

Characterization and prognostic factors of children with sepsis in a high complexity hospital

Caracterización y factores pronósticos de pacientes con sepsis en un hospital de alta complejidad

Maria Camila Franco^{a,b}, Laura F. Niño-Serna^c, Manuela Rendón^{a,d},
Marcela Betancourt^c, Catalina Torres^c, Isabel Cristina Maya^c

^aUniversidad Pontificia Bolivariana. Medellín, Colombia.

^bUniversidad CES. Medellín, Colombia.

^cHospital Pablo Tobón Uribe. Medellín, Colombia.

^dResidente de Pediatría.

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What do we know about the subject matter of this study?

Sepsis is the leading cause of death in children, with higher rates in low- and middle-income countries. There are few studies in Latin America, most of them limited to patients admitted to the ICU.

What does this study contribute to what is already known?

In a cohort of children with sepsis in a high-complexity hospital, evaluated before admission to the ICU and with a high rate of organ dysfunction, we found insufficient bundle compliance, specifically to early antibiotic use and intravenous fluids therapy.

Abstract

Objective: To describe the clinical and laboratory characteristics of patients with sepsis admitted to a high-complexity healthcare center in Latin America. **Patients and Method:** Descriptive observational study. Patients between one month to 17 years of age with sepsis diagnosis were included. Studied variables included demographics, clinical and laboratory characteristics, and treatment administered, determining predictors of mortality. A descriptive analysis was performed using the Chi-square or Fisher test. **Results:** 186 patients were included and 72% of them had comorbidities. Respiratory disease was the most frequent source of sepsis (29%), followed by gastrointestinal infection (11%) and catheter-related bacteremia (11%). 60% of patients had at least one organ dysfunction, the most frequent being respiratory dysfunction (70%). 60% of the patients presented multiple organ dysfunction syndrome (MODS). Blood cultures showed a positive result in 37% of cases. The two most common first-hour interventions included IV resuscitation fluids (67%) and antibiotics (36%). Va-

Keywords:

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sopressor support and mechanical ventilation were used in 33% and 34% of patients, respectively. Overall mortality was 12% and was higher in patients diagnosed with MODS (59%) or who presented with some organ dysfunction. **Conclusion:** Organ dysfunction was frequent. Patients with some type of organ dysfunction or MODS presented higher mortality. Despite global and institutional guidelines focused on improving diagnosis and treatment, in less than half of the patients sepsis was adequately detected and first-hour IV fluids and antibiotics administration rates were below 70%.

Introduction

Sepsis is the leading cause of death in children, becoming a public health problem¹, with an estimated 48.9 million cases and 11 million deaths annually, representing 19.7% of all deaths worldwide². In Latin America, there is a reported prevalence between 12% and 35%, with a mortality rate between 18% and 56%³.

However, the prevalence of sepsis, severe sepsis, and septic shock presents important variations in relation to the definitions used and the source of the cohorts evaluated and maybe even higher in low-income countries since the final common pathway of the main causes of death in children (pneumonia, diarrhea, dengue, malaria) is organ dysfunction due to sepsis, not coded in death certificates⁴. Additionally, limitations in access to medical care, the burden of chronic non-communicable diseases, and the availability of resources, among others, are determinant factors for the development of sepsis in children in low- and middle-income countries and are not considered in guideline recommendations.

Our objective was to describe the clinical and paraclinical characteristics, bundle compliance, outcome, and mortality of pediatric patients diagnosed with sepsis.

Patients and Method

Study design

Retrospective observational study of a group of patients seen at the *Hospital Pablo Tobón Uribe* (HPTU) between 2016 and 2020. The HPTU is a high-complexity hospital in Medellín, Colombia, which has 78 pediatric hospitalization beds, an emergency department, and 27 pediatric and neonatal critical care beds, caring for patients with oncological comorbidities, transplanted, immunocompromised, and with rare diseases.

