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Prevalence and antimicrobial resistance pattern of bacterial isolates among children suspected for septicemia and urinary tract infections at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

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Abstract

Background: Blood stream and urinary tract infections are the major causes of mortality and morbidity of the pediatric population. Hence the aim of this study was to determine the prevalence and antimicrobial resistance pattern of bacterial isolates among children suspected for septicemia and urinary tract infections.

Method: An institutional based cross sectional study was conducted from January to March 2014. A total of 322 study participants who were suspected for septicemia and/or UTI were recruited. All blood & urine samples were cultured on blood and MacConkey agar. Culture positives were characterized by gram stain, colony morphology and conventional biochemical tests. Antimicrobial susceptibility testing was performed for all bacterial isolates using disk diffusion method. Data was analyzed using SPSS version 20.

Result: The overall prevalence of bacterial isolates from blood and urine cultures was 13.0% (n=23/177) and 22.1% (n=32/145) respectively. *Coagulase negative Staphylococci* 39.1% (n=9/23) from blood & *Klebsiella pneumoniae* 43.8% (n=19/32) from urine cultures were the most frequent isolated bacteria. Multidrug resistance was recorded in 89.1% (n=49/55) of all bacterial isolates. Gram positive and Gram negative isolates showed 71.42% and 95.11% MDR respectively. Amoxicillin (89.1%) and cefotaxime (85.5%) showed the highest level of resistance.

Conclusion: Standard infection control programs have to implemented and followed to minimize blood stream and urinary tract infections. The possible choices of antibiotic options for treatment of these infections are few due to wide scale resistance to commonly used antibiotics. To prevent further emergence and spread of MDR bacteria rational use of antibiotics and regular monitoring of antimicrobial resistance patterns is essential.

Key terms: Septicemia, UTI, multidrug resistance, Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

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INTRODUCTION

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Bacterial infections of the pediatric population continue to be an important cause of morbidity and mortality [1]. One of the main causes of this morbidity and mortality for pediatric groups is blood stream infection which continues a serious problem [2]. Bacteremia is defined as continuous or transient presence of microorganism within the blood stream while septicemia is its dissemination throughout the body with evidence of systemic responses towards microorganisms with variable severity [3]. Major clinical presentations of septicemia patients are fever, difficulty in breathing, tachycardia, malaise, refusal of foods or lethargy which required medical emergency of urgent rational antibiotics therapy [4]. Mortality rate of children in sub Saharan countries including Ethiopia due to septicemia approaches to 53% which makes it a significant health problem [5, 6].

The organisms responsible for bacteremia vary across geographical boundaries [7]. In USA and Europe the commonest clinically significant causes of blood stream infections are *Escherichia coli* and *Staphylococci aureus* however in Sub-Saharan Africa *Staphylococci aureus*, *Klebsiella species* and *Salmonella species* are the primary causative pathogens [8]. In addition organisms like *Coagulase negative staphylococci*, *Pseudomonas* species, *Salmonella* species and *Acinetobacter* species are potential pathogens of septicemia [9]. These pathogens are medically important because of their frequent isolation and high antibiotic resistance level which reached to worrying level [9, 10].

In addition to blood stream infections the pediatric populations are affected due to urinary tract infections (UTI) which is believed that by the age of seven 8% of girls and 2% of boys will have at least one episode [11]. Bacterial proliferation in one or more parts of the urinary system such as the kidney, ureters, bladder or urethra results in urinary tract infections [12]. In case of symptomatic UTI, it is accompanied with a variety of clinical signs including dysuria, pyuria, strong urge to urinate frequently, painful burning sensation, discomfortable pressure and bloody urine [13]. Likewise to septicemia the etiologic agents of UTI are variable and usually dependant on time, geographical location and age of patients [14]. *Escherichia coli, Klebsiella spp., Proteus spp., Enterobacter spp., Citrobacter spp. and Enterococci* are the commonest uropathogens [15].

