Original Article

A study of association of platelet count, prothrombin time and partial thromboplastin time with ocular haemorrhage in seropositive dengue fever patients

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Abstract

Introduction: Dengue fever has been known for more than a century in the tropical countries. Dengue fever has emerged as one of the most important arthropod tropical infections in the recent years with an estimated 2.5 billion people at risk all over the world. **Aims and Objectives:** To study association of platelet count, prothrombin time and partial thromboplastin time with ocular haemorrhage in seropositive dengue fever patients. **Methodology:** The present study was conducted in the Department of ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on a patients with dengue fever during the period of October 2011 to September 2012.One year cross-sectional study. Prevalence rate of ocular manifestations of DF as the percentage of the total patients examined having ocular manifestation of DF. P value is calculated to study association of plateletcount with the ocular complication. **Result:** Of all the laboratory parameters evaluated, marked thrombocytopenia (platelet count less than 50,000/µL) was present in 73% of patients.35 out of 73 patients who had thrombocytopenia had ocular haemorrhage, and the association was statistically significant ($p<0.026$). 38 patients out of 73 who had thrombocytopenia did not had ocular findings which was also significant. Prothrombin time (PT) and partial thromboplastin time (PTT) were carried out in 95 patients. Although 89.7% of patients with ocular haemorrhage had prolonged APTT values, the association was not statistically significant ($p>0.463$). PT was prolonged in 61.5% of patients with ocular haemorrhage ($p>0.430$). **Conclusion:** The study concluded that dengue is a significant cause of ocular disease with 40(40%) patients having ocular manifestations it has been found that there is close correlation with ocular manifestations of dengue and thrombocytopenia (platelet count <50,000cells/µl) which was statistically significant**.**

Keywords: Dengue Fever,Laboratory Findings in Dengue Patients. Ocular Manifestations in Dengue Patients.

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INTRODUCTION

Dengue fever has been known for more than a century in the tropical countries. Dengue fever has emerged as one of the most important arthropod tropical infections in the recent years with an estimated 2.5 billion people at risk all over the world.[1] Arboviruses (Arthropod borne viruses) are viruses of vertebrates, biologically transmitted by hematophagous insect vector. They multiply in blood sucking insects and are transmitted by bite to vertebrate hosts. Taxonomically, Arboviruses belong to families as diverse as Togaviridae, Bunyaviridae, Reoviridae, Arenaviridae and Rhabdoviridae. Infection with dengue virus is witnessing a global resurgence over last 15 to 20 years. Of the estimated 50 to 100 million cases occurring annually, about 5,00,000 cases require hospitalization.[2] Among children of South East Asian Region Countries, these infections including dengue fever (DF), dengue haemorrhagic fever are self-limiting. This mosquito born viral diseases caused by the bite of female anopheles

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Aedesaegypti leading to Dengue haemmohragic fever (DHF) and dengue shock syndrome (DSS) are the leading causes of hospitalization and death. A total of 2500 million people worldwide are at risk of dengue virus infection. Dengue affects more than 100 countries in all continents except Europe.[3]

