

Under-five children's Bacterial Blood Stream Infection in Southern Ethiopia

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Abstract

Background

Under-five children's blood stream infections mainly due to resistant pathogens found to be a higher risk of hospital mortality in low and middle income countries. This study intended to assess the bacterial profile and drug resistance of isolates of blood stream infection among under-5 children in Southern Ethiopia.

Methods

Retrospectively lab recorded data's were retrieved to assess the bacterial isolates and rates antibiotic resistance at Hawassa University Comprehensive Specialized Hospital.

Results

Of 323 bloods culture performed 116 (35.9%) were positive for potential bacterial BSI. Positivity of blood culture decrease with age, hence neonates blood stream infection were higher than other age groups (OR, 3; 95% CI 1.5–5.1; $p = 0.001$). The major gram positive isolate *CoNS* and *S.aureus* have shown highest level of resistance to penicillin 61.3.0% and tetracycline 78.8% whereas less level of resistance was reported to Meropenem 6.4%, Ceftriaxone 13% and doxycycline 13%. Although most of gram negatives isolates were resistant for tested antibiotics, *K.pneumoniae* has shown lesser resistance to cefotaxime and chloramphenicol.

Conclusion

A high level of blood stream infection accompanied by high drug resistant isolates was reported. The great burden in neonate than other children was reported. As a result to reduce the burden the hospital administrators need to facilities effective infection prevention and control programmes, effective hygiene practices and well-functioning environment along with educating patient about proper hygiene practices.

Background

Blood stream infection (BSI) is the most common causes of morbidity and mortality in children across the world[1]. The burden of sepsis is most likely highest in low- and middle-income countries. It is estimated about 3 million newborn and 1.2 million children suffer from sepsis globally every year. Unless diagnosed on time and treated promptly, it can lead to septic shock, multiple organ failure and death. Antimicrobial resistance is a major factor determining clinical unresponsiveness to treatment and rapid evolution to sepsis and septic shock. Sepsis patients with resistant pathogens have been found to have a higher risk of hospital mortality[2].

Although, BSI can be preventable with timely attention, coherent antimicrobial therapy and supportive care, so far higher death rates reported in developing countries[3]. The rate of BSI estimated to be 3–20 times higher in developing countries due to lack of adequate and regular microbiology laboratory in these country[4].

Fever may be the only manifestation of childhood invasive infection. Nevertheless in Ethiopia with the added burden of malaria, HIV infection, tuberculosis and malnutrition, the treatment of fever is often syndromic, targeting multiple possible aetiologies, without necessarily considering BSI as a potential cause[5]. That is why in developing country like Ethiopia, where malaria is endemic, most febrile children misleadingly managed as malarial infection and only very little proportion of them empirically managed as bacterial infection. As timely treatment of bacteremia and appropriate use of antibiotics for children is crucial most recommended replacement of presumptive treatment of malaria by test before treat as strategy for management of other febrile illness [6].

In southern Ethiopia, there is no reported data on blood stream bacterial infection among under-5 children. As a result this study provides information for local hospitals in the regions for empirical choice of antibiotics in the treatment of child bacteremia.

Methods

A retrospective study was conducted in Hawassa University comprehensive and specialized hospital (HUCSH). HUCSH is a teaching hospital providing both inpatient and outpatient services to more than 5 million people in the region. The microbiology lab is the only regional referral laboratory where patients from the region as well from parts of the region referred for bacteriological. All bacteremia-suspected patients were sent to microbiology lab for blood culture diagnosis of bacteremia and sensitivity tests.

We retrieved all microbiological reports on bacterial pathogens from January first 2019 to March 30, 2020. This study was approved by IRB of Hawassa University College of Medicine and health sciences. Administrative permission to access data was requested through the hospital laboratory manager of Hawassa University College of Medicine and health sciences. All data obtained in the course of the study were reserved confidential and used only for this study. We have no inclusion criteria except we reject unsuitably recorded data's like illegible or incomplete in a sense of either age or final culture results.

