and may lead to mortality. Therefore, it is important to identify the adherence of EDs, hospitals, and healthcare providers to the diagnostic and treatment criteria and guidelines for sepsis; this can be a topic that requires further investigation.

Sepsis often presents a wide variety of manifestations that can resemble varied medical conditions [4]. Regarding diagnosis in our analysis, one study revealed no combination of common signs in those with sepsis or severe sepsis, which made diagnosis difficult, whereas septic shock was confirmed based on a combination of symptoms [17]. Another study reported a high rate of recognition of septic shock, and one-half of the cases were due to sepsis; however, the study didn't report the criteria they followed to diagnose the condition [18]. It was reported that the recognition of sepsis wasn't varied by chronic conditions of children [19]. However, there is a lack of studies regarding reporting the exact symptoms and the most common symptoms related to sepsis and septic shock, as well as the criteria they adopted.

It was reported that defining sepsis is challenging due to differences in consensus opinions on the relevance and applicability of criteria to children [5]. Also, the definition and diagnosis of sepsis are hard due to insufficiently specific screening tools [12]. Additionally, the non-specific manifestations of sepsis highlight the urgent need for more effective and precise diagnosis methods [4]. CRP has long been used as a biomarker for children's sepsis [25], and it displayed better specificity and sensitivity compared to several hematological tests for children's sepsis, such as absolute neutrophil count, white cell count, erythrocyte sedimentation rate, neutrophil-to-lymphocyte ratio, and other acute phase reactants [25-27]. The advantages of CRP are that it is familiar to clinicians, has good feasibility [28], and there is a correlation between the elevation of CRP and disease severity [29]. Nonetheless, it is known that CRP has poorer specificity in early disease [30-32]. Also, PCT has exhibited better diagnostic accuracy compared to other acute phase parameters [33], and it is more useful in children compared to adults [34]. Also, PCT is specifically beneficial for pediatric emergencies regarding the identification of late-onset neonatal sepsis [12]. Nonetheless, it was stated that there is insufficient evidence regarding the cost-effectiveness and feasibility of PCT as a diagnostic marker for general use in the healthcare system [35]. One study in the current analysis revealed that CRP, PCT, and young age could be significant predictors of increased admission due to

sepsis [15]. However, the study didn't report the feasibility or cost-effectiveness of PCT in ED settings.

It was revealed that the variable application of sepsis criteria in studies, in addition to the lack of specificity in the 2005 criteria for SIRS [36], and subsequent definition of sepsis contributed to the lack of high-quality evidence for the current therapeutic regimen for children with sepsis [37]. The SSC highlighted the importance of timely recognition of children's sepsis using this as a trigger to launch a sepsis treatment bundle [7], but there is a lack of robust, high-quality evidence for current therapeutic regimens specifically for pediatrics [37]. However, the clinical guidelines recommended initiation of antibiotics [38]. Early management of children's sepsis can considerably reduce mortality rates based on previous observational data [39, 40]. In the present analysis, the studies that reported sepsis treatment reported the provision of antibiotics. However, the studies didn't specify or state the antibiotics used for the management of sepsis or additional therapeutic modalities.

Broad-spectrum antibiotics are widely recommended to be provided within one hour of diagnosis [7]. Additionally, the selection of empiric broad-spectrum antimicrobials should be dependent on local epidemiology and resistance patterns [1]. Based on evidence and biological rationale, blood culture collection and treatment with antibiotics represent widely accepted bundle components [7, 41]. Only one study in the present review reported the usage of broad-spectrum antibiotics, and they were provided to the patients within one hour of sepsis recognition, which goes with the recommendation. However, the study reported that broad-spectrum antibiotics were provided to the majority of cases, and I didn't report the exact proportion of patients who received the therapy [20].

Children with septic shock should receive antibiotics within one hour to achieve optimal outcomes and reduce mortality [7, 38]. However, one study in our analysis focused on sepsis, severe sepsis, and septic shock reported that septic shock cases received antibiotics at two hours, and fluid at 2.5 hours, which reveals a delay in the provision of treatment. This delay in antibiotic provision to septic shock patients may explain the higher mortality rate, which reached to 70%, and it was significantly higher compared to those with sepsis and severe sepsis [17]. This indicates the importance of the initiation of early treatment for sepsis patients.

