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Study of 'Fever without source' in Infants and young children

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Abstract

Background: Fever is one of the most common as well as trouble some manifestation in paediatric practice, both for paediatricians and parents. It is a simply noted an good marker of illness. Fever could be benign presentation of simple viral infection or it can be a presentation of life threatening bacterial infection like sepsis and pyogenic meningitis. It is a common, terrifying, physiologic response that has been the source of biggest complaint throughout the history of paediatric practice.

Methods: Analytical Cross-sectional Study.

Results: In present study, 60 cases were included. Age group between 1-3 months was 3.3% (n=2) of the patients, 4-36 months was 31.6% (n=19) of the patients and 37-60 months was 65% (n=39) of the patients. Female n=31 more than male n=29. Final diagnosis was of UTI in 11.6% (n=7) of the cases taken in the study. Sepsis was diagnosed in 10% (n=6), Rickettsial Fever was diagnosed in 13.3% (n=8), Typhoid fever was diagnosed in 11.6% (n=7), Dengue was diagnosed in 3.3% (n=2) and Kawasaki's disease was diagnosed in 5% (n=3) of the patients. Rest 45% (n=27) of the patients where cause was unknown.

Conclusion: UTI, Rickettsial infection and Enteric fever were among common cause of Fever without source. "Fever without source" pose a diagnostic dilemma and require detail evaluation to detect underlying etiology of infection, Systemic illness or Occult bacteremia. Majority of the patients no etiology was found in our study, In spite of thorough investigation.

Keywords: Fever, fever without source

Introduction

Fever is defined as rise of body temperature above the normal range and diurnal variation where body temperature is low in morning and on higher side during evening [1]. Or practical propose fever is defined as rectal temperature $>38.3^{\circ}\text{C}$ [1]. Fever without Source-Fever without focus comprises in the event of fever for under 7 days in a children whose clinical history and cautious physical assessment don't reveal the reason for the fever [17]. Less than 5 years of age children more susceptible for fever without source.

Fever is one of the most common as well as trouble-some manifestation in paediatric practice, both for paediatricians and parents. It is a simply noted and good marker of illness. In Greek 'Pyrexia'-meaning Fire, In Latin 'Febrile'-meaning Fever. It is a common, terrifying, physiologic response that has been the source of biggest complaint throughout the history of paediatric practice.

Fever often occurs in response to infection, inflammation and trauma. However, this view of fever is merely an oversimplification as a growing body of evidence now suggests that fever represents a complex adaptive response of the host to various immune challenges whether infectious or non-infectious. Although elevated body temperature is an indispensable component of the febrile response, it is not synonymous with fever. It is generally agreed that fever is a regulated rise in body temperature above normal daily fluctuations occurring in conjunction with an elevated thermoregulatory set point [1-5].

The normal body temperature ranges from $37^{\circ}\text{C}/98.6^{\circ}\text{F}$ and $37.5^{\circ}\text{C}/99.5^{\circ}\text{F}$. Evening temperatures being 0.5°C higher than in the morning. Rectal temperature $>$ oral temperature (0.5°C) $>$ axillary temperature (1°C) A rectal temperature with a glass- mercury or digital-electronic thermometer is considered the gold standard for taking temperatures Liebermeisters rule -The heart beat rises about 10-15 beats/min for each degree centigrade rise of body temperature.

It is Important to find out the cause of fever without source and treat because fever itself has detrimental effects on body function like febrile seizures and increased BMR.

Acute febrile illness is one of the most frequent illnesses of paediatric patients and it accounts for approximately 25% of the emergency department visits. In general, the fever source can be identified during the initial evaluation after careful anamnesis and physical examination [5-9]. However, in approximately 20% of the cases, the pediatrician may deal with a febrile child whose main focus of infection cannot be identified based on the data provided by the patient's clinical history and detailed clinical examination. This is called 'fever without source' (FWS) [7-13].