Since bacterial pathogens of septicemia and UTIs are variable regionally, infection control and treatment depends on knowledge of common causative organisms and their antibiotic resistance level in local scenario [7, 14, 16].

MATERIALS AND METHODS

Institutional based cross-sectional study was conducted from January to March 2014 at Tikur Anbessa Specialized Hospital which is the biggest referral hospital of Ethiopia located in the capital city Addis Ababa. A total of 322 study participants (<15years) were recruited using convenient sampling technique. The sample size was calculated based on single population proportion using previous study done in Ethiopia [17]. Patients who took antibiotics currently within the last two weeks and non volunteers were excluded. Demographic characteristics of patients were recorded using predesigned sheets after obtaining informed consent. From septicemia suspected children, 3-5ml of blood was collected aseptically using blood sample collection sets and antiseptics (70% alcohol and 2% tincture iodine) and transferred to blood culture bottle containing sterile brain heart infusion (Oxoid, England). A minimum blood to-broth ratio of 1 in 10 was maintained. From those UTI suspected children first morning mid stream urine samples were collected using sterile wide mouth container. The study participants' parents or guardians were given appropriate sample collection instructions before providing urine samples. Blood specimens within 30 minutes and urine specimens immediately after collection were brought to microbiology laboratory for bacterial analysis.

CULTURE AND IDENTIFICATION

Blood culture bottles were incubated at 37^{o}C and were inspected for the signs of bacterial growth daily for seven days. Turbid blood samples before the seventh day and none-turbid blood samples on the seventh day were sub-cultured on blood agar (Oxoid, England) and MacConkey agar (BD, USA) at 37^{o}C for 24 hours aerobically. Using a sterile calibrated wire loop (0.001 ml), all urine samples were inoculated to blood agar (Oxoid, England) and MacConkey agar (BD, USA) and incubated at 37^{o}C for 24 hours. For identification of *Staphylococci* mannitol salt agar (Oxoid, England) and DNAse agar (Oxoid, England) were also used. The number of colonies and numbers of different colony morphologies were counted for estimation of colony-forming units (CFU) per ml of urine and $\geq 10^5$CFU/ml of urine were considered as significant bacteriuria. All positive cultures were characterized by colony characteristics, Gram stain and standard biochemical tests [12]. Biochemical tests that were used to classify Gram positive bacteria at species level were catalase, serological test and for Gram negative bacteria triple sugar iron, indole, citrate, urea, Lysine decarboxylase (LDC) and motility were used.

DRUG SUSCEPTIBILITY PATTERNS

The disk diffusion was performed and after 16-18hours of incubation at 37^{o}C zone of inhibition was measured and interpreted as recommended by the Clinical and Laboratory Standards Institute (CLSI) [18]. Using a sterile wire loop, 3-5 pure colonies were picked from blood agar for Gram positives and MacConkey agar for Gram negatives and emulsified in nutrient broth. Standard inoculums adjusted to 0.5 McFarland using McFarland Densitometer was swabbed onto Muller-Hinton agar (dispensed on 100mm plate). Accordingly the CLSI guideline for each category of bacteria, drug susceptibility testing was performed against amoxicillin (30µg, BD), amoxicillin-clavulanic acid (30µg, BD), oxacillin (5µg, BD), chloramphenicol (30µg, BD), gentamicin (10µg, BD), TMP-SXT (1.25µg, BD), cefotaxime (30µg, BD), cefoxitin (30µg, Oxoid), tetracycline (30µg, BD), nitrofurantoin (300µg, BD), norfloxacin (5µg, BD), imipenem (10µg, Oxoid) and meropenem (10µg, Oxoid). Oxacillin susceptibility pattern of *Staphylococcus aureus* and *Coagulase negative Staphylococci* was interpreted using 30 µg cefoxitin. Availability and frequency of prescriptions were given attention to select those antibiotics used for the management of bacterial infections in Ethiopia keeping the CLSI guidelines. Level of drug resistance was interpreted as high, intermediate and low when the percentage of resistance was >80%, 60-80% and<60% respectively [17]. In this study multidrug resistance was defined as simultaneous resistance to two or more classes of antimicrobial agents.

