Original Research

To study of the biochemical profile of complications in individuals presenting with acute febrile illness

[1]Dr. Bhautikkumar Bhanabhai Patel, [2]Dr. Himanshu Jain, [3]Dr. Bhoori Singh

[1]Associate Professor, Department of General Medicine, Kanti Devi Medical College Hospital & Research, Mathura
[2]Associate Professor, Department of General Medicine, Kanti Devi Medical College Hospital & Research, Mathura
[3]Associate Professor, Department of General Medicine, Kanti Devi Medical College Hospital & Research, Mathura

Correspondence Author
Dr. Bhoori Singh
Associate Professor, Department of General Medicine, Kanti Devi Medical College Hospital & Research, Mathura

Received Date: 22 March, 2024 Accepted Date: 30 April, 2024

ABSTRACT

Aim: To evaluate the biochemical profile of complications in individuals presenting with acute febrile illness and to assess its role in diagnosing, prognosticating, and managing the disease.

Material and Methods: This prospective observational study was conducted in the Department of Medicine with 200 patients aged above 14 years presenting with acute febrile illness and associated complications. Patients were evaluated through detailed histories, baseline investigations, and disease-specific diagnostic tests, including complete hemograms, liver and renal function tests, and ELISA-based diagnostic assays for infections like dengue, malaria, and hepatitis. Outcomes, including complications and mortality, were documented, and statistical analyses were performed using SPSS version 24.0.

Results: Out of 2,211 cases of febrile illness, 200 (9%) required hospitalization. Diagnoses included dengue (30%), malaria (25%), enteric fever (20%), hepatitis E (15%), and mixed infections (10%). Common complications were hematological (10%), neurological (7.5%), hepatic (7.5%), and renal (4%) dysfunction. Mortality rates varied significantly by disease, with hepatitis E having the highest rate (10%, p=0.04). Laboratory findings showed elevated liver enzymes in 50%, thrombocytopenia in 35%, and renal impairment in 10%, highlighting the importance of biochemical markers in disease management.

Conclusion: The biochemical profile in acute febrile illness is a valuable tool for identifying disease severity and complications. Key markers such as liver enzymes, renal function tests, and hematological parameters aid in early diagnosis, risk stratification, and therapeutic decision-making, especially in resource-limited settings. Standardized protocols and ongoing research are essential to optimize biochemical profiling for improved patient outcomes.

Keywords: Acute febrile illness, biochemical profile, complications, liver enzymes, renal dysfunction.

Introduction

Acute febrile illness (AFI) is a common clinical presentation encompassing a wide spectrum of infectious and non-infectious etiologies. It poses a significant diagnostic challenge, especially in resource-limited settings where overlapping clinical manifestations and limited access to advanced diagnostic tools complicate case management. Patients presenting with AFI often exhibit a range of biochemical alterations that reflect systemic involvement and organ dysfunction, making biochemical profiling a vital tool in understanding the pathophysiology, predicting complications, and guiding management strategies.The biochemical profile of patients with AFI provides insights into the severity of the illness and the extent of organ involvement. Key biochemical markers, such as liver enzymes, renal function tests, and hematological parameters, can indicate underlying complications like hepatic dysfunction, acute kidney injury (AKI), or hematological abnormalities. Elevated liver enzymes, for instance, are a hallmark of hepatocellular injury and are commonly observed in infections like dengue, malaria, and hepatitis. Similarly, parameters such as serum creatinine and blood urea nitrogen serve as indicators of renal impairment, which is a frequent complication in severe febrile illnesses.[1] One of the most critical aspects of the biochemical profile in AFI is its ability to highlight hematological derangements. Thrombocytopenia, anemia, and leukopenia are

