BACTERIAL PROFILE AND ANTIMICROBIAL SUSCEPTIBILITY PATTERN IN SEPTICEMIA SUSPECTED CHILDREN AND AVAILABLE TREATMENT OPTIONS

Shaista Bakhat[1], Saman Nadeem[2], Ashfaq Hussain[3], Santosh Kumar Sidhwani[4], Hina Wasti[5], Yasmeen Taj[6], Faisal Faheem[7]

Correspondence

[1]Shaista Bakhat, Assistant Professor, Department of Pathology, Bahria University of Health Sciences, Karachi
✆: +92-3322039311
✉: shaistakhurram2@gmail.com
[2]Assistant Professor, Deparment of Microbiology, Jinnah Medical & Dental College, Karachi
[3]Microbiologist, Pakistan Navy Ship Shifa Hospital, Bahria University, Karachi
[4]Associate Professor, Department of Pathology, Ziauddin University, Karachi
[5]Assistant Professor, Histopathology, Bahria University of Health Science, Karachi
[6]Professor / Head of Department Pathology, Bahria University of Health Sciences
[7]Senior Lecturer / Statistician, Bahria University of Health Sciences, Karachi

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ABSTRACT

OBJECTIVES

Septicaemia (blood poisoning) is one of the chief sources of global morbidity and mortality in pediatric patients and presents with multidrug and extensive drug resistance. This study aims to detect the major causative agents, antimicrobial susceptibility patterns and associated factors of bacteraemia among pediatric patients.

METHODOLOGY

This retrospective cross-sectional study was done at National Medical Center, Karachi microbiology laboratory. Clinical specimens consist of blood. Blood samples were processed in BACTEC's automated blood culture system, and positive samples were sub-cultured on blood, Mac-Conkey. Final identification was done by API 20E and API 20NE (Biomerieux) and confirmed by MicroScan (Beckman coulter)®. The antimicrobial susceptibility was performed by using Bauer– Kirby disk diffusion method.

RESULTS

A total of 395 pediatric patients were taken in the study. Out of these patients, 226 (57.2 %) were female. The children with age 1-4 years were highly affected. Almost 50% were handled in emergency and transferred for admission. 36.2% of patients were exposed to intravenous devices. 89 (22.5%) patients had a history of prolonged use of antibiotics. Most patients with pneumonia presented with septicemia as a complication, and were detected by Klebsiella pneumonia (35.4%), Acinetobacter bauminii (25.3%) and Pseudomonas aeruginosa (20.3%).

CONCLUSION

The study revealed that gram-negative organisms are the predominant causative organisms of septicaemia. Antibiotic resistance to Carbapenem is gradually increased in the case of Acinetobacter bauminii and Escherichia coli. These issues can be overcome by early detection of microorganisms and establishing antibiotic stewardship.

KEYWORDS: *Antimicrobial Susceptibility, Multidrug Resistance, Pediatric, Septicemia Introduction*

INTRODUCTION

Septicemia is a life-threatening condition resulting from different bacteria within the bloodstream, capable of producing virulence factors that enable it to disseminate throughout the body and severely trigger human body response.[1] Microorganisms move to blood from different systems like the gastrointestinal tract, genitourinary system, respiratory system and skin.[2] Staphylococcus aureus, CoNS (Staphylococcus epidermidis and Staphylococcus saprophyticus), Enterococci, andalpha - hemolytic Streptococci are the major Gram - positive bacteria that lead to bacteremia. On the other hand, Gram-negative bacteria such as Salmonella typhi, Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumonia, and Acinetobacter species can cause septesemia.[3] Blood poisoning (Bacteremia) can occur in all age groups of the community, especially in children and immune-compromised people.[4] The incidence rate of bacteremia is amplified by prior hospitalization, duration of hospital stay, etiology of unknown fever, age groups, prolonged antibiotic therapy, complicated traumas, chronic debilitating illness, invasive medical measures, and HIV/AIDS are associated factors.[5] Antimicrobial resistance and involved etiological agents differ for different geographical areas and time periods.[6] Pediatric septicemic cases occur at a rate of 31.5 million each year all over the world, and as a consequence, the

