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Original Article

A Study on Clinical Profile of Children with Fever more than 5-day Duration in a Tertiary Care Hospital in Tirupati

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Abstract

Introduction: In children, fever is generally a sign of infection. Fever due to other causes including malignancy is rare. The prognosis for the most common forms of pediatric infections is usually excellent, but this is not the case for some bacterial infections and malignancies.

Aims and Objectives: (1) Aims: To study the clinical profile of children with fever more than 5-day duration in children 1 month to 12 years of age. (2) Objectives: To document the clinical profile of children with fever more than 5-day duration. To document the outcome of children with fever more than 5-day duration.

Materials and Methods: Study design: Prospective study. Setting: In-patients from a tertiary care hospital. Participants: 106 (mean age: 5.9 years) children between 1 month and 12 years with fever more than 5 days duration (fever – axillary temperature >99°F and oral temperature >100°F).

Results: Among 106 children (57 males and 49 females), 83% had a fever for 6–10 days, 44.4% had vomiting, 41.5% had chills/rigors, 25.5% needed oxygen supplementation, 55.7% needed intravenous fluids, 30.2% had hospital stay >10 days, 59.4% had intensive care unit stay, 32.1% were diagnosed as scrub typhus/spotted fever; 91.5% improved, 3.8% died.

Conclusion: Children with prolonged fever had overall better outcomes when brought earlier to the hospital setting. Most of the cases (91.5%) recovered without complications. Early and proper work-up and intervention improve the outcome in prolonged fevers.

Key words: Fever, Infectious disease, Prolonged fever

INTRODUCTION

Fever is usually seen as a sign of infection in children. Fever due to other causes such as malignancy and immunological diseases is rare. The risk of severe illness in febrile children is high in developing countries such as India. It is important to differentiate between infectious and non-infectious causes and intervene accordingly to avoid complications. Fever is often accompanied by symptoms and signs that suggest a diagnosis or at least point to an organ system such as headache, cough, diarrhea, or dysuria. This distinction provides a convenient means of categorizing causes of fever in children:

- Localizing symptoms or signs
- Associated presentation, e.g., rash
- No localizing signs.

It may also be categorized as:

- Fever of short duration with localizing signs for which the diagnosis can be established by clinical history and physical examination, with or without laboratory tests
- Fever without localizing signs, for which the history and physical examination do not suggest a diagnosis but laboratory tests may establish an etiology
- Fever of unknown origin.

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It has to be accepted that the causes of prolonged fever are not similar around the globe, neither a state too. It varies geographically, socioeconomically, ethnically, seasonally, and so on. The level of health-care facilities, immunization practices, and advancement in diagnostic techniques, antibiotic policies, and hygienic practices also play a big role in determining the causes of prolonged fever.[1] With the development of some of these techniques and practices in our country, the spectrum of prolonged fever may vary from the previous years. Reviewing of earlier literature reveals the paucity of studies in India, especially in this particular region in the past few years. This study is an attempt to throw light on the clinical picture and outcome of a fever of more than 5-day duration.

Aims and Objectives

Aims of the study

The study aimed to study the clinical profile of children with fever more than 5-day duration in children 1 month to 12 years of age.

Objectives of the study

- To document the clinical profile of children with fever more than 5-day duration
- To document the outcome of children with fever more than 5-day duration.

MATERIALS AND METHODS

Study Design

Prospective observational study.

Study Period

1 year from the time of IEC approval.

Study Subjects

In-patients aged 1 month to 12 years of age with fever more than 5-day duration.

Study Settings

Pediatrics ward and pediatric intensive care unit (PICU), a tertiary care hospital in Andhra Pradesh.

Sample Size

One hundred and six; the minimum sample size required was calculated using the following formula and was found to be 100.

$$\text{Sample size} = \frac{Z1-\alpha/2^2\, p(1-p)}{d^2}$$

Z = 1.96
p = 7%
d = 5%.

Statistics

Data were entered in Microsoft Excel and analyzed in terms of frequencies and percentages.

Inclusion Criteria

- Children of both genders, from 1 month to 12 years of age coming to S.V.R.R.G.G. Hospital for treatment of fever of more than 5 days duration
- Children whose parents have given informed written consent.

