Global Pediatric Health
Volume 9: 1–10
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DOI: 10.1177/2333794X221118017
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Update on Pediatric Sepsis in Mexico

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Abstract

The main objective of this work was to determine and update the causal agents' antibiotic sensitivity and resistance patterns on pediatric sepsis in a population of northeast Mexico. It is a cross-sectional study showing the results of blood cultures of pediatric patients with a presumptive diagnosis of sepsis were reviewed according to the SOFA criteria during 2020 in a public hospital in Mexico. A total of 207 blood cultures were performed and analyzed. The main isolated microorganisms were Staphylococcus, followed by Klebsiella and Escherichia. Several microorganisms showed 100% of sensitivity to different antibiotics or antifungals, some of them include Vancomycin, Voriconazole, Meropenem, Ciprofloxacin, and Cefotaxime. Bacteria of genre Staphylococcus showed its highest sensitivity rate to Tigecycline with 63.3%. Too Staphylococcus showed the highest resistance rate to Oxacillin with 50%. Although the patterns of sepsis-causing germs are similar to those previously reported, the development of new drugs with greater efficacy is the main contribution.

Keywords

sepsis, blood culture, anti-infective agents, microbial sensitivity tests, drug resistance

Received May 6, 2022. Accepted for publication July 18, 2022.

Introduction

Sepsis is a systemic inflammatory response that occurs as a reaction to an infection by bacteria, fungi or viruses.[1] In this clinical condition, microorganisms enter the bloodstream causing a serious detriment in the homeostasis of patients; hypoperfusion, tissue damage and multiple organ failure, causing increased risk of death in patients.[2]

In 2016, a group of specialized health workers known as Sepsis-3 updated the clinical criteria for sepsis, excluding the need for systemic inflammatory response syndrome and introducing a flow chart that includes rapid organ sequence evaluation (related to sepsis), and Sequential Organ Failure Assessment (SOFA) that included several clinical and lab findings. A SOFA score ≥ 2 is suggestive of sepsis. However, the clinical decision to make the diagnosis of sepsis is not yet definitively established by risk stratification scores, because this tool has not yet undergone clinical decision-making analysis[3,4]

There are large differences between adult and pediatric sepsis, in pathophysiology, clinical presentation, microorganisms, and therapeutic approaches. Therefore, the diagnosis of sepsis in pediatric patients represents a significant diagnostic challenge.[5] An early empirical treatment is essential to determine the clinical evolution of pediatric patients with sepsis, when the treatment is started early (<3 hours of evolution) the mortality is 4.0% to 8.0%, while when implementing the treatment

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later (>3 hours of evolution), mortality increases up to 21.0%. Then, the implementation of a rational early antimicrobial therapy is necessary.[6]

The severity of sepsis depends on the characteristics of the causative germ and its pharmacological resistance. For this reason, early diagnosis and appropriate and timely treatment are essential to reduce mortality, complications, and hospital stay.[7]

Blood culture is the gold standard to determine the etiological agent for the diagnosis of bacteremia. This procedure delays the diagnosis by 3 to 6 days after blood sample. For this, the early use of empirical antimicrobial therapy is justified, however unspecific treatment favors the creation of multi-resistant strains and increases mortality.[8,9]

Seeking to have more efficient diagnostic tools, detection methods such as molecular diagnosis have been proposed, which allow the identification of microorganisms in a few hours. Molecular diagnosis is performed directly from the blood of patients and although its advantage is speed, its main limitation is the presence of contaminating inhibitors of DNA and PCR such as Fe+ and immunoglobulins.[10] Furthermore, in Mexico, PCR tests are not accessible in hospital laboratories that care for most patients with suspected sepsis.[11]

The purpose of this research was to determine the main causative agents of bacterial sepsis in pediatric patients by blood cultures and to establish the patterns of antimicrobial sensitivity and resistance in a regional hospital in northeastern Mexico.

Materials and Methods

An observational, descriptive, prospective and cross-sectional study, where the results of blood cultures of patients between 0 and 17 years of age with a presumptive diagnosis of sepsis were reviewed according to the SOFA criteria during the months of April to November 2020 in a public hospital, located in the northeast of Mexico. In this hospital, more than 250 cases of pediatric septicemia are reported yearly.

