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Research Article

INCIDENCE OF CO-INFECTION OF DENGUE FEVER AND MALARIA: A CROSS SECTIONAL STUDY FROM A TERTIARY CARE CENTER IN PAKISTAN

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Abstract:

Objective: To evaluate the frequency and the clinical profile of patients with concurrent dengue and malarial infections.

Methodology: A cross sectional descriptive study conducted at Medical Unit, The Liaquat University of Medical and Health Sciences, from September 2019 to November 2019. Patients presented with consistent signs of dengue fever were included in the study. Patients with flu or other diseases like typhoid, thalassemia were excluded from the study. Patients with co-infection of dengue and malaria were categorized as Group A while those with only dengue fever were regarded as Group B. Demographic and clinical variables; age, gender, complete blood count, peripheral film, thick and thin films, blood clot profile, liver function tests (LFT), presence of dengue IgM and IgG was recorded.

Results: A total of 147 (42.2%) of patients diagnosed with dengue fever were hospitalized in our hospital for the treatment and management of dengue fever. Out of these 46 (31.3%) also tested positive for malaria as a co-infection. In group A, the mean age was 28.5 + 9.4 years while in group B it was 23.4 + 6.8 years. Patients with a co-infection had severely low hemoglobin; 39.1% compared to those with only dengue fever; 31.7%. The platelet count was strikingly much lower in patients with a co-infection compared to those with solo dengue infection ($p=0.000$). Other parameters were comparable in both groups.

Conclusion: The present study indicates that the co-infection of dengue fever and malaria share similar and overlapping symptoms which makes it hard for a physician to diagnose.

Keywords: Aedes, anopheles, dengue fever, dengue hemorrhagic fever, flavivirus, malaria

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INTRODUCTION:

It is not infrequent to observe patients with a concurrent infection of both dengue fever as well as malarial infection [1]. Both infectious diseases are transmitted and spread through mosquitoes that act as the vector. Dengue fever is a disease caused by a dengue virus which is transmitted to humans through the bite of an *Aedes aegypti* mosquito [2]. The virus belongs to the family Flaviviridae, genus flavivirus and it is a single-stranded enveloped RNA virus. Whereas, malaria is a parasitic infection spread across the globe through a bite of the *Anopheles* mosquito which carries the parasite plasmodium in their gut [3].

Over four hundred million patients are diagnosed with dengue fever worldwide, annually [1]. The burden of the disease is increasing at an alarming rate in Pakistan where the first outbreak was observed in 1994 [4]. The second outbreak of dengue fever was observed in 2004 where a large number of patients were from Karachi, the largest city of Pakistan [5]. It is possible to have a co-infection of dengue fever and malaria among patients where both these diseases are prevalent especially in the rainy and post-rainy seasons [6]. Literature suggests that the dengue virus and malarial parasite may coexist and cause catastrophic damage to the patient's health which may be fatal [7]. There are four kinds of malaria parasite which can cause disease in humans. In Pakistan, two most commonly found types of malaria parasites are *Plasmodium falciparum* and *Plasmodium vivax*. The former can be potentially life threatening [8].

The local data is either outdated or limited by many parameters. Therefore, it is essential to assess the burden of the co-infection of dengue and malaria in our setting. Hence, the present study aimed to evaluate the frequency of patients presenting a co-infection of dengue fever and malaria in our setting and further stratify the patients according to the severity of the clinical course of the disease.

METHODOLOGY:

A cross sectional descriptive study was conducted from September 2019 to November 2019 for duration of 3 months. This study was conducted at Liaquat University of Medical and Health Sciences. Ethical approval was obtained before initiating the data collection for the study. Informed written consent was obtained from all patients included in the study. All patients who presented with the complaint of fever, myalgia, any rash, or other consistent signs with dengue fever were included in the study. Patients with a flu, or characteristic features of other diseases like typhoid, thalassemia, or with no associated dengue fever were excluded from the study. Patients were diagnosed for dengue

and malaria infection with the help of clinical history, physical examination, and the consistent clinical features. Laboratory tests including thick and thin films were also done for malarial infections and serological tests for determination of dengue IgM and IgG antibodies confirmed the dengue fever diagnosis.

Demographic profiles of patients such as age, gender and residence, and other related data was recorded in a predefined pro forma. Complete blood count with peripheral film, malarial parasite thick and thin film stained with Giemsa stain, blood clot profile, liver function tests (LFT), dengue IgM and IgG were also recorded.