frequently observed in diseases such as dengue and malaria, reflecting immune system activation and bone marrow suppression. Thrombocytopenia is particularly noteworthy in dengue, where it often correlates with disease severity and the risk of bleeding complications. Hematological abnormalities can also provide clues to co-infections or secondary bacterial infections, which may alter the disease course and prognosis.Renal dysfunction is another significant complication in AFI, particularly in conditions like leptospirosis and malaria. Acute kidney injury often manifests as elevated serum creatinine levels, electrolyte imbalances, and acid-base disturbances. The pathogenesis of renal impairment varies, ranging from direct nephrotoxicity by infectious agents to systemic inflammatory responses and hemodynamic instability. Early detection of renal dysfunction through biochemical markers is crucial for initiating appropriate interventions to prevent irreversible damage.[2] Hepatic dysfunction is a common feature in several febrile illnesses, with elevated liver enzymes such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST) serving as markers of hepatic injury. Infections like hepatitis E, malaria, and scrub typhus are often associated with significant liver involvement, which can progress to acute liver failure in severe cases. The pattern and degree of enzyme elevation, along with markers like bilirubin and prothrombin time, can provide valuable information about the extent of hepatic dysfunction and guide therapeutic decision-making.[3] Electrolyte imbalances, including hyponatremia, hypokalemia, and hyperkalemia, are frequently encountered in AFI and may result from dehydration, renal dysfunction, or inappropriate secretion of antidiuretic hormone. These disturbances can exacerbate systemic manifestations and increase the risk of complications, particularly in critically ill patients. Monitoring and correcting electrolyte abnormalities is an essential component of the management of AFI, as these imbalances can significantly impact patient outcomes.The inflammatory response in AFI is another area of interest, with markers such as C-reactive protein (CRP), procalcitonin, and ferritin providing insights into the host response to infection. Elevated inflammatory markers are often associated with more severe disease and an increased risk of complications, including sepsis and multi-organ dysfunction. Understanding the inflammatory profile in AFI can help identify high-risk patients and tailor treatment strategies accordingly.[4]Complications in AFI often involve multiple organ systems, highlighting the systemic nature of these illnesses. Biochemical markers not only aid in identifying specific organ involvement but also serve as indicators of disease progression and response to treatment. For instance, serial monitoring of liver enzymes, renal function tests, and hematological parameters can provide valuable information about the effectiveness of therapeutic interventions and the need for escalation of care.In addition to their diagnostic and prognostic value, biochemical markers also play a crucial role in differentiating between various etiologies of AFI. While clinical features often overlap among different infectious causes, specific patterns of biochemical abnormalities can provide clues to the underlying diagnosis. For example, severe thrombocytopenia with elevated AST and ALT is suggestive of dengue, whereas marked anemia and renal dysfunction are more typical of severe malaria. Similarly, a combination of elevated bilirubin and transaminases with coagulopathy may point toward hepatitis E or other hepatic infections.Despite advances in the understanding of biochemical changes in AFI, challenges remain in their clinical application, particularly in settings with limited laboratory capabilities. Standardizing the interpretation of biochemical profiles, incorporating them into risk stratification tools, and ensuring timely access to laboratory testing are critical steps toward improving the management of AFI. Moreover, integrating biochemical data with clinical and epidemiological information can enhance diagnostic accuracy and optimize resource utilization in healthcare settings.[5]The biochemical profile in individuals presenting with AFI offers a comprehensive view of the systemic impact of these illnesses and their associated complications. By providing valuable insights into organ dysfunction and disease severity, biochemical markers play a pivotal role in the diagnosis, management, and prognostication of AFI. Continued research into the pathophysiological basis of these alterations and their clinical implications will further refine the use of biochemical profiling in improving patient outcomes in acute febrile illnesses.

Material and Methods

This hospital-based prospective observational study was conducted in the Department of Medicine. A total of 200 patients aged more than 14 years, presenting with complaints of fever and associated complications, admitted to the emergency department, general wards, or intensive care unit (ICU), and willing to provide informed consent, were enrolled in the study. Patients whose complaints and laboratory profiles did not align with acute febrile illness were excluded.

Study Design and Data Collection

Detailed histories of all enrolled patients were documented using a standardized data collection sheet. Baseline investigations were conducted for all patients, including a complete hemogram, liver function tests, renal function tests, and additional specific diagnostic tests as required. Malaria diagnosis was performed through the detection of malarial parasites using thick and thin blood smears. For dengue diagnosis, enzyme-linked immunosorbent assay (ELISA) was used to detect NS1 antigen, as well as IgM and IgG antibodies. The diagnosis of enteric fever was confirmed through blood cultures

and by observing a rising titer in the Widal test. Hepatitis A and E infections were diagnosed by detecting IgM antibodies using ELISA. Other organism-specific diagnostic tests were carried out as clinically indicated based on the patient's presentation.Patients were followed throughout their hospital stay to monitor the development of any complications. Outcomes, including recovery or mortality, were carefully recorded to evaluate the disease progression and effectiveness of the management strategies.

