

Original article

Childhood Septicemia in Tripoli, Libya: Bacterial Etiology and Its Antibiotic-Resistant Pattern

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ABSTRACT

Background and aims. Septicemia is a frequently occurring illness, but it affects children, particularly newborns and young infants, more than any other age group. This study aimed to determine the prevalence of septicemia in children and their antibiotic resistance pattern. **Methods.** A retrospective cross-sectional study was carried out during the period from April 2021 to July 2022 on a total of 302 patients who attended different polyclinics in Tripoli, Libya. **Results.** Out of 302 blood cultures, only 60 (19.8%) were positive growth of bacteria. Gram-positive bacteria constituted 32(53.3%) while Gram-negative bacteria were 28(46.7%). The highest number of isolates were *Klebsiella pneumoniae* (28.3%) followed by *Staphylococcus aureus* (20.0%), *Staphylococcus epidermidis* (15.0%), *Staphylococcus haemolyticus* (10.0%). While, in *E. coli* (10.0%), *Pseudomonas aeruginosa*, *enterococcus faecalis* were the most frequent isolates (5%, each), followed by *Streptococcus* spp., (3.33%), *Acinetobacter baumannii* (1.66%), and *Burkholderia cepacia* (1.66%). Most of isolates were resistant to the commonly used antibiotics such as gentamicin, erythromycin, and ticarcillin. Overall, the majority of isolates were multidrug resistant. **Conclusion.** The study has brought attention to the significant impact of bacterial infection as a cause of septicemia in children at a healthcare facility in Tripoli.

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INTRODUCTION

In developing countries, septicemia is among the commonest causes of neonatal morbidity and mortality. It is responsible for about 30-50% of the total neonatal deaths in developing countries [1]. WHO has made septicemia a global health priority and passed a resolution to improve sepsis prevention, diagnosis, and management [2]. Septicemia occurs when a bacterial infection elsewhere in the body, such as the lungs or skin, enters the bloodstream and thus can quickly become life-threatening. If left untreated, septicemia can progress to sepsis.

Septicemia and sepsis aren't the same; sepsis is a serious complication of septicemia. Sepsis causes inflammation throughout the body. This inflammation can cause blood clots and block oxygen from reaching vital organs, resulting in organ failure [3]. Early diagnosis and appropriate treatment are essential to improve outcomes and reduce morbidity and mortality [1]. Globally, about 3 million newborns and 1.2 million children had an infection every year, leading to septicemia [4]. The resistant pathogens count to be a cause of sepsis leading to death in 3 out of 10 neonatal. Although it is a major cause of global morbidity and mortality, sepsis still lacks targeted therapy [5].

The majority of clinical trials and epidemiologic studies with septic children have been carried out in high-income nations [6–10]. Since infectious diseases make up a significant portion of the life-threatening conditions that affect children in low- and middle-income countries, there is a particular need for epidemiologic data on pediatric sepsis in

these regions [11]. These data must be available to develop public health policies, allocate scarce financial resources more sensibly, and reduce social and economic disparities in child mortality. The current state of pediatric septicemia in Libya is lacking, therefore the current study aimed to determine and identify the most causative agents of septicemia and their antimicrobial-resistant profile.

METHODS

Study design and setting

This was a retrospective cross-sectional study carried out over a period of 1 year from April 2021 to July 2022 on 302 patients who were examined for septicemia (161 blood cultures were isolated from the University Hospital of Tripoli, 134 blood cultures were isolated from Al-Jala Children's Hospital, and 7 blood cultures were isolated from Al-Andalus Medical Center).

The inclusion criteria were suspected septicemic inpatients whose blood samples were sent for culture sensitivity tests and were positive for bacterial growth. Only children were included in the study. The exclusion criteria were patients whose blood samples did not show any growth.

Data collection procedure

The current study was carried out after obtaining the ethics committee's clearance and approval. According to the inclusion criteria, patients were included in the study. After fully describing the study procedure to the satisfaction of all study participants and their legal representatives, written informed consent was obtained for reviewing the records and gathering data.

A suitable case record form was designed to collect all necessary & relevant information and details of antimicrobial agents used in empirical therapy were noted. A culture & sensitivity test was done on all blood samples. A suitable case record form was created to collect all necessary and relevant information and the antimicrobial agents used in empirical therapy were documented [12].

