

## A CLINICAL STUDY OF OCULAR MANIFESTATIONS OF DENGUE FEVER

## Ophthalmology

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## ABSTRACT

**Background:** Dengue is a vector borne disease by four different serotype of dengue virus transmitted by bite of female aedes mosquito. It is an acute febrile illness characterized by myalgia, joint pain, gastrointestinal manifestations. Complications like dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS), Extended dengue syndrome (EDS) may be fatal for patients. Ophthalmic manifestations like conjunctival chemosis and bleeding manifestations like subconjunctival haemorrhage, retinal haemorrhage associated with low platelet count. We determine different clinical spectrum of ophthalmic manifestation and correlation with platelet level.

**Materials And Method:** This study was a prospective, observational study conducted in Department of Ophthalmology comprising of 70 patients suffering from dengue selected from indoor of Department of Medicine of Govt. Medical College, Kota, a tertiary care hospital, during the period from August 2019- October 2019.

**Results:** Out of 70 patients (Age > 18 years) diagnosed as dengue were enrolled in our study out of which 43 patients were males (61.42%) and 27 patients were female (38.57%). Maximum number of cases was found in age group 40-50 years. Ocular findings were present in 29 patients (41.42%). Periorbital lid edema, conjunctival congestion and periorbital ecchymosis are detected in few cases. Subconjunctival haemorrhage (SCH) was most the most commonest ocular finding noted in 9 patients (12.85%).

Thrombocytopenia was noted in 41 patients (58.57%) of which 26 patients (63.41%) had ocular findings. Leucopenia was present in 29 patients (41.42%) of which 21 patients (72.41%) had ocular finding. Raised haematocrit is also associated with ocular manifestations.

**Conclusion:** The incidence of dengue fever is increasing so also ocular complications, hence all patients with dengue should be evaluated to prevent any serious ocular complications.

## KEYWORDS

Haemorrhagic fever, Subconjunctival haemorrhage, Thrombocytopenia

## INTRODUCTION

Dengue is a vector borne disease by four different serotypes of dengue virus transmitted by bite of female Aedes mosquito. It is an acute febrile illness characterized by myalgia, joint pain, gastro intestinal manifestations.<sup>(1)</sup>

Dengue viruses are arbo viruses capable of infecting humans, and causing disease. These infections may be asymptomatic or may lead to (a) classical dengue fever, or (b) dengue haemorrhagic fever without shock, or (c) dengue haemorrhagic fever with shock.

Manifestations of dengue in the eye, though rare in the past, are now more recently noted to be common in some outbreaks<sup>(2)</sup> & dengue is emerging day by day, & few patients come with ocular complain mainly retro orbital pain so it is an issue for ophthalmologist. Ocular involvement of dengue is still confusing but most common finding in anterior segment is subconjunctival hemorrhage<sup>(3)</sup> and posterior segment finding is retinal haemorrhage.<sup>(4)</sup>

Complications like dengue haemorrhagic fever (DHF), dengue shock syndrome (DSS) and Extended dengue syndrome (EDS) may be fatal for patients. Ophthalmic manifestations like conjunctival chemosis and bleeding manifestations like subconjunctival haemorrhage & retinal haemorrhages associated with low platelet count. We had studied different clinical spectrum of ocular manifestations and their correlation to platelet level.<sup>(5)</sup>

## OBJECTIVE:

To study the ocular manifestations associated with dengue fever

## MATERIALS AND METHODS

## Design Of Study:

This study was a prospective, observational study conducted in Department of Ophthalmology comprising of 70 patients suffering from dengue selected from indoor of Department of Medicine of Govt. Medical College, Kota, a tertiary care hospital, during the period from July 2019-January 2020. Patients follow-up varied from weeks to 6 months.

The study plan was approved by the ethical committee of the institute.

## Inclusion Criteria:

- Patients aged 18 years to 70 years, regardless of gender, and able to provide informed consent were selected. These patients were admitted to GMC, Kota & diagnosed with dengue fever according to WHO criteria

## Exclusion Criteria:

- Clinically unstable patients and patients with systemic illness and potentially similar ocular finding in dengue such as diabetes, hypertension and other correlated disease and pre-existing thrombocytopenia.
- History of ocular surgery, past ocular injury causing abnormal ocular morphology.
- Informed consent was taken from all patients during eye examination.

