BLOOD CULTURE AND BACTEREMIA PREDICTORS IN INFANTS LESS THAN ONE YEAR OF AGE WITH FEVER WITHOUT SOURCE (FWS)

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ABSTRACT: BACKGROUND: Fever is an extremely common occurrence in paediatric patients and the most common cause for a child to be taken to the doctor. Most of the infants less than 1yr of age have fever without focus. The aim of the study is to document the rate of bacteremia and their predictors in infants with fever without source. **OBJECTIVES:** To assess the rate of bacteremia in febrile infants attending OPD and inpatient department of pediatrics at a tertiary hospital and to analyze factors that predicts the possibility of having serious bacterial infection. METHODS: This is a hospital based prospective study carried out for a period of 1yr. The study included 85 infants from 1 month to 12 months of age who presented with fever without source (FWS). All infants with fever without source were subjected to septic screen, which includes CBC, CRP, Chest x-ray Urine routine, urine culture and Blood culture and sensitivity. Percentage of blood culture positivity among those febrile infants were calculated and tabulated. Most frequently isolated pathogen was documented. Predictors of serious bacterial infection among febrile infants were documented. **RESULTS:** Among 85 Febrile infants 57 infants have serious bacterial infection which constitutes around 67.05%. Among 57 Serious Bacterial Infection (SBI) patients, 35 patients had positive chest x-ray. 22 patients have abnormal leucocyte count. Positive blood culture and urine culture were 38.6% and 29.6% respectively. The p value for blood culture and urine culture were statistically significant. The most frequently isolated pathogen was Escherichia coli (E.coli), followed by staphylococcus aureus (Staph. aureus) in blood culture. The most frequently isolated pathogen was Escherichia coli in urine culture. CRP and Platelet count were not good predictors of bacteremia in febrile infants. CONCLUSION: A positive blood culture rate of 38.9% was found in infants with FWS. CRP and platelet count were not good bacteremia predictors in infants with fever without source. We recommend obtaining a blood and urine culture in infants with FWS, particularly those with elevated leucocyte count and positive chest x-ray.

KEYWORDS: Fever, Young infant, Blood culture, Diagnostic tests, Bacteremia.

INTRODUCTION: Fever is the most common reason for healthy young children to be brought to a pediatric emergency department. Most of these infants have fever without source (FWS). Despite the fact that most cases of FWS are caused by viral infections, for which no treatment is required, they can also be caused by a severe underlying bacterial infection, and mainly in infants less than 1yr.^{1,2,3} Infants eventually diagnosed with SBI can appear well and have nonspecific signs.⁴ Several management protocols have been designed to evaluate these children to identify those at high risk of developing SBI. The traditional approach to febrile young infants involves performing a white blood cell count (WBC) and blood and urine cultures, administering antibiotics, and admitting them to hospital.⁴⁻⁵ Recent articles analyzing the usefulness of classic indices such as WBC, absolute neutrophil count (ANC), and C-reactive protein (CRP) for predicting the risk of an SBI at this age have

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had Conflicting results.^{6,7,8} Infants have commonly been split into following 2 different age groups: neonates (0–28 days old), infants (1month-1yr). Serious bacterial infection (SBI) is found in 10% to 15% of febrile infants younger than 3 months.^{8,9,10} No data's are available to assess the rate of bacteremia in infants less than 1yr of age. The rate of SBI in young infants has apparently changed in recent years, as have the pathogens producing them.^{11,12,13,14} Group B Streptococcus, for example, a classic bacterial pathogen in these children, has been associated with high rates of meningitis (39%), no meningeal infection foci (10%), and sepsis (7%).¹⁵ The use of intrapartum antibiotic prophylaxis has reduced the incidence of early-onset infections caused by group B Streptococcus, but a parallel reduction in the incidence of late-onset diseases has not been reported.^{16,17,18} The early detection of urinary malformations using prenatal ultrasound and the introduction of the heptavalent pneumococcal conjugate vaccine¹⁹ have also decreased SBI rates in these patients.

OBJECTIVES: To assess the rate of bacteremia in febrile infants attending OPD and inpatient department of paediatrics at a tertiary hospital:

- 1. To analyze factors that predicts the possibility of having serious bacterial infection.
- 2. To describe the bacteria isolated in these children.

MATERIALS AND METHODS: This is a hospital based prospective study carried out for a period of 1yr (2010-2011). The study included 85 infants from 1 month to 12 months of age who presented with fever without source (FWS) attending OPD and inpatient department of pediatrics in our hospital (SMVMCH) which is a tertiary care center in Puducherry. Informed written consent has been taken from parents/guardians of the children.

Inclusion Criteria:

- 1. Infants with age between 1month and 1yr are included.
- 2. Infants with fever without source (FWS) are included.

