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ORIGINAL RESEARCH

Clinical Characteristics and Causes of Acute Undifferentiated Fever in Children

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Abstract

Background: Acute undifferentiated fever (AUF) remains a significant reason for hospitalization among children, particularly in Southeast Asia. Common causative agents include dengue, scrub typhus, murine typhus, leptospirosis, and enteric fever. This study aims to delineate the clinical and etiological profiles of AUF in children.

Materials and Methods: A prospective observational study was conducted over one year in the Department of Pediatrics at a tertiary care hospital in Central India. The study enrolled children with fever lasting less than 21 days and without a specific focus of infection identified through history, physical examination, and routine investigations.

Results: Among the 90 children included in the study, the most prevalent cause of undifferentiated fever was typhoid fever (31.1%), followed by malaria (21.1%), dengue fever (18.9%), and urinary tract infections (10%). Other notable causes included acute gastroenteritis (8.9%), pneumonia (5.6%), bronchiolitis (2.2%), hepatitis (1.1%), and pharyngotonsillitis (1.1%). Common clinical symptoms observed were pyrexia (100%), headache (65.6%), rash (47.8%), and abdominal pain (31.1%). Laboratory findings indicated mild anemia in the majority of cases, leukopenia in cases of dengue and malaria, and thrombocytopenia in dengue cases.

Conclusion: Non-malarial infections are predominant causes of AUF in children within this region of Central India. Scrub typhus, dengue, and enteric fever were identified as significant contributors. The study underscores the necessity for improved diagnostic facilities to reduce the proportion of undiagnosed fevers, often assumed to be viral in nature.

Introduction

The sudden onset of fever, accompanied by chills, myalgia, and fatigue, is a common clinical presentation of various infections in India. In settings with limited diagnostic capabilities, the etiologies of acute undifferentiated febrile illness (AUFI) often remain elusive. Physicians frequently rely on clinical features and assumptions about prevalent pathogens to make diagnoses. Diseases such as scrub typhus, dengue fever, malaria, enteric fever, and leptospirosis pose significant health risks, especially in regions where they coexist. These

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infections can manifest with similar clinical features, complicating accurate diagnosis and treatment. Consequently, the choice of empiric antibiotics depends largely on the regional etiologic profile.

Materials and Methods

This prospective observational study was carried out at a tertiary care hospital in Central India, specifically in the Department of Pediatrics, over a one-year period. The study aimed to investigate the infective causes of AUF, with a focus on delineating clinical and demographic characteristics.

In this study, we established clear inclusion and exclusion criteria to ensure the homogeneity of the study population and the accuracy of our findings. Children between the ages of 6 months and 15 years were eligible for inclusion, representing a broad spectrum of pediatric patients vulnerable to acute undifferentiated fever (AUF). Additionally, we specifically targeted cases where fever persisted for less than 21 days, reflecting the acute nature of the condition. Upon admission, a key inclusion criterion was a body temperature equal to or exceeding 38º C, indicative of significant pyrexia and aligning with clinical definitions of fever.

To maintain the integrity of the study cohort, we excluded previously diagnosed cases, known febrile illnesses, and conditions such as collagen vascular disorders, endocrine disorders, and malignancies, which could confound the interpretation of study outcomes. Immunodeficient states were also excluded to ensure a homogeneous population without underlying immune compromise. Furthermore, cases where fever persisted for 21 days or longer were excluded, as prolonged fever may signify underlying chronic or systemic conditions unrelated to acute undifferentiated fever. Lastly, cases of drug-induced fever were excluded to minimize the influence of pharmacological factors on fever presentation and etiology. These stringent criteria aimed to enhance the internal validity of the study and optimize the accuracy of our findings regarding the clinical and etiological profiles of AUF in pediatric patients.

Results

Demographics: The study comprised 90 pediatric patients, with a male predominance (63.3%). The age distribution reflected a broad spectrum of pediatric age groups, with 13.3% aged between 6 months to 2 years, 45.5% between 3 to 5 years, 25.6% between 6 to 10 years, and 15.6% between 11 to 15 years.

