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Original Research Article

Ocular manifestations of dengue fever: A cross-sectional study in a teaching hospital in Northwestern Karnataka

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Abstract

Background: Dengue is a viral infection transmitted to humans through the bites of infected mosquitoes of aedes family. Dengue fever has appeared as a global public health problem in the recent decades. Though dengue related ocular complications are not uncommon, they are often underreported. Dengue is known to cause wide spectrum of ocular manifestations in the affected patients.
Aim and Objective: The present study aimed to evaluate the prevalence of ophthalmic manifestations among Dengue Sero positive patients.
Materials and Methods: This was a cross-sectional study conducted on 170 dengue Sero positive confirmed patients admitted in medicine wards/ ICU at KLE'S Dr Prabhakar Kore Hospital of either sex of all age groups with no preexisting ocular ailments, willing to take part in the study formed the study sample.
After recording visual acuity using Snellen's visual acuity test, anterior segment examination was done by focused torch light/hand held slit lamp followed by posterior segment examination after pupillary dilation using IDO. Macular testing was done using Amsler's grid. Patients were assessed on the first day of admission, the third day and at the time of discharge. If required, they were asked to visit the Ophthalmology Outpatient Department. Daily Blood sample collection was done for routine investigations, such as liver and renal function tests, random blood sugar, serum electrolytes and also complete blood count. The relevant findings were documented and subjected to statistical analysis.
Results: The mean age of subjects was 43.10 ±16.13 years. The median age was 43 years, ranging from 18 years to 82 years. With respect to gender, 91 (53.52%) subjects were male, while 79 (46.47%) subjects were female. The distribution of subjects based on ocular symptoms reveals that the majority, 134 (78.82%) subjects, did not report any ocular symptoms (NIL). Among those who did, the most common symptom was redness, affecting 19 (11.18%) subjects, followed by blurring of vision (BOV) in 13 (7.65%) subjects. Less frequently reported symptoms included ocular pain in 5 (2.94%) subjects, floaters in 2 (1.18%) subjects, central scotoma in 2 (1.18%) subjects and metamorphopsia in 1 (0.59%) subject. The distribution of subjects based on bilateral ocular involvement shows that 21 (12.35%) subjects had bilateral involvement. Among the 62 eyes with ocular involvement, petechial haemorrhages in the conjunctiva were the most common finding, observed in 15 (24.19%) eyes. Subconjunctival haemorrhage (SCH) was the second most frequent, affecting 9 (14.52%) eyes. Dot blot haemorrhages were noted in 8 (12.90%) eyes, while uveitis was present in 5 (8.06%) eyes. Other findings included Roth's spots, optic disc haemorrhage, and macular edema, each affecting 4 (6.45%) eyes. Optic disc edema and cotton wool spots were found each in 3 (4.84%) eyes. Less common findings included hard exudates, macular haemorrhage and vascular sheathing, each in 2 (3.23%) eyes and vitreous haemorrhage in 1 (1.61%) eye. Presentation of dengue-related ocular signs and symptoms corresponded to the nadir of thrombocytopenia in our study.
Conclusion: Dengue fever can result in various manifestations in human eye. Regardless of age, a multidisciplinary approach to dengue fever management is crucial. Physicians should promptly refer patients to ophthalmologists and also Ophthalmologists must meticulously evaluate patients with dengue-related ophthalmic manifestations because some patients may have reduced visual acuity and show little or no response to treatment.

Keywords: Dengue, Fever, Thrombocytopenia, Haemorrhage, Vision.