mortality rate is high, with an estimated 7.5 million deaths yearly.[7] By 2020, Forty-one cent of all global bacteremic cases were reported by the World Health Organization (WHO) and in sub-Saharan African and Asia countries, 30– 70%, including children under the age of five, with a mortality rate of 42% among intensive care patients.[8] The incidence rate of blood poisoning in Pakistan was reported as 912 (95% confidence interval) with an 8% mortality rate.[9] Multidrug resistance among different pathogens has led to pandemic antimicrobial resistance in the last two decades.[10] Appropriate selection of antibiotics and timely has a key role in treating septicemic cases. However, antibiotic resistance is a fast-growing issue in low socioeconomic countries. Unsuitable sepsis therapy exacerbates the disease and increases the mortality rate and emergence of new drug-resistant strains.[11] Our study reveals that drug resistance as multidrug and extensive drug resistance is increased. We are standing on the edge of pan-drug resistance. This study aims to determine the early detection of bacteria and antimicrobial susceptibility patterns with associated factors that can make clinicians aware of the emergence of multi and extensively drug resistance that is a responsible threat in pediatric patients and provide guidelines to physicians to start the empirical therapy.

METHODOLOGY

This retrospective cross-sectional study was done at National Medical Center, Karachi microbiology laboratory. One investigator extracted the data from June 2019 to June 2021 through the lab LIMS system (Laboratory Information Management System) with the permission of hospital management. Pediatric patients with clinical presentation of septicemia were included in the research. Study participants who used antibiotic treatment within the last two weeks during the data collection time were excluded. Pediatric patients without caregivers during the data collection period were also excluded from the study. Phenotypic antimicrobial susceptibility patterns were carried out on isolates from clinical samples of pediatric patients hospitalized in the medical, surgical, and Intensive Care (ICU) units. Samples were also received from the outpatient department. Clinical specimens consist of blood and central venous pressure (CVP) tips. Blood samples were processed in BACTEC's automated blood culture system, and once they were flagged positive, gram staining was done, and samples were sub-cultured on blood, Mac-Conkey. Isolate identification was carried out by performing biochemical tests based on the gram stain interpretation. Final identification was done by API 20E and API 20NE (Biomerieux) and confirmed by MicroScan (Beckman coulter)®. The antimicrobial susceptibility was performed by standard susceptibility test using the Bauer– Kirby disk diffusion method. Antimicrobial disc contents were as follows: amikacin 30 µg(oxoid), gentamycin 10 µg(oxoid), ceftriaxone 30 µg(oxoid), ceftazidime 30 µg(oxoid), cefepime 30 µg(oxoid), piperacillin/ tazobactam 100/10 µg(oxoid), imipenem 10 µg (oxoid), meropenem 10 µg (oxoid), ciprofloxacin 5 µg (oxoid), levofloxacin 5 µg(oxoid), vancomycin 30 µg(oxoid). Antibiotic susceptibility interpretation was based on the Clinical and Laboratory Standards Institute (CLSI) Performance Standards for Antimicrobial Susceptibility Testing M100 criteria.[12] Information about age and gender was noted from medical records prepared by doctors and nurses daily.

RESULT

A total of 395 pediatric patients were taken in the study. Out of these patients, 226 (57.2 %) were female. The children with age 1-4 years were highly affected. Children with (BMI < 18.5kg/m^2) were considered malnourished and accounted for 16.7%% of the patients. The family consists of 5-9 members, and residents of an urban area are mostly prone to infection associated with complications (Table 1). Almost 50% were handled in emergency and transferred for admission. 36.2% of patients were exposed to intravenous devices. 89 (22.5%) patients had a history of prolonged use of antibiotics. Mostly septicemic patients were associated with respiratory diseases. (Table 2) Most patients with pneumonia presented with septicemia as a complication and were detected by Klebsiella pneumonia (35.4%), Acinetobacter bauminii (25.3%) and Pseudomonas aeruginosa (20.3%). (Table 3) Children presented with septicaemia mostly associated with age and pneumonia. (Table 4).