Change in the therapy following the result of the culture & sensitivity test was recorded and the change was by the antimicrobial sensitivity pattern.

Statistical analysis

Data were descriptively analyzed and presented as count and percentages using Microsoft Excel version 13.

RESULTS

In this study, 302 patients were examined and 60 of them were found to have positive blood cultures, which represents 20% of the total. The bacterial growth distribution from the 302 blood cultures was as follows: 31 (19.3%) from the University Hospital of Tripoli, 28 (20.9%) from Al-Jala Children's Hospital, and 1 (14.3%) from Al-Andalus Medical Center (Table 1).

Table 1. The total specimens of blood cultures.

Samples [n=302]	University hospital of Tripoli [n=161]	Al-jala Children's Hospital [n=134]	Al-andalus Medical Center [n=7]	Total
Growth of bacteria	31(19.3%)	28(20.9%)	1(14.3%)	60
No growth of bacteria	130(80.7%)	106(79.1%)	6(85.7%)	242

As shown in Figure 1, the majority of bacterial growth was isolated from the Special Care Baby Unit (SCBU) (n=30, 50%), followed by Pediatric Intensive Care Unit (P. ICU) (n=18, 30%), and Pediatric Oncology (P. ONCO) (n=6, 10%), Pediatric Respiratory Unit (P. RES) (n=4, 7%), Pediatric Gastroenterology (P. GASTRO) (n=1, 1.5%), and Outpatient Department (OPD) (n=1, 1.5%).

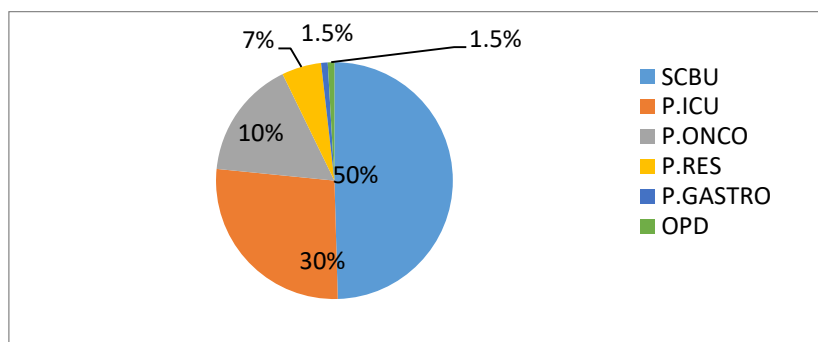


Figure 1. Distribution of positive growth among hospital departments:

Our study found cases of septicemia in children, with the majority occurring in the younger age groups of ≤ 28 days ($n=35$, 58%). Of these cases, 22 were from the university hospital of Tripoli and 13 were from Al-Jala Children's Hospital as shown in (Table 2).

Table 2. Result of age group's positive blood culture in children

Age	University Hospital of Tripoli	Al-Jala Children's Hospital	Al-Andalus Medical Center
≤ 28 days	22	13	0
>28 days–2 years	5	8	1
>2–12 years	4	7	0

According to Table 3, out of all the positive blood culture samples, 53.33% were Gram-positive bacteria and 46.66% were Gram-negative bacteria. The highest number of bacterial isolates was *Klebsiella pneumoniae* (*K. pneumoniae*) (28.3%), followed by *Staphylococcus aureus* (*S. aureus*) (20.0%), *Staphylococcus epidermidis* (*S. epidermidis*) (15.0%), *Staphylococcus haemolyticus* (*S. haemolyticus*) (10.0%), *E. coli* (10.0%), *Pseudomonas aeruginosa* (*P. aeruginosa*) (5%), *Enterococcus faecalis* (*E. faecalis*) (5%), *Streptococcus* spp., (3.33%), *Acinetobacter baumannii* (*A. baumannii*) (1.66%), and *Burkholderia cepacia* (*B. cepacia*) (1.66%).

