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Clinico-Epidemiological and Laboratory Profile of Children Presenting with Acute Undifferentiated Febrile Illness of Less Than 7 Days in Children (3 Months To 18 Years)

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Abstract

Introduction

Acute Undifferentiated Febrile Illness (AUFI) is a major cause of pediatric morbidity and mortality in tropical regions, with overlapping etiologies such as malaria, dengue, and scrub typhus complicating diagnosis. This study aimed to evaluate the clinical, epidemiological, and laboratory profiles of AUFI in children in Rajasthan, India, to enhance diagnostic strategies and guide empirical management.

Material & Methods

A hospital-based prospective study was conducted from May 2023 to April 2024 at the Pacific Institute of Medical Sciences in Udaipur, Rajasthan. Children aged 3 months to 18 years with AUFI (fever ≤7 days without localized symptoms) were enrolled. Exclusion criteria included chronic illnesses and fever with organ- specific manifestations. A structured Proforma was used to collect demographic, clinical, and epidemiological data. The diagnostic workup included blood counts, malaria and dengue serology, scrub typhus IgM ELISA, Typhidot IgM, C- reactive protein (CRP), liver function tests, blood and urine cultures, and chest X-rays (as indicated). Statistical analysis was performed using SPSS v28, with $p < 0.05$ considered statistically significant.

Results

Among 168 children, malaria was the most common diagnosis (40.5%), followed by dengue (15.5%) and undifferentiated febrile illness (19%). Peak incidence occurred post-monsoon (35.7%), with significant associations between malaria and anemia ($p<0.0001$) and dengue and leukopenia ($p<0.05$). Hospital stays >7 days were more frequent in undifferentiated cases ($p<0.01$). The discharge rate was 91.7%, with mortality highest in scrub typhus (7.1%).

Conclusion

Malaria remains the leading AUFI in children, with thrombocytopenia and thrombocytopenia serving as key diagnostic

markers. Improved diagnostics, vector surveillance, and seasonal intervention strategies are needed to reduce the AUFI burden and mortality.

Keywords: Fever, AUFI, Pediatric Febrile Illness, leukopenia, thrombocytopenia

Introduction

Fever, described by Sir William Osler as one of humanity's greatest enemies, is a physiological response to pyrogens that elevate the hypothalamic temperature set-point, typically defined as greater than 38°C orally or greater than 38.5°C rectally. It arises from infections (bacterial, viral, or parasitic), inflammatory conditions, or immunological disorders. It is classified by duration (acute: less than 7 days, subacute: 7–14 days, and chronic: more than 14 days) or pattern (intermittent, remittent, or continuous). While fever aids the host's defense, temperatures exceeding 40°C signal severe illness, requiring intervention. [1]

Acute Undifferentiated Febrile Illness (AUFI)—fever ≤7 days without localized symptoms—poses diagnostic challenges, especially in tropical regions where overlapping infections (e.g., dengue, malaria, scrub typhus) are endemic and require different treatment. In children, AUFI carries high morbidity and mortality due to non-specific presentations, risking delays in diagnosis and complications like sepsis, organ failure, or shock syndromes (e.g., dengue shock syndrome, severe malaria). Empirical antibiotic misuse further exacerbates antimicrobial resistance (AMR), complicating the treatment of drug-resistant typhoid, tuberculosis, and bacterial sepsis. [2,3]

Globally, AUFI disproportionately affects children in tropical areas, with viral (dengue, influenza, chikungunya) and bacterial (typhoid, scrub typhus, leptospirosis) pathogens predominating. Malaria remains endemic in Africa, Asia, and South America, while zoonotic infections rise with urbanization and climate change. In India, AUFI peaks during the monsoons, with dengue and chikungunya prevalent in urban areas and scrub typhus and leptospirosis in rural regions. Typhoid's multidrug-resistant strains and malaria's regional variability, notably in northeastern India, compound the burden (6). COVID-19 and influenza have further complicated AUFI diagnostics. [4]