## All Subjects Classified According To WHO Guideline:

Thrombocytopenia was taken as platelet count less than  $1 \text{ lakh/mm}^3$  leucopenia as white blood cells (WBC)  $< 5000 \text{ cells/mm}^3$  & hemoconcentration (haematocrit 20%) above baseline.

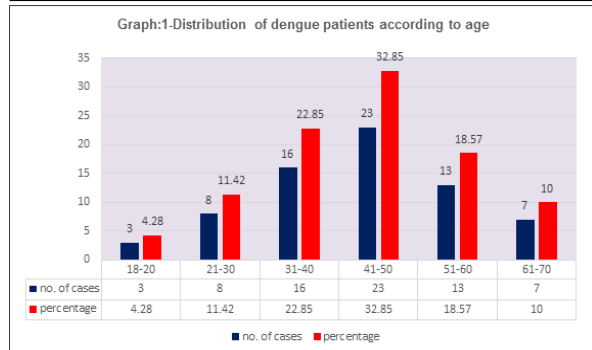
A detailed clinical history, systemic examination routine haematological examination i.e. haemoglobin, total leukocyte count, platelet count, malarial antigen, IgM, IgG antibodies and Widal test for typhoid, peripheral blood smear (PBF) test for malaria parasite was performed.

Complete ocular examination like best corrected visual acuity (BCVA) measured with Snellen acuity for both distance and near, slit lamp examination, intra ocular pressure by Non- contact tonometry, dilated fundus examination with indirect ophthalmoscopy with 20 D, Optical Coherence Tomography (OCT) for posterior segment finding and fundus photos were taken with fundus camera. The patients with positive ophthalmic finding were asked to follow-up.

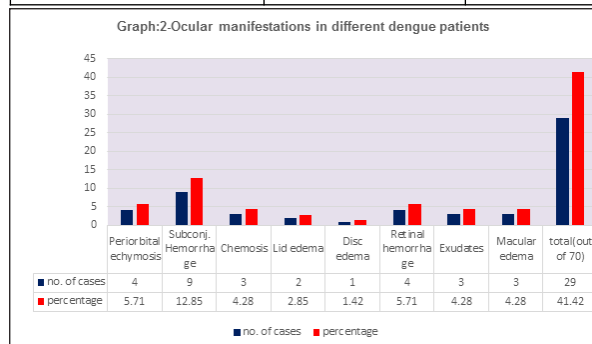
The sample size analysed for validity statistically with software SPSS 20.0.

**OBSERVATIONS & RESULTS:****Table 1: Age Distribution**

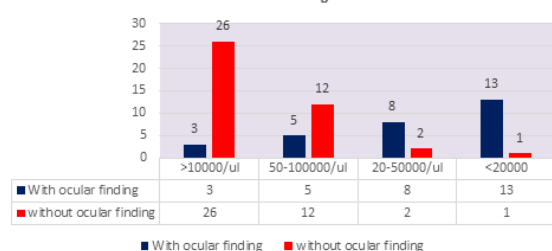
Age at presentation	Number of patients	Percentage
18-20	3	4.28%
21-30	8	11.42%
31-40	16	22.85%
41-50	23	32.85%
51-60	13	18.57%
60-70	7	10.00%
Total	70	

**Table-2: Ophthalmic Manifestations In Different Dengue Patients**

Ocular finding	Number of patients	% of total
Periorbital ecchymosis	4	5.71%
Subconjunctival haemorrhage	9	12.85%
Chemosis	3	4.28%
Lid edema	2	2.85%
disc edema	1	1.42%
Retinal haemorrhage	4	5.71%
Hard exudates	1	1.42%
Soft exudates	2	2.85%
Macular edema	3	4.28%

**Table 3: Laboratory Finding And Association With Ocular Manifestations:**

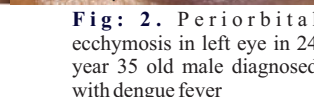
Laboratory parameter	With ocular finding	Without ocular finding
Platelets count		
>100000/ul	3	26
50-100000/ul	5	12
20-50000/ul	8	2
<20000/ul	13	1
Total WBC count		
>5000/ml	9	33
<5000/ml	21	8
PCV		
20-25	3	1
26-30	5	3
31-35	2	7
36-40	4	12
41-45	0	6
46-50	13	9
>50	2	2