The disease is caused by four serotypes of the dengue virus, any of which may be responsible for an epidemic. The clinical manifestations of dengue infection varies from asymptomatic to severe life threatening illness in the form of DHF/DSS. Dengue hemorrhagic fever or DSS may be fatal in 40% to 50% of untreated patients, however, with appropriate treatment the mortality can be brought down to one to five percent[4]. Epidemic transmission requires a favourable temperature (< 20^0C) and stagnant water for the breeding of Aedesaegypti. Outbreaks in urban areas infected with the Aedes mosquito may be explosive with attack rates reaching up to 70% of the population.[5]A higher temperature within range of mosquito viability leads to more infectious mosquitoes, which bite more frequently. The DHF / DSS remained a disease of children and young adults for two decades after its identification in the 1950s. The epidemics from Malaysia and Delhi, which occurred recently, show more affection of adults than children. The reasons for this change in epidemiology of DHF are not clear.[1] Laboratory diagnosis of dengue virus infection depends upon demonstration of specific antibodies in serum samples by haemagglutination inhibition, complement fixation, neutralization test or ELISA.[5] Dengue fever has been known for more than a century in the tropical countries. Dengue fever has emerged as one of the most important arthropod tropical infections in the recent years with an estimated 2.5 billion people at risk all over the world.[1] Infection with dengue virus is witnessing a global resurgence over last 15 to 20 years. Of the estimated 50 to 100 million cases occurring annually, about 5,00,000 cases require hospitalization.[2]Among children of South East Asian Region Countries, these infections including dengue fever (DF), dengue haemorrhagic feverare self-limiting. This mosquito born viral diseases caused by the bite of female anopheles Aedesaegypti leading to Dengue haemmohragic fever (DHF) and dengue shock syndrome (DSS) are the leading causes of hospitalization and death. It preceded by diarrheal disease and acute respiratory infections only. The resurgence of infections is attributed to decay in public health infrastructure, lack of mosquito control, unplanned urbanization and global population explosion. Increase in air travel and excellent mode of transport of pathogens also contributes spread. A total of 2500 million people worldwide are at risk of dengue virus infection. Dengue affects more than 100 countries in all continents except Europe.[3] Dengue as a disease has been poorly studied and important lacunae remain in the understanding of the presentations, the complications and the treatment of the disease. Outbreaks in urban areas infected with the Aedes mosquito may be explosive with attack rates reaching upto 70% of the population.[5]A higher temperature within range of mosquito viability leads to more infectious mosquitoes, which bite more frequently. Ocular manifestation of DF have received little attention in published literature. There are isolated reports of DF who primarily presented with visual impairment due to posterior segment involvement. Other manifestation are in form of retinal haemorrhages and retinopathy. DF and DHF can cause ophthalmic symptoms that were not previously well-described in the medical literature. Blurring of vision typically coincides with the nadir of thrombocytopenia and occurs ≈1 week after onset of fever.[6] Clinical features include retinal edema, blot haemorrhages, and vasculitis. Less common features include exudative retinal detachment, cotton wool spots, and anterior uveitis. Prognosis is generally good as the disease is often self-limiting, resolving spontaneously even without treatment. However, patients may experience mild relative central scotoma that may persist for months. The use of steroids in treating this inflammatory eye condition is controversial. A randomized controlled trial is under way to evaluate the effect of systemic steroids on dengue retinopathy; results will be reported in due course.[6]Ophthalmologic manifestations [6]. In the published literature significant number of patients presented with subconjunctivalhaemorrhage. The majority of patients had multiple, dot-like petechial haemorrhages. This pattern of subconjunctivalhaemorrhage has been reported to be occasionally associated with systemic conditions like meningococcal septicaemia, subacute bacterial endocarditis, measles, and sandfly fever, but not yet with dengue fever.[6]DF and DHF can cause ophthalmic symptoms that were not previously well-described in the medical literature.[7]The difference in severity and type presentation may be due to variation in virulence and serotype of the infecting virus.

AIMS AND OBJECTIVES

To study Prevalence of Ocular Manifestations in Patients with Dengue Fever

METHODOLOGY

The present study was conducted in the Department of ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on a patients with dengue fever during the period of October 2011 to September 2012.One year cross-sectional study. The

