Original Article

Association Between Dengue Skin Rash and Disease Outcome in A Tertiary Care Hospital

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Author`s Contribution

[1,2]Substantial contributions to the conception or design of the work; or the acquisition, [3,4]Data Collection, [5]Drafting the work or revising it critically for important intellectual content [6]Active participation in active methodology, analysis, or interpretation of data for the work

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ABSTRACT

Objective: The objective of this research work is to build upon existing knowledge by exploring the relationship between dengue skin rashes and disease course in a tertiary healthcare center.

Methods: This descriptive cross sectional study was conducted in Dermatology department at HBS General Hospital, Islamabad. from January 2024 to August 2024. Total 188 confirmed dengue fever patients was performed. Researchers documented demographic information together with clinical features as well as laboratory findings and disease outcomes of all these patients. Dermatologists evaluated the presence, morphology and distribution of skin rashes. Disease severity was classified according to the 2009 WHO dengue guidelines.

Results: Skin rash was observed in 17.6% (n = 33) of patients, with maculopapular rash being the most common type (75.8%, n = 25). Patients with skin rash had significantly milder disease outcomes. 87.9% of the patients with skin rash had non severe dengue while only 12.1% of patients with skin rash had severe dengue. While in the patients without skin rash, 69% had mild disease while 31% had severe dengue ($p < 0.001$). Laboratory findings revealed higher platelet counts (87,000 ± 23,000/µL vs. 53,000 ± 18,000/µL, $p < 0.001$) and lower hematocrit levels (37.9 ± 4.1% vs. 42.2 ± 5.0%, $p = 0.002$) in patients with rash. The patients with skin rash required less hospitalization of 4.4 ± 1.5 days compared to 6.6 ± 2.1 days ($p < 0.001$), while the occurrence of complications (9.1% vs. 25.8%) including hemorrhage and organ failure ($p = 0.003$) also showed lower rates. Multivariate analysis identified the absence of skin rash as an independent predictor of severe dengue (aOR = 3.18, 95% CI: 1.68–6.02, $p < 0.001$).

Conclusion: The presence of skin rash in dengue patients is associated with milder disease outcomes, which includes higher platelet counts, lower hematocrit levels, shorter hospitalization, and fewer complications. Routine clinical practice that includes dermatological examinations allows better risk stratification for dengue patients.

Keywords: Dengue fever, Skin rash, Disease severity, Prognostic marker.

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Introduction

Dengue fever (DF) represents a significant public health threat in tropical and subtropical countries. It stems from a flavivirus, dengue virus (DENV) transmitted by mosquito bites. According to the World Health Organization (WHO) annual report, DF affects 390 million people worldwide and half the population faces potential infection risks.[1] The clinical manifestations of

DF stretch across two extremes including minor febrile illness and major dengue fever causing plasma leakage, bleeding problems and organ dysfunction.[2] Cutaneous manifestations of DF include frequent appearances of different morphologies of skin rash. A clear connection between dermatological manifestations and disease severity remains unexplored. Thus, researchers need to conduct more analysis on this subject.

The Aedes aegypti mosquito primarily spreads the disease during the rainy season. The flaviviruses have a lipid envelope and are spherical and comparatively fragile (40–50 nm). A person may have an early onset of fever along with a range of nonspecific signs and symptoms after the virus incubates for 3 to 14 days (on average, 4 to 7 days) after being bitten by an infective mosquito.[6]

During this acute febrile phase, which could last anywhere from two to ten days, dengue viruses spread throughout the peripheral circulation. After an extrinsic incubation period of 8 to 12 days, other A. aegypti mosquitoes may contract the virus if they bite an infected individual during this febrile viremic stage. These mosquitoes may then spread the virus to other uninfected individuals. Clinically, there are two forms of DF: dengue shock syndrome (DSS) and dengue hemorrhagic fever (DHF).[7, 8]

Skin involvement is prevalent in DF patients. It might range from generalized morbilliform rash to confluent erythematous rash.[9] The diagnosis of DF may be aided by the initial appearance of a skin rash in the context of an acute febrile illness. It is currently unclear how the existence of a skin rash affects the severity, prognosis, and outcome of the disease. In this study, individuals with DF with and without skin rash were compared for differences in clinical presentation, laboratory data, illness course, morbidity, and prognosis.[10]

The complication of skin rash occurs frequently in dengue cases but remains under-investigated as a clinical symptom which presents as maculopapular or petechial eruption during both febrile and recuperation phases of the illness.[3] Research findings about dengue disease severity remain contradictory because studies present either positive or negative associations between rash appearance and disease outcome.[4] There exists an unexplained difference that shows researchers need to understand dermatological signs better in predicting disease course and patient results. The understanding of immunological and pathophysiological mechanisms involved in dengue-related skin rashes remains minimal because of which these clinical markers are inaccessible for early risk evaluation and management strategies.

