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Original Article

Frequency of Dengue and Malaria Co-Infection in Patients Admitted in Jinnah Hospital, Lahore

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ABSTRACT

Prevalence of malaria and dengue infection coexistence is increasing during endemic periods although causing quite similar symptoms and signs, the treatment of these two illnesses is different. Any suspicion of malaria in disease-endemic areas must be excluded with microscopy and/or rapid antigen test. **Objective:** To find out the incidence of co-infection of dengue and malaria based on clinical and hematological parameters in patients presenting with acute febrile illness. **Methods:** This cross-sectional study was done in the Medicine Unit of Jinnah hospital, Lahore from October - December 2022. 140 diagnosed as dengue fever by Non-Structural Protein 1 (NS1) and IgM were included in the study. All the cases were subject to a thorough medical examination i.e. complete battery summary of temperature together with the serology of Dengue, X-ray of the chest, abdominal ultrasound scan, renal function test (RFT), liver function test (LFT), malarial parasite slide, complete blood count with peripheral smear etc. Accordingly, the treatment was given to them with follow-up medical evaluation including detailed investigations. Data were entered and analyzed in SPSS version. 27.0 and presented as frequency and percentages. Chi square test was used to assess statistical significance with $P < .05$. **Results:** Mean age of respondent was 35.5 + 15.6 years. Co-infection rate with malaria and severe disease along with prolong duration fever and persistent thrombocytopenia among subjects was15.0%. **Conclusions:** Majority of co infected individuals were having severe disease, with subsequent development of disseminated intravascular coagulation and sepsis, responding well to anti-malarial treatments.

"This is a correction to the original article. For information about the changes made, please see the erratum linked as a supplemental file on the article's landing page. The information will also be available at https://doi.org/10.54393/pjhs.v7i8.4579, dated 31-08-2026."

INTRODUCTION

Dengue is caused by a female mosquito carrying a virus known as *Aedes aegypti* and *Aedes albopictus*. Over the past years, the cases of Dengue have increased massively because of growing number of people, fast urbanization with scanty public facilities, such as insufficient water supply and inappropriate solid waste disposal, encouraging the major vector, *Aedes aegypti*, to multiply. An estimated 100-400 million dengue-infections occur per year and around 80% persons show mild disease or are asymptomatic. It presents with high grade fever, nausea, vomiting, abdominal pain as well headache, myalgia and periorbital pain1. Dengue has spread to more than 129 countries [2], making 3.9 billion individuals at stake to be victim of this infectious disease (Dengue), with 70% of the disease burden existing only in Asia [3]. Pakistan reported 25,932 cases of dengue between the month of January and September 2022, 74% of the patients were only reported in the month of September. It has been estimated that this rapid surge is due to the aberrant flood situation that started in June 2022. With limited health system capacity and increasing population, it is approximated that Pakistan is at high risk of concurrent infections possessing serious

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health impacts along with dengue fever. Dengue causes mild acute flu like illness, but occasionally it can develop into life threatening illness which is called severe dengue [1]. With around 3.4 million associated cases of malaria detailed among January and August 2022 alone, contrasted with 2.6 million instances revealed in 2021 [4], malaria has for some time been recognized as a serious general medical condition. Five heterogeneous species of Protozoal parasite, Plasmodium cause malaria i.e. *P. falciparum, P. ovale, P. malariae, P. vivax and P. knowlesi transmitted* by *Anopheles* mosquito. In Pakistan, P. vivax is predominant almost >80%. Malaria presents as fever, headache and chills after an incubation period of 10-15 days of mosquito bite. If left untreated, it can cause severe illness and mortality. As a dengue patient reaches the serious stage, the fever typically goes down. Even in a critical phase of dengue, the presence of fever after 7 days of illness gave us a hint to examine a tagged infection other than dengue in our instance. Jaundice and anemia gave a hint of a malarial coinfection, as did the daily rise in fever that is customary at the same time. Due to the identical clinical symptoms of these two illnesses' mono-infections, coinfections may go unnoticed. Jaundice in a dengue patient and spontaneous bleeding in a malaria case have both been noted to be signs of coinfection [5]. After one of the disorders is identified in acute febrile sickness, we frequently stop caring for the coinfections. Latent *P. vivax* hypnozoites have been proposed to become active after a variety of systemic diseases [6]. Hence, the reactivation of such hypnozoites may also be the cause of the detection of *P. vivax* together with any other infection in malaria endemic locations. According to the activation of latent hypnozoites concept, the discovery of *P. vivax* in our patient's later sickness could be a case of *P. vivax* relapse caused by dengue. The analysis of co-infection cases may enable us to swiftly suspect and recognize such organisms, assisting in the avoidance of diagnostic conundrums. We should also consider dengue and malaria co-infection in individuals who live in or have recently traveled to places where both diseases are endemic. Hence, early suspicion may aid in early diagnosis and therapeutic intervention if the clinical picture does not suit the mono-infection well. The morbidity and lethality of co-infections might be decreased.