present study was conducted during October 2011 to October 2012.Patients admitted with diagnosis of dengue fever, confirmed by serological tests in inpatient wards at Medical, Pediatric and Ophthalmic departments belonging to age> 6 years and of either gender at KLE'S Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum, were enrolled in this study. All the patients with dengue fever admitted KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum during the study period that is 100 admissions were recorded during the study and same considered as sample size. One hundred consecutive patient admitted in Medical and Paediatric wards with diagnosis of serologically positive dengue fever. Participants not willing to give consent. Participants with history of diabetes mellitus, hypertension, anemia or any other systemic or ophthalmic disorder were excluded from the study. Diagnosis of dengue fever was based on clinical features and laboratory parameters. Serological evaluation was done by using the dengue Ig Mcapture ELISA TEST KIT. The ophthalmic evaluation was done in Ophthalmic OPD in all the patients except for those who were too ill to be moved to the OPD in whom the evaluation was done at bed side. Prevalence rate of ocular manifestations of DF as the percentage of the total patients examined having ocular manifestation of DF. P value is calculated to study association of plateletcount with the ocular complication.

RESULTS

Table 1: Laboratory findings and association with ocular haemorrhage

Laboratory Parameter	No (%) of patients		P - value
	With ocular haemorrhage	Without ocular haemorrhage	
>100 000/µL	1(2.5)	7 (11.7)	0.026
50 – 100 000/µL	4 (10.0)	15 (25.0)	
<50 000/µL	35 (87.5)	38 (63.3)	
Total	40 (100)	60 (100)	
Prothrombin time*			
Normal	15 (38.5)	16 (29.7)	0.430
Prolonged	24 (61.5)	40 (70.3)	
Total	39 (100)	56 (100)	
APTT*			
Normal	4 (10.3)	10 (17.9)	0.463
Prolonged	35 (89.7)	46 (82.1)	
Total	**39 (100)**	**56 (100)**	

* Prothrombin time and APTT were carried out in 95 patients only.