Bacteriological investigation

Our laboratory bacteriological analysis follows all standard operation procedures based on the Clinical and Laboratory Standards Institute's (CLSI). The collected clinical samples were submitted to the laboratory and processed following standard procedures. Hence according to CLSI, a 1-2 mL blood sample was collected aseptically and added to tryptic soya broth in a ratio of blood to broth 1:9 and incubated at 35-37°C. Visual inspection for possible microbial growth; like hemolysis, turbidity, gas production and pellicle formation was assessed until 5th days to report no bacterial growth. Turbid broth cultures were sub cultured into MacConkey agar, Blood agar plates and Chocolate agar plates (Oxoid™ Ltd, Thermo Fisher Scientific, and Waltham, MA, USA) and incubated at 37°C for 24–48 hours. The Chocolate agar-incubated cultures were carried out in a microaerophilic atmosphere by using a candle jar. Bacterial identification was done primary based on colony characteristics and Gram-stain reaction followed by proper biochemical tests. Antimicrobial susceptibility profile of isolates was determined by Kirby- Bauer disc diffusion method and the results were interpreted according to CLSI guidelines [7]. The following antibiotics were used; Pencilin (10 µg), Cotrimoxazole (25 µg), Tetracycline (30 µg), Amoxicillin-Calvulanic acid (20/10 µg), Ceftazidime (30 µg), cefotaxime(30 µg), Doxycycline(30 µg), Chloramphenicol, ceftriaxone (30 µg), ampicillin (10 µg) Erythromycin(15µg), gentamicin (10 µg), meropenem (10 µg, Amikacin(30 µg), ceftriaxone (30 µg)

Quality control

Our microbiology lab performs quality control of all culture system by using *E. coli* (ATCC-25922), *S. aureus* (ATCC- 25923) and *P. aeruginosa* (ATCC-27853) as positive and negative controls respectively. In addition the National laboratory, Ethiopian Public Health Institute (EPHI) supervised as well supplies all necessary quality issues,

Data analysis

The data was entered and analysed using SPSS version 20(IBM Corporation, Armonk, NY, USA). Descriptive statistics like frequency and percentages of categorical variables was calculated then compared using Chi-square test. The odds ratio (OR) with 95% confidence interval (95% CI) were calculated to estimate the relationship of outcome with independent variables. The significance level was $p < 0.05$.

Result

We processed a total of 323 blood cultures from child who were suspected for blood stream infection during the study period. The ratio of male were 172 (53.3%) and 151 (46.7%) females. From all processed clinical samples, 116/323 (35.9%) were culture positive for invasive bacterial infection. Among recorded 116 bacterial infections, 62 (53.4%) were male and 54 (46.6%) female. Dominant number of patients, 142 (44%) as well the highest positivity rate, 52.6% was recorded among the age group of 0–28 day neonates, $p = 0.003$ (Table 1).

Table 1
Age and sex distribution of under five children with blood stream infection

Demographic features	Positive No. (%)	Negative No. (%)	Total No. (%)	χ^2 (P-value)
Sex				
Male	62 (53.4)	110 (53.1)	172 (53.3)	0.96(0.003)
Female	54 (46.6)	97 (46.9)	151 (46.7)	
Age group				
0–28 day	61 (52.6)	81 (39.1)	142 (44)	11 (0.003)
29 day - 12 months	37 (31.9)	60 (29)	97 (30)	
1–5 year	18 (15.5)	66 (31.9)	84 (26)	
Total	116 (35.9)	207 (64.1)	323 (100)	

Bacterial Isolates

In this study a total of 116 bacteria were documented of these 62(53.4%) were gram positive bacteria. The frequent isolate were; *CoNS* 29 (24.8%), *Klebsiella pneumoniae* 25 (21.4%), and *S. aureus* 21 (17.9%) while *proteus* and *entrobacter* with 2(1.7%) were the least isolate found (Fig. 1). From

the isolated, Gram-positive bacteria were more prevalent than Gram-negative bacteria.

Table 2
Distribution of isolates from under five children with blood stream infection

variables	Total %	Bloodstream infection, n (%)	OR (95% CI)	p-value
sex				
male	172(35.3)	62 (36)	1.1 (0.64–1.6)	0.952
female	151(46.7)	54 (35.8)	1	
Age group				
0–28 day	142(44)	61 (43)	2.8 (1.5–5.1)	0.001
29 day - 12 months	97(30)	37 (38.1)	2.26 (1.2–4.4)	0.016
1–5 year	84(26)	18 (21.4)	1	

Antibiotic Resistance Of Gram Positive

As antibiotic resistancesummaries of gram positive bacterial isolates shown in Table 3, most of the isolates recorded resistance greater than 60% for Penicillin, Tetracycline and Erythromycin. *S. aureus* and *CoNS* show the list resistance to Ceftriaxone, Cefotaxime and Meropenem while commonly used drugs shows highest resistance. *S. aureus* also show highest resistances to, Penicillin, Tetracycline and Erythromycin. Similarly *Enterococci* reported list resistance to Ceftriaxone, Meropenem and Doxycycline.