Exclusion Criteria

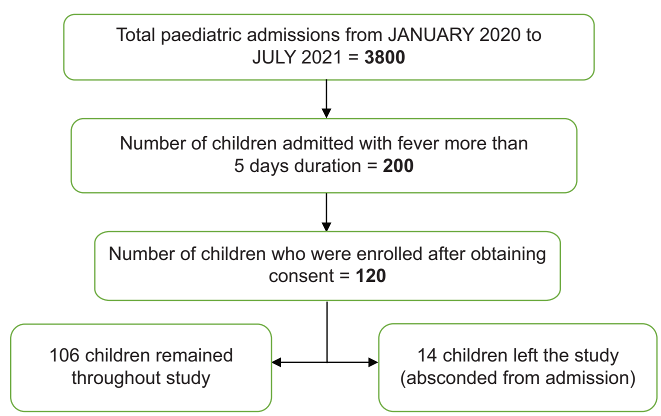
- Children who left part way through the study
- Insufficient data.

Methodology

The children from 1 month to 12 years of age who present with complaints of fever more than 5-day duration to the Department of Pediatrics, were triaged as per their presenting symptoms, signs, and vitals and were admitted in PICU or ward as per the needs. Detailed history and physical examinations were done and baseline investigations were sent.

Ethical Issues

Before the collection of data, all the subjects' parents are briefed about the purpose of the study and written informed consent will be obtained. All investigations were done free of cost, and no financial burden was imposed on the patient. Ethical clearance was obtained from the Institutional Ethics Committee, SV Medical College, Tirupati.



OBSERVATIONS AND RESULTS

Age and Gender Distribution of Cases

Out of 106 patients, 57 were males and 49 were females. The male: female ratio = 1.1:1 [Figure 1] Maximum number of cases was in the age group of more than 5 years (50.9%).

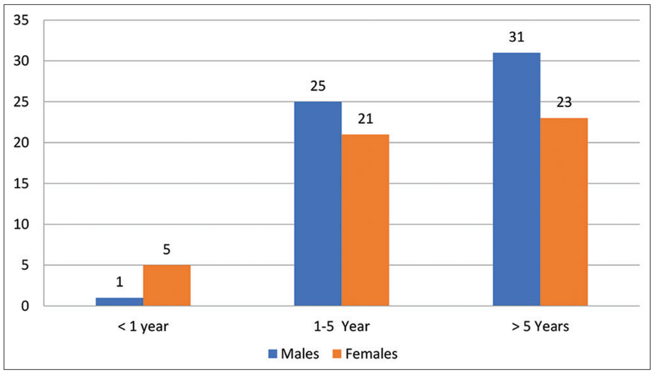


Figure 1: Age and gender distribution

Duration of Fever

About 83% of the cases had a fever lasting for 5–10 days, 4.7% had a fever lasting for 11–14 days, and 12.3% had a fever for more than 15 days.

In this study, the maximum number of cases (72.6%) was from November to March. The least cases were from April to July [Table 1].

Table 1: Month-wise/seasonal distribution of cases

Month	Number of cases	Percentage
January	13	12.3
February	22	20.7
March	20	18.9
April	0	0
May	2	1.9
June	1	0.9
July	2	1.9
August	13	12.3
September	9	8.5
October	2	1.8
November	13	12.3
December	9	8.5

Associated Symptoms and Signs

- 44.4% had vomiting as one of the associated complaints with fever, followed by chills/rigors (41.5% and cough 32%)
- 35.8% had hepatomegaly as a clinical finding followed by pallor (33.9%) [Table 2].
- The studies by Ahmed *et al.*[2] also revealed gastrointestinal symptoms were the most common. Yaramis *et al.*,[3] Sajid *et al.*,[4] Chitu and Chandhra[5] studies also showed gastrointestinal symptoms were the most common in more than two-thirds of cases.