Usually children with 'fever without source' pose a diagnostic dilemma and require detail evaluation to detect underlying etiology of infection, Systemic illness or Occult bacteremia is estimated to be present in 30% of febrile illness in newborn, 10 - 15% of infants < 3 months and 5% of children between 3 months to 5 years [2-4]. Common causes of fever without source are self limiting acute viral infections, Bacteremia, Septicemia, Urinary tract infection, Pneumonia, Typhoid fever, Malaria, Rickettsial infection, Leptospirosis. Other rare non infective causes of 'fever without source' are connective tissue disorders and haematological condition like leukemia and lymphoma.

Need of study

In a developing country, Infectious disease remains the most important causes of fever without source. Knowledge of the relative importance of different causes will help in planning intervention strategies for prevention and Treatment of 'fever without source'.

Material and Methods

Total 60 Patients were included in our study. This Analytical cross sectional study was conducted at Bharati Vidyapeeth (Deemed to be University) Medical College and Hospital, Sangli over a period of 18 months. Approval from IEC has been taken. All children from 1 month to 5 years fulfilling the criteria of 'fever without source'

Case Definition of 'Fever without source'

1. Children 1 month to 5 years with 1- History of fever for less than 7 days and atleast for 48 hours.
2. No source found on detail History and Examination.
3. Documentation of fever (38.3 °C and above) within 24 hours of admission.

Sample size

- p=prevalence = 5% parent reference
- q =100-p = 95%
- d = allowable error= 5%
- $\alpha = 5\%$
- z $\alpha = 1.96$
- minimal sample size
- $n = \frac{Z^2 pq}{d^2} = 44.75 = 45$.

Minimal sample size, calculated by using statistical formula with error 5% and level of significance 5% is 45.

Inclusion Criteria: Children 1 month to 5 years with

1. History of fever for less than 7 days and atleast for 48 hours.

2. No source found on detail History and Examination.
3. Documentation of fever (38.3 °C and above) within 24 hours of admission.

Exclusion criteria: Children suffering from chronic disease like Congenital heart disease, Chronic Renal Disease and Endocrine disease.

Statistical analysis: All the observational findings were recorded and entered into prestructured proform. The whole data was analysed with help of statistician. Frequency and percentage was obtained by using MS-Excel.

Results

The present cross-sectional study was done to study the etiology, clinical parameters and laboratory findings of children who presented with fever without source with various clinical outcomes.

- In our study, 60 patients were taken, 48.3% of the patients were male (n=29) and rest being female 51.6% (n=31).
- The patients aged between 1-3 months comprised of 3.3% (n=2) of the patients, 4-36 months were 31.6% (n=19) and 37-60 months were 65% (n=39). So, 37-60 months was the most common age group.
- We observed that all the patients presented was complaints of fever in n=60 (100%) the most commonest complaint on admission, Followed by Reduced appetite in 76.6% (n=46), Irritability in 70% (n=42), Generalized weakness 68.3% (n=41) of the patients.
- On examination, we observed that hepatomegaly was seen in 70% was the most common on admission of the patients followed by pallor in 63.3%, Hypotension and danger sign of shock in 5% (n=3) which was seen PICU admission patients.
- In our study mean haemoglobin was found 10.29 gm% lowest being 6.2 gm/dl and highest being 14 gm/dl, mean Total leucocytes count was 9741.6 cells per cumm lowest being 1000 per cumm and highest being 25000 per cumm, Mean Platelet was 315566.6 per ml lowest being 15000 per cumm and highest being 1072000 per cumm, and mean Q-CRP was 34.31mg/dl lowest being 0.25 mg/dl and highest being 185.3 mg/dl respectively.
- Other diagnostic test like blood culture and sensitivity was positive in 13.3% (n=8) patients, Urine culture and sensitivity was 11.6% (n=7), dengue serology in 3.3% (n=2), Weil felix test in 13.3% (n=8), No positive case of Leptospirosis and Brucellosis were found in our study.
- In our study most common organism isolated in blood culture and sensitivity was salmonella typhi
- We observed that USG abdomen was Normal in 51.6% (n=31) of the patients, in the remaining 35% (n=21) of patients were shown hepatomegaly, 1.6% (n=1) of patients were shown splenomegaly and 3.3% (n=2) of patient were shown ascites. X-ray chest does not shown any pneumonic patch.
- Rickettsial disease was seen in 11.6% (n=8) of the patients, Urinary tract infection was seen in 11.6% (n=7) of the patients, Typhoid fever was seen in 11.6% (n=7) of the patients, Sepsis was seen in 10% (n=6) of the patients, dengue was seen in 3.3% (n=2) of the