QUALITY CONTROL

Standard Operating Procedures (SOP) were strictly followed verifying that media meet expiration date and quality control parameters per CLSI [17]. Visual inspections of cracks in media or plastic petridishes, unequal fill, hemolysis, evidence of freezing, bubbles, and contamination was done. Quality control was performed to check the quality of medium. Each new lot was quality controlled before use by testing the *Escherichia coli ATCC 25922* and/or *Staphylococcus aureus ATCC 25923* standard control strains.

Statistical analysis and interpretation

The data was analyzed using SPSS version 20. The descriptive statistics (mean, percentages or frequency) was calculated. The bi-variant logistic regression analysis was used to see the relation between dependent variable and independent variables. Variables that showed a significant association were selected for further analysis using multiple logistic regression models with a p-value < 0.05 considered statistically significant.

Data quality Assurance

Socio-demographic characteristics of patients were collected using structured data collection sheets after getting informed consent. Blood and urine specimens were collected in accordance with SOPs and brought to bacteriology laboratory immediately for bacteriological analysis. Culture results were recorded carefully before data entry and the data was double checked by a different person before analysis.

Ethical clearance

The study was approved by "Department Research and Ethical Review Committee (DRERC)" of the Department of Medical Laboratory Science (MLS/483/15), School of Allied Health Sciences, College of Health Sciences, Addis Ababa University. Written permission letter was also obtained from the study site. The purpose and procedures of the study was explained to the study participants, participants' parents or guardians within the study period. Those participants who gave informed consent and those children who gave assent and whose parents or guardians gave informed consent were selected and enrolled as the participants of the study. A patient result was communicated to the attending physicians

RESULTS

Socio-demographic characteristics

Three hundred twenty two (n=322) septicemia and urinary tract infection suspected children were investigated during the study period. Among the total participants 55% (n=177/322 and 45% (n=145/322) of them were suspected for septicemia and UTI respectively. Of these patients, 53.4% (n=172/322) were males and 46.6% (n=150/322) were females with males to females ratio 1.15:1. Most of patients 98(30.4%) were between 1-6 years of age and their mean (std. deviation) of ages were 3.22(1.229) with age range of 0- 15

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years. Of them 38.5% (n=124/322) were out patients while the remaining 61.5% (n=198/322) were inpatients. Socio-demographic characteristics of patients have shown in table 1.

Table 1 Socio-demographic characteristics of septicemia and UTI suspected children.

Variables		Culture results					
		Septicemia (n=177)			UTI (n=145)		
		Positive	**Negative**	**Total**	**Positive**	**Negative**	**Total**
Gender	Male	15(14.7)	87(85.3)	102(100)	16(22.9)	54(77.1)	70(100)
	Female	8(10.7)	67(89.3)	75(100)	16(21.3)	59(78.7)	75(100)
	Total	23	154	177	32	113	145
Age in Year	0-30days	5(15.6)	27(84.4)	32(100)	3(50.0)	3(50.0)	6(100)
	30days-1	5(20.8)	19(79.2)	24(100)	5(21.7)	18(78.3)	23(100)
	1-6	6(12.5)	42(87.5)	48(100)	9(18.0)	41(82.0)	50(100)
	6-12	4(9.3)	39(90.7)	43(100)	11(26.2)	31(73.8)	42(100)
	12-15	3(10.0)	27(90.0)	30(100)	4(16.7)	20(83.3)	24(100)
Patient Type	Outpatient	1(2.1)	46(97.9)	47(100)	10(13.0)	67(87.0)	77(100)
	Inpatient	22(16.9)	108(83.1)	130(100)	22(32.4)	46(67.6)	68(100)

OPD= Outpatient department

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Prevalence of bacterial isolates of septicemia and UTIs

