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Clinical Profile and Etiology of Children Presenting with Prolonged Fever in a Tertiary Care Hospital

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Abstract

Introduction: *Prolonged fever in children, defined as fever persisting for ≥10 days without an initially identifiable cause, is a common yet diagnostically challenging clinical presentation, especially in resource-limited settings.* ***Aim of the study:*** *To determine the common causes of prolonged fever and its clinical presentation and outcome which may guide to narrow the diagnostic approach.* ***Materials and Methods:*** *A prospective observational study was conducted on 86 children aged 1 year to 12 years admitted with prolonged fever. Detailed history, clinical examination, and a stepwise diagnostic protocol—including baseline and targeted investigations—were used to determine underlying causes.* ***Result:*** *The majority were aged between 5 to 10 years (43.02%), followed by 1–5 years (33.72%) and 10-12 years (23.25%). In terms of gender males are predominate (56.97%). The common identifiable causes were Rickettsial fever (31.40%), Leukemia& lymphoma (11.63%), Enteric Fever (10.46%) and Bronchopneumonia (10.46%). In 6.97% of cases, the cause of prolonged fever remained undiagnosed . The most common associated clinical features included chills or rigors (43.02%), Pallor (36.05%), hepatomegaly (26.74%), cough (23.25) and vomiting (20.93%). Categorization of the diseases showed infectious cause predominant (73.25%) then malignancy (13.95%) and connective tissue /autoimmune disease (5.81%). Most hospital stays ranged from 8 to 14 days (50.00%), during which 86.04% recovered, 11.62% were referred, and one death occurred.* ***Conclusion:*** *Infectious diseases remain the predominant cause of prolonged fever in children in low-resource settings. However, a notable proportion had non-infectious or undiagnosed etiologies, highlighting the need for a structured, multi-tiered diagnostic approach. Early recognition and context-specific management strategies are essential to improve outcomes.*

Keywords: *Prolonged fever, pediatric, etiology, tuberculosis, Rickettsial fever, malignancy, undiagnosed fever.*

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Introduction:

Fever is the most common reason for a child to seek medical care.Prolonged fever in children is a frequently encountered yet diagnostically challenging clinical entity that accounts for a significant proportion of pediatric hospital visits and admissions globally[1]. It is estimated that 4% of all pediatric hospitalizations worldwide are due to fevers persisting beyond one to two weeks, reflecting a notable clinical and economic burden[2]. Prolonged fever—commonly defined as a body temperature ≥38°C (100.4°F), at least once a day lasting more than 7 to 10 days in the absence of an identifiable source despite initial clinical evaluation. Prolong fever may have a wide spectrum of underlying causes, including both common self-limiting infections and more serious, potentially life-threatening systemic diseases[3,4]. Prolong fever causes anxiety to parents , on other hand it causes confusion for the physician, leading to unnecessary laboratory tests and medications including multiple antibiotics. Four etiological catagories of diseases should be considered: infectious, /autoimmune, malignancy and miscellenious. The Infectious diseases remain the most prevalent cause, particularly in low- and middle-income countries, where diseases such as tuberculosis, malaria, enteric fever, and a growing burden of arboviral and rickettsial infections continue to dominate[5-8]. However, with the widespread implementation of vaccination programs, significant improvements in hygiene and sanitation practices, and evolving environmental and socioeconomic conditions, the relative contribution of non-infectious etiologies to prolonged fever has become increasingly evident. These include autoimmune diseases, connective tissue disorders, malignancies such as Acute leukemia, and lymphoma, as well as various inflammatory

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syndromes like Kawasaki disease, systemic juvenile idiopathic arthritis, and periodic fever syndromes, all of which are now recognized more frequently in clinical practice[1,9,10]. Moreover, the emergence of atypical infections, changing antimicrobial resistance patterns have further expanded the diagnostic spectrum[11]. The clinical approach to prolonged fever involves a meticulous and often staged diagnostic process, which begins with comprehensive history-taking and physical examination, followed by targeted investigations such as complete blood counts, inflammatory markers, cultures, and imaging studies[12]. In tertiary care like autoimmune panels, bone marrow studies, and imaging modalities such as CT or MRI can facilitate early diagnosis[1]. However, in resource-constrained environments, the lack of diagnostic infrastructure often leads to empiric treatment based on clinical suspicion, contributing to overuse of antimicrobials and potential delays in identifying non-infectious causes[13]. Importantly, certain cases remain undiagnosed despite extensive evaluation and may eventually resolve spontaneously, though some may harbor insidious pathologies that carry risks of progression or recurrence[14]. The clinical profile of children with prolonged fever varies by age, geographic location, immune status, nutritional state, and local endemic disease patterns—necessitating region-specific data to guide clinicians[15]. Understanding the evolving etiological profile and for diagnostic accuracy, optimizing antibiotics use and improving patient outcomes. On this background, the present study was designed to investigate the clinical profile and underlying causes of prolonged fever in pediatric patients, with the goal of contributing to evidence-based diagnostic and treatment strategies that are both effective and appropriate.