Some studies in our analysis focused on timing in the treatment of children's sepsis [14, 16, 17, 19, 21]. However, the time considered as a delay in treatment was varied between different studies; one study considered it at more than 5.5 hours (330 minutes) [14], and another study considered it more than one hour [16]. Delay in treatment was linked with higher mortality rates [14], but another study revealed the converse and reported that higher mortality rates and poorer outcomes were recorded for those who received antibiotics for sepsis within one hour of recognition compared to those who received antibiotics after one hour [21].

Only one study reported several variables contributed to the delay in treatment; however, the study didn't report the correlations and their significance between such factors and the treatment delay [16]. Nonetheless, another two studies in our analysis studied two factors; one study compared sepsis, severe sepsis, and septic shock and found that the delay in provision of therapy, including antibiotics and fluids, was longer for sepsis and severe sepsis compared to septic shock, but without reporting the significance of this variation [17]. The other study reported varied results in terms of the presence and absence of chronic diseases among the patients, where the absence and/or presence of chronic diseases significantly influenced the time to the first intravenous fluid, whereas it had no impact on the timing of therapy.

A sepsis care bundle involves initial resuscitation and treatment such as blood culture collection, commencement of antimicrobials, and administration of a fluid bolus, within 180 minutes for pediatrics with sepsis-associated organ dysfunction and within 60 minutes for those with septic shock [7]. Two studies in our analysis reported the implementation of several therapeutic interventions. The implementation of therapeutic interventions was based on the patient's condition and requirements. One study focused on septic shock patients reported adoption of several therapeutic interventions, including oxygen therapy, vascular filling, fluid, inotropes, and different antibiotics [18]. Another study reported that 70% of patients had hypotension and more than one-half of them exhibited resolution with no therapy within one hour [20]. Such findings indicate that the implementation of different therapeutic interventions

would be based on the patient's condition severity and requirements. Therefore, there should be a guideline to be followed to be aware of the correct and exact treatment that should be adopted.

Conclusion:
The definition and diagnosis of sepsis, especially among children, is hard due to several factors, including presentation of sepsis with a wide variety of symptoms resembling other medical conditions, the variations in consensus opinions on the applicability and relevance of criteria to children, and the lack of sufficiently effective and accurate diagnostic tools. Additionally, we found that most of the studies didn't adopt international criteria for defining sepsis in children. Early and immediate provision of treatment for septic patients is a crucial step for improving the outcomes of patients. However, there is a delay in the provision of treatment for septic patients. Additionally, few studies followed treatment guidelines.

Limitations, strengths, and recommendations:
There are some limitations in this review, including variations in the age of children; some studies included neonatal age, and some studies included patients'age of 20 years. The retrospective design of most studies is another limitation. Also, not all studies reported the criteria for diagnosing sepsis, the guidelines of treatment, and the exact therapy. Also, there are variations in defining the time of treatment delay. However, this review also has strengths, including the fact that it is the first systematic review that focuses on the current subject. Also, we declared the gaps in studies and literature to help establish further high-quality studies. Therefore, further studies are highly recommended.

