

The Epidemiology of SIRS in Children: A Literature Review

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Abstract

Systemic Inflammatory Response Syndrome (SIRS) is an early sign before sepsis with signs of fever or hypothermia, tachycardia, and leukocytosis or leukopenia. Sepsis can lead to Multiple Organ Dysfunction (MODS) even death. Almost 3 million children under 5 years of age died because of sepsis. The objective of this study is to provide a review regarding the epidemiology of SIRS in children. The prevalence of SIRS in children is common. Therefore, there still need research on the pediatric SIRS topic so that people can aware more about SIRS as a warning sign of sepsis as one of the global burden deaths that can lead to death.

Keywords: SIRS; Epidemiology; Children; Sepsis; Pediatrics; Prevalence

1. Introduction

Globally, sepsis can lead to a life-threatening condition. Children under 5 years old are at greater risk of sepsis. In 2017 World Health Organization estimated 20 million cases of sepsis and 2,9 million children under 5 years of age died because of it [1]. SIRS is an early sign before sepsis with signs of fever or hypothermia, tachycardia, and leukocytosis or leukopenia. SIRS that are not treated can lead to sepsis, shock septic, MODS (Multiple Organ Dysfunction Syndrome, even mortality[2]. Early recognition on SIRS hopefully can prevent SIRS develop to sepsis. The International Consensus Conference on pediatric determined SIRS is least two of the following criteria, one of which must be abnormal temperature or leukocyte count:

- Core temperature of $>38,5^{\circ}\text{C}$ or $<36^{\circ}\text{C}$.
- Tachycardia or bradycardia according to age group
- Tachypnea or bradypnea according to age group
- Abnormal leucocytes count according to age group.

However, there is a lack and difficulties of epidemiological data relating to SIRS in children. This literature review aims to review several available articles about epidemiology on SIRS populations in children in several various countries across the continent. Another aim of this study is to raise awareness and understanding about SIRS in children. In addition, this review describes and characterizes each country's SIRS situation.

2. Definition

Systemic Inflammation Response Syndrome (SIRS) is an excessive body defense response to localize dangerous stressors such as infection, trauma, acute inflammation, and so on, as well as eliminate endogenous and exogenous substances that cause systemic inflammation [3]. In 1992 the American College of Chest Physicians (ACCP) and the Society of Critical Medicine (SCCM) introduced the term SIRS as follows:

1. Core temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$
2. Heart Rate (HR) > 90 beats per minute
3. Respiratory rate (RR) > 20 times per minute, or CO_2 partial pressure < 32 mmHg / 4.3 kPa
4. Leukocyte count $> 12,000$ per microliter ($12 \times 10^9/\text{L}$) or $< 4,000$ per microliter ($4 \times 10^9/\text{L}$) or immature neutrophils (bands) $> 10\%$.

Sepsis is defined if ≥ 2 SIRS criteria are met and infection is suspected or confirmed [4].

In 2001, SCCM (Society of Critical Care Medicine) and other institutions held a consensus that gave rise to a definition of sepsis-2 which was the same as before (using SIRS and infection criteria)[5]. In 2016, a new definition of sepsis emerged, namely Sepsis-3, which defines sepsis as life-threatening organ dysfunction caused by the host response to infection[6]. Sepsis-3 is diagnosed using the qSOFA (quick Sepsis Related Organ Failure Assessment) criteria:

1. Decreased consciousness (GCS <15)
 2. Systolic pressure < 100 mmHg
 3. Respiratory Rate $> 22/\text{minute}$
- *If you meet 2 of the 3 criteria, means sepsis positive.

The United Nation Convention on the Rights of the Child (UN-CRC) stated on part 1 article 1, a child means every human being below the age of eighteen years unless under the law applicable to the child, majority is attained earlier. According to UNICEF, children are all people under 18 years of age [7], [8]. The International Pediatric Sepsis Consensus Conference (IPSCC) define SIRS in children (pSIRS) is characterized by the presence of at least 2 of the 4 criteria below, one of which must include an abnormal body temperature or leukocyte count [9]:

1. Fever (core body temperature >38.5) or hypothermia (core body temperature $<36^{\circ}\text{C}$)
2. Tachycardia or bradycardia (in children aged <1 year)
 - Tachycardia: The mean heart rate is > 2 SD from the normal (above normal) for age (absence of external stimulus, chronic drugs, or pain stimuli, or an unexplained persistent increase in heart rate over a 0.5 - 4 hours.
 - Bradycardia in children aged < 1 year: Mean heart rate < 10 th percentile (below normal) for age (absence of external vagal stimulus, β -blocker medication or congenital heart disease, or an unexplained persistent decrease in heart rate for 0.5 hours.
3. Tachypnea or mechanical ventilation
Mean respiratory rate (RR) $> 2\text{SD}$ from normal (above normal) for age or mechanical ventilation for acute process not associated with underlying neuromuscular disease or receipt of general anesthesia.
4. Increase or decrease in the number of leukocytes based on age (not secondary to chemotherapy-induced leukopenia) or immature neutrophils (band) $> 10\%$.

