

NORMALIZATION AND RECOVERY TIME OF BLOOD CELL COUNTS IN UNCOMPLICATED DENGUE

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Abstract

Objectives: - To determine the recovery time using laboratory tests during the evolution of uncomplicated dengue.

Study design: Descriptive Cross sectional Study.

Place and duration of study: At CMH Quetta, from Jan 2024 to Dec2024.

Methodology: The study was conducted on serological dengue positive patients of both genders ranging from age 5-50 years. Sample was calculated by sample size calculator Open epi through non-probability consecutive sampling keeping confidence interval at 95% and margin of error as 5%. Data was analyzed using SPSS version 25.0. The chi-square test was used for statistical analysis between laboratory tests and duration of recovery. Descriptive statistics were compared using the chi-square test for the variables of gender and age. A p-value less than 0.01 was regarded as statistically significant.

Results: A total of 100 dengue positive patients were categorized into five age groups spanning each decade, with a mean age of 30.7 years. Thrombocytopenia was observed in 78 patients, while 22 had normal platelet counts. 73 patients exhibited leucopenia. The main laboratory abnormalities found in dengue positive patients were thrombocytopenia and leucopenia.

Conclusion: - Majority of the dengue positive patients regained their normal white cell count and platelet levels after 5 days of initial diagnostic laboratory tests.

INTRODUCTION

Dengue fever stands as one of the most significant rapidly spreading viral diseases, transmitted through the bite of mosquitoes, particularly prevalent in sub-tropical and tropical regions.^{1,2} The Aedes aegypti mosquito carries the virus, leading to symptoms such as acute fever for 3 to 5 days, muscle pain, severe headaches, joint pain, and gastrointestinal issues, among others.^{1,3} Presently, over 125 countries, including Pakistan, are endemic to dengue, with multiple outbreaks occurring

throughout the year, peaking post-monsoon. Various factors contribute to its widespread, including viral genomic evolution, climate change, and social factors like urbanization, population growth, socioeconomic factors, travel and global trade.⁴

More than 70% of the global burden of dengue is borne by Asian countries, significantly affecting children's morbidity and mortality. Recognizing its severity, the World Health Organization (WHO) has classified dengue as

one of the most important neglected tropical diseases from 2015 to 2020.^{5,6} Additionally, other diseases like leptospirosis, malaria, and influenza A, present with similar symptoms, necessitating laboratory confirmation for accurate diagnosis.^{5,7,8} Correct diagnosis of the pathogen is important as each requires different treatment options.⁸ Common diagnostic methods include PCR for virus detection, NS1 protein detection, and serological tests for host immune response.

Given the varying kinetics of biomarkers, no single assay can definitively diagnose dengue. However, combining NS1 detection with IgM and/or IgG detection improves diagnostic accuracy.⁸ Nonetheless, in underdeveloped countries or small local hospitals, these tests may be inaccessible or costly, making clinical assessment crucial. Studies have shown that dengue patients often exhibit leukopenia and thrombocytopenia, making these parameters valuable in diagnosing dengue, especially in resource-limited settings like Pakistan. Identifying the positive predictive value of these parameters can aid in distinguishing dengue from other febrile illnesses, thereby reducing unnecessary referrals to central labs.⁹ In this context, the present study aimed to assess the hematological dynamics and their recovery time in patients with uncomplicated dengue.

Operational Definitions

Thrombocytopenia: A platelet count that falls below the lower limit of normal (<150,000/microliter) in adults.

Leucopenia: A condition in which there is an abnormally reduced amount of white blood cells (<4000/microliter) in adults.