Table 3
Antimicrobial resistance patterns of gram positive bacteria

Antibiotics	<i>CoNS</i> 29 (%)	<i>S.aureus</i> 21 (%)	<i>Enterococcus</i> 5 (%)	<i>S. pyogens</i> 7 (%)	Total n (%)
Penicillin	17(58.6)	15 (71.4)	3(60)	3(42.8)	38 (61.3)
Tetracycline	-	17(81)	5(100)	4(57.2)	26 (78.8)
Amoxicillin and Calvulanic acid	6(20.6)	4 (19)	1(20)	3(42.8)	14 (22.6)
Amikacin	5 (17.3)	5 (23.8)	1(20)	1(14.3)	12 (19.4)
Ceftazidime	6(20.6)	7 (33.3)	2(40)	2(28.6)	17 (27.4)
Cefotaxime	5 (17.3)	2 (9.5)	2(40)	1(14.3)	10 (16.1)
Cotrimoxazole	14(48.3)	8(38)	3(60)	4(57.2)	39 (62.9)
Chloramphenicol	12 (41.4)	9(42.8)	1(20)	-	22(40)
Ceftriaxone	1 (3.5)	6 (28.5)	0	1(14.3)	8(12.9)
Gentamicin	4 (13.8)	13(61.9)	3(60)	3(42.8)	23 (37)
Meropenem	1 (3.5)	1(4.7)	1(20)	1(14.3)	4(6.4)
Erythromycin	18 (62)	15 (71.4)	4(80)	-	37(67.3)
Doxycycline	3 (10.5)	2 (9.5)	2(40)	1(14.3)	8 (13)
Ciprofloxacin	5 (17.3)	2 (9.5)	-	1(14.3)	8(14)

Antibiotic Resistance Pattern Of Gram Negatives

Yet again the most frequent isolate, *K.pneumoniae* recorded the high resistance almost for all common antibiotics mainly to ampicillin, Ceftazidime and Ciprofloxacin however, least resistance documented to Chloramphenicol and Cefotaxime. In contrast *P.aeruginosa* and *E.coli* confirmed highest resistance to Chloramphenicol although still they showed high resistance for the rest of other antibiotics. Ceftriaxone seems the least resisted drug for *E. coli* and Cefotaxime and Ceftriaxone appears least resisted by other isolates of gram negatives (Table 4).

Table 4
Antimicrobial resistance patterns of gram negative bacteria

Antibiotics	<i>K.pneumoniae</i> 25(%)	<i>Paeruginosa</i> 9 (%)	<i>E.coli</i> , 6 (%)	<i>Citrobacter</i> 7 (%)	<i>Salmonella</i> <i>entica</i> , 4 (%)	<i>Entrobacter</i> <i>spp</i> 2(%),	<i>P.mirabilis</i> 2(%)	Total, n(%)
Ampicillin	21(84)	8(88.8)	4(66.6)	5(71.4)	3 (75)	2(100)	1(50)	44 (80)
Amoxicillin and Calvulanic acid	15(60)	7(77.8)	3(50)	4(57)	2(50)	1(50)	1(50)	33(60)
Cefepime	17(68)	4(44.4)	3(50)	6(85.7)	2(50)	1(50)	1(50)	34 (61.2)
Cefotaxime	9(36)	5(55.5)	2(33.3)	3(42.8)	1(25)	0(0)	0(0)	20(36.4)
Cotrimoxazole	12(48)	3(33.3)	3(50)	4(57)	2(50)	1(50)	0(0)	25(45.5)
Chloramphenicol	7(28)	7(77.8)	3(50)	4(57)	1(25)	1(50)	1(50)	24(43.6)
Ceftriaxone	17(68)	4(44.4)	2(33.3)	2(28.6)	3(75)	0(0)	0(0)	28(50.9)
Gentamicin	17(68)	5(55.5)	2(33.3)	2(28.6)	2(50)	0(0)	2(100)	30(54.5)
Ciprofloxacin	18(72)	6(66.6)	3(50)	4(57)	2(50)	0(0)	1(50)	34 (61.2)
Ceftazidime	18(72)	3(33.3)	4(66.6)	5(71.4)	3(75)	2(100)	1(50)	36(65.5)
Amikacin	12(48)	3(33.3)	3(50)	4(57)	2(50)	1(50)	0(0)	25(45.5)

Discussion

Bacterial blood stream infection of children is one of the most serious problems worldwide[2]. The lack of proper microbiological analysis in developing country like Ethiopia has challenged the process of reducing the burden.