**Graph :3-Correlation of platelet count with or without ocular finding****RESULTS:**

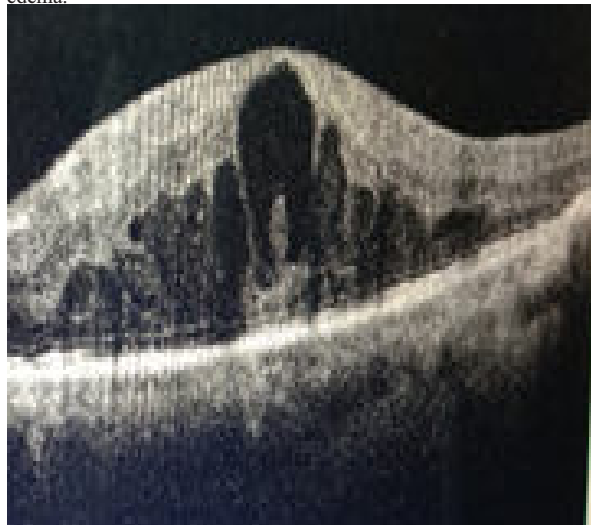
A total of 70 patients (Age 18 -70 years) diagnosed as dengue were enrolled in our study out of which 43 patients were males (61.42%) and 27 patients were female (38.57%). Maximum number of cases was found in age group 40-50 years. Median duration of stay in hospital was 7-10 days. Patient mainly belong to low socioeconomic status with predominant labourers and working class.

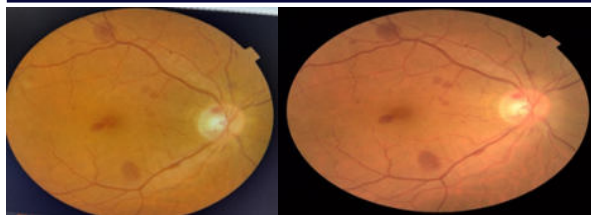
In our study, all cases presented with fever, myalgia, headache others clinical features are nausea, abdominal pain, loose motion, pruritus, joint pain etc. Visual complaints were noted in 18 patients (25.71%), retro-orbital pain in 4 patients (5.71%). Platelet counts was variable in our study. The lowest platelet count noted was 18000/uL. Thrombocytopenia was noted in 41 patients 58.57%). Leucopenia were noted in 29(41.42%). Out of 70,80% patients were NS1 positive, IgM positive in 17.14%, IgM and IgG positive in 2.85%,all patients having IgG and IgM positive have eye manifestations.

Ocular findings were present in 29 patients (41.42%).Anterior segment findings were present in 18 patients.4 Patients (5.71%) had Periorbital ecchymosis, 3 patients (4.28%) had chemosis, 2 patients (2.85%) had lid edema. Subconjunctival haemorrhage (SCH) was most commonest ocular finding noted in 9 patients (12.85%).

**Fig.1:** Subconjunctival haemorrhage in LE of old male diagnosed with dengue fever**Fig. 2.** Periorbital ecchymosis in left eye in 24 year 35 old male diagnosed with dengue fever

Posterior segment findings were present in 11 patients. 4 Patients (5.71%) had superficial retinal haemorrhage, 1 patient (1.42%) had hard exudate, 2 patients (2.85%) had soft exudate and 1 patient (1.42%) had bilateral disc edema and 3 patients (4.28%) had macular edema.

**Fig.3:** OCT shows macular edema in a dengue patient



**Fig.4&5:** Fundus Photograph Showing Retinal Haemorrhage Following Dengue Fever

In laboratory parameters thrombocytopenia was noted in 41 patients (58.57%) of which 26 patients (63.41%) had ocular findings. Leucopenia was present in 29 patients (41.42%) of which 21 patients (72.41%) had ocular finding. Raised haematocrit was also associated with ocular manifestations.