Table 2: Associated clinical features (symptoms and signs)

S. No.	Associated clinical features	No. of patients	Percentage
1	Chills/rigors	44	41.5
2	Myalgia	10	9.4
3	Abdominal pain	25	23.6
4	Vomiting	47	44.4
5	Loose stools	9	8.5
6	Cold	27	25.5
7	Cough	34	32.1
8	Gum bleed/other mucosal bleed	5	4.7
9	Rash	23	21.7
10	Petechiae	1	0.9
11	Dysuria	9	8.5
12	GIT bleed	3	2.8
13	Loss of weight	2	1.9
14	Headache	11	10.4
15	Conjunctival congestion	10	9.4
16	Altered sensorium	13	12.3
17	Convulsions	16	15.1
18	Dehydration	2	1.9
19	Oliguria	16	15.1
20	Dyspnea	16	15.1
21	Pallor	36	33.9
22	Lymph node enlargement	29	27.4
23	Edema	16	15.1
24	Jaundice	5	4.7
25	Hypotension	7	6.6
26	Hepatomegaly	38	35.8
27	Splenomegaly	22	20.8
28	Added respiratory sounds	6	5.7

Laboratory Investigations and Imaging

41.5% had Hb% <10 g%.

The total WBC count was more than 11000 in 40.6% of the cases, whereas it was <4000 in 4.7% of the cases [Table 3].

- Scrub immunoglobulin M (IgM) was positive in 32.1% of the cases
- Dengue serology (NS1/IgM) was positive in 1.9%,
- The WIDAL test was positive for 3.8%.
- Blood culture and sensitivity yielded growth in 2.8% of the cases. (*Pseudomonas* and *Acinetobacter*, *Streptococcus*, and non-fermentative Gram negative *bacilli*)
- Urine culture and sensitivity were positive in 5.7% of the cases (*Escherichia coli*, *Pseudomonas*, and *Candida*)
- Peripheral smear showed changes in 29.2% of cases. (microcytic hypochromic anemia, dimorphic anemia, blast cells, and *Plasmodium vivax* were seen as findings)
- Ultrasound (USG) abdomen showed a normal study in 76.4%, showed hepatomegaly alone in 11.3%, splenomegaly alone in 2.8%, and both hepatosplenomegaly in 8.5%
- USG chest showed changes in three cases
- Chest X-ray showed significant changes in 8.5% of cases (pleural effusion and consolidation).

Table 3: Total leukocyte count levels and number of cases

Total WBC count	No. of cases	Percentage
<4.000	7	6.6
4.000–11.000	56	52.8
>11.000	43	40.6

Hospital Stay

- Among the 106 cases, 60 (56.6%) had a hospital stay of 5–10 days, 32 (30.2%) had more than 10 days of hospital stay whereas 14 (13.2%) had <5 days of hospital stay [Table 4]
- The cases which improved: 54 had 5–10 days of stay and 31 had more than 10 days of stay
- The referred cases: Four stayed for 5–10 days and two stayed for <5 days
- The cases that succumbed to the disease: Two stayed for 5–10 days, one died within 1 day, and one died after 10 days of hospital stay.
- Transfusion was done in 10.4% (packed red blood cells/fresh frozen plasma/whole blood/platelet concentrates, as per requirement)
- 63 cases (59.4%) had ICU stay. Among them, 24 (38.1%) had ICU stays up to 24 h, 27 (42.9%) had ICU stay of 24–72 h, whereas 12 (19%) had more than 72 h of ICU stay [Table 5 and Figure 2].
- 27 cases (25.5%) out of 106 required Oxygen supplementation. Out of which, 12 (44.5%) required it for ≤24 h, 5 (18.5%) required it for more than 72 h [Table 6 anf Figure 3].
- 59 cases (55.7%) were given intravenous (IV) fluids. Among them, 32 (54.2%) were given IV fluids for a duration of 24–72 h, and 19 (32.2%) were given for up to 24 h Treatment included administration of antibiotics, steroids, and Ig as per the clinical diagnosis and progression of the disease.

