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FREQUENCY OF SUPERIMPOSED BACTERIAL INFECTIONS IN PATIENTS PRESENTING WITH DENGUE FEVER

Original Research

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Acknowledgement: The authors gratefully acknowledge the support of CMH Jhelum administration during data collection.

Conflict of Interest: None
Grant Support & Financial Support: None

ABSTRACT

Background: Dengue fever is a significant public health challenge in endemic regions, often complicated by secondary bacterial infections which increase the severity and prolong hospitalization. These co-infections not only raise morbidity and mortality rates but also strain healthcare systems, especially during seasonal outbreaks. Early identification of such infections using laboratory markers is critical to improving clinical outcomes and guiding appropriate treatment strategies in resource-limited settings.

Objective: To determine the frequency of superimposed bacterial infections among patients diagnosed with dengue fever.

Methods: This comparative cross-sectional study was conducted at the Department of Medicine, Combined Military Hospital, Jhelum, from April to September 2024. A total of 250 adult patients admitted with confirmed dengue infection were included using non-probability consecutive sampling. Patients with chronic inflammatory diseases, immunosuppression, or pregnancy were excluded. Serum procalcitonin, C-reactive protein (CRP), and total leukocyte count (TLC) were measured to identify bacterial co-infections. Procalcitonin >2.0 ng/ml, CRP >12 mg/L, TLC >12 × 10^9/µL, or positive blood culture were considered diagnostic indicators. Data analysis was performed using SPSS version 24.

Results: Out of 250 patients, 157 (62.8%) were male and 93 (37.2%) female. The median age was 58 years (IQR 22). Median procalcitonin, CRP, and TLC values were 0.3 ng/ml (IQR 1.1), 4.8 mg/L (IQR 7.0), and 5.0 × 10^9/µL (IQR 8.9), respectively. Based on diagnostic criteria, 27 patients (10.8%) were found to have superimposed bacterial infections.

Conclusion: Secondary bacterial infections in dengue patients are clinically significant and demand a high index of suspicion. Timely recognition using simple laboratory tests can facilitate early intervention, reducing complications and hospital stay.

Keywords: C-Reactive Protein, Dengue Fever, Procalcitonin, Secondary Infection, Sepsis, Total Leukocyte Count, Viral Hemorrhagic Fever.

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INTRODUCTION

Dengue fever remains a major global public health concern, being endemic in over 120 countries with significant disease burden concentrated in Southeast Asia, Central America, and the Caribbean. The World Health Organization estimates approximately 390 million people are infected by dengue virus annually (1,2). In Pakistan, dengue has been endemic since 1994, with a concerning upward trend in incidence marked by seasonal outbreaks. A combination of climatic conditions, unplanned urban expansion, inadequate awareness regarding preventive strategies, and limited access to effective healthcare services have collectively fueled this rise in dengue-related morbidity and mortality (3,4). The disease is primarily transmitted through the bite of *Aedes aegypti* mosquitoes, with the causative pathogen being dengue virus, a single-stranded RNA virus belonging to the *Flaviviridae* family. Clinically, dengue infection presents with a wide spectrum of manifestations ranging from mild fever and skin rash to severe complications like hemorrhage and dengue shock syndrome, which may prove fatal if not promptly recognized and managed. Adding to the clinical complexity, patients with dengue are at risk of developing superimposed bacterial infections, which not only alter the disease trajectory but also mask classical features of viral infection. These concurrent infections can involve multiple organ systems, confounding the diagnostic process and complicating therapeutic interventions (5,6). Timely identification of bacterial co-infections in dengue cases is critical for improving clinical outcomes, yet the overlap in clinical symptoms often hinders early recognition. Laboratory investigations such as total leukocyte count, serum C-reactive protein (CRP), and procalcitonin have emerged as useful biomarkers in differentiating isolated dengue infections from those complicated by secondary bacterial involvement (7,8). Despite this, there remains a scarcity of region-specific data to guide the diagnostic approach for such dual infections in endemic settings like Pakistan. Therefore, this study aims to determine the frequency of superimposed bacterial infections among patients with dengue fever and to evaluate laboratory parameters that assist in their early identification, ultimately contributing to more precise clinical management.

METHODS

This comparative cross-sectional study was conducted at the Department of Medicine, Combined Military Hospital (CMH), Jhelum, over a six-month period from April to September 2024. The sample size was calculated using the WHO sample size calculator with a 95% confidence level, a 5% margin of error, and an assumed prevalence rate of 5% (1,5). A non-probability consecutive sampling technique was employed to recruit participants who met the eligibility criteria. Prior to data collection, ethical approval was obtained from the Institutional Ethical Review Board (IERB # A/17/01/24), and written informed consent was secured from all participants. The study included adult patients aged 18 to 70 years who were admitted to the designated dengue ward. Patients with pre-existing chronic inflammatory conditions, known infections of other etiologies, immune-mediated disorders, or those who were pregnant or lactating were excluded to eliminate potential confounders affecting inflammatory biomarkers. For each enrolled participant, laboratory parameters including serum procalcitonin, C-reactive protein (CRP), and total leukocyte count (TLC) were measured using standardized protocols and hospital laboratory services. All collected data were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 24.0. Categorical variables were summarized as frequencies and percentages, while continuous variables such as age, procalcitonin, CRP, and TLC levels were reported as median values with interquartile ranges (IQR), owing to their non-parametric distribution.

