Ocular manifestations in patients diagnosed with dengue in a reference hospital in the city of Manaus, Brazil

Alterações oculares em pacientes diagnosticados com dengue em um hospital de referência na cidade de Manaus

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ABSTRACT

Objective: To determine the prevalence of ocular alterations in patients diagnosed with dengue, admitted to a reference center for infectious and parasitic diseases in Manaus (AM), Brazil.

Methods: This was an observational, analytical, and prospective case series study with 33 patients admitted to the hospital with positive clinical pathology tests during a 90-day period of a dengue epidemic in 2011. The investigations included measurement of visual acuity, macular assessment with Amsler grid test, fundus biomicroscopy, retinography and optical coherence tomography.

Results: The average age of the patients was 35.48 years (minimum age 17 years and maximum 69 years). The main symptoms reported were blurred vision, followed by retro-ocular pain, photopsia, halos, foreign bodies, scotoma, double vision, and floaters. Visual acuity ranged from 20/20 to 20/40 (median 20/30). Macular assessment with Amsler Grid Test was unsatisfactory in three patients. The most common retinal findings were perimacular edema, macular edema, retinal hemorrhage, vasculitis, and changes in the retinal pigment epithelium. Optical coherence tomography showed retinal edema in 16 patients (51.51%).

Conclusions: In all cases, the disease was self-limiting and resolved spontaneously without treatment. Therefore, this study confirms that ocular manifestations in dengue fever are varied and frequent.

RESUMO

Objetivo: Determinar a prevalência de alterações oculares em pacientes com diagnóstico de dengue, internados em um centro de referência para doenças infecciosas e parasitárias em Manaus (AM), Brasil.

Métodos: Estudo observacional, analítico e prospectivo de série de casos de 33 pacientes admitidos no hospital com exames de patologia clínica positivos durante um período de 90 dias de uma epidemia de dengue em 2011. As investigações incluíram medida da acuidade visual, avaliação macular com tela de Amsler, biomicroscopia de fundo de olho, retinografia e tomografia de coerência ótica.

Resultados: A idade média dos pacientes foi de 35,48 anos (idade mínima de 17 anos e máxima de 69 anos). Os principais sintomas relatados foram visão turva, seguida de dor retro-ocular, fotopsia, halos, corpos estranhos, escotoma, visão dupla e moscas volantes. A acuidade visual variou entre 20/20 e 20/40 (mediana 20/30). A avaliação macular com a tela de Amsler foi insatisfatória em três doentes. Os achados retinianos mais comuns foram edema perimacular, edema macular, hemorragia retiniana, vasculite e alterações no epitélio pigmentar da retina. A tomografia de coerência óptica mostrou edema da retina em 16 doentes (51,51%).

Conclusões: Em todos os casos, a doença foi autolimitada e resolveu-se espontaneamente sem tratamento. Este estudo confirma, portanto, que as manifestações oculares da dengue são variadas e frequentes.

INTRODUCTION

Dengue is the most common viral disease affecting human health worldwide. It is an acute disease caused by a virus of the genus *Flavivirus* of the family *Flaviviridae* and is transmitted by the bite of an infected female mosquito of the genus *Aedes*, with *Aedes* (Stegomyia) *aegypti* being the main vector.[1]

There are currently four known viral serotypes, DENV-1, DENV-2, DENV-3 and DENV-4, all of which can cause disease ranging from asymptomatic or oligosymptomatic infections to more severe forms such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), which can be fatal.[1,2]

The first reports of this disease occurred in North America, Asia, and Africa in the mid-13th century.[3] During this period, dengue was considered a non-fatal and occasional disease with sparse and intermittent epidemics.[4,5] However, after World War II, outbreaks occurred in Asia and spread to the Pacific and the Americas.[6]

Today, the disease is prevalent in all tropical and subtropical regions, mainly in urban and semi-urban areas. It is considered a re-emerging disease with increasing incidence in Asia, Africa, and Central and South America, and represents a serious public health problem worldwide.[2]

This infection occurs when infected female mosquitoes inoculate human skin with a viral load of DENV, which multiplies in the regional lymph nodes and then spreads into the bloodstream over a period of 4 to 7 days.[7]