patients, Kawasaki’s disease was seen in 5% (n=3) of the patients. In 45% of the patients no etiology was found in our study.

- Urinary tract infection, Rickettsial infection and Typhoid fever were among common cause of Fever without focus/source.
- In our study were 2 cases of Dengue infection were diagnosed as fever without source. They responded to fluid therapy and supportive line of management.
- Three cases of Fever without source diagnosed as kawasaki’s disease in our study, they responded to IvIg therapy.
- In 45% of the patients no etiology was found in our study, In spite of thorough investigation. Most of these patients were suffering from nonspecific viral infection and responded to supportive therapy over period of treatment, some of the patients respond to empirical antibiotic therapy.
- No death happen in the study group patient.

Discussion

We observed clinical parameters, fever was present all the patients n=60 (100%). Rash was present in 33.3% (n=20) of the patients, Irritability in 70% (n=42), Bodyache in 25% (n=15), Joint pain in 5% (n=3), Reduced appetite in 76.6% (n=46), Headache in 23.3% (n=14) and Abdominal pain in 18.3% (n=11) as well. On examination, we observed that high body temperature in all patients 100% (n= 60), Hypotension in 5% (n=3), on admission 5% of patients present with hypotension and along with other signs of shock. So patient admitted at PICU for critical care management. Prehypertension (90-95 centile) 11.6% (n=7), those patients admitted with blood pressure on higher side (BP-between 90-95th centile) whom careful blood pressure monitoring were done. Pallor in 63.3% (n=38), Jaundice in 1.6% (n=1), Rash in 33.3% (n=20), Hepatomegaly in 70% (n=42) and Splenomegaly in 16.6% (n=10) was present.

In a similar study, George O. Akpede, *et al.* In Nigeria (Country in West Africa) studied with complaints of Fever, chills, Sign of sepsis and sign of meningitis. K. Kaushal *et al.* study observed fever with urinary symptoms in acute renal injury, diarrhea of the patients. Omolola *et al.* study observed that the common presenting complaints with fever, anorexia, Convulsion, Diarrhea, lethargy, Rigors, restlessness, Breathlessness, Excessive crying, Vomiting, Cough, weakness and Irritability. On systemic examination both splenomegaly, hepatomegaly of the patients.

In our study UTI have been diagnosed in seven patients. Urinary tract infection was the most common infection bacterial infection. Eight patients were diagnosed to have Rickettsial disease. All the cases were diagnosed on the basis of weil felix test were agglutination titre (>1:160). This positive weil felix test was supported by other biochemical parameters like Hypoalbuminemia and Hyponatremia. Seven patients were diagnosed to have Typhoid fever. Typhoid fever was the common systemic bacterial infection. All the enteric positive patients have grown *salmonella typhi* on blood culture. In my study were 2 cases of Dengue infection were diagnosed as fever without source.