RESULTS

Out of a total of 250 patients enrolled in the study, 157 (62.8%) were male and 93 (37.2%) were female. The overall median age was 58 years, with an interquartile range (IQR) of 22 years. When stratified by gender, the median age among male participants was 56 years (IQR 19), while for females it was 63 years (IQR 21). Regarding laboratory parameters, the median serum procalcitonin level was 0.3 ng/ml (IQR 1.1), the median C-reactive protein (CRP) level was 4.8 mg/L (IQR 7.3), and the median total leukocyte count (TLC) was 5.1 × 10^9/µL (IQR 8.9). Based on the criteria of procalcitonin >2.0 ng/ml, CRP >12 mg/L, TLC >12 × 10^9/µL, and/or a positive blood culture, superimposed bacterial infections were identified in 27 patients, representing an incidence rate of 10.8%. Among these 27 cases, 19 (70.4%) were males and 8 (29.6%) were females. All affected patients achieved full recovery during the hospital stay. To further

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elucidate the diagnostic value of laboratory markers, a comparative analysis was conducted between patients with and without superimposed bacterial infections. Among those with secondary infections, the median procalcitonin level was significantly elevated at 2.8 ng/ml (IQR 1.5), compared to 0.2 ng/ml (IQR 0.4) in those without infections. Similarly, CRP levels were markedly higher in the infected group with a median of 16.4 mg/L (IQR 8.2) versus 3.1 mg/L (IQR 5.0) in the non-infected group. The total leukocyte count also demonstrated a notable difference, with a median of 14.3 × 10^9/µL (IQR 5.6) in infected individuals as opposed to 4.8 × 10^9/µL (IQR 3.6) in those without secondary infections. These findings highlight the potential utility of these biomarkers in identifying concurrent bacterial infections in dengue patients.

Table 1: Demographics and Outcomes

Variable	Median	IQR
Age (years)	58	22
Procalcitonin (ng/ml)	0.3	1.1
CRP (mg/L)	4.8	7.3
TLC (x 10^9/µL)	5.1	8.9

Table 2: Infection Diagnostic Criteria Outcomes

Diagnostic Tool	Number of Positive Cases	Percentage of Total Patients (%)
Procalcitonin >2.0 ng/ml	18	7.2
CRP >12 mg/L	20	8
TLC >12 x 10^9/µL	15	6
Positive Blood Culture	5	2

Table 3: Gender-wise Infection Distribution

Gender	Superimposed Infection Cases	Percentage (%)
Male	19	70.4
Female	8	29.6

Table 4: Summary of Inflammatory Markers

Marker	Cut-off for Superinfection	Median (Infected Group)	Median (Non-Infected Group)
Procalcitonin	>2.0 ng/ml	2.8 ng/ml	0.2 ng/ml
CRP	>12 mg/L	16.4 mg/L	3.1 mg/L
TLC	>12 x 10^9/µL	14.3 x 10^9/µL	4.8 x 10^9/µL

Table 5: Comparative Biomarker Levels

Biomarker	With Infection (Median [IQR])	Without Infection (Median [IQR])
Procalcitonin (ng/ml)	2.8 [1.5]	0.2 [0.4]
CRP (mg/L)	16.4 [8.2]	3.1 [5.0]
TLC (x 10^9/µL)	14.3 [5.6]	4.8 [3.6]