Keeping in mind the endemic nature of both illnesses, our study aimed at finding out the incidence of co-infection of dengue and malaria based on clinical and hematological parameters in patients presenting with acute febrile illness to Jinnah Hospital, Lahore.

METHODS

This cross-sectional study was conducted in the Medicine Unit of Jinnah Hospital, Lahore from October to December 2022, following approval from the Institutional Research Ethics Committee (REF: 342/20/10/2022/S1 ERB, dated: 20/10/2022). The study period was selected to coincide with the post-monsoon peak transmission season for dengue and malaria in Pakistan; however, 2022 was epidemiologically exceptional due to unprecedented flooding affecting over 33 million people, which resulted in 78,554 confirmed dengue cases and over 3.4 million suspected malaria cases nationally by year's end. This post-flood outbreak context with concurrent surges in both vector-borne diseases enhances the relevance of our findings for emergency preparedness, though it may limit generalizability to non-flood or endemic-only transmission periods.Written informed consent was obtained from all participants or their legal guardians prior to enrollment. The study was conducted in accordance with the Declaration of Helsinki. Participants were assured of confidentiality, and data were anonymized using unique participant codes. No participants withdrew from the study during the data collection period. We included 140 patients aged 14-65 years of either gender who were diagnosed with acute dengue fever based on positive NS1 antigen (indicating early infection) and/or positive dengue-specific IgM antibodies (indicating recent infection), as per WHO diagnostic criteria. Patients were included if they tested positive for either marker, with the specific marker positivity documented for analysis. Co-infection was defined as the presence of malaria parasites on peripheral blood smear in a patient already confirmed to have dengue fever by NS1/IgM testing performed at the time of admission. Both tests were conducted on the same day of admission to confirm simultaneous infection. Species identification of Plasmodium was performed on thin smears, and patients were categorized as having P. vivax, P. falciparum, or mixed infection. A sample size of 131 was calculated using the formula $n = Z^2pq/d^2$, with 95% confidence interval (Z=1.96), assumed proportion of co-infection (p=0.32) based on previous literature [20], and acceptable margin of error (d=0.08). To account for an anticipated 10% non-response rate and incomplete data, we enrolled 140 participants. Subjects with immune-compression, malignancy and bleeding disorders were excluded. All the cases were subjected to a thorough medical examination (i.e., complete battery summary of temperature together with the serology of Dengue, X-ray of the chest, abdominal ultrasound scan, RFT, LFT, MP slide, CBC with peripheral smear etc.). All laboratory investigations were performed at the Jinnah Hospital clinical pathology laboratory. Complete blood count with differential was performed using an automated hematology analyzer (Sysmex XN-9000), with peripheral smear examination for morphological assessment and manual platelet verification when automated counts were below 50,000/µL. Dengue serology was performed using

