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Clinicohematological Profile of Acute Febrile Illness in Pediatric Populations: An Experience of Tertiary Care Teaching Hospital in Gujarat

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ABSTRACT

Acute febrile illness (AFI) constitutes a significant cause of hospital admissions among the pediatric population, leading to substantial morbidity and mortality in children globally. Common etiological agents encountered in Indian clinical contexts include chikungunya fever, dengue, malaria, typhoid. This study aimed to investigate the spectrum of AFI among pediatric patients, assess hematological parameters, identify specific causative agents, and evaluate the prognostic implications of these parameters. The study enrolled pediatric patients presenting with AFI at the outpatient department. Hematological profiles and biochemical investigations were conducted for all cases of AFI, with subsequent correlation analysis. Appropriate statistical methods were employed for data analysis. Statistically significant leukopenia was observed in cases of malaria and typhoid fever. Moreover, a significant difference in the severity of thrombocytopenia was noted between dengue fever and malaria. This study underscores the importance of both clinical and hematological parameters in the context of AFI. It concludes that these parameters collectively offer valuable insights for diagnosing the etiology of AFI.

INTRODUCTION

Acute febrile illness (AFI) manifests as a sudden onset of fever resulting from the invasion of the body by an infectious agent. It stands as a predominant complaint among pediatric patients seeking clinical attention, often leading to hospital admissions, morbidity, and fatalities among children worldwide. In India, prevalent causes of AFI encompass dengue, typhoid, malaria, and chikungunya fever[1,2]. Dengue and chikungunya fever, both arboviral diseases transmitted through mosquito bites, primarily by Aedes aegypti and Aedes albopictus, are endemic in tropical regions like India. They typically present with similar symptoms such as fever, body aches, skin eruptions, nausea, vomiting, and debility. Chikungunya is more frequently associated with acute arthritis and rashes, while dengue, particularly in cases of dengue hemorrhagic fever, may lead to bleeding and shock due to plasma leakage. The dengue virus (DENV), comprising four serotypes (DENV 1–4) within the flavivirus genus, is among the most prevalent arthropod-borne viral infections[3,4].

Notably, the World Health Organization (WHO) has included dengue in its targeted initiatives against neglected tropical diseases from 2015 to 2020. However, the reporting of dengue cases in India is often inadequate due to non-standardized national surveillance systems, primarily reliant on clinical diagnoses lacking essential laboratory confirmations [5,6]. This study aims to examine the spectrum of AFI in the pediatric population, alongside assessing hematological parameters for diagnosing AFI cases using a predefined set of laboratory tests. Additionally, the prognostic significance of these hematological parameters is under scrutiny.

MATERIAL AND METHODS

This cross-sectional investigation spanned a 3-month duration and took place at a tertiary healthcare facility in Gujarat. The study enrolled pediatric patients attending the outpatient department with AFI, following approval from the Institutional Ethics Committee and obtaining informed consent from parents or guardians. 145 children aged between 2 and 14 years, displaying fever for up to 7 days, constituted the study cohort. Patients presenting beyond 5 days of fever onset or declining consent were excluded.

Blood samples were procured within 5 days of fever onset, collected in plain vials for acute sera and ethylenediaminetetraacetic acid (EDTA) vials for hematological assessments. Complete blood counts were performed using the Automated Cell Counter (Sysmex). Malaria cases were confirmed via microscopy or rapid diagnostic tests for malaria antigens. Dengue detection utilized non-structural protein 1 enzyme-linked immunosorbent assay (ELISA) antigen tests on acute serum samples, while dengue and chikungunya immunoglobulin M antibody tests were ELISA-based. Liver function tests (LFT) encompassing alkaline phosphatase, aspartate aminotransferase, and alanine aminotransferase were conducted using Siemens automated biochemistry analyzer. Commercial testing kits were employed to investigate other febrile etiologies such as typhoid. Hematological and biochemical profiles were evaluated and correlated, including complete hemogram and peripheral blood smear examination for microscopy.

Leukopenia was defined as <4000/mm^3 and thrombocytopenia as <150,000/mm^3. Derangement in LFT was characterized by serum glutamic pyruvic transaminase (SGPT) value >35 IU/L and serum bilirubin value >1.2 mg/dL. Statistical analysis involved tabulating patient data and utilizing the Chi-square method, with p-values <0.05 deemed statistically significant to identify correlations among various febrile illness parameters.

