



ANTIMICROBIAL SUSCEPTIBILITY PATTERNS OF BLOOD CULTURE POSITIVE
SEPSIS AGE ≥ 1 MONTH ≤ 14 YEARS ADMITTED TO ST. PAUL'S HOSPITAL
MILLENNIUM MEDICAL COLLEGE PEDIATRIC UNIT OVER THREE YEARS
PERIOD, ADDIS ABABA ETHIOPIA FROM JANUARY 2016 TO DECEMBER 2018
A RETROSPECTIVE STUDY

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Information Sheet

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The List of abbreviations and acronyms

AST: Antimicrobial susceptibility testing

BA: Blood agar

BC: blood culture

CI: Confidence interval

CONS: Coagulase-negative staphylococci

CLSI: Clinical Laboratory Standards Institute

DMLT: Department of Medical Laboratory Technology

R: resistance

EOPD: emergency outpatient department

GP: gram positive

GN: gram negative

MRSA: methicillin resistance staphylococcus aureus

NICU: neonatal intensive care unit

PW: pediatric ward

S: sensitive

SPP: Species

SPHMMC: St. Paul's Hospital Millennium Medical College

WHO: World Health Organization

PPS probability proportional size

Abstract

Background: Blood stream infections remain one of the most important causes of morbidity and mortality in pediatric age group. Due to inappropriate use of antibiotics, antibiotic resistance is increasing and treatment of blood stream infections becomes more difficult by time.

Objective: The aim of the present study was to determine the bacterial profile of bloodstream infections and their antibiotic susceptibility pattern at SPHMMC pediatric unit Addis Ababa, Ethiopia.

Methodology: retrospective study of 310 patients blood culture result from Clinical Microbiology laboratory unit of SPHMMC Addis Ababa was reviewed from January, 2016 to December, 2018 . Data was entered and analyzed by using SPSS version 25.0 statistical software and results were expressed using frequency and percentages, Tables and graphs were used to summarize the results. Ethical clearance was acquired from faculty ethical committee of SPHMMC.

Result: Out of the total 310 suspected sepsis 72 (23.2%) culture positive were isolated. Out in 310 patents 175(56.5%) were male and 135(43.5%) were female. All pediatric patients with suspected sepsis and admitted during the study period age distribution 188(60.6%) $\geq$ 1 month to 1 years, 59(18.7%) > 1 year to 5 years and 63(20.6%) were 5 year to 14 years whose blood culture done were included to this study Klebsiella Pneumonia 24(33.3%) followed by Staphylococcus 19(26.4%,), Coagulase-negative staphylococci 14(19.4%,) Most of the isolates show a high level of resistance to Trimethoprim-Sulfamethoxazole, Penicillin , Ampicillin, Gentamycin , and Ceftriaxone which we used empirically in our set up ,

Conclusions:

In this study the overall prevalence of blood stream infection was high 72(23.2%). This study provides some insight into the local trends and bacterial etiology of bloodstream infections among pediatric. Gram Positive bacteria are the major contributors of BSI in our patients. A higher rate of antimicrobial resistance among gram negative and gram positive organisms is an alarming issue. Exact contributing factors for the bloodstream infections (BSI) within these groups need to be further elucidated. Rational use of antibiotics, formulation of antibiotic policy, and prompt therapy of bloodstream infections for the effective management and prevention of drug resistance are urgently needed in our setting.

Keywords: Prevalence, Blood culture, Bacterial isolates Antimicrobial susceptibility pattern, SPHMMC

1. Introduction

1.1 Background

Bloodstream infections (BSIs) are defined as the presence of viable infectious microorganism in the bloodstream causing clinical illness [1]. They are among the leading causes of mortality and morbidity worldwide [2]. The term bloodstream infection and bacteremia are synonymously used which generally refer to the significant growth of a microorganism in a blood culture obtained from the patient with clinical signs of infection [3]. In clinical practice, bacteremia may range from self-limiting infections to life threatening septicemia that requires prompt and rational antimicrobial treatment [4]. However, in the developing countries, changing epidemiology, lack of standard antimicrobial guidelines in locality, emergence of antimicrobial resistance, and paucity of good diagnostic facilities are major denominators for surge in BSI associated morbidity and mortality [5]. BSI remains one of the most important causes of morbidity and mortality throughout the world. Approximately 200,000 cases of bacteremia occur annually with mortality rates ranging from 20-50% worldwide [6]. BSI accounts for 10-20% of all nosocomial infections and is the eighth leading cause of mortality, in the United States some 17% of result in death [7]. In sub Saharan countries including Ethiopia septicemia is an important cause of illness and death in children. The prevalence of resistance organisms is increasing in both out-patient and hospitalized patients with septicemia and it varies accordingly with geographical regional location. Clinicians should be well knowledgeable about their regional antibiotic sensitivity and resistance patterns for determining the empirical therapy till they get the culture results or even if they have no culture report facilities in rural areas. 53% which makes it a significant health problem in developing countries [8]. In many studies a wide range of bacteria has been described in febrile patients including gram negative bacteria such as *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella* species, *Neisseria meningitidis*, Hemophilic influenza, and gram positive such as Coagulase negative staphylococci (CONS), *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Streptococcus agalactiae*, and *Enterococcus faecium* [9-13]. The diagnosis of these infections can be confirmed by blood culture, which is routinely available in few hospitals in developing