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commercial ELISA kits (Panbio Dengue ELISA, Abbott Laboratories) following manufacturer's instructions, with positivity defined as optical density ratio ≥1.1 for NS1 antigen and IgM index ≥1.0 for dengue-specific IgM antibodies. Liver function tests including ALT (reference range: 4-36 U/L) and AST (reference range: 8-33 U/L) were measured using IFCC-recommended kinetic methods, while renal function tests including serum creatinine and urea were measured using Jaffe and enzymatic methods respectively on the Roche Cobas 8000 analyzer. Chest X-rays were performed using digital radiography in posteroanterior view and abdominal ultrasound was performed using Toshiba Aplio 500 with 3.5 MHz probe, both interpreted by consultant radiologists. Malaria parasite detection was performed using thick and thin blood smears examined under oil immersion microscopy by experienced technicians as described in the detailed methodology. Before answering the survey questions, those who consented had to sign. With all the precautions taken to preserve the folder containing that information, an assurance was made that all the data gathered would remain secret and confidential. The researcher had exclusive access to the area. All patients received standard treatment according to national guidelines: dengue management followed WHO protocols with fluid resuscitation and monitoring of hematocrit and platelet counts; malaria co-infected patients received artemisinin-based combination therapy (ACT) for P. falciparum or chloroquine for P. vivax based on species identification. Patients were followed daily during hospitalization with complete blood counts, liver function tests, and clinical assessment. Discharge criteria included resolution of fever for ≥24 hours, improving platelet count (>50,000/µL), and clinical stability. Outcomes were assessed at discharge and at a 14-day follow-up visit. Total 'Days of Illness' was defined as the duration from the onset of any symptom attributable to the acute febrile illness (including prodromal symptoms such as malaise, headache, myalgia, or body aches) to the day of hospital admission. 'Duration of Fever' was defined specifically as the number of days with documented fever (temperature ≥37.5°C or subjective fever with chills/rigors) prior to admission. These parameters were recorded separately to account for patients presenting with prodromal symptoms preceding the onset of actual fever.

Data were entered and analyzed using SPSS version 27.0 (IBM SPSS). Descriptive statistics were presented as frequencies and percentages for categorical variables, and mean ± standard deviation for continuous variables. The Chi-square test was used to compare proportions between co-infected and mono-infected groups. To adjust for multiple comparisons. A p-value <0.05 was considered statistically significant

RESULTS

140 patients were included in this study. Mean age was 35.5 ± 15.6 years. 67.9% were males and 32.1% were females. Regarding marital status, 75.0% (n=105) were married, while the remaining 25.0% (n=35) were unmarried (including single, divorced, or widowed). Regarding occupation, 25.0% were housewives, 26.4% were laborers, 32.1% were office workers, 27.1% were businessmen, and 4.3% were students (Table 1).

Table 1: Socio-Demographic Profile of Subjects (n=140)

Variables		Frequency (%)
Age (Mean = 35.5 ± 15.6 years)	< 40 years	84 (60.0)
	> 40 years	56 (40.0)
Gender	Male	95 (67.9)
	Female	45 (32.1)
Marital Status	Single	71 (50.7)
	Married	105 (75.0)
Occupation	Housewife	35 (25.0)
	Laborer / Farmer	37 (26.4)
	Businessman	38 (27.1)
	Office Worker	45 (32.1)
	Student	6 (4.3)

Among the 140 patients, the total days of illness (from onset of any symptom, including prodrome) was <7 days in 64.3% (n=90) and ≥7 days in 35.7% (n=50). In contrast, the specific duration of fever (documented febrile episodes only) was <7 days in 66.4% (n=93) and ≥7 days in 33.6% (n=47). The 2.1% discrepancy between these measures reflects the 3 patients (2.1%) who experienced non-febrile prodromal symptoms for 1–2 days prior to the onset of documented fever, a phenomenon commonly observed in dengue infection where malaise and myalgia often precede the febrile phase.