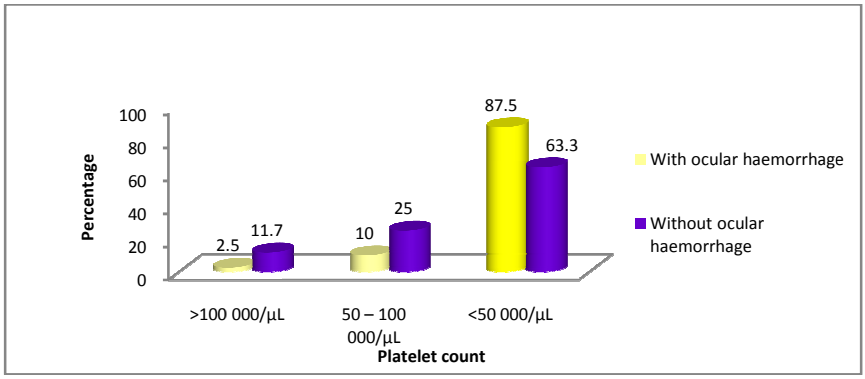

Figure 1: Laboratory findings and association with ocular haemorrhage

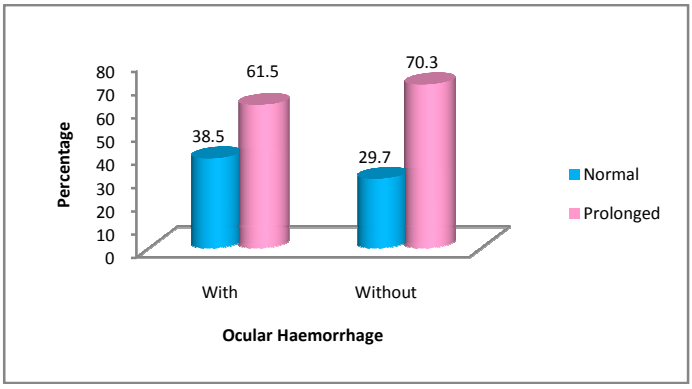

Figure 2: Prothrombin time with Ocular Haemorrhage

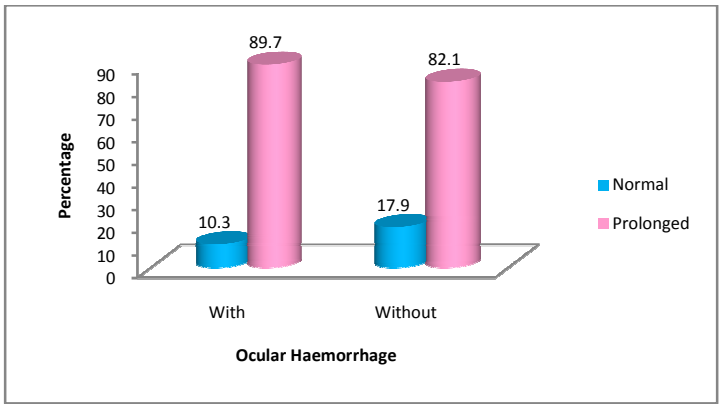

Figure 3: APTT time with Ocular Haemorrhage

Of all the laboratory parameters evaluated, marked thrombocytopenia (platelet count less than 50,000/µL) was present in 73% of patients.35 out of 73 patients who had thrombocytopenia had ocular haemorrhage, and the association was statistically significant (*p<0.026*). 38 patients out of 73 who had thrombocytopenia did not had ocular findings which was also significant. Prothrombin time (PT) and partial thromboplastin time (PTT) were carried out in 95 patients. Although 89.7% of patients with ocular haemorrhage had prolonged APTT values, the association was not statistically significant (*p>0.463*). PT was prolonged in 61.5% of patients with ocular haemorrhage (*p>0.430)(Table 1).*

DISCUSSION

The pathophysiologic mechanisms involved in dengue infection are complex and not completely understood. The various manifestations of the disease are believed to be a result of either direct viral invasion or a complex immune-mediated process. It has been speculated that viral invasion of endothelial cells, dendritic cells, monocytes, and hepatocytes causes apoptosis and cellular dysfunction. This may be followed by the transient aberrant immune response, resulting in CD4/CD8 ratio inversion and cytokine overproduction, that has deleterious effects on these cells. In addition, overproduction of interlukin-6 triggers the formation of autoantibodies against platelets and endothelial cells, and this results in further immune mediated damages. Subconjunctivalhaemorrhages, retinal haemorrhages, and exudates, which could be due to generalized increased capillary permeability, plasma leakage, and haemorrhagic diathesis associated with endothelial dysfunction, platelet destruction, and consumptive coagulopathy.[6] The pathogenesis of cotton wool spots may be related to occlusion of pre-capillary arterioles in the retinal nerve fiber layer by immune complex deposition. Lim *et al* in their study suggested the possibility of specific autoantibodies being produced against retina, retinal pigment epithelium, or choroid, but precise mechanisms responsible for the various ocular alterations in dengue still remain unknown. Haemorhagic manifestations of dengue fever are believed to be multifocal in origin. Gomber *et al*, however, reported that there was no significant association between thrombocytopenia and haemorrhagic manifestations, signifying that there may be other factors like platelet dysfunction and disseminated intravascular coagulopathy, responsible for bleeding. Blurring of vision typically coincides with the nadir of thrombocytopenia and occurs ≈1 week after onset of fever.[5.] Less common features include exudative retinal detachment, cotton wool spots, and anterior uveitis. Prognosis is generally good as the disease is often self-limiting, According to Harutoglou *et al*, most of findings resolve spontaneously even without treatment. However, patients may experience mild relative central scotoma that may persist for months. The use of steroids in treating this inflammatory eye condition is controversial. A randomized controlled trial is under way to evaluate the effect of systemic steroids on dengue retinopathy.[7] There are isolated reports of dengue fever patients who primarily presented with visual impairment due to posterior segment involvement. 8 patients in our series had posterior segment findings, including dilatation and tortuosity of vessels as only finding in 5 (5%) patients, macular haemmohrage in1(1%) patient and, isolated superficial retinal haemorrhages in 2 (2%)patients In our study 40 % patients had ocular manifestations while 60 % were asymptomatic. In our series, 37(37%) patients had classic dengue fever and remaining 63 (63%) patients had dengue haemmorrhagic fever, out of which 44(44%) patients were categorised into DHF grade II and remaining were in other category. Ocular findings were present in 35 patients that means 90 % patient with DHF grade II. As compared to other studies, the difference in the severity and type of presentation in our series may be