Diagnosis

- 32.1% of the cases were diagnosed as scrub typhus/rickettsial fever. 7.5% cases of pneumonia and 7.5% cases of meningitis were also diagnosed [Table 7]
- Scrub typhus was the most common cause of fever more than 7 days in a study by Sumathisri *et al.*,[6] followed by enteric fever, pneumonia, and urinary tract infection. This similarity in the most common etiology might be due to the geographical nearness of the places where both studies were conducted and also due to the fact that both studies were separated by only 5 years gap
- Patil *et al.*,[7] Rekha *et al.*,[8] and Anand *et al.*,[9] study results shows undiagnosed fever was the most common etiology followed by dengue fever and enteric fever Shankar Raikar *et al.*,[13] and Shruti K Bhalara *et al.*,[14] studies revealed that Dengue fever was the most common etiology followed by malaria and sepsis. In contrast Suresh *et al.*,[10] Kumar and Chandhra,[11] and Gandhi and Akhaolkar[12] studies showed malaria as the most common etiology followed by dengue and undiagnosed fever.

Among the children diagnosed with scrub typhus, 24 (70.5%) had chills/rigors, and 20 (58.8%) had vomiting as an associated complaint. Twenty-eight (82.4%) were found to have an eschar. 16 (47%) of the children had hepatomegaly, 9 (26.5%) had splenomegaly, and 9 (26.5%) had pallor. Platelet count <1.5 lakh was there for 19 (55.8%) of those children.

Table 4: Duration of stay and outcome

Duration of stay	No. of cases (%)	Recovered cases (%)	Referred cases (%)	Death (%)
<5 days	14 (13.2)	11 (11.5)	2 (33.3)	1 (25)
5–10 days	60 (50.6)	54 (56.3)	4 (66.7)	2 (50)
>10 days	32 (30.2)	31 (32.2)	0 (0)	1 (25)

Table 5: Duration of ICU stay

Duration of ICU stay	No. of cases	Percentage
≤24 h	24	38.1
24–72 h	27	42.9
>72 h	12	19

ICU: Intensive care unit

Table 6: Duration of Oxygen supplementation

Duration of Oxygen supplementation	No. of cases	Percentage
≤24 h	12	44.5
24–72 h	10	37
>72 h	5	18.5

Table 7: Final diagnoses of the cases

S. No.	Diagnosis	Frequency	Percentage
1	Scrub typhus/Rickettsial fever	34	32.1
2	Pneumonia/lower respiratory tract infection	11	10.4
3	Meningitis	8	7.5
4	Malaria	5	4.8
5	Urinary tract infection	5	4.8
6	Enteric fever	5	4.8
7	Meningoencephalitis	5	4.8
8	Leukemia	4	3.8
9	Acute encephalitis syndrome (etiology undiagnosed)	4	3.8
10	Dengue fever	3	2.8
11	Viral hepatitis	3	2.8
12	Acute gastroenteritis	2	1.9
13	Kawasaki disease	2	1.9
14	Chronic suppurative otitis media	2	1.9
15	Septicemia	2	1.9
16	Viral fever	2	1.9
17	Septic arthritis	1	0.9
18	Liver abscess	1	0.9
19	Cellulitis	1	0.9
20	Disseminated BCGosis	1	0.9
21	Steven Johnson syndrome	1	0.9
22	Viral hemorrhagic fever	1	0.9
23	Aplastic anemia	1	0.9
24	MIS-C	1	0.9
25	Scarlet fever	1	0.9