AUFI's causes are diverse, including parasitic infections such as malaria (Plasmodium spp.), which is endemic in India and accounts for 1.7% of global cases. Notably, Rajasthan experiences seasonal spikes, with 72.61% of cases occurring from September to November. [5] Viral causes, such as dengue, affect 33 million people annually in India, particularly children aged 5–15. Rajasthan reported 63,000 cases in 2015, with Udaipur being a high-burden district. [6] Bacterial infections, such as scrub typhus (Orientia tsutsugamushi), are also emerging, with pediatric cases in rural Rajasthan linked to severe complications, necessitating early diagnosis. [7] Additionally, other conditions such as typhoid, UTIs, and rickettsial infections contribute significantly to AUFI cases. [8] Malaria caused 20.6% of under-14 deaths in India. [9] The incidence of dengue in children in Rajasthan ranges from 35 to 60 cases per 1,000 person-years, while scrub typhus requires improved diagnostics. [10,11]

Objectives

This study aims to:

- Analyze AUFI's clinical-laboratory profile in children aged 3 months to 18 years.
- Identify regional pathogens and seasonal trends to guide empirical therapy.

By refining diagnostic algorithms and public health strategies, the study aims to mitigate the impact of AUFI on pediatric health in high-burden regions, such as Rajasthan.

Material and methods

This hospital-based prospective study was conducted in the Department of Pediatrics at the Pacific Institute of Medical Sciences, Udaipur, Rajasthan, over a one-year period (May 2023–April 2024). The study enrolled children aged 3 months to 18 years who were admitted with acute undifferentiated febrile illness (AUFI), defined as fever (≥38°C axillary or ≥38.5°C rectal or oral) of ≤7 days' duration without a localized infection. Exclusion criteria included fever with respiratory, central nervous system (CNS), or gastrointestinal symptoms; chronic illnesses (e.g., congenital heart disease, immunodeficiency); or denial of parental consent. A structured Proforma captured demographic data (age, sex, socioeconomic status using Modified Kuppuswamy Scale, 2022), clinical data (anthropometry, vital signs, systemic examination), and epidemiological data.

All participants underwent a standardized diagnostic workup, which included a complete blood count, peripheral blood film, malaria RDT, dengue NS1/IgM/IgG ELISA, scrub typhus IgM ELISA, Typhidot IgM, C-reactive protein (CRP), liver function tests, blood and urine cultures, and a chest X-ray (as indicated). Etiological definitions included: malaria (positive RDT/microscopy), dengue (NS1/IgM positivity), scrub typhus (IgM ELISA ≥1.1 OD), enteric fever (Typhidot IgM positivity), and UTI (≥10^5 CFU/mL or pyuria with positive dipstick). Statistical analysis employed descriptive statistics (frequencies, means) and inferential tests (chi-square, logistic regression) using SPSS v28 ($p < 0.05$ considered significant), with sensitivity analyses conducted for missing data. Ethical approval was obtained from the institutional ethics committee.

Results

The study of 168 children with acute undifferentiated febrile illness revealed malaria as the most common cause (40.5%), showing strong associations with anemia ($p<0.0001$) and thrombocytopenia ($p<0.01$). Dengue fever is the second most common known cause (15.5%), showing a significant association with leukopenia ($p < 0.05$). In contrast, undifferentiated illness (19%) exhibits a correlation with prolonged hospitalization (>7 days, $p < 0.01$) and poorer outcomes. Most cases occurred post-monsoon (35.7%), particularly malaria ($p\approx< 0.0000005$). Clinically, pallor (27.4%) was the most common finding in malaria ($p<0.01$), while 41% showed no abnormalities. Laboratory findings demonstrated thrombocytopenia in 42.9% of cases [malaria (23.8%, $p < 0.01$), and dengue (11.9%, $p < 0.01$)], anemia in 45.2% cases with malaria showing significant association with p value 0f < 0.0001, and universal but nonspecific elevation of CRP (86.9%, $p = 0.9996$). The majority (52.4%) required 4-7 days of hospitalization, with 91.7% discharged successfully. Mortality was 3.6%, highest in scrub typhus (7.1% of total). These findings highlight the continued dominance of malaria in pediatric febrile illnesses, the diagnostic value of thrombocytopenia and leukopenia for dengue, and the concerning outcomes of undifferentiated cases that require further investigation.

