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Manifestation and outcome of concurrent malaria and dengue infection

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ABSTRACT

Objective: Studies on concurrent infection of dengue and malaria are uncommon in India. Therefore, in this study, we compared the clinical features and outcome of concurrent infection with mono-infection of dengue and malaria.

Methods: All the patients of fever within 7 days duration were investigated for dengue, malaria and other causes of fever. Patients of concurrent dengue and malaria (Group A) were compared with dengue mono-infection (Group B) and malaria mono-infection (Group C). Biochemical and haematological investigations were done and compared.

Results: During the study period 367 patients of dengue were admitted. Concurrent infection of dengue and malaria was found in 27 (7.4%) patients. There were 27 (5.8), 340 (72.5), and 102 (21.7%) patients in Groups A, B, and C respectively. The clinical features of concurrent infection were more like dengue than malaria. Unlike malaria the outcome of concurrent infection is good.

Conclusion: Concurrent infection of dengue and malaria is not uncommon. For the diagnosis investigations for both the infections should be carried out routinely.

Key words Severe malaria; sub-conjuctival haemorrhage; thrombocytopenia

INTRODUCTION

Malaria and dengue are two common vector-borne diseases in India. The former is a parasitic disease transmitted by *Anopheles* mosquito and the latter is a viral disease transmitted by *Aedes* mosquito. In a geographical area where both the vectors co-exist, simultaneous occurrence of malaria and dengue in an individual cannot be ruled out. But studies on concurrent infections are scarce in India and only limited to few case reports[1, 2]. Therefore, we have undertaken this prospective study to find out the incidence, clinical presentations, and outcome of dengue and malaria co-infection. The differences of co-infection with malaria and dengue mono-infection were also studied.

MATERIAL & METHODS

We have conducted this prospective observational study at V.S.S. Medical College, Burla, Odisha, India during an outbreak of dengue fever from June to September 2011 after taking clearance from the Ethical Committee. During the study period all the patients who attended the outdoor of Department of Medicine and Emergency Department with history of fever for <7 days were included in the study. All the patients were investigated for dengue and dengue positive patients were admitted for observation. Dengue negative patients were investigated for malaria and other causes of fever. Patients of dengue were further investigated for malaria to detect dengue and malaria co-infection. After diagnosis, patients were grouped into dengue and malaria co-infection (Group A), dengue mono-infection (Group B) and malaria mono-infection (Group C). Differences between qualitative values were determined by χ^2-test and quantitative values by unpaired '*t*' test. *P*- value <0.05 is considered as significant.

The diagnosis of dengue was made with detection of IgM antibody and NS-1 antigen by rapid diagnostic test (*Advantage* Dengue NS1 Ag and Ab Combi card of J Mitra & Co. Pvt. Ltd., New Delhi). For diagnosis of malaria peripheral blood smear (thick and thin) was obtained and stained with Giemsa stain for detection of malaria parasites.

The detailed clinical history, examination, and laboratory investigations were done in all the cases. We collected blood at the time of admission for complete blood count (CBC), fasting blood glucose, blood urea, serum creatinine, sodium, potassium, bilirubin, serum glutamate-oxaloacetate transaminase (SGOT), serum glutamate-pyruvate transaminase (SGPT), and alkaline phosphatase (ALP). The parasitic count made from the peripheral blood smear was expressed as number of asexual parasites per micro litre of blood and was calculated from the number of parasitized cells per 200 leukocytes in a thick film, i.e. No. of parasites 'x' total leukocyte count/200. CBC and parasitic count were repeated every 24 h till the normal

isation of the platelet count and to know the parasitic clearance. Temperature was recorded every 12 h to assess fever clearance time. All patients were followed up for 2 wk.

Patients of dengue were treated symptomatically. Patients with thrombocytopenia and bleeding manifestations were treated with platelet concentrate. Patients of dengue and malaria co-infection were considered as severe malaria and treated with inj. Artesunate as per WHO guidelines[3] along with treatment for dengue fever. Supportive fluid therapy was administered as per the requirement. Patients of severe malaria were treated according to the guidelines of the WHO[3].

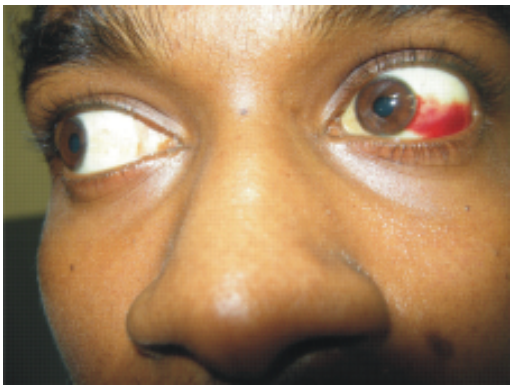

Fig.1: Patient of dengue and falciparum malaria with sub-conjuctival haemorrhage.