The research by Mishra AK et al.[5] explores the relationship between dengue skin rash and disease outcomes in tertiary care hospital. Dermatological examinations performed on dengue patients reveal that skin rashes could potentially serve as signs indicating disease prognosis. These findings lack broader application because the study only took place at one hospital and dengue represents differently within varied populations across worldwide locations. Additional research studies must confirm the observed relationships and investigate what biological factors link skin conditions to dengue fever severity.

Our research analyzes clinical data from patients with DF to determine risk assessment strategies that help patient care management through skin rash assessment. This research investigates the connection of immunological markers to dengue-associated skin rash pathogenesis while establishing fundamental knowledge for further investigation.

Methodology

This descriptive cross sectional study was conducted in Dermatology department at HBS General Hospital, Islamabad. from January 2024 to August 2024. The study was initiated following Institutional Ethics Committee approval and informed written consent was taken from all participants. The patient sample for this research consisted of 188 cases of diagnosed DF. The WHO sample size calculator calculated the proper sample size under the following parameters: 95% confidence level with 14.2% anticipated population proportion (rate of skin rash among DF patients) and 5% absolute precision.

All patients of any age or gender who received DF diagnosis at hospital admission during the study period were included in the study. Patients received DF confirmation through NS1 antigen tests and IgM ELISA or RT-PCR diagnostics in accordance with WHO diagnostic protocols. The study excluded patients who had insufficient medical record documentation or co-occurring infections or alternative febrile illnesses that could masquerade as DF.

A standardized form was utilized to collect information about demographic data along with clinical and laboratory findings to assess the disease outcomes. The researchers documented clinical indicators which

included patients' skin rash types (maculopapular, petechial or others), fever duration, bleeding and plasma leakage manifestations (ascites and pleural effusion). The laboratory analysis included both platelets count and hematocrit levels, liver function tests and serological testing. The research evaluated disease severity according to non-severe dengue and dengue with warning symptoms and severe dengue using the 2009 WHO dengue classification system. Characteristics of skin rashes during DF were determined through assessments performed by dermatologists and physicians who used morphology, distribution, and relationship to febrile periods to classify the rashes. Only specific cases required photographic evidence to confirm disease categories and validate rating agreement among investigators.

The main research objective focused on the relationship between skin rashes and the level of disease severity among the participants. Secondary outcomes included the relationship between the type of rash and clinical parameters such as platelet count, hematocrit levels, duration of hospitalization, and the need for intensive care. Complications such as hemorrhage, organ failure, and mortality were also recorded and analyzed. Statistical analysis was performed using SPSS version 25.0 software. Descriptive statistics like mean ± SD, frequency and percentages were used to summarize demographic and clinical characteristics. The categorical variables were compared using the chi-square test or Fisher's exact test. Continuous variables were analyzed using the Student's t-test. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 188 patients with confirmed DF were included in this study. The demographic and clinical characteristics of the study population are summarized in Table I. The mean age of the participants was 32.5 ± 14.2 years, with a slight male predominance (56.4%, n = 106). Among the study population, 72.3% (n = 136) were classified as having non-severe dengue, while 27.7% (n = 52) had severe dengue, including dengue with warning signs and severe dengue, as per the 2009 WHO classification guidelines. Skin rash was observed in 17.6% (n = 33) of the patients, with maculopapular rash being the most common type (75.8%, n = 25), followed by petechial rash (18.2%, n = 6) and other types (6.1%, n = 2). The presence of skin rash was significantly associated with milder disease outcomes ($p < 0.001$). Among patients with skin rash, 87.9% (n = 29) had non-severe dengue, compared to 12.1% (n = 4) with severe dengue. In contrast, among patients without skin rash, 69.0% (n = 107) had non-severe dengue, while 31.0% (n = 48) had severe dengue. Comorbidities such as hypertension and diabetes mellitus were present in 14.9% (n = 28) and 11.7% (n = 22) of the study population, respectively, with no significant differences between patients with and without skin rash ($p > 0.05$).