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1. Introduction

Dengue fever has appeared as a global public health problem in the recent decades. The clinical spectrum of the disease can vary from dengue fever to dengue haemorrhagic fever and dengue shock syndrome. Dengue is extensively spread mosquito-borne viral disease, transmitted to humans by the bite of infected mosquitoes of Aedes species. Dengue infection in humans is caused by four serotypes of the dengue virus (DEN-1, DEN-2, DEN-3, and DEN-4), all belonging to the Flavivirus genus. According to the WHO 1997 classification, symptomatic cases of dengue virus infection are categorized into dengue fever (DF), dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS). The updated WHO classification from 2009 organizes dengue patients based on varying severity levels: dengue without warning signs, dengue with warning signs—which encompasses persistent vomiting, abdominal pain, fluid accumulation, mucosal bleeding, lethargy, liver enlargement, and rising haematocrit along with falling platelets—and severe dengue.[1-3] Dengue fever is prevalent in over 100 countries, with the highest incidence reported in the Americas, South-East Asia, and Western Pacific regions as recognized by the WHO.[2] In India, dengue is highly prevalent across all states and is one of the common causes for hospital admissions. Previously, a few decades earlier Dengue fever had largely urban distribution but now it's reported from semi-urban as well as rural parts.[4,5]

The magnitude of the disease has raised significantly and has extended geographically to many previously unaffected areas also because of greatly increased human travel which has lead to carry the infectious agents even to the areas in which it was hitherto absent and stands as the most important arthropod-borne viral disease of humans and the fastest spreading mosquito borne viral disease worldwide.[2]

Dengue is a viral infection transmitted to humans through the bites of infected mosquitoes of aedes family namely aedes aegypti, aedes albopictus, aedes scutellaris or aedes polynesiensis.[6,7]

Other modes of dengue transmission include perinatal transmission, breast milk, blood transfusion and organ transplantation.

Dengue is known to cause complications like cardiomyopathy, hepatic injury, pneumonia, orchitis, oophoritis, seizures, neurological issues like myelitis, encephalopathy and encephalitis, ischaemic and haemorrhagic stroke and also ophthalmic complications but many times ophthalmic complications are often overlooked.

Dengue related ocular complications are not uncommon but they are often underreported.

The wide spectrum of ocular complications of dengue fever includes retrobulbar pain, blurring of vision, impaired colour vision, sub conjunctival haemorrhage, anterior uveitis, posterior segment findings include retinal oedema, retinal vascular diseases, cotton wool spots, exudative retinal detachment, optic neuritis, ischaemic optic neuropathy, branch/ central retinal artery occlusion and retinal pigment epithelial disturbance, maculopathy and many more.

In this study the authors aim to estimate the prevalence of ocular manifestations in Dengue Sero positive patients in north-western Karnataka population.

2. Materials and Methods

This was a cross-sectional study done at KLE'S Dr Prabhakar Kore Hospital & MRC on 170 dengue seropositive patients who formed the study sample. The study was done over a period of 8 months from 1/3/2023 to 30/10/2023 after obtaining Ethical committee clearance from the Institutional ethics committee, where the study was carried out.

2.1. Inclusion criteria

Dengue seropositive patients admitted in medicine wards/ ICU at KLE'S Dr Prabhakar Kore Hospital of either sex of all age groups with no pre-existing ocular ailments, willing to be part of the study formed the study sample.

2.2. Exclusion criteria

Patients with diabetes/ hypertension/ haemoglobinopathies/ malignancy/ cardiac disease / renal failure / liver failure/ pre-existing history of uveitis/ glaucoma/ ocular trauma / corneal degenerations/ dystrophies and patients unwilling to take part in the study were kept out from the study.

After recording visual acuity using Snellen's visual acuity test, focused torch light/hand held slit lamp was used for anterior segment examination followed by posterior segment examination after pupillary dilatation using Indirect Ophthalmoscope with 20 D lens. Amsler's grid testing was done to check for visual distortions, conditions affecting macula. Patients were examined on first day of examination followed by 3rd day and at the time of discharge, if it was necessary they were asked to come to Ophthalmology Outpatient Department. Blood sample collection was done every day and subjected to routine investigations like Complete Blood Count, Random Blood Sugar, Liver Function Tests, Renal Function Tests and serum electrolytes test.

2.3. Statistical analysis

The documented data is analysed using statistical software R version 4.4.0 and Microsoft Excel. Categorical variables are mentioned in the form of frequency tables. Continuous variables are mentioned in Mean ± SD / Median (Min, Max) form.

3. Results

Data contains measurement on 170 subjects who formed the study population. The following table shows the demographic details of the study subjects.