countries[14]. Bacterial pathogens isolated from BSI are a leading cause of significant patient morbidity and mortality. The impact of specific etiologic agents on BSI patient outcome are tremendous; BSI increases the mortality rate, prolongs patient stay in an intensive care unit and in the hospital, and leads to increased health care costs [15,16]. The timely and appropriate use of antibiotics is currently the only way to treat bacteremia. However, many bacterial pathogens have become resistant to antibiotic regimens and become a serious public health concern with economic and social implications throughout the world. Antibiotics resistance is a growing problem in developing countries such as Ethiopia. In Ethiopia the unregulated over-the-counter sale of these antimicrobials, mainly for self-treatment of suspected infection in humans, and to a lesser extent for use in animals without prescription, would inevitably lead to emergence and rapid dissemination of resistance [17]. Many studies have found that inadequate empirical therapy of bacteremia infections is associated with adverse outcomes, including increased mortality and increased drug resistance emergence [18-19]. However, there are only a few studies from Ethiopia, which have studied the organisms involved in BSI and their susceptibility pattern. We therefore conducted this study to determine the common bacterial agents associated with BSI and their antimicrobial susceptibility patterns in SPHMMC tertiary teaching Hospital in A.A, Ethiopia

1.2 .Statement of the problem

One of the more alarming recent trends in infectious diseases is the increasing frequency of antimicrobial resistance among microbial pathogens causing nosocomial and community acquired infections. Numerous classes of antimicrobial agents have become less effective as a result of the emergence of antimicrobial resistance, often as result of selective pressure of antimicrobial usage. [20] The need to use empiric antibiotic therapy based on local patterns and deescalate and escalating upon receiving blood culture results is key.

We, therefore, should equip the available microbiology laboratories so that we may continuously profile the etiologies of sepsis and their antimicrobial susceptibility in our setting.

An informed choice of antibiotics in our setting will reduce mortality from sepsis while also bringing down the cost of healthcare through reduced days of hospitalization. Antimicrobial resistance exacts a high economic and human cost. Drug-resistant organisms frequently do not respond to therapy, resulting in hospitalization, increasing utilization of diagnostic services, and

mortality. Ethiopian hospitals consume about 50% of the national drug budget, which are considered to have high drug budget compared to the population segment using these health facilities. However, very little is known culture isolate drug sensitivity pattern (particularly antibiotics) is used in hospitals like in other health facilities. The aim of the present study was to determine the bacterial profile of bloodstream infections and their antibiotic susceptibility pattern and in children. Doing this research will help treatment guideline development and will serve as base line for subsequent researches.

1.3. Significance of the study

Sepsis is a major cause of morbidity and mortality in African and across the world. We will clearly defined ways of improving these outcomes. Key among them is the creation of antibiogram that helps in the early initiation of appropriate empiric antibiotic therapy. De-escalation of antibiotics is also dependent upon the isolation of a particular causative agent and the culture and susceptibility patterns thereof. Knowledge of the isolates and drug susceptibility profiles of and blood stream pathogens in pediatrics helps to selection of appropriate antibiotics for empiric treatment. Bacteria isolated and maintained in this study will be used for further studies such as determining mechanisms of development of drug resistance

Thus, it is necessary to inform the clinicians and other health care professionals about the bacterial profile of a particular area and their antimicrobial susceptibility patterns to design an empirical treatment policy for the patients.

2. Literature Review

2.1 Bacterial isolate and drug sensitivity in south Asia , NEPAL .

Hospital based cross sectional study carried out between March 2015 and August 2016 (over a period of 18 months) at the Department of Microbiology, Manmohan Memorial Teaching Hospital, a tertiary care referral center with 300 patient beds, in Kathmandu, Nepal. Out of 3,088 blood cultures during the period, 231 (7.48%) were positive for significant growth of bacterial pathogen suggesting bloodstream infection. Staphylococcus aureus was the leading pathogen involved in pediatric cases (, 45.6%) was resistance to of beta-lactam antibiotics, fluoroquinolones, aminoglycosides, and carbapenems [21].

2.1.1 Bacterial isolate and drug sensitivity in Asia, India Antimicrobial susceptibility testing was done for bacterial isolates from positive blood cultures in India journal of global infectious disease from Oct 2014-Dec. A total of eight pathogenic bacterial genera were identified and their antimicrobial susceptibility pattern was noted. *Staphylococcus* spp. were most prevalent (33%), followed by *Klebsiella pneumoniae* (20%), *Escherichia coli* (13%), *Acinetobacter* spp. (13%), *Enterococcus* spp. (12%), *Pseudomonas aeruginosa* (3%), *Proteus* spp. (2%), and *Citrobacter* spp. (2%) [22].

2.1.1.2 Bacterial isolate and drug sensitivity in Africa in Cape Town, South Africa

A retrospective descriptive cohort study was conducted at a pediatric referral hospital in Cape Town, South Africa. The National Health Laboratory Service (NHLS) microbiology database was accessed to identify positive blood culture specimens during the period 2011–2012. Of the 693 unique bacterial and fungal BSI episodes identified during the study period, 248 (35.8%) were community-acquired (CA), 371 (53.5%) hospital-acquired (HA) and 74 (10.7%) healthcare-associated (HCA). The overall risk was 6.7 BSI episodes per 1000 admissions. *Escherichia coli*, *Staphylococcus aureus* and *Streptococcus pneumoniae* were the most frequent causes of CA-BSI and *Klebsiella pneumoniae*, *Acinetobacter baumannii* and *S. aureus* were most commonly isolated in HA-BSI [23].

2.1.1.3 Descriptive cross sectional study Bacterial isolate and drug sensitivity in Kenyatta National Hospital in Africa.