Table 1: Demographic Characteristics of Septicemic Patients

Variables	Frequency	%age
Sex		
Female	226	57.2
Male	169	42.8
Age (years)		
< 1	46	11.6
1-4	172	43.5
5-9	109	27.6
10-15	68	17.2
Pediatric BMI		
< 18.5 Kg/m^2	66	16.7
18.5-24.9 Kg/m^2	303	76.7
> 25 Kg/m^2	26	6.6
Resident		
Urban	273	69.1
Rural	122	30.9
Family size		
<=4	61	15.4
5-9	282	71.4
>=10	52	13.2

Table 2: Clinical Profile of Septicaemic Patients

Variables	Frequency	%age
Admission to the hospital		
Yes	195	49.4
No	200	50.6
Medical devices used		
Intravenous Device	143	36.2
Endotracheal tube	64	16.2
Surgery	20	5.1
Nothing	168	42.5
Chronic use of antibiotics		
Yes	89	22.5
No	306	77.5
Comorbidities		
Burn cases	56	14.2
Respiratory disease	101	25.6
Febrile Illness	151	38.2
Wound cases	27	6.8
Urinary tract disease	18	4.6
Gastrointestinal disease	16	4.1
Skin disease	26	6.6

Table 3: Distribution of Bacterial Isolates

		Frequency	%age
Valid	Klebsiella pneumoniae	140	35.4%
	Acinetobacter bauminii	100	25.3%
	Pseudomonas aeruginosa	80	20.3%
	Escherichia coli	20	05.1%
	Salmonella typhi	05	01.3%
	Staphylococcus aurius	10	02.5%
	Enterobacter	40	10.1%

Table 4: Factors Associated with Septicemia

		Pediatric_Septicemia		Total	P-Value
		Positive (n=31)	Negative (n=364)		
Age	< 1	0	46	46	0.003
		0.0%	100.0%	100.0%	
	1-4	10	162	172	
		5.8%	94.2%	100.0%	
	5-9	09	100	109	
		8.3%	91.7%	100.0%	
	10-15	12	56	68	
		17.6%	82.4%	100.0%	
Diagnosis	Burn cases	10	46	56	0.000
		17.9%	82.1%	100.0%	
	Respiratory disease	101	0	101	
		100%	0.0%	100.0%	
	Febrile Illness	0	151	151	
		0.0%	100.0%	100.0%	
	Wound cases	09	18	27	
		33.3%	66.7%	100.0%	
	Urinary tract disease	0	18	18	
		0.0%	100.0%	100.0%	
	Gastrointestinal disease	12	04	16	
		75.0%	25.0%	100.0%	
	Skin disease	0	26	26	
		0.0%	100.0%	100.0%	
Antibiotic_use_prolong	Yes	10	79	89	0.177
		11.2%	88.8%	100.0%	
	No	21	285	306	
		6.9%	93.1%	100.0%	