Sample size was calculated as proportion study, considering a confidence level of 95.0%, precision of 3.0%, and the probability of isolating the germ with patterns of sensitivity and resistance to antibiotics of 15.0%, using these data a sample size of 172 blood cultures was calculated. The sampling was realized in a non-probabilistic way for convenience starting in April 2020 and until November 2020.

Patients between 0 and 17 years of age admitted to any of the pediatric services of hospital who meet the following clinical criteria were included:

Sepsis in neonates, suspicion of neonatal sepsis with vertical transmission clinical criteria

Poor clinical evolution, fever > 38.3°C/Hypothermia <35.5°C, difficulty feeding, hypoactivity, unexplained tachycardia, digestive signs (rejection of the takes, vomiting/diarrhea, abdominal distension, hepatomegaly, jaundice) respiratory signs: (Grunting, nasal flaring, retractions, irregular breathing patterns, tachypnea, cyanosis. apnea periods), neurological signs: (hypoactivity /irritability, hypotonia/hypertonia, tremors/seizures, tense fontanelle). These clinical criteria plus the presence of risk factors for vertically transmitted infection or diagnostic confirmation of vertical sepsis (risk of sepsis).

as altered hematic biometry: (Leukocytosis/leukopenia with $<5000/mm^3$, immature/mature neutrophil index > 0.2 or immature/total > 0.16, thrombocytopenia $< 150\,000/mm^3$, alteration of acute phase reactants, C-reactive protein >10-15 mg/dL. procalcitonin > 0.5 ng/dL after 72 hours of life.

Nosocomial or late sepsis (since the third day of life and before the month of life). Clinical signs: Unexpected evolution, unexplained tachycardia, increased ventilatory requirements, need to reintroduce mechanical ventilation without apparent respiratory cause.

Sepsis in pediatric patients, Clinical Data: Alteration of the neurological state, fever >38.3°C/Hypothermia <35.5°C, tachypnea (>2 SD for age), tachycardia/bradycardia (>2 SD for age), capillary filling>2 seconds, hot/cold extremities, decreased peripheral pulses, decreased urinary output. A score of 2 or higher on the SOFA scale for pediatric patients, plus, alteration of hematic biometry: Leukocytosis/leukopenia depending on the age of the patient (not secondary to chemotherapy), presence of 10% or more of immature forms of neutrophils.[12]

The exclusion criteria were patients who for any reason could not have a blood culture. Those patients with incomplete data were eliminated from the analysis.

The procedures to be performed on recruited patients are described below: The first step was the registry of protocol al Ethics and research committee. Once registered recruitment of patients happens in all pediatric departments of the hospital. Parents of patients who meet inclusion criteria were invited to participate in this study and sign informed consent. Additionally, pediatrics patients with mental and psychological state allowed understand protocol terms to sign an assent informed document to participate.

After signing the informed consent, all patients were subjected to a duplicate blood culture and handled by the hospital laboratory and external laboratory. In addition, the patient's sociodemographic data and comorbidities were taken from his file. All data was handled confidentially for the investigation but open to the treating physician.

The blood culture was taken with sterile measures. Two blood cultures were taken separated by a short time interval (between 15 and 20 minutes). Blood cultures were always taken by trained personnel. The material was prepared on a procedure tray prior to taking the sample under strict aseptic technique. The cleaning and puncture procedures were carried out in accordance with the guidelines proposed by the CLSI.[13] Then, 5 to 10 mL of samples were collected, except in preterm infants, in whom a 3 to 5 mL sample was collected. The integrity of the bottle and the turbidity or hemolysis in the culture were verified. For this study, the system used was Bactec FX-40 from BD (Becton-Dickinson®). The flasks remained at 37°C for a period of 5 to 7 days in incubation and from 7 to 21 days in the case of suspicion of difficult-to-culture microorganisms. The material required was in accordance with the guidelines proposed by the CLSI.[13]