The overall prevalence of bacterial isolates from sepcemia suspected children was 13.0% (n=23/177) while from those UTI suspected children was 22.1% (n=32/145). From the total bacterial isolates 56.4% (n=31/55) of culture positives were from males while 43.64% (n=24/55) were from females. Among the tal bacteria isolates Gram positive and Gram negatives constitutes 25.5% (n=14/55) and 74.5% (n=41/55) respectively with a ratio of Gram positives to Gram negatives of 0.34:1. The most frequent isolated bacteria were *Klebiesella pneumoniae* 34.5% (n=19/55), *CONS* 16.4% (n=9/55) and *E. coli* 10.9% (n=6/55) (figure 1). The spectrum of BSI and UTI was varied with the age of patients (Table 1) where the highest culture positives 20.3% were found among infants. However there was no stastical significant association between the age of patients and culture results (OR=0.84, 95%CI=0.314-2.65, P = 0.695). In this study 80% (n=44/55) of pathogens were isolated from hospitalized patients which showed statistically significant association with culture results (OR=2.935, 95%CI=1.452-5.934, P = 0.003). In our study from blood culture *Coagulase negative Staphylococci* 39.1% (n=9/23) was the most frequent isolated bacte-

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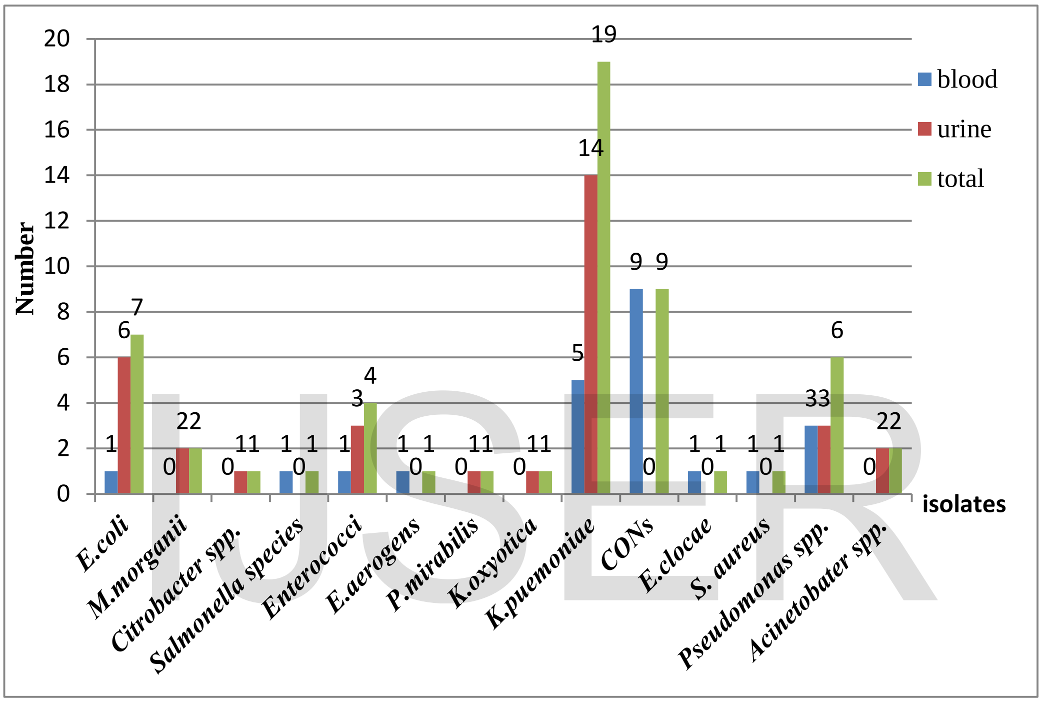
ria followed by *K. pneumoniae* 21.7% (n=5/23).