Table 1: Demographic details of the subjects

Variables	Sub Category	Number of subjects (%)
Age (years)	Mean ± SD Median (Min, Max)	43.10 ± 16.13 43 (18, 82)
Gender	Male	91 (53.52%)
	Female	79 (46.47%)

The mean age of subjects was 43.10 years ± 16.13 years. The median age was 43 years, which ranged from 18 years to 82 years. In terms of gender, 91 (53.52%) subjects were male, while 79 (46.47%) subjects were female. All subjects were confirmed dengue- Sero- positive cases.

The following **Table 2** gives the distribution of subjects according to ocular symptoms.

Table 2: Distribution of subjects according to ocular symptoms

Ocular symptoms	Number of subjects (%)
BOV	13 (7.65%)
Central scotoma	2 (1.18%)
Redness	19 (11.18%)
Floaters	2 (1.18%)
Metamorphopsia	1 (0.59%)
Ocular pain	5 (2.94%)
No ocular symptoms (NIL)	134 (78.82%)

The distribution of subjects based on ocular symptoms reveals that the majority, 134 (78.82%) subjects, did not report any ocular symptoms (NIL) and were completely normal ophthalmologically. Among those who did, the most common symptom was redness, affecting 19 (11.18%) subjects, followed by blurring of vision (BOV) in 13 (7.65%) subjects. Less frequently reported symptoms included ocular pain in 5 (2.94%) subjects, floaters in 2 (1.18%) subjects, central scotoma in 2 (1.18%) subjects, and metamorphopsia in 1 (0.59%) subject.

The **Table 3** gives the distribution of subjects according to ocular findings.

The distribution of ocular findings shows that most subjects had no abnormalities, with 129 subjects (75.88%) in the right eye (RE) and 149 (87.65%) in the left eye (LE) subjects reporting no findings. The most common abnormality was petechial haemorrhages in the conjunctiva, affecting 10 (5.88%) subjects in the RE and 5 (2.94%) subjects in the LE. Dot blot haemorrhages were seen in 6 (3.53%) subjects in the RE and 2 (1.18%) subjects in the LE. Subconjunctival haemorrhage (SCH) occurred in 6 (3.53%) subjects in the RE and 3 (1.76%) subjects in the LE. Other findings included cotton wool spots, optic disc edema, and optic disc haemorrhages, each affecting 2 subjects (1.18%) or fewer in both eyes. Overall, ocular abnormalities were more frequent in the RE than the LE.

Table 3: Distribution subjects according to ocular findings

Ocular findings	RE	LE
Cotton wool spots	2 (1.18%)	1 (0.59%)
Dot blot haemorrhages	6 (3.53%)	2 (1.18%)
Hard exudates	1 (0.59%)	1 (0.59%)
Macular oedema	3 (1.76%)	1 (0.59%)
Macular haemorrhage	1 (0.59%)	1 (0.59%)
Optic Disc oedema	2 (1.18%)	1 (0.59%)
Optic disc haemorrhage	2 (1.18%)	2 (1.18%)
Petechial haem in conjunctiva	10 (5.88%)	5 (2.94%)
Roths spots	3 (1.76%)	1 (0.59%)
SCH	6 (3.53%)	3 (1.76%)
Uveitis	3 (1.76%)	2 (1.18%)
Vascular sheathing	1 (0.59%)	1 (0.59%)
Vitreous haemorrhage	1 (0.59%)	0
NIL	129 (75.88%)	149 (87.65%)

The following **Table 4** gives the distribution of subjects based on bilateral involvement.

Table 4: Distribution of subjects based bilateral involvement

Bilateral involvement	Number of subjects (%)
No	20 (11.76%)
Yes	21 (12.35%)
NA	129 (75.88%)

The distribution of subjects based on bilateral ocular involvement shows that 21 (12.35%) subjects had bilateral involvement, while 20 (11.76%) subjects had no bilateral involvement. The majority of subjects, 129 (75.88%), were classified as not applicable (NA), indicating no ocular findings for these participants.