attributed to variations in the virulence and serotype of the infecting virus.[8] Our study revealed that 87.5 % of patients with ocular haemorrhage (subconjunctival or retinal) had marked thrombocytopenia (platelet counts less than 50,000/µL) and the association was statistically significant *(p<0.026)*.The correlation with other parameters, like prolonged PT, PTT tests were not significant.(Table 1) which is consistent with other several studies. Ocular alterations in dengue are usually self-limiting. According to Haritoglou *et al*, most of the findings resolve without specific treatment, but occasionally visual recovery may be prolonged or vision may remain permanently impaired in patients with a severe maculopathy. In our study, one patient had visual impairment till the time of discharge. We are not able to comment on the recovery in this case, as we lost follow up of this patient. Lim *et al* in a recent report suggested the use of peri-ocular steroids for treatment of vision threatening maculopathy in dengue patients.[9] Their study, however, included 6 patients only, thus inferences regarding definitive management these findings are in confirmation with Spitznas(in German) 1978[10], Wen *et al*(inchinese) 1989[11], Haritoglou *et al* (in German) 2000[12], Haritoglou *et al* 2002[13,] Cruz Villegas *et al* 2003[14].

REFERENCES

1. Pande JN, Kabra SK. Dengue hemorrhagic fever and shock syndrome. Natl Med J India. 1996; 9(6): 256-8.
2. Singh M. Medical emergencies in children. 4th Ed. New Delhi: Sagar Publications; 2004.
3. Halstead SB. Dengue hemorrhagic fever. A pubic health problem and a field for research. Bull World Health Organ 1980; 58(1):1-21.
4. Cohen SN, Halstead SB. Shock associated with dengue infection. J Paediatr 1966; 68(3): 448-55.
5. Halstead SB. The XXth century dengue pandemic: need for surveillance and res. World Health Stat Q 1992; 45 (2-3): 292-8.
6. Harpreet K Kapoor; SaloniBhai et al. Ocular manifestations of dengue fever in East Indian epidemic.Can J Opthalmol 2006;41:741-6.
7. Stephen C.B. Teoh et al.A re-look at ocular complications in dengue fever and dengue haemorrhagic fever. Dengue Bulletin-volume 30, 2006.
8. Haritoglou C, Scholz F, Bialasiewicz A, Klauss V. [Ocular manifestation in dengue fever]. Ophthalmologe 2000 Jun; 97(6):433-6.
9. Lim WK, Mathur R et al. Ocular manifestation of dengue fever. Opthalmology 2004:111:2057-64.
10. Spitznas M. [Macular haemorrhage in dengue fever (author's transl)]. KlinMonatsblAugenheilkd 1979 Sep; 175(3):429.
11. Wen KH, Sheu MM, Chung CB, Wang HZ, Chen CW. [The ocular fundus findings indengue fever]. Gaoxiong Yi XueKeXueZaZhi 1989 Jan; 5(1):24-30.
12. Haritoglou C, Scholz F, Bialasiewicz A, Klauss V. [Ocular manifestation in dengue fever]. Ophthalmologe 2000 Jun;97(6):433-6.
13. Haritoglou C, Dotse SD, Rudolph G, Stephan CM, Thurau SR, Klauss V. A tourist with dengue fever and visual loss. Lancet. 2002;360:1070
14. Cruz-Villegas V, Berrocal AM, Davis JL. Bilateral choroidal effusionsassociated with dengue fever. Retina. 2003:23:576–8.

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