For the cultivation procedure: the flasks that the team tested as positive, that showed evidence of development or that were about to be discarded, were subcultured. Finally, if bacteria were observed in the smear, the result was recorded and a subculture was carried out, otherwise the bottle was discarded following biosafety regulations. Based on the results observed at the gram staining, the appropriate culture media were selected for the isolation and identification of the microorganism. One milliliter of the culture was deposited on a plate in Blood Agar, EMB Agar, Vogel Johnson agar, Chocolate Agar. 1 mL of the broth was applied in a tube containing Thioglycolate medium. The culture boxes were incubated for 24 to 48 hours at 37°C in a BD BACTEC™ FX40 automated blood culture system, it is an automated blood culture instrument used for the growth and detection of organisms (unless the presumed isolated microorganism required other conditions) in accordance with the guidelines proposed by the CLSI.[13]

For the identification of the microorganism and to know the patterns of susceptibility and resistance to antibiotics, this procedure was followed:

1.- The culture media that presented bacterial development underwent a Gram stain to the different colonies and the results were recorded.
2.- The identification of the microorganism was carried out by means of complementary biochemical tests that were applied according to the protocol established for each microorganism.
3.- Then we proceeded with the susceptibility tests.
4.- Once the microorganism was identified, the pertinent susceptibility tests were carried out in accordance with the guidelines proposed by the CLSI.[13]

All data were collected in a data sheet in Excel® (Microsoft Office®) designed expressly for this research work, this sheet contains the sociodemographic variables of the minors and in it the report of the blood culture, the bacteria or isolated bacteria was attached. and the pattern of susceptibility and resistance reported.

The data were captured in a Microsoft Office® Excel database and analyzed with the statistical software SPSS® version 22 of IBM statistics. The analysis was basically descriptive where the frequency (proportion) with which a certain bacterium is isolated in this population was calculated, later the cross analysis was carried out to determine the isolation proportions of bacteria according to the stage, age, gender, department, and comorbidities. The relationship of certain bacteria with the evolution of the patients and the main proportions of sensitive and resistant antibiotics according to the isolated bacteria were described.

Results

A total of 207 blood cultures were performed, 59.9% of them correspond to samples from male patients. The age range of patients merge from newborn to teenager, where percentage of newborns was 54.6%, young infants 18.4%, older infants 4.8%, preschool 6.8%, scholar 11.1%, and finally teenager have a percentage of 4.3%.

Regarding the distribution by area of hospital stay, 41.6% corresponded to the medical pediatric area, 12.5% to the surgical pediatric area, and 45.9% to the nursery.

Almost all (98.6%) of the patients presented comorbidities; prematurity was present in 31.4% of blood samples taken, risk of sepsis in 15.0%, late sepsis in 13.0%, early sepsis in 4.3%, patients with respiratory distress syndrome have 8.3%, pneumonia 6.8%, necrotizing enterocolitis 2.4%., hydrocephalus 4.8%, meningitis, 3.4%, and encephalopathy 1.0%. Over more, patients with immunosuppression had 8.2%, malnutrition in 8.2% and other comorbidities 15.5%. Only 1.4% do not had any comorbidity.

Regarding the site of the blood culture collection, 65.5% of these were obtained by peripheral puncture, while 34.7% were obtained from the central venous catheter. Of the 207 patients who underwent a blood culture, 91.8% were discharged due to improvement, while 8.2% died.

The main proportions of microorganisms grouped according to their genera can be observed in Table 1. The main isolated microorganisms in general were Staphylococcus (39.5%), followed by bacteria of the genera Klebsiella and Escherichia with 14.5% and 9.2% respectively. A total of 76 positive blood cultures were reported, corresponding to 36.7% and 131 negative blood cultures with 63.2%.

Table 1. Shows the Proportions of Microorganisms Isolated From Blood Cultures.