Note: A total of 62 eyes from 41 patients (24.12%) had ocular findings, while the majority (129 patients, 75.88%) had no ocular involvement.

The **Table 5** gives the distribution of eyes according to ocular finding.

Table 5: Distribution of eyes according to ocular finding

Parameters	Number of eyes	% among eyes with ocular involvement (n=62)
Cotton wool spots	3	4.84%
Dot blot haemorrhages	8	12.90%
Hard exudates	2	3.23%
Macular oedema	4	6.45%
Macular haemorrhage	2	3.23%
Optic Disc oedema	3	4.84%
Optic disc haemorrhage	4	6.45%
Petechial haem in conjunctiva	15	24.19%
Roths spots	4	6.45%
SCH	9	14.52%
Uveitis	5	8.06%
Vascular sheathing	2	3.23%
Vitreous haemorrhage	1	1.61%

Among the 62 eyes with ocular involvement, petechial haemorrhages in the conjunctiva were the most common finding, observed in 15 (24.19%) eyes. Subconjunctival haemorrhage (SCH) was the second most frequent, affecting 9 (14.52%) eyes. Dot blot haemorrhages were noted in 8 (12.90%) eyes, while uveitis was present in 5 (8.06%) eyes. Other findings included Roth's spots, optic disc haemorrhage, and macular oedema, each affecting 4 (6.45%) eyes. Cotton wool spots and optic disc oedema were found each in 3 (4.84%) eyes. Less common findings included hard exudates, macular haemorrhage, and vascular sheathing, each in 2 (3.23%) eyes, and vitreous haemorrhage in 1 (1.61%) eye.

The following **Table 6** gives the distribution of ocular finding day and Thrombocytopenia Day.

Table 6: Distribution of ocular finding day and thrombocytopenia day (lower limits of platelet count) (<50,000/mm^3)

Variables	Mean ± SD	Median (Min, Max)
Ocular finding day	7.71 ± 1.65	7 (5, 14)
Thrombocytopenia day	7.27 ± 0.78	7 (6, 10)

The average day for the onset of ocular findings was 7.71 ± 1.65 days, with a median of 7 days (spanning from 5 to 14 days). In the case of thrombocytopenia, the average day of occurrence was marginally earlier at 7.27 ± 0.78 days, also with a median of 7 days (spanning from 6 to 10 days). This indicates that both ocular findings and nadir of thrombocytopenia (50,000/ mm^3) typically appeared around the same time with a slight variation in the onset.

4. Discussion

Dengue fever is endemic in many countries across the world including India. It is more common in tropical and subtropical climates. The magnitude of dengue has witnessed upsurge due to population explosion, global warming, unplanned urbanization, improper mosquito control and inefficient health care facilities. Also increased human travel has contributed to the spread of the infectious agent even to the areas in which it was hitherto absent.[8-11]

World Health Organization in its 2012 report, stated dengue ranks as the most important mosquito borne viral disease in the world causing global burden.[12] Globally, dengue is now endemic in more than125 countries. Nearly 75% of the world's population exposed to dengue is from Asia Pacific part of the world.[13,14] The world health organization estimates that 50 to 100 million dengue infections occur annually with over 20,000 dengue related deaths every year.[7,12,15] Dengue is very well known to cause multi organ system damage, though Ocular involvement in dengue is not rare it often remains under emphasized. This study describes the prevalence of ocular manifestations in dengue sero positive cases in north-western Karnataka.

In the current study a total of 170 subjects formed the study sample. Their age ranged from 18 years and 82 years. Mean age was 43.10 ± 16.13 years. Among them 91 (53.52%) subjects were male, while 79 (46.47%) subjects were female. Indicating slight male preponderance. Similar parameters were noticed in a study by Wagle AM et al[15] in Singapore where in 40.8 years (range 18- 87 years) was the average age of the study population and majority were males (74.3%). A study done by Mbu-Nyamsi, D et al[16] during dengue epidemic in Reunion Island showed average age of 41.9 years which is close to our observation.

