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Challenges to Medical Training and Sharing Knowledge During the Pandemic

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"He who studies medicine without books sails an uncharted sea, but he who studies medicine without patients does not go to sea at all". These are the words of Sir William Osler, who crafted the first residency programme for speciality training for physicians. A competent doctor is not born, but made- taught and trained through a structured programme guided by mentors who have mastered their craft. And over the years, this traditional technique of medical training was followed across all specialities. However things took a drastic turn, when the pandemic struck the world in 2019. There was a decision to suspend all clinical rotations indefinitely, and medical trainees were instructed to avoid activities involving direct patient contact. Several weeks into this disruption, focus was shifted towards creating a new normal. The possibilities of online teaching platforms and tools, which were sparingly explored previously, were adopted in a large scale, and this showed that even in a virtual platform, it is possible to achieve a number of teaching objectives. Although the waves of the pandemic seem to have waned off, many changes are here to stay.

Online Teaching Resources

In an effort to continue the educational process, the teaching institutions worldwide resorted to online teaching.These can be generally delivered to students in two main formats: asynchronous, which includes recorded videos and podcasts, and synchronous (live) distance education, such as Webinars and virtual classrooms.[1]

One of the positive aspects of online teaching is the flexibility of time and location and the subsequent increased convenience. Another advantage is that online teaching is more cost-effective than classroom-based learning, as it does not require educators to move, while more individuals across different institutions (or even countries) can attend the programme.[2]

The main drawback of this method is that it hinders the students from developing the necessary communication and empathy skills for interacting with patients and also denies opportunities to learn and practise the art of proper clinical examination.[3]

Without a doubt, one can say that surgical training has been significantly affected by the pandemic.[4] Ideal surgical training model is an apprenticeship model, where a mentor continuously supervises and assesses their mentees, giving increasing responsibilities and level of independence. With the advent of Covid 19, at first, due to the lockdown, elective cases were kept on hold for a long period. Then the massive waves of covid infections devoured all the resources- hospital space, manpower, oxygen, etc. The mentors and mentees were always in the front line providing care to the affected. As a result, neither the units were to perform the requisite number of operations nor the trainees were able to attend enough theater days.

Dissertations and research

Post graduate training programme requires the candidates to conduct research and present it in a dissertation or thesis. The pandemic and its effect took a serious toll on these research activities. Non-follow-up of enrolled patients and difficulty in recruiting new patients for the study were major problems. One would not be wrong in assuming that the post graduates, could not have performed high-quality research due to the scarcity of clinical material, absence of proper supervision, and mental stress.[5]

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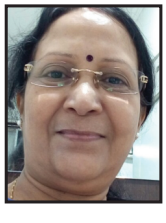

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Examinations

The Pandemic had its effect on examinations too. Firstly, many examinations had to be postponed or cancelled, which resulted in undue extension of a particular course and/ or lack of enough residents in the units. Secondly, the universities had to change the manner in which the examinations were held. The traditional method involving clinical examination of real patients was no longer possible. Students were given case scenarios and had to answer the requested questions6. It is doubtful that, by this method, proper assessment of candidates' clinical skills and conceptual understanding of medicine can be made.

Adverse effect on Health

The pandemic added new stressors while worsening the existing ones. Extra covid duties without proper duty offs took a toll on the mental and physical health.[7] The disrupted traditional learning processes and failure to achieve academic milestones have contributed to the students' anxiety.

Conclusion

The pandemic threw a host of new challenges for medical residents education and training. Online teaching techniques were the most frequently attempted solution to cope with social distancing constraints

Still medical education was highly impacted by the COVID-19 pandemic particularly in surgical specialties. The short-term impact of the pandemic on postgraduate medical education and training is clear as day, however, the long-term effects can only be speculated.

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There are no conflicts of interest.

Review Article

Ophthalmic Manifestations of Covid19 : A Review Study

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Abstract

COVID-19, caused by the Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged as a global pandemic in the year 2020 and is now known to affect almost every organ system of the human body. Various articles regarding the ophthalmic manifestations of the disease, have been published in literature, by many ophthalmologists and physicians. This review aims at summarizing all the possible ocular implications of the virus, thereby helping ophthalmologists in recognizing and treating such ocular pathologies with a high index of clinical suspicion. Google Scholar, Web of Science and PubMed databases were searched from 1st January 2020 to 30th June 2021 and English literature relevant to our search was included in the review. A total of 48 case reports, 15 case series, 20 cross-sectional/case control/cohort observational studies and 2 prospective interventional studies were included. Conjunctivitis was found to be the most common ophthalmic manifestation. Other anterior segment, posterior segment, neuro-ophthalmic and orbital manifestations were also reported. Viral ribonucleic acid has been isolated from conjunctival swabs, though the viral load has been found to be very low as compared to oropharyngeal and nasopharyngeal swabs, hence minimizing the risk of disease transmission via ocular secretions. Ocular toxicities of drugs used in the treatment of COVID-19, have also been reported in literature. Since ocular manifestations can be the presenting symptoms of SARS-CoV-2 infection, ophthalmologists are expected to be prudent in the diagnosis, thereby limiting the spread of the disease as well as avoiding life-threatening and vision-threatening complications.

Keywords : Ophthalmic manifestations; COVID-19; SARS-CoV-2; Pandemic; Conjunctivitis; Review of literature

Introduction

In December 2019, in Wuhan, China, the Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was detected initially and the Coronavirus disease 2019 (COVID-19) spread rapidly across the world and was declared a global pandemic on the 11th of March 2020.[1] As on 1st July 2021, 183,153,754 cases have been reported all over the world, of which, 325,191 people have succumbed to this deadly disease.[2]

There is no particular pathognomonic symptom to detect COVID-19, as a result of which the clinical diagnosis may become challenging. Several symptoms such as fever, cough, sore throat, malaise, nasal obstruction, breathlessness, headache, loss of smell or taste, etc. have been commonly reported among the patients suffering from COVID-19, however these symptoms may not always be present.[3] Some patients may show gastrointestinal symptoms such as abdominal pain, diarrhea, loss of appetite, vomiting, etc. while others may exhibit uncommon symptoms such as skin rash, discoloration of fingers or toes, renal and ocular symptoms.[4]

Most of the clinical research on SARS-CoV-2, reported in literature, is mainly focused on the respiratory manifestations of the disease. However, there have been several cases of extrapulmonary; mainly ocular complications of COVID-19. The ophthalmic manifestations commonly reported are conjunctivitis, chemosis, dry eye, ocular irritation, itching, photophobia and blurring of vision.[5] Conjunctivitis has even been reported as a presenting symptom of COVID-19 in some studies.[6]

This review of literature has been aimed at summarizing the relevant published articles on the ophthalmic manifestations of COVID-19, which indeed can help physicians across the globe in early diagnosis and prompt management of the disease.

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Methods

For this review of literature, Google Scholar, Web of Science and PubMeddatabases were searched from 1st January 2020 to 30th June 2021 and English literature relevant to our search was included in the review. Also, the references of related studies were reviewed for potentially eligible literature.

Inclusion Criteria

Empirical observational studies including case control, cohort, cross-sectional, interventional studies, case reports and case series, which have reported the ophthalmic manifestations seen in COVID-19 patients with active infection, were included in this review.

Exclusion Criteria

Reviews and meta-analysis, commentaries and editorials were excluded from the review.

A total of 48 case reports, 15 case series, 20 cross-sectional/case control/cohort observational studies and 2 prospective interventional studies were reviewed. The ocular manifestations associated with COVID-19, which have been reported in the above-mentioned studies, were tabulated and Microsoft Excel was used to perform the statistical analysis.

Literature Review

1. Eyelid, conjunctiva and anterior segment manifestations of COVID-19:

As per our review, about 46 articles have been published in English literature, pertaining to ocular surface and anterior segment manifestations of COVID-19. The mean age of the study population was found to be 51.75 years and ocular manifestations were seen in 436 patients out of the total 8477 patients studied in these articles. Ocular symptoms/findings were the presenting complaints or concurrent presentation in most of the patients with COVID-19. However, it was seen that some patients developed the ocular symptoms/signs, a few days after being detected positive for SARS-CoV-2. Six studies have reported anterior segment manifestations of COVID-19 among newborns and pediatric patients. Among the neonates, the mean age was 35.2 weeks, whereas it was 6.65 years in the pediatric age group. A total of 65 children were reported to have ocular manifestations.

Conjunctivitis was the most commonly reported ocular surface manifestation. Most of the patients presented with symptoms of unilateral or bilateral conjunctival congestion, foreign body sensation, itching, tearing and discharge. On examination, majority of the COVID-19 patients with respiratory tract symptoms, showed presence of follicular conjunctivitis. A case report published by Navel et al. highlights the case of a 63 year old male from France with severe SARS-CoV-2 infection, manifesting hemorrhagic and pseudo membranous conjunctivitis, 3 weeks after the onset of his respiratory tract symptoms. This is by far the only reported case of pseudo membranous conjunctivitis associated with COVID-19.[7] Case reports published by Cheema et al. and Guo et al., have reported kerato conjunctivitis in patients with mild and moderate COVID-19 infection respectively.[8,9] Studies performed by Abrishami et al. and Tyagi et al., have also reported keratitis as one of the ocular manifestation associated with COVID-19.[10,11] In all these cases, the conjunctival swab was tested positive for SARS-CoV-2, indicating an infective etiology for the ocular surface involvement. Conjunctivitis was treated with topical antibiotics and mild steroids and debridement (for pseudomembranous conjunctivitis) and a course of oral antivirals (for keratoconjunctivitis) and showed resolution.[7,8,9,10,11] In a cross-sectional study conducted by Ceran et al. in Turkey, out of the 93 patients included in the study, only 20 patients were found to have ocular involvement, out of which 2 patients were diagnosed with episcleritis.[12] Episcleritis has also been reported by Mangana et al. and Otaif et al. in a31 year old female in whom it developed a week after being diagnosed with COVID-19 and a 29 year old male, in whom it was the presenting symptom of COVID-19, respectively. In both these cases, however, it was a self limiting condition.[13,14] Cases of subconjunctival and scleral hemorrhage associated with SARS-CoV-2 infection, have also been reported in literature.[11,15,16] The common eyelid manifestations associated with COVID-19 were eyelid edema, erythema, tenderness, lid margin hyperemia, crusted lashes and meibomitis.

We found a total of 4 case series, 1 case report and 1 cross-sectional study, in English literature, which have reported the eyelid, ocular surface and anterior segment manifestations of COVID-19 in the pediatric and neonatal age group. In the cross-sectional study conducted by Maet al., in Wuhan, China, 27 out of 216 COVID-19 positive children showed ocular signs and symptoms suggestive of conjunctivitis.[17] Cases reported by Valenteet al. and Sanaei Dashti et al. also reported acute viral conjunctivitis as the most common manifestation of COVID-19.[18,19] The conjunctivitis was mild and self limiting in these cases. Alcalde et al. reported the case of a 13 year old boy, who presented with unilateral episcleritis associated with COVID-19, for which he was treated with topical corticosteroids and showed good response, but 10 days later was diagnosed with post-infectious unilateral optic neuritis.[20] More severe ocular manifestations such as bilateral non granulomatous acute anterior uveitis and severe corneal punctuate epitheliopathy have been reported by Öztürk et al.,in children.[21] A case series conducted on 15 newborn infants by Pérez-Chimal et al., reported periorbital edema as the most common sign in all babies with ocular manifestations of COVID-19. The other manifestations reported were conjunctival chemosis, hemorrhagic conjunctivitis, corneal edema, rubeosis iridis and posterior synechiae.[22]

Table 1 represents the studies which have reported the ocular surface and anterior segment symptoms and signs in COVID-19 positive patients.

Table 1: Eyelid, Ocular surface and anterior segment manifestations of COVID-19

Sr. No.	Name of Study	Authors	Journal	Year	Type of study	Sample size	Location	Ocular manifestations reported
1.	Ocular manifestations and clinical characteristics of 535 cases of COVID-19 in Wuhan, China: a cross-sectional study	Chen *et al.*[23]	*Acta ophthalmologica*	2020	Cross-sectional study	535	China	Conjunctival congestion, discharge, ocular pain, foreign body sensation, photophobia, dry eye, blurred vision, tearing, itching.
2.	Characteristics of ocular findings of patients with coronavirus disease 2019 (COVID-19) in Hubei Province, China	Wu *et al.*[24]	*JAMA ophthalmology*	2020	Case series	38	China	Conjunctival hyperemia, chemosis, epiphora and increased secretions.
3.	Ocular manifestations and clinical characteristics of children with laboratory-confirmed COVID-19 in Wuhan, China	Ma *et al.*[17]	*JAMA ophthalmology*	2020	Cross-sectional study	216	China	Conjunctival discharge, eye rubbing, conjunctival congestion, ocular pain, tearing, eyelid swelling.
4.	Ocular manifestations of coronavirus disease 2019	Ceran *et al.*[12]	*Graefe's Archive for Clinical and Experimental Ophthalmology*	2020	Cross-sectional study	93	Turkey	Hyperemia, photophobia, itching, epiphora, burning sensation, follicular conjunctivitis, increased secretion, gritty feeling, blurred vision, chemosis, episcleritis.
5.	Ocular manifestation as first sign of coronavirus disease 2019 (COVID-19): interest of telemedicine during the pandemic context	Daruich *et al.*[25]	*Journal francais d'ophtalmologie*	2020	Case Report	1	Argentina	Conjunctival hyperemia with eyelid edema and foreign body sensation.
6.	Ocular manifestations of hospitalized patients with COVID-19 in northeast of Iran	Abrishami *et al.*[10]	*Ocular immunology and inflammation*	2020	Cross-sectional study	142	Iran	Conjunctival hyperemia, tearing, irritation, itching, foreign body sensation, chemosis, periorbital pain, photophobia, blurred vision, keratitis.
7.	Ocular manifestations of a hospitalised patient with confirmed 2019 novel coronavirus disease	Chen *et al.*[26]	*British Journal of Ophthalmology*	2020	Case Report	1	China	Acute follicular conjunctivitis.
8.	SARS-CoV-2 isolation from ocular secretions of a patient with COVID-19 in Italy with prolonged viral RNA detection	Colavita *et al.*[27]	*Annals of Internal Medicine*	2020	Case Report	1	Italy	Acute conjunctivitis.
9.	Ocular manifestations and viral shedding in tears of pediatric patients with coronavirus disease 2019: a preliminary report	Valente *et al.*[18]	*Journal of American Association for Pediatric Ophthalmology and Strabismus*.	2020	Case Series	27	Italy	Acute conjunctivitis with conjunctival hyperemia and increased secretions.
10.	An adult with COVID-19 kawasaki-like syndrome and ocular manifestations	Lidder *et al.*[28]	*American journal of ophthalmology case reports*	2020	Case Report	1	USA	Photophobia and conjunctival hyperemia with lid erythema and swelling.
11.	Clinical profile and prevalence of conjunctivitis in mild COVID-19 patients in a tertiary care COVID-19 hospital: A retrospective cross-sectional study	Sindhuja *et al.*[29]	*Indian Journal of Ophthalmology*	2020	Cross-sectional study	127	India	Conjunctival congestion, burning sensation, watering, painful eyelid swelling.