Genre	Frequency	Percentage
Staphylococcus	30/76	39.5
Klebsiella	11/76	14.5
Escherichia	7/76	9.2
Enterobacter	7/76	9.2
Acinetobacter	6/76	7.9
Candida	6/76	7.9
Pseudomonas	4/76	5.3
Stenotrophomonas	3/76	3.9
Streptococcus	1/76	1.3
Ralstonia	1/76	1.3
Positive	76/207	36.7
Negative	131/207	63.29

The most frequently isolated species in blood cultures can be seen in Table 2. The most frequently isolated microorganisms were *Staphylococcus hominis, Klebsiella pneumoniae, Escherichia coli, Enterobacter cloacae, Acinetobacter baumannii, Candida parapsilosis, Pseudomonas aeruginosa, Stenotrophomonas maltophilia, Streptococcus anginosus*, and *Ralstonia mannitolilytica.*

The distribution of microorganisms by age stage was, in the newborn stage the predominant genera was Staphylococcus with 50.0% and in second place the genera Klebsiella with 18.4%. The identified genera with the highest frequency in younger infants was Staphylococcus with 39.1%, followed by Enterobacterales and Pseudomonas with 13.0% each. Older infants presented isolation of gram-negative bacteria in 75.0%, amongst them 25.0% corresponded to each of the following: Klebsiella, Escherichia and Pseudomonas. In scholar patients, Enterobacteria, Pseudomonas and Acinetobacter predominated with 20.0% each. Finally, in adolescents, 50.0% of the frequency corresponded to Acinetobacter and 50.0% Candida. All these outcomes are swowed in the table 3.

Next, the distribution of isolated bacteria is described according to the comorbidity of the patients: Blood culture isolated microorganisms in preterm infants were mainly Staphylococcus 55.0%, followed by Klebsiella 20.0%, Enterobacter and Escherichia 10.0%, the less frequent was Candida 5.0%. In patients with early sepsis, only Escherichia and Staphylococcus were isolated 50.0% each. In late sepsis most common isolated microorganism were Staphylococcus 35.3%, followed by Enterobacter and Klebsiella 23.5%, Candida 11.8% and Acinetobacter 5.9%. In patients with diagnosis risk of sepsis, Escherichia was isolated in 50.0%, while Klebsiella and Staphylococcus have 25.0% each. In patients with respiratory distress syndrome, only Klebsiella and Staphylococcus were isolated in 50.0% each. In patients with pneumonia Staphylococcus 40.0%, Candida, Klebsiella, and Streptococcus 20.0% were isolated. In blood samples from necrotizing enterocolitis patients, only Staphylococcus with was isolated (100.0%). Most common microorganism isolated in patients with hydrocephalia were Pseudomonas and Streptococcus 28.6%; followed by Acinetobacter, Escherichia, Staphylococcus with 14.3%. In samples from patients with meningitis, Klebsiella was isolated in 100%. In patients with encephalitis, were isolated Acinetobacter and Pseudomonas 50.0% each. In patients with immunosuppression, Acinetobacter, Candida, Enterobacter, and Staphylococcus were isolated in 25.0% each. In patients with diagnosis of malnutrition, Staphylococcus was most frequently isolated (42.9%), followed by Acinetobacter, Klebsiella, Pseudomonas, and Ralstonia 14.3%.

The susceptibility of microorganisms to antibiotics is shown in Table 4. The highest susceptibility rate is shown by several antibiotics and antifungals, and it corresponds to a 100.0%. Staphylococcus showed the highest sensitivity to Tigecycline at a 63.3% rate, followed by Vancomycin with 53.0% and Doxycycline 33.3%. The Klebsiella genera showed a sensitivity of 100.0% to Meropenem, 45.5% to Ertapenem and 36.4% to Ciprofloxacin. Escherichia genera also had a susceptibility of 100.0% to Meropenem, and a 71.4% to Cefotaxime and Ertapenem equally. The Enterobacter genera had a susceptibility of 100% to Meropenem and Ciprofloxacin but showed no susceptibility to other drugs. Regarding the Acinetobacter genera, it only showed a susceptibility of 50.0% to Trimethoprim and sulfamethoxazole and 33.0% to Ciprofloxacin. The Candida genera presented a 100% susceptibility to Voriconazol, followed by 50.0% of Amphotericin B and 16.7% to Caspofungin. Pseudomona genera showed a susceptibility of 100.0% to Meropenem, 75.0% Ciprofloxacin and 25.0% to Vancomycin. The Stenotrophomonas genera showed sole susceptibility to Trimethoprim and sulfamethoxazole with 66.7%. Streptococcus showed a 100.0% sensitivity to Vancomycin and Cefotaxime only. Finally, the Ralstonia genera only showed a susceptibility of 100.0% to Ciprofloxacin.