The patients were treated and managed according to the latest guidelines provided by the World Health Organization. Antimalarial therapy for *Plasmodium falciparum* was given to each patient; quinine sulfate 600 mg three times a day adjunctive to doxycycline 100 mg daily for at least a week. For *Plasmodium vivax*, artemether 20 mg and lumefantrine 120 mg tablets twice daily for three days followed by primaquine 0.6 mg/kg given once daily for two weeks. In patients with low platelet count of less than $20,000 \times 10^9/\text{litre}$, fresh frozen plasma or thrombocyte concentrates were used.

Statistical analysis

Data was entered into statistical package for social sciences (spss v.24) and analyzed by an expert statistician. Categorical data was presented as frequency and percentage. Continuous data was presented as mean plus standard deviation. Association between demographic and clinical parameters as independent variables with the co-infection of dengue and malaria was assessed using t-test and chi square where appropriate. A p-value of 0.05 was considered as statistically significant.

RESULTS:

A total of 348 patients were assessed during the study period presenting with complaints of fever and symptoms consistent with dengue fever. Out of these, 221 (63.5%) patients tested positive for dengue IgM antibodies. 147 (42.2%) of them were hospitalized in our hospital for the treatment and management of dengue. Out of these 46 (31.3%) were also positive for malaria as a co-infection. Patients with co-infection of dengue and malaria were categorized as Group A while those with only dengue fever were regarded as Group B.

In group A, the mean age was 28.5 ± 9.4 years while in group B it was 23.4 ± 6.8 years. The age in both groups ranged between 8 years to 64 years. There were 98 (66.7%) male patients while 49 (33.3%) were female patients. Details are shown in Table 1 and figure 1.

Gender distribution in the study (n=147)

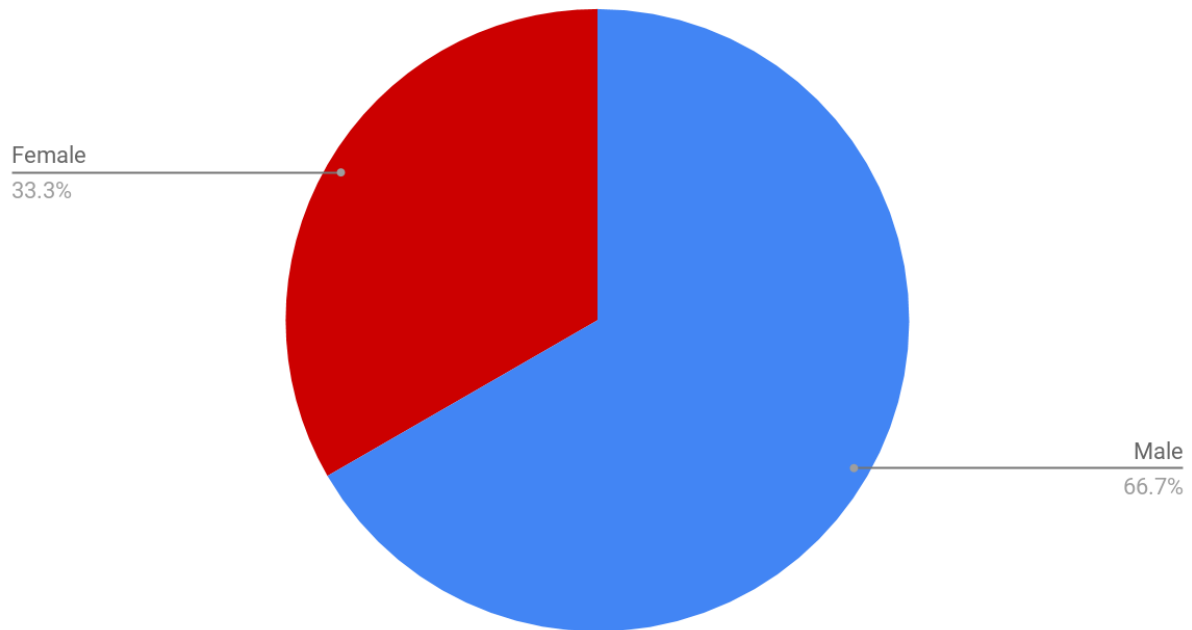


Figure 1. Gender distribution in the study population (n=147)

Out of the 46 patients with a co-infection of malaria, 10 (21.3%) were infected with *Plasmodium falciparum* while 36 (78.7%) had *Plasmodium vivax* parasite (See Figure 2).

