Original Research Article

Comparison of clinical course, Laboratory Profile, severity and outcome of co-infection with mono-infection of malaria and dengue

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Abstract

Introduction: Dengue and malaria both vector-borne diseases are prevalent in many areas of the world as well as in India.Co-infection of malaria & dengue is not very common.The aim of the present study was to compare the clinical course, laboratory features, severity and outcome of co-infection with mono-infection of malaria and dengue.**Materials and Methods:** A total of 160 consenting consecutive patients were included in the study, who were either males or females older than 14 years of age with a confirmed diagnosis of malaria and dengue. Patients in whom *Plasmodium falciparum* or *Plasmodium vivax* malaria was diagnosed on peripheral smear or test positive for antigen; dengue was diagnosed by test positive for NS1 antigen, positive IgM or PCR. The P value less than 0.05 were taken as statistically significant.**Result:** Consequently, 160 patients were enrolled in this study in which 2 were excluded. Among the 160 patients, 107 (66.9%) were males and 53 (33.1%) were females.. The mean age was 36.2 years. Among the 158 febrile cases included, 78 (49.4%) were dengue, 65(41.1%) were diagnosed with malaria and 15 (9.5%)with co-infection.**Conclusion:** we observed that haematological profile can be helpful in predicting the need for ICU care and mortality. Hemoconcentration among patients with dengue fever is not a frequent presentation though its presence may favour the diagnosis of Dengue.

Keywords: coinfection, monoinfection, malaria, dengue

Introduction

Vector-borne diseases are infections transmitted by the bite of infected arthropod species, such as mosquitoes, ticks sandflies etc. Dengue and malaria both of these vector-borne diseases are present in many areas of the world. However, co-infection of dengue and malaria is not a common finding. These are continued to be a major health problem in some of the most populated areas of the world. Many tropical and sub-tropical countries are endemic for both dengue and malaria. The two diseases share many clinical features and may be clinically indistinguishable. It is important, however, to differentiate between the two conditions, as malaria is treatable and any delay in treatment may result in a poor outcome.Malaria and Dengue attribute to considerable morbidity and at times mortality in the Indian subcontinent. The clinical course ranges from benign presentation with early resolution to fulminant course with complications like bleeding, renal failure, respiratory distress, hypotension and death.Anopheline transmission of malarial parasites and concurrent viral Dengue coinfection by Aedes mosquito is possible and documented in our geographic setting[1-4].The influence of co-infections on severity is not straightforward, therefore,the aim of this study was to differentiate clinical and biological picture of co-infections from infections alone and determine whether patients infected by both malaria and dengue (MD) were more severe than either infection alone (respectively M and D). Dengue and malaria being among the most common vector borne diseases result in majority of acute febrile illnesses in the tropics, particularly during the monsoons. The classical concept of malaria occurring in rural and dengue in urban settings, is now contradicted and simultaneous infections from the overlap of mosquito biotypes is increasingly being documented. The aim of the present study was to compare the clinical course, laboratory features, severity and outcome of coinfection with monoinfection of malaria and dengue.

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Materials and Methods

This observational study was conducted between April 2019 to December 2019 in the Department of General Medicine, SVS Medical College, Mahabubnagar,Telangana State, india. Study Participants were selected from patients attended OPD in General Medicine department.Ethical clearance was obtained prior to the study. Informed consent were taken from all the participants. A total of 160 consenting consecutive patients were included in the study, which were either males or females older than 14 years of age with a confirmed diagnosis of malaria and dengue. patients in whom Plasmodium falciparum or Plasmodium vivax malaria was diagnosed on peripheral smear or test positive for antigen; dengue was diagnosed by test positive for NS1 antigen, positive IgM or PCR.

Three groups, isolated dengue monoinfection, isolated malaria and those positive for both dengue and malaria were included in this mutually exclusive study. Patients with a concomitant proven hematological disorder due to secondary causes, such as chronic liver disease, drug use, or associated dengue fever, were excluded from the study as were patients already on antimalarial therapy, those with primary hematological disorders, and pregnant females with malaria. A detailed history and physical examination were performed for each patient. Fever patterns, presence of jaundice, hepatosplenomegaly, lymphadenopathy, skin petechial hemorrhages, chills and rigors, and urine color were specifically noted. Clinical comparison of signs and symptoms, severity and outcome as per predefined clinical criteria was systematically carried out. Relevant laboratory parameters were compared. Statistical analysis of data as per protocol was performed. Baseline hematological parameters such as hemoglobin, platelets, leukocyte counts, and their differential counts were classified into normal and pathological counter parts. Frequencies and percentages were calculated for the patients falling into each of these categories. The percentages of patients who presented with the clinical features

were calculated and stratified according to the Plasmodium species. The P value less than 0.05 were taken as statistically significant.