Out of the 232 blood samples drawn for culture, a total of 15 (6.5%) grew pathologically significant bacteria. The most common organisms were gram positive bacteria with Coagulase negative *Staphylococcus aureus* being the most common at 40%. As far as the susceptibility to antibiotics was concerned, the majority of the bacteria were susceptible to the most commonly used antibiotics, with the least resistance against carbapenems and third generation cephalosporins. The highest resistance was against the penicillins and the macrolides (24).

2.1.1.4 Bacterial isolate and drug sensitivity in Ethiopia

This laboratory based retrospective study of 390 blood culture and susceptibility tests was conducted in Bacteriology Laboratory of the University of Gondar Teaching Hospital from September 2006 to January 2012 (27). Out of 390 blood culture results, 71 (18.2%) were culture

positive. The predominant bacteria isolated from blood culture were Coagulase negative staphylococci 30 (42.3%), followed by *S. aureus* 17 (23.9%) and *Klebsiella* spp 9 (12.9%), *E. coli* 5 (7.0%), *Pseudomonas aeruginosa* 4 (5.6%) and *Salmonella* spp. 3 (4.2%). The gram positive and gram negative bacteria constituted 49 (69%) and 22 (31%) of the culture isolates; respectively. The isolates showed high rates of resistance to most antibiotics tested. The range of resistance for Gram positive and Gram negative were from 23.5% – 58.8%, and 20%– 100% respectively. This retrospective cross-sectional study was conducted from March to May 2013 at the University of Gondar(28). Among a total of 856 blood samples analyzed, 169 (19.7%) cases were bacteremia confirmed. From the confirmed cases, 98 (58%) were male and 71 (42%) female. Culture positivity rate was highest (44%) in the age group of ≤ 28 days followed by the age group of 29 days–5 years. coagulase-negative staphylococci were the most common causative agent for bacteremia among the Gram-positive isolates. The overall antimicrobial susceptibility pattern of the Gram-positive isolates was an intermediate level of resistance (60%–80%), but Gram-negative bacteria showed a high level of resistance (>80%) against ampicillin and amoxicillin..A descriptive cross sectional study was conducted based on the two years records of culture and drug susceptibility test results of blood in the clinical microbiology laboratory unit from January, 2015 to December, 2016 in Addis Ababa, Ethiopia (29). A total of 500 blood culture specimens from patients with suspected bacteremia were processed from January 2015 to December 2016(29). Of these patients 231 (46.2%) were females and 259 (51.8%) were males, the age of the patients were ranged from a day to 86 years. majority of the patients 264 (52.8%) were less than one year. The overall prevalence of blood culture positive of bacteremia suspected patients was 164/500 (32.8%). Of these culture positive samples 98/259 (37.8%) were males and 66/231 (28.6%) were females . Of the culture positive results 128/164 (78.04%) were gram positive and 36/164 (21.95%) were gram negative bacteria.Among gram positive isolates 82 (64.56%) was *Staphylococcus* species, 43 (33.85%) was Coagulase negative *Staphylococcus* (CoNS), 3 (2.36%) was *Streptococcus* species and of the total of 36 gram negative bacteria isolates constituted 23 (63.90%), 6 (16.71%), 4 (11.11%), 2 (5.5%), and 1 (2.77%) were *Klebsiella pneumoniae*, *Escherichia coli*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Nisseria meningitidis* respectively. *Staphylococcus aureus* 70/82 (85.4%) was resistance to Trimethoprim-sulphamethoxazole, 68/82 (82.9%) was resistance to Penicillin, 62/82 (75.6%) was resistance to Erythromycin, 61/82 (74.3%) was resistance to Tetracycline,

61/82 (74.3%) was resistance to Doxycycline, 60/82 (73.1%) was resistance to Gentamycin and 55/82 (67.1%) was resistance to Clarithromycin whereas majority of *Staphylococcus aureus* showed least resistance to Chloramphenicol and Clindamycin which was 38/82 (46.3%) and 4/82 (4.8%) respectively⁹ (29).

3. Objectives

3.1 General objective

The aim of the present study was to determine the bacterial profile of bloodstream infections and their antibiotic susceptibility pattern at SPHMMC pediatric unit Addis Ababa, Ethiopia.

Retrospective study

3.2 Specific objectives

To evaluate the magnitude of blood culture positive in pediatric sepsis

To assess drug sensitivity pattern in blood culture positive pediatric sepsis

To determine common microorganism isolated from blood culture positive of pediatric sepsis

4. Materials and method

4.1. Study area

St Paul's Millennium Medical College, as it is known today, was established through a decree of the Council of Ministers in 2010, although the medical school opened in 2007 and the hospital was established in 1968 by the late Emperor Haile Selassie. It is second largest government hospital serving both teaching and care with catchment population more than 5 million, currently it has 350 beds with an annual average of 300,000 patients. It has over 1500 clinical and non-clinical staff. The hospital also has 13 departments including pediatric and child which occupied 33 beds in pediatric ward, 4 beds in pediatric ICU and 12 beds in pediatric emergency OPD served average 6480 patients of 1800 patients are septic patients

4.2. Study period

This study was conducted from March—August, 2019.

4.3 Study design

A retrospective study was conducted based on review of records of 310 patients for whom blood culture were routinely processed in department of Pediatrics SPHMMC from January 2016 – December 2018

4.4 Source population

All pediatric age group admitted to the hospital's pediatric unit with suspected sepsis worked up for sepsis during the study period that was included in the study.