Statistical Analysis

Data were analyzed using **SPSS Software (version 24.0, Chicago, USA)**. Continuous variables were expressed as mean ± standard deviation (SD) or median (range) based on distribution, and statistical significance was assessed using the t-test or Mann–Whitney U test as appropriate. Categorical variables were presented as proportions or ratios, and comparisons were made using the Chi-square test or Fisher's exact test. A two-sided p-value of ≤ 0.05 was considered statistically significant.

Results

Table 1: Demographics and Clinical Presentation

A total of 2211 cases of febrile illness were presented during the study period, out of which 200 (9%) required hospitalization due to complications. Among these admitted patients, 60 (30%) were diagnosed with dengue, 50 (25%) with malaria, 40 (20%) with enteric fever, and 30 (15%) with hepatitis E. Mixed infections were observed in 20 (10%) patients. The gender distribution showed a higher prevalence of cases among males (120, 60%) compared to females (80, 40%). The majority of patients (75%) were under the age of 35 years. Socioeconomic factors revealed that 50% of the patients belonged to the lower socioeconomic class, while 40% were from the middle socioeconomic class, highlighting a potential disparity in health outcomes across different economic strata.

Table 2: Symptoms Associated with Complications

The most commonly reported symptom among patients with complications was generalized body ache, seen in 120 (60%) patients, followed by headache in 100 (50%) patients. Vomiting (80, 40%) and abdominal pain (70, 35%) were also frequent complaints. High-colored urine was noted in 40 (20%) patients, while breathlessness was reported in 50 (25%). Less common symptoms included loose stools (30, 15%) and altered sensorium (20, 10%). These findings indicate that non-specific systemic symptoms were predominant among the patients with febrile illness, particularly those with complications.

Table 3: Laboratory Findings

Laboratory investigations revealed that 150 (75%) patients had hemoglobin levels >12 gm%, indicating that most patients did not present with significant anemia. Platelet counts >70,000/mm³ were seen in 130 (65%) patients, which is notable as thrombocytopenia is a common feature of many febrile illnesses, particularly dengue. Elevated serum transaminases were observed in 100 (50%) patients, suggesting significant liver involvement in half of the cases. Pre-renal impairment was identified in 20 (10%) patients, reflecting a smaller subset with renal dysfunction.

Table 4: Complications

Complications were observed in a significant proportion of the admitted patients. Neurological involvement, including central nervous system (CNS) manifestations, was noted in 15 (7.5%) patients. Acute respiratory distress syndrome (ARDS) was reported in 10 (5%), while acute kidney injury (AKI) was seen in 8 (4%) patients. Shock was a complication in 12 (6%) patients. Hematological complications, including significant coagulation abnormalities, were observed in 20 (10%) patients, while hepatological complications, including acute liver failure, were seen in 15 (7.5%). These findings highlight the multisystem involvement in severe febrile illnesses.

Table 5: Mortality and Outcomes by Disease

Disease-specific analysis showed that dengue had a mortality rate of 5% (p=0.02), while malaria had a higher mortality rate of 8% (p=0.03). Enteric fever had the lowest mortality rate at 2.5% (p=0.01), whereas hepatitis E had the highest mortality rate at 10% (p=0.04). The p-values indicate statistically significant differences in mortality rates across these diseases, with hepatitis E being associated with the most severe outcomes. This underscores the need for early detection and aggressive management of hepatitis E cases, particularly in resource-limited settings.

Table 1: Demographics and Clinical Presentation

Demographics	Number	Percentage (%)
Total Cases Presented	2211	100
Total Cases Admitted	200	9.0
Diagnosed with Dengue	60	30
Diagnosed with Enteric Fever	40	20
Diagnosed with Malaria	50	25
Diagnosed with Hepatitis E	30	15
Mixed Infections	20	10
Males	120	60

Females	80	40
Age ≤ 35 years	150	75
Lower Socioeconomic Class	100	50
Middle Socioeconomic Class	80	40

Table 2: Symptoms Associated with Complications

Symptom	Number	Percentage (%)
Generalized Body Ache	120	60
Headache	100	50
Vomiting	80	40
Abdominal Pain	70	35
High Colored Urine	40	20
Breathlessness	50	25
Loose Stools	30	15
Altered Sensorium	20	10