Where as in a study done by Anjum MAR et al in Dhaka the mean age of the study population was 31.6 years With male and female ratio being 1.42: 1, showing lesser mean age and more male preponderance as compared to ours.[17]

Also, study by Vijita et al showed 37.62±18.68 years (Range 14 to 81 years) as the average age in their study population which is less as compared to ours, with 78% male and 21.7% female population, showing very high male preponderance as compared to our study.[18]

In Punjab, Singh et al had 112 dengue positive patients whose age ranged from 18years and 60 years, average age was 35± 15 years, slightly less than ours, 60 were men and 52 were women.[19] Also, Teoh SCB et al did a study on a relatively small population of 50 dengue sero positive cases.[20] Totally they had 34 men and 16 women with age ranging between 20 and 69 years (average 32±11 years, less than ours). In another study conducted by Kapoor HK et al the

average age was 31.3 years, less than the present study with 63.4% being men.[21]

In the current study the prevalence of ocular manifestations in dengue Sero positive patients was 24.12% that is out of 170 patients a total of 62 eyes from 41 patients had ocular findings. Where as prevalence rates observed in other studies were more compared to ours, in a study done in Dhaka, Bangladesh by Anjum MAR et al 1457 patients out of 4030 (36.12%) had ocular complaints.[17] Also in a study done by Kapoor HK et al in Ludhiana, Punjab stated that 54 patients out of 134 (40.3%) had ocular signs which was more as compared to the current study.[21]

Similarly, A study done by Sujata et al in Bangalore reported ocular findings in 68 patients out of 120 patients (56.7%).[22] Wagle AM et al reported that totally in 109 patients who completed ocular examination in the study, 52 patients (47.7%) had ocular signs which were high as compared to the present study.[15]

Whereas a study done by Singh et al in Punjab noted a prevalence of 9.82% which was low as compared to our study.[19]

In the current study out of 41 patients who had ocular involvement 21 (12.35%) subjects had bilateral involvement, while 20 (11.76%) subjects had only one eye involvement. Vijitha et al conducted a study which showed bilateral ocular involvement in 6 out of 23 patients which was less as compared to ours.[18] A study done by Lim WK, et al stated that most cases are bilateral but asymmetric.[23]

Singh et al from Punjab reported 5 out of 11 ocular findings positive dengue patients (45.45%) had bilateral involvement.[19] Teoh SCB et al reported 15 out of 50 patients (30%) had both eyes affected in their study.[20]

It is well known fact that the pathological process of ophthalmic manifestations in dengue is complex and its clinical manifestations are varied. The various ocular symptoms reported in the present study were blurring of vision, redness, metamorphopsia, central scotoma, floaters and ocular pain. The most common symptom was redness, affecting 19 (11.18%) subjects, followed by blurring of vision (BOV) in 13 (7.65%) subjects. Less frequently reported symptoms included ocular pain in 5 (2.94%) subjects, floaters in 2 (1.18%) subjects, central scotoma in 2 (1.18%) subjects, and metamorphopsia in 1 (0.59%) subject.

Similarly, a study on dengue fever epidemics by Wagle AM et al reported ocular symptoms like blurred vision (3, 2.7%) retro orbital pain (2, 1.8%) impaired colour vision (1, 0.9%) and metamorphopsia (1, 0.9%).[15]

Vijitha et al also stated that presenting ocular symptoms included decreased vision (29, 100%), eye pain (22, 75.9%), redness (21, 72.4%), watering and discharge (13, 44.8%), bleeding from the eye (2, 6.9%).[18] Mbu-Nyamsi, D et al during dengue epidemic in Reunion Island reported scotoma (71.4%), also abrupt reduction in visual acuity (39.2%) as the ocular symptom in their study.[16]

In the current study among the 62 eyes with ocular involvement, petechial haemorrhages in the conjunctiva were the most common finding, observed in 15 (24.19%) eyes. Subconjunctival haemorrhage (SCH) was the second most frequent, affecting 9 (14.52%) eyes. Dot blot haemorrhages were noted in 8 (12.90%) eyes, while uveitis was present in 5 (8.06%) eyes. Other findings included Roth's spots, optic disc haemorrhage, and macular oedema, each affecting 4 (6.45%) eyes. Cotton wool spots and optic disc oedema were found each in 3 (4.84%) eyes. Less common findings included hard exudates, macular haemorrhage and vascular sheathing, each in 2 (3.23%) eyes, and vitreous haemorrhage in 1 (1.61%) eye.