Exclusion Criteria:

- 1. Infants with age less than 1month and >1yr.
- 2. Infants with obvious focus of infection.
- 3. Children whose parents refuse to consent.
- 4. Infants with chronic disorders or previous underlying diseases are excluded.

Our Pediatric Emergency Department algorithm for the management of infants less than 1yr of age with FWS recommends urine dipstick testing, CBC, CRP, blood culture, and urine culture for all children. Gram stain of urine is not routinely performed. We consider performing a chest x-ray, lumbar puncture, including Gram stain, bacterial culture, on an individual basis.

If an infant is well-appearing, and all ancillary tests appear to be normal, we recommend that the patient be discharged without antibiotic treatment after several hours of observation in the Pediatric Emergency Department, generally up to 24 hours after fever developed (This means that if an infant is brought to the Pediatric Emergency Department 6 hours after fever was first registered, this infant remains in our Observation Unit for about 18 hours for clinical evaluation). We recommend hospital admission for infants less than 1yr of age, those with abnormal laboratory tests and when the clinical situation worsens during the patient's stay in the Observation Unit.

DEFINITION:

- 1. FWS: Axillary or rectal temperature at home, or rectal temperature in the Pediatric Emergency Department, of _38°C, without catarrhal or respiratory symptoms/signs (Such as tachypnea) or a diarrheal process, in patients with normal physical examination, according to the diagnostic codes issued by the Spanish Society of Pediatric Emergencies (SEUP). 22 Infants were included even if fever was assessed by parents at home without using a thermometer.
- 2. Well-Appearing: Defined by a normal pediatric assessment after being evaluated by a pediatric emergency physician during the first hour after attending the Pediatric Emergency Department. Appearance, respiratory and circulatory items had to be classified as normal for infants to be classified as well-appearing, and data had to be reflected on the patient's charts.
- **3. Positive Blood Culture:** Blood culture from which a true bacterial pathogen was grown (Streptococcus pneumoniae, Neisseria meningitidis, Enterococcus, Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus, group A and B Streptococcus, Listeria monocytogenes, or Salmonella species). Staphylococcus epidermidis, Propionibacterium acnes, and diphtheroids grown from previously healthy immunocompetent infants (With no history of heart disease, ventriculoperitoneal shunt, indwelling catheter, or other prosthetic devices) were categorized as contaminants.
- 4. SBI: isolation of a bacterial pathogen from the cerebrospinal fluid (CSF), blood, or urine.
- **5. Bacterial Meningitis:** (a) positive CSF culture or CSF gram stain (b) positive blood culture with pleocytosis.
- 6. Occult Bacteremia: Positive blood culture in a well-appearing infant diagnosed with FWS.
- **7. Urinary Tract Infection (UTI):** Growth of more than 50,000 colony forming units/mm3 of a unique bacterial pathogen in a urine sample collected by bladder catheterization. Growth of 10,000 to 50,000 colony forming units/mm3 was also considered an UTI when associated with leukocyturia and or nitrituria.
- **8. Previously Healthy Infant:** To be classified as previously healthy, the patient must meet all the following criteria: born at term (After _37 weeks' gestation), not treated for unexplained hyperbilirubinemia, not hospitalized longer than the mother, not receiving current or prior antimicrobial therapy, no previous hospitalization, and no chronic or underlying illness.

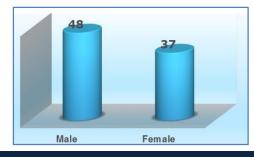
STATISTICAL ANALYSES: Statistical analyses were conducted using the Statistical Program for the Social Sciences version 15(SPSS 15) Data are expressed as the mean and standard deviation for quantitative variables or numbers and percentages for categorical variables. Continuous data were compared using the Student t test. Categorical data were examined using chi square test. Statistical significance was defined as P value< 0.05. Prevalence rates were expressed as a percentage with their respective confidence intervals (CI).

This study was forwarded by the Research Committee of the Pediatric Emergency Department and approved by the ethical committee of the college.

RESULTS: During the study period, 85 infants whose age is between 1 month and 1 yr with FWS were investigated and the results are documented below.

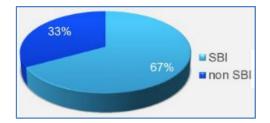
Sex wise Distribution of Cases:

- Total number of patients studied 85.
- Male 48 patients (56.47%).
- Females 37 patients (43.52%).