Laboratory findings and clinical outcomes, as detailed in Table II, revealed significant differences between patients with and without skin rash. Patients with skin rash had higher mean platelet counts (87,000 ± 23,000/μL) compared to those without rash (53,000 ± 18,000/μL, $p < 0.001$). Similarly, hematocrit levels were lower in patients with skin rash (37.9 ± 4.1%) than in those without rash (42.2 ± 5.0%, $p = 0.002$). No significant differences were observed in white blood cell counts or liver function tests (alanine aminotransferase and aspartate aminotransferase) between the two groups ($p > 0.05$). The duration of hospitalization was significantly shorter in patients with skin rash (4.4 ± 1.5 days) compared to those without rash (6.6 ± 2.1 days, $p < 0.001$). Additionally, patients with skin rash were less likely to require intensive care (6.1%, n = 2) compared to those without rash (23.9%, n = 37, $p = 0.002$). Complications such as hemorrhage and organ failure were also less frequent in patients with skin rash (9.1%, n = 3) than in those without rash (25.8%, n = 40, $p = 0.003$).

Multivariate logistic regression analysis, as shown in Table III, identified the absence of skin rash as an independent predictor of severe dengue (adjusted odds ratio [aOR] = 3.18, 95% confidence interval [CI]: 1.68–6.02, $p < 0.001$), after adjusting for age, sex, and comorbidities. Other significant predictors of severe dengue included thrombocytopenia (platelet count < 50,000/μL, aOR = 2.70, 95% CI: 1.40–5.20, $p = 0.003$) and elevated hematocrit levels (aOR = 2.10, 95% CI: 1.16–3.80, $p = 0.014$). Age > 50 years was also associated with an increased risk of severe dengue (aOR = 1.85, 95% CI: 1.02–3.35, $p = 0.042$), while the presence of comorbidities showed a trend toward significance (aOR = 1.72, 95% CI: 0.95–3.12, $p = 0.074$).

In conclusion, the presence of skin rash in dengue patients, though observed in only 17.6% of cases, was associated with milder disease outcomes, higher platelet counts, lower hematocrit levels, shorter hospitalization, and fewer complications. Findings demonstrate that skin

Table I: Demographic and Clinical Characteristics of the Study Population. (n = 188)

Characteristic	Total (n = 188)	With Skin Rash (n = 33)	Without Skin Rash (n = 155)	p-value
Age (years)				
Mean ± SD	32.5 ± 14.2	31.8 ± 13.5	32.7 ± 14.4	0.712
Gender, n (%)				
Male	106 (56.4%)	18 (54.5%)	88 (56.8%)	0.812
Female	82 (43.6%)	15 (45.5%)	67 (43.2%)	
Disease Severity, n (%)				
Non-severe dengue	136 (72.3%)	29 (87.9%)	107 (69.0%)	<0.001
Severe dengue	52 (27.7%)	4 (12.1%)	48 (31.0%)	
Type of Rash, n (%)				
Maculopapular	-	25 (75.8%)	-	-
Petechial	-	6 (18.2%)	-	-
Other	-	2 (6.1%)	-	-
Hypertension, n (%)				
Yes	28 (14.9%)	4 (12.1%)	24 (15.5%)	0.621
No	160 (85.1%)	29 (87.9%)	131 (84.5%)	
Diabetes mellitus, n (%)				
Yes	22 (11.7%)	3 (9.1%)	19 (12.3%)	0.589
No	166 (88.3%)	30 (90.9%)	136 (87.7%)	

Table II: Laboratory Findings and Clinical Outcomes by Skin Rash Status.

Parameter	With Skin Rash (n = 33)	Without Skin Rash (n = 155)	p-value
Platelet count (×10³/µL),			
Mean ± SD	87,000 ± 23,000	53,000 ± 18,000	<0.001
Hematocrit (%),			
Mean ± SD	37.9 ± 4.1	42.2 ± 5.0	0.002
White blood cell count (×10³/µL),			
Mean ± SD	4.2 ± 1.8	3.8 ± 1.6	0.215
Liver function tests, mean ± SD			
Alanine aminotransferase (U/L)	68.5 ± 32.4	72.3 ± 35.1	0.541
Aspartate aminotransferase (U/L)	75.2 ± 34.7	78.6 ± 37.2	0.623
Hospitalization duration (days),			
Mean ± SD	4.4 ± 1.5	6.6 ± 2.1	<0.001
Intensive care required,			
n (%)	2 (6.1%)	37 (23.9%)	0.002
Complications, n (%)			
Overall Complications	3 (9.1%)	40 (25.8%)	0.003
Hemorrhage	2 (6.1%)	25 (16.1%)	0.112
Organ failure	1 (3.0%)	15 (9.7%)	0.201

Table III: Multivariate Logistic Regression Analysis for Predictors of Severe Dengue.