Population

Children between 1 month and 17 years of age with ICD-10 diagnosis for sepsis in the clinical history (A021, A400 to A403, A408 to A415, A418, A419 to A421, and

B377) were included. At the time of this study, the new guidelines “2020 Surviving Sepsis Campaign”⁵ and the “Latin American Consensus on the Management of Sepsis in Children”⁶ were not yet available so, for the final selection, we included patients with a diagnosis of sepsis according to the definitions of the international consensus on pediatric sepsis published in 2005⁷, in force for the study period (table 1)^{2,3,5,7-10}. Patients referred from another institution were excluded.

Data and variable analysis

Demographic variables, comorbidities, focus of infection, sepsis characteristics and severity, vital signs, and paraclinical variables at sepsis diagnosis (blood count, C-reactive protein -CRP-, lactate, laboratory tests, cultures, identification of respiratory viruses, FilmArray® gastrointestinal or CNS panel) were recorded as well as therapeutic interventions (latency of fluid and antibiotic administration, vasoactive and ventilatory support), sepsis-Bundle compliance⁵, and mortality at 90 days (table 1).

Statistical analysis

For qualitative variables, frequencies and proportions were calculated and for quantitative variables, normality was assessed using the Shapiro-Wilk test, expressed as median and interquartile range (IQR). An exploratory analysis was performed where some characteristics related to sepsis were compared between deceased and surviving patients through the Chi-square or Fisher's exact test as appropriate. SPSS version 20 was used. The study was approved by the institution's ethics committee (Act No. 2020.003).

Results

Demographic characteristics

Of 279 eligible patients, 93 were excluded because they did not meet sepsis criteria, resulting in a total sample of 186 patients, where 61% were male. The age was 9.3 years (0.67-12.5), 39% were infants, 34% were adolescents, and a lower percentage were schoolchildren (27%). 72% had relevant comorbidities, the most common being oncological ones (23%), immuno-

suppressive treatment (23%), and neurologic diseases (20%). The main causes of admission were community-acquired pneumonia (29%), sepsis of gastrointestinal origin (11%), and catheter-related bloodstream infection (CRBSI) (11%). 61% of the sepsis diagnosis was made in the emergency department, 20% during hospitalization, and 17% in the Pediatric Intensive Care Unit (PICU) (table 2). Hospital stay was 15 days (8-31) and PICU stay was 7 days (3-13).

Clinical characteristics

Of the variables used for diagnosing sepsis, alterations in heart rate (84%) and temperature (76%) were the most frequently identified, followed by respiratory rate (55%) and capillary refill time (36%), the latter being recorded in only 76%. Mental status was recorded in 90% of patients and was abnormal in 24%. Regarding temperature at the time of sepsis diagnosis, hypothermia was present in 21% of oncologic patients,