Cross tests were carried out to establish the resistance of the microorganisms to the different antibiotics and antifungals and this information was showed in Table 5: The antibiotic that showed the highest resistance rate was Oxacillin, with 50.0% for Staphylococcus, continuing with this genus of microorganisms, 43.0% resistance to erythromycin and 16.7% for the trimethoprim-sulfamethoxazole. The Klebsiella genera presented 45.0% resistance to trimethoprim, followed by 27.0% for

Table 2. Shows the Distribution of Isolated Bacteria by Genre and Species.

Genre	Species	Frequency	Percentage
Staphylococcus	Aeurus	9/30	30
	Hominis	7/30	23.3
	Epidermidis	6/30	20
	Lentus	4/30	13.3
	Capitis	1/30	3.3
	Haemolyticus	3/30	10
Klebsiella	Pneumoniae	10/11	90
	Oxytoca	1/11	10
Escherichia	Coli	7/7	100
Enterobacter	Cloacae	7/7	100
Acinetobacter	Baumanni	4/6	66.6
	Haemolyticus	2/6	33.3
Candida	Parapsilosis	4/6	66.6
	Tropicalis	2/6	33.3
Pseudomonas	Aeruginosa	3/4	75
	Atutzeri	1/4	25
Stenotrophomonas	Maltophila	3/3	100
Streptococcus	Anginousus	1/1	100
Ralstonia	Manitolityca	1/1	100

ceftriaxone as well as ampicillin. Regarding Escherichia, 87.0% resistance was found for quinolones, and 27.0% for sulfa drugs; of the Enterobacterales genera, 100.0% were resistant to cefuroxime, 42.0% showed resistance to trimethoprim-sulfamethoxazole as well as to ceftriaxone; continuing with the Acinetobacter genera; it was found that 67.0% were resistant to cefepime, followed by 33.0% for ceftazidime, ceftriaxone, and ciprofloxacin. 50.0% of Pseudomonas showed resistance to amikacin and ceftazidime, respectively. 33% of the genus Stenotrophomonas were resistant to trimethoprim-sulfamethoxazole. Of the Streptococci, 100.0% showed a rate of resistance to ceftriaxone and ampicillin. 100.0% of the Ralstonia genus showed resistance to fourth generation cephalosporins and ampicillin. Finally, the fungi presented 50.0% resistance to fluconazole and 33.0% to caspofungin.

Discussion

As aforementioned, sepsis in the pediatric patient requires prompt recognition and opportune treatment with empirical antibiotic therapy based on the most frequent microorganisms per group age; however, an appropriate spectrum antibiotic regimen should be changed once the causative pathogen is identified. Most of the incidence studies in pediatric patients with sepsis are based on the US population, unfortunately the incidence of sepsis and isolated microorganisms in the Latin American population is different.[14,15] For this reason, studies should be carried out to review the most common isolated microorganisms and the patterns of susceptibility and resistance to antibiotics in Latin-American populations; as this allows offering more appropriate initial treatments, thereby reducing mortality and complications.

Our main outcomes will support changes in traditional antibiotic schemes based in another context. As previously described[16] Staphylococcus was the most common agent isolated by blood cultures. Although *S. epidermidis* and *S. hominis* can be contaminants of the cultures, they can behave as pathogens in immunocompromised patients, as the cultures were performed under the highest possible aseptic conditions, so we consider them as pathogens, although we do not rule out the possibility of contamination in a little more 23% of positive cultures of Staphylococcus. This bacterium was the main causal agent in newborn and young infants. In a previous study carried out in a neonatal intensive care unit in Mexico City,[17] the most common isolated bacteria were Enterobacterales (67.0%). In the same study, they find that 65.5% of Staphylococcus species isolated shown resistance to oxacillin; meanwhile, in our study, only 50.0% of this species were resistant to oxacillin. In a previous report from Australia more than 2000 samples of patients with bacteremia have been reviewed, they found that methicillin-sensitive staphylococci do not show resistance to other antibiotics, while methicillin-resistant staphylococci, have up 42.0% of resistance to erythromycin. These outcomes were similar at founded in our study were 43.0% of the staphylococcus isolated showed

Table 3. Distribution of Microorganisms by Stage.