The dengue virus can also reach the visual system and cause visual damage. It can reach the eyes, both through the bloodstream and the neurological pathway, and cause changes in the structures of the eye and its attachments.[8] Complications affecting the visual systems are numerous and have been reported especially in the last decades.[9] The main manifestations are retro-orbital pain,[10] retinal hemorrhages, and subconjunctival hemorrhages.[11] Other ocular manifestations such as optic neuritis,[12] exudative maculopathy,[10] choroidal effusion,[13] Roth spots,[14] vasculitis, exudative retinal detachment, and anterior uveitis are rare.[15]

Given the importance of vision (responsible for 80% of human integration with the environment) and the high incidence of dengue fever in the state of Amazonas, Brazil, it is essential to study the ophthalmic manifestations of this disease to promote eye health, prevent blindness, and restore vision. The objective of this study was to determine the prevalence of ocular alterations in patients diagnosed with dengue, admitted to a reference center for infectious and parasitic diseases in Manaus (AM), Brazil.

METHODS

This was an observational, analytical, prospective case series study. The study included 33 patients admitted to Fundação de Medicina Tropical Heitor Vieira Dourado for different clinical forms of dengue fever between March and May 2011.

The study included female and male patients above 14 years of age who signed an Informed Consent Form.

Patients were admitted to the hospital with suspected dengue fever and the presence of one or more of the following symptoms: abdominal pain, persistent vomiting, lipothymia, hemorrhage, dyspnea, jaundice, sudden decrease in platelets or sudden increase in hematocrit, and the presence of fever lasting up to 7 days. They were also accompanied by at least two of the following symptoms: arthralgia, myalgia, headache, retro-ocular pain, rash and asthenia, a negative Plasmodium test and a blood sample for a specific dengue test.

Patients under 14 years of age, those who did not sign the Informed Consent Form, and those with an unconfirmed diagnosis of dengue infection by laboratory test (RT-PCR, NS-1, or MAC-ELISA) were excluded from the study.

The study was approved by the Research Ethics Committee of the Amazonas Tropical Medicine Foundation, no. 2041, on June 4, 2011.

To collect information, a clinical form was used, containing patient details such as name, research code, age, sex, date of ophthalmological examination, ocular symptoms, and diagnostic ophthalmological examination aimed at detecting changes in the visual apparatus in dengue fever.

The ophthalmologic examination was conducted at the Instituto de Oftalmologia de Manaus (IOM) and included visual acuity measurement with Snellen chart macular evaluation with Amsler grid test, biomicroscopy of ocular structures and fundus (Topcon SL-D2 slit lamp and 90D lens), optical coherence tomography (OCT; Zeiss Cirrus HD-OCT), and color retinography of the posterior pole (Topcon TRC 50 retinography), the latter limited to the enrollment of patients with evidence of changes in the retina.

Data were recorded in a database and analyzed using standard quantitative descriptive analysis methods. The Chi-squared test was used for categorical variables, and Fisher's exact test was used when certain necessary assumptions were not met. Quantitative variables were assessed using Student's t-test, and in cases where this was not appropriate, the data were subjected to the non-parametric Mann-Whitney test. The significance level of the test was 5%, with a confidence level of 95%. Analyses

were conducted using the statistical software Minitab 14 (academic version) and R version 2.11.

RESULTS

A total of 33 patients were examined, including 17 males, aged between 17 and 69 years, with a mean of 35.48 years (Table 1).

Table 1. Characteristics of the studied population

	Cases n
Gender	
Male	17
Female	16
Age, years old	
10-19	3
20-29	13
30-39	4
40-49	8
50-59	3
≥60	2

Ocular symptoms were reported by 87.87% of the patients, distributed as follows: blurred vision (60.60%), retro-ocular pain (57.57%), photopsia (51.51%), halos (12.12%), scotoma (9.09%), foreign body sensation (9.09%), double vision (6.06%), and floaters (3.03%), as described in Table 2.

Table 2. Frequency of ocular symptoms

Symptoms	Cases n(%)
Blurred vision	20 (60.60)
Retro ocular pain	19 (57.57)
Photopsia	16 (48.50)
Halos	4 (12.12)
Scotoma	3 (9.09)
Foreign body sensation	3 (9.09)
Double vision	2 (6.06)
Floaters	1 (3.03)

Visual acuity was reduced in seven patients (21.21%), ranging from 20/25 to 20/40 (Table 3).