References:
1-Alsharif SM, Altaieb TT, Alabbad YM, et al. Strategies for early identification and management of sepsis in children. Int J Community Med Public Health. 2024 Sep;11(9):3677-3682.
2-Laih, C.-Y.; Hsiao, P.-J.; Wang, Y.-D.; Lee, S.W.; Huang, C.-P.; Chen, W.-C.; Yang, C.-R.; Wu, H.-C.; Chang, C.-H.; Lai, C.-M. PD35-03 QSOFA (quick sequential organ failure assessment score) and sofa scores are valuable tools to predict postoperative sepsis resulting from ureteroscopic lithotripsy (URSL). J. Urol. **2018**, 199, e721–e722.
3-Singer, M.; Deutschman, C.S.; Seymour, C.W.; Shankar-Hari, M.; Annane, D.; Bauer, M.; Bellomo, R.; Bernard, G.R.; Chiche, J.-D.; Coopersmith, C.M.; et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA **2016**, 315,801.
4-Piccioni A, Baroni S, Rozzi G, Belvederi F, Leggeri S, Spagnuolo F, Novelli M, Pignataro G, Candelli M, Covino M, Gasbarrini A. Evaluation of presepsin for early diagnosis of sepsis in the emergency department. Journal of Clinical Medicine. 2025 Apr 4;14(7):2480.
5-Miranda M, Nadel S. Pediatric Sepsis: a Summary of Current Definitions and Management Recommendations. Curr Pediatr Rep 2023;11:29-39.
6-Agyeman PKA, Schlapbach LJ, Giannoni E, Stocker M, Posfay-Barbe KM, Heininger U, et al. Epidemiology of blood culture-proven bacterial sepsis in children in Switzerland: a population-based cohort study. The Lancet Child Adolescent Health. 2017;1(2):124-33.
7-Weiss SL, Peters MJ, Alhazzani W, Agus MSD, Flori HR, Inwald DP, et al. Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children. Pediatr Crit Care Med. 2020;21(2):e52-106.
8-Fleischmann-Struzek C, Goldfarb DM, Schlattmann P, Schlapbach LJ, Reinhart K, Kissoon N. The global burden of paediatric and neonatal sepsis: a systematic review. The Lancet Resp Med. 2018;6(3):223-30
9-Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR, et al. Global, regional, and national sepsis incidence and mortality, 1990㪥2017: analysis for the Global Burden of Disease Study. The Lancet. 2020;395(10219):200-11.
10-Srzic, I. Sepsis definition: Whats new in the Treatment Guidelines. Acta Clin. Croat. **2022**, 61 (Suppl. S1), 67.
11-Schlapbach LJ, Weiss SL, Wolf J. Reducing collateral damage from mandates for time to antibiotics in pediatric sepsis—primum non nocere. JAMA Pediatr. 2019;173(5):409-10.

12-Hibberd O, Karageorgos S, Ranaweera M, Mullally PJ, Athanasiou D, Roland D. Recognising and managing sepsis in children's emergency care: a clinical practice review. Pediatric Medicine. 2025 Jan 1;8:11.
13-Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71.
14- Lane RD, Richardson T, Scott HF, Paul RM, Balamuth F, Eisenberg MA, Riggs R, Huskins WC, Horvat CM, Keeney GE, Hueschen LA. Delays to antibiotics in the emergency department and risk of mortality in children with sepsis. JAMA network open. 2024 Jun 5;7(6):e2413955.
15- Lee TA, Chen CY, Chang YJ, Guo BC, Lin WY, Wu CH, Wu HP. Presentations of Children with Suspected Sepsis Caused by Acute Infectious Diarrhea in the Pediatric Emergency Department. Children. 2024 Jan 29;11(2):171.
16- Mwanza ZV, White BS, Britton PN, McCaskill ME. Timing of antibiotics in febrile children meeting sepsis criteria at a paediatric emergency department. Emergency Medicine Australasia. 2023 Oct;35(5):855-61.
17- Monteiro Medeiros DN, Cintra Nunes Mafra AC, Carla de Souza D, Juan Troster E. Epidemiology and treatment of sepsis at a public pediatric emergency department. Einstein (16794508). 2022 Jan 1;20.
18- Zohoun L, Lalya F, Dossou-Togbe L. Management of Shock in the PediatricEmergency Unit of the National Teaching Hospital HKM (CNHU-HKM) in Cotonou. Annals of Pediatrics. 2021; 4(1)1080.
19- Hegamyer E, Smith N, Thompson AD, Depiero AD. Treatment of suspected sepsis and septic shock in children with chronic disease seen in the pediatric emergency department. The American Journal of Emergency Medicine. 2021 Jun 1;44:56-61.
20- Greenwald E, Olds E, Leonard J, Davies SJ, Brant J, Scott HF. Pediatric sepsis in community emergency care settings: guideline concordance and outcomes. Pediatric emergency care. 2021 Dec 1;37(12):e1571-7.
21- Creedon JK, Vargas S, Asaro LA, Wypij D, Paul R, Melendez E. Timing of antibiotic administration in pediatric sepsis. Pediatric emergency care. 2020 Oct 1;36(10):464-7.
22- Schlapbach LJ, Chiletti R, Straney L, Festa M, Alexander D, Butt W, et al. Defining benefit threshold for extracorporeal membrane oxygenation in children with sepsis—a binational multicenter cohort study. Crit Care. 2019;23(1):429.
23-Kannikeswaran N, Mahajan P. Pediatric Sepsis: New Strategies for Reducing Sepsis Related Mortality. Indian Pediatr. 2023;60(12):981-4.
24- Harley A, Latour JM, Schlapbach LJ. The role of parental concerns in the recognition of sepsis in children: a literature review. Front Pediatr. 2019;7:161.
25- Pulliam PN, Attia MW, Cronan KM. C-reactive protein in febrile children 1 to 36 months of age with clinically undetectable serious bacterial infection. Pediatrics 2001;108:1275-9.
26- Chang SSY, Lim AZ, Ong GY, et al. Predictors of serious bacterial infections using serum biomarkers in an infant population aged 0 to 90 days: a prospective cohort study. BMJ Paediatr Open 2021;5:e000861.
27- dos Anjos BL, Grotto HZ. Evaluation of C-reactive protein and serum amyloid A in the detection of inflammatory and infectious diseases in children. Clin Chem Lab Med 2010;48:493-9.
28- Andreola B, Bressan S, Callegaro S, et al. Procalcitonin and C-reactive protein as diagnostic markers of severe bacterial infections in febrile infants and children in the emergency department. Pediatr Infect Dis J 2007;26:672-7.
29- Gendrel D, Raymond J, Coste J, et al. Comparison of procalcitonin with C-reactive protein, interleukin 6 and interferon-alpha for differentiation of bacterial vs. viral infections. Pediatr Infect Dis J 1999;18:875-81.
30- Luaces-Cubells C, Mintegi S, García-García JJ, et al. Procalcitonin to detect invasive bacterial infection in non-toxic-appearing infants with fever without apparent source in the emergency department. Pediatr Infect Dis J 2012;31:645-7.
31- Velasco R, Gomez B, Labiano I, et al. Performance of Febrile Infant Algorithms by Duration of Fever. Pediatrics 2024;153:e2023064342.