In this study among urine cultures *K. pneumoniae* 15.6% (n=14/32) were the most frequent isolates followed by *E. coli* 15.6% (n=5/32), *Pseudomonas spp.* 9.4% (n=3/32) and *Enterococci spp.* 9.4% (n=3/32



CONs-----------Coagulase negative Staphylococci

Figure 1 A bar graph showing frequency and types of bacterial isolates from septicemia and UTI suspected children

Antibiotic resistance patterns

The overall multidrug resistance level (MDR ≥2 different classes of antibiotics) of all bacterial isolates was 89.1% (n=49/55) (table 2). Antimicrobial resistance level for Gram positive isolates were ranging from 0-100% with an MDR level of 71.4% (n=10/14). All gram positive isolates showed high level of resistance (>80%) for amoxicillin and sulphamethoxazole-trimethoprim; intermediate level of resistance (60-80%) to amoxicillin-clavulanic acid, chloramphenicol, gentamicin, tetracycline and low level of resistance for norfloxacin and nitrofurantoin. In the same manner antimicrobial resistance patterns of Gram-negative organisms were ranging from 0 to 100% with an MDR level of 95.1% (n=39/41).

Table 2 Multidrug resistance level of bacteria isolates

	Organism isolated	No. of bacteria Tested	MDR level in No. (%)
	E. coli	6	6(100)
	M. morganii	2	2(100)
	Citrobacter spp.	1	1(100)
Gram negative	*Salmonella spp.*	1	1(100)
	E. aerogens	1	1(100)
	P. mirabilis	1	0(0)
	K. oxytoca	1	1(100)
	K. pneumoniae	19	18(94.7)
	E. cloacae	1	1(100)
	Pseudomonas spp.	6	6(100)
	Acinetobacter spp.	2	2(100)
	Total	**41**	**39(95.11%)**
Gram positive	*CONS*	9	6(66.67)
	Enterococcus spp.	4	3(75.0)
	S. aureus	1	1(100)
	Total	**14**	**10(71.48)**
Total		**55**	**49(89.1)**

CONs--*Coagulase negative Staphylococci*, *MDR*----*multidrug resistance*

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All gram negative isolates showed high level of resistance (>80%) for amoxicillin, sulphamethoxazole-trimethoprim and cefotaxime; intermediate level of resistance (60-80%) to amoxicillin-clavulanic acid, chloramphenicol, gentamicin, tetracycline and low level of resistance for cefoxitin, norfloxacin, nitrofurantoin, imipenem and meropenem.

The most frequent Gram positive bacteria *Coagulase negative staphylococci* 69.2% (n=9/14) showed 66.7% (n=6/9) of MDR level. It demonstrated intermediate level of resistance to amoxicillin (77.8%), cefotaxime (77.8%), sulphamethoxazole-trimethoprim (77.8%) and tetracycline (66.7%). It showed better susceptibility for norfloxacin (77.8%), amoxicillin-clavulanic acid (77.8%) and oxacillin (75%) compared to other tested drugs. Similarly the most frequent Gram negative isolates *k. pneumoniae* 46.34% (n=19/41) showed that 94.7% (n=18/19) of multidrug resistance level. It demonstrated to high level of resistance to cefotaxime (100%), amoxicillin (94.7%), amoxicillin-clavulanic acid (89.5%), gentamicin (89.5%) and sulphamethoxazole-trimethoprim (84.2%). As compared to other tested drugs it showed lowered resistance for imipenem (10.5%), meropenem (15.8%), norfloxacin (15.8%), and cefoxitin (36.8%) respectively (table 3).

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Table3. Antimicrobial resistance levels of bacterial isolates.