Result

Table 1: Comparison of clinical features of co-infection and isolated dengue

Clinical features	Co-infection	Isolated dengue	P value
Fever	13 (86.6)	76 (97.4)	0.243
Chills / rigors	12 (80)	64 (97.4)	0.341
Retro-orbital pain	14 (93.3)	75 (96.2)	0.202
Myalgia	14 (93.3)	76 (97.4)	0.134
Headache	14 (93.3)	62 (79.5)	0.451
Epigastric distress	13 (86.6)	62 (79.5)	0.501
Rash / petechiae	9 (60)	58 (74.4)	0.624
Facial flushing	7 (46)	54 (69.2)	0.955
Palmar erythema	10 (66.7)	58 (74.4)	0.268

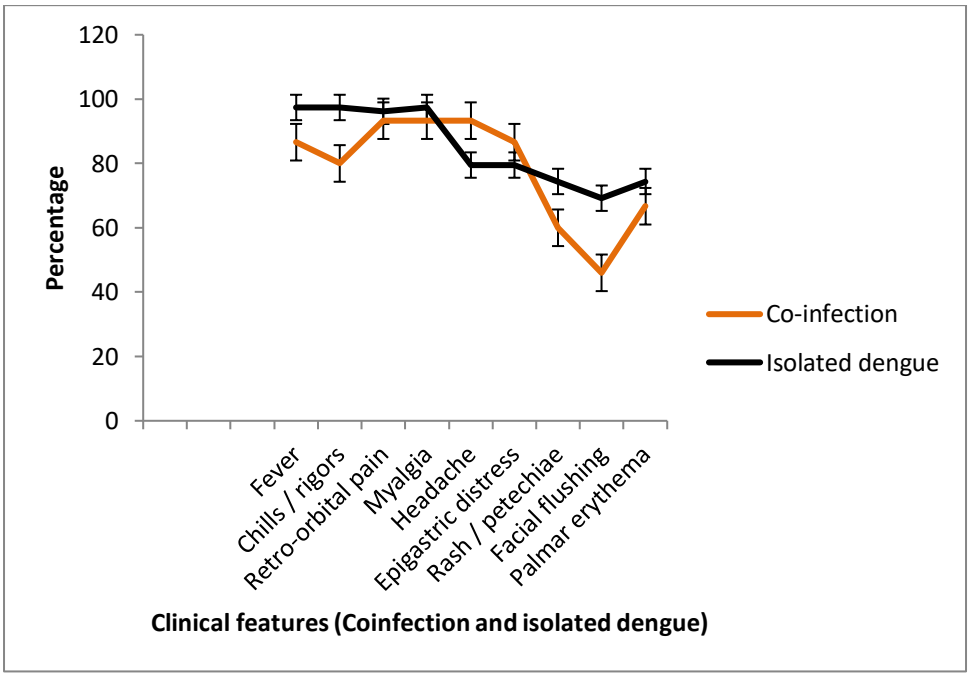

Fig 1: Comparison of clinical features of co-infection and isolated dengue

Table 2: Comparison of clinical features of co-infection and isolated malaria

Clinical features	Co-infection	Isolated Malaria	P value
Fever	13 (86.6)	62 (95.4)	0.023
Chills / rigors	12 (80)	43 (66.2)	0.246
Retro-orbital pain	14 (93.3)	54 (83.1)	0.006
Myalgia	14 (93.3)	48 (73.8)	0.043
Headache	14 (93.3)	31 (47.7)	0.043
Epigastric distress	13 (86.6)	7 (10.8)	0.002
Rash / petechiae	9 (60)	4 (6.4)	0.001
Facial flushing	7 (46)	2 (3.1)	0.004
Palmar erythema	10 (66.7)	1 (1.5)	0.001