Predictor	Adjusted Odds Ratio (aOR)	95% Confidence Interval (CI)	p-value
Absence of skin rash	3.18	1.68–6.02	<0.001
Thrombocytopenia (<50,000/µL)	2.70	1.40–5.20	0.003
Elevated hematocrit	2.10	1.16–3.80	0.014
Age > 50 years	1.85	1.02–3.35	0.042
Presence of comorbidities	1.72	0.95–3.12	0.074

rash has the potential to serve as a clinical tool for both measuring disease severity and directing patient treatment strategies among patients in regions where dengue is prevalent.

Discussion

The findings of this research shows how dengue patients with skin rash face milder disease progression which demonstrates skin symptoms' value as clinical predictors for dengue severity. Skin rash was observed among 17.6% of participants. Maculopapular rash (75.8%)

appeared most often followed by petechial rash (18.2%) and other rash types (6.1%). Previous research has established maculopapular rash as the most typical skin manifestation of dengue wherein this rash develops either during the febrile stage or recovery period of the illness.[11, 12] Skin rash showed a powerful relationship with non-severe dengue because 87.9% of patients who had skin rash developed milder disease manifestations. The research findings agree with Saad A, et al. [13]] who discovered positive outcomes in dengue patients were linked to skin rash development.

Current understanding of dengue-associated skin rash pathophysiology shows incomplete clarity because experts believe an immune reaction leads to the symptoms, the rash develops because of cytokine release and vascular endothelial activation processes that occur as the host immune system fights dengue virus infection.[14] Rash development demonstrates an efficient immune response that both inhibits virus spread and blocks the occurrence of severe plasma leakage and hemorrhage. The observed higher platelet counts combined with lower hematocrit levels in patients with skin rash in our study supports that their thrombocytopenia and hemo-concentration are less severe than those who do not develop rash. Findings from our study align with earlier studies showing skin rash appears with milder hematological side effects and better clinical results.[15, 16]

Patients who develop skin rash show both reduced hospital stay and require fewer intensive care services indicating good disease outcomes. Resource-limited healthcare settings can benefit from the presence of skin rash to help prioritize patient care and distribute resources effectively. The occurrence of rash in dengue patients leads to decreased complications in hemorrhage and organ failure making rash an efficient marker for better clinical outcomes. Research carried out by[17] Thomas et al. and[12] Mahboob A, et al. revealed dengue patients with skin rash had lower rates of complications.

Multivariate logistic regression determined that patients without skin rash had three times the risk (aOR = 3.18, 95% CI: 1.68–6.02) of severe dengue ($p < 0.001$). So, dermatological examination remains essential for proper clinical assessment of dengue patients according to this research discovery. The presence of thrombocytopenia along with elevated hematocrit levels served as two major indicators for severe dengue disease. Severe dengue risk increased by 85% in individuals older than 50 years (aOR = 1.85, 95% CI: 1.02–3.35, $p = 0.042$) according to research.[18]

The relationship between comorbidities and severe dengue showed an unproven pattern as well as insignificant statistical outcome in this study (aOR = 1.72, 95% CI: 0.95–3.12, $p = 0.074$). The research outcome corresponds with previous findings of Ng WY et al, [19] and Khan MA, et al[20], because hypertension and diabetes mellitus along with other comorbidities intensify dengue severity by reducing immune response and weakening vascular integrity. Additional studies utilizing bigger participant numbers must investigate how comorbidities affect dengue disease progression.

Individuals with skin rash from dengue infection demonstrate the least severe disease progression alongside elevated platelet levels coupled with decreased hematocrit markers and a shorter duration of hospital care and lower complication rates. Healthcare institutions within dengue-endemic areas can benefit from skin rash observations to gauge patient conditions for enhanced treatment and management. Dermatological examination included in standard medical assessments allows healthcare staff to evaluate patient risk better and deliver better treatment outcomes particularly under diagnostic equipment limitations.

Conclusion

The research shows that 17.6% of patients developed rash symptoms which appeared mostly as maculopapular rashes and such cases corresponded to milder dengue disease outcomes. The appearance of rash in patients correlated with better platelet counts and decreased hematocrit levels as well as accelerated recovery and reduced complications. On the other hand, absence of rash was found to be an independent predictor of severe disease progression. The results indicate skin rash functions as an important distinctive feature that helps physicians identify patients with lower disease severity when managing patients especially in under-resourced medical environments. Dermatological examinations help healthcare providers detect dengue patients who have lower chances of developing dangerous disease manifestations because the dermatological assessment remains straightforward and non-invasive. Additional studies need to confirm these findings to identify the biological processes which drive this relationship. Regular assessment of patients' skin rashes through clinical practice standards will create better outcomes for dengue treatment among endemic regions.

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