4.5 Study population

All pediatrics age >1month up to 14 years of old with sepsis whose blood culture sent for analysis during the study period

5.6 Sample Size Determination and Sampling Technique

5.6.1 Sample size

The amount of sample size that infer the target population in this study was calculated for estimating a single population proportion at 95% confidence interval (CI) ($Z_{\alpha/2} = 1.96$), 5% margin of error

$$n = \frac{z^2 p(1-p)}{d^2} = \frac{(1.96)^2 (0.28) (0.72)}{(0.05)^2} = 309$$

where n = sample size

z = confidence interval 95%

p = estimate of proportion

d = margin of error

The prevalence was taken from the previous study in Ethiopia Wasihun et al. Springer 2015 Mekelle (25)

4.7 .1 Sampling Technics

A convenient sampling technique was employed for that pediatrics fulfills the inclusion criteria during the study period

5.8 Inclusion criteria

All pediatric age group admitted to the SPHMMC pediatric unit with diagnosed of sepsis and blood culture done during the study period

5.9 Exclusion criteria

Pediatric suspected sepsis whose blood culture result lost was excluded from the study.

4.10 Study variables

4.10.1 Dependent variables

Bacterial isolation rate and drug sensitivity pattern of pediatric BSI

4.10.2 Independent variables

Age, sex, Weight

Time growth, time of culture sent

Previous antibacterial therapy

Application of indwelling medical device

Hospitalization period

Co-morbidities,

Clinical, signs and symptoms of sepsis for each patient

.

4.11 Data Collection

Data were collected by trained data collector who was general practitioner. He extracted the data like demographic ,Age, Sex ,card number of the patient and blood culture result both negative and positive manually from the microbiology registration books of the hospital laboratory using data abstraction checklists. MRN of each patient with blood culture done patients age (≥ 1 month < 14 year) were retrieved in the chart room of the hospital. Chart of patients with culture done was clerked and all clinical presentation of each septic patient was documented using standard questioner and was checked for its completeness and consistency.

All blood culture result done during the study period were involved and a predefined data collection tool was used to extract all socio-demographic data and other relevant information such as weight, previous antibacterial therapy, and application of indwelling medical device, hospitalization period, clinical signs and symptoms of sepsis for each patient. All the bacterial isolates and their drug sensitivity pattern were seen from blood culture report paper from both SPHMMC and EPHI bacteriology department. Blood culture report paper from both SPHMMC and EPHI bacteriology department shows bacterial species name and its drug sensitivity pattern against to amikacin, amoxicillin/clavulanate, ampicillin, penicillin , vancomycin, ceftazidime,

ceftriaxone, , chloroamphenicoloxacillin, ciprofloxacin, gentamicin, meropenem, nitrofurantoin, , trimethoprim and sulfamethoxazole .Sample size calculated based on previous prevalence study among children suspected of septicemia and in mekele which the P 28% [25].

4.12 Data Analysis

Data was entered to statistical package for the social science (SPSS versions 25) and was analyzed to make inferences on the frequency of occurrence of sepsis and to show bacterial sensitivity pattern to locally prescribe antibiotic. Descriptive statistics using frequency tables, figures, text

4.13 .Data Quality Assurance

The questionnaire was pretested and the pretest results was not included in the study. The main investigator was supervise the data collection, each day the collected data was checked for accuracy and completeness. The participant's names were not collected and the data was de-identified after the questionnaire was completed and all blood culture positive and negative samples was taken. The collected data was stored in a secure location and only the lead investigator was access to this location.

5.14. Operative definition

Case definition: Any patient with suspected sepsis whose blood culture was positive for any pathologic bacteria.

Sepsis: Sepsis is defined as the presence (probable or documented) of infection together with systemic manifestations of infection. Diagnostic criteria for sepsis include infection (documented or suspected)

Bacteremia: Bacteremia is the presence of viable bacteria in the blood.

5. Result

5.1 Characteristic of study population

During the study period 310 blood samples from clinically suspected cases of pediatric septicemia were obtained. Of this, 175(56.5%) were Male and 135(43.5%) were Female resulting in an overall male to female ratio of 1.29:1. Among admitted cases the mean length of hospital stay from the date of admission to blood sample collection for culture was 5 days with a

range of 1 to 35, days 161(51.9%) stayed > 10 days . Indwelling medical device such as intravenous (IV) usage were observed in 214 (69%) of the study.

Blood culture were done 192(61.9%), and 118(38.1%) community acquired and Hospital acquired infection respectively. Patients investigated for blood stream infections, the commonest clinical finding were fever (auxiliary temp>37.5°C) 296(95.5%), followed tachypnea 240 (77.45%), feeding/sucking failure 238(76.8%) , hypothermia (Temp < 36°C),149(48%) and Lethargy 193(62%). More than one clinical features of sepsis were observed in the majority of the study subjects.

