

Original Research Article

Study of the utility of blood culture in febrile children aged between 3 months to 12 years admitted in a tertiary centre

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ABSTRACT

Background: Fever, the most common complaint that led patients to seek healthcare, indicates an underlying infection which could either be simple self-limiting viral infections or life threatening bacterial infections. It's greatest challenge is the risk of occult bacteraemia, for which blood culture is the gold standard for the diagnosis. Objectives was to determine the proportion of blood culture positives among febrile children and to describe the bacteriological profile and antibiogram of blood culture isolates.

Methods: A cross sectional study was done in the Department of Paediatrics and Microbiology, RIMS Hospital, Imphal. After obtaining consent (verbal assent in >7 years), blood culture samples were drawn from 200 children aged between 3 months to 12 years. The data was analysed using descriptive statistics. Chi square test was used and p-value of less than 0.05 taken as statistically significant.

Results: Culture positivity was seen in 17 cases (8.5%) of which, participants who were less than 1 year of age and without proper immunisation record showed the highest positivity rate. It was higher in fever with localizing signs (9.2%) than those with fever without focus (7.8%). Gram positives constituted 11 (64.7%) of the isolates while 35.3% were Gram negatives. *Staphylococcus aureus* was the only Gram positive isolate. Of them, 4 were MRSA but all the strains were sensitive to Vancomycin and Linezolid. The most common Gram negative isolate was *Acinetobacter spp* and 80% of them were sensitive to Aminoglycosides while most of the Gram negatives were resistant to Ampicillin and 3rd generation Cephalosporins. All *Acinetobacter spp* were sensitive to Carbapenems but the only *Pseudomonas spp* isolated was sensitive only to Colistin.

Conclusions: Blood culture positivity rate is relatively low in this study. However, studies with larger sample sizes are recommended to validate the findings. We emphasise the need for antibiotic stewardship.

Keywords: Antibiogram, Bacteraemia, Blood culture, Blood stream, Infections fever with localising signs

INTRODUCTION

Fever is one of the most common complaint that led patients to seek healthcare. Fever is defined as a rectal temperature of $\geq 38^{\circ}\text{C}$ (100.4°F), and a value of $>40^{\circ}\text{C}$ (104°F) is called hyperpyrexia.^{1,2} Body temperature fluctuates in a defined normal range ($36.6\text{-}37.9^{\circ}\text{C}$ / $97.9\text{-}100.2^{\circ}\text{F}$ rectally), so that the highest point is reached in early evenings and the lowest point in the morning. Any

abnormal rise in body temperature should be considered a symptom of an underlying condition.^{2,3}

Fever may herald the onset of a serious and life-threatening disease such as meningitis, pneumonia or it may be the sole manifestation of a mild self-limited viral infection.⁴ Several studies confirm the observation that most acute febrile illnesses in children are of presumed viral etiology and require little more than supportive

therapy. Hence, the most important issue for physicians is to focus on the fever's etiology and to rule out serious diseases as the mortality may be as high as 30% if there is bacteremia.^{5,6} Consequently, early diagnosis and appropriate treatment of blood stream infection (BSI) can make the difference between life and death.⁷

Although distinguishing a child with a viral illness from one with bacterial disease is usually not difficult, there may be considerable overlap in the clinical appearance of children with fever without source due to viral etiology and those with occult bacterial infection. Investigations like complete blood cell count, urine analysis, C-Reactive Protein (CRP) may be useful in determining bacterial infection, but blood culture remains the gold standard method for detection of presence of pathogen in children suspected of serious bacterial infection.⁷

Blood cultures remain the mainstay of laboratory diagnosis of bloodstream infections (BSI) in infants and children. Recovery of a pathogen is always advantageous, as it confirms the diagnosis of bacteremia and allows identification and susceptibility testing on the organism to optimize antimicrobial therapy and duration. A negative blood culture is just as important, as it rules bacteremia and prompts continued investigation of other infectious or non-infectious etiologies or cessation of unnecessary empirical antimicrobial therapy.⁸

Considering this background, this study was conducted to reduce BSI related mortality by early identification of etiological agents and administration of targeted antimicrobial therapy. This study will also help physicians in providing empirical therapy based on the prevalent organisms and their antibiotic sensitivity pattern and developing rational antibiotic policy.