Table 3. The frequency of bacterial types isolated from positive blood culture

Bacterial Types N=60		University hospital of Tripoli (n=31)	Al-Jala Children's Hospital (n=28)	Al-andalus Medical Center (n=1)	Total of isolate (n=60)
Gram-positive 32 (53.33%)	<i>S.aureus</i>	0	12(20.0%)	0	12(20%)
	<i>S. epidermidis</i>	9 (15.0%)	0	0	9 (15%)
	<i>S.haemolyticus</i>	6 (10.0%)	0	0	6(10%)
	<i>Enterococcus faecalis</i>	3 (5%)	0	0	3 (5%)
	<i>Streptococcus</i> SSP	1 (1.6%)	0	1 (1.6%)	2 (3.33%)
Gram-negative 28 (46.66%)	<i>K. pneumoniae</i>	8 (13.3)	9 (15.0%)	0	17 (28.3%)
	<i>E. coli</i>	6 (10.0%)	0	0	6(10.0%)
	<i>P. aeruginosa</i>	2(3.33%)	1 (1.6%)	0	3 (5%)
	<i>A. baumannii</i>	1 (1.6%)	0	0	1 (1.6%)
	<i>B. cepacia</i>	1 (1.6%)	0	0	1 (1.6%)

Since the appearance of *S. aureus* in Al-Jala Children's Hospital only, $n = 12$, which had a high resistance to erythromycin (E), Gentamicin (GN), while being sensitive to Vancomycin (VA). Among the Gram-positive bacteria, *S. epidermidis* showed complete resistance to benzylpenicillin (p), Oxacillin (ox). However, the majority of the isolated strains are resistant to genamycin (CN), including *S. haemolyticus* which is also highly resistant to gentamicin.CN), benzylpenicillin (p), and oxacillin (ox) *Enterococcus faecalis* was found to be resistant to the antibiotic Trimethoprim/Sulfamethoxazole (sxt), while *Streptococcus.ssp* displayed resistance to benzylpenicillin (p) and Oxacillin. This was revealed in the test results (Table 4).

Table 4. Antibiotic resistance pattern of predominant gram-positive bacteria

Antibiotic	<i>S.aureus</i> (n=12)	<i>S. epidermidis</i> (n=9)	<i>S.haemolyticus</i> (n=6)	<i>Enterococcus faecalis</i> (n=3)	<i>Streptococcus ssp</i> (n=2)
Gentamicin	8(66%)	7(77%)	6(100%)	1(33%)	0(0)
Benzylpenicillin	ND	9(100%)	6(100%)	2(66%)	2(100%)
Oxacillin	ND	9(100%)	6(100%)	2(66%)	2(100%)
Tetracycline	ND	5(55%)	0(s)	1(33%)	1(50%)
Tobramycin	ND	8(88%)	6(100%)	1(33%)	1(50%)
Levofloxacin	ND	5(55%)	5(83%)	1(33%)	1(50%)
Moxifloxacin	6(50%)	5(55%)	5(83%)	1(33%)	1(50%)
Clindamycin	8(66%)	5(55%)	6(100%)	2(66%)	0(0)
Erythromycin	12(100%)	8(88%)	6(100%)	1(33%)	2(100%)
Linezolid	ND	9(100%)	6(100%)	0(0)	2(100%)
Fusidic Acid	ND	6(66%)	1(16%)	2(66%)	0(0)
Vancomycin	2(17%)	0(0)	3(50%)	0(0)	0(0)
Nitrofurantoin	ND	7(77%)	4(66%)	1(33%)	1(50%)
Tigecycline	ND	6(66%)	0(0)	0(0)	0(0)
Fosfomycin	ND	5(55%)	4(66%)	1(33%)	1(50%)
Trimethoprim / Sulfamethoxazole	ND	4(55%)	2(33%)	3(100%)	2(100%)

*ND (Non-Done)

In Gram-negative bacteria, *K. pneumoniae* showed high resistance to Ticarcillin (Tic), Piperacillin (PRL), Tazobactam (CAz), while *P. aeruginosa* was found to be completely resistant to Ticarcillin (Tic) and Ciprofloxacin (Cip). Most antibiotics were effective against *B. cepacia*, with the exception of Ticarcillin (Tic) and Colistin (CT) which showed resistance. In contrast, *A.baumannii* showed resistance to many types of antibiotics (Table 5).

