

Co-existence of Dengue Fever & Malaria in Thrombocytopenic Patients Presented with Acute Febrile Illness

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ABSTRACT

Background: Dengue fever and malaria both can present with thrombocytopenia and is regarded as a strong predictor of dengue fever. Thrombocytopenia is also considered criterion of disease severity, bad prognostic factor and its presence is associated with increase probability of malaria.

Objective: To determine frequency of co-existence of dengue fever and malaria in thrombocytopenic patients presented with acute febrile illness in tertiary care hospital.

Methods: Cross-sectional, observational study conducted at the department of Emergency Medicine, Ziauddin University Hospital, Karachi from April 2013 to January 2014. A total of 159 patients meeting inclusion criteria were included in this study. 5ml of blood by venupuncture in EDTA anti-coagulant for platelet count and preparing thick and thin films and 2 ml of blood in plain bottle for detection of dengue specific IgM was collected from all patients. Thick films are used to identify malarial parasites and thin films to identify specie. Dengue fever was diagnosed on positive dengue IgM. Co-existence was labeled as positive if malarial parasites and dengue IgM found to be present at the same time. This diffusion susceptibility test was use to determine susceptibility of bacterial agents to antibiotics. Data was analyzed by descriptive statistics using SPSS software version 19.

Results: Overall mean (\pm SD) age was 38.3 (\pm 7.9) years, with Male to female ratio was 1.1: 1. Co-infections (Dengue and Malaria) were diagnosed in 5 (5.6%) of cases. From 5 cases, 3 (60%) were male and 2 (40%) were female. Mean (\pm SD) age of 5 positive cases of co-infection was 37.8 (\pm 8.3) years.

Conclusion: Concurrent infections were found 5.6% in this study, however, this percentage is slightly low; and special consideration should be given to the likelihood of co-infection with dengue and malaria.

KEY WORDS: *Dengue Fever, Malaria, Immunoglobulin-M (IgM), Febrile Illness, Thrombocytopenia.*

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INTRODUCTION

Dengue Virus is becoming an increasing health problem. Over 99% cases of viral hemorrhagic fever reported worldwide are due to dengue hemorrhagic fever (DHF).¹ Dengue fever is cause by dengue viruses (DENVs) which are members of Flaviviridae family.² It has been estimated that 2.5 billion people live in areas which are at risk of epidemic transmission and over 50 million of DENV infections occur globally each year.^{3,4} Since we are living in region where malaria is endemic and is considered as the most common cause of fever and in general practice empirical anti-malarial therapy is common, it is important to distinguish the two conditions due to clinical similarities and unexpected progress of dengue fever (DF) to DHF and dengue shock syndrome (DSS).⁵

Both dengue fever and malaria can present with thrombocytopenia. Thrombocytopenia is a consistent finding in dengue fever and is regarded as a strong predictor of dengue fever. [6] Thrombocytopenia is also considered criterion of disease severity, bad prognostic factor and its presence is associated with increase probability of malaria.^{7,8}

In a local study Ali et.al showed that Out of 11 patients diagnosed as having dengue fever on serology 9 (81.8%) also had co-existence of malaria and thrombocytopenia was present in 90% of such patients.⁵ Out of 11 DENV positive patients three patients died and first DENV positive patients who died was prescribed anti-malarial by general practitioner in outdoor.⁵ On autopsy plasmodium falciparum rings were found in blood and DENV IgM was detected in serum samples⁵

Due to clinical similarities in two conditions and possibility of extensive mosquito exposure, high co-existence of both conditions cannot be excluded.⁵ This study aims to determine frequency of co-existing dengue fever and malaria in thrombocytopenic patients presenting with acute febrile illness so that magnitude of the condition could be assessed. The findings could

be used to plan that all patients with acute febrile illness with thrombocytopenia must be screened for dengue fever without delay.

METHODOLOGY

This study was carried out at the department of emergency medicine, Ziauddin University Hospital, Karachi, Pakistan. Patients of either gender with more than 12 years of age presenting to Ziauddin Hospital Karachi with acute febrile illness and found to have thrombocytopenia were included in the study while patients known to have disease causing thrombocytopenia e.g. systemic lupus erythematosus, idiopathic thrombocytopenic purpura and patients with other causes of acute febrile illness such as pneumonia, meningitis, enteric fever etc. diagnosed on blood culture, chest X-ray sputum C/S, urine D/R were excluded from the study.