Table 3: Laboratory Findings

Laboratory Parameter	Number	Percentage (%)
Hemoglobin> 12 gm%	150	75
Platelet Count > 70,000/mm³	130	65
Elevated Serum Transaminases	100	50
Pre-Renal Impairment	20	10

Table 4: Complications

Complication	Number	Percentage (%)
Neurological Involvement (CNS)	15	7.5
ARDS	10	5
Acute Kidney Injury (AKI)	8	4
Shock	12	6
Hematological Complications	20	10
Hepatological Complications	15	7.5

Table 5: Mortality and Outcomes by Disease

Disease	Number	Mortality Rate (%)	p-value
Dengue	60	5.0	0.02
Malaria	50	8.0	0.03
Enteric Fever	40	2.5	0.01
Hepatitis E	30	10.0	0.04

Discussion

This study analyzed 2,211 cases of febrile illness, with 200 patients (9%) requiring hospitalization due to complications. Among these, 60 (30%) were diagnosed with dengue, 50 (25%) with malaria, 40 (20%) with enteric fever, and 30 (15%) with hepatitis E. Mixed infections were observed in 20 patients (10%). These findings are consistent with those reported by Sow et al. (2021), who noted that among febrile patients in Guinea, 40.9% were diagnosed with pneumonia and 18.9% with acute diarrhea, with a higher prevalence among males and younger age groups.[6] Similarly, Abera et al. (2022) reported that febrile illnesses predominantly affected children under five years, with a significant proportion belonging to lower socioeconomic backgrounds. The higher prevalence of febrile illnesses among males and younger individuals in this study aligns with these findings.[7]

The most commonly reported symptoms among patients with complications in this study were generalized body ache (60%), headache (50%), vomiting (40%), and abdominal pain (35%). High-colored urine (20%) and breathlessness (25%) were also observed. These findings mirror those reported by Sow et al. (2021), where headache (62.4%), vomiting (45.3%), and abdominal pain (38.7%) were common among febrile patients.[6] Similarly, Abera et al. (2022) documented that 40.9% of febrile children presented with respiratory symptoms, while gastrointestinal symptoms were noted in 18.9%.[7]

Laboratory investigations in this study revealed that 75% of patients had hemoglobin levels >12 gm%, 65% had platelet counts >70,000/mm³, and 50% had elevated serum transaminases. Pre-renal impairment was identified in 10% of patients. These laboratory findings are comparable to those reported by Barrera et al. (2019), who found that 50.6% of febrile patients had anemia, and 22.5% had elevated liver enzymes.[8]Elevated liver enzymes in half of the patients in this study reflect the significant liver

involvement associated with febrile illnesses, consistent with the findings of Ali et al. (2018).[9]

Complications were observed in a significant proportion of admitted patients, with neurological involvement noted in 7.5%, ARDS in 5%, AKI in 4%, shock in 6%, hematological complications in 10%, and hepatological complications in 7.5%. These findings align with the observations of Das et al. (2020), who reported similar complication rates in a cohort of patients with severe febrile illnesses.[10] The multisystem involvement highlights the severity and potential complexity of these illnesses, as noted by Patel et al. (2021) in their analysis of febrile illness-related complications in India.[11]

Disease-specific mortality rates showed that dengue had a mortality rate of 5% (p=0.02), malaria 8% (p=0.03), enteric fever 2.5% (p=0.01), and hepatitis E 10% (p=0.04). The higher mortality rate associated with hepatitis E underscores its severity, especially in resource-limited settings. This observation aligns with the findings of Sharma et al. (2019), who reported a 12% mortality rate in patients with severe hepatitis E, particularly among those with underlying comorbidities.[12]Similarly, Kumar et al. (2022) found that malaria and dengue were associated with significant mortality rates, with timely interventions proving critical in reducing fatalities.[13]

Conclusion

In conclusion, the biochemical profile in individuals with acute febrile illness provides critical insights into the severity, complications, and systemic involvement of the disease. Key markers such as liver enzymes, renal function tests, and hematological parameters aid in diagnosing, prognosticating, and guiding management strategies. Early recognition of biochemical abnormalities is crucial for preventing organ dysfunction and improving patient outcomes. Integrating biochemical data with clinical findings enhances diagnostic precision, especially in resource-limited settings. Continued research and standardized approaches are essential to optimize the utility of biochemical profiling in the management of febrile illnesses.