Table 5. Antibiotic resistance pattern of predominantly gram-negative bacteria in the university hospital of Tripoli

Antibiotic	<i>K. pneumoniae</i> (n=8)	<i>P. aeruginosa</i> (n=2)	<i>B. cepacia</i> (n=1)	<i>A. baumannii</i> (n=1)
Ticarcillin	8(100%)	2(100%)	1(100%)	1(100%)
Piperacillin	8(100%)	0(0)	0(0)	0(0)
Tazobactam	8(100%)	1(50%)	0(0)	1(100%)
Ceftazidime	8(100%)	1(50%)	0(0)	0(0)
Imipenem	7(87%)	2(100%)	0(0)	1(100%)
Meropenem	4(50%)	0(0)	0(0)	0(0)
Amikacin	0(0)	0(0)	0(0)	1(100%)
Gentamicin	7(87%)	0(0)	0(0)	1(100%)
Tobramycin	5(62%)	0(0)	0(0)	1(100%)
Ciprofloxacin	7(87%)	2(100%)	0(0)	0(0)
Minocycline	4(50%)	1(50%)	0(0)	1(100%)
Colistin	0(0)	2(100%)	1(100%)	1(100%)
Trimethoprim/ Sulfamethoxazole	6(75%)	2(100%)	0(0)	0(0)

At Al-Jala Children's Hospital, it was found that *K. pneumonia* among Gram-negative bacteria was resistant to Piperacillin (Tic) and displayed resistance to some other antibiotics. On the other hand, *P. aeruginosa* was found to be sensitive to most types of antibiotics (Table 6).

Table 6: Antibiotic resistance pattern of predominantly gram-negative bacteria in Al-Jala Children's Hospital.

Antibiotic	<i>K. pneumoniae</i> (n=9)	<i>P. aeruginosa</i> (n=1)	<i>E. coli</i> (n=6)
Piperacillin	9(100%)	0(s)	3(50%)
Tazobactam	8(88%)	1(100%)	4(66%)
Ceftazidime	6(75%)	0(0)	4(66%)
Imipenem	8(88%)	0(0)	3(50%)
Amikacin	2(22%)	0(0)	0(0)
Gentamicin	7(77%)	1(100%)	3(50%)
Ciprofloxacin	7(77%)	1(100%)	1(16%)
Colistin	2(22%)	1(100%)	3(50%)
Trimethoprim/ Sulfamethoxazole	5(55%)	0(0)	3(50%)

DISCUSSION

Even in developed countries, sepsis is still a leading cause of death among hospitalized infants and children [12]. This study discovered a diverse array of bacterial pathogens that contribute to bloodstream infections. The most prevalent microorganisms were Gram-positive bacteria (53.33%), such as *Staphylococcus aureus* (20.0%) and *Staphylococcus epidermidis* (15.0%). Commensal Gram-positive cocci can be found on human body surfaces and may infect intravenous devices, leading to infections in hospitalized patients, especially neonates and pediatric patients. Studies have shown that Gram-positive bacteria are the primary cause of pediatric septicemia, with a prevalence rate of 20-25%. In our study, Gram-negative bacteria accounted for 46.66% of cases. Similar findings have been reported in other studies from India and South Africa, where Gram-negative bacteria were also found to be the predominant cause of septicemia. Rapid detection and identification of bacteria in blood is crucial for patient care, as the mortality rate associated with bloodstream infections is very high [13-14].

In this study, the most common gram-negative bacteria found was *K. pneumoniae*, accounting for 28.3% of cases. This differs from a previous study conducted by Karambin et al., where gram-negative bacteria accounted for 90.6% of cases, and *Enterobacter* was identified as the most common pathogen [15]. According to a report by Movahedian et al, gram-negative bacteria were found to have a prevalence rate of 72.1%. The most common pathogen among them was *P. aeruginosa* [16]. However, the results indicate that a significant number of bacteria present were gram-negative, specifically *K. pneumoniae* (28.3%) and *S. haemolyticus* (10.0%). This finding is consistent with a previous report from Pakistan (17). *Klebsiella pneumoniae* is a type of bacteria that is normally found in the digestive system but can become the main cause of infections in both community and hospital settings. These infections can include septicemia, urinary tract infections, and pneumonia. They are more frequently seen in newborns than in other groups of people [18]. Global surveillance reports suggest that bloodstream isolates are the most suitable candidates for studying the antimicrobial susceptibility of human bacterial pathogens [19-20]. This study conducted antimicrobial susceptibility testing on all bacterial strains using various antimicrobial agents in accordance with the Clinical Laboratory Standards Institute guideline.