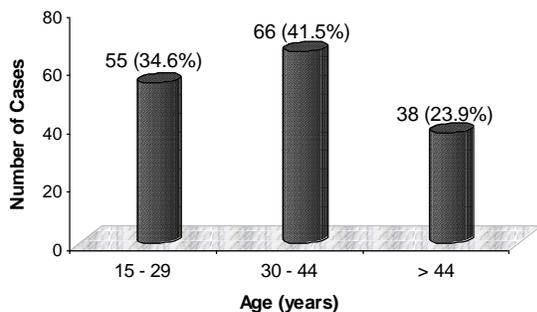
A total of 159 patient's fulfilling inclusion criteria were included in the study. 5ml of blood by venupuncture in EDTA anti-coagulant for platelet count and preparing thick and thin films and 2 ml of blood in plain bottle for detection of dengue specific IgM was collected from all patients. Thick films are used to identify malarial parasites and thin films to identify specie. Dengue fever was diagnosed on positive dengue IgM. To minimize bias all specimen was sent to single central laboratory of the hospital. A proforma especially designed for the study was used to documents findings such as patients age, gender, name, malaria parasite, dengue IgM by the researcher. Co-existence was labeled as positive if malarial parasites and dengue IgM was found to be present at the same time.

Data was entered in computer and analyzed by SPSS version 19.0 frequency and percentages were calculated for categorical variables such as gender, co-existing dengue fever and malaria. Mean standard deviation was calculated for numerical variables like age. Stratification was done in terms of age and gender to see the effect of that on outcome.

RESULTS

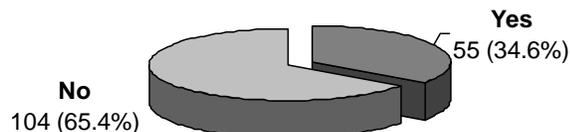
During the study, a total of 159 cases with thrombocytopenia of age > 12 years were included. From 159 cases, 82 (51.6%) were male and 77 (48.4%) were female. Mean (\pm SD) age of 159 cases was 38.3 (\pm 7.9) years with range = 15 – 53 years. Majority 66 (41.5%) of cases had age between 30 – 44 years. (Figure 1).

Figure 1.



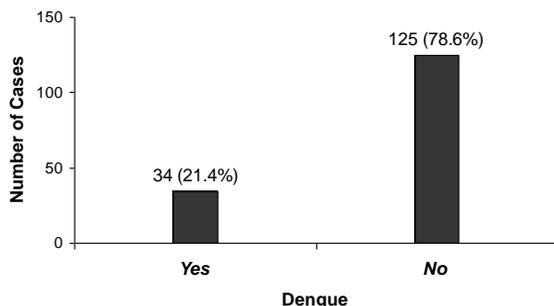
Out of 159 thrombocytopenic cases presented with acute febrile illness, malaria was diagnosed in 55 (34.6%) cases (Figure 2).

Figure 2.



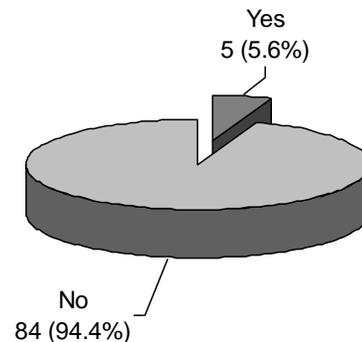
Dengue fever was diagnosed on positive dengue IgM. Out of 159 cases, 34 (21.4%) of cases were diagnosed as dengue (Figure 3).

Figure 3.



Co-infections (Dengue and Malaria) were diagnosed in 5 (5.6%) cases (Figure 4).

Figure 4.



Out of 5 positive cases of co-infection, 3 (60%) were male and 2 (40%) were female. Mean (\pm SD) age of 5 positive cases of co-infection was 37.8 (\pm 8.3) years with range = 15 – 52 years. Majority 3 (60%) of cases had age between 30 – 44 years.

DISCUSSION

Despite an extensive overlap between dengue and malaria widespread areas, there are limited literatures published on co-infections. Febrile patients who are living in or returning from the endemic areas, dengue and malaria must be suspected in these patients. Dengue is usually ruled out after the confirmation of malaria. There are two methods for the confirmation of dengue: in acute phase (0 – 4 days after the start of fever) by RT-PCR, which is quicker and more precise, and other methods is dengue-specific IgM sero-conversion.