12.	Corona virus disease-19 (COVID-19) presenting as conjunctivitis: atypically high-risk during a pandemic	Khavandi *et al.*[30]	*Contact Lens & Anterior Eye*	2020	Case Report	1	Iran	Follicular conjunctivitis with mucoid discharge.
13.	Characteristics of ocular manifestations of patients with coronavirus disease 2019 in Daegu Province, Korea	Lee *et al.*[31]	*Journal of Korean Medical Science*	2020	Case Series	103	Korea	Conjunctival congestion, visual disturbances, ocular discomfort, itching sensation, epiphora, ocular pain.
14.	Conjunctivitis can be the only presenting sign and symptom of COVID-19	Scalinci *et al.*[32]	*IDCases*	2020	Case Series	5	Italy	Acute conjunctivitis with chemosis, epiphora, photophobia.
15.	Detection of severe acute respiratory syndrome Coronavirus-2 in the tears of patients with Coronavirus disease 2019	Karimi *et al.*[33]	*Eye*	2020	Case Series	43	Iran	Conjunctivitis with conjunctival erythema and discharge, foreign body sensation.
16.	Conjunctivitis in COVID-19 patients: frequency and clinical presentation	Güemes-Villahoz *et al.*[15]	*Graefe's Archive for Clinical and Experimental Ophthalmology*	2020	Cross-sectional study	301	Spain	Conjunctivitis, conjunctival hyperemia, discharge, tearing, foreign body sensation, subconjunctival hemorrhage.
17.	Ocular surface manifestation of COVID-19 and tear film analysis	Meduri *et al.*[34]	*Scientific Reports*	2020	Case Series	29	Italy	Lid margin hyperemia, meibomitis, conjunctival hyperemia, tearing, foreign body sensation, ocular pain, tearing, dryness.
18.	Ocular Features and Associated Systemic Findings in SARS-CoV-2 Infection	Cavalleri *et al.*[35]	*Ocular Immunology and Inflammation*	2020	Cross-sectional study	172	Italy	Conjunctival hyperemia, epiphora, foreign body sensation, itching, lid swelling, discharge.
19.	More than loss of taste and smell: burning watering eyes in coronavirus disease 2019.	Rokohl *et al.*[36]	*Clinical Microbiology and Infection*	2020	Prospective observational study	108	Germany	Burning sensation, epiphora, redness.
20.	Late manifestation of follicular conjunctivitis in ventilated patient following COVID-19 positive severe pneumonia	Nayak *et al.*[37]	*Indian Journal of Ophthalmology*	2020	Case Report	1	India	Follicular conjunctivitis.
21.	Clinical characteristics of coronavirus disease 2019 in China	Guan *et al.*[38]	*New England journal of medicine*	2020	Retrospective cohort	1099	China	Conjunctivitis.
22.	Unilateral conjunctivitis as first presentation of Coronavirus Disease 2019 (COVID-19): A telemedicine diagnosis	Daruich *et al.*[39]	*Journal francais d'ophtalmologie*	2020	Case report	1	Argentina	Conjunctival hyperemia, eyelid edema.
23.	COVID-19 emergency in the cruise's ship: a case report of conjunctivitis	Salducci *et al.*[40]	*Clinical Therapeutics*	2020	Case report	1	Italy	Conjunctivitis.
24.	Ophthalmologic evidence against the interpersonal transmission of 2019 novel coronavirus through conjunctiva	Zhou *et al.*[41]	*MedRxiv*	2020	Retrospective cohort	67	China	Conjunctivitis.
25.	Evaluation of coronavirus in tears and conjunctival secretions of patients with SARS-**CoV-2** infection.	Xia *et al.*[42]	*Journal of medical virology*	2020	Prospective interventional	30	China	Conjunctivitis.

26.	Evaluation of conjunctival swab PCR results in patients with SARS-CoV-2 infection	Atum *et al*.[43]	*Ocular immunology and inflammation*	2020	Prospective interventional	40	Turkey	Conjunctivitis.
27.	The evidence of SARS-CoV-2 infection on ocular surface	Zhang *et al*.[44]	*The Ocular Surface*	2020	Cross-sectional study	72	China	Conjunctivitis.
28.	Screening for novel coronavirus related conjunctivitis among the patients with corona virus disease-19.	Lan *et al*.[45]	*Chinese journal of ophthalmology*	2020	Cross-sectional study	81	China	Dryness, conjunctival chemosis, swelling, itching.
29.	Evaluation of ocular symptoms and tropism of SARS-**CoV-2 in** patients confirmed with COVID-**19**	Hong *et al*.[46]	*Acta ophthalmologica*	2020	Cross-sectional study	56	China	Redness, dryness, foreign body sensation, pain.
30.	Assessing viral shedding and infectivity of tears in coronavirus disease 2019 (COVID-19) patients.	Seah *et al*.[47]	*Ophthalmology*	2020	Case series	17	Singapore	Conjunctival injection, chemosis.
31.	Ocular findings and proportion with conjunctival SARS-COV-2 in COVID-19 patients	Zhou *et al*.[48]	*Ophthalmology*	2020	Cross-sectional study	121	China	Itching, redness, tearing, foreign body sensation.
32.	Viral shedding in tears of COVID-19 cases presenting as conjunctivitis.	Goel *et al*.[49]	*Indian Journal of Ophthalmology*	2020	Case report	2	India	Conjunctivitis.
33.	Retinal involvement and ocular findings in COVID-19 pneumonia patients	Pirraglia *et al*.[50]	*Scientific Reports*	2020	Cross-sectional study	43	Italy	Bilateral conjunctivitis with conjunctival hyperemia.
34.	Keratoconjunctivitis as the initial medical presentation of the novel coronavirus disease 2019 (COVID-19)	Cheema *et al*.[8]	*Canadian journal of ophthalmology*	2020	Case Report	1	Canada	Keratoconjunctivitis.
35.	Relapsing viral keratoconjunctivitis in COVID-19: a case report.	Guo *et al*.[9]	*Virology Journal*	2020	Case report	1	China	Relapsing viral keratoconjunctivitis.
36.	Haemorrhagic conjunctivitis with pseudomembranous related to SARS-CoV-2.	Navel *et al*.[7]	*American journal of ophthalmology case reports*	2020	Case report	1	France	Hemorrhagic, pseudomembranous conjunctivitis.
37.	Episcleritis as an ocular manifestation in a patient with COVID-**19**	Mangana *et al*.[13]	*Acta ophthalmologica*	2020	Case Report	1	Spain	Nodular episcleritis.
38.	Episcleritis as a possible presenting sign of the novel coronavirus disease: A case report	Otaif *et al*.[14]	*American Journal of Ophthalmology Case Reports*	2020	Case Report	1	Saudi Arabia	Episcleritis.
39.	Ocular involvement in coronavirus disease 2019 (COVID-19): a clinical and molecular analysis	Shemer *et al*.[51]	*International ophthalmology*	2021	Case control study	48	Israel	Conjunctivitis, irritation, foreign body sensation, discharge, eyelid edema.
40.	Ophthalmic manifestations in the COVID-19 clinical spectrum	Kumar *et al*.[52]	*Indian Journal of Ophthalmology*	2021	Prospective observational study	2742	India	Acute conjunctivitis, diffuse conjunctival congestion, hyperlacrimation, follicular conjunctivitis, chemosis, orbital cellulitis.

41.	Ocular Manifestations of Hospitalized COVID-19 Patients in a Tertiary Care Academic Medical Center in the United States: A Cross-Sectional Study	Feng *et al*.[16]	*Clinical Ophthalmology (Auckland, NZ)*	2021	Cross-sectional study	400	USA	Conjunctival injection, visual disturbances, ocular irritation, discharge, itching, scleral hemorrhage.
42.	Ocular Manifestations in Covid-19 Positive Patients Admitted to a Tertiary Care Centre in Uttarakhand, India: A Prospective Study	Tyagi *et al*.[11]	*International Journal of Health and Clinical Research*	2021	Prospective cohort study	1950	India	Conjunctival congestion, conjunctivitis, subconjunctival hemorrhage, superficial punctuate keratitis.
43.	COVID-19 ocular findings in children: a case series	Alcalde *et al*.[20]	*World Journal of Pediatrics*	2021	Case Series	17	Spain	Conjunctivitis, episcleritis, retinal vasculitis, post-infectious retrobulbar optic neuritis.
44.	Ophthalmic manifestations associated with SARS-CoV-2 in newborn infants: a preliminary report.	Pérez-Chimal *et al*.[22]	*Journal of American Association for Pediatric Ophthalmology and Strabismus*	2021	Case series	15	Mexico	Periorbital edema, conjunctival chemosis, hemorrhagic conjunctivitis, corneal edema, rubeosis iridis and posterior synechiae.
45.	Bilateral Acute Anterior Uveitis and Corneal Punctate Epitheliopathy in Children Diagnosed with Multisystem Inflammatory Syndrome Secondary to COVID-**19**	Öztürk *et al*.[21]	*Ocular immunology and inflammation*	2021	Case series	5	Turkey	Bilateral non granulomatous acute anterior uveitis, severe corneal punctuate epitheliopathy.
46.	Ocular Complication of a Child with Confirmed 2019 Novel Coronavirus Disease: A Case Report	Sanaei Dashti *et al*.[19]	*Archives of Pediatric Infectious Diseases* In Press	2021	Case Report	1	Iran	Viral conjunctivitis.

2. **Ocular posterior segment manifestations of COVID-19**

According to our literature review, around 15 studies, reporting posterior segment manifestations of COVID-19, have been published in the English language. The mean age of the study population was found to be 51.25 years. A total of 38 patients were reported to have posterior segment involvement, out of which majority were males.

Retinal vascular occlusions such as unilateral and bilateral central retinal vein occlusion, hemiretinal and branch retinal vein occlusion and central retinal artery occlusion, concurrently or following COVID-19 infection, have been reported by several authors. A case report published by Dumitrascu et al., reports the finding of acute incomplete ophthalmic artery occlusion in a 48 year old COVID-19 positive male patient, who was suffering from deep vein thrombosis and was receiving anticoagulation with apixaban for the same.[53] In most of the case reports published, the retinal vascular event was not accompanied by any other systemic comorbidities in the patients, however, they were seen to be associated with a rise in the serum inflammatory markers such as D-dimer, ferritin, C-reactive protein, fibrinogen, prothrombin time, activated partial thromboplastin time and Interleukin 6. Rarer conditions such as acute macular neuroretinopathy (AMN) and paracentral acute middle maculopathy (PAMM) have been reported by Gascon et al. and Zamani et al. in a 53 year old male and 35 year old female with COVID-19, respectively.[54,55] Zago Filho et al. reported vitritis with outer retinal abnormalities in a 57 year old female, with mild COVID-19 illness.[56] The posterior segment finding of acute retinal necrosis was reported in a 75 year old immunocompromised female, by Gupta et al., which was diagnosed to be secondary to Varicella zoster virus infection and triggered by COVID-19, possibly by the ability of the SARS-CoV-2 to compromise the blood retinal barrier and causing a more severe inflammatory response.[57] Alcalde et al., reported the case of a 11 year old patient, who was diagnosed with unilateral retinal vasculitis with retinal exudates and perivascular infiltrates, 2 weeks after being infected with COVID-19 and the condition was seen to resolve spontaneously without any specific treatment.[20] Studies published by Sanjay et al. and Goyal et al., have reported the finding of Central serous chorioretinopathy (CSCR), roughly 2 weeks after the COVID-19 infection, pointing out the possibility of this being a consequence of long term steroid administration.[58,59] A cross-sectional study published by

Periera et al., has reported retinal findings such as peripheral retinal hemorrhages, cotton wool spots, macular retinal pigment epithelialmottling, macular hemorrhages and hard exudates, peripapillary hemorrhages and retinal sectoral pallor, however these findings cannot be solely correlated to COVID-19, due to presence of other confounding factors in these patients.[60] In a case series published by Lecler et al., 9 patients showed the presence of nodules at the posterior pole of the globe, on magnetic resonance imaging scans. All these nodules were located in the macular region and were mostly bilateral and associated with severe COVID-19 illness. Though the nature of these nodules in not exactly known, authors have postulated a viral, vasculitic or autoimmune etiology.[61]

Table 2 summarizes the studies which have reported the posterior segment manifestations related to COVID-19.

Table 2: Posterior segment manifestations of COVID-19

Sr. No.	Name of Study	Authors	Journal	Year	Type of study	Sample size	Location	Ocular manifestations reported
1.	Retinal vein occlusion in COVID-19: A novel entity.	Sheth *et al.*[62]	*Indian Journal of Ophthalmology*	2020	Case Report	1	India	Vasculitic inferior hemiretinal vein occlusion with superonasal branch retinal vein occlusion and macular edema.
2.	Impending central retinal vein occlusion in a patient with coronavirus disease 2019 (COVID-19).	Invernizzi *et al.*[63]	*Ocular immunology and inflammation*	2020	Case Report	1	Italy	Impending Central retinal vein occlusion.
3.	Central retinal vein occlusion with COVID-19 infection as the presumptive etiology	Walinjkar *et al.*[64]	*Indian Journal of Ophthalmology*	2020	Case Report	1	India	Central retinal vein occlusion.
4.	Bilateral Central Retinal Vein Occlusion in a 40-Year-Old Man with Severe Coronavirus Disease 2019 (COVID-19) Pneumonia.	Gaba *et al.*[65]	*The American Journal of Case Reports*	2020	Case Report	1	UAE	Bilateral Central retinal vein occlusion.
5.	Unique case of central retinal artery occlusion secondary to COVID-19 disease	Acharya *et al.*[66]	*IDCases*	2020	Case Report	1	USA	Central retinal artery occlusion.
6.	Acute ophthalmic artery occlusion in a COVID-19 patient on apixaban	Dumitrascu *et al.*[53]	*Journal of Stroke and Cerebrovascular Diseases*	2020	Case Report	1	USA	Incomplete ophthalmic artery occlusion.
7.	Covid-19-associated retinopathy: a case report.	Gascon *et al.*[54]	*Ocular immunology and inflammation*	2020	Case Report	1	France	Acute macular neuroretinopathy (AMN), Paracentral acute middle maculopathy (PAMM).
8.	Acute macular neuroretinopathy in a patient with acute myeloid leukemia and deceased by COVID-19: a case report	Zamani *et al.*[55]	*Journal of Ophthalmic Inflammation and Infection*	2020	Case Report	1	Iran	Acute macular neuroretinopathy (AMN).
9.	Vitritis and Outer Retinal Abnormalities in a Patient with COVID-19	Zago Filho *et al.*[56]	*Ocular immunology and inflammation*	2020	Case Report	1	Brazil	Vitritis with outer retinal abnormalities.
10.	Atypical bilateral acute retinal necrosis in a coronavirus disease 2019 positive immunosuppressed patient	Gupta *et al.*[57]	*European journal of ophthalmology*	2020	Case Report	1	London	Acute retinal necrosis caused by VZV, triggered by COVID-19.
11.	Retinal findings in hospitalized patients with severe COVID-19	Pereira *et al.*[60]	*British Journal of Ophthalmology*	2020	Cross-sectional study	18	Brazil	Peripheral retinal hemorrhages, macular retinal pigment epithelial hyperplasia, retinal sectoral pallor, macular hemorrhages and hard exudates with peripapillary flame shaped hemorrhages, cotton wool spots.
12.	COVID-19 ocular findings in children: a case series	Alcalde *et al.*[20]	*World Journal of Pediatrics*	2021	Case Series	17	Spain	Conjunctivitis, episcleritis, retinal vasculitis, post-infectious retrobulbar optic neuritis.

13.	"Old wine in a new bottle"-post COVID-19 infection, central serous chorioretinopathy and the steroids.	Sanjay *et al*.[58]	*Journal of Ophthalmic Inflammation and Infection*	2021	Case Report	1	India	Central serous chorioretinopathy.
14.	Retinal manifestations in patients following COVID-19 infection: A consecutive case series.	Goyal *et al*.[59]	*Indian Journal of Ophthalmology*	2021	Case Series	7	India	Central serous chorioretinopathy, retinal hemorrhages.
15.	Ocular MRI findings in patients with severe COVID-19: a retrospective multicenter observational study	Lecler *et al*.[61]	*Radiology*	2021	Case Series	129	France	Nodules at the posterior pole of the globe.

3. Neuro-ophthalmic manifestations of COVID-19:

We found around 16 studies published in English literature, which have reported the neuro-ophthalmic manifestations related to COVID-19. The mean age of the study population was 41.92 years and most of the affected individuals were found to be males. Of these, only few patients were known to be suffering from comorbidities such as diabetes, hypertension and hyperlipidemia.

Cases of unilateral and bilateral optic neuritis have been reported in young to middle aged patients diagnosed with mild to moderate COVID-19 illness, by Sawalha et al., Zhou et al. and Sharma et al.[67,68,69] François et al., reported the case of a 58 year old female, who presented with blurring of vision and ocular redness, 8 days after being tested positive for COVID-19 and was diagnosed to have unilateral panuveitis with severe optic neuropathy.[70] A possible mechanism of neurotropism of the SARS-CoV-2 has been postulated in the neuro-ophthalmic manifestations of COVID-19. Ortiz-Seller et al., reported a rare case of Adie's tonic pupil in a 51 year old woman, who presented with retro-orbital pain and difficulty in reading, 2 days after being diagnosed with COVID-19 and showed complete recovery with oral steroids.[71] Two cases of Miller Fischer syndrome have been reported in middle aged males with mild COVID-19 illness, within a week of the onset of the disease.[72,73] Among the cranial nerve palsies, 6th nerve palsy was seen more commonly and reported in 7 patients in the articles published by Greer et al. and Falconeet al., followed by pupil sparing, incomplete 3rd nerve palsy which was reported in a 24 year old female by Belghmaidi et al.[74,75,76] Most of these patients were seen to be suffering from mild COVID-19 illness. Assini et al. reported 2 cases of bilateral ptosis with Guillain-Barré syndrome, 20 days after severe COVID-19 infection, whereas a case of ocular myasthenia gravis was reported in a 65 year old woman by Sriwastava et al., roughly 2 weeks after the onset of other systemic symptoms of COVID-19 infection.[77,78] A rare case of papillophlebitis was reported in a middle aged male from Spain, 42 days after being tested for positive for COVID-19 and was probably attributable to the coagulopathy or cytokine storm, seen in the later stages of the infection.[79] There have been case reports and case series which have highlighted the neuro-ophthalmic manifestations related to SARS-CoV-2 infection in children. Alcalde et al. reported the case of a 13 year old boy, who presented with unilateral episcleritis associated with COVID-19, for which he was treated with topical corticosteroids and showed good response, but 10 days later was diagnosed with post-infectious unilateral optic neuritis.[20] The case of a 10 year old girl with optic neuritis secondary to COVID-19 was reported by Parvez et al.[80] In both these cases, the optic neuritis was seen to respond well to systemic steroid therapy with good visual outcomes. Theophanous et al. reported a case of right sided facial palsy in a child with hyper IgM syndrome, agammaglobulinaemia, sleep apnea and asthma.[81]

Table 3 highlights the studies which have reported the neuro-ophthalmic manifestations of COVID-19.