RESULTS AND DISCUSSIONS

A total of 145 febrile patients, aged between 2 and 14 years, were enrolled in the study, predominantly comprising males. The largest subgroup consisted of 46 children aged 2 to 4 years. The mean age of the patients was 7.1 years (Table 1). The majority of cases were attributed to malaria, followed by typhoid fever (Fig. 1).

Patients exhibited diverse clinical manifestations, including fever, vomiting, myalgia, rashes, abdominal pain, and arthralgia. Fever was universal among all patients, with a maximum duration of 7 days. Headache was a prevalent symptom, particularly among dengue and malaria cases, while vomiting predominated in typhoid cases, and arthralgia was prominent in chikungunya cases (Table 2).

Regarding hematological parameters, the correlation with hemoglobin levels was statistically insignificant across all diseases. Leukopenia showed statistical significance (p=0.003) only in cases of typhoid fever, while its association was insignificant in malaria, dengue, and chikungunya fever (p=0.39). The severity of thrombocytopenia significantly differed in dengue fever (p=0.009), whereas it was statistically insignificant in malaria and typhoid fever (p=0.68 and 0.43, respectively) (Table 3).

Table 1: Demographic characteristics of study participants

Variable	n	Percentage
Gender		
Male	84	57.93
Female	61	42.07
Total	145	100.00
Age Group		
2-4 years	46	31.72
4-6 years	17	11.72
6-8 years	18	12.41
8-10 years	17	11.72
10-12 years	24	16.55
12-14 years	23	15.86
Total	145	100.00

Table 2: Signs and symptoms observed in AFI cases

	Dengue		Malaria		Typhoid		Chikungunya	
Symptoms	n	%	n	%	n	%	n	%
Abdominal pain	12	70.59	15	19.23	20	48.78	4	44.44
Arthralgia	7	41.18	16	20.51	15	36.59	9	100.00
Bleeding manifestations	6	35.29	4	5.13	0	0.00	0	0.00
Diarrhea	12	70.59	30	38.46	26	63.41	3	33.33
Headache	15	88.24	35	44.87	23	56.10	4	44.44
Jaundice	3	17.65	29	37.18	7	17.07	0	0.00
Myalgia	6	35.29	29	37.18	17	41.46	6	66.67
Rashes	9	52.94	9	11.54	12	29.27	6	66.67
Vomiting	12	70.59	41	52.56	26	63.41	4	44.44

Table 3: Haematological parameters in AFI cases

	Dengue		Malaria		Typhoid		Chikungunya	
Parameter	n	%	n	%	n	%	n	%
Anemia (Hb <12 mg/dl)	12	70.59	38	48.72	38	92.68	0	0.00
PCV (<45%)	15	88.24	71	91.03	71	173.17	0	0.00
Leukopenia (<4000/mm3)	6	35.29	26	33.33	26	63.41	7	77.78
Neutrophils (<40%)	10	58.82	28	35.90	28	68.29	4	44.44
Lymphocytes (>45%)	6	35.29	29	37.18	29	70.73	3	33.33
Platelets (100,000–150,000/µl)	3	17.65	22	28.21	22	53.66	7	77.78
50,000–100,000/µl	7	41.18	44	56.41	44	107.32	1	11.11
<50,000/µl	9	52.94	13	16.67	13	31.71	0	0.00

Table 4: Biochemical parameters in AFI cases

	Dengue		Malaria		Typhoid		Chikungunya	
Parameter	n	%	n	%	n	%	n	%
SGOT >40 IU/ml	10	58.82	28	35.90	22	53.66	9	100.00
SGPT >35 IU/ml	9	52.94	36	46.15	23	56.10	7	77.78
Alkaline Phosphatase elevation	6	35.29	61	78.21	19	46.34	1	11.11
Serum bilirubin >1.2 mg/ml	3	17.65	12	15.38	6	14.63	-	-

Among dengue fever patients, elevated serum glutamic-oxaloacetic transaminase (SGOT) levels were prevalent, while raised alkaline phosphatase was common in malaria patients. Approximately 57.1% of typhoid patients exhibited elevated serum glutamic pyruvic transaminase (SGPT) levels, while abnormalities in both SGOT and SGPT were observed in chikungunya patients (Table 4).