Category	Subgroup	n (%) or Value	Significant Associations (p-value)
Demographics	Age (11-15 years)	56 (33.3%)	-
	Female gender	90 (53.6%)	-
	Lower middle SES	48 (28.6%)	-
Seasonality	Post-monsoon peak	60 (35.7%)	Malaria ($p\approx0.0000005$)
Clinical Findings	Pallor	46 (27.4%)	Malaria ($p<0.01$)
	Hepatosplenomegaly	29 (17.3%)	-
	No abnormalities	69 (41.1%)	Undifferentiated illness ($p<0.01$)
Diagnoses	Malaria	68 (40.5%)	-
	Dengue fever	26 (15.5%)	-
	Undifferentiated illness	32 (19.0%)	-
Lab Abnormalities	Anemia	76 (45.2%)	Malaria ($p<0.0001$)
	Leukopenia	58 (34.5%)	Dengue ($p<0.05$)
	Thrombocytopenia	72 (42.9%)	Malaria ($p<0.01$), Dengue ($p<0.01$)
	Elevated CRP	146 (86.9%)	Non-specific ($p=0.9996$)
Hospital Course	4-7 day stay	88 (52.4%)	-
	> 7-day stay	54 (32.1%)	Undifferentiated illness ($p<0.01$)
Outcomes	Discharged	154 (91.7%)	-
	Mortality	6 (3.6%)	Scrub typhus (7.1%)

Discussion

The present study evaluated the clinical, epidemiological, and laboratory characteristics of acute undifferentiated febrile illnesses (AUFI) in children aged 3 months to 18 years at a tertiary care hospital in Rajasthan. The study found that the most affected age group was 11–15 years (33.3%), aligning with findings from Prabha S et al. [12] and Mittal C et al. [13], but differing from Desari R et al. [14], who reported a higher prevalence in younger children (3–5 years). A female preponderance (M: F ratio, 0.86) was observed, contrary to studies by Nagar et al. [15] and Mittal et al. [13], which reported a male predominance. Lower socio- economic groups were more affected, a finding consistent with those of Herrick et al. [16] and Rauf et al. [17]

Seasonal variation was significant, with peak AUFI cases occurring during the monsoon and post-monsoon seasons (July–October), consistent with the findings of Rauf et al. [17]. Mittal et al. [13] Malaria and dengue peaked between July and November, aligning with studies by Kumar A et al. [18] and Mishra S et al. [19] Scrub typhus was most common from August to November, as reported by Kumar et al. [18] UTIs exhibited a different seasonal trend, peaking between January and May, which contrasts with the findings of Bhonsle K et al. [20], who reported a peak during the rainy season.
Among diagnoses, malaria was the most prevalent (40.4%), significantly higher than in studies by Mittal et al. [13] (16.5%) and Morch et al. [21] (17%), possibly due to the geographical location of most of the patients near hilly backwater. Dengue (15.4%), UTIs (8.92%), scrub typhus (8.33%), and enteric fever (7.73%) were comparable to those reported in prior studies. Laboratory findings highlighted anemia in malaria patients, thrombocytopenia in dengue cases, and elevated CRP in scrub typhus and enteric fever, aligning with studies by Prabha S et al. [12], Utuk et al. [22], and Das et al. [23] These findings reinforce the need for region-specific diagnostic and preventive strategies to improve AUFI management in pediatric populations.

Conclusion

This study emphasizes the seasonal prevalence and clinical profile of AUFIs in children, with malaria (40.48%) being predominant. Key markers included leukopenia for dengue and CRP elevation for inflammatory responses. Despite a 91.7% overall discharge rate, scrub typhus had a higher mortality rate than the rest. Limitations included a single-center design, short duration, and diagnostic constraints. Future research should focus on advanced diagnostics, multicenter studies, vector surveillance, and biomarker exploration to improve AUFI diagnosis, management, and outcomes, especially during peak transmission seasons.

Conflict of Interest-Nil

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