



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 was 15.0%. **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.

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 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 after approval from the Jinnah hospital Research Ethics Committee (REF: 342/20/10/2022/S1 ERB, dated: 20/10/2022); research was given the go-ahead (REC) in the Medicine Unit of Jinnah

hospital, Lahore from October - December 2022. A sample size of 131 was calculated with 95% confidence interval and acceptable difference of 0.08% with assumed proportion of patients having co infection with malaria and dengue of 0.32 [20]. 140 cases with age ranging from 14 to 65 years of either gender diagnosed with dengue fever by NS1 and IgM were included in the study. 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.). An introduction and people who participated in the study were spoken to before the questionnaire was given to them. 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. 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 among patient with co-infection with $p < .05$ was taken as statistically significant.

RESULTS

140 patients were included in this study. Mean age was 35.5 \pm 15.6 years. 67.9% were males and 32.1% were females. 75.0% were married. Regarding occupation, 25.0% were housewives, 26.4% were laborers and 32.1% were office workers, 27.1% were businessmen and 4.35 were students (Table 1).

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

Variables	Frequency (%)	
Age (Mean = 35.5 \pm 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 140 patients, 64.3% had illness for < 7 days. 66.4% were admitted with fever <7 and 33.6% >7 days. 32.1% had active vomiting and 28.6% had bleeding with tender hepatomegaly in 22.1% of the patients (Table 2).

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)
Tender Hepatomegaly	No	109 (77.9)
	Yes	31 (22.1)

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) value was > 35 in 2.1% patients and 15.0% were positive for myeloperoxidase (MP) in blood (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 - 50	102 (72.9)
	< 35	35 (25.0)
	> 50	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 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 infecting 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]. 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]. 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% had platelets between 10,000 – 50,000 whereas 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. Zaki found malaria and dengue fever are both endemic in India, with active transmission being reported from many areas. Thus, there is a possibility of coexisting malaria and dengue infection in the same patient. The patient described in the case presented with fever, myalgia and had thrombocytopenia. During the course in hospital, he developed myositis, rhabdomyolysis and renal failure [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]. Kotepui et al., stressed on 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.

CONCLUSIONS

Majority of co infected individuals have severe disease. Co-infected individuals responded well to anti-malarial treatment despite going into disseminated intravascular coagulation and sepsis and there was no mortality found either in co-infected or dengue mono infected individuals.

Authors Contribution

Conceptualization: SS¹

Methodology: SS²

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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