	Staphylococcus	Klebsiella	Escherichia	Enterobacter	Acinetobacter	Candida	Pseudomonas	Stenotrophomonas	Streptococcus	Ralstonia
Newborn	19/39	7/39	4/39	3/39	1/39	3/39	3/39	0/39	0/39	1/39
	48.7%	17.9%	10.2%	7.7%	2.6%	7.7%	7.7%	0%	0%	2.6%
Young infant	9/23	3/23	1/23	3/23	2/23	0/23	3/23	2/23	2/23	0/23
	39.1%	13%	4.3%	13%	8.7%	0%	13%	8.7%	8.7%	0%
Older infant	0/4	1/4	1/4	0/4	0/4	1/4	1/4	0/4	0/4	0/4
	0%	25%	25%	0%	0%	25%	25%	0%	0%	0%
Preschool	0/3	0/3	0/3	0/3	1/3	0/3	0/3	0/3	2/3	0/3
	0%	0%	0%	0%	33.3%	0%	0%	0%	66.7%	0%
Scholar	0/5	0/5	0/5	1/5	1/5	0/5	1/5	1/5	1/5	0/5
	0%	0%	0%	20%	20%	0%	20%	20%	20%	0%
Teenager	0/2	0/2	0/2	0/2	1/2	1/2	0/2	0/2	0/2	0/2
	0%	0%	0%	0%	50%	50%	0%	0%	0%	0%

resistance to erythromycin.[18] In this way, in newborns and young infants, the recommendation must include antibiotics to treat Staphylococcus infections.[19] Although, Vancomycin and Doxycycline are commonly used to treat infections by *Staphylococcus aureus* however, in this study the antimicrobial with the highest sensitivity founded was Tigecycline with a 63.3% susceptibility rate, which is uncommonly used to treat these infections, and it could be considered as option of treatment in these cases.

In our investigation, in older infants enterobacteria and pseudomonas were the main family of bacteria causal of sepsis. All of them, Enterobacterales and Pseudomonadaceae families were 100%sensitive to meropenem. Considering that: meropenem and imipenem are the drugs recommended for treatment of Enterobacterales resistant to beta lactamase in critically ill patients[20]; then, meropenem must be included in the early treatment scheme. Our outcomes showed that gram-negative bacteria, such as Klebsiella, Escherichia, and Enterobacter showed a high resistance to Trimetoprim-Sulfametoxazol with 45.5%, 16.7%,and 28.6% respectively. Gram-negative bacteria are commonly treated with ureidopenicillins, carbapenems, fluoroquinolones, cephalosporins and many other drugs but their widespread use has led to antimicrobial resistance and her use must be analyzed.[21,22] Ceftazolone/tazobactam and ceftazidime/avibactam are the newest drugs approved by FDA for treating gram-negatives.[23]

in our study, in pre-escolar stage the main causal agent was Streptococcus, we found 100.0% resistance to ampicillin and third generation cephalosporins, specifically ceftriaxone. Controversially, in a systematic review and meta-analysis in low- and middle-income countries, most of Streptococcus isolated were sensible to ampicillin and third generation cephalosporins.[24] In the same way, Droz et al establish that the percentage of susceptibility to cephalosporins is 93.0% in Africa and 78.0% in Asia.[25]

A prevalence of non-fermenting aerobic gram-negative bacilli was founded in our study on scholar and teenager sepsis, of them 67.0% of the *Acinetobacter* species isolated showed resistance to cefepime, and 33.0% were resistant to each one off follows: ceftriaxone, ciprofloxacin, and ceftazidime. In previous studies, *Acinetobacter* has shown significant resistance to multiple antibiotic treatments, which has been accounted as a challenge to modern medicine while treating clinical illnesses regarding the afore mentioned microbe.[26]

In conclusion, in this study, the most frequently identified microorganisms were *Staphylococcus*, *Klebsiella* and *Escherichia*, respectively. Our results coincide with previous reports which establish that *Staphylococcus* is the microorganism that most commonly causes sepsis. The highest resistance rate for *Staphylococcus* was 50.0% to Oxacillin, a commonly used antibiotic for treating this microbe. This study found a *Staphylococcus* susceptibility of 63.0% to Tigerglycine, which is interesting as it is an unconventional treatment for this microorganism and could be considered as an alternative therapeutic option. *Klebsiella*, *Escherichia*, and *Enterobacter* presented a 100.0% susceptibility to Meropenem. Our results show that *Streptococcus* showed a 100.0% resistance to both ampicillin and ceftriaxone while it has been established that it has a worldwide 70.0% susceptibility. Another hand, *Streptococcus* showed 100.0% susceptibility to vancomycin and cefotaxime.