Figure 1 Age distribution of pediatric patient with Blood Stream Infection Admitted to SPHMMC Recovered from Blood Culture from January 2016 To December 2018, Addis Ababa, Ethiopia

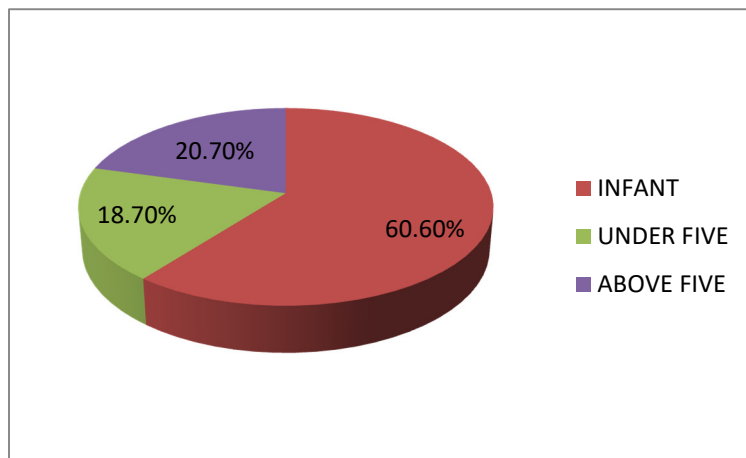


Figure 2 sex distribution of pediatric patient with Blood Stream Infection Admitted to SPHMMC Recovered from Blood Culture from January 2016 To December 2018, Addis Ababa, Ethiopia

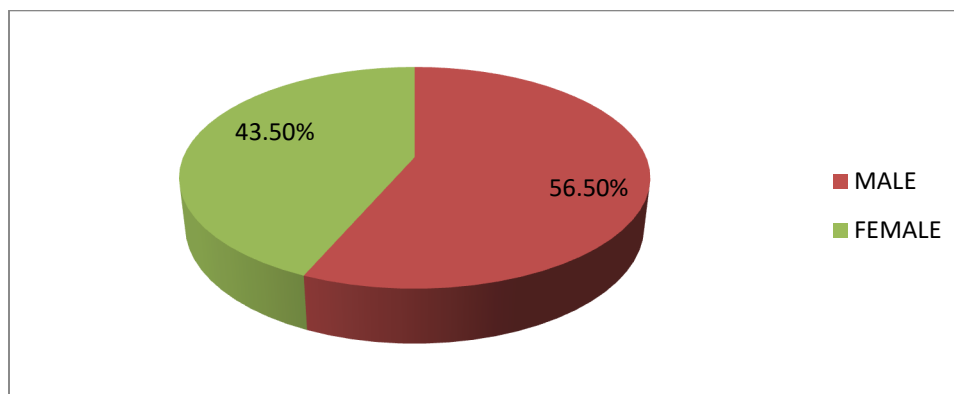


Table 1 Main Clinical Symptoms and with sepsis Of Blood Stream Infected Patients Admitted to SPHMMC Recovered from Blood Culture from January 2016 To December 2018, Addis Ababa, Ethiopia

Clinical symptom	Frequency	Percent	Total
Tachypnea	297	95.5%	310
Bradycardia	80	26.2%	310
Tachycardia	293	94.8%	310
Bradypnea	89	28.7%	310
Fever ($\geq 37.5^{\circ}\text{C}$)	296	95.5%	310
Hypothermia ($<36.5^{\circ}\text{C}$)	149	48%	310
Loss appetite	238	76.8%	310
Lethargy	193	62%	310
Leukopia (wbc <5000)	28	9%	310
Normal WBC(5000-10000)	188	60.6%	310
Leukocytosis (wbc >1500)	94	30%	310
Indwelling medical device	214	69%	310
Pre-sample antibiotic history	224	72%	310
Culture result	72	23.2%	310

6.2 Culture result:

Out of 310 children with clinical sepsis positive blood culture was found in 72 (23.2%). The Gram positive and Gram negative bacteria accounted for 40 (55.5%) and 32 (44.4%), respectively. The commonest Gram positive bacterial isolates were *Staphylococcus aureus* 19 (26.4%). Among Gram negative bacterial isolates the most predominate organisms were *Klebsiella pneumonia*, 24 (33.3%) see figure 1

Figure 3 Frequency Of Bacterial Species Isolates From Blood Stream Infected Patients Admitted To SPHMMC Recovered From Blood Culture January 2016 To December 2018 , Addis Ababa, Ethiopia