Table 1. Definitions used in the study⁵

Sepsis	Confirmed or suspected infection associated with the presence of systemic inflammatory response syndrome (SIRS), defined as the presence of 2 or more of the following: temperature $> 38.5^{\circ}$ or $< 36^{\circ}$, heart rate $> 2SD$ for age, or in children under 1 year $< P10$, respiratory rate $> 2SD$ for age or mechanical ventilation for acute disease, elevated or decreased leukocyte count for age, or more than 10% immature neutrophils.
Severe sepsis	Sepsis plus one organ dysfunction.
Septic shock	Sepsis and cardiovascular organ dysfunction persisted after administration of isotonic fluids at > 40 cc/kg within one hour.
Organ dysfunction	Organ dysfunction associated with sepsis is defined as a severe infection that leads to an alteration in the function of an organ, whether or not it is of cardiovascular origin. It is important to highlight that the Surviving Sepsis guideline does not establish a specific definition for organic dysfunction, since given the multiple methods to identify this situation in children, it is difficult to reach a consensus on its definition in this population ⁵
Cardiovascular dysfunction	Despite the administration of isotonic fluids greater than 40 ml/Kg in 1 hour: Hypotension: BP less than the 5th percentile or 2 SD for age or Need for vasoactive drugs to maintain BP in the normal range (dopamine greater than 5 micrograms/kg/minute or dobutamine, epinephrine, or norepinephrine at any dose) or Two of the following: <ul style="list-style-type: none"> Unexplained metabolic acidosis: Base deficit > 5 mEq/L or increased arterial lactate 2 times the normal value (2 mmol/L). Oliguria: urinary output less than 0.5 ml/Kg/hour. Prolonged capillary refill: greater than 3 seconds. Difference between central and peripheral temperature greater than $3^{\circ}C$
Respiratory dysfunction	PaO ₂ /FIO ₂ : less than 300 in the absence of cyanotic heart disease or pre-existing lung disease or PaCO ₂ greater than 65 or 20 mmHg above baseline PaCO ₂ or oxygen requirements greater than 50% to maintain SpO ₂ greater than 92% or Need for invasive or non-invasive mechanical ventilation.
Neurologic dysfunction	Glasgow scale less than or equal to 11 or Acute change in mental status with a decrease on the Glasgow scale greater than 3 points from the abnormal level.
Hematologic dysfunction	Platelet count less than 80,000/mm ³ or a 50% decrease in platelet count from the highest value recorded in the previous 3 days (for chronic hematology and cancer patients) or INR greater than 2
Renal dysfunction	Serum creatinine greater than or equal to 2 times the normal limit for age or a 2-fold increase from baseline creatinine.
Hepatic dysfunction	Total bilirubin greater than or equal to 4 mg/dL or ALT 2 times the upper limit for age.
Multiple organ dysfunction syndrome (MODS)	Dysfunction of 3 or more organs
Bundle 2020	Package of measures for the management of sepsis according to the surviving sepsis 2020 campaign, which consists of a bolus of fluids (10-20 mL/kg), antibiotics, and blood cultures within the first hour of detection of sepsis in patients with septic shock and within 3 hours in patients without shock.
Adequate detection of sepsis	Identification of SIRS associated with confirmed or suspected infection, within the first hour of presenting the clinical changes and/or the laboratory results.
Late detection of sepsis	Identification of SIRS associated with confirmed or suspected infection, after the first hour of presenting the clinical changes and/or the laboratory results.

Infection site	<ul style="list-style-type: none"> • Pneumonia: patient with symptoms compatible with community-acquired pneumonia, with pneumonic consolidation on chest X-rays, with no other sepsis foci. • Undetermined: without a clear origin of the infection. • Gastrointestinal: patient with symptoms of gastrointestinal infection • CRBSI: positive blood cultures and clinical manifestations associated with infection (fever and/or hypotension) in a patient who has a central intravascular device, and in whom there is no other apparent source of infection other than the catheter.⁸ • Urinary tract infection: patient with symptoms compatible with urinary tract infection and urine culture with more than 100,000 CFU taken by bladder catheter. • Primary bloodstream infection: patient with two positive blood cultures for the same organism. • Skin: patient with clinical evidence of skin infection such as cellulitis, erysipelas, necrotizing infection, or abscess.⁹ • Osteoarticular: patient with septic arthritis and osteomyelitis confirmed by culture of joint fluid or bone or by suggestive magnetic resonance imaging.¹⁰ • CNS: patient with symptoms of meningitis/encephalitis, with CSF cytochemical compatible with infection and/or positive CSF culture or film array or PCR isolation. • Surgical site infection: local inflammatory changes in the surgical wound or tomography compatible with infection and/or positive culture. • Peritoneal infection: clinical suggestive of peritonitis with laboratory findings and positive culture.
Vital signs	<p>The following vital signs were considered at the time of diagnosis of sepsis:</p> <p>Heart rate, blood pressure, respiratory rate, temperature, oxygen saturation.</p>

⁸At the time this research began, the research group did not yet have the new definitions published in the latest available guidelines "surviving pediatric sepsis 2020"⁵, therefore, the previously proposed definitions were used to establish sepsis (International Consensus of pediatric sepsis published in 2005)⁷. SE: standard deviation; BP: blood pressure; SpO₂: oxygen saturation; INR: international normalized ratio; ALT: alanine aminotransferase; CRBSI: Catheter-related bloodstream infection; CFU: colony forming unit; CNS: central nervous system; CSF: cerebrospinal fluid; mmHg: millimeters of mercury; PCR: polymerase chain reaction.

22% of transplanted patients, 23.5% of patients with liver disease, and 28.5% of preterm infants (table 3).