## DISCUSSION

The dengue virus forms a distinct complex within the genus flavivirus based on antigenic and biological characteristics. There are 4 virus serotypes which are designated as DENV-1, DENV-2, DENV-3 and DENV-4. Infection with any one serotype confers lifelong immunity to that virus serotype. Although all 4 serotypes are antigenically similar, they are different enough to elicit cross-protection for only a few months after infection by any one of them.<sup>(6)</sup>

Secondary infection with dengue serotype 2 or multiple infection with different serotypes lead to severe form dengue DHF/DSS.<sup>(7)</sup>

All 4 serotypes have been associated with epidemics of dengue fever (with or without DHF) with varying degree of severity.

The incidence, clinical manifestation and geographical distribution of dengue have increased due to increase in global temperature and population growth rate, unplanned urbanization, inefficient mosquito control, frequent air travel, and lack of health care facilities.<sup>(1,8,9)</sup>

Dengue affects human of all age group with a male preponderance. Our study is similar to that by Kapoor et al<sup>(10)</sup> and Hussain et al<sup>(11)</sup> with regard to male preponderance.

In our study ocular manifestations of dengue has been reported in form of subconjunctival haemorrhage (SCH), lid swelling and ecchymosis<sup>(10,11)</sup> and in posterior segment finding in form of disc edema, retinal haemorrhage, exudates and macular edema.<sup>(11,12)</sup>

In our study 2 patients presented with atypical presentations i.e. Bilateral lid edema with ecchymosis. Similar presentation was reported by Vinod et al<sup>(12)</sup>

Posterior segment finding in form of retinal haemorrhage, soft exudate, hard exudate and disc edema.<sup>(14)</sup> None of patients in our study had anterior uveitis, proptosis, retrobulbar haemorrhage and retinal vasculitis<sup>(10)</sup>.

The most common ocular manifestation in our patients was subconjunctival haemorrhage followed by retinal haemorrhages. It was similar to the studies by Kapoor et al<sup>(10)</sup> and Hussain et al<sup>(11)</sup>

The ocular finding were varied involving both anterior and posterior segments in contrast to study reported by Lim et al.<sup>(13)</sup> wherein the ocular features were limited to the macula.

There are 4 different serotype in dengue, variation in virus strain within and between different serotype disease influence disease severity. In our study we encountered mostly dengue fever patients of which 41.42% have ocular manifestations.<sup>(15)</sup> The pathophysiology of dengue infections is complex and not completely understood. Various manifestations of dengue due to direct virus invasion or complex immune mechanism comprise of complex immune activation and cytokine production are involved in mechanism of plasma leakage. Ocular finding in our patients like SCH, hard exudate and retinal haemorrhage diathesis due to endothelial dysfunction. The pathogenesis of soft exudate in dengue may be due to occlusion of pre capillary arterioles in nerve fibre layer by immune complex deposits. Lim et al<sup>(13)</sup> suspected there is a possibility of production of specific antibody against retina, retinal pigment epithelium or choroid. The

exact mechanism of various ocular manifestations in dengue are still unclear.

Thrombocytopenia is a consistent finding in dengue infection, prolong plasma prothrombin time (PTT) and reduced fibrinogen concentration and other abnormal haemostatic indices evident and these correlates with severity of plasma leakage.<sup>(16)</sup>

According to Wills et al these abnormality correlates with timing and severity of plasma leakage rather than clinical manifestations.<sup>(17)</sup>

Thrombocytopenia and abnormal coagulation profiles have been reported to have predictive value for systemic bleeds.<sup>(11)</sup>

## CONCLUSION

There is increase in epidemicity of dengue infections and thus ophthalmic manifestations are expected to rise. The treating physician should be aware of various ocular manifestations in dengue. They should promptly refer patients who have deteriorated blood parameters, patients complaining of blurring of vision, dengue re-infection cases and patients of DHF, DSS and EDS to ophthalmologist for earlier evaluation. Though most common manifestation is subconjunctival haemorrhage, retinal haemorrhage can also occur. Hence, thrombocytopenia should be corrected at earliest to avoid ocular complications.

Ophthalmologist should also be aware of various ocular manifestations, as early referral for supportive therapy can decrease mortality by appropriate treatment.

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