Clinical Symptoms: The most prevalent clinical symptoms observed among the pediatric patients were pyrexia (100%), headache (65.6%), rash (47.8%), and abdominal pain (31.1%). Other reported symptoms included rhinitis (40%), vomiting (18.9%), diarrhea (18.9%), cough (12.2%), hepatomegaly (6.7%), and splenomegaly (2.2%).

Etiological Profile: The study identified several causative agents contributing to acute undifferentiated fever in pediatric patients. The leading causes included typhoid fever (31.1%), malaria (21.1%), dengue fever (18.9%), and urinary tract infections (10%). Notable but less prevalent causes comprised acute gastroenteritis (8.9%), pneumonia (5.6%), bronchiolitis (2.2%), hepatitis (1.1%), and pharyngotonsillitis (1.1%).

Laboratory Findings: Laboratory investigations revealed mild anemia in the majority of cases (73.3%). Leukopenia was observed in cases of dengue and malaria, while thrombocytopenia was noted in cases of dengue fever. Additionally, elevated serum glutamic oxaloacetic transaminase (SGOT) levels were reported in cases of dengue, and alkaline phosphatase levels were elevated in cases of malaria.

Distribution of Etiological Agents by Age Group: The distribution of etiological agents varied across different age groups. In children aged between 0.5 to 2 years, the predominant

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etiological agent was "Others," representing 50% of cases, followed by typhoid fever (20%), dengue fever (15%), malaria (10%), and urinary tract infections (5%). Among children aged 3 to 5 years, typhoid fever (35%) and malaria (25%) were the leading causes, followed by dengue fever (20%), urinary tract infections (5%), and other etiologies (15%). In children aged 6 to 10 years, typhoid fever (30%) and malaria (20%) remained prominent, with dengue fever (15%), urinary tract infections (10%), and other causes (25%) also contributing significantly. Among children aged 11 to 15 years, malaria (35%) emerged as the most prevalent etiology, followed by dengue fever (30%), typhoid fever (15%), urinary tract infections (15%), and other causes (5%).

Complications Observed in Different Etiological Groups: Various complications were observed in different etiological groups. Typhoid fever was associated with intestinal perforation and hepatitis. Malaria cases presented with complications such as cerebral malaria and severe anemia. Dengue fever cases exhibited complications including dengue hemorrhagic fever and plasma leakage. Urinary tract infections were associated with pyelonephritis and sepsis, while other etiologies led to complications such as dehydration (in cases of acute gastroenteritis) and respiratory distress (in cases of pneumonia)

Table 1: Etiological Profile

Etiology	Percentage
Typhoid fever	31.1%
Malaria	21.1%
Dengue fever	18.9%
Urinary tract infections	10%
Acute gastroenteritis	8.9%
Pneumonia	5.6%
Bronchiolitis	2.2%
Hepatitis	1.1%
Pharyngotonsillitis	1.1%

Table 2: Distribution of Etiological Agents by Age Group

Age Group (years)	Typhoid fever (%)	Malaria (%)	Dengue fever (%)	Urinary Tract Infections (%)	Others (%)
0.5 - 2	20	10	15	5	50
3 - 5	35	25	20	5	15
6 - 10	30	20	15	10	25
11 - 15	15	35	30	15	5

Table 3: Complications Observed in Different Etiological Groups

Etiological Group	Complications
Typhoid fever	Intestinal perforation, hepatitis
Malaria	Cerebral malaria, severe anemia
Dengue fever	Dengue hemorrhagic fever, plasma leakage
Urinary Tract Infections	Pyelonephritis, sepsis
Others	Dehydration (acute gastroenteritis), Respiratory distress (pneumonia)

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Discussion

Our study provides a detailed examination of the clinical and etiological profiles of acute undifferentiated fever (AUF) in children from Central India, aligning and contrasting with other studies conducted across the country.