Organ dysfunction

60% of the patients presented at least one organ dysfunction and of these, 60% presented multiple organ dysfunction syndrome (MODS). Among the patients with organ dysfunction, the most frequent was respiratory (70%), followed by cardiovascular (68%), hematologic (39%), neurologic (14%), renal (13.5%), and hepatic (11%) dysfunction.

Laboratory results

The most frequent alteration was the leukocyte count (80%), presenting leukocytosis in 45% and leukopenia in 35%. Bandemia was present in 7%. Lactate was 1.7 mg/dL (1.2-2.5), being above 2 mg/dL in 36% of cases (table 4). Renal function was preserved in most patients (70%). Altered glycemia levels were found in 16% and bilirubin levels in 9%, while the presence of hypocalcemia was observed in 69%, mainly in oncologic patients.

Microbiology

Aerobic blood cultures were indicated in 67% of the patients, with positive results in 37%, and *Staph-*

yllococcus aureus being the most frequent microorganism (n = 16, 41%), with fatal outcomes in 2 of them, followed by Gram-negative bacilli such as *Escherichia coli* (13%) and *Klebsiella pneumoniae* (8%).

Viral studies were indicated in 52% of the patients (respiratory viral panel 35%), obtaining positive results in 20%. Respiratory syncytial virus was the most frequent isolate (53%) and, to a lesser extent, cytomegalovirus, dengue, herpes simplex type 1, influenza, metapneumovirus, rotavirus, and SARS-CoV-2. Five cases of fungal infection were identified, corresponding to 22% of the total isolates; *Candida glabrata* was the most commonly identified fungus (40%).

Treatment

Regarding the treatment administered (table 5), 67% of the population received crystalloids bolus, either normal saline or Ringer's Lactate, at 10-20 mL/kg dose, and 36% received empirical broad-spectrum antibiotic in the first hour. 13% of the patients in the cohort received antibiotic treatment before the diagnosis of sepsis. The time elapsed between diagnosis and antibiotic initiation was 125.5 minutes (60-223). Vasoactive support lasted 4 days (2-8), requiring two or more drugs in 41 patients (66%); the duration of invasive ventilatory support was 1 day (1-4) and 7 days for non-

Table 2. Baseline characteristics in the cohort of patients diagnosed with sepsis

Characteristics	Total, n = 186 n (%)
Sex	
Male	114 (61)
Comorbidity	134 (72)
Oncologic diseases ^a	43 (23)
Immunosuppression ^b	42 (23)
Neurologic diseases ^c	38 (20)
Respiratory diseases	30 (16)
Other	30 (16)
Gastrointestinal diseases	26 (14)
Congenital anomalies	25 (13)
Transplant	19 (10)
Liver diseases	18 (10)
Kidney diseases	18 (10)
Prematurity	16 (9)
Heart diseases	16 (9)
Recent surgery	15 (8)
IEM	10 (5)
Benign hematologic diseases	9 (5)
Endocrinology diseases	6 (3)
Psychiatric diseases	4 (2)
Immunodeficiencies	2 (1)
Source of infection	
Lung	54 (29)
Unknown	22 (12)
Gastrointestinal	21 (11)
CRBSI	20 (11)
Urinary	19 (10)
BSI	17 (9)
Skin	11 (6)
Osteoarticular	11 (6)
CNS	4 (2)
SSI	2 (1)
Peritoneal	2 (1)
Unit	
Emergency room	113 (61)
Inpatient care	37 (20)
Pediatric and neonatal critical care	31 (17)

^aPatients with confirmed neoplastic disease, whether hematological or solid organ; ^bPatients with primary or acquired immunodeficiency or chronic immunosuppressive management with steroids, biological therapy, immunomodulators in transplantation or autoimmune disease; ^cInclude patients with epilepsy and infantile cerebral palsy; CNS: central nervous system. IEM: inborn errors of metabolism. BSI: bloodstream infection. CRBSI: Catheter-related bloodstream infection. SSI: surgical site infection.

invasive (3.5-10). Vasoactive support and mechanical ventilation were required in 50 patients (27%), with a PICU stay of 11 days (7-16.7) and hospital stay of 24.5 days (18.7-36.2).