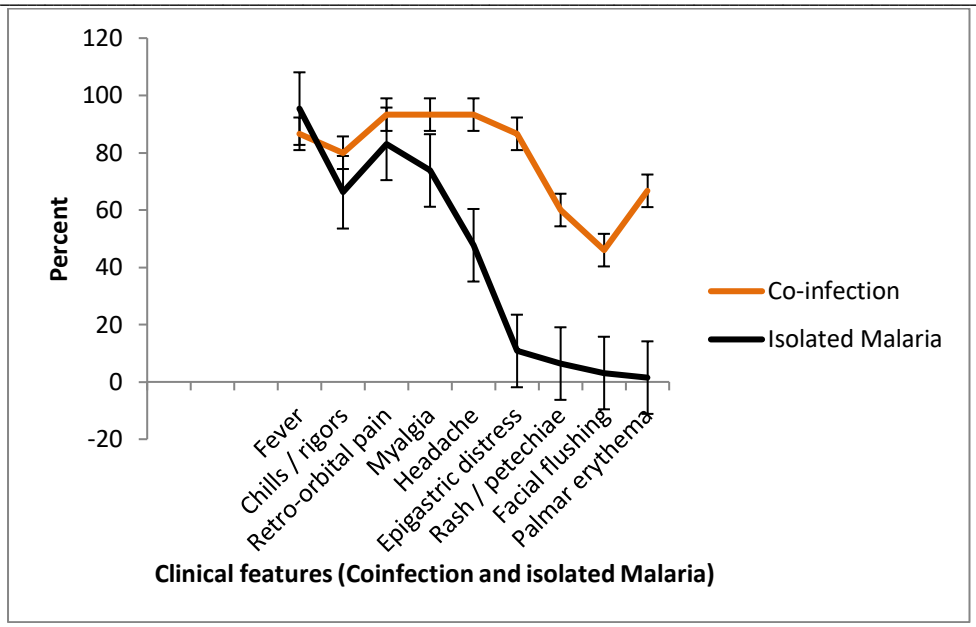

Fig 2: Comparison of clinical features of co-infection and isolated malaria

Table 3: Comparison of severity of lab parameters between co-infection and isolated dengue

Investigations	Co-infection	Isolated dengue	P value
Haemoglobin	8.9±2.1	9.1±0.4	0.001
Haematocrit	42.8±2.6	43.5±0.5	0.001
WBC	2019±280	2160±146	0.023
Platelets	48352±3892	21780±4819	0.004
ALT	103.2±19.1	104.9±13.4	0.482
AST	108.9±11.4	116.1±10.5	0.023

(Mann Whitney U test)

Table 4: Comparison of severity of lab parameters between co-infection and isolated Malaria

Investigations	Co-infection	Isolated Malaria	P value
Haemoglobin	8.9±2.1	7.9±0.7	0.001
Haematocrit	42.8±2.6	39.4±3.4	0.142
WBC	2019±280	3264±132	0.003
Platelets	48352±3892	69942±6994	0.004
ALT	103.2±19.1	82.9±10.1	0.002
AST	108.9±11.4	94.2±8.7	0.002

(Mann Whitney U test)

Consequently, 160 patients were enrolled in this study in which 2 were excluded. Among the 160 patients, 107 (66.9%) were males and 53 (33.1%) were females.. The mean age was 36.2 years. Among the 158 febrile cases included, 78 (49.4%) were dengue, 65(41.1%) were diagnosed with malaria and only 15 (9.5%)with co-infection.

The data was entered using MS-Excel-2007 and analyzed using SPSS -16 software. Descriptive analysis for numerical data consists of mean with standard deviation (SD) and for categorical data consists of frequencies and percentage for various parameters.

The coinfection and dengue groups presented with a similar clinical picture, with severe retro orbital pain, myalgia, rash and abdominal pain, though epigastric distress predominated in the coinfection group. Table 1 and 2 and Figure 1,2 showing the Comparison of clinical features of co-infection with isolated dengue and malaria. Among compared laboratory parameters, transaminitis was statistically significant in the co-infection group (p value <0.001). Anaemia was significant in the malaria group whereas the dengue group presented with raised haematocrit. The coinfection group with low haemoglobin and haematocrit was consistent with malaria coinfection. Thrombocytopenia was common to all groups, though highly significant in the dengue group (p<0.001). Leucopenia was significant in the coinfection and dengue groups compared to the malaria group. Table 3 and 4 showing the Comparison of severity of lab parameters between co-infection with isolated dengue and malaria. Among the severity parameters, bleeding manifestations, renal dysfunction and jaundice, was notable in the coinfection group, compared to the malaria group.