Table 3 : Neuro-ophthalmicmanifestations of COVID-19

Sr. No.	Name of Study	Authors	Journal	Year	Type of study	Sample size	Location	Ocular manifestations reported
1.	COVID-19-Induced Acute Bilateral Optic Neuritis.	Sawalha *et al*.[67]	*Journal of Investigative Medicine High Impact Case Reports*	2020	Case Report	1	USA	Bilateral optic neuritis.
2.	Myelin oligodendrocyte glycoprotein antibody–associated optic neuritis and myelitis in COVID-19.	Zhou *et al*.[68]	*Journal of Neuro-Ophthalmology*	2020	Case Report	1	USA	Parainfectious demyelinating optic neuritis.

3.	Ophthalmic and Neuro-ophthalmic Manifestations of Coronavirus Disease 2019 (COVID-19).	Ortiz-Seller *et al*.[71]	*Ocular Immunology and Inflammation*	2020	Case Report	1	Spain	Inflammatory chorioretinal disease with Adie's syndrome.
4.	COVID-19 presenting with ophthalmoparesis from cranial nerve palsy.	Dinkin *et al*.[72]	*Neurology*	2020	Case Report	1	USA	Miller Fischer Syndrome.
5.	Miller Fisher Syndrome and polyneuritis cranialis in COVID-19.	Gutiérrez-Ortiz *et al*.[73]	*Neurology*	2020	Case Report	1	Spain	Miller Fischer Syndrome.
6.	Isolated Cranial Nerve 6 Palsy in 6 Patients With COVID-19 Infection	Greer *et al*.[74]	*Journal of Neuro-Ophthalmology*	2020	Case Series	6	USA	Sixth nerve palsy.
7.	Acute abducens nerve palsy in a patient with the novel coronavirus disease (COVID-19).	Falcone *et al*.[75]	*Journal of American Association for Pediatric Ophthalmology and Strabismus*	2020	Case Report	1	USA	Sixth nerve palsy.
8.	Third Cranial Nerve Palsy Presenting with Unilateral Diplopia and Strabismus in a 24-Year-Old Woman with COVID-19	Belghmaidi *et al*.[76]	*The American Journal of Case Reports*	2020	Case Report	1	Morocco	Pupil sparing, incomplete third nerve palsy.
9.	New clinical manifestation of COVID-19 related Guillain-Barré syndrome highly responsive to intravenous immunoglobulins: two Italian cases	Assini *et al*.[77]	*Neurological Sciences*	2020	Case Report	2	Italy	Bilateral ptosis with Guillain-Barré syndrome.
10.	New onset of ocular myasthenia gravis in a patient with COVID-19: a novel case report and literature review	Sriwastava *et al*.[78]	*Journal of neurology*	2020	Case Report	1	USA	Ocular myasthenia gravis.
11.	Papillophlebitis in a COVID-19 patient: Inflammation and hypercoagulable state.	Insausti-García *et al*.[79]	*European journal of ophthalmology*	2020	Case Report	1	Spain	Papillophlebitis.
12.	Bell's palsy in a pediatric patient with hyper IgM syndrome and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).	Theophanous *et al*.[81]	*Brain and Development*	2021	Case Report	1	USA	Bell's palsy.
13.	Coronavirus disease 2019–Associated ocular neuropathy with panuveitis: a case Report	François *et al*.[70]	*JAMA ophthalmology*	2021	Case Report	1	France	Severe optic neuropathy with panuveitis.
14.	COVID-19 ocular findings in children: a case series	Alcalde *et al*.[20]	*World Journal of Pediatrics*	2021	Case Series	17	Spain	Conjunctivitis, episcleritis, retinal vasculitis, post-infectious retrobulbar optic neuritis.
15.	Unilateral inferior altitudinal visual field defect related to COVID-19.	Sharma *et al*.[69]	*Indian Journal of Ophthalmology*	2021	Case report	1	India	Parainfectious optic neuritis.
16.	Optic Neuritis in a Child With COVID-19: A Rare Association	Parvez *et al*.[80]	*Cureus*	2021	Case Report	1	UAE	Optic neuritis.

4. Orbital manifestations of COVID-19:

Several cases of rhino-orbital-cerebral mucormycosis have been reported in literature owing to the rampant use of corticosteroids in the management of COVID-19 especially in patients with other comorbidities such as diabetes mellitus. A review article published by Singh et al., has reported 101 cases of mucormycosis in patients suffering from COVID-19, out of which 82 cases have been reported in India.[82] Though not exhaustively, we have tried to include the most unique and important articles which have reported cases of rhino-orbital-cerebral mucormycosis occurring concurrently in patients suffering from COVID-19 infection.Other orbital manifestations in the setting of COVID-19 illness, have also been reported by a few authors. The mean age of these study subjects was 48.3 years.Turbin et al., reported the cases of 2 young adolescent boys who were diagnosed with orbital cellulitis, which was in fact the presenting symptom of the moderate to severe COVID-19 illness.[83] Martínez Díaz et al. reported the case of a 22 year old male with COVID-19 associated acute dacryoadenitis.[84] In a prospective observational study conducted by Kumar et al., 1 patient was reported to have features indicative of orbital cellulitis.[52] Shires et al. reported the case of a 76 year old male with hypertension, diabetes and testicular cancer and who developed an orbital abscess with globe perforation, several days after being diagnosed positive for COVID-19.[85]

Table 4 is a representation of the orbital manifestations of COVID-19.

Table 4- Orbitalmanifestations of COVID-19

Sr. No.	Name of Study	Authors	Journal	Year	Type of study	Sample size	Location	Ocular manifestations reported
1.	COVID-19 mimicking dengue fever with the initial manifestation of retro-orbital pain–a rare case	Ruiy *et al.*[86]	*Journal of the Formosan Medical Association*	2020	Case Report	1	Taiwan	Bilateral retro-orbital pain.
2.	Orbital cellulitis, sinusitis and intracranial abnormalities in two adolescents with COVID-19.	Turbin *et al.*[83]	*Orbit*	2020	Case series	2	USA	Orbital cellulitis.
3.	Rhino-orbital mucormycosis associated with COVID-19.	Mehta *et al.*[87]	*Cureus*	2020	Case Report	1	India	Rhino-Orbital-Cerebral mucormycosis.
4.	Acute dacryoadenitis in a patient with SARS-CoV-2 infection	Martínez Díaz *et al.*[84]	*Orbit*	2021	Case Report	1	London	Acute dacryoadenitis.
5.	Ophthalmic manifestations in the COVID-19 clinical spectrum	Kumar *et al.*[52]	*Indian Journal of Ophthalmology*	2021	Prospective observational study	2742	India	Acute conjunctivitis, diffuse conjunctival congestion, hyperlacrimation, follicular conjunctivitis, chemosis, orbital cellulitis.
6.	Unusual cause of acute sinusitis and orbital abscess in COVID-19 positive patient: Case report	Shires *et al.*[85]	*International Journal of Surgery Case Reports*	2021	Case Report	1	USA	Orbital abscess.
7.	Mucormycosis with orbital compartment syndrome in a patient with COVID-19.	Werthman-Ehrenreich *et al.*[88]	*The American journal of emergency medicine*	2021	Case Report	1	USA	Rhino-Orbital-Cerebral mucormycosis.
8.	Acute invasive rhino-orbital mucormycosis in a patient with COVID-19-associated acute respiratory distress syndrome.	Mekonnen *et al.*[89]	*Ophthalmic plastic and reconstructive surgery*	2021	Case Report	1	USA	Rhino-Orbital-Cerebral mucormycosis.
9.	Mucor in a viral land: a tale of two pathogens	Sen *et al.*[90]	*Indian journal of ophthalmology*	2021	Case Series	6	India	Rhino-Orbital-Cerebral mucormycosis.
10.	Rhino-orbital mucormycosis in a COVID-19 patient.	Baskar *et al.*[91]	*BMJ Case Reports*	2021	Case Report	1	India	Rhino-Orbital-Cerebral mucormycosis.
11.	Rhino-orbital mucormycosis during steroid therapy in COVID-19 patients: a case report.	Veisi *et al.*[92]	*European Journal of Ophthalmology*	2021	Case Report	2	Iran	Rhino-Orbital-Cerebral mucormycosis.

Discussion

COVID-19, which was first reported in Wuhan, China in late December 2019, rapidly spread across all parts of the globe and emerged as a global pandemic on March 2020.[4] Thousands of articles have been published in literature on COVID-19, since then. From being asymptomatic to having severe life threatening complications, the patients with COVID-19 show a wide spectrum of multisystemic manifestations. It is now a well known fact that the SARS-CoV-2 can affect almost each and every organ of the body. There are various studies in literature, which have reported the ophthalmic manifestations of COVID-19. The hypothesized pathogenesis for ocular manifestations in patients diagnosed with COVID-19 is related to the presence of human angiotensin-converting enzyme II (ACE2) protein, which is believed to be the cell receptor for SARS-CoV-2, in the epithelial cells of eyes, in addition to lungs, kidneys and intestines. Recent studieshave shown that viral invasion may also be mediated via the novel route of CD147 receptor.[93] In the review of literature which we conducted, we found that ocular manifestations were seen in approximately 10% of the patients suffering from the disease. Majority of the patients showed ocular surface and anterior segment manifestations, most common being conjunctivitis, which presented as unilateral or bilateral conjunctival congestion, foreign body sensation, itching, tearing and discharge. Ribonucleic acid of SARS-CoV-2 has been detected in the conjunctival swabs of patients with ocular surface involvement.[94] The route of transmission of the virus to the eye is believed to be through direct inoculation of the ocular surface by infective droplets, by its migration from the respiratory tract via the nasolacrimal duct or involvement of the lacrimal glands through the hematogenous route.[95] However, there has been no evidence of viral replication in the ocular tissues. Since the viral load in the ocular surface samples has been found to be relatively low as compared to the nasopharyngeal and oropharyngeal collections, the transmission of COVID-19 through ocular surface, carries a very low risk.[95] However, it is advisable to use personal protective equipment such as goggles and slit-lamp breath shields as well as proper sanitization techniques, while conducting patient's ocular examination.

In addition to the eyelid, ocular surface and anterior segment manifestations, several reports of the posterior segment, neuro-ophthalmic and orbital manifestations seen in patients with COVID-19 illness have also been published in literature. Although we have tried to limit our review only to the ocular manifestations noted concurrently or within the infective period of COVID-19, there have been various reports, in which ocular features have been noted long after the subsidence of the COVID-19 illness, owing to the immunological effects of the virus.[4,94]

Ocular toxicities of the drugs commonly used in the treatment of COVID-19 have also been noted. Retinal toxicity is a known complication associated with the long term of chloroquine and hydroxychloroquine, but is not generally seen with short term use in COVID-19. Antivirals drugs used in the management of COVID-19 are also known to cause ocular toxicity, however it is very uncommon. Systemic corticosteroids, which are being used rampantly in the management of COVID-19, are known to cause cataract, glaucoma and central serous chorioretinopathy, in the long run.[96]

As per our review, ocular manifestations were seen as the presenting symptom of COVID-19 in approximately 3% of patients, which necessitates the awareness about these ocular manifestations among ophthalmologists, so that a high index of clinical suspicion about COVID-19 is kept in mind, while treating such patients.

Conclusion

This article provides a broad overview of all the possible ocular manifestations, reported in patients with varying severity of COVID-19 illness, and is expected to help the treating ophthalmologists in identifying these ocular pathologies and treating them with a high index of clinical suspicion, especially when the presentation is unusual. This would further help in early diagnosis of COVID-19 and limiting disease transmission. Physicians and ophthalmologists are encouraged to report more and more unusual presentations of COVID-19, to allow a better understanding of the disease entity, prevalence of ocular manifestations associated with it and the risk of its transmission.

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Water-Associated Eye Diseases (WEDs)

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Abstract

The ocular diseases, caused by exposure to contaminated water produces a wide spectrum of condition that ranges from asymptomatic , slightly discomfort to severe reaction depending on agent and host response. These conditions are directly related to human contact with water and can occur through toxic, allergic, inflammatory or infective mechanisms. The non-infective causes can include chemicals used to clean swimming pools, oil spills and water-sport related injuries. Similarly, a number of infective organisms causing ocular diseases are transmitted through water. This can have a significant impact on the quality of life and socio-economic factors, locally as well as internationally. These are diseases that we know how to treat or prevent, but without adequate attention, they cause severe disfigurement, disabilities, and social stigma. The present article gives a comprehensive review of water-associated eye diseases, its epidemiology, clinical presentation and current management. It also highlights the future challenges and possible solutions to these problems. Awareness of this entity is absolutely essential to arrive at an accurate diagnosis and to prevent its potential reversible and irreversible ocular complications.

The online search was conducted utilizing search engines such as PubMed, Google Scholar, etc for relevant terms.

Keywords : Trachoma; Acanthamoeba keratitis; Atypical Mycobacterium; toxoplasmosis; Pseudomonas; Chloramines

Introduction

Water is an essential component of all organisms. It has multiple roles in human society. Its essential for drinking and is used for many purposes. There are wide varieties of source of water. Each presenting a potential source of illness depending upon factors such as general level of sanitization, cultural and socioeconomic characteristic, sewage disposal practice, development and degree of industrialization, endemic diseases, climate and geological and hydrological conditions.[1,2]

Water-associated diseases are mainly classified into five categories as water-based, water-borne, water-related, water-washed, and water-dispersed.[3] (1) Water-based etiological agents are mainly worms which spend a part of their life cycle in water bodies. (2) Water-borne diseases are contamination of water by pathogens and their transmission can be described as 5F concept which are fluids, finger, food, fields, and flies. (3) Water-related infectious diseases are zoonotic in nature where breeding of vectors may serve as an initial replication of pathogens and eventually results in the disease. (4) Water-washed diseases are associated with poor personal and domestic hygiene. (5) Water-dispersed diseases are infections whose pathogens can proliferate in freshwater and enter the body through the respiratory tract, these can be dispersed as aerosols from air-conditioning systems.[3,4] Water-associated eye diseases (WEDs) are all ocular diseases occurring as a result of water exposure. The contaminants and pollutants in water can be infectious, toxic or allergic in nature. Although the condition is mild and self-limiting in most cases, but with comorbidity or in situations such as immunocompromise or extremes of age, this can prove devastating and blinding.[5]

The Incidence of WEDs in developed countries are low compared with under developed countries. United States Environmental Protection Agency reported that every year 1.8–3.5 million persons are affected by recreational water-borne illnesses (RWI) in the USA alone. RWI being attributed to contamination of water bodies by infectious agents from sewer overflows.[6] WEDs can have a significant impact on the economy, locally as well as internationally. People who are infected by a WEDs are usually confronted with related costs and not seldom with a huge financial burden. This is especially the case in less developed countries. The financial losses are mostly caused by e.g. costs for medical treatment and medication, costs for transport, special food, and by the

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loss of manpower. It is estimated that around 37.7 million Indians are affected by water-borne diseases annually and 73 million working days are lost due to water-borne disease each year. The resulting economic burden is estimated at $600 million a year.[7]

A continuous exposure to infectious agents, mechanical trauma, chemicals and toxins can affect the quality of life. This article is an attempt to serve as a guide and stimulant for documentation, investigation, prevention and reporting of WEDs. WEDs can be divided in two groups, infectious condition and Non-infectious condition.