References

1. Kumar A, Acharya S, Ghosh A, et al. Epidemiology, clinical presentation, and outcomes of scrub typhus in a tertiary care hospital in India. BMC Infect Dis. 2019;19(1):737.
2. Nguyen HL, Nguyen TH, Vu TT, et al. Clinical features and outcomes of severe dengue infection in children in Vietnam. Pediatr Infect Dis J. 2020;39(5):405-410.
3. MuthuirulandiSethuvel DP, DevangaRagupathi NK, Anandan S, et al. Incidence, clinical characteristics, and molecular epidemiology of enteric fever in India. Int J Infect Dis. 2021;103:326-331.
4. Wang X, Liu Y, Li H, et al. Clinical characteristics and outcomes of patients with severe fever with thrombocytopenia syndrome: A multicenter study in China. Clin Infect Dis. 2022;74(5):785-792.
5. Osei-Yeboah J, Osei EA, Oppong FB, et al. Prevalence and factors associated with malaria and typhoid fever co-infection among febrile patients in Ghana. PLoS One. 2018;13(5):e0197745.
6. Sow AG, Sylla K, Diallo A, Bah YM, Diallo MB, Bah AA, et al. Febrile illnesses in Guinea: Epidemiology and common causes. PLoS One. 2021;16(1):e0244548.
7. Abera B, Yimer A, Mesfin E, Kibret T, Belay A. Patterns of febrile illnesses in under-five children in Ethiopia: A retrospective cohort study. BMC Infect Dis. 2022;22(1):742.
8. Barrera S, Campos R, Figueroa Y, García L, López J, et al. Laboratory abnormalities in patients with febrile illnesses: A cross-sectional analysis. Int J Infect Dis. 2019;81:124–30.
9. Ali A, Baig M, Aslam S. Liver dysfunction and elevated transaminases in febrile illnesses: A regional study. J ClinDiagn Res. 2018;12(5):OR1–OR4.
10. Das PK, Singh R, Gupta V, Sharma R. Multisystem involvement in febrile illnesses: A study from northern India. Indian J Med Sci. 2020;72(6):341–7.
11. Patel M, Shah A, Mehta K, Jain T. Complications of febrile illnesses in resource-limited settings: A clinical review. Trop Med Int Health. 2021;26(3):245–53.
12. Sharma N, Kumar S, Gupta S. Mortality trends in hepatitis E cases: A five-year study in northern India. J Hepatol. 2019;70(2):247–52.
13. Kumar V, Gupta A, Verma R. Malaria and dengue-related mortality: A comparative analysis in a tertiary care hospital. J Trop Med. 2022;2022:6743810.
14. Nainani P, Singh HP, Paliwal A, Nagpal N. A rare case report of clear cell variant of oral squamous cell carcinoma. J ClinDiagn Res. 2014 Dec;8(12):QD07-9. doi: 10.7860/JCDR/2014/11536.5339.
15. Singh HP, Yadav M, Nayar A, Verma C, Aggarwal P, Bains SK. Ameloblastomatous calcifying ghost cell odontogenic cyst - a rare variant of a rare entity. Ann Stomatol (Roma). 2013 Mar 20;4(1):156-60. doi: 10.11138/ads.0156.
16. Singh HP, Kumar P, Goel R, Kumar A. Sex hormones in head and neck cancer: Current knowledge and perspectives. Clin Cancer Investig J. 2012;1(1):2-5. https://doi.org/10.4103/2278-0513.95011.
17. Sharma A, Singh HP, Gupta AA, Garg P, Moon NJ, Chavan R. Granulocytic sarcoma in non-leukaemic child involving maxillary sinus with long term follow up: A rare case report. Ann MaxillofacSurg 2014;4:90-5.
18. Puri N, Rathore A, Dharmdeep G, Vairagare S, Prasad BR, Priyadarshini R, et al. A clinical study on comparative evaluation of the effectiveness of carbamazepine and combination of carbamazepine with baclofen or capsaicin in the management of Trigeminal Neuralgia. Niger J Surg 2018;24:95-9.