Discussion

Patients with isolated malaria had a significantly lower hemoglobin concentration and hematocrit at presentation than cases of isolated dengue.Patients with dengue–malaria co-infection had a significantly lower rate of jaundice than those with isolated dengue. The remaining clinical and laboratory parameters were comparable. There was no between-group difference in terms of severity of the disease. The first case of concurrent DENV and P. falciparum was reported in 2005,[5]and this was followed by reports of mixed infections with

DENV and P. vivax,[6]P. falciparum, or both.Carme et al. evaluated 1723 consecutive febrile patients in Cayenne Hospital, French Guiana, and found dengue in 238 (13.8%), malaria in 393 (22.8%), and mixed dengue and malaria infection in 17(1%) patients [7]. P. falciparum was the predominant Plasmodium species found. Rapid diagnostic tests were used for the detection of IgM and NS1 for diagnosing dengue infection. Due to the high false-positivity and low specificity of rapid diagnostic tests for IgM,[8] there may have been an over-estimation of the dengue–malaria co-infection rate. The results of these and other studies may not be comparable due to the variable patient selection criteria and diagnostic methods used. Our study shows that the rate of malaria infection was higher than the rate of dengue infection in patients admitted as probable cases of dengue fever. Even amongst the confirmed cases of dengue infection, there were more cases of dengue–malaria co-infection than isolated dengue infection.It was noticed that epigastric distress, abdominal pain and hepatomegaly was very frequent in the coinfection group, characterizing potential dengue severity. Transaminitis with jaundice and hepatomegaly corroborated these findings. Bleeding manifestations too were notable in this group. This can be attributed to increased capillary fragility, endothelial damage and coagulation abnormalities related to dual infection, rather than the low platelet counts. Among compared haematological parameters, anemia was notable in the malaria and raised hematocrit in the dengue groups respectively, whereas, the coinfection group presented with low haematocrit and anaemia.Co-infected patients presented deep thrombocytopenia more frequently than patients with single infections. Low platelets are common in dengue and malaria. In febrile patients living or returning from endemic areas, it is a good predictive factor of malaria[9,10]and in case of negative malaria diagnosis it is a good predictive factor of dengue[9]. During malaria attack in adults, thrombocytopaenia is generally not considered to be a risk factor of haemorrhage and increased mortality[10]. Nevertheless, in non-immunized children with a malaria attack, a platelet count below 100 109/L has been demonstrated to be a predictive factor of mortality[11]. Furthermore, a study performed in France on 21,888 cases of imported P. falciparum malaria showed that thrombocytopaenia below 50 109/L was associated with an increased risk of mortality[12].Considering dengue fever, high thrombocytopaenia is a known severity criterion and is linked to a higher mortality[13]. In the present study, severe thrombocytopaenia was not really accompanied with a recrudescence of haemorrhagic signs. No significant difference for the thrombocytopaenia between P. vivax and P. falciparum was observed. During malaria attacks, thrombocytopaenia generally worsens linearly with the increase of PL. This relationship did not clearly appear in patients co-infected with dengue so it is notable that deep thrombocytopaenia apparently occurred even with low parasite loads when associated with dengue virus[14].Anaemia was more frequent in patients with dual infection. There was a convergence of indirect signs, such as pallor and transfusion need and elevated total bilirubin, probably in relation to increased haemolysis. Anaemia is a classical symptom of malaria but it is barely described in dengue fever. concurrent dengue and malaria infection tends to be more severe than single infections notably for haematologic abnormalities, such as thrombocytopaenia and anaemia, known risk factors of severe dengue fever and/or malaria. However,whether this increased severity results from longer evolution duration or increased virulence or both remains to be determined. The study was retrospective so the results should be interpreted with caution. Whether prospective studies with homogeneous biological diagnosis methods and patient groups would be necessary to confirm the greatest severity of co-infection, the feasibility of such a study is questionable because of the very low prevalence of dual infection.

Conclusion

Co-infections of malaria & dengue is quite uncommon but it could become a serious medical problem. Since the biological and clinical characteristics of dengue and malaria are very similar, all clinicians treating patients in or returning from endemic areas should systematically order examinations for both diagnoses, even if one or the other is positive. We observed that Laboratory profile can be helpful in predicting the need for ICU care and mortality. Hemoconcentration among patients with dengue fever is not a frequent presentation though its presence may favor the diagnosis of Dengue. The two infections are clinically indistinguishable and specific diagnostic testing is needed to confirm the diagnosis.

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