Infectious conditions

A large variety of pathogens are present in water. Some are as normal inhabitants others as contaminants. We take a concise look at the common infective agents causing WEDs. (**Table-1**)

Trachoma

Trachoma is caused by Chlamydia trachomatis, a Gram-negative obligate intracellular bacteria, serotypes A, B, Ba and C. It is spread by direct contact, contact with fomites, poor personal and family hygiene (towels and/or washcloths). Although trachoma was eliminated from much of the developed world, this disease persists in many parts of the developing world, particularly in communities without adequate access to clean water and sanitation.[8,9]

India is recognized as one of the major endemic zones of chlamydial eye infection. The bacterium has an incubation period of 6 to 12 days, after which the affected individual experiences symptoms of conjunctivitis, or irritation similar to "pink eye". The infection evokes an intense mixed inflammatory response in the conjunctiva initiated by the cytokines and interferon released by the infected cells. Initially, the neutrophils infiltrate the conjunctiva followed by lymphocytes, macrophages, plasma cells, and eosinophils. Trachoma usually affects both the eyes and symptoms include itching, irritation, discharge, swelling of eyelids, photophobia, and pain. Blinding endemic trachoma results from multiple episodes of reinfection that maintains the intense inflammation in the conjunctiva. Scars on the inside of the eyelids contract, disrupting the lid margin and causing the eyelashes to rotate inwards until they rest against the eye. With each excruciating blink, the lashes damage the sensitive cornea leading to corneal opacity and irreversible blindness.[9]

The World Health Organization (WHO) recommends a simplified grading system for trachoma, (1) Trachomatous inflammation, follicular (TF)—Five or more follicles of >0.5 mm on the upper tarsal conjunctiva (2) Trachomatous inflammation, intense (TI)—Papillary hypertrophy and inflammatory thickening of the upper tarsal conjunctiva obscuring more than half the deep tarsal vessels, (3) Trachomatous scarring (TS)—Presence of scarring in tarsal conjunctiva, (4) Trachomatous trichiasis (TT)—At least one ingrown eyelash touching the globe, or evidence of epilation (eyelash removal), (5) Corneal opacity (CO)—Corneal opacity blurring part of the pupil margin.[10]

The earliest and easiest method of laboratory diagnosis is by direct detection of inclusion bodies (Halberstaedter-Prowazek bodies) with Giemsa staining of conjunctival smears. Other methods are enzyme immunoassay (EIA), Tissue culture isolation (gold standard), PCR.[9] In vivo confocal microscopy (IVCM) provides non-invasive procedure that can be used to quantify connective tissue scarring and measure the degree of inflammatory cell infiltrate.[8]

Treatment done by Antibiotic, First choice is Azithromycin (For children single oral dose of 20 mg/kg and for adult single dose of 1 gm) or second choice is topical tetracycline (1% eye ointment twice a day for six weeks). Azithromycin can be used in children from the age of six months and in pregnancy. Antibiotic treatment reduces the risk of active trachoma in individuals infected with chlamydial trachomatis.[11] Surgery needed for individuals with trichiasis, a bilamellar tarsal rotation procedure is warranted to direct the lashes away from the globe. Early intervention is beneficial as the rate of recurrence is higher in more advanced disease.[9]

The WHO-recommended SAFE strategy includes; Surgery to correct advanced stages of the disease, Antibiotics to treat active infection, using azithromycin, Facial cleanliness to reduce disease transmission and Environmental change to increase access to clean water and improved sanitation. Intensive community-based health education programs to promote face-washing can reduce the rates of active trachoma, especially intense trachoma.[12]

Atypical mycobacteria

The Mycobacterium tuberculosis complex (M. tuberculosis, M. bovis, and M. africanum) is composed of species pathogenic for man and animal, and "nontuberculosis mycobacteria" (NTM) or "mycobacteria other than M. tuberculosis", include the formerly called "atypical" mycobacteria. In contrast to tuberculous bacteria that live and grow in human tissue, nontuberculous bacteria are free-living saprophytes that are widely distributed in the environment: water, soil, dust, and aerosols.[13,14] They have been recovered from many piped and treated drinking waters throughout the world. NTM are not contaminants picked up from another source, but residents able to survive and grow in water. The physiological characteristics of NTM have provided an understanding of their ecological distribution and their high resistance to disinfection by chlorine undoubtedly contributes to their persistence in drinking water systems. Several experimental data suggest a role for protozoa present in water environments as host for pathogenic mycobacteria, such as M. avium. These attributes favor their survival and even occasional growth in natural waters such as fresh water, salt water, and estuaries, in piped and treated waters such as drinking and domestic waters, swimming pools and aquaria, public baths, and whirlpools. Increases in the immunodeficient population and the prevalence of NTM in water systems contribute to an emerging problem of waterborne mycobacterial infections. Von Reyn et al. were among the first to document a relationship between infections in AIDS patients, and water as the source of the M. avium

complex and the possibility that potable water is a source of the nosocomial spread of M. avium infections in hospitals. Recirculating hot water systems, used in many institutions such as hospitals, hotels, apartments, and office buildings, may allow thermotrophic and chlorine-resistant mycobacteria to persist and colonize once they have been introduced from municipal systems.[13]

Ocular NTM infections most commonly seen as keratitis following LASIK procedures, corneal surgery, contact lens wear or foreign body injury. Clinical feature include decreased vision, a variable degree of pain and photophobia. Their course is waxing and waning. They have ability to form biofilms under low nutrient conditions and typical crack-windshield appearance on cornea.[14]

Diagnosis is by stain, culture media and PCR. Corneal scraping from the lesions is the gold standard to identify NTM on specific solid agar media such as Lowenstein-Jensen medium, MacConkey agar etc. PCR is relatively faster and more specific.[14]

Treatment needs prolonged therapy. A combined medical and surgical approach is often required with frequent follow up. They are most sensitive to clarithromycin and amikacin followed by linezolid, gatifloxacin, moxifloxacin and ciprofloxacin. Surgical debridement and/or Lasik flap elevation and irrigation required in refractory cases.[14]

Pseudomonas

Among the causative organisms of bacterial keratitis, Pseudomonas aeruginosa is of particular concern for several reasons. P. aeruginosa, which causes a significant proportion of bacterial keratitis, is responsible for 6% to 39% of cases in the United States and 8% to 21% in South India. Pseudomonas aeruginosa, agram-negative bacillus is widely found in the environment. In lake and reservoir waters, the concentration can reach 10/100 ml to >1000/100 ml. Ocular infection can be acquired following exposure to inadequately chlorinated hot tubs, whirlpools or swimming pools. A severe form of infection leading to corneal ulcers is seen in contact lens users who use home-made saline solutions.[15] Pseudomonas aeruginosa is reported to form biofilms.[14] Previous history of refractive surgery, associated trauma, ocular surface disease and immunosuppression are additional risk factors.[15]

Ocular manifestation is redness, pain and decreased vision. On examination, an epithelial defect with infiltrate and often a hypopyon is present. The condition may progress to corneal perforation and eventual endophthalmitis. A characteristic feature of Pseudomonas infection is a diffuse epithelial graying glistening appearance, away from the main lesion.[16]

Diagnosis is made by Gram's stain and culture-sensitivity of scrapings from the corneal infiltrate. Samples from the contact lens solution and lens case should also be taken for microbiologic workup.[15,16]

Treatment of choice is governed by the sensitivity results. However, empirical treatment with a newer Fluroquinolone (e.g. gatifloxacin) or combination therapy with a cephalosporin and an aminoglycoside can be started while waiting for the results. In a study, P. aeruginosa was found to be highly sensitive to ceftazidime, ciprofloxacin, and amikacin.[17] Steroids for Corneal Ulcers Trial (SCUT) did not find a significant benefit with corticosteroid treatment, but they also did not find any increase in adverse events.[18]

Acanthamoeba

Acanthamoeba species are the causative agents of a sight-threatening infection of the cornea known as Acanthamoeba keratitis (AK).Five species have been reported. Acanthamoeba, are generally free-living protozoa in trophozoite and cyst form. Acanthamoebae are present in fresh water, brackish water and sea water bodies. They are also found in swimming pools, hot tubs, drinking water systems, heating-ventilating-air-conditioning (HVAC) systems and humidifiers.[19] The occurrence of Acanthamoeba in water resources has an added danger since these amoebae can harbor pathogenic micro-organisms such as Legionella, Pseudomonas and Helicobacte.[19,20]

Although contact lens (CL) wear is the leading risk factor for AK, Acanthamoeba spp. can cause infection in non-contact lens wearers also. Poor contact-lens hygiene is a significant risk factor for developing Acanthamoeba keratitis. Wearing of contact-lenses during swimming or showering can significantly increase the risk of infection from Acanthamoebae.[20]

Common symptoms are massive pain, photophobia and tearing. Acanthamoeba keratitis is characterized by an initial limbitis with anterior stromal and perineural infiltrates (radial keratoneuritis). There can be overlying punctate or pseudo-dendritic keratitis. The infiltrates enlarge and join to form a central or paracentral ring abscess. Subsequently, satellite lesions, stromal opacification, scleritis and corneal thinning with descematocele formation may occur. Occasionally, corneal perforation may lead to endophthalmitis.[5]

Diagnosis made by two methods. First non-invasive confocal microscopy, Acanthamoeba being seen as double wall cyst. Other methods being invasive, include staining, culture media and PCR.

Polyhexamethylene biguanide (PHMB) and chlorhexidine have been reported to be the most effective drugs for treatment of infection and in combination they have been reported to be effective against both cysts and trophozoites. Propamidine isethionate (Brolene) may be accompanied by drug toxicity and resistance. Neomycin and Imadazoles also effective in controlling disease. Unresponsive cases may need PK, DALK, laser photo therapeutic keratectomy (PTK), AMG etc.[5,20]

Public health awareness, e.g. warning signs in the area, to educate the public against water-related activities while using contact lenses is necessary to prevent Acanthamoeba infections.[20] Chlorine conventionally used for water treatment does not eliminate Acanthamoebae.[5] Thus, improved purification processes such as correct filter pore sizes are crucial factors in eliminating Acanthamoebae from water sources.

Giardiasis

This is an infection caused by the protozoa Giardia lamblia. Giardiae occur in 2 stages: cysts and trophozoits. Cysts are excreted in feces and can survive for 2–3 months under ideal conditions. Transmission is by ingestion of cysts in contaminated water or directly through the fecal/oral route. A few outbreaks of Giardiasis have been reported due to mass exposure to contaminated water or direct contact with the infected patients (e.g. in child care centers).[21]

The ocular manifestation include: iridocyclitis, choroiditis, retinal hemorrhages, retinal vasculitis and a peculiar "salt and pepper" retinal degeneration.[22]

Diagnosis is made bydirect observation of the cysts or trophozoites in fecal samples. Other tests include ELISA, immunochromatogenic tests, direct immunofluorescence and PCR assays.[21,22]

Treatment of Giardiasis is with metronidazole, tinidazole, albendazole, furazolidine or paromomycin.[21,22]

Toxoplasmosis

Taxoplasmosis is caused by Toxoplasma gondii , an obligate intracellular protozoan parasite.[22] Ingestion of water contaminated with oocytes from the feces of infected cats can cause infection in humans.The definitive hosts for T. gondii are cats. Warm blooded animals like mice, livestock and humans act as intermediate hosts. There are 3 infective stages of T. gondii: (i) Sporocysts (Oocysts), which get excreted in cat feces. (ii) Bradyzoites, which remain encysted in tissue. (iii) Tachyzoites, the proliferative phase responsible for tissue destruction and inflammation. The oocysts can wash into water bodies from soil and hosts acquire infection by exposure to water contaminated by them.[5,23]

The disease present as Focal retinitis, a solitary inflammatory focus, often near a healed chorioretinal scar. There is dense vitritis, making visualization of the lesion difficult, giving a headlight in the fog appearance. In some cases, inflammation surrounding the optic nerve head may lead to optic disc inflammation itself (Jensen choroiditis).[5]

Diagnosis is made by Laboratory investigations, Sabine Feldman Dye test; Indirect Fluorescent antibody Assay (IFA); direct agglutination test; Latex Agglutination Test (LAT); Microparticle Enzyme Immuno Assay (MEIA); Enzyme-linked Fluorescent Assay (ELFA) and ELISA.[23] Classically, Ocular toxoplasmosis has been treated with "Triple Therapy" consisting of Pyrimethamine (loading dose of 50–100 mg, then, 25–50 mg once daily), Sulfadiazine (2–4 g loading dose, then 1 g 4 times daily) and oral corticosteroids (0.5–1.0 mg/kg body weight daily). In "Quadruple Therapy" Clindamycin (300 mg four times daily for 3 weeks) is added to the above. (This medication is combined with Sulfadiazine to prevent pseudomembranous colitis). Other alternatives are: Cotrimoxazole twice daily for 4–6 weeks; Atovaquone 750 mg three times per day; or Azithromycin 500 mg per day for 3 days. In pregnant patients Spiramycin 3 g per day can be used in the first trimester and triple therapy thereafter. Intravitreal Clindamycin (1.0/0.1 ml–1.5 mg/0.1 ml) is also favored currently.[24,25]

Leptospirosis

Humans become infected with the pathogenic organism, Leptospira interrogans, through water or soil contaminated by urine of infected animals.[18] Its spirochaetes. Its the most widespread zoonosis in the world. The prevalence ranges from 0.1 to 1/100,000 per year in temperate areas to 10 or more/100,000 per year in the humid tropical areas. During outbreaks, e.g. after floods and in high-risk groups, 100 or more/100,000 persons may be infected.[5] Leptospirosis occurs as a zoonosis in rodents, dogs, cattle, pigs and wild animals. The leptospires are excreted from the reservoirs in kidneys, leading to contamination of water bodies. The organism can survive in water for several months. Humans are infected by drinking or bathing in contaminated water. In humans the organisms usually gain entry through abraded skin or intact mucosa. This may lead to either a self-limiting anicteric syndrome or icteric leptospirosis (Weil's disease).[26]

Ocular manifestations is by bilateral conjunctival suffusion, non granulomatous anterior uveitis, hypopyon, cataract, interstitial keratitis, vitreous inflammatory reaction and membranes, retinal vasculitis, papillitis and often, panuveitis. In severe systemic infection, the eyes characteristically show circumciliary congestion and yellowish sclera.[18]

Diagnosis is made by Microscopic Agglutination Test (MAT), ELISA, macroscopic agglutination, indirect haemagglutination, lepto dipstick, microcapsule agglutination tests and lateral flow assay. PCR tests are also being available recently.[27]

Treatment is with oral doxycycline, amoxicillin or ampicillin in mild to moderate illness. In cases with severe infection, the drugs of choice are intravenous Penicillin G, Cefotaxime or Ceftriaxone.[27]

Toxocariasis

Toxocariasis caused by human infection with the larvae of Toxocara canis, Toxocara cati, Ascaris suum or some new species being reported recently. Human is merely an accidental but more or less normal intermediate or paratenic host, who are infected accidentally by ingestion of invasive eggs through contaminated water.[22]

Ocular larva migrans syndrome (OLM) is a localized manifestation of Toxocara infection, usually caused by a single second-stage larva. OLM is unilateral in 90% of the cases. It can present as Chronic endophthalmitis (CE), posterior pole granuloma (PPG) or a peripheral granuloma (PG). CE is usually seen in children 2–9 years of age. There is a pan-uveitis, with the peripheral retina covered with dense greyish-white exudates. PPG occurs in older children (6–14 years). It presents as a round, yellowish-white, solid granuloma on the posterior pole. A PG appears as a white, hemispherical granuloma in any quadrant of the fundus. There can be vitreous bands seen, causing dragging of the disc and macula and tractional retinal detachments.[22,28]

Other complications of OLM include: fulminant

endophthalmitis, papillitis, secondary glaucoma and choroidal neovascular membranes.[28]

Laboratory diagnosis is done by an ELISA test. It is non-specific and any positive titre can be considered as significant in association with clinical findings. Other tests include: an ELISA test for toxocara excretory-secretory antigen (TES-Ag) and Toxocara Goldmann-Witman (GW) coefficient analysis of aqueous and serum. Treatment includes: Thiabendazole (25 mg/kg body weight, up to 3 gm/day for 5 days), Albendazole (800 mg twice daily for 6 days) or Mebendazole (100–200 mg twice daily for 5 days). Argon laser can be utilized to kill live larvae seen in the retina. Complications of the infection, such as retinal detachment, persistent vitreous opacification and epi-retinal membrane formation, require surgery.[22,28]

Schistosomiasis

Disease caused by parasitic flatworm called schistosomes. The disease is spread by contact with fresh water contaminated with the parasites. These parasites are released from infected freshwater snails.[20] The disease is especially common among children in developing countries, as they are more likely to play in contaminated water.