Methodology

An analytical cross-sectional study was carried out at CMH Quetta with approval from the ethical committee of the hospital, in collaboration with the Pathology Department. The study spanned for six months from Jan 2024 to June 2024. The study included 100 patients of 5-50 years of age. Adults and children of both genders, admitted to pediatric and medical wards with acute dengue infection were enrolled. Sample was calculated by sample

size calculator Open epi through non-probability consecutive sampling keeping confidence level at 95% and margin of error as 5%. Dengue infection was confirmed using an Indirect ELISA for anti DENV IgM. Patients in shock, with chronic illnesses upon presentation, with Dengue Hemorrhagic Fever, Severe Dengue Fever or initially diagnosed with non-dengue illnesses were excluded. The duration of recovery was divided into three categories. First category was from 0-4 days, second category from 5-8 days and third category was from 9-12 days. The first day of the disease was considered the onset of symptoms related to dengue fever and the laboratory profile was evaluated for the first 12 days. The variables selected were leukocyte and platelet count. Informed consent was obtained from all patients before enrollment. Laboratory test charges were covered by the hospital administration. Venous blood samples of 2.5 ml were collected in EDTA - containing CP bottles and analyzed using an automated Haematology analyzer Sysmex XT 2000i system. Total leucocyte count (TLC) and platelet count were recorded in a designed proforma. Data analysis was performed using SPSS version 25, employing descriptive statistics to calculate qualitative and quantitative variables. Gender, presence of thrombocytopenia, and leucopenia were presented as frequencies and percentages, while age was expressed as mean and standard deviation. The chi-square test was used for statistical analysis. Descriptive statistics were compared using the chi-square test for the variables of gender and age. A p-value less than 0.01 was regarded as statistically significant.

Results

In the study, 100 patients with confirmed dengue infection through IgM ELISA were included, with ages ranging from 5 to 60 years. Patients were categorized into three age groups which include less than 20 years, 20 to 40 years and more than 40 years of age, with a mean age of 30.7 years. Table I displays the frequency of thrombocytopenia in males and females across age groups, with a notable prevalence in the <20-year age group for both genders, along with an additional peak in females aged >40 years. Of the total patients, 50 were male and 50 were

female. Thrombocytopenia was observed in 78 patients, while 22 had normal platelet counts. Additionally, 73 patients exhibited leucopenia. Among the thrombocytopenic patients, 66 also had leucopenia. The correlation between thrombocytopenia and TLC is depicted in Table II and further supported by the correlation matrix in Table III. 62 patients with thrombocytopenia and 60 patients with leucopenia had regained normal levels after 5

days as compared to only 16 patients with thrombocytopenia and 13 patients with leucopenia who regained normal levels within 5 days of initial laboratory tests. The positive predictive value (PPV) of thrombocytopenia was 81%, while that of leucopenia was found to be 75% in patients of acute dengue infection. The PPV for the combination of leucopenia and thrombocytopenia was 88%.

Table I: Frequency of Thrombocytopenia relative to age group (n=100)

Age	Male			Female			p-value
	No	Yes	Total Patients	No	Yes	Total Patients	
<20	7	16	23	3	12	15	0.000
20-40	5	12	17	3	13	16	
>40	2	8	10	2	17	19	
Total	14	36	50	8	42	50	

Table II: Incidence of Thrombocytopenia relative to TLC (n=100)

TLC	Thrombocytopenia			p-value
	No	Yes	Total	
Leucopenia present	7	66	73	0.000
Leucopenia absent	15	12	27	
Total	22	78	100	

Table III: Correlation Matrix (n=100)

	TLC	Thrombocytopenia
TLC	1	0.390**
Thrombocytopenia	0.390**	1

** . Correlation is significant at 0.01 level (2-tailed).

Discussion

Dengue fever poses a significant health challenge in countries like Pakistan, where resources for diagnosis are limited, leading to a reliance on clinical judgment rather than extensive laboratory testing. Several global studies have indicated that certain routine blood tests can aid in diagnosing dengue fever, particularly in resource-poor settings. For instance, parameters like white cell count, platelet count, liver function tests, C-reactive protein levels, and coagulation profiles have been found to correlate with dengue infection. In our own study conducted in Pakistan, we observed that thrombocytopenia and low total leukocyte count (TLC) were significant indicators of acute dengue infection, aligning

with the concept of marrow suppression during the disease's acute phase.