PSCC (Pediatric Sepsis Consensus Congress) separates children's SIRS vital signs based on physiological and clinical changes according to age group and laboratory test results into 6 categories, that is newborns, neonates, infants, toddlers, school age and adolescents. This division is also divided based on risk factors for infection and the administration of antibiotics [9]. SIRS classification in children can be seen on table 1.

Table 1. SIRS classification-based age of children [9]

Age Group	Heart Rate (beats/min)		Respiratory Rate (breaths/min)	Leukocyte Count (Leukocyte x 10 ³ /mm ³)	Systolic Blood Pressure (mmHg)
	Tachycardia	Bradycardia			
Infant: 1 mo - 1 y	>180	<90	>34	>17,5 or <5	<100
Toddler and Preschool: 2 - 5 y	>140	NA	>22	>15,5 or <6	<94
Schol Age of Child: 6 - 12 y	>130	NA	>18	>13,5 or <4,5	<105
Adolescent and Young Adult: 13 - <18y	>110	NA	>14	>11 or <4,5	<117

3. Epidemiology of SIRS in Children

Table 2. Studies on the prevalence of SIRS in various countries

Author (year) [ref.]	Place, Country	Title	Study Design	Period	Study Setting (ED/PICU/all)	Study population	Prevalence of SIRS
Laphra, 2021 [10]	Bangkok, Thailand	Characteristics and Outcome of Children with Systemic Inflammatory Response Syndrome due to Sepsis and non-Sepsis in a Tertiary Care Center in Thailand	Prospective observational study	January - December 2019	Pediatric Tertiary University Hospital	All eligible patients	51,3% (n= 229 / 446)
Ganjoo et. al, 2014 [11]	Srinagar, Northern India	Clinical Epidemiology of SIRS and Sepsis in Newly Admitted Children	Prospective study	June 2011 - May 2012	Pediatric General Hospital (General Wards & PICU) - Tertiary Care Hospital	All children admitted at referral care centre in Northern India	23% (n= 201/865)
Foo et al, 2018 [12]	London, UK	Presumed Systemic Inflammatory Response Syndrome in the Pediatric Emergency Department	Descriptive retrospective cohort study	April - March 2013	PED of London Health Sciences Centre - Tertiary Care Center	All children present to the PED	15,3% (n= 216/1416)
Pavare, 2009 [13]	Latvia, Europe	Prevalence of Systemic Inflammatory Response Syndrome (SIRS) in Hospitalized Children: A Point Prevalence Study	Descriptive Prospective point prevalence study	January-February 2007	Tertiary Level Hospital	All patients treated in hospital	7% (n=66/943)
Scott et al, 2015 [14]	Colorado,	The Prevalence and Diagnostic Utility of Systemic Inflammatory Response Syndrome Vital Signs in A Pediatric Emergency Department	Retrospective descriptive study	April 2011 - March 2012\	ED tertiary pediatric hospital	All visits to ED pediatric hospital	15,2% (n=6.122 /40.356)
Horeczko and Green, 2013 [15]	California, United States	Emergency Department Presentation of the Pediatric Systemic Inflammatory Response Syndrome	Retrospective analysis	2007 - 2010	general ED conducted by CDC	National Ambulatory Medical Care Survey	21,7% (n= 24.970.364 /114.817.502)

Carvalho et al, 2005[16]	Brazil	Prevalence of Systemic Inflammatory Syndromes at a Tertiary Pediatric Intensive Care Unit	Cross-sectional, prospective, observational study	August 1999 – July 2000	PICU Tertiary Care Hospital	All patient admitted to PICU	68% (n=304/447)
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3.1. Asia

A prospective observational study that was conducted at a tertiary care center in Bangkok, Thailand from January to December 2019 resulting prevalence of SIRS 51.3% (n: 229/446). and among them 177 (77.3%) had sepsis. Of patients with SIRS, 120 (52.4%) were boys and the average age is 24 months. The most common underlying diseases were congenital heart diseases (27,5%)[10].