In similar study, S.Sangeeth *et al.* [18] showed blood culture was positive in 7.17% (n=15) patients, Rapid Dengue test was positive in 15.79% (n=33), Typhoid fever was 0.96% (n=2), Leptospirosis test was 2.39% (n=5), Peripheral smear for malaria parasite was positive in 6.22% (n=13), Lumbar

puncture was positive in 1.91% (n=4), myocarditis was 0.47% (n=1), X-ray chest showed patchy pneumonia was in 6.86% (n=14), septic arthritis was 0.96% (n=2), UTI was 8.61% (n=18) and unknown cause was 48.33% (n=101). Vinchurkar *et al.* [21] showed systemic bacterial illness in 36.2% (n=37) and 63.8% (n=65) had non bacterial infection. B.M. Machado *et al.* (19) in 9.3% (n=20) had serious bacterial infection. Among all the cases of serious bacterial infection, they identified one patient of occult bacteremia, three patients of pneumonia and 16 cases of urinary tract infections, 49.8%(n=107) patients, spontaneous resolution of fever without any antibiotic treatment; in 40.9% (n=88), benign self-restricted illness was recognized.

In our study, Etiology are Rickettsial disease was seen in 11.6% (n=8) of the patients, Urinary tract infection was seen in 11.6% (n=7) of the patients, Typhoid fever was seen in 11.6% (n=7) of the patients, Sepsis was seen in 10% (n=6) of the patients, dengue was seen in 3.3% (n=2) of the patients, Kawasaki’s disease was seen in 5%(n=3) of the patients. In 45% of the patients no etiology was found in our study, In spite of thorough investigation.

In similar study, S. Sangeeth *et al.* showed 7.17% (n=15) patients of bacteremia, Dengue was 15.79% (n=33), Enteric fever was 0.96% (n=2), Leptospirosis was 2.39%(n=5), malaria was 6.22% (n=13), Meningitis was 1.91%(n=4), myocarditis was 0.47% (n=1), Pneumonia was 6.86% (n=14), septic arthritis was 0.96% (n=2), UTI was 8.61% (n=18) and unknown cause was 48.33% (n=101). Omolola. *et al.*, bacteremia was found in 7.17% (n=12) cases, bacteremia in children age between 1-3month was 5%. B M Machado *et al.* (37), it showed urinary tract infection was 7.4% (n=16). R K Kaushal *et al.*, it showed urinary tract infection was 8.4%. L.Kapilan *et al.*, it showed dengue in 74.5%(n=143).

Table 1: Age and Sex wise Distribution

Age	No of patients (n=60)	Male (n=29)	Female(n=31)
1 month –3 months	2(3.3%)	1 (3.4%)	1 (3.2%)
4–36 months	19 (31.6%)	12 (41.3%)	7(22.5%)
37 – 60 months	39 (65%)	16(55.1%)	23(74.1%)

Table 2: Etiology of total cases of ‘fever without source’.

Sr No	Etiology	Total
		No of case (n=60)
1	UTI	7 (11.6%)
2	Sepsis	6 (10%)
3	Dengue	2(3.3%)
4	Kawasaki disease	3 (5%)
5	Rickettsial disease	8 (13.3%)
6	Typhoid fever	7 (11.6%)
7	Unknown cause	27 (45%)

Conclusion

1. Fever without source account of 3% of total PICU and Paediatric ward patients admission.
2. Urinary tract infection, Rickettsial infection and Typhoid fever were among common cause of Fever without focus/source.
3. ‘Fever without source’ pose a diagnostic dilemma and require detail evaluation to detect underlying etiology of infection, Systemic illness or Occult bacteremia.
4. Majority of the patients no etiology was found in our study, In spite of thorough investigation. Most of these

patients were suffering from nonspecific viral infection as they required over 4-7 days of hospitalization with supportive treatment.

5. Three cases of Fever without focus/source diagnosed as kawasaki's disease in our study, they responded to IvIg therapy.

The present study had following limitations: 1- The small sample size study, In spite of small sample size, we observed results are similar to bigger size study. 2-Hospital based study were led in a tertiary referral centre were generally sick children are got admitted.

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Conflict of Interest: None

Ethics Approval: This study protocol was approved by Chairman, Institutional Ethics committee Bharati vidyapeeth (Deemed to be university) medical college and Hospital Sangli Maharashtra.

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