Outcomes

Mortality was 12% (22 children), with no statistically significant difference in terms of sepsis detection ($p = 0.2$). Higher mortality was present in patients with some organ dysfunction ($p = 0.01$) and MODS ($p = 0.01$) (table 6). Of the patients who died, all had been admitted to the PICU and had some type of organ dysfunction.

Adequate detection of sepsis occurred in 90 patients (48%).

In patients in whom the Bundle was complied with, there were 3 deaths (9%) while in those in whom it was not complied with there were 19 (12%). Non-compliance with this bundle was due to 3 factors: late detection (24%), initiation of fluids after the first hour (33%), and late initiation of antibiotics (64%), the latter due to late medical orders (average 46.5 minutes), late administration (125.5 minutes), or difficulties with the pediatric patient's venous access.

Four patients (2%) required cardiopulmonary resuscitation maneuvers in the first 48 hours after diagnosis; 2 of these patients died.

Discussion

The main findings in our cohort were the high frequency of comorbidities (~3/4) and at least one organ dysfunction, the most frequent being respiratory (70%). Adequate detection of sepsis was infrequent (~1/2), while fluid resuscitation and antibiotic administration in the first hour were suboptimal, with a latency close to 2 hours. Overall mortality was 12%, higher in patients with some organ dysfunction and MODS.

Despite initiatives to improve early diagnosis and treatment of pediatric sepsis, such as the ACCM/PALS pediatric sepsis treatment guidelines¹¹, the Latin American Consensus⁶, the Global Pediatric Sepsis Initiative¹², and the Surviving Sepsis Campaign⁵, mortality remains high, between 4% and 50%, depending on the severity of the disease, risk factors, and geographic location¹³⁻¹⁵. In Colombia, the estimated overall mortality rate in children is 18%¹⁶. In this series, the overall mortality rate was similar to that found in the SPROUT study of PICUs in South America and lower than that estimated in a Colombian study conducted in 2013¹⁶; however, it should be noted that the aforementioned study was conducted only in patients admitted to PICUs, therefore, of greater severity and higher mortality risk than the patients in this study.

Table 3. The temperature at the time of diagnosis of sepsis according to comorbidities

Comorbidities	n	Temperature at the time of sepsis diagnosis			
		Normal n (%)	Febricula ^a n (%)	Fever ^b n (%)	Hypothermia ^c n (%)
Prematurity	14	4 (28.5)	1 (7)	5 (36)	4 (28.5)
Malformation	25	4 (16)	2 (8)	15 (60)	4 (16)
Heart disease	16	0 (0)	3 (19)	13 (81)	0 (0)
Respiratory disease	29	6 (21)	1 (3)	18 (62)	4 (14)
Neurologic disease	37	8 (22)	4 (11)	22 (59)	3 (8)
Oncologic disease	42	6 (14)	0 (0)	27 (64)	9 (21)
Hematologic disease	8	1 (12.5)	1 (12.5)	5 (62.5)	1 (12.5)
Recent surgery	14	0 (0)	1 (7)	10 (71)	3 (21)
Gastrointestinal disease	26	5 (19)	0 (0)	19 (73)	2 (8)
Liver disease	17	4 (23.5)	0 (0)	9 (53)	4 (23.5)
Renal disease	18	5 (28)	1 (5)	12 (67)	0 (0)
Primary immunodeficiency	2	0 (0)	0 (0)	2 (100)	0 (0)
Transplant	18	3 (17)	1 (5)	10 (56)	4 (22)
Immunosuppression	41	6 (15)	1 (2)	26 (63)	8 (20)

^aFebricula (slight fever): body temperature between 37,5 and 38°C, ^bFever: body temperature >38°C. ^cHypothermia: body temperature less than 36°C.

The impact of sepsis on infant mortality is even more worrisome in low- and middle-income countries, where low immunization rates and poor sanitary conditions are associated with a higher prevalence of infectious diseases; it may also be related to inadequate treatment and late recognition (52% in our study), findings similar to those reported in other Latin American studies^{13,15,17}. This is especially worrisome since our institution implemented the “sepsis code” strategy several years ago, aimed at early detection.