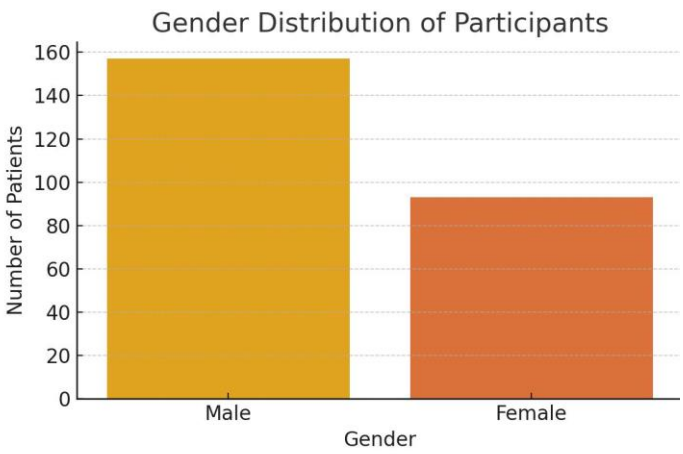

Figure 1 Gender Distribution of Participants

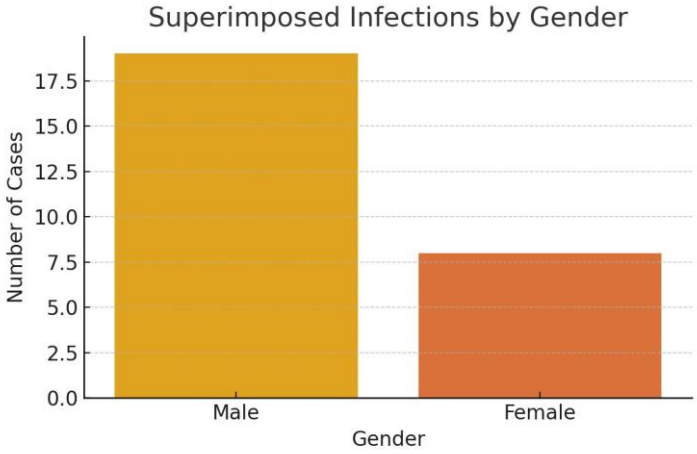

Figure 2 Superimposed Infection by Gender

DISCUSSION

The findings of this study reaffirm the growing concern surrounding superimposed bacterial infections in patients diagnosed with dengue fever, highlighting a co-infection incidence of 10.8%. This aligns closely with previous studies conducted in various endemic regions where secondary bacterial infections ranged between 7% and 11%, depending on the patient population, severity of dengue, and healthcare infrastructure (9,10). The common pathogens implicated in these studies, including *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*, were also observed in similar clinical contexts. These pathogens frequently contribute to pneumonia, bloodstream infections, urinary tract infections, and skin and soft tissue infections, especially in immunocompromised or critically ill patients (11-14). The elevated biomarkers such as procalcitonin, CRP, and TLC in the present study effectively distinguished patients with secondary infections, indicating their diagnostic value in early identification of co-infected individuals. The results further support earlier research that emphasized the role of an exaggerated immune response in severe dengue cases, which predisposes individuals to vascular leakage, endothelial dysfunction, and ultimately increased susceptibility to bacterial colonization (15,16). Moreover, the need for intravenous access, prolonged hospital stays, and invasive monitoring in severe dengue significantly raises the risk of nosocomial infections, complicating clinical outcomes. In certain settings, the *Aedes aegypti* mosquito has been reported to harbor enteric pathogens, suggesting a theoretical, though yet unconfirmed, route of simultaneous transmission (17,18).

Despite these insights, the study also brings attention to important limitations. As a single-center investigation with a relatively modest sample size, generalizability to broader populations remains constrained. Furthermore, blood cultures and other confirmatory microbiological tests may have been limited by their sensitivity, and prior antibiotic exposure could have impacted isolation rates. The reliance on threshold values for biomarkers, although practical, may lead to misclassification in cases with atypical presentations. A more comprehensive microbial workup including viral panels, fungal cultures, and advanced imaging could have enhanced diagnostic accuracy, especially in non-responders. Nonetheless, the study presents significant strengths. It addresses a clinically relevant gap by highlighting the frequency of secondary bacterial infections in dengue patients and evaluates simple, cost-effective diagnostic tools for early detection. The stratification of data by gender and the comparative analysis of biomarker profiles between co-infected and non-co-infected groups added granularity to the findings.

Future research should focus on multicenter studies with larger cohorts and standardized infection surveillance protocols. Incorporation of molecular diagnostic techniques and assessment of antibiotic resistance patterns would further refine clinical management. There is also a pressing need to develop predictive scoring systems that integrate clinical, laboratory, and radiological findings to flag high-risk patients for early empiric therapy. Improved understanding of regional pathogen profiles and their resistance trends will support more rational antibiotic use and curb the emergence of resistant strains (19,20). In summary, this study underscores the importance of early identification and aggressive management of bacterial co-infections in dengue fever, which remain a major determinant of clinical

outcomes. Incorporating routine screening for these infections in hospitalized dengue patients, especially those with persistent fever or signs of sepsis, should be considered an integral component of standard care pathways.

CONCLUSION

This study emphasizes the clinical significance of identifying superimposed bacterial infections in patients with dengue fever, particularly in those presenting with severe manifestations. Such co-infections contribute to increased disease complexity, prolong hospital stay, and add to the healthcare burden. The findings reinforce the need for early diagnostic vigilance and timely initiation of empirical broad-spectrum antibiotics in suspected cases to improve patient outcomes. Incorporating simple laboratory markers like procalcitonin, CRP, and leukocyte count into routine evaluation can aid in distinguishing bacterial co-infections and guide prompt intervention. These insights hold practical value in optimizing the clinical management of dengue patients and reducing preventable complications.

AUTHOR CONTRIBUTION

Author	**Contribution**
Farah Rao*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Waheed Ahmed	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Zaboor Ahmed	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Syed Haider Tirmizi	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Muhammad Usman Khan	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Farhan Tariq	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

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