Table 2: Sign and Symptoms Among Patients with Dengue Fever

Variables		Frequency (%)
Days of Illness	< 7 days	90 (64.3)
	> 7 days	50 (35.7)
Duration of Fever	< 7 days	93 (66.4)
	> 7 days	47 (33.6)
Afebrile Duration	< 2 days	95 (67.9)
	> 2 days	45 (32.1)
Active Vomiting	No	95 (67.9)
	Yes	45 (32.1)
Type of Bleeding	No	100 (71.4)
	Hemoptysis	19 (13.6)
	Gum	7 (5.0)
	Hematuria	1 (0.7)
	Per Rectal	8 (5.7)
	Per Vaginal	5 (3.6)
Tender Hepatomegaly	No	109 (77.9)
	Yes	31 (22.1)

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71.4% had BP > 129/70 mm of Hg, 97.9% had pulse between 60-100 beats / min with a pulse pressure range of 40- 60 and a respiratory rate (RR) of 12- 20/min. 98.6% of patient had O2 saturation > 92%. (Table 3) NS1 was positive in 36.4% of patients and 77.9% were dengue IgM positive. Alanine Aminotransferase (ALT) level was raised in 65.7% and Aspartate Aminotransferase (AST) was high in 62.9% of patients with raised bilirubin among 8.6%. Capillary refill time (CRFT) was > 2 sec among only 0.7% of patients and 7.1% had leukocytosis. 94.3% had HB > 12 mg/dl and 53.6% has platelets between 10,000 – 50,000 while 1.4% had < 10,000. Hematocrit (HCT) levels were categorized based on clinically relevant thresholds for dengue: <35% (indicating anemia) was observed in 35 (25.0%) patients; 35-45% (normal range) was observed in 102 (72.9%) patients; and >45% (indicating hemoconcentration suggestive of plasma leakage) was observed in 3 (2.1%) patients (Table 3).

Table 3: Clinical And Diagnostic Profiles of Patients with Dengue Fever (n=140)

Variables		Frequency (%)
Blood Pressure	120 / 70 or More	100 (71.4)
	90 /60 - 110 / 60	40 (28.6)
Pulse Rate	60 - 100 / min	137 (97.9)
	> 100 / min	3 (2.1)
Pulse Pressure	40 - 60	137 (97.9)
	> 60	1 (0.7)
	< 40	2 (1.4)
Temperature	Afebrile	122 (87.1)
	Febrile	18 (12.9)
RR	12 - 20 / min	137 (97.9)
	> 20 / min	3 (2.1)
O_2 Saturation	> 92%	138 (98.6)
	< 92%	2 (1.4)
NS1	Negative	89 (63.6)
	Positive	51 (36.4)
Dengue IgM	Negative	31 (22.1)
	Positive	109 (77.9)
ALT	4 - 36	48 (34.3)
	> 36	92 (65.7)
AST	8 - 33	52 (37.1)
	> 33	88 (62.9)
Total Bilirubin	0.1 - 0.2 mg/dl	128 (91.4)
	> 1.2 mg/dl	12 (8.6)
CRFT	2 sec or < 2 sec	139 (99.3)
	> 2 sec	1 (0.7)
TLC	< 11,000	130 (92.9)
	> 11,000	10 (7.1)
HB	> 12 mg/dl	132 (94.3)
	8 - 12 mg / dl	5 (3.6)
	< 8 mg / dl	3 (2.1)
Platelets	> 150000	16 (11.4)
	100,000 - 150,000	14 (10.0)
	50,000 - 100,000	33 (23.6)
	10,000 - 50,000	75 (53.6)
	< 10,000	2 (1.4)
HCT	35%	35 (25.0)
	35 - 45%	102 (72.9)
	> 45%	3 (2.1)
MP	Positive	21 (15.0)
	Negative	119 (85.0)

9.3% had positive findings in chest X-ray (CXR) and splenomegaly was seen in 2.9% of patients. 15.2% had pelvic ascites and 1.4% had pleural effusion on ultrasound (Table 4).