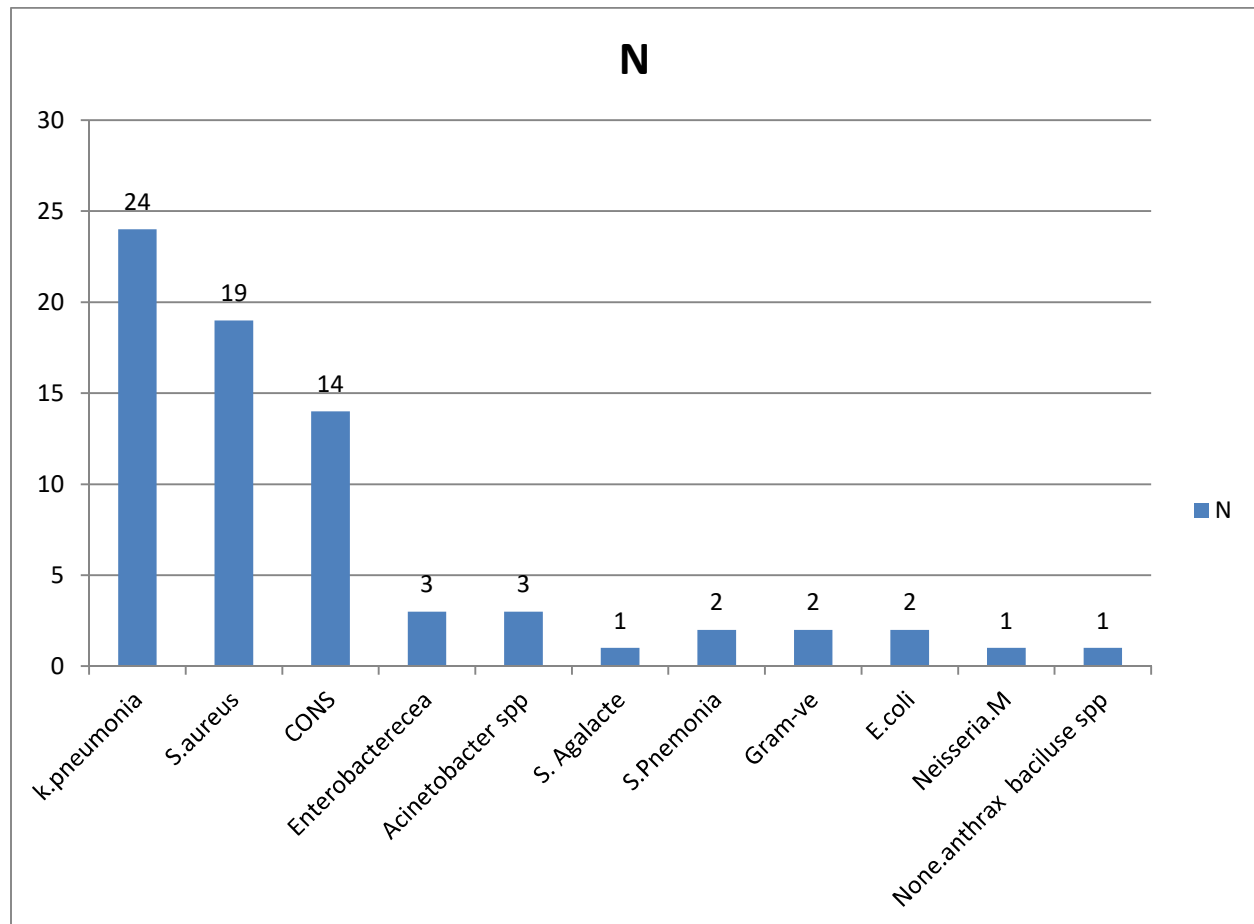


Table 2 Bacterial species isolates from blood stream infected patients recovered from blood culture SPHMMC by Age category from January 2016 To December 2018 Addis Ababa, Ethiopia

Age category	Common Bacterial isolate							
	k.pneumonia	Frequency	S.aureus	Frequency	CONS	Frequency	Enterobacteriaceae	Frequency
1 month to 1 year	20	83.3%	8	42%	11	78.5%	1	33%
>1 year to 5 year	3	12.5%	2	10.5%		000	1	33.3%
>5 year to 14 years	1	4.1%	9	47.3%	3	21.4%	1	33.3%
total	24	100%	19	100%	14	100%	3	100%

6.3 Antimicrobial sensitivity and resistance pattern of blood culture isolate

Antimicrobial agents were used before and after blood culture result. Out of 310 the patients, 224 (72.3%) had received antibiotic empirically before of sampling, 61/72 had positive blood culture. Ampicillin, Gentamicin and ceftriaxone were among the most common empirically used antibiotics during our study.

Drug sensitivity test against 14 antimicrobial agents were done. The highest degree of resistance in Gram positive bacteria like *Staphylococcus aureus* was seen against Penicillin, Ampicillin, Co-trimoxazole and Ceftriaxone.

Most of *Staphylococcus aureus* isolate were sensitive for Vancomycin ,Oxacillin and Chloramphenicol ,18/19(94.7%) 15/19(78.9%), 17/19(89.5%) respectively and 100% sensitive to clindamycin and meropenem see Table 3.

Gram negative bacteria like *Klabseilla pneumonia* was 100% resistant to Ampicillin, Gentamicin, Co-trimoxazole and Ceftriaxone .

Klabseilla pneumonia was 23/24(95.8%) sensitive to Ciprofloxacin and 100% sensitive to Amikacine, Meropenem see Tab

Table 3: Show Antibiotics sensitivity and resistance pattern of Gram positive bacteria isolated from patients of blood stream infection From January 2016 to December 2018, Addis Ababa, Ethiopia.

Culture isolate organism	Antibiotics Sensitivity and Resistance of (%)									
	Total	P	AMP	ERY	SXT	CRO	OXA	VCO	CLN	MERO
S.AUREUS	19	100% R	100% R	100% R	84.2 % R	94.7 % R	78.9 %	94.7 % S	100% S	100%
CONS	14	100% R	100% R	85.7 % R	85.7 % R	100% R	NA	78% S	NA	100% S
S.PNEUMONIA	2	100% R	100% R	100% R	100% R	100% R	NA	100% S	100% S	100% S
S. AGALACTIAE	2	100% S	100% S	100% S	100% S	100% S	100% S	100% S	100% S	100% S

Key: CONS: Coagulase negative *Staphylococcus*; CRO: Ceftriaxone; P: Penicillin; AMP: Ampicillin; ERY: Erythromycin; SXT: Trimethoprim-sulphamethoxazole; CLN: Clindamycin; ; CHL: Chloramphenicol; CIP: Ciprofloxacin; OXA: oxacillin , VCO :vancomycin

N.B 100% of the isolated in this study ,S: sensitive R: résistance NA: not done

Table 4: Show Antibiotics resistance pattern of Gram Negative bacteria isolated from patients of blood stream infection From January 2016 to December 2018, Addis Ababa, Ethiopia