CONs--Coagulase negative Staphylococci, NA --Not applicable: AML--amoxicillin, AmC--amoxicillin-Clavulanic acid, SXT—

Isolated bacteria	Antimicrobial resistance of bacterial isolates from blood and urine cultures (no.(%))												
	AML	**AMC**	**SXT**	**FOX**	**C**	**CTX**	**GE**	**NOR**	**TE**	**FN**	**OX**	**IMI**	**MEM**
E. coli(n=6)	6(100)	6(100)	6(100)	3(50)	4(66.7	4(66.7	4(66.7)	4(66.7	5(83.3)	0(0)	NA	0(0)	0(0)
M. morganii(n=2)	2(100)	2(100)	2(100)	2(100)	2(100)	2(100)	2(100)	2(100)	2(100)	2(100)	NA	2(100)	0(0)
Citrobacter spp. (n=1)	1(100)	1(100)	I(100)	1(100)	1(100)	1(100)	1(100)	1(100)	1(100)	0(0)	NA	0(0)	0(0)
Salmonella spp. (n=1)	1(100)	0(0)	1(100)	0(0)	0(0)	0(0)	0(0)	0(0)	1(100)	0(0)	NA	0(00	0(0)
Enterococcus spp. (n=4)	2(50.0	2(50)	2(50)	2(50)	4(100)	3(75)	2(50)	2(50)	2(50)	2(50)	2(50)	NA	NA
E. aerogens(n=1)	1(100)	1(100)	1(100)	1(100)	0(100)	1(100)	1(100)	1(100)	1(100)	0(0)	NA	0(0)	0(0)
P. mirabilis(n=1)	1(100)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	NA	0(0)	0(0)
K. oxytoca(n=1)	1(100)	1(100)	1(100)	1(100)	0(00)	1(100)	0(0)	0(0)	1(100)	1(100	NA	0(0)	1(100
K. pneumoniae (n=19)	18(94.7)	17(89.5)	16(84.2)	7(36.8)	11(57.9)	19(100)	17(89.5)	3(15.8)	14(73.7)	9(47.9)	NA	2(10.5)	3(15.8)
CONS(n=9)	7(77.8)	2(22.2)	7(77.8)	NA	4(44.4)	7(77.8)	3(33.3)	2(22.2)	6(66.7)	2(12.5)	2(25)	NA	NA
E. cloacae(n=1)	0(0)	0(0)	1(100)	0(0)	1(100)	1(100)	1(100)	1(100)	0(0)	0(0)	NA	0(0)	0(0)
S. aureus(n=1)	1(100)	1(100)	0(0)	NA	0(0)	1(100)	1(100)	0(0)	1(100)	0(0)	1(100)	NA	NA
Pseudomonas spp. (n=6)	6(100)	6(100)	6(100)	5(83.3)	5(83.3)	5(83.3)	5(83.3)	3(50)	5(83.3)	4(80)	NA	0(0)	1(16.7)
Acinetobacter spp. (n=2)	2(100)	2(100)	2(0)	1(50)	1(50	2(100)	2(100	0(0)	1(50)	2(100	NA	1(50	1(50)
Total(n=55*)*	**49(89.1)**	**41(74.5)**	**46(83.6)**	**22(40)**	**34(61.8)**	**47(85.5)**	**39(70.9)**	**19(34.5)**	**40(72.7)**	**21(39.6)**	**5(38.5)**	**5(12.2)**	**6(14.6)**

sulphamethoxazole-trimethoprim, FOX--Cefoxitin, C--chloramphenicol, CTX--cefotaxime, GM--gentamicin, TE--tetracycline, FN—nitrofurantoin, NOR--norfloxacin, OX--oxacillin, IMI--imipenem, MEM—meropenem