ocular involvement is rare. Present as uveitis or subretinal granuloma. Diagnosis is made by direct isolation of the eggs or larvae in the eye. Isolation of eggs in urine or stools can help in diagnoses. Specific and highly sensitive PCR based assays have been developed for the detection of schistosome DNA in faeces or sera and plasma. Antibody detection can be useful in a few specific circumstances, but its application is limited. If not treated, symptoms will persist. The treatment of choice for all forms of schistosomiasis is Praziquantel. Other drugs used to treat schistosomiasis are oxamniquine and metrifonate.[29]

Non-infectious conditions

Swimming pool related

Swimming leads to exposure of eye with contaminated water. This leads to redness, irritation and rubbing of eye that further cause corneal abrasion or secondary infection. Usually the swimmer present with burning sensation, photophobia and blurred vision.[5] The Centers for Disease Control (CDC) conducted a study to assess illness and injuries caused by swimming pool disinfectants and chemicals in the USA. According to this study, as many as 33% cases from SENSOR (Sentinel Event Notification System for Occupational Risk) and 42% from NEISS (National Electronic Injury Surveillance System) had ocular illnesses attributable to swimming pool additives. A study on indoor swimming pool workers in Italy also reported red eyes in 48.9% and itchy eyes in 44.4% of the respondents.[5]

The pathogenesis of such eye irritation after swimming is down to chlorine's pH level, Chloramines, specially nitrogen trichloride or trichloramine (NCl3). A number of chlorine containing agents (such as Calcium- or Sodium-hypochlorite and Chlorinated isocyanuric acid) are used to disinfect swimming pool water.[30] The free chlorine reacts with nitrogen-containing matter introduced into the pool water by swimmers (urine/urea, sweat, skin squama, cosmetics) leading to the formation of a number of "disinfection by-products" (DBPs) including trihalomethanes and chloramines.[31] Trichloramine is regarded as the main causal agent responsible for ocular irritation.[30,31]

Water's normal pH level is 7 (neutral); below 7 indicates a more acidic level, and values above 7 suggest alkaline levels. The pool water's pH should be between 7.2 and 7.8 to be safe for swimmers to use, while also ensuring that bacteria levels are kept low. Ideally, chlorine in the pool would have a pH of 6.5 as this is when it's 100% effective against bacteria. However, 6.5 is far too acidic for our skin, which is why the recommended level is between 7.2-7.8. At this less acidic level, the chlorine doesn't break down the germs, fats and oils in the water as effectively, which is how bacteria and infections still remain in the water. It is the partially broken-down compounds which cause irritation to eyes as the chlorine can't work properly. Similarly, itchy eyes can also happen when there is too much chlorine in the water, it's all about finding the perfect balance.[32]

Saltwater is often touted as a "more natural approach" than chlorinated water, as it's "safe on skin, hair, and your eyes". Saltwater pools rely on salt to keep them clean, instead of utilizing chlorine tablets or other stronger chemicals. Chlorine is actually a by-product of salt so, even if a pool is just saltwater, there will still be small amounts of chlorine in it. While chlorine is known to cause some swelling in the eye's cornea, saltwater doesn't have the same effect. This is because the concentration of water in your eyes is actually very similar to sea water, and so is much gentler on your eyes than chemicals such as chlorine.[32]

Swimming pool related incidents can be reduced by prophylactic measures aimed at minimizing DBPs such as: controlling all technical parameters during the water disinfection process, regulation of water quality, ensuring good public hygiene (showering before entering swimming pools and wearing proper clothing) and undertaking regular public education and awareness campaigns.[31]

Radiation injuries due to long periods in the sea

Individuals who spend a lot of time at sea are highly exposed to UV radiation. UV radiation is invisible to the human eye and is subdivided into three categories: UV-A (400-320 nm), UV-B (320-280 nm) and UV-C (280-220 nm). The ozone layer filters out UV-C. The UV radiation that reaches the Earth is composed of about 95% UV-A and 5% UV-B. UV-A radiation has lower energy, but penetrates much deeper into the eye and may also cause posterior segment eye injury. UV-B is mostly absorbed by the cornea, and less by the lens, causing damage to these tissues, but rarely reaching the posterior segment. UV-B is the most harmful, probably because of its higher level of energy.[33]

Several ocular pathologies may be caused or worsened

by exposure to UV radiation, especially by UV-B. UV light is reflected off surfaces, in a variable percentage depending on the surface: the snow can reflect about 80 to 94% of UV-B radiation, the foam of the sea about 25%, the white sand of the beach about 15% and seawater reflects between 5 to 8%. Reflected UV radiation is added to the incident UV radiation, enhancing exposure to the total UV radiation. The greater the proximity to the reflecting surface, the greater the exposure of our eyes to reflected radiation.[33]

Direct sunlight is harmful to the eye, the reflected UV rays can be even more, because we are looking down and around (exposure to reflected radiation) more often than we are looking up, directly at the sun (exposure to direct radiation)

Acute exposure to high levels of UV radiation may cause temporary photochemical lesion in the keratotic cells, called photokeratitis, also known as ultraviolet burn. Symptoms appear a few hours after exposure, with tearing, foreign body sensation, blurred vision, pain, and intense photophobia, presenting with conjunctival hyperemia and superficial punctate keratitis. Treatment includes ocular occlusion with antibiotic ointment for a minimum of 24 hours.

Chronic exposure to UV radiation is clinically and epidemiologically more important than acute exposure. The cornea absorbs most UV radiation, not only from direct irradiation but also from oblique rays. UV-B radiation induces oxidative stress and damages corneal epithelial, may cause pterigium, pinguecula, ocular surface squamous neoplasms etc.

The best way to prevent injuries is by using an ultraviolet filter, which can be incorporated into spectacles and contact lenses.[33]

Water sports related

WEDs during water sports can have multiple mechanisms. They can be chemicals from pollutants or mechanical injuries from sport equipments, such as masks and diving boards. In February 2015, some of the competitors in a kayaking contest in New Zealand developed sudden ocular pain and reduced vision. The condition was suspected to be due to exposure to dishwashing liquid or fire-retardant residues in the river water. In a water-jet related incident, high pressure from the vehicle was reportedly responsible for Descemet's membrane ruptures in an individual.[5]

Oil spills

Barrels of crude oil released into the ocean due to accident or explosion in the carrier or oil refinery. It has adverse effects on the health of cleanup workers, fishermen, and others as well as on the ecosystem. These incident leads to oil spill response and cleanup (OSRC) activity. Dispersants are applied to the surface either through aerial spraying or by vessels within 3 nautical miles (5.5km) of the involve area. Dispersants are typically used to reduce the interfacial tension between crude oil and water and facilitate the breakup of oil slicks into small droplets that are thought to be more easily dispersed by natural processes such as wind and wave action. Dispersants are composed of propylene glycol, 2-butoxyethanol and organic salts including dioctyl sodium sulfosuccinate (DOSS). These usually leads to burning sensation, itching and redness.[34]

These non-specific conditions are usually self-limiting and resolve with minimal sequelae

Precautions to prevent water-associated disease:

- Ensure the water is visibly clean and free from sand and silt. Filter the water to get rid of visible dirt.
- Drink only clean and safe water – either portable water or water filtered through water purifiers.
- Get water purifying devices like filters, RO unit, etc., regularly serviced and maintained.
- Ensure stored water is germ-free.
- Add antiseptic liquid, such as Dettol in dubious-looking bathing water.
- Hand hygiene – regularly wash hands with soap after returning home, after using the toilet, before and after preparing food, before eating or drinking anything.
- Teach hand hygiene to children. Children should make it a habit to always wash hands when returning home after playing games.
- Ensure food is washed and thoroughly cooked.
- Use disposable glass and plates whenever possible when eating outside food, particularly street food.
- Avoid eating stale cooked food, unrefrigerated food kept exposed outside for long hours.[35]

Conclusion

The knowledge of the different types of water-associated diseases has come to the forefront with the advent of globalization over the past few decades. Several pathogenic microorganisms which were previously unknown have become the focus of major research in this field. Rural populations are more at risk from water-associated illnesses, but everyone faces risks of polluted or contaminated water. Water-associated illness can affect anyone, anywhere. Due to increasing contamination of water bodies, Industrial excreta and global warming, the water quality is severely affected. There are very high levels of subclinical and acute ocular disorders among humans due to water-associated diseases. There is also a risk of development of resistant species of organisms which may be difficult to manage. The present article gives a comprehensive review of water-associated eye diseases, its epidemiology, clinical presentation and current management. It also highlights the future challenges and possible solutions to these problems. Awareness of this entity is absolutely essential to arrive at an accurate diagnosis and to prevent its potential reversible and irreversible ocular complications. In such a scenario it is worth revisiting the common causes of such water-associated eye diseases (WEDs).

Table 1 : Water-associated Eye Diseases (WEDs)

		Infectious Condition
1-	Bacteria	Chlamydia Trochomatis
		Nontuberculous Mycobacteria
		Pseudomonas aeruginosa
2-	Protozoan	Acanthamoeba
		Giardiasis
		Leishmaniasis
		Microsporidiosis
		Rhinosporidiosis
		Taxoplasmosis
3-	Helminthic Round Worm	Angiostringyliasis
		Bancroftian and Brugian Filariasis
		Baylisascariasis
		Dirofilariasis
		Loiasis
		Onchocerciasis
		Toxocariasis
		Trichinosis
4-	Helminthic Flat Worm	Cysticercosis
		Fascioliasis
		Hydatid Cyst
		Schistosomiasis
		Non-Infectious Condition
1	Swimming pool related	
2	Radiation injuries due to long periods in the sea	
3	Water sports related	
4	Oil spills	

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Corona Virus (Covid-19) –Knowledge, Attitude and Practices of Patients Attending Ophthalmology Clinic

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Abstract

Aim: To assess KAP towards COVID-19 among ophthalmic patients at a tertiary care center.

Methods: An open ended questionnaire with 24 questions was used to evaluate the KAP towards COVID 19 among consecutive OPD patients.

Results: Of the 500 participants in the age group of 18 -80 years, 52.8% were males. Highest mean knowledge score (15.73±3.65) was observed in the age group 30-60 years. The overall attitude of participants on following infection prevention guidelines was strong (14.73±2.00). Practice patterns of age group 31-60 was significantly better than that of > 60 years. The vulnerability to infection and the poorer practice patterns among the older age group signifies the need for targeted awareness programs focusing on them. Gender had no impact on KAP Scores. The main source of information was TV /newspapers (75.3%) suggesting that media should be frequently used to disseminate information on COVID-19 by the stakeholders.

Conclusion: Although our patients had reasonably good KAP scores, targeted health education interventions can increase the awareness and can help prevent the spread of COVID-19 across the population.

Keywords : COVID-19; Knowledge; Attitude; Practice; Social distancing; awareness

Introduction

CORONA VIRUS DISEASE (COVID-19) was first identified in December 2019 in Wuhan, China.[1,2] The disease has spread globally affecting 227 countries and territories and has become a life threatening pandemic disease. SARS-COV-2 is transmitted from person-to-person through inhalation of aerosols from an infected individual.[1] Old age and patients with pre-existing illnesses (like hypertension, diabetes cardiac disease, lung disease or cancer) have been identified as potential risk factors for severe disease and mortality.[3,4] More information about the distribution, transmission, pathophysiology, treatment, and preventive methods of COVID-19 are being studied. World Health Organization (WHO) recommends prevention of human-to-human transmission by protecting the close contacts.[5]

Primary preventive measures include regular hand washing, social distancing, and respiratory hygiene (covering mouth and nose while coughing or sneezing).[6,7] Transmission of SARS-CoV-2 virus also occur within the healthcare system as well.[8,9] Various studies have suggested that ocular surfaces can be a potential source of transmission.[10,11,12] The detection of SARS-CoV-2 virus in ocular secretions suggests infectivity.[13]

The higher viral load in the nasal cavity compared to throat suggests higher potential for transmission of the disease through close face to face settings like slit lamp examination. SARS-CoV-2 remains viable in aerosols for at least 3 hours. Air forced tonometry generates micro-aerosol droplets. This also pose a risk for transmission of the disease in the ophthalmology clinic.[14]

A poor understanding of the disease among population can result in rapid spread of infections and poor containment of the disease. The purpose of the study is to analyze the KAP of patients regarding COVID-19 and to create awareness regarding disease preventive practices.

Aims and objectives

To analyze the Knowledge, Attitude and Practices

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regarding COVID-19 among patients attending ophthalmology clinic and to create awareness among the patients regarding preventive measures towards COVID-19

Materials and methods

The Prospective, Cross sectional hospital study was conducted in a tertiary eye care hospital. The study protocol, questionnaire validation and consent form were approved by Institutional Ethics Committee (IEC). The study adhered to the tenets of the Declaration of Helsinki and written informed consent was obtained from each participant of the study for publication.

All patients above 18 years who were presenting to the eye care hospital during the lockdown period from August 2020-October 2020 were invited to participate in questionnaire survey after OPD registration. Patients with ocular emergencies like severe pain/ trauma were excluded from the study. The study participants were informed in their own vernacular language about the objectives of the survey and confidentiality of their responses. Data were collected in their own vernacular language by interview method using a pre-validated questionnaire and response was noted by the observer. Respondents were given awareness regarding correct practices and prevention methods at the end of the session.

Statistical Analysis

Categorical data was represented in the form of frequency and percentage. Quantitative data was representedas meanand standard deviation. Comparison of variables has been done with Unpaired t test.ANOVA test was applied for the comparison of more than two groups along with Post Hoc multiple comparison. A p value of <0.05 was considered statistically significant.Data was analyzed with IBM SPSS Version 22 for windows.

Results

Demographic characteristics

A total of 500 participants were included in the study. It comprised of participants in the age group 18-80 years, 20.8 % were of the age group 21-30, 19.2% were of the age group 31-40 and 19% were 41-50years.Of these, males constituted about 52.8% of the total sample. All the patients were aware of the symptoms of COVID-19. Nearly 206 cases (41.2%) patients presented for emergency eye conditions like trauma/redness, 170 cases (34%) came for regular eye checkup and 124 cases (24.8%) came for follow up of chronic conditions like glaucoma. For about 75% of participants, the primary source of COVID-19 awarenesswas from the newspaper or TV.

Table : 1

Age	No of Cases	Percent
⩽ 20	63	12.6
21-30	104	20.8
31-40	96	19.2
41-50	95	19.0
51-60	65	13.0
61-70	60	12.0
71-80	17	3.4
Total	500	100.0

Knowledge assessment

Table : 2

Question	TRUE (%)	FALSE (%)	I DON'T KNOW (%)
1. The main clinical symptoms of COVID-19 are Cough ,Fever Sore throat, Runny nose, Myalgia ,Diarrhea	500 (100)	0	0
2.Currently there is no effective cure for COVID-19, but early symptomatic and supportive treatment can help patients recover from the infection	383 (76.6)	46 (9.2)	71 (14.2)
3.The COVID-19 virus spreads via respiratory droplets of infected individuals	407 (81.4)	15 (3.0)	78(15.6)
4.In the absence of fever,COVID-19+ patient cannot transmit the virus	133 (26.6)	243 (48.6)	124 (24.8)
5.Not all persons with COVID-19 will develop severe cases	418 (83.6)	32 (6.4)	50 (10.0)
6.Only those who are elderly, with chronic illnesses and obesity are more likely to get severe cases	360 (72)	97 (19.4)	43(8.6)
7.Wearing masks can prevent from acquiring infection by the COVID-19 virus	474 (94.8)	14 (2.8)	12 (2.4)
8. To prevent the infection by COVID-19, individuals should avoid going to crowded places	464 (92.8)	18 (3.6)	18 (3.6)
9.Isolation and treatment of people who are infected with the COVID-19 virus are effective ways to reduce the spread of the virus	446 (89.2)	16 (3.20	38 (7.6)
10. People who have contact with someone infected with the COVID-19 virus should be immediately isolated in a proper place.	443 (88.6)	15 (3.0)	42 (8.4)
11.Infection can be transmitted via contact with fomites like door handles	323 (64.6)	60 (12)	117 (23.4)

The knowledge of participants with regards to symptoms, spread, and prevention of COVID-19 was good, with a mean knowledge score of 15.80 .Thehighest mean knowledge score (15.73±3.65) was observed in the age group 30-60 years. Knowledge among patients aged >60 years was poorer compared to the other age groups. The result of the knowledge survey is presented in Table 2. All patientshad good knowledge about the main symptoms of COVID-19. Furthermost, 89.2 % of the participants were aware that early symptomatic and supportive treatment can help most patients recover from the infection. Awareness about the prevention and treatment was good among the participants, such that nearly everyone (92.8%) knew that COVID-19 can be prevented by avoiding crowded places such as market, train stations and avoiding public transportation. Furthermore, 88.6 % of participants knew that people who had contact with COVID-19 infected person be immediately isolated in a proper place.But only 64.6 %were aware of possible COVID-19 transmission through fomites like door handles.