RESULTS

During the period of study, 546 patents of acute onset of fever were admitted and 77 patients had fever due to causes other than dengue and malaria, hence, excluded from analysis. Out of 469 patients, dengue and malaria was diagnosed in 367 (78.2%) and 102 (21.7%) patients respectively. Out of 367 patients of dengue, concurrent infection of dengue and malaria was found in 27 (7.4%) patients. Hence, there were 27 (5.8%), 340 (72.5%), and 102 (21.7%) patients in Groups A, B, and C respectively.

The clinical features of Group A were continuous fever, back pain, headache, running nose, and bleeding manifestations which were comparable with the clinical features of Group B (Table 1). Bleeding manifestations like purpuric rashes over skin, melaena with or without haematemesis, epistaxis, and sub-conjuctival haemorrhage was present in 5 (50%), 3 (30%), 1 (10%), and 1 (10%) cases of co-infection and 78 (55.7%), 47 (33.5%), 10 (7.1%), and 5 (3.5%) cases of dengue mono-infection respectively. Sub-conjuctival haemorrhage ($p = 0.001$) was significantly different, whereas other manifestations were not different significantly ($p = 0.8$), hence, comparable with dengue. A patient of co-infection with sub-conjuctival haemorrhage was shown in Fig. 1. Retrobulbar headache was present in 33.3% (5/15) of Group A patients compared to 48.1% (130/270) patients of dengue ($p < 0.01$). Bleeding manifestations were more among patients with Group B (42.1%) which was significantly more than Group A (37.1%, $p = 0.01$).

The clinical features of malaria were fever (100%), headache (34.3%) and associated features of severe malaria that included loss of consciousness (n = 90, 88.2%), jaundice (n = 60, 58.8%), oliguria (n = 54, 52.9%). Intermittent fever with typical paroxysm was present in 65 (63.7%) cases. Multiple complications of coma, jaundice, and oliguria were found in 40 (39.2%) cases. Among the patients of co-infection, intermittent fever with typical paroxysm was absent in all the cases ($p = 0.001$). We did not encounter complications like cerebral malaria, renal failure, and multiple organ failure in any case with concurrent dengue and malaria except one case (3.7%) with jaundice. Bleeding manifestations were absent signifi-

Table 1. Clinical features of co-infection with mono-infection

Features	Co-infection (A)	Dengue (B)	Malaria (C)	*P*-value	
				A 'x' B	A 'x' C
No. of subjects	27	340	102		
Male	18 (66.7)	220 (64.7)	68 (66.6)	0.7	0.7
Female	9 (33.3)	120 (35.2)	34 (33.3)	0.8	0.8
Fever	27 (100)	340 (100)	102 (100)	*	
Running nose	21 (77.8)	268 (78.9)	4 (3.9)	0.8	0.002
Myalgia	16 (59.3)	204 (60)	15 (14.7)	0.7	0.001
Headache	15 (55.6)	270 (79.4)	35 (34.3)	0.1	0.3
Bleeding manifestations	10 (37.1)	140 (41.2)	2 (1.9)	0.01	0.001
Back pain	9 (33.3)	250 (73.5)	8 (7.8)	0.02	0.001
Severe malaria	1 (3.7)	0	90 (88.2)	+	0.001

*Same percentage, no comparison necessary; +Not comparable; Figures in parentheses indicate percentages.

Table 2. Haematological and biochemical parameters

Investigations	Co-infection (A)	Dengue (B)	Malaria (C)	*P*-value	
				A 'x' B	A 'x' C
Parasitic count (No./mm^3)	5098.8 ± 542.6	0	6489.4 ± 432.8	*	0.01
Haemoglobin (g/dl)	10.7 ± 1	10.8 ± 2.9	6.8 ± 1.2	0.7	0.001
Leukocyte count (No./mm^3)	4244.4 ± 728.1	4512.8 ± 920.9	6109.6 ± 765.8	0.8	0.001
Platelet count (No./mm^3)	58230.7 ± 5893.0	48000.6 ± 9235.8	145000.7 ± 908.6	0.8	0.001
FBS (g/dl)	88.7 ± 11.1	80.5 ± 11.7	78.9 ± 9.6	0.8	0.6
B. urea (g/dl)	27.9 ± 2.9	25.8 ± 10.5	41.8 ± 6.9	0.8	0.002
S. creatinine (mg/dl)	0.9 ± 0.2	1.1 ± 0.5	3.9 ± 1.2	0.9	0.001
S. bilirubin (mg/dl)	0.7 ± 0.3	0.8 ± 0.3	4.8 ± 2.1	0.7	0.002
SGOT (IU/l)	34 ± 5.3	32.8 ± 6.8	51.7 ± 11.2	0.5	0.001
SGPT (IU/l)	32.8 ± 6.8	34.8 ± 5.6	45.9 ± 14.6	0.7	0.001
Alkaline phosphatase (IU/l)	78.8 ± 9.9	87.5 ± 8.9	102.6 ± 14.7	0.8	0.001
S. sodium (mEq/l)	138.5 ± 2.9	136.8 ± 3.8	135 ± 2.5	0.8	0.7
S. potassium (mEq/l)	3.7 ± 0.2	3.8 ± 0.7	3.9 ± 1.2	0.7	0.8

*Not comparable.

cantly ($p = 0.001$) among patients with Group C (1.9%) compared to Group A (37.1%). Hepatosplenomegaly was not found in any case of Group A and B whereas it was found in 62 (60.8%) cases of Group C ($p = 0.001$).