Materials and Methods:

This prospective observational study was conducted at the Department of Pediatrics, Khulna Medical College Hospital, Khulna, over a one year period from January 2024 to December 2024. A total of 86 children who presented with prolonged fever were enrolled based on predefined inclusion and exclusion criteria. Prolonged fever was defined as fever lasting at least 10 days at the time of presentation, as reported by the caregivers and verified by healthcare staff through serial axillary and/or oral temperature measurements. Inclusion Criteria were children aged 1 year to 12 years, fever persisting for at least 10 days at presentation and admitted to the pediatric ward during the study period. Exclusion Criteria were children with known immunocompromised conditions at presentation (undergoing chemotherapy, Steroid therapy for >14 days, diagnosed case of aplastic anemia and thalassemia), Children who left against medical advice before diagnosis or treatment completion.

Ethical Considerations:

Prior to enrollment, parents or legal guardians were informed about the purpose and nature of the study, and written informed consent was obtained. The study was conducted in accordance with ethical principles, and ethical clearance was obtained from the Institutional Ethics Committee.

Data Collection:

After obtaining informed consent from parents or legal guardians, data were collected using a structured questionnaire. Samples were taken as consecutive manner. Information gathered included demographic details (age and gender), clinical features, and relevant epidemiological history such as travel, contacts, parasite exposure, family history and prior medication.

Thorough clinical examination was done on admission and serial temperature charting and daily systemic assessments were recorded throughout hospitalization.

Diagnostic Workup:

All enrolled patients underwent a series of baseline investigations to determine the underlying etiology of prolonged fever. These included complete blood count (CBC), peripheral blood film (PBF), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), urine routine and microscopy & culture, chest X-ray, blood cultures and tripple antigen test. Based on the presence of clinical suspicion or diagnostic clues, a set of targeted investigations were performed selectively. These included Mantoux test, gastric lavage and stool for Gene Xpert, Ultrasonogram, cerebrospinal fluid (CSF) study, echocardiography, and serological tests for HIV, ICT for Malaria, autoimmune/rheumatological markers like ANA, anti-dsDNA. Where necessary, advanced imaging techniques such as CT scan, MRI, and biopsy were done to establish a definitive diagnosis.

Statistical Analysis:

All data collected from the structured questionnaire were first checked for completeness and accuracy. Data were then analyzed accordingly. Categorical variables were summarized as frequencies (n) and percentages (%). No inferential statistics (e.g., chi-square test, t-test, or regression analysis) were applied, as the primary aim of the study was to describe the clinical spectrum and not to establish causal associations or risk factors.

Result:

The majority were aged between 5 to 10 years (43.02%), followed by 1–5 years (33.72%) and 10-12 years (23.25%). In terms of gender distribution males are predominate (56.97%) (Table I). The common identifiable causes were Rickettsial fever (31.40%), Leukemia& lymphoma (11.63%), Enteric Fever (10.46%) and Bronchopneumonia(10.46%). A small number of patients were diagnosed with serious conditions such as Infective Endocarditis, Empyema Thoracis, complicated Meningoencephalitis, Liver abscess (each 1.16%). In 6.97% of cases, the cause of prolonged fever remained undiagnosed (Table II). The most common associated clinical features included chills or rigors (43.02%), Pallor (36.05%), hepatomegaly (26.74%),cough (23.25) and vomiting (20.93%), (Table III). Categorization of the diseases showed infectious cause predominant (73.25%) then

malignancy (13.95%) and connective tissue /autoimmune disease (5.81%) (Table IV). Most hospital stays ranged from 8 to 14 days (50.00%), among them 86.04% recovered, 11.62% were referred and death occured 4.65% of total cases(Table V).

Table I: Demographic characteristics of the study population (n=86)

Demographic data	Frequency (n)	Percentage (%)
Age group		
1-5 year	29	33.72
5-10 year	37	43.02
10-12 year	20	23.25
Gender		
Males	49	56.97
Females	37	43.02

Table II: Etiologies of prolonged fever among patients (n=86)

Etiology	Frequency (n)	Percentage (%)
Rickettsial fever	27	31.40
Leukemia/lymphoma	10	11.63
Enteric fever	9	10.46
Bronchopneumonia	9	10.46
Lobar Pneumonia	5	5.81
UTI	4	4.65
SOJIA	3	3.48
SLE	2	2.33
Septic Arthritis	2	2.33
Tuberculosis	2	2.33
Aplastic anaemia	2	2.33
Infective endocarditis	1	1.16
Empyema Thoracis	1	1.16
Meningoencephalitis with subdural effusion	1	1.16
Dengue with complications	1	1.16
Liver abscess	1	1.16
Undiagnosed	6	6.97

Table III: Clinical features (According to system involved) of participants (n=86)