MIS-C: Multisystem inflammatory syndrome in children

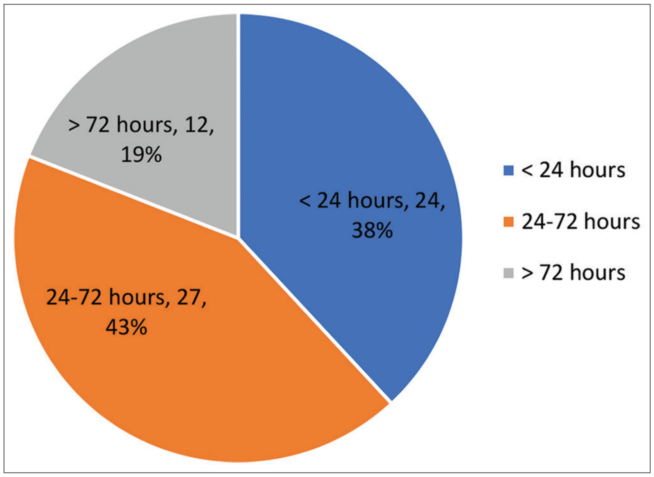


Figure 2: Pie-chart depicting duration of intensive care unit stay for patients

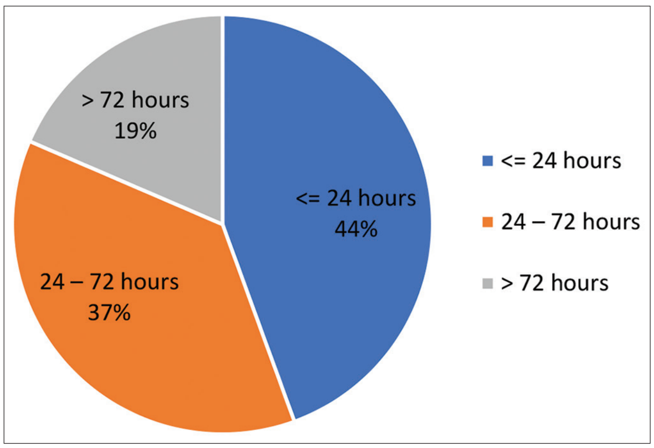


Figure 3: Duration of Oxygen supplementation

Table 8: Significance of different parameters to recovery

Parameter and relation to recovery	*P*-value
Duration of fever	0.002
Duration of total stay	0.002
Duration of ICU stay	0.043
O_2 supplementation and i.v. fluids	>0.05
Hemoglobin	<0.05
Age	0.007
Gender (Males vs. Females)	0.004
Without petechiae versus with petechiae	0.038
Without weight loss versus with weight loss	0.005
Without pallor versus with pallor	<0.001
Without hypotension versus with hypotension	0.001
Without hepatomegaly versus with hepatomegaly	0.027
Transfusions (−vs.+)	<0.001
Complications (−vs.+)	0.001

ICU: Intensive care unit, IV: Intravenous

Outcome

- Ninety-seven (91.5%) improved with or without complications or sequelae, 5 (4.7%) were referred to higher center for further management, 4 (3.8%) died.
- Significantly higher duration of stay was reported among the patients who tested negative for Scrub IgM (*P* −0.014) (Signifying that children with scrub typhus recovered quickly on administration of doxycycline), positive blood culture (*P* −0.047), without hepatomegaly (*P* −0.007), without splenomegaly (*P* −0.036) (Since in most of the cases the presence of splenomegaly and/or hepatomegaly helped in identifying the illness quickly and also in initiating appropriate treatment earlier) and with complications (*P* < 0.001) [Table 7].

Association Laboratory Findings with the Duration of Stay (Mann–Whitney Test)

Significantly higher duration of stay was reported among the patients who tested negative for scrub IgM (*P* −0.014), positive blood culture (*P* −0.047), without hepatomegaly (*P* −0.007), without splenomegaly (*P* −0.036), and with complications (*P* < 0.001).

Correlation of Variables with Duration of Stay (Spearman correlation)

There was a significant mild positive correlation between the IV fluid duration and the duration of the stay (*P* −0.009). The longer the duration of iv fluid administration, the longer the hospital stay.

Limitations of this Study

This study was conducted in a Government medical college amidst the COVID-19 pandemic. Since the hospital was dealing with COVID-19 cases in large numbers, there was a significant refusal on the part of patients' families to get the children admitted for complaints of fever.

There was difficulty in getting many of the tests done because of the resource-limited nature of the time.

Most of the children who were admitted with fever in our hospital had already been treated with antibiotics in peripheral centers by other practitioners which led to poor yield of blood culture and urine culture.

CONCLUSION

- There is no gender predilection for prolonged fevers (male: female = 1.1:1)
- The mean duration of fever was 10.3 days
- 72.6% of cases were from November to March
- Gastrointestinal complaints were the most commonly associated complaint
- About 89.6% (95) had infectious causes of fever and 3.7% (4) were due to malignancy
- Scrub typhus (32.1%) was the most common etiology among the infectious causes

- The mean duration of hospital stay for children was 9.6 days
- Children with anemia had worse outcomes than other children
- About 91.5% recovered with or without any complications/sequelae.

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