Attitude assessment

The overall attitude of participants on following infection prevention guidelines were strong with a mean (SD) score of 14.73 ± 2. Majoirty of the patients had a positive attitude towards COVID-19 and agreed that hand wash and face masks can help prevent the spread of infection. Significant difference was noted in mean attitude scores with respect to the demographic variables between the age groups below 30 and above 30 years. The result of the attitude assessment is presented in Table 3.

Table : 3

1.Wearing a well-fitting face mask is effective in preventing COVID-19	a)Strongly Disagree 14 (2.4%)	b) Disagree 4(0.8%)	c) Neutral 52(10.4%)	d) Agree 334 (66.8%)	e) Strongly Agree 98 (19.6%)
2.Using a hand wash can prevent you from getting COVID-19	a) Strongly Disagree 6 (1.2%)	b) Disagree 5 (1%)	c) Neutral 21 (4.2%)	d) Agree 273(54.6%)	e) Strongly Agree 197 (39.4%)
3.Hospital visit can increase the risk of getting infection	a)Strongly Disagree 6(1.2%)	b) Disagree 62 (12.4%)	c) Neutral 54 (10.8%)	d) Agree 239(47.8%)	e) Strongly Agree 141(28.2%)
4.In your locality ,COVID -19 cases are well controlled	a)Strongly Disagree 122(24.4%)	b) Disagree 133 (26.6%)	c) Neutral 117(23.4%)	d) Agree 114(22.8%)	e) Strongly Agree 15(3%)

Practice patterns

Practice pattern among participants were similarly high, with a mean (SD) score of 17.38 +- 2.20. The result of the practice pattern is presented in Table 4.

8% of the participants knew that 2 arm distance to be maintained with other person.66% of the participants always wore a mask.56.8% washed their hands 5-10 times in a day and 55% used soap to clean their hands. However, 3.4% of the patients did not use masks regularly, frequently visited crowded places(7.4%) and reused the same mask for >2 weeks (30.4%).

Table : 4

1. In recent days, have you gone to any crowded place?	a)Always 37(7.4%)	b)Occasional 267 (53.4%)	c) Never 197(39.4%)
2. How much distance you should keep with the other person to avoid spread of infection?	a)I don't know 61 (12.2%)	b) 1 arm distance 186 (37.2%)	c) 2 arm distance 254(50.8%)
3. How frequently do you wash hands in a day?	a)<5 times 146(29.2%)	b) 5-10 times 284(56.8%)	c)>10 times 71(14.2%)
4. What do you use to clean your hands?	a)Only water 55(11%)	b)soap 275(55%)	c)Hand sanitizer 172(34.4%)
5. In recent days, how frequently have you worn a mask?	a)never 17(3.4%)	b)Occasional 151 (30.8%)	c)always 333(66.6%)
6.What type of mask do you use	a)cloth mask 365 (73%)	b)surgical mask 82(16.4%)	c) N95 mask 53(10.6%)
7. How long do you use one mask?	a)>2 weeks 78 (15.6%)	b)1 week 268(53.6%)	>2 weeks 154 (30.8%)

Demographic variables and KAP scores

Analysis of KAP scores with respect to demographic characteristics. Table 5 describes the scores of knowledge, attitude, and practices towards COVID-19. KAP scores with respect to demographic variables such as gender and age are described in table 6 and table 7 respectively. The knowledge scores of the female were slightly higher than that of males, although the difference was not significant (P-0.35). Higher scores of females were observed in the attitude as well. Practice scoresamong females was less compared with that of malesand the difference was significant (P<0.03)

Table : 5

KAP Scores	Mean	Std. Deviation	Minimum	Maximum
Knowledge	15.80	3.58	12.00	32.00
Attitude	14.73	2.00	4.00	20.00
Practice	17.38	2.44	10.00	24.00

Table : 6

KAP Scores	Male		Female		Unpaired t test	
	Mean	Std. Deviation	Mean	Std. Deviation	P Value	Sig
Knowledge	15.65	3.42	15.96	3.76	0.35	NS
Attitude	14.69	2.23	14.78	1.70	0.60	NS
Practice	17.24	2.20	16.79	2.45	P<0.03	Sig

Table : 7

KAP	Age Groups	N	Mean	Std. Deviation	ANOVA
Knowledge	⩽ 30	167	15.16	2.58	P<0.001, Highly Sig
	31-60	256	15.73	3.64	
	> 60	77	17.44	4.64	
Attitude	⩽ 30	167	15.05	2.18	P<0.03, Sig
	31-60	256	14.55	1.74	
	> 60	77	14.64	2.31	
Practice	⩽ 30	167	17.22	2.44	P<0.02, Sig
	31-60	256	17.10	2.24	
	> 60	77	16.36	2.31	

Table 8 shows the comparison between the age groups and their knowledge, attitude and practice scores. Knowledge score of patients in the age group less than 30 years was highly significant than that of the age groupmore than 60 years (P - 0.001).Attitude score of participants in the age group <30 years was significantly higher than that of the age group >60 years (P-0.02) .Practicepatterns were significantlybetter among patients of age group 31-60 years as compared to age>60 years (P-.002). TABLE 8

Table : 8

Tukey's Post Hoc Multiple Comparisons		
KAP	Groups	Sig.
Knowledge	⩽ 30 Vs >60	0.001, Highly Sig
	31-60 Vs > 60	0.001, Highly Sig
Attitude	31-60 Vs > 60	0.02, Sig
	⩽ 30 Vs >60	0.02, Sig
Practice	31-60 Vs > 60	0.02, Sig

Discussion

The novel COVID-19 virus has resulted in an unprecedented crisis within a short time. Considering the uniqueness of the disease and the uncertainties associated with its pathogenesis, it is crucial to actively engage the population to curtail the rapid spread of the disease. To date, there has been limited published data on knowledge, attitude, and practice (KAP) patterns toward COVID 19 among ophthalmic patients presenting to a hospital. Understanding KAP among patients is valuable considering the various amount of exposure risks that exists during their treatment visits to the Hospital.

In the present study, the knowledge, attitude and practice patterns of patients attending a tertiary hospital towards COVID-19 were assessed. A mean knowledge score of 15.80 with standard deviation of ±3.58was obtained, indicating good knowledge among the participants, with highest mean knowledge score (17.44±4.64) observed in the age group above60 years.

Knowledge and attitude patterns of age group above 60 years was poorer compared to the other age groups .The vulnerability of this age group to infection and the poorer practice patterns is a matter of concern. This signifies the need for targeted awareness programs focusing on older age groups. The main source of information regarding COVID-19 was TV /newspapers (75.3%).This suggests that media should be frequently used to disseminate information on COVID-19 by the stakeholders.

72% of the patients had a positive attitude towards COVID-19 and agreed that hand wash and face masks can help prevent the spread of infection. Significant difference was noted in mean attitude scores with respect to the demographic variables between the age groups <30 and above 30years.3% of the patients did not use masks regularly, frequently visited crowded places(6%) and reused the same mask for >2 weeks(9%).This emphasizes the need for awareness campaigns targeting these specific groups with low KAP scores.

Better knowledge can avert negative attitudes and thus promote positive preventive and therapeutic practices. The result of the study also emphasizes the need for better public health policies and tailored strategies to help curtail the pandemic.

Conclusion

In summary, the present study was able to provide a comprehensive analysis of the COVID-19 KAP among patients attending ophthalmology clinic. Althoughthese patients had an acceptable awarenessand knowledge on COVID-19 and showed a positive attitude on overcoming the pandemic, innovative awareness and preventive measures are urgently needed. Considering the high number of elderly people in our study population who had lower KAP scores, targeted health education interventions and policies has to be implemented. This can increase the awareness among the public andalso helpto prevent the spread of COVID-19 across the population.

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There are no conflicts of interest.

Original Article

Intellectual Disability Readdressed with Ocular Manifestations

Dinesh Sharma, Anju Kochar, Kalpana Jain, J M Manohar

Abstract

Purpose : We conducted this study to determine the association of ocular involvement, refractive error, and other disabilities with reference to intelligence quotient (IQ) and disability percentage in subjects with permanent intellectual disability in the north western part of Rajasthan.

Method : Total 101 patients were evaluated from the villages to the Medical College level (Primary, secondary and tertiary level of health care system) for ocular involvement by diffuse light, slit-lamp biomicroscopy, direct and indirect ophthalmoscopic examination, and with the autorefractometer.

Results : Hypermetropia and hypermetropic astigmatism were the most common type of refractive errors among the intellectually disabled patients. IQ level is inversely proportional to the level of hypermetropia and hypermetropic astigmatism. Mental retardation was associated with other ocular conditions like strabismus, nystagmus, and amblyopia. .These morbidities are directly proportional to the severity of mental retardation and inversely proportional to the level of IQ.

Keywords : mental retardation; intellectual disability; hypermetropia; astigmatism; IQ

Method

The study was done in hundred and one intellectually disabled subjects, who were examined in various villages, tehsils, sub-divisional district headquarters, and in the Medical College of Bikaner and Churu districts located in the Thar desert of the north-western part of Rajasthan near Indo-Pak border. (primary, secondary, and tertiary level). These patients were examined in various camps, organized by the Government of Rajasthan from 2012 to 2020 in various disability certificate camps and in routine OPD for providing disability certificates for various Government welfare schemes. Cases referred from the Psychiatry department for ophthalmic reference in the Eye Department of S.P. Medical college were also included in the study

Figure .1 Geographic representation of the area of study

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Case selection criteria

1. Subjects with permanent disabilities.
2. Age group from 8 to 50 years.
3. Intellectually disabled patients having more than forty percent disabilities (>40%) as per the Gazette of India.
4. IQ level <70
5. Patients sufficient to cooperate for Ophthalmic examination.

Case exclusion criteria

Criteria for the exclusion of patients were

1. Highly uncooperative patients.
2. Severely mentally retarded patients. (IQ<10)
3. Patients with <40% of mental illness.

Limitations of the study

1. Cooperation from subjects was the biggest hindrance in our study.
2. Detailed fundus examination was not possible since cooperation from patients was a challenge.

Mode of examination

A comprehensive eye examination was done by diffuse light examination, Slit lamp biomicroscopy, direct and indirect ophthalmoscopy and Autorefractometry. Vision was recorded on Snellen's chart and subjective correction given. Data was collected ,tabulated , analyzed and inferences drawn. Patients were referred to the department of Psychiatry for calculation of IQ.

Mental retardation and intelligence quotient (IQ)

The formula used to calculate the approximate Intelligence quotient was taken as per the Government of India's gazette. IQ calculation was done by psychiatrist and calculation of IQ was done by standard formula i.e.

IQ= Mental age/chronological age x 100

Level of intelligence- classified as follows

Idiot	---	0-24
Imbecile	---	25-49
Moron	---	50-69
Borderline	---	70-79
Low normal	---	80-89
Normal	---	90-109
Superior	---	110-119
Very superior	---	120-139
Near-Genius	---	140 and above

Disability calculation

Disability calculation was done as per the Gazette of India, The intellectual disability calculation was done based on the VSMS score(Vineland social maturity scale). The following score is used for disability calculation:

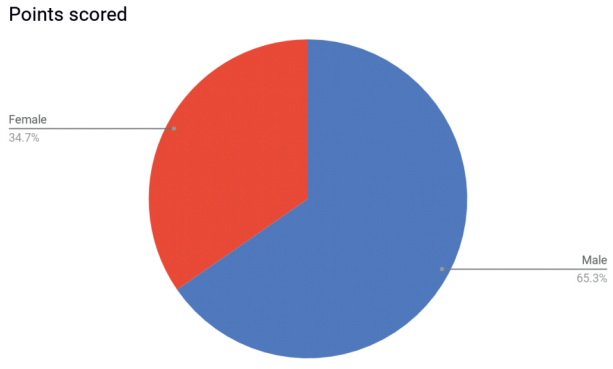
1. VSMS score 0-20: Profound Disability-100%
2. VSMS score 21-35: Severe Disability-90%
3. VSMS score 36-54: Moderate Disability-75%
4. VSMS score 55-69: Mild Disability-50%
5. VSMS score 70-84: Borderline Disability-25%

(VSMS-Vineland Social Maturity Scale)

OBSERVATIONS

The observations are as follows-

Table -1 : Male-female ratio



Sex	
F	35
M	66
Grand Total	**101**

Table -2 : Intelligence Quotient (IQ) and its relation to Refractive errors (Spherical +cylinder)

IQ	No. of Patients.	RE Spherical	RE Cylindrical
<20	18	08	08
<40	24	32	32
<60	54	105	103
<70	05	10	10
Grand Total	**101**	**155**	**153**

Table-3 : Alignment (Convergence/divergence out of 101 pts.) [Convergent 45°cases 7(06.93%)., convergent 70°and 20 ° cases 3 each (02.97%)]

S.N.	Alignment	Number	%
1.	Convergent	13	12.87%
2.	Divergent	02	01.98
Total	--	15	14.85%

Table-4 : Cornea involvement

Cornea	COUNTS
Megalocornea	1
Microcornea	9
Normal - sized	88
Opacity	3
Grand Total	**101**

Table-5 : Lens involvement (Out of 101)

S.N.	Lens	Number	%
1.	Cataract	5	04.95%
2.	Inferonasal subluxation	2	01.98%
3.	Superotemporal subluxation	2	01.98%
4.	Microspherophakia	2	01.98%
5.	Normal lens	87	86.13%
6.	Not seen	3	02.97%

Table-6 : Alignment and ocular movement

Ocular Movement	COUNT
NORMAL	84
NYSTAGMUS	12
RESTRICTED	5
Grand Total	**101**

Table-7 : Visual acuity Both Eyes (approximate)

Both Eye	COUNT
6/12	8
6/18	5
6/24	10
1/60	2
2/60	1
3/60	10
6/36	19
6/60	27
PL/PR	6
UC	13
Grand Total	**101**

Table-8 : Disability percentage and ocular involvement in percentile

S.N.	Disability %	Number	%
1.	>40	37	36.63%
2.	>60	7	06.93%
3.	>70	3	02.97%
4.	>80	19	18.81%
5.	100	35	34.35%
Total	--	101	99.69%

Table-9 : Refractive error Spherical (Both eyes)

S.N.	Spherical	Number	%
1.	+0 to +10	100	49.50%
2	10 to -0	55	27.22%
3.	Error	23	11.38%
4.	Uncooperative	24	11.88%
5.	Total	202	99.98%

Table- 10 : Refractive Error Cylindrical (both eyes)

S.n.	cylinder	Number	%
1.	+0 to +10	91	45.04%
2.	-0 to -10	62	30.69%
3.	Error	25	12.37%
4.	Uncooperative	24	11.88%
5.	Total	202	99.98%

Table 11: (A and B). Refractive error in relation to IQ

(A) Both Eye spherical vs IQ distribution

IQ→ ↓ Sph	IQ<20	IQ<40	IQ<60	IQ<70	TOTAL	Total/ %
+0 to+10	8	21	63	08	**100**	**49.50%**
-10 to -0	00	11	42	2	55	27.22%
Error	10	10	3	00	23	11.88%
uncooperative	18	6	00	00	24	11.38%
Total	36	48	108	10	202	99.98%

(B) Both Eyes cylinder vs IQ distribution						
IQ→ ↓ Cyl	IQ<20	IQ<40	IQ<60	IQ<70	Total	%
+0 to+10	6	24	59	2	91	**45.04%**
-10 to-0	2	8	44	8	62	30.69%
Error	10	10	3	5	25	12.37%
Uncooperative	18	06	00	00	24	11.88%
Total	36	48	106	15	202	99.98%

Table-12 : Other associated ophthalmic co-morbidities (out of 101pts.)

S.N.	comorbidities with MR	number	%
1.	Multiple disability	12	11.88%
2.	Blind	5	04.95%
3.	Low vision	2	01.98%
4.	Temporary blind	1	00.99%
5.	Deaf	4	03.96%
6.	Cerebral palsy	2	01.98%
7.	Microcephaly	1	00.99%
8.	Nyctalopia	1	00.99%
9.	Family history of MR	2	01.98%
10.	Entropion B/L both eyes	1	00.99%
Total		**31**	**30.69 %**

Results

There were 35 females(34.65%) as against 66 males (65.34%) intellectually disabled subjects enrolled in the study. (**Table 1**)

The maximum patients which we examined were around IQ 60 followed by IQ 40, IQ 20, and least were around IQ 70. About the relation with IQ, 5 patients (04.95%) with IQ around 70 were found. A total of 54 patients(53.46%) were of IQ around 60 and thus made this study possible. Patients with IQ around 40 were 24 in number (23.76%).