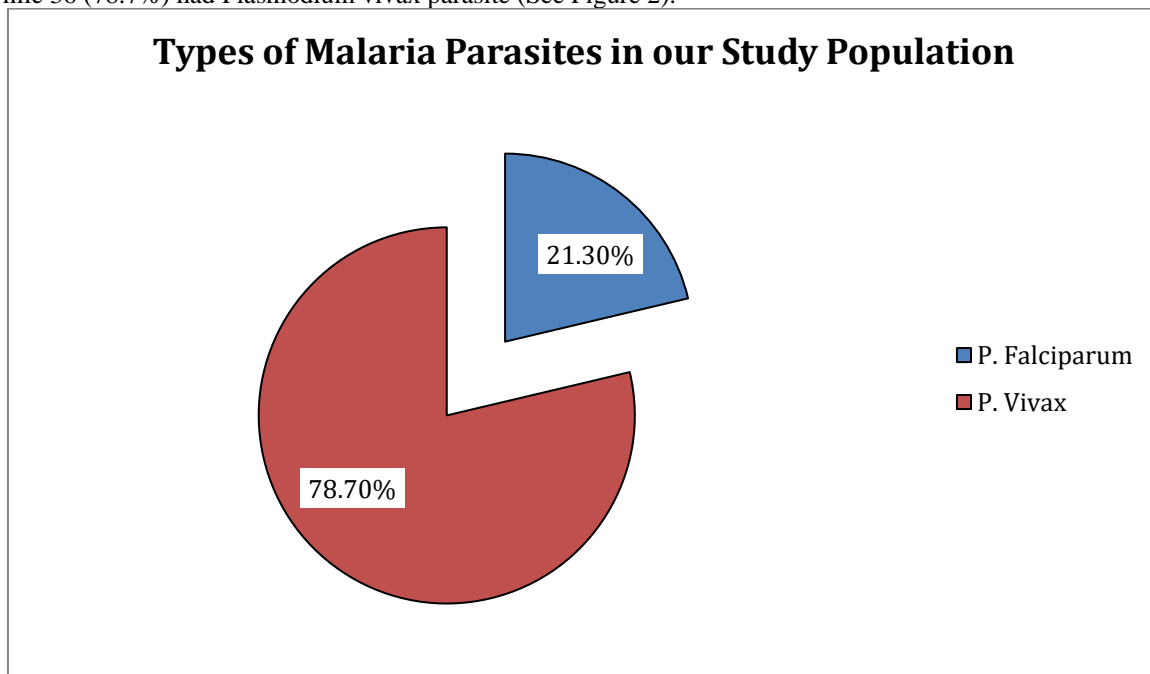


Figure 2. Distribution of malaria parasite in study patients n=46

When laboratory parameters were assessed, it was found that patients with a co-infection with both dengue and malaria had severely low hemoglobin; 39.1% compared to those with only dengue fever; 31.7%. The hematocrit level was also much lower in group A (84.6%) compared to group B (78.2%), however, it was not significant. The platelet count was strikingly much lower in patients with a co-infection compared to those with solo dengue infection ($p=0.000$). Other parameters were equal in both groups.

Table 1. Demographic and Clinical profile of patients in group A and group B

Characteristics	Group A (Dengue & Malaria) n=46	Group B (Dengue only) n=101	P-value
Age groups <i>10 years or less</i> <i>11 to 19 years</i> <i>20 to 46 years</i>	8 (17.4%) 11 (23.9%) 29 (63%)	21 (20.8%) 27 (26.7%) 53 (52.5%)	0.084
Presenting signs & symptoms <i>High grade fever</i> <i>Headache</i> <i>Nausea and vomiting</i> <i>Muscle ache/Myalgias</i> <i>Rash</i> <i>Loss of appetite</i> <i>Abdominal pain</i>	46 (100%) 34 (74%) 27 (58.9%) 29 (63%) 21 (45.7%) 19 (41.3%) 42 (91.3%)	101 (100%) 71 (70.3%) 89(88.1%) 59 (58.4%) 20 (19.8%) 26 (25.7%) 32 (31.7%)	1 0.897 0.03 0.745 0.000 0.002 0.000
Hemoglobin (mg/dL) <i><6</i> <i>6-10</i> <i>>10</i>	18 (39.1%) 14 (30.4%) 14 (30.4%)	32 (31.7%) 51 (50.5%) 17 (16.9%)	0.001
Platelet count (per mm³) <i>< 20,000</i> <i>20,000-50,000</i> <i>50,000-10,0000</i>	34 (73.9%) 10 (21.7%) 2 (4.3%)	41 (40.6%) 52 (51.5%) 8 (7.9%)	0.000