In the other hand, research conducted by Ganjoo and colleagues in tertiary care hospital in Srinagar, Northern India shows that the prevalence of SIRS among hospitalized children was 23% (n:201/865). Among these patients, 79% (n:159/201) had SIRS associated with infection. In this prospective study from June 2011 – May 2012, shows that 64% (n: 129/201) had sepsis and 15% (n: 30) had severe sepsis. Also 19 patients had septic shock. Most SIRS patients were in the 2-5 years old group (n: 94/201). Boys have a higher number (n: 124/201) than the girls (n: 77/201). The majority cases of SIRS were pulmonary (44%)[11].

3.2. Europe

Foo et al conducted a retrospective cohort study to determine the prevalence of pediatric SIRS (pSIRS) and sepsis in Pediatric Emergency Department (PED) London Health Sciences Centre, also a tertiary care center, for 16 days throughout the 2012 year. The study resulting pSIRS incidence was 15.3% (n: 216/1416). The median age in this study is 4 years old and most of the children in 2-5 years of age category Infection incidence was 76,4% (n=165) and mostly diagnosed with a lower respiratory tract infection (n: 46). In this study also found that children with SIRS had a longer length of hospital stay. However, the gender percentage wasn't examined[12].

Not only in London, a publication of Pavare and his colleague were performed in The Children's Clinical University Hospital (tertiary level hospital) in Latvia. This study was conducted in early 2007. The prevalence of SIRS in this study was quite small, just 7% (n:66/943). Eight percent (n:5/66) of SIRS patients developed sepsis. Like the other study, most of SIRS patients were aged 2-5 years (39%). More than half SIRS patients had an infectious disease. There's a slightly higher number in boys than girls (n:36vs30) There were no data about the majority of the main diagnosis. [13].

3.3. United States

A study that presence SIRS prevalence is conducted in a tertiary academic free-standing pediatric hospital in Colorado. This retrospective descriptive cohort study is taken from April 2011 until March 2012. The prevalence of SIRS in children under 18 years of age that admitted to Emergency Department was 15,2% (n: 2.122/40.356) which is quite common. The highest percentage of SIRS children was in the 1 – 4 years age groups and the lowest percentage was found in adolescent group (15 – 17 years old). Boys were the most dominant to presents SIRS vital signs (52,8%). [14]

In another study in California [17] shows that the prevalence of SIRS Children in Emergency Department was 21.7% (n: 24,970.364/114,817.502). This retrospective analysis of data was collected in the National Hospital Ambulatory Medical Care Survey for 4 years from 2007-2010. Horeczko and Green estimate each year approximately there were 6.2 million visits in ED by children that have SIRS. This study shows that 1-5 years group was the most likely to have SIRS. The results of this study show that boys have a higher presentation than girls (50.7% vs 49.3%). Fifty three percent of SIRS patients were found to have infection.

Another study in Brazil conducted by Carvalho et al observe the prevalence of SIRS at a tertiary care Pediatric Intensive Care Unit (PICU). As a result, SIRS sign was found in 68% (n=304/447) of children in PICU. The median age in this study was 24 months and 54% were male. Two – thirds of them had infectious SIRS. In this study also observed SIRS mortality (12%; n=36) and SIRS length of stay in the ICU (median = 3 days). It also shows how infection was responsible for higher risk of death (14.9% vs 6.3%) and a longer stay in ICU (3 vs 2 days) than the non-infectious one. [16]

Researchers had difficulty in finding the prevalence of SIRS in children, perhaps because SIRS criteria are no longer used in determining sepsis these days. However, researchers managed to find several research. The studies above were heterogenous in design, population, sample size and settings. Most of them were conducted at a tertiary care hospital in the hope that it can generalize this review and represent the country itself. It is concluded that the SIRS rate in tertiary hospitals worldwide is quite common, at 29%. The highest average prevalence is in Asia continent at 37%, followed by America at 35% and finally Europe which has an average prevalence of only 11%. Both in the ER, PICU and in the pediatrics department all showed diverse results. SIRS were more common than girls although not very significant. Children that had SIRS usually under 5 years of age (2-5 years old category). Almost half of the patients usually have an infection which means they may develop sepsis and progress to severe sepsis and shock. From the results of the research above, it was also found that somewhat LOS and death rates were higher in patients with SIRS than non-SIRS. Even though only several literatures were reviewed, it is hoped that this literature is sufficient to represent the global prevalence. In the future, it is hoped that more research will be carried out on SIRS and sepsis to increase awareness of countries in the region.

Conclusion

There's still limited data on epidemiology of SIRS in children to represent worldwide. This compilation of articles proves that the prevalence of SIRS in children is quite common and eventually it can develop into sepsis. Therefore, there still need research on the pediatric SIRS topic so that people can aware more about SIRS as a warning sign of sepsis as one of the global burden deaths that can lead to death.

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