This study revealed that a highest prevalence of (35.9%) bacterial BSI among children compared to similar studies in different corner of the country; Jimma 8.8%[8], Addis Ababa 32.8%[9] and other African countries like Tanzania 14.2%[10]; 24%[11], Gabon 17%[12], Burkina Faso 6%[13] in S. Africa 5.5% [14]; 5.7%[5] and among Iranian neonates 6.4% [15]. Our results are comparable to study done in Gondar, northern Ethiopia (39.5.9%)[16]. While it was lower compared to the study done in Gondar 46.6%[17] among neonates suspected to sepsis. Possible reason for variation might be the variation in clinical indication for blood culture and patient age group. In our set up blood culture demanded after explicate diagnosis of other doubts due to the fact that blood culture is costly and take long time. Moreover poor effective hygiene practices and well-functioning environmental also poor patient hygienic practices might increase the rate of infection.

In Ethiopia, bacterial sepsis was reported as the leading cause of neonatal death [18]. One of the systematic review study in Ethiopia has reported that a pooled prevalence of neonatal sepsis in Ethiopia was 49.98%[19]. Likewise in this study higher rate of blood stream infection recorded with the odds of neonates being more positive in blood stream infection than other age group of under 5 children (OR, 3; 95% CI 1.5–5.1; p = 0.001) (Table 2). Most other study also reported neonates BSI higher compared to [16, 19].

Regarding isolate, the current study has found that almost 43% of the isolates were *CoNS* and *S. aureus* followed by *Klebsiella* 21.4% which is similar with other studies in Ethiopia, in Arsi[20] and Gondar[16] also with most of other studies in Africa. When we look report from African study, BSI study on neonatal in Tanzania reported that *S. aureus* 36.5% and *Klebsiella* 29.7% dominate all isolates recognized[21] there is also agreement with report from S. Africa were *S. aureus*, *Klebsiella* and *E. coli* are predominant isolate BSI among children[5]. Type of isolates in this study is still similar to that reported in other African studies for instant report from S. Africa shows predominate isolates *S. aureus*, *Klebsiella*[14] among blood cultured samples of children. Again In Zimbabwe, *CoNS* and *S. aureus*[22] were dominant. This might show sort of nosocomial infection due to procedural insertion of different medical device to child. At the mean time health workers poor effective hygiene practices and well-functioning environment that can source birth canal contamination of *Klebsiella* to neonatal [21]. Likewise to this study a systematic review study done in resource limited countries had also reported that Gram-negative organisms, *Klebsiella pneumoniae*[23] was dominant isolate from child blood culture. In the other hand study from Ghana reported non-typhoidal salmonellae was dominant[24]

As usual gram positive isolates shows highest level of resistance to penicillin 61.3.0% and tetracycline 78.8% which is similar with report in Jimma[8] and Gondar[16] also comparable with report of systematic review which covers most of the regions found in Ethiopia [25]. *S. aureus* and *CoNS* shown high level of resistance penicillin (59%, 71.4%), Amoxicillin and Calvulanic acid (20.6%, 19%), tetracycline (80%) and Erythromycin (62% 71.4%), which is again similar with systematic review done in Ethiopia [26]. However less level of resistance was reported to Meropenem (6.4), Ceftriaxone (13%) and doxycycline (13%) that is comparable with previous study in the region[27].

The overall BSI rates of gram negative isolates were 17% and almost all resisted Ampicillin (80%), Ciprofloxacin (61.2%) and Ceftazidime (65.5%). As displayed in 4, most of the isolates are resistant for the tested antibiotics 36% -80% of resistance. The predominate isolate, *K.pneumoniae* have shown leaser resistance tocefotaxime and chloramphenicol while *P. aeruginosa* and *E.coli* resist more than 50%. Though comparison of our finding with others report is difficult due to the fact that antibiotic resistance vary place to place in addition to lack of consistency in the measurement and reporting of susceptibility data makes it difficult to compare findings among different countries and laboratories, sometimes even within one country[28]. But most of the study revealed high resistance of gram negatives. In fact in resource limited countries large regional variations in resistance rates to locally prescribed antibiotics is common [16, 23].Due to concerning other gram negative isolates we are unable to discuss on rate of resistance due to leaser number of observation.

Conclusion

In general the finding in this study indicates high level of BSI among under-five children. A high drug resistance to locally used antibiotics also surge the challenge. Therefore we recommend for local health professionals to see choicesof best drug fromreported compiled date for their routine empirical treatment of blood stream bacterial infections. Furthermore the hospital administrators should facilities mainly on having functioning infection prevention and control programmes, effective hygiene practices and precautions, along with a clean, well-functioning environment and equipment also educating patient about effective hygiene practices.

Limitations

First as it is retrospective study from registered in laboratory log book we didn't got different documented independent variables for possible causal effect association. Hence we did not investigate risk factor for infection as well for drug resistance. Second, due to lack of appropriate facility anaerobicwere not included.Third we have excluded vancomycin resistance test due to lack ofuniformity.