DISCUSSION:

The dengue fever is a rising issue and a concern of public health especially in areas where urbanization is rapidly not controlled. Dengue virus is caused by a flavivirus which is transmitted to humans through an *Aedes aegypti* mosquito bite which acts as its reservoir and a vector [9]. Malaria is also a serious health hazard in Pakistan, which is another infection spread through a malarial parasite called plasmodium which is of four types including *P. falciparum*, *vivax*, *ovale*, and *malariae* [8-10]. It is also driven and transmitted by the *Anopheles* mosquito and can be fatal in many instances [11]. Both these diseases are highly prevalent in Pakistan [12]. About a hundred million patients are diagnosed with dengue fever annually with 200,000 cases being reported from South East Asia, alone [13].

It is common for both dengue and malaria infection to coexist at the same time in areas where both of these diseases are endemic. Co-infection of these infectious diseases may cause similar symptoms that may cause impediment in adequate diagnosis subsequently leading to a delay in treatment and management [14]. The sufferers of the co-infection of dengue and malaria are reported to have a more

severe clinical course and poor outcome. The incidence of bleeding manifestations, rash and anemia are often more highlights in the patients with both infections at a time [15].

In the present study, frequency of patients with the co-infection of dengue and malaria was assessed along with the evaluation of demographic and clinical parameters in these patients. We reported a strikingly high rate of co-infection i.e. forty six out of the 147 patients that were hospitalized for treatment during the study, were diagnosed with both dengue fever and malaria infection. In contrast, a local study reported a much lower incidence of 26 (23.21%) patients with concurrent infection of dengue and malaria in 2009 [16]. Similarly, in another study a much lower frequency of 7.1% (17 of 238) of co-infection was reported [17]. The disparity can be explained by the population increase, rampant urbanization, and innumerable congested shanty towns all over the city, Karachi, Pakistan.

The present study reported that there were about three-fourth patients infected with *P. vivax* while about 20 percent had *P. falciparum* parasite. In contrast to the present findings, an earlier local

study by Khan HU, et al, found that 57 (58.17%) patients had *P. falciparum* while 40 (40.81%) had *P. Vivax* and only 1 patient had *P. malariae* in their study population [8].

In the present study, it was observed that the patients with concomitant infection of dengue fever and malaria suffered from a much severe disease and worsening symptoms and deranged laboratory parameters compared to those with only dengue fever. It was reported that the majority of the patients with a co-infection had low hemoglobin, hematocrit, and a severe form of thrombocytopenia ($p=0.000$). These findings of the present study are in line with the previous literature [15-18]. In a local study by Assir et al, it was indicated that patients with coinfection of dengue and malaria had a lower incidence of jaundice compared to those with isolated dengue fever. Nevertheless, other measures for severity of disease remained comparable in all three groups [15].

In contrast, a study from India authored by Mohapatra et al, indicated that the patients with concurrent infection of dengue with malaria had a better patient outcome in comparison with the patients diagnosed with malaria alone [19]. The difference in our findings can be explained by analyzing that the patients with co-infection in their study sought early medical treatment i.e. within an average of 2.2 ± 0.4 days therefore, accessibility to prompt treatment and urgent primary care was a significant contributor in regards to the evidently good outcome. Another contributing factor for good patient prognosis was the low parasitic count in patients with a co-infection.

Despite our best efforts to minimize limitations, there are certain obstacles we faced during the study. The number of patients presenting with the complaints of fever and consistent picture of dengue fever were over three hundred or so. However, only half of the patients sought treatment at our tertiary care center. The reason for their departure was that the many of the patients belonged to rural areas and were from low socioeconomic class. They were unable to afford treatment at our hospital. Other reasons included; inaccessibility to proper medication and pharmacy and non-availability of free accommodation in the city since many patients were referred to the tertiary care hospital by their local quacks or physician in their hometown.

CONCLUSION:

It is important to remember that dengue and malaria can coexist and may cause much more damage to the patient. Our study indicates that the co-infection of dengue fever and malaria share similar and overlapping symptoms which makes it

very hard for a physician to diagnose. The co-infection is associated with a much more serious clinical course compared to dengue fever alone. It should be given special attention since delay in diagnosis can have catastrophic consequences for the patient's outcome.

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