Patients with IQ around 20 were 18 (17.82%). Among these 5 patients (27.77%) were associated with multiple disabilities. (**Table 2**)

Strabismus is common in mentally retarded patients. In this study out of 101 patients, 15 patients(14.85%) were found with varying degrees of strabismus out of 101 patients. In which convergent squint was in 12 patients (11.88%) In this sub-classification 6 each was of 20 and 45 degrees (05.94% each) while 2 cases(01.98%) were divergent. Out of two,1 divergent case was associated with optic atrophy. (**Table 3**)

The involvement of the cornea is also common. In this study cornea was involved in 13 patients (12.87%). Microcornea was observed in 9 cases (08.91%) Corneal opacity in 3 cases (02.97%). Megalocornea in 1 case (00.99%). (Table 4)

Iris coloboma with mental retardation was associated in one case (01.99 %). (**Table 5**) The crystalline lens is frequently involved in mentally retarded persons in the form of cataract, subluxation, and microspherophakia.etc.In this study, 5 cases were found bilateral cataract (04.95%) and 1 patient (00.99%) was a confirmed case of Homocystinuria as per record. Out of 5 cataract patients, 2 cases (01.96%) were having congenital cataracts as per history. Early development of cataracts was noted in 2 cases (01.98%). Among these 1 patient had given the history of taking some drug (thioridazine and chlorpromazine for a long time).

Out of 101 patients, 12 patients were had nystagmus (11.88 %) while two patients(01.98%) with restricted ocular movements in all cardinal positions of gaze were found. (**Table 6**)

With regard to visual acuity it was found that 26.73% of patients were had vision around 6/60 and 18.81% had acuity of vision around 6/36, Patients with vision around 3/60 were 09.90%, Patients below 2/60 vision were 02.87 %, Patients with vision 6/24 or better were 14.85%. Uncooperative patients were 12.87%. Patients who showed to be PL and PR positive were 05.94%. (**Table 7**)

During the fundus examination, we have seen one patient having bilateral optic disc atrophy (00.99%) and on the other hand, one patient showed leukocoria (00.99%).

In our study, we found that disability percentage is directly proportional to ocular defects and poor vision. (**Table 8**)

In this study total, 35 patients(34.65%) were having 100% mental disabilities, while 37(36.63%) with disability around 40 %, were of patients with multiple disabilities, low socioeconomic stratum, and other factors.

Regarding the relation between refractive error and mental retardation, hypermetropia was found in 100 eyes (49.50%) while myopia was seen in 55 eyes (27.72%)

On the other hand, hypermetropic astigmatism is high among the patients 90 eyes(44.55%) while myopic astigmatism was found in 62 eyes (30.69%). The rest of the patients either were uncooperative for taking autorefractometer reading or autorefractometer showed error due to varying reasons. (**Table 9 to 11 A and B**)

Cycloplegic refraction of both eyes of 101 cases (total 202 eyes), by Auto Refractometer by using Tropicamide 0.8 % w/v and phenylephrine 5% w/v topical drops were done. The inference was that Hypermetropia was the major type of refractive error among mentally retarded patients that is 100(49.50 %). Myopia was in 55 eyes (27.22 %), while uncooperative patients in whom we could not manage to take

AR reading were 24 eyes in number (11.88 %) while in 23 eyes (11.38%) there was an error in reading due to varying causes like corneal opacity, cataract, and nystagmus, etc.

Hypermetropic astigmatism was found in 91 eyes (45.04%) while Myopic astigmatism was in 62 eyes ((30.69%). There was an error in AR reading in 21 cases (10.39%) due to varying causes like corneal opacity, cataract, and nystagmus, etc. In subjects with IQ <20, hypermetropia was only 8 but on the other hand errors and total uncooperative patients are as much as high 28 cases in comparison to higher IQ groups. If the correct AR reading or examination would have been possible then this result slightly could be different (see table)

Table12 shows other associated disabilities which were present in 31 subjects (30.69%) of total patients. Multiple disabilities (More than one disability in one patient) was in found in 12 patients (11.88%), complete blindness (100% as per gazette of India) was seen in 5 (04.95%). Patients associated with deafness were 4 in number (03.96%). Patients with low vision, cerebral palsy, and patients with a family history of mental retardation were 2 each (01.98%). Patients with temporary blindness (which could be improved by penetrating keratoplasty), Microcephaly, Nyctalopia, and bilateral both eyes entropion was found in 1 patient each (00.99%).

Discussion

There was a male preponderance in our study, the ratio being 13:7 male versus female.Sex differences in M: F ratio may because of sex discrepancy in the western part of Rajasthan where males are given more social importance over females in the community. The community provides early and more medical help to males than females. Some other reasons may also be there like genetic preponderance etc, This study supports study done by Minakshi vashist et al[1] which showed pravelence is higher in males (78.04%) as compared to females (21.06% in Hatyna state.

Out of 101 patients, 12 patients had nystagmus (11.88 %) while two patients with restriction of ocular movement in all cardinal positions of gaze were found. This study in in concordance with the study done by Rajesh Subhas Joshi et al[2] (Indian journal of Psychiatry) and studt done by Parikshit Gogate et al[3] which shows the incidence of strabismus 10.31 % in patients of learning disability and nystagmus (6.08%) respectively. Restricted movement may be explained due to the maldevelopment of the central nervous system and brain.

Megalocornea is rare in intellectually disabled subjects and very rare in megalocornea mental retardation and /or seizures syndrome. In this study 1 patient with megalocornea was found to have multiple disabilities viz mental retardation and Buphthalmos in one case.Corneal dystrophy though frequently associated with mental retardation , was not found in a single case in this series.

Regarding Corneal opacity, in our study, 2 cases were due to old healed corneal ulcer (01.98%), and 1 case, as per history was due to old chickenpox (or viral keratitis)

Megalocornea Intellectual Disability Syndrome is a rare disease in which additional findings may include an unusually prominent forehead (frontal bossing), widely spaced eyes (ocular hyperterelorism), downwardly slanting eyelid folds. It is x -linked recessive disorder said to be around 37-50 cases in the world.)

A correlation between central corneal thickness and intellectual disability has been observed in several studies. Children with greater intellectual disability have more central corneal thickness. However, measuring central corneal thickness was beyond the scope our study so data regarding this feature is not available in this study. The reason being lack of facility to measure central corneal thickness, especially in rural areas and primary and secondary levels of health care units of the community.

Coloboma may be associated with mental retardation. According to a study by Mette Warburg et al[4] among 96 mentally retarded patients with coloboma and / microphthalmia, 15 had multiple malformations. Coloboma with multiple anomalies sometimes associated with neural crest defects, midline structural abnormalities, and congenital heart disease suggesting that there is a definite association between coloboma and mental retardation. Many syndromes with coloboma, microphthalmos, microstomia, hearing defects are well-known disease entities.

In our study, one case of bilateral iris coloboma was associated with congenital lenticular changes, hearing defect, Slurring of speech with mild mental retardation.

Examining visual acuity in a mentally retarded person is a challenge. Many patients were cooperative enough to get themselves examined with the help of their relatives or parents with the Snellen Chart. But, many were very uncooperative and irritable. Only gross judgment of visual acuity in such patients was possible. We noted visual acuity by showing them a tree, birds, door, window, animals, motor vehicle, or other types of object varying distances. Vision may or may not be directly associated with mental retardation but underlying pathology or maldevelopment of the brain or central nervous system does exist.

Gustavson syndrome including optic atrophy with severe mental retardation, microcephaly, severe hearing defect, spasticity, epileptic seizures with restricted movement of the large joints was observed in one of the subjects in this series also.

Regarding IQ, it is stated that there is a maldevelopment of the brain, which may usually be associated with maldevelopments other organs at a particular time of gestational age. No disabilities were associated with patients with IQs more than 60. This seems that level of IQ is inversely proportional to the multiple disabilities.

Regarding relation with refractive error, our results correlates with a study done by Rabindra Ghising et al[5] in the students of Kathmandu valley and Mary Thomas et al[6] and On the other hand contrary to our study, a study done by Shin Yeuong et al[7] and clinical epidemiological research in investigative ophthalmology and visual science) states that there is a novel association between myopia and cognitive dysfunctions. Kalaiselvi G et al[8] also showed contrary results. Here the possibility of contrast in our results may be due to differences in their criteria and Indian criteria for

grading of cognitive functions and mental retardation. Secondly, genetic and/or demographic variation may also be the other cause.

An important inference drawn from our study was that the IQ level is inversely proportional to the level of hypermetropia and hypermetropic astigmatism. Moreover, it also indicates that hypermetropic astigmatism is more common than the other types of astigmatism.

Perhaps, no such study has been done which shows the relation of against the rule astigmatism and mental retardation to the best of our knowledge.

Arsen Akinci et al[9] in their study of refractive errors and ocular findings in children with intellectual disability, also showed that the children with intellectual disability had significantly more nystagmus, strabismus, astigmatism, and hypermetropia than controls. Our study is in agreement with this conclusion. A possibility, that a small brain in the small head (microcephaly, which is present in 1 case) may be associated with lesser sulci and gyri with a lesser surface area of brain parenchyma thus a low level of intelligence a low IQ cannot be denied. A complete MRI of such patients could prove this observation better. Similarly, small heads with small orbits and small eyes explain hypermetropia in such patients.

Maldevelopment of the brain and central nervous system intrauterine could be a cause of strabismus observed in this study and similar results were found in a study done by Gurvindner Kaur et al[10] which showed 18.1 % and 10.37% of strabismus in children with learning disability and mental retardation respectively (In our study the convergence was 12.87% and divergence was 01.98%).

This study showed the presence of ocular problems with other comorbidity is high in mental retardation. Patients with mental retardation and other disabilities (other than visual impairment) are at a higher risk of visual impairment as compared to the normal population. The majority of the ocular disorders, like refractive errors and strabismus, are easily treatable. As these patients depend on their visual inputs for social and academic or general activities if any, early detection and prompt treatment of even a minor visual problem are of utmost importance for them.

Visual disabilities always aggravate or add the morbidity to their preexisting mental retardation and other disabilities, it will affect the overall development of the patients right from an early age much more than it affects a normal person. Unfortunately, patients with

other disabilities are at a significantly higher risk of visual impairment too and vice versa. Refractive errors are easily corrected by prescribing spectacles thereby, improving the quality of life of such subjects.

The majority of the cases of strabismus can be corrected by either surgery or spectacles. Thus, a simple and timely intervention in the form of spectacles and other modes of treatments can make a huge difference in the lives of patients with mental retardation and other disabilities. The very fact that the majority of the causes of visual impairment like refractive errors, amblyopia, and strabismus are easily treatable, signifies the need for regular ocular examination in children with disabilities. The parents, caregivers, and medical professionals need to be sensitized and motivated for the regular ophthalmic examination of these patients, even if the disability is not visual. Protocols should be made regarding, mandatory vision screening in all mentally retarded patients.

Unfortunately, difficulties lie in the felt need of the patients because patients never seek medical advice on their own. He or she always remains dependent on their parents, caretakers, and guardians. Truly speaking even medical professionals does not take due interest and do not care to examine such patients and help them out of situation in whatever way possible.

Conclusion

Our study shows that hypermetropia and hypermetropic astigmatism are high among the mentally retarded patients and IQ level is inversely proportional to the level of hypermetropia and hypermetropic astigmatism. Moreover, it also indicates that irregular hypermetropic astigmatism is more than the other types of astigmatism. Mental retardation was associated with other ocular conditions like strabismus, nystagmus, and amblyopia etc.these morbidities are directly proportional to the severity of mental retardation and inversely proportional to the level of IQ.

Recommendation

Our recommendation is that, all patients with intellectual disability, should undergo an annual ophthalmological examination specifically for refractive errors like hypermetropia and hypermetropic astigmatism. Early detection and treatment of ocular problems and correction of their refractive errors are essential to prevent visual impairment as well as amblyopia in the future. This also improves the quality of life and makes mentally retarded patients more acceptable by society. Poor vision aggravates and makes it difficult to manage all the other disabilities, thus increases the familial, social, and economic burden on the individual, nation, and the world.

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There are no conflicts of interest.

Visual Impairment in Chronic Kidney Disease Patients

Jyotika Prasanna Mishrikotkar, Rujuta Ranjeet Sapkal

Abstract

Aim: To study the prevalence and identifiable cause of visual impairment in Chronic Kidney Disease patients (CKD)

Material and Method: A prospective, cross-sectional study was conducted on 118 patients with CKD attending tertiary health care center and evaluated them on following basis: Uncorrected and best corrected Visual acuity, IOP measurement, Slit lamp and Fundus examination. OCT Macula and Disc, Fundus Photo and Perimetry were done wherever needed

Results: Out of the 118 patients studied, 74(62.71%) were males and 44(37.28%) were females with most common age group being 31-50 years (39.83%). Out of 118 patients, 10(8.47%) were found to have visual impairment with cataract being the most common cause in 60%. About 70.336% had comorbidities with Hypertension being most common in 37.28% followed by Hypertension and Diabetes in 20.338%

Conclusion: The study reinforces the need of eye screening in patients with comorbidities enabling early detection and treatment before irreversible vision loss occurs.

Keywords : CKD; Visual Impairment; Hypertension; Diabetes; Cataract; Glaucoma

Introduction

Chronic kidney disease (CKD) is a burgeoning global public health concern.[1] In India, the prevalence of CKD was found to be 17.2 percent.[2,3] The visual system is damaged as a result of Uraemia, Metabolic Imbalances, Hypertension, or Haemodialysis treatment.[4] The renal and retinal circulations are anatomically, physiologically, and pathologically similar. As a matter of fact, analyzing retinal microvasculature allows for the detection of early microcirculatory changes attributed to CKD Disease.

Age-related ocular diseases end up sharing cardiovascular risk factors and pathogenic processes, such as oxidative stress and inflammation, which are two of the key pathogenic mechanisms inherent in CKD. As a result, CKD patients may be more likely to develop age-related ocular diseases.[5] The metabolic control of the disease state can be speculated by the ocular status. Some of the causes of visual impairment that could be present in a Chronic Kidney Disease Patient are: Amblyopia, Cataract, ARMD, Glaucoma, Optic Disc Edema, Retinopathy, Maculopathy, Retinal vascular diseases, Retinal detachment.

Screening patients with CKD enables early detection of potentially vision-threatening complications, allowing timely intervention. There is no consistent statistically significant relation between VI, specific eye diseases, and CKD. Understanding whether or not there are valid links between CKD and certain eye diseases might lead to the formulation of new screening methods and therapeutic strategies for both conditions.

Our study aims to find out the prevalence of visual impairment and theidentifiable cause of visual impairment in CKD patients. It also highlights the importance of timely ocular evaluation.

Materials and Methods

We conducted a prospective cross-sectional studyon all patients having CKD attending our tertiary care centre during a period of 3 months from 22nd December, 2020 to 22nd March, 2021. All patients with Chronic Kidney Disease irrespective of age and gender were included in the study. Patients not willing to participate, unwilling for dilated evaluation and those who couldn't be mobilized for slit lamp evaluation were excluded. The study adhered to the tenets of the Declaration of Helsinki and written informed consent was

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obtained from each participant of the study for publication.