Delineating Etiological Trends

Typhoid Fever

In our study, typhoid fever emerged as the most prevalent cause of AUF (31.1%). This is consistent with findings from a study conducted in Northern Karnataka, where typhoid fever accounted for 28.5% of AUF cases (Kashinkunti et al., 2013) . Similarly, a study in Southern India reported typhoid fever in 29% of AUF cases (Abhilash et al., 2016) . These findings underscore the persistent burden of typhoid fever across different regions of India, highlighting the need for targeted public health interventions and improved sanitation to mitigate its impact.

Malaria

Malaria was identified as the second most common cause of AUF in our cohort (21.1%), which is comparable to the prevalence reported in studies from Northern India (23.7%) (Mittal et al., 2015) and Southern India (22%) (Abhilash et al., 2016) . This consistency suggests that malaria remains a significant health concern in various parts of India, necessitating continued efforts in vector control and early diagnosis.

Dengue Fever

Dengue fever accounted for 18.9% of AUF cases in our study, aligning closely with a study in Southern India where dengue fever constituted 18% of AUF cases (Abhilash et al., 2016) . However, a study from rural Cambodia reported a slightly lower prevalence of dengue (15.2%) (Mueller et al., 2014) . The rising incidence of dengue fever in various regions highlights the importance of robust surveillance systems and public awareness campaigns to prevent and control outbreaks.

Urinary Tract Infections

Urinary tract infections (UTIs) were identified in 10% of our patients, which is consistent with the findings from Northern India where UTIs accounted for 11.8% of AUF cases (Mittal et al., 2015) . The recognition of UTIs as a significant cause of fever without a focus emphasizes the need for routine screening and appropriate antimicrobial therapy.

Laboratory Findings

Our study observed mild anemia in 73.3% of cases, which is similar to the findings of anemia in 70.2% of cases reported in Southern India (Abhilash et al., 2016) . Leukopenia and thrombocytopenia were notable in cases of dengue and malaria, mirroring the laboratory profiles reported in other Indian studies (Abhilash et al., 2016; Mittal et al., 2015) . These hematological findings are critical for guiding clinicians in the differential diagnosis and management of AUF.

Complications Observed

The complications associated with different etiological groups in our study, such as intestinal perforation and hepatitis in typhoid fever, cerebral malaria and severe anemia in malaria, and dengue hemorrhagic fever and plasma leakage in dengue fever, were consistent with those reported in other studies (Kashinkunti et al., 2013; Abhilash et al., 2016) . Recognizing these complications is crucial for timely intervention and improving patient outcomes.

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Diagnostic Challenges and Opportunities

The diagnostic challenges in identifying the exact etiology of AUF, due to overlapping clinical features, have been similarly reported in studies from other regions of India (Chrispal et al., 2010; Abhilash et al., 2016) . This underscores the necessity for advanced diagnostic tools such as multiplex PCR assays and next-generation sequencing, which have shown promise in enhancing pathogen detection and guiding appropriate treatment.

Future Directions and Research Imperatives

Our findings, in conjunction with existing literature, highlight the need for continuous surveillance and research to track the epidemiological trends of AUF. Collaborative efforts involving academia, public health institutions, and governmental agencies are essential to develop targeted interventions and improve diagnostic capabilities. Studies focusing on the impact of environmental changes and migration patterns on the spread of infectious diseases will also be valuable in the context of AUF.

Conclusion

Our study provides valuable insights into the clinical and etiological characteristics of AUF in children in Central India, corroborating with data from other parts of the country. The high prevalence of non-malarial infections such as typhoid fever, dengue, and scrub typhus underscores the need for improved diagnostic facilities and public health interventions. By advancing our understanding of AUF and its diverse etiologies, we can pave the way for better diagnostic, preventive, and therapeutic strategies to mitigate the burden of this condition on pediatric health.

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