Aims and objectives was to determine the proportion of blood stream infection among febrile children aged between 3 months to 12 years, to identify etiological agent causing blood stream infection and to study antibiotic susceptibility pattern of the bacterial isolates.

METHODS

This was a cross sectional study carried out in the Department of Pediatrics and Microbiology, RIMS, Imphal. Study population includes Children 3 months to 12 years of age admitted in a tertiary centre.

Inclusion criteria

- Hospitalised children with fever for at least 3 days
- Those who gave consent/assent

Exclusion criteria

- Patient with primary or secondary immunodeficiency
- Patient with indwelling catheters
- Patient taking immunosuppressants.

- Patient with malignancy or tuberculosis
- Patients with heart diseases (congenital/acquired, with or without prosthetic valves)

Sample size was 200 by taking 23.1% as culture positivity rate as per Mehrotra et al.

Study variables

Independent criteria

- Demographics profiles - age, gender, immunization status
- Presence of fever and administration of antibiotic before admission
- Duration of fever
- Degree of fever
- Presence of associated symptoms (cough, rash, ear ache, altered mental status, chills and rigor, joint pain, seizure, dysuria, sore throat)
- Antibiotic treatment at home.

RESULTS

In this study on the utility of blood culture in febrile children aged between 3 months to 12 years in this centre, authors had enrolled 200 consenting patients and the blood culture samples were taken as laid down in the protocol. Of the 200 culture reports, 179 (89.5%) were sterile, 17 (8.5%) positive while 4 (2%) were reported as contaminated as shown in Table 1. Deducing the bacteriological profile further, amongst the culture positive reports, *Staphylococcus aureus* was 64.7% (N11), *Acinetobacter spp.* constitutes 29.4% (N5) while *pseudomonas* was grown in only 5.9% (N1) as shown in Table 2.

Table 1: Distribution of participants by blood culture report (N=200).

Blood culture report	N	Percentage
Positive	17	8.5
Sterile	179	89.5
Contaminated	4	2.0

Table 2: Distribution of participants by bacterial profile (N=17).

Bacterial profile	N	Percentage
<i>Staphylococcus aureus</i>	11	64.7
<i>Acinetobacter spp.</i>	5	29.4
<i>Pseudomonas aeruginosa</i>	1	5.9

The antibiotic sensitivity pattern showed that the only Gram-positive organism identified, *Staphylococcus aureus*, was 100% sensitive to Vancomycin and Linezolid although 4 (36.3%) were identified as MRSA with Cefoxitin disc by Kirby-Bauer diffusion method. It was also observed that 54.5% were resistant to both Penicillin

and Azithromycin respectively while 18% to multidrug resistant. Cotrimoxazole. Most of the Gram-negative isolates were

Table 3: Distribution of participants by antibiotic sensitivity (N=17).

Antibiotics sensitivity	<i>Staphylococcus aureus</i> (n=11)		<i>Acinetobacter spp</i> (n=5)		<i>Pseudomonas aeruginosa</i> (n=1)		Total	
	S	R	S	R	S	R	S	R
Gentamicin	10	1	3	1	0	1	13	3
Vancomycin	11	0	0	0	0	0	11	0
Linezolid	11	0	0	0	0	0	11	0
Ciprofloxacin	5	6	5	0	0	1	10	7
Amikacin	4	1	4	1	0	1	8	3
Clindamycin	8	3	0	0	0	0	8	2
Amoxi-clav	6	5	-	-	0	0	6	5
Erythromycin	6	5	-	-	0	0	6	5
Cefoxitin	7	4	-	-	0	0	7	4
Imipenem	0	0	5	0	0	1	5	1
Piperacillin/Tazobactam	10	1	3	2	0	1	13	4
Colistin	0	0	5	0	1	0	6	0
Cefipime	0	0	3	2	0	1	1	3
Ceftazidime	0	0	3	2	0	1	3	3
Meropenem	0	0	4	1	0	1	4	1
Tobramycin	0	0	4	1	0	1	0	1
Aztreonam	0	0	4	1	0	1	1	2
Netilmicin	0	0	4	1	0	1	0	1
Cefoperazone/Sal-bactam	0	0	4	1	0	1	1	2
Doripenem	0	0	5	0	0	0	5	0
Levofloxacin	0	0	3	2	0	0	3	2
Tigecycline	3	8	0	0	0	1	3	9
Ceftazidime	0	0	3	2	0	0	3	2
Ampicillin	1	10	1	4	0	0	2	14
Tetracycline	10	1	4	1	0	0	14	2
Doxycycline	3	8	0	0	0	0	3	8
Azithromycin	5	6	0	0	0	0	5	6
Chloramphenicol	6	5	2	3	0	0	8	8
Penicillin	5	6	0	0	0	0	5	6
Cotrimoxazole	9	2	1	4	0	0	10	6

Table 4: Patient characteristics among blood culture positive (N=17).