Referring to the published case reports,⁹⁻¹² the dengue infection's diagnosis is based on positive dengue IgM; while, this cannot vogue the recent dengue virus, because IgM can endure for months and cross-react along with other arboviruses.¹³ The RT-PCR requires advance laboratory settings and cannot be performed on site, while a new test, Platelia, which is easily available and can be included in any laboratory and shows particularly early-acute phase samples.¹⁴ To find out the frequency of malaria and dengue co-infection, the Platelia test must be used in all cases of malaria-like or dengue-like syndrome, even when then diagnosis of malaria is positive, in all

areas where both dengue and malaria infections could overlap.

Both dengue fever and malaria can present with thrombocytopenia. Thrombocytopenia is a consistent finding in dengue fever and is regarded as a strong predictor of dengue fever.⁶ Thrombocytopenia is also considered criterion of disease severity, bad prognostic factor and its presence is associated with increase probability of malaria.^{7,8}

Many etiologic agents with mixed infections are not rare in malaria.¹⁵ Despite limited data available, dengue and malaria co-infection can be common in areas having both diseases are co-endemic.¹⁶

A study of management and diagnostic techniques of malaria and dengue co-infection shows patients who present with dual infection having prolonged fever which is more than seven days associated with bleeding manifestation, anemia, myalgia and rashes.¹⁷ Also, according to Vasconcelos et al, arboviral infection which causes continuous fever can cover periodic fever associated with malarial parasites.¹⁸ Out of 159 thrombocytopenic cases presented with acute febrile illness, malaria was diagnosed in 55 (34.6%) cases while 34 (21.4%) of cases were diagnosed as dengue.

Of the 89 patients of malaria and dengue in this study, 5.6% had concurrent malaria and dengue. This percentage is relatively high as compared with other international studies. A study from France reported that 1% concurrent dengue and malaria.¹⁹ Another study from Brazil reported 1.8% concurrent dengue and malaria.²⁰ Very high percentage was found in a local study Ali et.al showed that Out of 11 patients diagnosed as having dengue fever on serology 9 (81.8%) also had co-existence of malaria and thrombocytopenia was present in 90% of such patients.⁵ In this study from 5 positive cases of

co-infection, 3 (60%) were male and 2 (40%) were female. Mean (\pm SD) age of positive cases of co-infection was 37.8 (\pm 8.3) years.

We acknowledge the fact that a small number of patient were assessed during the study, however, it is important to understand that malaria and dengue co-infection requires special focus because delayed diagnosis can lead to lethal complications.¹⁶⁻²¹

These two syndromes as a co-infection can cause similar symptoms or may overlap symptoms; the diagnosis of dengue or malaria based purely on clinical grounds is very difficult and challenging for physician¹⁶ and it is also possible that either clinical range of disease or cure may also be affected, so it is very important to note that both diseases have similar clinical pattern, so the diagnosis could be made concurrently specially in those patients who are living in or returning from endemic areas or during dengue breakout.²²⁻²³

CONCLUSION

Concurrent infections were found 5.7% in this study. Although this percentage is slightly low; special focus should be given to the likelihood of co-infection with dengue and malaria. In the emergency department; the peculiarity between dengue and malaria should be made because in both situations, timely diagnosis is necessary for patient care. Finally, it is important to note that both diseases have similar clinical findings, thus the diagnosis could be made concurrently for dengue and malaria in patients living or returning from areas where both diseases are widespread or during dengue outbreaks.

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REFERENCES

¹ Rigau-Perez JG, Clark GG, Gulber DJ, Reitee P, Sanders EJ, Vorndam AV. Dengue and dengue hemorrhagic fever. *Lancet* 1998;352:971-977.

² Henchal EA, Putnak JR. The dengue viruses. *Clin Microbiol Rev* 1990;3: 376-396.

³ Pinheiro FP, Corber SJ. Global situation of dengue and dengue hemorrhagic fever and its emergence in Americas. *World Health Stat* 1997;50:161-169.

⁴ Guzman MG, Kouri G. Dengue: an update. *Lancet infect Dis* 2002;2:33-42.