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Table 3. Visual acuity of patients participating in the study

Corrected visual acuity	Cases n(%)
20/20	26 (78.79)
20/25 to 20/40	7 (21.21)

Macular evaluation by the Amsler grid test was unsatisfactory in three patients (Table 4).

Table 4. Assessment of the Amsler grid of the patients participating in the study

Amsler grid	Cases n(%)
Insatisfactory	3 (9.09)
Satisfactory	30 (90.91)

Fundus biomicroscopy revealed changes in ten patients (30.30%) with one or more abnormalities (Table 5): RPE spots, 9.09%; retinal hemorrhages, 6.06%; hard exudates, 6.06%; perifoveal edema, 6.06%; and vascular sheath, 3.03%.

Table 5. Results of fundus biomicroscopy of the patients participating in the study

Manifestations	Cases n(%)
RPE spots	3 (9.09)
Retinal hemorrhage	2 (6.06)
Hard exudates	2 (6.06)
Perifoveal edema	2 (6.06)
Vascular sheath	1 (3.03)

RPE: retinal pigment epithelium.

Optical coherence tomography showed retinal edema in 16 patients (51.51%), with increased thickness in the perimacular area in 15 cases (45.45%) and in the macular area in 1 case (3.03%), as shown in Table 6.

Table 6. Optical coherence tomography results

	Cases
Central retinal thickness	254.03 micrometers
Retinal edema, n (%)	16 (51.51)

DISCUSSION

This study investigated the presence of ocular changes in patients with a confirmed diagnosis of dengue fever. There was no statistical difference in the incidence of ocular damage between men and women. In a study conducted by Costa et al.[16] in a hospital in Juiz de Fora (MG), Brazil, 92 patients with a confirmed diagnosis of dengue were evaluated, and there was no statistical difference between the sexes. This suggests that the diagnosis of dengue is not related to the sex of the patient.

In this study, ten patients (30.30%) were found to have fundus biomicroscopic changes. The changes found included flecks in the RPE, hard exudates, retinal hemorrhages, perifoveal edema, and vascular sheath.

In this sense, Bacsal et al. [17] evaluated 41 patients diagnosed with dengue maculopathy using retinal angiography and optical coherence tomography (OCT) and found various ocular changes, including retinal hemorrhages, vascular changes, optic disc edema, retinal precipitates, vitreous hemorrhages, among others.

Optical coherence tomography was able to reveal the details of the changes occurring in the retina, thereby contributing to a better understanding and knowledge of the disease. It confirmed retinal edema in most patients.

The exact pathophysiological mechanism of ophthalmic complications caused by dengue is still unclear, but many studies have suggested that an immunological process is a likely mechanism for these manifestations.[15,18]

The occurrence of ophthalmic complications may be related to hyperpermeability mediated by immunologic and inflammatory mechanisms associated with the onset of symptoms in the convalescent phase, approximately one week after the onset of dengue.[19] It is known that interactions between the virus, the immune response, and the vascular endothelium lead to acute plasma leakage, favoring the formation of edema.[15] In the eye, this would lead first to an increase in subretinal fluid and then to inflammatory processes that could result, for example, in a generalized infection in the patient's eye as a result of the breakdown of the blood-retinal barrier.

Most patients recovered vision and had best corrected visual acuity <20/40.[20,21] To date, there is no randomized controlled trial and no known effective treatment for this type of symptom. However, any maculopathy or insult to the macula and RPE may cause the patient to develop choroidal neovascularization. These new abnormal subretinal vessels can bleed and cause scarring of the macula if left untreated, leading to irreversible blindness. Therefore, continuous monitoring is recommended.[22,23]

CONCLUSION

In all cases, the disease was self-limiting and resolved spontaneously without treatment. Therefore, this study confirms that ocular manifestations in dengue fever are varied and frequent.

CONTRIBUTIONS OF AUTHORS

Chaves Filho CC, Ferreira LCL, and Lacerda MVG contributed to the conception and design of the study. Chaves Filho CC and Chaves CMO contributed to the analysis and interpretation of the data, writing, and critically reviewing the content of the manuscript. All authors have approved the final version of the manuscript and are responsible for all aspects of it, including ensuring its accuracy and integrity.

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