System Involved	Clinical features	Frequency (n)	Percentage (%)
General	Marked Anorexia	29	33.72
	Myalgia	6	6.97
	Loss of weight	10	11.62
	Chills/rigors	37	43.02
Gastrointestinal	Abdominal pain	5	5.81
	Vomiting	18	20.93
	Loose stools	5	5.81
	Dehydration	4	4.65
Respiratory	Rhinorrhoea	16	18.60
	Cough	20	23.25
	Dyspnea	15	17.44
	Added respiratory sounds	15	17.44
Hematological	Pallor	31	36.05
	Jaundice	1	1.16
	Petechiae/Purpura	3	3.48
	Gum bleed/other mucosal bleeding	3	3.48
	Lymph node enlargement	6	6.97
	Hepatomegaly	23	26.74
	Spleenomegaly	13	15.11
Renal	Dysuria	4	4.65
	Oliguria	9	10.46
	Edema	2	2.32
Cardiac	Hypotension	4	4.65
	Cardiac murmur	2	2.32
Central Nervous System	Headache	16	18.60
	Conjunctival congestion	3	3.48
	Convulsions	1	1.16
	Altered sensorium	4	4.65
Locomotor	Joint pain &swelling	3	3.48

Table IV: Categorization of the diseases according to final diagnosis

Disease catagory	Number of cases (n=86)	Percentages (%)
Infections	63	73.25
Malignancy	12	13.95
Autoimmune / Connective tissue disease	5	5.81
Miscellaneous	2	2.32
Undiagnosed	6	6.97

Table V: Duration of hospital stay and outcome of study population (n=86)

Duration of stay	No. of cases (%)	Recovered cases (%)	Referred cases (%)	Death (%)
1-7 days	29 (33.72%)	24 (82.75)	3(10.34)	2 (6.89)
8-14 days	43(50%)	37(86.04)	5 (11.62)	1 (2.32)
>14 days	13(15.11%)	11 (84.61)	1 (7.69)	1 (7.69)
Total	86	73(84.88)	9(10.46)	4(4.65)

Discussion:

Children presenting with prolonged fever can exhibit diverse clinical profiles, reflecting a wide spectrum of etiological categories including infectious, connective tissue disease/ inflammatory, malignancy, and miscellaneous causes[1]. This prospective study evaluated the clinical spectrum, etiologies, and outcomes of children presenting with prolonged fever in a tertiary care setting. Prolonged fever in pediatric populations remains a diagnostic challenge, particularly in low- and middle-income countries, where infections and non-infectious etiologies coexist in varying proportions. In our study cohort (n=86), children aged 5- 10 years comprised the largest age group (43.02%), followed by the 1–5 years (33.72%) and 10 - 12 years (23.25%) age groups. This age distribution aligns with findings from studies by Sumathisri et al. who observed a higher prevalence of prolonged fever presentations in school-aged children[16]. Males constituted 56.97% of our cohort, indicating a mild male preponderance. This male predominance is echoed in studies by Lim et al. and Shoman et al., which reported similar gender distributions[17,18]. Infectious causes dominated the etiology, accounting for 73.25 of cases. Rickettsial Fever was the leading cause (31.40%) consistent with observations from Southeast Asian studies, where these vector-borne illnesses are prevalent[19,20]. Leukemia/lymphoma was the most frequent non-infectious etiology (11.63%), followed by rare cases such as systemic-onset juvenile idiopathic arthritis (SOJIA) and this findings are in line with study by Shoman et al., which

underscore the importance of malignancies and autoimmune disorders in the differential diagnosis of fever of unknown origin (FUO)[18]. Unfortunately, 6.97% of the patients remained undiagnosed despite extensive workup. A comparable proportion of undiagnosed fever cases, approximately 12%, was reported by both Avinash et al. and Joshi et al. In contrast, Sumathisri et al. documented a lower rate, with only 4% of patients remaining without a definitive diagnosis[16,21,22].

The clinical features were diverse. The most common symptoms included chills or rigors (43.02%), cough (23.25) and vomiting (20.93%), Pallor (36.05%), Hepatomegaly (26.74%), respiratory added sound (17.44%) and splenomegaly (15.11%) were significant examination findings. These features suggest a predominance of systemic infections, and are supported by studies from Agrawal et al. and Anand et al., which noted similar clinical profiles in pediatric fever cohorts[23,24]. Regarding patient outcomes, most recovered with supportive and specific therapy. Only 4 patients (4.65%) died, indicating favorable outcomes with timely diagnosis and treatment. Similar low mortality rates have been reported in previous study[25]. The duration of hospital stay was 8 - 14 days in 50% of cases, A small number of patients required referral for specialized care, particularly those with complex or non-infectious causes. This trend is supported by findings in previous studies that associate delayed diagnosis or referral with prolonged hospitalization[26,27].Undiagnosed causes are the most challenging cases worldwide. In our study undiagnosed causes accounted for 6.97%.This result comparable with another study which showed 18.84%[28].

Conclusion:

Prolonged fever in children presents a wide diagnostic spectrum, predominantly led by infectious causes in our center. Among them Rickettsial fever is most common. However, hematological malignancies were found as an emerging causes. A systematic, protocol-based approach combining clinical evaluation with relevant investigations can improve diagnostic yield and patients outcome. Further large-scale, multi-center studies are recommended to validate findings and guide policy-making in pediatric febrile illness management.

Conflict of Interest: None.

Ethical approval: The study was approved by the Institutional Ethics Committee.

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