Culture isolate organism	total	Antibiotics Sensitivity and Resistance of (%)								
		P	AMP	GEN	SXT	CRO	AMI	CHL	CIP	MERO
K.PNEUMONIA	24	(100% R)	19(100% R)	100% R	100% R	83.3% R	100%	100%	95.8% S	100% S
ENTEROBACTERE CEAE	3	100% R	100% R	100% R	100% R	100% R	100% S	100%	100% S	100% S
ACINETOBACTER SPP	2	100% R	100% R	100% R	100% R	100% R	100% S	100%	100% S	100% S
ESCHERICHIA COLI	2	100% R	100% R	100% R	100% R	100% S	100% S	100%	100% S	100% S
NEISSERIA.M	1	100% R	100% R	100% R	100% R	100% S	100% S	100%	100% S	100% S

Key: ; CRO: Ceftriaxone; P: Penicillin; AMP: Ampicillin; ERY: Erythromycin; SXT: Trimethoprim-sulphamethoxazole; ; CIP: Ciprofloxacin; AMI: Amikacin MERO:meropenem Sensitive , R resistance

Table 5 Antimicrobial susceptibility pattern of bacterial isolates from blood culture of pediatric patients at SPHMMC hospital Addis Ababa Ethiopia 2019, summery

Culture isolate organism	Antibiotics Sensitivity and Resistance of (%)													
	P	A M P	E R Y	S X T	CR O	OX A	V C O	C H L	C L N	ME RO	CI P	A M I	GE M	C H L
S.AUREUS (N=19)	R	R	R	R	R	78.9 %sR	S	S	S	S	N A	N A	NA	S
CONS (N=14)	R	R	R	R	R	NA	S	S	S	S	57 % S	N A	R	S
S.PNEUMONIA(N=2)	R	R	R	R	R	NA	S	S	S	S	S	N A	R	S
S. AGALACTIAE (N=2)	S	S	S	S	S	S	S	S	S	S	S			
K.PNEUMONIA (N=24)	R	R	N A	R	83. 3% S	NA	N A	S	R	S	S	S	R	S
ENTEROBACTE RECEAE(N=3)	R	R	N A	S	S	NA	N A	S	N A	S	S	S	S	S
ACINETOBACT ER SPP(N=3)	R	R	R	R	R	NA	N A	S	N A	S	S		R	S
ESCHERICHIA COLI(N =2)	R	R	R	N A	R	S	N A	N A	S	S	S		S	S
NEISSERIA.M(N =1)	R	R	R	R	S		N A	N A	S	S	N A	S	R	S

Key: ; CRO: Ceftriaxone; P: Penicillin; AMP: Ampicillin; ERY: Erythromycin; SXT: Trimethoprim-sulphamethoxazole; ; CIP: Ciprofloxacin; AMI: Amikacin MERO:meropenem Sensitive , R resistance VCO: vancomycin OXA: oxacillin NA : note done

7. Discussion

Bloodstream infections remained a challenge for the infectious disease physicians due to the changing bacterial etiology and emergence of antimicrobial resistance. Early detection of causative organism and determination of its antimicrobial susceptibility profile are necessary to help clinicians decide appropriate empirical therapy, which ultimately decreases the emergence of resistance (30). Our study evaluates the incidences of bloodstream infections, bacterial etiology, and antimicrobial susceptibilities among the pediatric patients. In this study the overall frequency of bacteria isolated from blood culture was 23.2%. Comparatively, similar rates of BSI have been reported from, Addis Ababa (21.4%), Gondar (18.2%) and Mekelle (28%) [25, 27, 28,], We have much higher bacterial isolation as compared to Kenya 6.5% and Nepal 7.48%) [24, 21]. Most possible explanation could be due to the difference in blood culture system, study population, the study design, geographical location, etiological agents, and infection control policies between countries. Furthermore, lower rates of BSI may be ascribed to the injudicious use of antibiotics not only by clinicians before referring to the tertiary care center but also by patients themselves.

Fifty five percent of our findings showed that BSI was caused by Gram positive bacteria and 44% was caused by Gram negative bacteria. Similar Study findings also reported that higher BSI caused by Gram positive bacteria than Gram negative bacteria organisms reported from Mekelle (72.2% vs. 27.8%) and Addis Ababa (77% vs 22.6) (25, 29). Another study reported from India was India (33% vs . 20%) and Nepal (89.19 and 10.81%) also showed higher BSI caused by Gram positive bacteria than Gram negative bacteria respectively [21, 22] Most probable reason could be Gram positive bacteria have virulence factors that prevent them from the host innate immune system and enable them to cross mucosal barriers, disseminate and replicate in distant organs.

This study revealed that *S. aureus* and *CONS* were the first and second most prevalent GPB agents isolated in this study area (26.4% and 19.4%). This has also been reported by other studies conducted in Addis Ababa, Nepal and India, two studies (21, 22, 26, 27, and 29). The probable reason for highest incidence of these bacteria could be commonly found in the hospital environment which might be contaminate among admitted patients and increase the infection rate. *K. pneumoniae* was the predominant isolated Gram negative bacteria with prevalence rates of (33.3%) . Our blood culture finding is higher for *K. pneumoniae* as compared to other

studies in Ethiopia Addis Ababa (14.06%) Gendar (12.7%) Mekelle (0.2%) (25, 27, 29).The variation in the BSI rates among these studies may be attributable to sampling volume of blood culture, culture system, and medium formulation as well as type of patients enrolled in the study.