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Discussion

Prevalence of bacteria isolates among septicemia and UTI suspected children

The overall prevalence 17.1% (n=55/322) of bacterial isolates from septicemia and UTI suspected children was almost similar with studies done in Ethiopia (18.2%) [6] and Nigeria (21.7%) [4]. However, this finding was relatively lower than studies done in Gondar Ethiopia (25.6%, 32.1%) [17, 21] and much lower than a study done in Addis Ababa Ethiopia (44.7%) [22]. On the other hand, our finding was higher than studies done in Ethiopia which was 8.8% [23] and in Pakistan which was 13.2% [24]. The possible explanations could be the difference in methodology used, the study design, nature of patient population, epidemiological difference of etiological agents and seasonal variations [17]. In this study 80% (n=44/55) of bacteria were isolated from hospitalized patients and there was a statistical significant association between being out patient or inpatient with culture results (OR=2.935, 95% CI =1.452-5.934, P = 0.003). Similar finding was seen from a study done in Ethiopia which showed relatively higher prevalence of bacterial isolated from hospitalized patients than out patients [6]. In the present study 25.5% (n=14/55) of infections were caused by Gram-positive and 74.5% (n=41/55) by Gram-negative bacteria with Gram positives to Gram negatives ratio of 0.34:1.

In our study the most frequent isolates of blood cultures were Gram positive organisms which showed similarity with other studies [21, 24]. *Coagulase negative Staphylococci* 39.1% (n=9/23) were the commonest etiologies of blood culture which was in line with other studies [23, 24]. A study from other parts of Ethiopia [6] showed a similar finding with our study where the primary pathogen of blood stream infections was *CONS* 42.3%. To the contrary our finding was higher than compared to other studies done in different parts of Ethiopia like Gondar (6.8%) and Jimma (26.1%) [21, 23] and a study done in India (12.3%) [25]. Since long ago *CONS*s have been regarded as non pathogenic however their increasing incidence in different infections like bacteremia related to indwelling devices, central nervous systems shunt infections, native or prosthetic valve endocarditis and UTIs left them as important pathogens. Additionally it is an important cause of morbidity and mortality of immunocompromised individuals [23].

Klebsiella pneumoniae 21.7% (n=5/23) were the most common isolates of blood cultures which showed similarity with other studies [5, 23, 26] and it was in line with a previous study done in Addis Ababa, Ethiopia [22]. However it showed disagreement with a study done in Nigeria where the most common isolated bacteria in blood cultures were *E. coli* and *S. aureus* [8]. Geographical variation, nature of patient population and epidemiological difference of the etiological agent could explain this difference [17]. The high occurrence of *Pseudomonas spp.* and *Acinetobacter spp.* in blood were often concern as these bacteria were associated with high degree of resistance to many antibiotics (they showed 100% MDR). Other bacterial isolates in blood cultures were *salmonella species* 4.3% (n=1/23), *Enterobacter cloacae* 4.3% (n=1/23), *Enterococci* 4.3% (n=1/23) and *Enterobac-*

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ter aerogens 4.3% (n=1/23).

The prevalence of UTI 22.1% (n=32/145) among children was in line with the findings of other study done in Ethiopia (22.7%) [27]. However the present finding was lower than as compared to other findings in different parts of the world (36.68%, 71.72%) [26, 28]. Highest positive urine cultures 50% (n=3/6) was seen in age group of 0-30days though the age groups of 1-6years were the most UTI suspected group. In our study the most frequent isolated bacteria in urine cultures were *Klebsiella pneumoniae 43.75*% (n=14/32) which disagreed with other study that reported *Escherichia coli* a primary pathogens of UTI [17]. Bacterial prevalence is mostly affected by difference in identification methods which makes comparison difficult. In addition bacterial etiologies of UTI can show geographic variation and may even vary over time within a population [27]. The second common bacterial isolates of urine cultures were *Escherichia coli* 15.6% (n=5/32) which showed similarity with a study done in India [28]. Other UTI isolates were *Enterococci* 9.4% (n=3/32), *Pseudomonas spp.* 9.4% (n=3/32), *Morganella morganii* 6.3% (n=2/32), *Acinetobacter spp.* 6.3% (n=2/32), *Citrobacter spp.* 3.1% (n=1/32), *Enterobacter cloacae* 3.1% (n=1/32), *Klebsiella oxytoca* 3.1% (n=1/32) and *Proteus mirabilis* 3.1% (n=1/32).