Characteristics	N	Percentage (%)	
Gender	Male	10	58.82
	Female	7	41.18
Age (In months)	3-12	11	64.72
	13-60	4	23.52
	>60-120	2	11.76
	>120		
Immunisation status	Completely immunised	1	5.90
	Partially immunised	10	58.82
	Non immunised	6	35.28
Antibiotic used	5	29.41	
Presence of fever localising signs	10	58.82	
Duration of fever / Median (In days)	6.5 (4-9)		
Temp median range (In Fahrenheit)	101.6 (101.1-102.2)		

Ampicillin (80%) and Chloramphenicol (60%) were the least effective drugs. Majority of the Gram-negatives were sensitive to Imipenem (83.3%) and Gentamicin and Amikacin (66.7%). Of those cultures where *Acinetobacter spp* were isolated, 80% of them were sensitive to aminoglycosides. The only *Pseudomonas spp* was sensitive only to Colistin as shown in Table 3.

The gender characteristics amongst the culture positives showed a slightly higher incidence in males (58.8%) over females (41.1%). Age-wise, infants showed a higher positivity rate over other age groups as 11 (64.7%) of the infants showed positive blood cultures while 4 (23.5%) and 2 (11.7%) were of the age groups of 13-60 months and >60-120 months respectively. The children who completed their immunisation as schedule showed a much lower positivity rate at 5.9% (N1) over the partially immunized (58.8%) and the unimmunized (35.2%). 5 (29.4%). Of the culture positives, 5 (29.4%) had already received over-the-counter antibiotics before being sampled 10(58.8%) presented with localising signs of infection. The mean temperature in blood culture positive group was 38.7°C and the mean duration of fever was 6.5 days. It is worth mentioning that 49% of the study population had already received antibiotic at home prior to hospital admission as shown in Table 4.

DISCUSSION

Our study recruited 200 febrile children aged between 3 months and 12 years to find out the rate of blood stream infections, prevalent organisms and the pattern of antibiotic susceptibility. The participants who were admitted in the Paediatrics ward with fever for at least three days were subjected to blood culture before antibiotic therapy was initiated. It involved history taking, clinical assessment and laboratory tests. The study has found that bacteraemia was not a common cause of fever among febrile under twelve children admitted in RIMS, Manipur, India. The prevalence of bacteraemia was only 8.5%. Thus, fever could be attributed to other causes like viral and fungal infections.¹ The other attributable cause could be the introduction of vaccines in these age groups. The mean temperature in blood culture positive group was 38.7°C and the mean duration of fever was 6.5 days.

It is worth mentioning that 49% of the study population had already received antibiotic at home prior to hospital admission. Shah SS et al also reported that 38% of the participants used antibiotics before evaluation.² The lower rate of bacteraemia may be contributed by less sample size, study with larger number of participants for better interpretation of prevalence of bacteraemia is required.

The blood culture positivity of 17 (8.5%) seen in our study was in contrast with Arora U et al and Sharma M et al who reported 20% and 33.9% respectively.^{3,4} But this finding is similar to a study conducted by Msafiri et al, in

which the prevalence of bacteraemia was 10.8%.⁵ The incidence of bacteraemia varied widely among different studies conducted in India. Differences in results could be because the other studies included newborn and older children with suspected sepsis where the chance of blood culture positivity is much higher.^{3,6} Of those cultures where *Acinetobacter spp* was isolated, 80% of them were sensitive to aminoglycosides. This was similar to study done by Vaghela HG et al where majority of *Staphylococcus aureus* was resistant to Penicillin but highly sensitive to Gentamicin.⁶ They also found that *Acinetobacter spp* were sensitive to Carbapenems. The only *Pseudomonas aeruginosa* identified was sensitive only to Colistin. The only possible explanation for this is easy availability of over the counter and irrational use of antibiotic in certain health settings in the study area.