Most children who die of sepsis suffer refractory shock or MODS, with deaths occurring predominantly within the initial 48-72 hours of treatment¹⁶⁻¹⁸. In this cohort, mortality was higher when the patient had MODS (60%), being higher than that reported by other authors, (19%-36%)^{16,18}, which may be explained by demographic differences with the referred studies. Mortality was lower compared with other authors (64%-73%)^{19,20}.

In general, children with sepsis present with non-specific signs and symptoms at the onset of the disease, preserving their hemodynamic stability due to compensatory mechanisms¹¹. However, most algorithms continue to be based on the abnormality of vital signs, which are also found to be altered in a large proportion of children with self-limited febrile infections.

There is controversy about the role of tachycardia in emergency care as it is an appropriate indicator of severe infection²¹, despite that most children with sepsis have tachycardia abnormalities. Additionally, multiple studies have questioned the limitations of inter-rater variability and interpretation of prolonged capillary refill time, often used in clinical sepsis scores^{22,23}. The study by Fleming et al. found no association between capillary refill and serious infections in the emergency department, contrary to the common perception of its usefulness as a reliable clinical sign of peripheral perfusion in the case of sepsis in clinical settings²². In our study, capillary refill was recorded in ¾ of the patients, observing that was abnormal in 36% of these, reflecting this variability. In recent years, new technologies have been developed to assess capillary refill in order to achieve a more accurate measurement for the clinician²⁴.

In contrast to what has been reported in studies in South America (less than 50%) and Central America (less than 10%)^{14,15,17}, 60% of patients developed MODS. This may be explained by the complexity of the hospital where the study was conducted, a national referral center with a significant flow of patients with underlying comorbidities (72%), the most frequent being immunosuppressed patients and those with

Table 4. Laboratory results in patients with sepsis

Laboratory	n/N (%)
Leukocytes (cell/mm ³) ^a	13500 (6100 - 19350)
Leukocytosis (<2 SD for age)	82/184 (45)
Leukopenia (>2 SD for age)	19/184 (35)
Bands (%) ^a	7 (3.5 - 13.5)
Bandemia (> 10%)	13/186 (7)
Platelet count (cell/mm ³) ^a	234000 (94500 - 394750)
Thrombocytopenia (< 150000)	59/184 (32)
Thrombocytosis (> 450000)	28/184 (15)
CRP (mg/dl) ^a	7.2 (2.4 - 17.3)
Serum creatinine (mg/dl) ^a	0.51 (0.40 - 0.71)
Less than 2 times ULN	27/145 (19)
More than 2 times ULN	16/145 (11)
Total bilirubin (mg/dl) ^a	0.8 (0.4 - 1.8)
Less than 4	61/67 (91)
More than or equal to 4	6/67 (9)
ALT (U/l) ^a	28 (16 - 48.7)
PaFiO ₂	
Mild hypoxemia (300-200 mmHg)	17/100 (17)
Moderate hypoxemia (200-100 mmHg)	24/100 (24)
Severe hypoxemia (0-100 mmHg)	11/100 (11)
PaCO ₂	
Hypercapnia (>45 mm Hg)	48/102 (47)
Hypocapnia (< 35 mm Hg)	17/102 (17)
BE (mEq/l) ^a	-3 (-5.7 - 0.9)
More than -5	87/119 (73)
Less than -5	32/119 (27)
Lactate (mg/dl) ^a	1.7 (1.2 - 2.5)
Between 1 and 2	56/124 (45)
More than 2	45/124 (36)
Glycemic (mg/dl) ^a	108 (92 - 142)
Hyperglycemia (> 180 mg/dl)	16/122 (13)
Hypoglycemia (< 60 mg/dl)	4/122 (3)
Ionized calcium (mmol/l) ^a	1 (0.9 - 1.1)
Hypocalcemia (< 1 mmol/L)	84/121 (69)
Hypercalcemia (> 1.3 mmol/L)	3/121 (3)

^aMedian (Interquartile range). CRP: C-reactive protein, ULN: upper limit of normal. ALT: alanine aminotransferase, PaFiO₂: ratio of arterial oxygen partial pressure (PaO₂) to fractional inspired oxygen (FiO₂), PaCO₂: partial pressure of Carbone Dioxide, BE: base excess.