AFIs impose a significant health burden, particularly in developing nations, notably affecting children and resulting in substantial loss of healthy life years. Common etiological agents in South Asia include dengue, typhoid, and paratyphoid among patients presenting with fever[7-10]. Thrombocytopenia combined with anemia serves as a crucial diagnostic indicator for malaria in individuals with AFI[11-13]. In cases of severe falciparum malaria, thrombocytopenia is attributed to disseminated intravascular coagulation and platelet endothelial activation, while in uncomplicated malaria such as Plasmodium vivax, macrophage activation, antiplatelet antibodies, sequestration in non-splenic areas, and pseudothrombocytopenia due to platelet clump formation are implicated[14].

Our investigation revealed that among 100 fever patients, dengue was detected in 11.72%, malaria in 53.79%, typhoid in 28.28%, and chikungunya in 6.21% of cases, aligning with prior studies indicating the persistence of dengue fever, typhoid fever, and malaria as significant public health concerns in many developing regions[15]. Among dengue patients in our study, prevalent symptoms included headache, vomiting, and gastrointestinal manifestations like abdominal pain and diarrhea, consistent with earlier findings reporting fever, conjunctival congestion, and myalgia as common clinical presentations. Petechiae emerged as the primary bleeding manifestation among dengue patients in our study, diverging from previous observations of skin bleeding preceding gum bleeding[16].

Constitutional symptoms such as headache, myalgia, cough, rhinitis, and anorexia were more pronounced in chikungunya fever. Arthralgia predominated as the leading symptom in chikungunya patients in our study, followed by myalgia, vomiting, and rashes, consistent with prior research associating chikungunya with polyarthralgia, headache, and myalgia/arthralgia of greater severity compared to other diseases and skin rashes[17]. Transient thrombocytopenia commonly accompanies systemic infections presenting as febrile illness, notably in tropical infections such as malaria, dengue, chikungunya, and various viral infections, as well as typhoid fever. Malaria fever emerged as the primary cause of thrombocytopenia in our study, differing from previous studies attributing septicemia or dengue as the major etiology[18-20]. Severe thrombocytopenia was notably significant in dengue patients compared to those with malaria, typhoid, and chikungunya.

Hematocrit changes exceeding 20% and established cutoffs from previous studies served as indicators of hemoconcentration for diagnosing and

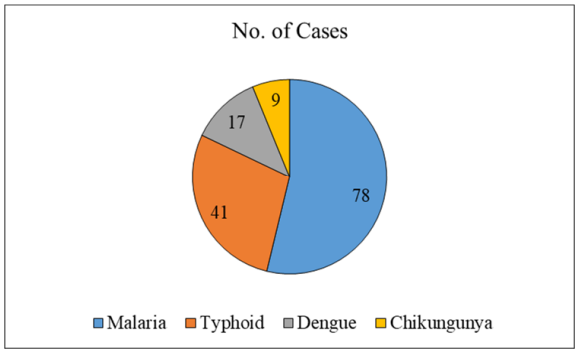

Fig. 1: Diagnosis of AFI in study population

monitoring severe dengue infection[21-23]. Platelet counts showed a significant association with disease severity in dengue fever, suggesting their utility as predictive parameters[24]. Contributing factors to thrombocytopenia in dengue include decreased red blood cell deformability, splenic phagocytosis, peripheral destruction, and excessive platelet removal [25,26].

Anemia, leukopenia, and thrombocytopenia are commonly observed in typhoid fever due to bone marrow suppression and hemophagocytosis. Leukopenia was particularly notable in typhoid patients in our study, contrasting with its statistical insignificance in dengue, malaria, and chikungunya patients[27]. Mild to moderate thrombocytopenia was prevalent among typhoid patients, yet without any bleeding manifestations. In chikungunya patients, mild platelet count decreases were observed in some cases, with one case presenting severe thrombocytopenia, contrasting with normal platelet counts in dengue patients[28].

Liver enzyme derangement is common in AFI, with dengue fever exhibiting a more rapid increase in aspartate aminotransferase levels compared to other illnesses[29]. Typhoid patients in our study displayed raised levels of liver enzymes, consistent with prior findings indicating various mechanisms contributing to hepatic injury in typhoid fever[30-32].

Limitations of our study include its focus on patients primarily from lower or middle socioeconomic strata, limiting generalizability, and the relatively small sample size for individual diagnoses, suggesting the need for larger-scale studies to better evaluate these parameters' roles.

CONCLUSION

Platelet count serves as a predictive indicator for dengue fever, while leukopenia is indicative of typhoid fever, thereby serving as predictive markers for diagnosing these febrile illnesses in endemic regions. Clinical and hematological parameters collectively offer valuable insights for diagnosing the etiology of AFI in pediatric population.

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