Antimicrobial resistance patterns of bacterial isolates

The overall 89.1% (n=49/55) multidrug resistance level of our finding was different from other studies done in Ethiopia which showed an MDR level of 95.2% and 47.85% [17, 27]. Antimicrobial resistance levels for Gram positive and Gram negative isolates were ranging from 0-100% and most of them showed multiple drug resistance which was comparatively similar with a study done in other part of Ethiopia [23]. Gram positive and Gram negative isolates showed 71.48% (n=10/14) and 95.11% (n=39/41) MDR level respectively which was similar with a study done in Gondar, Ethiopia [17]. However our study result was higher than a study done previously at the same hospital, Tikur Anbessa Specialized Hospital, which showed 45.7% and 84.2% MDR level of Gram positive and Gram negative bacteria respectively [22]. This MDR increment showed that antimicrobial resistance is changing over time which might suggest a very high resistance gene pool due to gross misuse and inappropriate usage of antibacterial agents [6] together with incorrect administration of antimicrobial agents in empirical therapies and lack of appropriate infection control strategies [19].

In our study *CONs (*MDR=66.7% (n=6/9)) showed intermediate level of resistance to amoxicillin (77.8%), sulphamethoxazole-trimethoprim (77.8%) and tetracycline (66.7%). It showed better susceptibility for norfloxacin (77.8%), amoxicillin-clavulanic acid (77.8%) and oxacillin (75%) compared to other tested drugs which was in line with other study [23]. From the Gram negative isolates *K. pneumoniae showed* 94.7% (n=18/19) of MDR level: which showed highest level of resistance to cefotaxime (100%), amoxicillin (94.7%), amoxicillin-clavulanic acid (89.5%), gentamicin (89.5%) and sulphamethoxazole-trimethoprim (84.2%). Similarity was found with other studies done in Ethiopia [21] and Nigeria [4]. These bacteria showed better susceptibility for norfloxacin (80%), imipenem (80%), meropenem

(70%), cefoxitin (50%) and nitrofurantoin (50%) as compared to other tested antibiotics.

Amoxicillin (MDR=89.1%) was the most highly resistant drugs which was a similar finding with studies done in other parts of Ethiopia (93.5%) [30] and (83.9%)[28]. To the contrary lower resistance level of amoxicillin was observed in other studies done in Ethiopia [17] and India (69%) [29].In our study *Klebsiella pneumoniae* 94.7% (n=18/19), *E. coli* 100% (n=6/6) and *Pseudomonas spp.*100% (n=6/6) showed high level of resistance to amoxicillin. Cefotaxime (MDR=85.5%) was the second drug that showed high level of resistance which agreed with other study (MDR was 83%) [15]. However a lower resistance level of cefotaxime was observed in a study done from India (MDR=46.15%) [26]. *Klebsiella pneumoniae* 100% (n=19/19), *Acinetobacter spp.* 100% (n=2/2) and *E. coli* 4(66.7%) showed high resistance level for Cefotaxime. It is supported by a study conducted in India in which cefotaxime resistance for *Klebsiella* species and *E. coli* were 88% and 87% respectively [31]. Hundred percent of cefotaxime resistance for *Klebsiella species* was also showed from a study in Nigeria [4]. This might be due to the selective pressure created to the third generation cephalosporin agents [32]. Among the common tested drugs norfloxacin (63.9%) showed a better susceptibility for most multidrug resistant bacteria isolates in our study as compared to other tested drugs. It was supported with other studies [14, 17].

Conclusion

Blood stream infections and UTIs among children were predominantly caused by *Coagulase negative Staphylococci* and *Klebsiella pneumoniae* respectively. MDR level of bacterial isolates was high 89.1% (n=49/55) and most pathogens were highly resistant for multiple antibiotics. The choice of drugs for the treatment of bacterial isolates especially for bacterial strains resistant to most classes of antibiotics is quite narrow due to their wide scale resistance for most common drugs which have been used previously. To prevent further emergence and spread of MDR bacterial pathogens rational use of antibiotics and regular monitoring of antimicrobial resistance patterns are essential and mandatory.

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