Table 5. Treatment and interventions

Treatment	n (%)
Fluid bolus in the first hour	124 (67)
Blood culture in the first hour	89 (48)
Antibiotic administration in the first hour	66 (36)
Vasoactive*	62 (33)
Norepinephrine	46 (25)
Milrinone	38 (20)
Epinephrine	35 (19)
Vasopressin	16 (9)
Dopamine	7 (4)
Steroids	26 (14)
Transfusions*	71 (38)
Red cells	64 (57)
Platelets	36 (32)
Plasma	10 (9)
Cryoprecipitate	2 (2)
Mechanical ventilation	64 (34)
IMV	60 (93)
NIMV**	14 (7)
2020 Sepsis-Bundle compliance	32 (17)

IMV: invasive mechanical ventilation, NIMV: none invasive mechanical ventilation. *A patient could have received more than one vasoactive or more than one transfusion.

**Of these patients, 10 received IMV.

oncologic disease, in contrast to other studies, where respiratory and neurological diseases predominate^{13,16}. Globally, the respiratory system continues to be the main focus, being found in 37% to 40% of the patients and, in second place, bloodstream infection in 19% to 25%, similar to our results^{22,25,26}.

Similar to our study, the proportion of microbiological isolation ranges between 26%-65%, which confirms the difficulties in isolating a causal etiological agent, with underestimates of viral sepsis^{4,13,26-29}. In pediatrics, bacteria continue to be the main causative agent identified, similar to our study, where *S. aureus* predominated, followed by Gram-negative bacteria^{19,27,27,30,31}. The low frequency of viral sepsis is likely because of the low availability of viral panel or FilmArray given the cost and resources in our milieu, which prevented its routine use^{32,33}.

Early diagnosis and treatment are very important to reverse septic shock, where the persistence of shock

Table 6. Comparison of some important characteristics related to sepsis between deceased and surviving patients

Characteristics	Deceased N = 22	Survivors N = 164	P value
Sepsis detection			
Appropriate	8 (36%)	82 (50%)	0.2 ^a
Late	14 (64%)	82 (50%)	
Antibiotic in the first hour			
Yes	1 (5%)	30 (18%)	0.08 ^b
No	21 (95%)	134 (82%)	
Crystalloids bolus in the first hour			
Yes	4 (18%)	34 (21%)	0.5 ^b
No	18 (82%)	130 (79%)	
Any organ dysfunction (n = 111)			
Yes	22 (100%)	89 (54%)	0.01^b
No	0 (0%)	75 (46%)	
Multi-organ dysfunction (n = 67)			
Yes	13 (59%)	54 (33%)	0.01^a
No	9 (41%)	110 (67%)	

^aChi-square test. ^bFisher's exact test. The statistically significant p-value is in bold.

adversely affects survival in a time-dependent manner, however, timely recognition and treatment (fluids in the first hour and antibiotics) can improve the prognosis and continues to be present in the treatment guidelines for sepsis and septic shock, both Latin American and international ones^{6,11,30}.

A limitation of this study was its retrospective design, where there was a loss of data in some variables, which may cause an over or underestimation of the presence of organ dysfunction since the paraclinical tests to evaluate it were not requested in all patients of the cohort and in the clinical assessment, in addition to the limitation in the report of mental status and capillary refill, which makes it possible for sepsis to be recognized late in the presence of signs of severity. In addition, this study was performed in a highly complex hospital, where the severity of the patients may be greater than in other settings, which limits the generalization of the results.

In conclusion, in this cohort of patients, organ dysfunction was frequent as was MODS, with higher mortality in these patients. Comorbidities were frequent. Adequate detection of sepsis was present in only 48% and compliance with sepsis care bundles was low (17%). Despite worldwide and institutional initiatives focused on improving diagnosis and treatment, the initiation of intravenous fluids and antibiotics administration in the first hour was below 70%.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: This study was approved by the respective Research Ethics Committee. The authors state that the information has been obtained anonymously from previous data.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

Financial Disclosure

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