Table 5: Antimicrobial Susceptibility Pattern of Microorganisms

Bacterial isolates		Antimicrobial drugs																
		AK	AMC	AMP	TZP	ATM	CFM	CIP	CN	SXT	CRO	IPM	MEM	PB	CXM	FX	FOS
Klebsiellapneumonia	S	47	20	-	32	18	26	26	35	34	17	68	35	80	-	-	-
	R	33	60		48	62	54	54	45	46	63	12	45	0			
Pseudmonas aeruginosa	S	20	-	-	20	20	-	20	20	-	-	20	20	20	-	-	--
	R	0			0	0		0	0			0	0	0			
Acinetobactorbauminii	S	28	-	18	15	-	1	4	22	20	20	25	38	20	20	87	98
	R	72		82	85		99	96	78	80	80	75	62	80	80	13	2
Escherichia coli	S	-	94	7	65	-	23	27	72	-	30	70	71	99	91	82	67
	R		46	133	75		73	113	68		110	70	69	41	21	58	73
Salmonella typhi	S	-	-	110	-	-	-	110	-	-	5	-	5	-	-	-	-
	R			5				23			0		0				
Staphylococcus aureus	S	-	-	120	-	-	-	10	10	-	-	-	-	-	-	-	-
	R			10				0	0								
Enterococcus	S	-	-	40	-	-	-	-	40	-	-	-	-	-	-	-	-
	R			0					0								

Abbreviations: CRO, ceftriaxone; AMC, amoxicillin; AMP, ampicillin; DOX, AMX amoxicillin; CLT, CIP ciprofloxacin; AK Amikacin, TZP Tazobactum, ATM Aztreonam, CFM Cefixime, CN Cefalaxin, SXT trimethoprim sulphamethoxazole IPM Imipenem, MEM Meropenem, PB Polymyxin, FOS Fosfomycin, FX cefoxitin S, sensitive; R, resistance.

DISCUSSION

Our study revealed that the overall culture positivity rate was 7.09% which was per a study conducted in the United States (7.7%), [and] Italy (8.2%), Northern Ethiopia (7.4%).[13,14,15] Similar results were reported from another study conducted in Turkey, with 8% sepsis in pediatric patients.[16] On the other hand, these cases were reported with a low ratio in developed and advanced countries, like 2-3%. This variation is related to socio-demographic factors and advanced healthcare facilities technologies.[17] But a situation was observed at Dhaka with a 69.35% sepsis rate in neonates. This

increases the mortality rate in low socioeconomic countries. There is an urgent need to conduct more research on the early detection of microorganisms, antibiotic profiles and prompt medical assistance.[18] It may indicate that in our study, patients participated in a decreased number of single-centred studies. In our study, Klebsiella pneumonia is the leading cause of septicemia, followed by Acinetobacter bauminii and Pseudomonas aeruginosa , per a study in China.[19] Klebsiella pneumonia blood infections in children are highly critical and were also supported by a survey of South Africa.[20] Our study's risk factors are associated with age and respiratory infections like pneumonia. Septicemia is the body's extreme response, commonly present in children. Association, a study revealed that in the U.S., more than 70,000 infants and children presented with sepsis or blood poisoning each year, and 7000 out of it led to death.[21] Same results were shown by one study conducted in Bangladesh.[22] Pneumonia is caused by *Klebsiella pneumonia,* also reported by a Chinese study.[23] our research results are also supported by a study conducted in China.[24] We observed in our study that septicemia is caused by gram-negative organisms more than gram-positive organisms, which is under study.[25]

LIMITATIONS

The sample size of this study is small.

CONCLUSION

The study revealed that gram-negative organisms are the predominant causative organisms (Klebsiella pneumonia, Pseudomonas aeruginosa and Acinetobacter bauminii) of septicaemia in children. Antibiotic resistance to last resort Carbapenem is gradually increased in the case of Acinetobacter bauminii and Escherichia coli. These issues can be overcome by early detection of microorganisms and establishing antibiotic stewardship.

CONFLICT OF INTEREST: None

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CONTRIBUTORS

1. ***Shaista Bakhat*** - *Concept & Design; Drafting Manuscript; Critical Revision; Supervision*
2. ***Saman Nadeem*** - *Concept & Design; Data Acquisition*
3. ***Ashfaq Hussain*** - *Data Acquisition*
4. ***Santosh Kumar Sidhwani*** - *Drafting Manuscript*
5. ***Hina Wasti*** - *Drafting Manuscript*
6. ***Yasmeen Taj*** - *Drafting Manuscript*
7. ***Fasial Faheem*** - *Data Analysis/Interpretation*