Our research echoes findings from other studies, such as one by Ho et al., which demonstrated a positive predictive value (PPV) of 89.5% for a combination of leukopenia, thrombocytopenia, elevated aspartate aminotransferase (AST), and low C-reactive protein (CRP) levels.¹⁰ However, our study, unlike some others, focused on minimal parameters derived from routine complete blood count (CBC) tests, aiming for a practical and cost-effective approach to aid prompt diagnosis by physicians in resource-constrained settings like Pakistan.

Comparatively, Chen et al. highlighted a PPV of 100% for the combination of leukopenia,

thrombocytopenia, and elevated transaminase levels in pediatric dengue patients, employing a broader array of clinical markers and diagnostic methods.¹¹ In contrast, our study encompassed a wider age range and relied solely on CBC results obtained on a random day, thus presenting a more streamlined approach to diagnosis.

Moreover, studies utilizing advanced diagnostic techniques like detecting non-structural protein NS1 or viral-specific nucleic acids have shown higher PPVs, as seen in Mussio et al. and Liu et al.¹² However, our study's focus on IgM positivity and exclusion of such advanced methods may have contributed to comparatively lower PPVs.

A study undertaken in China aimed to identify predictive laboratory markers for early diagnosis of dengue infection.¹³ The positive predictive value of leukopenia and thrombocytopenia for DENV infection were 96.9% and 93.0%, respectively. These values obtained are again higher than ours [66% and 81% respectively] as the Viral RNA was detected by real-time RT-PCR, and viral-specific NS1 antigen was detected using enzyme linked immuno sorbent assay being more sensitive methods in picking up the disease in its earlier phase. More over the study was carried out in an epidemic where as our study was conducted in acute febrile illness in an endemic area. The findings were consistent with a study done by Liu et al, which showed that prolonged APTT, leucopenia, thrombocytopenia and raised AST has a PPV of greater than 80% and is useful in evaluating the likelihood of acute dengue infection.¹⁴

Despite these differences, the consistency in findings across studies underscores the importance of certain laboratory parameters in diagnosing acute dengue infection. Notably, the variation in parameters considered for PPV calculation reflects the need for tailored approaches to suit the resource availability and practicality of implementation in diverse healthcare settings.

Limitations:

The study's limitations include its cross-sectional design, which restricts the ability to determine a causal relationship between lab findings and duration of recovery. In future, it

would be beneficial to conduct a longitudinal study to establish a cause-and-effect relationship. Our study's limitations include a smaller sample size and reliance solely on IgM positivity, its emphasis on minimal parameters from routine tests serves a crucial purpose in resource-constrained settings. By providing a practical and cost-effective approach to aid diagnosis, our findings aim to assist physicians in efficiently narrowing down differentials and selectively conducting diagnostic tests in highly suspected cases.

Conclusion

In patients showing symptoms of acute fever, especially during the post-monsoon period, analyzing blood counts becomes crucial for early detection of dengue fever, particularly in areas with limited diagnostic resources. Given dengue fever's endemic status in Pakistan and its serious complications, there's an urgent need for further research into its diagnosis and prognosis to facilitate early detection and management.

Conducting time trend analyses of various parameters like platelet count, ANC, eosinophil count, hematocrit, and chemical markers such as AST is essential for understanding disease progression, facilitating early recovery, and managing complications promptly. Exploring new parameters like IPF could aid in early diagnosis, treatment monitoring, and prognosis assessment of acute dengue fever. It's also vital to conduct studies with larger sample sizes, segregating data by age groups, to better comprehend disease severity across different age demographics. Establishing review boards and committees for continuous evaluation of diagnosis, treatment, prevention, and control policies for dengue fever is imperative.

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Author's Contributions:

The authors accept responsibility for all aspects of the study, ensuring that any questions

regarding the accuracy or integrity of the work are addressed and resolved appropriately.

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