Drug sensitivity pattern

The antibiotic susceptibility spectrum of bacterial pathogens significantly varies according to the patient population, their age, and the strains. . Most of the Gram positive bacteria and Gram negative bacteria were multi drug resistance, with a very high resistance to beta lactam antibiotics (100% resistant to Penicillin, Ampicillin) and macrolide (100% resistant to Erythromycin. Third generation cephalosporin's (100% resistance to ceftriaxone) and both GPB and GNB were resistance to Gentamycin. This was higher drug resistance BSI as compared to study reports in Ethiopia (4.8% to 85.4% and 40% to 100%) vs. (83%- 100%) for both gram positive and gram negative organisms (29, 25), other ways similar reports from Nepal, India and Kenya (21,22,24) . In our study *Staphylococcus aureus* was 100% resistance to penicillin, ampicillin and cotrimoxazole. other study Ethiopia , Addis Ababa *Staphylococcus aureus* was resistance , (85.4%), (82.9%), (75.6%) to cotrimoxazole , to Penicillin, to Erythromycin respectively . In Nepal *Staphylococcus aureus* was resistance (80% and 100%), (26.6% and 84.0%), 51.1% and 84.0%) to ampicillin ,cotrimoxazole ,erythromycin .India similar to our finding *Staphylococcus aureus* was (100%) resistance to penicillin, ampicillin, cotrimoxazole (21,22 , 23, 29)). The increased resistant blood isolates in this study may be a signal of indiscriminate and continuous use of sub-therapeutic doses of commonly available antimicrobials, or we are over prescribing violating the rational use of Antibiotics. *K. pneumoniae* was highly sensitive to Amikacin , Ciprofloxacin and Meropenem . *Staphylococcus aureus* and CONS highly sensitive to Vancomycine , Oxacillin ,Chloramphenicol and Clindamycin in this study . There are similar study reports from Ethiopia, South Africa, and India (25. 22, 24)

The results of this study showed that BSI was more prevalent in under one year's old ages. This finding was supported by different other studies (25, and 29). This is might be due to their low immune response There was no a statistically significant Association between age of patients and BSI P-Value (0.287). This is might be due to their low immune response. The increased resistant blood isolates in this study may be a signal of indiscriminate and continuous

use of sub-therapeutic doses of commonly available antimicrobials, or we are over prescribing violating the rational use of Antibiotics.

7.1 Conclusion

In this study the overall prevalence of blood stream infection was high 72(23.2%). This study provides some insight into the local trends and bacterial etiology of bloodstream infections among pediatric. Gram Positive bacteria are the major contributors of BSI in our patients. A higher rate of antimicrobial resistance among gram negative and gram positive organisms is an alarming issue. Exact contributing factors for the bloodstream infections (BSI) within these groups need to be further elucidated. Rational use of antibiotics, formulation of antibiotic policy, and prompt therapy of bloodstream infections for the effective management and prevention of drug resistance are urgently needed in our setting.

7.2 Limitations

Since it is retrospective study, the study population was not systematically selected, so that the Results may not be truly representative.

Risk factors and associated clinical outcomes were also not evaluated

7.3 Recommendation

- ✓ Large prospective systematic study design is recommended to know the genetic cause of drug resistance
- ✓ Update on Guideline is recommended to the department to practice empirical treatment infectious disease based on this finding

Declarationss

Ethics approval and consent to participate

Ethical clearance and approval was obtained from the Ethical review committee of SPHMMC. The culture sample was used only for the purpose of the study; the privacy of personal information were ensured and that no payments was made in return for enrollment. The collected data was kept in a secure location only the lead investigator has access to and it was de-identified once data collection was completed blood culture positive and negative samples were taken. Lastly, appropriate treatment guide was provided to the respective pediatric unite immediately whenever data been needed diagnosed

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ANNEXES

Background characteristics Variables

MRN-----

Sex Female ----- Male -----

Age

.

>1 month –1 years -----

>1–5 years -----

5----14 years _____

Clinical signs and symptoms of sepsis for each patient

Clinical features of children investigated for blood stream tract infection

Tachypnea

Bradypnea	yes	no
-----------	-----	----

Tachycardia

Bradycardia	yes	no
-------------	-----	----

Fever ($\geq 37.5^{\circ}\text{C}$)	yes	no
---------------------------------------	-----	----

Hypothermia ($<36.5^{\circ}\text{C}$)	yes	no
---	-----	----

Failure to feed/suck	yes	no
----------------------	-----	----

Cough	yes	no
-------	-----	----

Apnea or shortness of breath		yes
no		

Vomiting	yes	no
----------	-----	----

Diarrhea	yes	no
----------	-----	----

Lethargy	yes	no
----------	-----	----

Seizures	yes	no
----------	-----	----

Shock/Coma	yes	no
------------	-----	----

Length of Hospital stay

≤ 10 days-----

>10 days -----

Indwelling medical device	yes	no
---------------------------	-----	----

yes no

yes no

If yes

Pneumonia

Meningitis

Chronic heart disease

Anthropometry

Weight----- Height ----- Wt/Ag ----- Wt/ Ht ----- Ht/Ag----

MUAC -----

WBC _____

Blood culture positive

Organism identified in culture report _____

Susceptibility test result

Organism1	S& R .P	Drug	Organism 2	S &R.P		
		Amikacin				
		Ampicillin				
		Augmentin				
		Azithromycin				
		Cefazolin				
		Cefotaxime				
		Ceftriaxone				
		Ciprofloxacin				
		clindamycin				
		Erythromycin				
		Gentamycin				
		Meropenem				
		Oxacillin				
		Penicillin				