Biochemical investigations of Groups A and B were within normal limits (Table 2). But among patients with malaria mono-infection, there was abnormality of liver and renal parameters due to severe malaria (jaundice and renal failure). Among the haematological parameters, platelet count was low in both the Groups A (58230.7 ± 5893/mm^3) and Group B (48000.6 ± 9235.8/mm^3), $p = 0.8$). Leukopenia was also found in both the Groups A and B. But comparison of haematological parameters among Group A and C showed that the former had thrombocytopenia and leukopenia without anaemia, whereas the latter group had anaemia with normal platelet and leukocyte count ($p = 0.001$). The parasitic count of co-infection was 5098.8 ± 542.6/mm^3, which was lower than malaria 6489.4 ± 432.8/mm^3 ($p = 0.01$).

Plasmodium falciprum, *P.vivax*, and mixed species infection (*P. falciprum* + *P. vivax*) was found in 24 (88.8%), 2 (7.4%), and 1 (3.7%) cases respectively among co-infections. Among the patients of malaria mono-infection *P. falciprum* and mixed species infection was found in 98 (96%) and 4 (3.9%) patients.

The mean interval of onset of fever to the hospitalization of Groups A, B, and C patients was 2.2 ± 0.4 days, 2.8 ± 0.6 days (A 'x' B, $p = 0.8$), and 5.5 ± 0.9 days (A 'x' C, $p = 0.001$) respectively. All the patients of co-infection recovered with treatment within 7 days. There was also no death among the patients of concurrent infection and dengue but 11 (10.7%) patients of malaria died.

DISCUSSION

The present study showed three notable findings. First, it showed that malaria and dengue co-infection is not uncommon in a locality where both the vectors co-exist. Second, in concurrent infection, the clinical features of dengue fever are predominant over malaria. Third, severe malaria is uncommon among the patients with co-infection, hence, the outcome is good.

The present study also showed that the incidence of concurrent dengue and malaria among the patients of dengue fever was 7.4%. Out of all the cases with fever, concurrent infection was 5.8%. In French Guiana, the incidence of co-infection among the patients of dengue fever was 7.1% (17 of 238), which is similar to the present study. It was high in Pakistan and was found in 23.2% of cases[4,5]. Hence, the incidence of the co-infection may vary in different geographical areas. As the incidence is of the hospitalized patients, therefore, it is not representative of a community or a local population. Further, vector load estimation of a geographical area would be helpful in determining the concurrent infection in a locality. But we could not determine in this study. Other studies had also this limitation[4, 5].

In the present study, *P. falciparum* was present in majority of the cases (88.8%). However, *P. vivax* and mixed (*P. vivax* and *P. falciparum*) infection was found in 2 and 1 cases respectively. *Plasmodium vivax* was the common species found in both French Guiana and Pakistan. In the former study *P. vivax* was found in 63.9% and *P. falciparum* in 33.8% cases where as in the latter *P. vivax* was found in 96.2% (25 of 26) cases[4, 5]. This is due

to the species prevalence in a particular locality.

The clinical features of concurrent infection were more like dengue mono-infection than malaria mono-infection. Therefore, clinically, it is difficult to diagnose concurrent dengue and malaria. Intermittent fever with typical paroxysm and complications like cerebral malaria, renal failure and multi-organ failure were also absent among the patients with concurrent infection. On the other hand, bleeding manifestations similar to dengue were common among the patients with concurrent dengue and malaria infection. Therefore, screening for malaria in patients with dengue is necessary for diagnosis of such cases.

Absence of severe malaria was also observed in other available studies[4,5]. Thrombocytopenia, leukocytopenia, and anaemia have been reported in 84.6, 34.6, and 34.6% cases respectively from Pakistan[5]. Deranged liver function was also found in that study[5].

It is notable that bleeding manifestations are uncommon in falciparum malaria, whereas in dengue haemorrhagic manifestations are common. However, when both the diseases can induce thrombocytopenia, it is difficult to decide which one is responsible for the causation of bleeding. Therefore, malaria with bleeding manifestations are considered as severe malaria and treated accordingly[8]. Patients without bleeding were also treated as severe malaria because such patients may develop bleeding during the hospital stay. But there is no recommendation for treatment of malaria in such clinical situation.

In the present study, irrespective of the *Plasmodium* species infection, the outcome of concurrent dengue and malaria is good. The benign outcome has also been observed in other two studies[4, 5]. The good outcome and absence of severe malaria may be explained as follows. First, the patients of concurrent dengue and malaria sought medical treatment earlier (2.2 ± 0.4 days) than patients of malaria (5.5 ± 0.9 days)[6, 7]. Therefore, early diagnosis and treatment with antimalarial drugs was possible. Secondly, low parasitic count which has been observed among the patients of concurrent infection may be another contributing factor for good outcome.

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