Conclusion

These results allow clinical pediatricians working in this setting to use rational treatments that are likely to be associated with better therapeutic success based on the commonly reported microorganisms, as well as their resistance and susceptibility. For although the microorganisms associated with sepsis appear to be the same; however, in the cultures performed, drugs with greater susceptibility were found. Finally, these outcomes were used to suggest changes in the empirical treatment scheme of our institution.

Table 4. General Rate of Sensitivity to Antibiotics.

	Staphylococcus (30)	Klebsiella (11)	Escherichia (11)	Enterobacter (9)	Acinetobacter (6)	Candida (6)	Pseudomona (4)	Stenotrophomonas (3)	Streptococcus (1)	Ralstonia (1)
Vancomycin	17/30	0/11	0/11	0/9	0/6	0/6	1/4	0/3	1/1	0/1
	56.6%	0%	0%	0%	0%	0%	25%	0%	100%	0%
Voriconazole	0/30	0/11	0/11	0/9	0/6	6/6	0/4	0/3	0/1	0/1
	0%	0%	0%	0%	0%	100%	0%	0%	0%	0%
Caspofungin	0/30	0/11	0/11	0/9	0/6	1/6	0/4	0/3	0/1	0/1
	0%	0%	0%	0%	0%	16.7%	0%	0%	0%	0%
Amphotericin B	0/30	0/11	0/11	0/9	0/6	3/6	0/4	0/3	0/1	0/1
	0%	0%	0%	0%	0%	50%	0%	0%	0%	0%
Meropenem	0/30	11/11	11/11	9/9	0/6	0/6	4/4	0/3	0/1	0/1
	0%	100%	100%	100%	0%	0%	100%	0%	0%	0%
Gentamicin	4/30	0/11	0/11	0/9	0/6	0/6	0/4	0/3	0/1	0/1
	13.3%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Trimethoprim and sulfamethoxazole	0/30	0/11	0/11	0/9	3/6	0/6	0/4	2/3	0/1	0/1
	0%	0%	0%	0%	50%	0%	0%	66.7%	0%	0%
Ciprofloxacin	5/30	4/11	0/11	9/9	2/6	0/6	3/4	0/3	0/1	1/1
	16.7%	36.4%	0%	100%	33.3%	0%	75%	0%	0%	100%
Cefotaxime	15/30	1/11	8/11	0/9	0/6	0/6	0/4	0/3	1/1	0/1
	50%	9.1%	72.7%	0%	0%	0%	0%	0%	100%	0%
Oxacillin	8/30	0/11	0/11	0/9	0/6	0/6	0/4	0/3	0/1	0/1
	26.7%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Tigecycline	19/30	1/11	1/11	0/9	0/6	0/6	0/4	0/3	0/1	0/1
	63.3%	9.1%	9.1%	0%	0%	0%	0%	0%	0%	0%
Doxycycline	10/30	0/11	0/11	0/9	0/6	0/6	0/4	0/3	0/1	0/1
	33.3%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Ertapenem	0/30	5/11	8/11	0/9	0/6	0/6	0/4	0/3	0/1	0/1
	0%	45.5%	72.7%	0%	0%	0%	0%	0%	0%	0%
Rifampicin	5/30	0/11	0/11	0/9	0/6	0/6	0/4	0/3	0/1	0/1
	16.7%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Amikacin	0/30	1/11	0/11	0/9	0/6	0/6	0/4	0/3	0/1	0/1
	0%	9.1%	0%	0%	0%	0%	0%	0%	0%	0%

Table 5. General Rate of Resistance to Antibiotics.