Study done by Singh et al mentioned dot and blot haemorrhages (50%) macular haemorrhages (31.25%), cotton wool spots (31.25%), Roth spots (18.75%), sub conjunctival haemorrhage (12.5%) vascular sheathing (12.5%) hard exudates (6.25%).[19]

AM Wagle et al noticed yellowish white subretinal dots at the level of retinal pigment epithelium in the macula (41, 37.6%) retinal haemorrhages (15, 13.7%) cotton wool spots (13, 11.9%) and sub conjunctival haemorrhage (3, 2.7%) in their study.[15]

A study conducted by Kapoor et al reported majority cases of dengue-related subconjunctival haemorrhages and in 50 patients with subconjunctival haemorrhage, 42 cases (84%, $n = 50$) had petechial haemorrhages in the conjunctiva and eight cases (16%, $n = 50$) showed haemorrhages in one to four quadrants,[21] the spectrum of manifestations in all these studies were less as compared to ours.

In our study, the mean day for the appearance of ocular findings was 7.71 ± 1.65 days, with a median of 7 days (range from 5 to 14 days). The mean day of occurrence of nadir of thrombocytopenia (<50,000) was slightly earlier at 7.27 ± 0.78 days, with a median of 7 days (range 6 to 10 days). This indicates that both ocular findings and the nadir of thrombocytopenia typically appeared around the same time with a slight variation in the onset. Also, it has been reported that ophthalmic complications are usually seen in young adults who often present at the nadir of thrombocytopenia.[24]

The primary causes of the reduction in visual acuity were macular involvement from vascular blockage, disc oedema, hemorrhage, or oedema. The patients came with complaints of symptoms such as diminution of vision, scotomas, red eye, ocular pain and metamorphopsia.

As long as the patient stayed in hospital, monitoring of CBC was done every day. Lowest levels of thrombocytopenia (<50,000) were seen on the 7th day with a range of 6^{th} to 10^{th} day of the onset of symptoms. Presentation of ocular signs

and symptoms due to dengue correlated with the nadir of thrombocytopenia in our study. The ocular findings in the current study population showed a self-resolving pattern with symptomatic medical management.

This study describes the wide variety of ocular complications of dengue infections. With increasing epidemicity and co-circulation of multiple dengue serotypes, the occurrence of dengue fever and even dengue haemorrhagic fever is bound to increase leading to increase in dengue ophthalmic morbidity. So, there is a need for heightened awareness of dengue related ophthalmic manifestations among clinicians as well as general public. Dengue Awareness programs in the form of scientific talks, video enabled lectures should be run in High schools and colleges by NGO'S and government health agencies.

5. Limitations

The sample size was small and it was restricted to a single centre.

6. Conclusion

With the rise in incidence rates of dengue fever, there is a necessity to understand the role of multidisciplinary approach in treating dengue seropositive cases. The ocular complications connected with dengue fever are not uncommon, the diverse array of ocular and adnexal manifestations in dengue/ dengue haemhorrhagic fever ranging from simple subconjunctival haemorrhage to retinal vasculitis which may result in irreversible loss of vision or impairment of vision demanding timely ophthalmic intervention. Hence, physicians should promptly refer dengue seropositive patients for ophthalmic evaluation. The current study illustrates the intricacies of symptomatology, thrombocytopenia relation with ocular symptoms and also complications. The prevalence and salient features of ocular involvement in dengue depicted in this study emphasizes the importance for thorough evaluation, timely intervention and need to generate public awareness.

7. Source of Funding

No any financial support sought or granted for this study.

8. Conflicts of Interest

There are no conflicts of interest pertaining to this study.

9. Ethical Approval

Ethical No.: MDC/DOME/528.

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