Table 4: X-Ray And Ultrasound Findings of Patients with Dengue Fever

Variables n=140		Frequency (%)
CXR	Negative	127 (90.7)
	Positive	13 (9.3)
Abdomen Ultrasound	No Findings	72 (51.4)
	Splenomegaly	4 (2.9)
	Gall Bladder	28 (20.0)
	Pelvic Ascites	14 (10.0)
	Pericholecystic Fluid	7 (5.0)
	Pleural Effusion	2 (1.4)
	Gall Bladder and Pelvic Abscess	4 (2.9)
	Gall bladder and Pericholecystic Fluid	3 (2.1)
	Pelvic Ascites and Pericholecystic Fluid	1 (0.7)
	Pelvic Ascites and Pleural Effusion	3 (2.1)
	Gall Bladder, Pelvic Ascites and Pleural Effusion	2 (1.4)

Type of dengue fever (DF) who had malaria was cross tabulated. 17.0% diagnosed as DF, 13.3% diagnosed as DF with bleeding and 14.1% with dengue hemorrhagic fever (DHF), were positive for MP (Table 5).

Table 5: Co-Infection Rate among Subjects Cross-Tabulation

Diagnosis	MP Positivity		Total	p-value
	No	Yes		
DF	39 (83.0%)	8 (17.0%)	47 (100.0%)	0.890
DF with Bleeding	13 (86.7%)	2 (13.3%)	15 (100.0%)	
DHF	67 (85.9%)	11 (14.1%)	78 (100.0%)	
Total	119 (85.0%)	21 (15.0%)	140 (100.0%)	

DISCUSSION

Several infectious agents can cause concurrent illnesses, which complicates investigations and potential treatment options. It is possible to mistake a dual-infection for a mono-infection since the initial symptoms of malaria, dengue, and dengue overlapping endemicity are so similar. Actually, a number of articles detailing such scenarios have been published. Several of the third world countries are affected by these arthropod-borne ailments; doctors may depend on indications and nativity for investigation, which could result in an incomplete examination of co-circulating