	Staphylococcus (30)	Klebsiella (11)	Escherichia (11)	Enterobacter (9)	Acinetobacter (6)	Candida (6)	Pseudomonas (4)	Stenotrophomonas (3)	Streptococcus (1)	Ralstonia (1)
Oxacillin	15/30	0/11	0/11	0/9	0/6	0/6	0/4	0/3	0/1	0/1
	50%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Levofloxacin	3/30	0/11	0/11	0/9	0/6	0/6	0/4	0/3	0/1	0/1
	10%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Caspofungin	0/30	0/11	0/11	0/9	0/6	2/6	0/4	0/3	0/1	0/1
	0%	0%	0%	0%	0%	33.3%	0%	0%	0%	0%
Fluconazole	0/30	0/11	0/11	0/9	0/6	3/6	0/4	0/3	0/1	0/1
	0%	0%	0%	0%	0%	50%	0%	0%	0%	0%
Ceftazidime	0/30	1/11	0/11	0/9	2/6	0/6	2/4	0/3	0/1	1/1
	0%	9.1%	0%	0%	33.3%	0%	50%	0%	0%	100%
Ciprofloxacin	2/30	0/11	9/11	0/9	2/6	0/6	0/4	0/3	0/1	0/1
	6.7%	0%	81.8%	0%	33.3%	0%	0%	0%	0%	0%
Trimethoprim	5/30	5/11	3/11	4/9	1/6	0/6	0/4	1/3	0/1	0/1
	16.7%	45.5%	27.7%	44.4%	16.7%	0%	0%	33.3%	0%	0%
Cefuroxime	0/30	1/11	0/11	9/9	0/6	0/6	0/4	0/3	0/1	0/1
	0%	9.1%	0%	100%	0%	0%	0%	0%	0%	0%
Erythromycin	12/30	0/11	0/11	0/9	0/6	0/6	0/4	0/3	0/1	0/1
	43.3%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Ceftriaxone	0/30	3/11	1/11	4/9	2/6	0/6	0/4	0/3	1/1	0/1
	0%	27.3%	9.1%	44.4%	33.3%	0%	0%	0%	100 %	0%
Ampicillin	1/30	3/11	0/11	0/9	0/6	0/6	0/4	0/3	1/1	1/1
	3.3%	27.3%	0%	0%	0%	0%	0%	0%	100%	100%
Amikacin	0/30	0/11	0/11	0/9	1/6	0/6	2/4	0/3	0/1	0/1
	0%	0%	0%	0%	16.7%	0%	50%	0%	0%	0%
Cefepime	0/30	0/11	0/11	0/9	4/6	0/6	0/4	0/3	0/1	0/1
	0%	0%	0%	0%	67.7%	0%	0%	0%	0%	0%
Piperacillin-tazobactam	0/30	0/11	2/11	0/9	0/6	0/6	0/4	0/3	0/1	0/1
	0%	0%	18.2%	0%	0%	0%	0%	0%	0%	0%

Acknowledgments

The authors thank the staff of Hospital Regional # 6, the coordination of education and research for the facilities granted to carry out this research and the University of Monterrey for the support received for the translation and publication of this manuscript. We must thank "Dirección General de Calidad y Educación en Salud, Secretaría de Salud, México" for the support given to Estefanía Mattenberger-Cantú during her social service.

Authors' Contributions

CADB and FGS were responsible for the concept; RSF and FGS for the design; RSF, MGMT, and LEGT for supervision; MGMT and LEGT for materials; CABD, EMC, GBGM, and PAMD for data collection and/or processing; EMC, GBGM, and PAMD for the analysis and/or interpretation; CABD, EMC, GBGM, and PAMD for the literature review; FGS RSF for writing; and MGMT, LEGT, CABD, EMC for critical review.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work wasn't supported by any institution nor received any type of funding.

Ethical Considerations

This research is registered on the national registry committee of research and ethics of Mexican institute of social security by the number R-2020-1909-020 with the folio number F-2020-1909-015 in September 2020. Letters of assent and informed consent were included for each patient. All results were handled with strict confidentiality; however, they were open to the patients' treating physicians. As a benefit of this project, all the minors received the results of the blood cultures that served the treating physicians to make their therapeutic decisions.

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