32- Olaciregui I, Hernández U, Muñoz JA, et al. Markers that predict serious bacterial infection in infants under 3 months of age presenting with fever of unknown origin. Arch Dis Child 2009;94:501-5.
33- Pourakbari B, Mamishi S, Zafari J, et al. Evaluation of procalcitonin and neopterin level in serum of patients with acute bacterial infection. Braz J Infect Dis 2010;14:252-5.
34- Mills GD, Lala HM, Oehley MR, et al. Elevated procalcitonin as a diagnostic marker in meningococcal disease. Eur J Clin Microbiol Infect Dis 2006;25:501-9.
35- National Institute for Health and Care Excellence. Procalcitonin testing for diagnosing and monitoring sepsis (ADVIA Centaur BRAHMS PCT assay, BRAHMS PCT Sensitive Kryptor assay, Elecsys BRAHMS PCT assay, LIAISON BRAHMS PCT assay and VIDAS BRAHMS PCT assay). 2015. Available online: https://www.nice.org.uk/guidance/dg18
36- Goldstein B, Giroir B, Randolph A. International pediatric sepsis consensusconference: definitions for sepsis and organ dysfunction in pediatrics. PediatrCrit Care Med 2005;6(1):2–8.
37- Harley A, Schlapbach LJ, Johnston AN, Massey D. Challenges in the recognition and management of paediatric sepsis—the journey. Australasian Emergency Care. 2022 Mar 1;25(1):23-9.
38- Karageorgos S, Hibberd O, Mullally PJW, et al. Antibiotic Use for Common Infections in Pediatric Emergency Departments: A Narrative Review. Antibiotics (Basel) 2023;12:1092.
39- Evans IVR, Phillips GS, Alpern ER, Angus DC, Friedrich ME, Kissoon N, et al.Association between the New York sepsis care mandate and in-hospitalmortality for pediatric sepsis. J Am Med Assoc 2018;320(4):358–67.
40- Cruz AT, Lane RD, Balamuth F, Aronson PL, Ashby DW, Neuman MI, et al.Updates on pediatric sepsis. JACEP Open 2020;5(1):981–3.
41- Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al.Surviving sepsis campaign: international guidelines for management of sepsisand septic shock: 2016. Crit Care Med 2017;45(3).