⁵ Ali N, Nadeem A, Anwar M, Tariq WZ, Chotani RA. Dengue fever in malaria endemic areas. *J Coll Physicians Surg Pak* 2005;16:340-342.

- ⁶ Ahmed S, Ali N, Ashraf S, Ilyas M, Tariq WZ, Chotani RA. Dengue fever outbreak: A clinical management experience. *J Coll Physicians Surg Pak* 2008;18:8-12.
- ⁷ Mahmood A, Yasir M. Thrombocytopenia; a predictor of malaria among febrile patients in Liberia. *Infect Dis J Pak* 2005;14:41-44.
- ⁸ Lathia TB, Joshi R. Can hematological parameters discriminate malaria from nonmalarious acute febrile illness in the tropics? *Indian J Med Sci.* 2004;58:239-244.
- ⁹ Charrel RN, Brouqui P, Foucault C, de Lamballerie X. Concurrent dengue and malaria. *Emerg Infect Dis.* 2005;11:1153-1154.
- ¹⁰ Deresinski S. Concurrent Plasmodium vivax malaria and dengue. *Emerg Infect Dis.* 2006;12:1802.
- ¹¹ Thangaratham PS, Jeevan MK, Rajendran R, Samuel PP, Tyagi BK. Dual infection by dengue virus and Plasmodium vivax in Alappuzha District, Kerala, India. *Jpn J Infect Dis.* 2006;59:211-212.
- ¹² Ward DI. A case of fatal Plasmodium falciparum malaria complicated by acute dengue fever in East Timor. *Am J Trop Med Hyg.* 2006;75:182-185.
- ¹³ Allwinn R, Doerr HW, Emmerich P, Schmitz H, Preiser W. Crossreactivity in flavivirus serology: new implications of an old finding? *Med Microbiol Immunol.* 2002;190:199-202.
- ¹⁴ Dussart P, Labeau B, Lagathu G, Louis P, Nunes MR, Rodrigues SG, et al. Evaluation of an enzyme immunoassay for detection of dengue virus NS1 antigen in human serum. *Clin Vaccine Immunol.* 2006;13:1185-9.
- ¹⁵ Singhsilarak T, Phongtananant S, Jenjittikul M, Watt G, Tangpakdee N, Popak N, et al. Possible acute coinfections in Thai malaria patients. *Southeast Asian J Trop Med Public Health* 2006;37:1-4.
- ¹⁶ Ward DI. A case of fatal Plasmodium falciparum malaria complicated by acute dengue fever in East Timor. *Am J Trop Med Hyg* 2006;75:182-185.
- ¹⁷ Abbasi A, Butt N, Sheikh QH, Bhutto AR, Munir SM, Ahmed SM. Clinical Features, Diagnostic Techniques and Management of Dual Dengue and Malaria Infection. *J Coll Physicians Surg Pak* 2009;19:25-29.
- ¹⁸ Vasconcelos PFC, Rosa APAT, Rosa JFST, Dégallier N. Concomitant Infections by Malaria and Arboviruses in the Brazilian Amazon Region. *Rev Latinoam Microbiol* 1990;32:291-294.
- ¹⁹ Carme B, Matheus S, Donutil G, Raulin O, Nacher M, Morvan J. Concurrent Dengue and Malaria in Cayenne Hospital, French Guiana. *Emerg Infect Dis* 2009;15:668-671.
- ²⁰ Santana VD, Lavezzo LC, Mondini A, Terzian AC, Bronzoni RV, Rossit AR et al. Concurrent dengue and malaria in the Amazon region. *Rev Soc Bras Med Trop* 2010;43:508-511
- ²¹ Charrel RN, Brouqui P, Foucault C, Lamballerie X. Concurrent Dengue and Malaria. *Emerg Infect Dis* 2007;11:1153-1154.
- ²² Bhalla A, Sharma N, Sharma A, Suri V. Concurrent infection with Dengue and Malaria. *Indian J Med Sci* 2006;60:330-331.
- ²³ Thangaratham PS, Jeevan MK, Rajendran R, Samuel PP, Tyagi BK. Dual Infection by Dengue Virus and Plasmodium vivax in Alappuzha District, Kerala, India. *Jpn J Infect Dis* 2006;59:211-212.
- ²⁴ Gubler DJ. Dengue and dengue hemorrhagic fever. *Clin Microbiol Rev* 1998;11:480-496.