Based on the results of the antibiotic resistance patterns, it was found that most of the isolates showed resistance to commonly used antibiotics such as Gentamicin, Erythromycin, and Ticarcillin. Among the Gram-positive bacteria that were isolated, staphylococci were found to be more susceptible to vancomycin. This pattern is consistent with what has been observed in other parts of the world [21-23]. Besides, *Staphylococcus aureus* showed resistance against gentamicin and Erythromycin, contrary to the report from Pakistan [24]. Based on the findings, it was discovered that the *Streptococcus* isolates responded well to gentamicin. However, *K. pneumoniae* showed resistance to Ceftazidime and Ciprofloxacin, whereas *P. aeruginosa* was sensitive to Ceftazidime. These results align with a study conducted in Bangladesh in 2021 [25].

In the present study, the prevalence of MDR isolated was remarkable. The emergence of MDR strains is causing growing health concerns and there are several reports which indicate the increasing prevalence of MDR strains in healthcare settings [21,26]. In agreement with our finding, some previous international reports showed the prevalence of MDR strains in bloodstream infection [27,28]. Where other studies discovered that MDR isolates played a significant role in the occurrence of bloodstream infections. However, there are some locally available antibiotics that have shown promising results against MDR isolates. This information can help physicians prescribe safe and effective treatments for their patients [29].

CONCLUSION

Based on our findings, *K. pneumoniae*, *S. aureus*, and *S. epidermidis* were identified as the primary pathogens responsible for bloodstream infections in Libyan children. The majority of the bacteria identified were Gram-positive, and most of them showed resistance to commonly used antibiotics. This study brings attention to the rise of bacteria that are resistant to antibiotics, which could be caused by inadequate infection control measures and inappropriate use of antibiotics. To manage these antibiotic-resistant pathogens, it is crucial to strictly follow infection control protocols and implement a comprehensive antibiotic policy across all hospitals.

Conflict of Interest

There are no financial, personal, or professional conflicts of interest to declare.

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تسمم الدم عند الأطفال في طرابلس ، ليبيا: المسببات البكتيرية ونمطها المقاوم للمضادات الحيوية

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المستخلص

الخلفية والأهداف: يُعد تسمم الدم مرضًا متكرر الحدوث ، ولكنه يصيب الأطفال ، وخاصة الأطفال حديثي الولادة وصغار الأطفال ، أكثر من أي فئة عمرية أخرى. هدفت هذه الدراسة إلى تحديد مدى انتشار تسمم الدم لدى الأطفال ونمط مقاومتهم للمضادات الحيوية. **طرق الدراسة:** تم إجراء دراسة مقطعية بأثر رجعي خلال الفترة من أبريل 2021 إلى يوليو 2022 على ما مجموعه 302 مريضًا حضروا عيادات مختلفة في طرابلس ، ليبيا. **النتائج:** من بين 302 عينة دم ، كان 60 فقط (19.8٪) نموًا إيجابيًا للبكتيريا. شكلت البكتيريا موجبة الجرام 32 (53.3٪) بينما كانت البكتيريا سالبة الجرام 28 (46.7٪). أعلى عدد من العزلات كانت (28.3٪) *Klebsiella pneumoniae* تليها *Staphylococcus aureus* (20.0٪) ، (15.0٪) *Staphylococcus epidermidis* ، (10.0٪) *Staphylococcus haemolyticus* بينما في (10.0٪) *E. coli* ، *Pseudomonas aeruginosa* و *enterococcus faecalis* كانت العزلات الأكثر شيوعًا (5٪) ، لكل منهما) ، تليها (3.33٪) *Streptococcus ssp.* ، (1.66٪) *Acinetobacter baumannii* ، و *Burkholderia cepacia* (1.66٪). كانت معظم العزلات مقاومة للمضادات الحيوية الشائعة الاستخدام مثل الجنتاميسين والإريثروميسين والتيكارسيلين. بشكل عام ، كانت غالبية العزلات مقاومة للأدوية المتعددة. **الخلاصة:** لفتت الدراسة الانتباه إلى التأثير الكبير للعدوى البكتيرية كسبب لتسمم الدم لدى الأطفال في مرفق للرعاية الصحية في طرابلس.

الكلمات الدالة: حساسية المضادات الحيوية ، ثقافة الدم ، تسمم الدم ، طب الأطفال