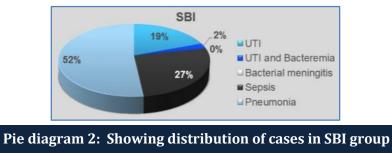
Bar diagram showing age wise distribution of cases

Distribution of cases	Number of cases	
SBI	57	
Non SBI	28	
Table 1: Distribution of cases in SBI Vs non SBI infants		



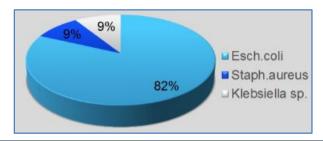
Pie-diagram 1: Distribution of cases in SBI V/s non SBI infants

SBI(57)	Number of Cases	
UTI	16	
UTI and Bacteremia	2	
Bacterial meningitis	Nil	
Sepsis	22	
Pneumonia	35	
Table 2: Showing distribution of cases in SBI group		



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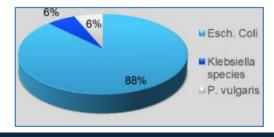
Isolated Bacteria	Number of Cases	
E. coli	18	
Staph. aureus	2	
Klebsiella species	2	
Table 3: Bacteria isolated from blood culture		



Pie-diagram 3: Bacteria isolated from blood culture

Isolated bacteria	Number of cases
E. coli	14
Klebsiella species	1
Proteus vulgaris	1
Table 4: bactoria isolat	

Table 4: bacteria isolated from urine culture



Pie-diagram 4: Bacteria isolated from urine culture

Variables	SBI (n=57)	Non-SBI (n=28)	P value	
Chest X ray	35(64.8)	6(19.4)	< 0.004**	
Abnormal CRP	34(63.0)	17(58.1)	0.817	
Anemic	41(75.9)	24(80.6)	0.788	
Abnormal TLC	31(57.4)	9(29.0)	0.014*	
Abnormal platelet count	17(31.5)	10(32.3)	1.000	
Positive blood culture	22(38.9)	4(12.9)	0.014*	
Positive urine culture	16(29.6)	1(3.2)	0.004**	
Table 5: Distribution of lab parameters in SBI Vs non SBI group				

* -95% CI, ** -99% CI.

DISCUSSION:

- Among 85 Febrile infants 57 infants have serious bacterial infection which constitutes around 67.05%.
- Among 85 febrile infants 48 infants were male and 37 infants were female.
- Among 57 SBI patients 16 cases had UTI, 2 cases had UTI with septicemia, 22 cases had sepsis, 35 cases had pneumonia.
- Among 57 SBI PATIENTS, 35 patients (64.8%) had positive chest x-ray whose p value is statistically significant.
- 57.4% patients had abnormal leucocyte count whose p value is statistically significant.
- Positive blood culture and urine culture were 22(38.9%) and 16(29.6%) respectively. The p value for blood culture and urine culture were statistically significant
- Out of 85 patients 76 patients are anemic, but there is no significant difference between SBI and non SBI group.
- Out of 85 patients 51 patients had positive CRP with no difference in SBI and non SBI group.
- 27 patients had abnormal platelet count with no difference in SBI and non SBI group.
- The most frequently isolated pathogen was E.coli, followed by staph. aureus in blood culture which is confirmed by standard biochemical test.
- The most frequently isolated pathogen was Escherichia coli in urine culture which is confirmed by standard biochemical test.
- White blood cell count was higher than C-reactive protein value (CRP) which was statistically significant.
- CRP and Platelet count were not good predictors of bacteremia in febrile infants.
- According to our results, the blood culture-positive rate is related to following 2 factors that can be easily evaluated when evaluating a febrile infant: general appearance and urine dipstick result. These factors can help identify infants at increased risk of having bacteremia.
- The blood culture-positive rate in febrile infants with a positive urine culture in our sample was significant, thus highlighting the importance of obtaining a blood culture in young febrile infants with a suspected UTI.
- The bacteremia rate detected in young infants with a UTI in previous studies was lesser, Bachur and Caputo¹⁶ reported an incidence of 21% for infants less than 1yr, whereas in our study bacterial isolation for septicemia and UTI were 38.9 and 29.6 respectively.
- In our study, CRP, and platelet count were not good predictors of bacteremia in febrile infants as test sensitivity in terms of positive blood culture was quite low and even the use of our low-risk SBI criteria gave a sensitivity of only 87%.
- Hsiao and Baker¹⁷ reviewed some of the recent literature on these classic markers In their 2005 manuscript, they concluded that WBC was neither sensitive nor specific as an indicator of bacteremia and other SBI in infants and that although CRP seems to be a reliable indicator of bacterial infection in children, no study have targeted young infants. But in our study there is a statistical significance of leucocytosis with positive blood culture.

Limitations of Study:

- 1. It is not a multicenter study, so the results might not apply to other populations.
- 2. The availability of a larger sample would have allowed us to analyze test performance levels in different age groups.

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The fact that all infants enrolled in this study were evaluated by an experienced pediatric emergency physician in the first hour after arriving in the emergency department can be considered a constraint as regards making these outcomes more widespread.

CONCLUSION:

- A positive blood culture rate of 38.9% was found in infants with FWS.
- CRP and platelet count were not good bacteremia predictors in infants with fever without source.
- We recommend obtaining a blood and urine culture in infants with FWS, particularly those with elevated leucocyte count and positive chest x-ray.

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