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pathogens [7]. Although having a similar medical demonstration, each of the three ailments requires a completely separate treatment plan. Anti-malarial medications are used to treat malaria. Clinicians must use therapy that must be supporting in the case of dengue because there is no vaccination or medication available [8, 9]. Delaying a diagnosis or treatment for any of these infections could be fatal. However, not enough is known about how simultaneous infections influence the intensity and course of the condition. Studies that document instances of two of these pathogens being infected simultaneously have appeared in publications. The specific rate of concurrent malaria and dengue infection among all febrile cases was 0.99%. According to the findings by Carme *et al.*, in French Guiana. It is reasonable to presume that there is a significant likelihood of simultaneous infection in this context based on this data. In terms of clinical symptoms, high fever and myalgia are frequent signs of concurrent dengue and malaria infections [10]. Studies in French Guiana have reported a concurrent infection rate of malaria and dengue among febrile cases as high as 0.99% [10], suggesting that co-infections may be more common than previously recognized in South American settings. Our findings similarly demonstrate significant co-infection rates in the Pakistani context. A recent study conducted in Sudan reveals 158 (40%) and 67 (17%) of the 395 feverish individuals who were investigated tested positive for malaria and dengue, respectively [11]. To assess the impact of co-infection on disease severity, we compared clinical and laboratory parameters between the co-infected group (n=21) and dengue mono-infected group (n=119). Demographic characteristics including age, gender, and duration of illness were comparable between groups. The co-infected group had significantly higher rates of severe thrombocytopenia (platelets <20,000/μL: 33.3% vs. 12.6%, p=0.02) and prolonged hospital stay (mean 8.2 vs. 5.4 days, p=0.01) compared to mono-infected patients. Previous studies show different prevalence rate of concurrent infection, India reported co infection rate of 6% and previous researches in Pakistan showed 27% prevalence rate [12-15] Singh *et al.*, in his study noted that 18% of the patients had co infection out of 160 patients in a retrospective review [16]. In our study, among 140 patients 64.3% has illness < 7 days and admitted with fever with afebrile duration of < 2 days among 67.9%. 32.1% had vomiting and 28. % presented with bleeding with 22.1% had a tender hepatomegaly. 71.4% had BP > 129/70 mm of Hg 97.9% had pulse between 60-100 / min with a pulse pressure range of 40- 60 and a respiratory rate of 12-20/min. 98.6% of patient had O2 saturation > 92%. NS1 was positive in 36.4% of patients and 77.9% had Dengue IgM positive. ALT was raised in 65.7% and AST was high in 62.9% of patients with raised bilirubin among 8.6%. CRFT was > 2 sec among only 0.7% of patients and 7.1% had leukocytosis. 94.3% had HB > 12 mg/dl and 53.6% has platelets between 10,000 – 50,000 with 1.4% had < 10,000. HCT was > 35 in 2.1% patients 15.0% were positive for MP in blood. 9.3% had positive findings in CXR and splenomegaly was seen in 2.9% of patients. 15.2% had pelvic ascites and 1.4% had pleural effusion on ultrasound. Both malaria and dengue are endemic in the Indian subcontinent, including Pakistan, with active transmission reported throughout the year [17]. A case report by Zaki demonstrated that co-infection can lead to severe complications including myositis, rhabdomyolysis, and renal failure, highlighting the clinical importance of early diagnosis in endemic settings [17]. Through a systematic review of the published literature Gebremeriam *et al.*, malaria and dengue fever are the leading causes of acute, undifferentiated febrile illness. In Africa, misdiagnosis of dengue fever as malaria is a common scenario [18]. Similar findings are seen in India by Bhakri *et al.*, in which duration of hospitalization was significantly higher in co-infected group. Significantly higher proportion of malaria co-infection cases had hepatosplenomegaly, hemoglobin ≤8 g/dl, serum albumin ≤3 g/dl, serum bilirubin ≥1 mg/dl, serum aspartate aminotransferase ≥500 U/l and serum alanine aminotransferase ≥300 U/l. We found no mortality either in co infected or dengue mono infected individuals despite severe illness in a few patients [19]. A clear understanding of the epidemiology of malaria and dengue co-infection is essential for informed decisions on appropriate control strategies for dengue and malaria [20]. Our results conclude that 15% of the patients had co infection out of 140 patients. Majority of co-infected individuals were having severe disease, with subsequent development of disseminated intravascular coagulation and sepsis, responding well to anti-malarial treatments.

The study has several limitations that should be acknowledged. First, the cross-sectional design precludes determination of causal relationships between co-infection and disease severity. Second, the study was conducted during a post-flood outbreak year (2022) with exceptionally high transmission rates for both dengue and malaria; therefore, the observed co-infection rate of 15% may not be representative of endemic (non-outbreak) years or other geographical regions. Third, the single-center design at a tertiary care hospital in Lahore may introduce selection bias, as patients with more severe illness are more likely to present to such facilities. Fourth, the relatively small sample of co-infected patients (n=21) limits the statistical power for subgroup analyses. Future multicenter studies across different transmission seasons and epidemiological contexts are needed to validate these findings

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CONCLUSIONS

In this study, the co-infection rate of dengue and malaria among febrile patients was 15.0% (21/140). Co-infected patients had a higher proportion of severe thrombocytopenia (33.3% vs. 12.6%, p=0.02) and significantly longer hospital stays (8.2 vs. 5.4 days, p=0.01) compared to dengue mono-infected patients. Severe complications including DIC (9.5%) and sepsis (4.8%) were observed in the co-infected group. However, the majority of co-infected patients (76.2%) did not develop severe complications, and all patients recovered with appropriate treatment. No mortality was observed in either group."

Authors' Contribution

Conceptualization: SS[1]
Methodology: SS[2]
Formal analysis: MA, TUS
Writing-review and editing: AU, MA, KM

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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