Male dominance was seen in this study with 122 males and 78 females (1.5:1) and more number of blood culture positive was seen in male (64.7%). This finding was consistent with the findings by Salameh KM et al which showed the ratio as 1.3:1.⁷ The male gender dominance in this could be attributed to the male gender preference in the society.

The maximum number of children belonged to 1-5 years of age (39%) followed by children less than 1 year of age (34%). The incidence of blood stream infection was much higher in the first year of life than in older children (64.7%) which was similar to findings in Mc Gowen JE et al.⁸ This is could be due to the immature and less effective adaptive immune system compared to older children. Similar finding was observed by Kumar YG et al where serious blood stream infection constituted 67.05% among febrile infants.⁹

The only Gram positive identified, *Staphylococcus aureus* was 100% sensitive to Vancomycin and Linezolid although 4 (36.3%) were identified as MRSA with Cefoxitin disc by Kirby-Bauer diffusion method. It was also observed that 54.5% were resistant to Penicillin, 54.5% to Azithromycin and 18% to Cotrimoxazole. This finding is similar to that of Tiwari DK et al, where 77.78% of *Staphylococcus* were resistant to penicillin and 33.33% were MRSA.¹⁰

It was also observed that, among the 17 positive blood cultures, the incidence of Gram positive organism was 64.7% while 35.3% of the isolates were Gram negative. *Staphylococcus aureus* was the predominant organism identified 11 (64.7%) followed by *Acinetobacter spp* 5 (29.4%) and *Pseudomonas aeruginosa* 1 (5.8%). This finding was in accordance with Eshwara VK et al, where 52.67 % of the isolates were Gram positive bacteria and 47.33% were Gram negatives.¹¹ But in most studies, Gram negative organisms have taken over the Gram positive especially in the hospital settings and among young infants. Eshwara VK et al, also reported that *Staphylococcus aureus* was a significant cause of BSI and 54% was MRSA BSI.¹¹ Most of the Gram-negative

isolates were multidrug resistant. Ampicillin (80%) and Chloramphenicol (60%) were the least effective drugs. Majority of the Gram negatives were sensitive to Imipenem (83.33%) and Gentamicin and Amikacin (66.7%). Majority of the participants (60%) presented with localizing signs/source, the commonest being cough and dyspnoea. Out of 17 culture positives, 11 (64.7%) occurred with a source. Greehow TL et al, and Murillo TA et al had shown similar findings where 77% of bacteraemia occurred with a focus.^{12,13} Baraff LJ et al, also had similar findings.¹⁴ Parental pressure for performing unnecessary testing and requesting unnecessary antibiotics for what appears to be routine viral illness remains a major problem today. Many parents have been conditioned to believe that testing and antibiotics are a necessary part of the management of fever, considering the low rate of culture positivity and the clinicians suspicion for viral illnesses.¹⁵ Special attention should be directed to CRP, WBC and Hb when selecting patients for antibiotic treatment in the emergency department.¹⁶ In this study, authors are able to know the common etiological agent involved in sepsis as does Brockmann VP et al.¹⁷ Authors were able to identify the antibiotic sensitivity patterns among various organisms which provide valid data for initiation of appropriate treatment.¹⁸

Our study has certain limitations. Most of the patients were already on over-the-counter antibiotics by the time they reported to the facility. Another limitation was the lesser sample size. Studies on larger sample size is recommended for better interpretation of the results. The studies on the health care associated blood stream infections is also needed at present. Other authors like Bressan S et al also suggested the need for a more conservative approach in infants and children.¹⁹ It should also be noted that our finding of low bacteraemia do not apply to children admitted to intensive care setting where the rate of bacteraemia is nearly two fold higher.

CONCLUSION

The rationale for obtaining blood cultures in febrile children relates to the ability to give target therapy when the causative organism is identified. However, instituting early empirical antibiotic therapy based on the prevalent organisms and their susceptibility pattern is an integral part of initial treatment of sepsis. The blood culture positivity rate was low as compared to studies done in other parts of the country. Nonetheless, isolation of high rates of MRSA and the detection of highly resistant strains of Gram negatives warrants continuous monitoring. Poor infection control practices coupled with inappropriate and irrational use of antibiotics are the main culprits for the widespread antimicrobial resistance. Strict adherence to infection control practices and following the core principles of antibiotic stewardship would definitely go a long way to help prevent emergence of resistance. However, a study with larger sample size is recommended to consolidate the findings of this study.

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