Abbreviations

ATCC: American type culture collection; BSI:blood stream infection; CLSI:Clinical and laboratory standard Institute; CoNS:Coagulase-negative staphylococcus; HUCSH:Hawassa University Comprehensive Specialized Hospital; IRB:Institutional Review Board; SNNPR:Southern Nation Nationalities' and peoples' region; SOP:Standard operating procedure; SPSS:Statistical package for social sciences; WHO:World Health Organisation

Declarations

Ethics approval and consent to participate

This study was approved by IRB of Hawassa University College of Medicine and health sciences. Administrative permission to access data was requested through the hospital laboratory manager of Hawassa University College of Medicine and health sciences. We have got waiver from hospital laboratory and all data obtained in the course of the study were reserved confidential and used only for this study.

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Authors' contributions

All authors; MH, TA, EA, AA, MA, and EM: participated in conception of the study, collected the data,interpretation of data and drafting the manuscript. MH and TA: design of study and critically reviewing the manuscript for important intellectual content. All authors read and approved the final manuscript for publication.

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Competing of interests

The authors declare that they have no competing interests.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author on upon reasonable request

Consent for publication

Not applicable.

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Figures

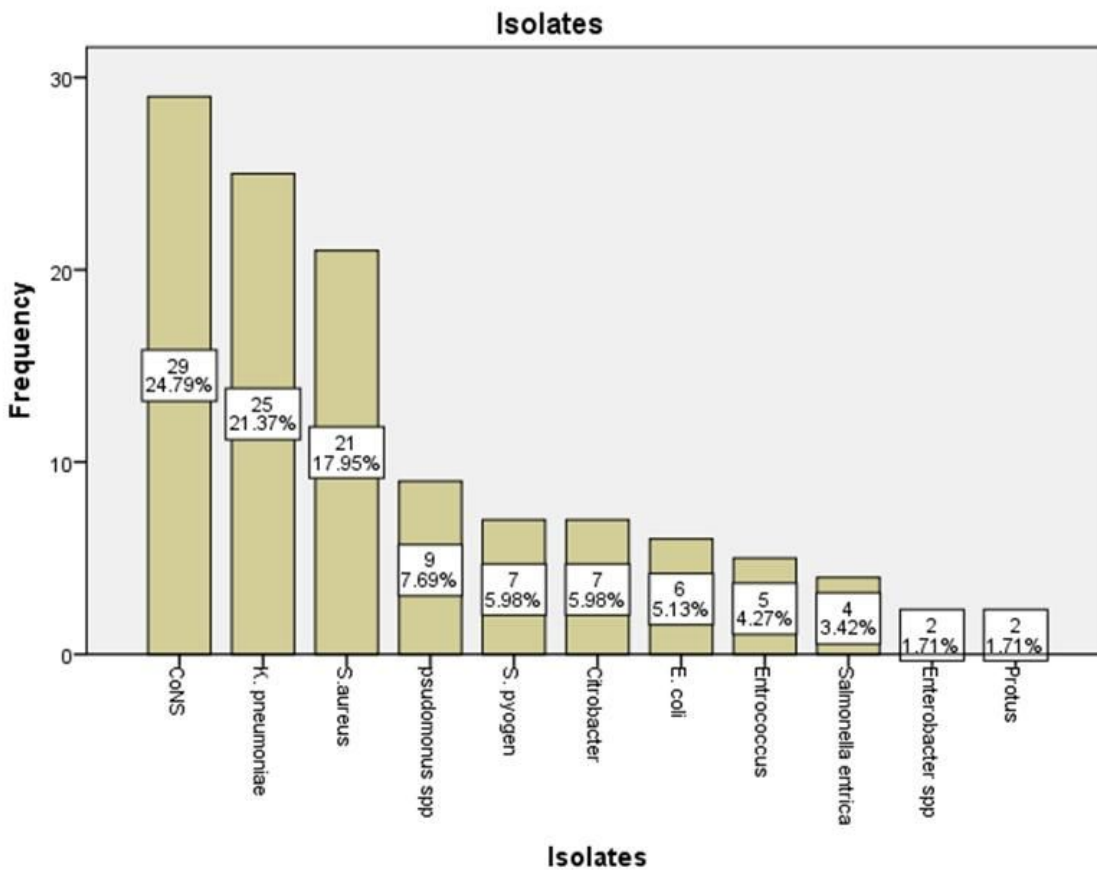


Figure 1

The frequent isolates from under five children with blood stream infection