All the cases were evaluated on the following grounds : Vision on Snellen's chart, IOPmeasurement on Applanation Tonometer, Slit lamp examination, Fundus examination using 90 D and IDO. OCT Macula, OCT Disc, Fundus Photo and Perimetry were done wherever needed. Visual Impairment was defined as VA <6/18 best corrected in the better eye and Blind as VA < 3/60 best corrected in the better eye< 3/60 best corrected in the better eye.[6]

Statistical analysis was done using SPSS software

Results

A total of 118 CKD patients were evaluated during our study period. Of them, 74 (62.71%) were males whereas 44 (37.29%) were females with a male to female ratio of 1.68:1. The most common age group in our study was between 31-50 years (39.83%) followed by 51-70 years (30.50%), >70 years (19.49%) and <30 years (10.17%) with a mean age of 55.39 years

(**Table 2**) Visual impairment was found in 10 (8.47 %) cases amongst 118 CKD cases with cataract being the most common cause in 6 (5.08 %) followed by glaucoma in 2 (1.69 %), age related macular oedema in 1 (0.85 %) and diabetic retinopathy in 1 (0.85 %) cases. (**Table 3**) Co- morbidities were present in 83 (70.31 %) cases. Hypertension was the most common co-morbidity seen in 44 (37.28 %), hypertension with diabetes in 24 (4.23 %)and only diabetes in 15 (12.7%)

(**Table 4**) shows role of various visual impairment variables having an impact on CKD. Statistically significant result found for age group 31 to 50 (p=0.0116), CKD patients with only diabetes and and hypertension with diabetes comorbidity (p=0.0002)

Discussion

Chronic Kidney Disease (CKD) is an inevitable terminal event of chronic renal parenchymaldisease due to various causes and is known more for its morbidity and mortality. The effects of the altered functioning of the renal system are reflected in every organ system of the body. CKD refers to a variety of pathophysiological conditions that are linked to poor kidney function and a progressive decline of glomerular filtration rate (GFR).Unless treated, it may lead to grave consequences; CKD leads to impairment of excretory, metabolic and endocrine functions of the kidney that leads to the development of clinical syndrome of uremia which includes features like anemia, metabolic bone disease, neuropathy, myopathy, endocrine abnormalities, hypertension, dyslipidemia, acidosis susceptibility to infections and various cardiovascular diseases. A total of 118 CKD patients were evaluated during our study period. We noted a male pre-ponderance with 74 (62.71%) males and 44 females (37.29%) along with a male to female ratio of 1.68:1. This could be attributed social & cultural norms where females aregenerally neglected and underdiagnosed. Likewise, Navdeep Gupta et al[7], in their study "An eye on chronic kidney disease, "included 106 patients, 69 of whom were males and 37 of whom were females (M: F=1.9:1). Dahal P et al[8] enrolled 300 patients in their study of "Ocular findings in chronic renal failure, Journal of College of Medical Sciences-Nepal," and the male to female ratio was 2.5:1.

The most common age group in our study was between 31-50 years (39.83%) followed by 51-70 years (30.50%), >70 years (19.49%) and <30 years (10.17%). The mean age group in our study was 55.39 years.Our results were similar to those of Gao et al.[9] in their study of "Ocular fundus pathology and chronic kidney disease in a Chinese population," where the average age of 9644 participants was 52.8 16.0 years.

Of the total 118 patients, visual impairment was present in 10 patients(8.47%). Cataract being the most common cause in 6 (5.08 %) followed by glaucoma in 2 (1.69 %), age related macular oedema in 1 (0.85 %) and diabetic retinopathy in 1 (0.85 %) cases.Zhu et al. 10in their study noted that visual impairment in CKD patients was around 7.7% 10Wong et al in the Singaporean Population eye- based study observed greater visual impairment in CKD patients around 36.1%[11] with cataract and retinopathy being the leading causes of visual impairment accounting for 34.9% and 10.4% respectively.

Atherosclerosis, endothelial dysfunction, oxidative stress, inflammation, renin-angiotensin system dysfunction, and Ca-P dysregulation (from vitamin D deficiency, hypocalcemia) are all potential pathogenetic mechanisms of cataract formation in CKD.

Comorbidities were present in 83 (70.31 %) cases. Hypertension was the most common co-morbidity seen in 44 (37.28 %), hypertension with diabetes in 24 (20.33 %)and only diabetes in 15 (12.7%). Similarly, Dahal P et al.[8] et al noted that about 41 % had HTN. However, approximately 32.6% had diabetes in contrast to our study.

Conversely, Manjula Devi et al's[12] study of "ocular findings in patients with chronic renal disease," diabetes and hypertension were found together in 40% of the patients, hypertension in 25%. However, the percentage of only diabetes in 16% was comparable to our study

Visual impairment was seen in 21.27 % cases in the most common age group of 31-50 years in our study with a significant p value (0.0116)

Of the total 74 males, visual impairment was found in 12.16% and a p value 0.692 indicating no significant corelation between gender and visual impairment.

Statistically significant result were also found for, CKD patients with only diabetes and and hypertension with diabetes comorbidity (p=0.0002)

A similar study done in our institution by Sapkal et al.[13] in a total of 158 eyes of 84 patients were examined, showed male preponderance. A greater prevalence in older population was observed then with higher association of HTN in 61 (72.61%) patients as compared to diabetes in 26 (30.9%) patients.

Conclusion

Chronic kidney disease is a rising irreversible multisystem disorder. Diabetes mellitus and hypertension - major disorders associated with chronic kidney disease. High prevalence and strong associations of VI and major eye diseases with CKD in the potentially useful age group 31-50 years. Early screening of this productive population can prevent potential reversible causes of visual impairment thereby improving the quality of life and economic burden. Irreversible vision loss can occur if not detected early improvising the importance of public health initiatives and early eye screening in the high-risk individuals.

Table 1: Distribution of patients with CKD according to age and gender

Sr No,	Age group (Years)	Male Number of Case N (%)	Female Number of Case N (%)	Total
1	**< 30**	8 (6.77 %)	4 (3.38 %)	12(10.17%)
2	**31 to 50**	26 (22.03 %)	21 (17.79 %)	47(39.83%)
3	**51 to 70**	25 (21.18 %)	11 (9.32 %)	36(30.50%)
4	**> 70**	15 (12.71 %)	8 (6.77 %)	23(19.49%)
	Total	**74 (62.71 %)**	**44 (37.29 %)**	**118(100%)**

Table 2: Distribution of patients with CKD according to the cause of Visual Impairment

Visual Impairment	Number of Case (N)	Percentage (%)
PRESENT	**10**	**8.47%**
Cataract	6	5.08 %
Glaucoma	2	1.69 %
Age related Macular Degeneration (ARMD)	1	0.85 %
Diabetic Retinopathy (DR)	1	0.85 %
ABSENT	**108**	**91.53 %**
TOTAL	**118**	**100 %**

Table 3: Distribution of CKD patients according to the comorbidites

Comorbidity	Number of Case (N)	Percentage (%)
PRESENT	83	70.31%
Hypertension	44	37.28 %
Diabetes	15	12.7%
Hypertension with Diabetes	24	20.33 %
ABSENT	35	29.69 %
TOTAL	**118**	**100 %**

Table 4: Visual Impairment variables in CKD

Sr No,	Variables	Visual Impairment		Total	Odds Ratio (95 % CI)	P Value
		Present N (%)	Absent N (%)			
1	**Age (31 to 50 Years)**	10 (21.27 %)	37 (78.73 %)	47 (100 %)	40.0400 (2.2828 to 702.2979)	0.0116
2	**Male Sex**	9 (12.16 %)	65 (87.84 %)	74 (100 %)	5.9538 (0.7279 to 48.6999)	0.0962
3	**Hypertension**	4(9%)	40(91%)	44(100%)	1.1333	0.8530
4	**Diabetes**	8 (10 %)	7 (90 %)	15 (100 %)	57.71 (0.1387 to 10.7668)	<0.0001
5	**Hypertension with Diabetes**	8 (33.33 %)	16 (66.67 %)	24 (100 %)	23.0000 (4.4707 to 118.3252)	0.0002

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There are no conflicts of interest.

Clinical Outcomes of Ocular Surface in Patients Treated with Vitamin D Oral Replacement

Aditi Sharma, (Maj) Abha Gahlot, Divya Singh, Arpit

Abstract

Purpose : To analyze the clinical outcomes of the ocular surface in patients with vitamin D deficiency after oral replacement. Duration of Study : August 2019 to January 2020(6 months).

Place of Study : Department of ophthalmology, Sharda Hospital ,Greater Noida , Uttar Pradesh.

Methods : A total of 40 patients with vitamin D deficiency were enrolled in the study. The patients received 50,000 units of oral vitamin D weekly over a period of 8 weeks. After 8 weeks, 1,500-2,000 units/d were administered for 24 weeks. Eyelid margin score, meibomian gland expressibility score, Oxford grading, Schirmer I test, tear breakup time, tear osmolarity, and the Ocular Surface Disease Index score were evaluated at baseline, and at 8, 12, and 24 weeks.

Results : The meibomian gland expressibility score, Schirmer I, tear breakup time, tear osmolarity, and Ocular Surface Disease Index score showed improvement 8 weeks after vitamin D supplementation . Compared with the pretreatment values, the eyelid margin score and Oxford grading were decreased at week 12 ($p<0.05$).

Conclusion : Vitamin D replacement appears to improve ocular surface in individuals with vitamin D deficiency.

Keywords : Dry eye syndrome; Vitamin D deficiency; Dietary supplements

Introduction

Vitamin D, produced in the skin following exposure to sunlight, is a fat-soluble vitamin. It plays vital roles in cartilage and bone metabolism,[1] as well as immunomodulation.[2]

Vitamin D and the vitamin D receptor regulate genes that contribute to inflammation, immunity, and cellular proliferation.[3] Vitamin D deficiency, a common health problem worldwide, may cause ocular diseases, such as myopia, age-related macular degeneration, diabetic retinopathy, uveitis, and dry eye syndrome (DES).[4,5] Ocular inflammation and increased osmolarity are the leading problems in patients with DES.[6] DES results in discomfort, visual disturbance, and tear film stability that damages the ocular surface.[6] It is assumed to be a localized autoimmune disease.

Recently, it was found to be related to vitamin D deficiency because of its anti-inflammatory action.[7,8,9] DES exerts a negative effect on quality of life, and patients with DES mostly complain of chronic ocular fatigue and pain.[10]

Vitamin D supplementation has been widely used for the treatment of several diseases. It has been reported to strengthen immunity, relieve inflammation, and regulate the cell cycle.[11,12,13] Recently, vitamin D was suggested to play a role in modulating corneal wound healing and enhancing the function of the corneal epithelial barrier.[14,15] Patients with vitamin D deficiency are typically followed up in endocrinology clinics, and most of them are unaware of the eye-related complaints. For this reason, we aimed to investigate the ocular surface health in patients with vitamin D deficiency, evaluate their tendency toward DES, and demonstrate the effect of treatment with vitamin D on the ocular surface.

Methods

The study was performed in adherence to the tenets of the Declaration of Helsinki and approved by the local ethics committee. Forty patients (aged >18 years), newly diagnosed with vitamin D deficiency (serum 25-hydroxyvitamin D levels (<20 ng/mL) in an endocrinology and metabolism

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outpatient clinic, were enrolled in this study. The mean age of the patients was 48.4 ± 11.08 years. There were 34 women and 6 men. Patients with meibomian gland disease, with or without DES were included. However, patients with any serious systemic disease (e.g., primary Sjögren's syndrome) or other systemic rheumatic disease history, vitamin B12 deficiency, pregnancy, breast feeding, history of smoking, current drug use, active ocular infection or allergy, previous eye surgery, and use of contact lenses were excluded.

Prior to the initiation of vitamin D supplementation, the patients underwent a complete ophthalmological examination. The patients received 50,000 units of oral vitamin D weekly, over a period of 8 weeks. After 8 weeks, 1,500-2,000 units/d were administered for 24 weeks.[16] The eyelid margin score (LMS), meibomian gland expressibility score (MGS), Oxford grading, Schirmer I test, tear breakup time (TBUT), tear osmolarity, and Ocular Surface Disease Index (OSDI) score were evaluated at baseline, and at 8, 12, and 24 weeks. The patients were maintained at 21°C and in 40% humid environment for 1 h while completing the OSDI questionnaire. All measurements were performed by one examiner with same order after waiting patients in the same room (E.E.K.). The right eyes of the patients were examined.
LMS was evaluated as follows: eyelid margin irregularity (presence/absence), vascularity of the eyelid margin (presence/absence), occlusion of glands at the lid margin (presence/absence), and displacement of the mucocutaneous junction (presence/absence), scored on a 0-3 scale. MGS was interpreted in accordance with the quality of meibomian gland secretion, scored on a 0-3 scale : (grade 0: clear meibum, easily expressed; grade 1: cloudy meibum, easily expressed; grade 2: cloudy meibum, expressed with moderate pressure; grade 3: meibum not expressible, even with hard pressure).[17]

The Schirmer I test was performed by placing a 5 × 35 mm strip of standard filter paper in the lower eyelid one-third of the distance from the lateral canthus and recording the wetted distance (in mm) after 5 min. TBUT was evaluated by examining the fluorescein-stained tear film with a biomicroscope using cobalt blue light and measuring the time between a blink and the first appearance of a dry spot. After staining with fluorescein, corneal punctate erosion staining was recorded using the standardized Oxford grading system.[18] Measurement of tear osmolarity was conducted using a TearLab osmometer (TearLab Corp, San Diego, CA, USA). Tears were collected from the inferior lateral tear meniscus.

Three consecutive measurements were obtained, and their mean was used for further evaluation. The OSDI questionnaire consists of three main sections concerning ocular symptoms, visual function, and environmental factors.[19]

Statistical analysis

All data are presented as mean ± standard deviation. Paired-sample t-tests were used to compare the eyelid margin, meibomian gland expressibility score, Oxford grading, Schirmer I test, TBUT, tear osmolarity, and OSDI score at baseline, and 8, 12, and 24 weeks after vitamin D supplementation.

The SPSS version 22 for Windows (IBM Corp., Armonk, NY, USA) software was used for all analyses. A ($p<0.05$) denoted statistical significance. With the 40 patients enrolled in this study, we had 80% power to detect an effect size (W) of 0.714 using a two-degree of freedom chi-squared test with $\alpha=0.05$.

Results

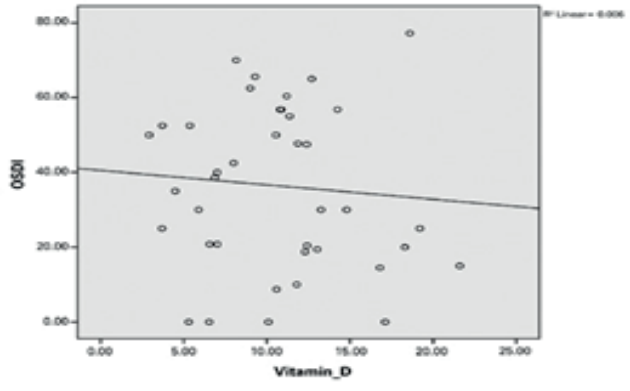
The mean levels of 25(OH)D in the serum at baseline were 10.71 ± 4.59 ng/mL. The correlation between the levels of vitamin D and LMS, MGS, Oxford, Schirmer I, TBUT, tear osmolarity, and OSDI is shown in figure 1.

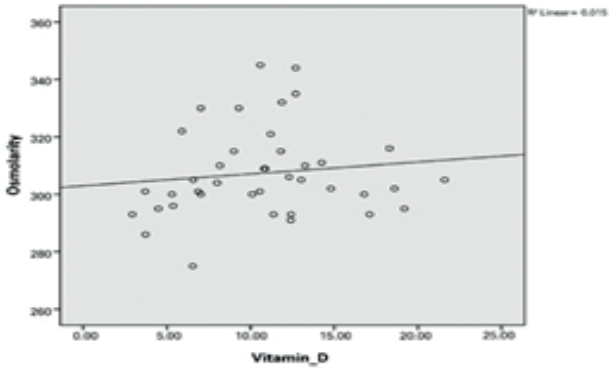
The effects of treatment with vitamin D on ocular surface parameters were evaluated (Table 1). MGS also improved after treatment compared with its level at baseline ($p<0.05$)The Oxford grading and eyelid marginscores decreased significantly after 12 weeks of treatment ($p<0.001$)The Schirmer I test score increased from 13.10 ± 8.01 mm at baseline to 17.33 ± 7.29 mm after 24 weeks ($p=0.002$, $p<0.001$,$p<0.001$) respectively.

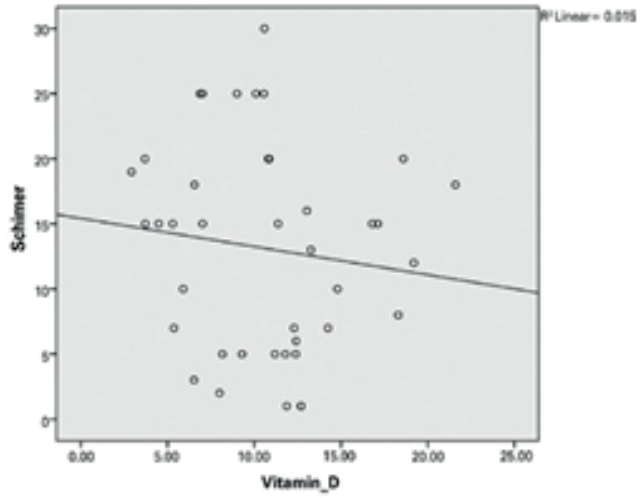
TBUT improved from 5.53 ± 3.12 s to 9.13 ± 3.01 s. Tear osmolarity was 307.4 ± 15.4 mOsm/L at baseline and 302.7 ± 10.6 after 24 weeks (all $p<0.001$)

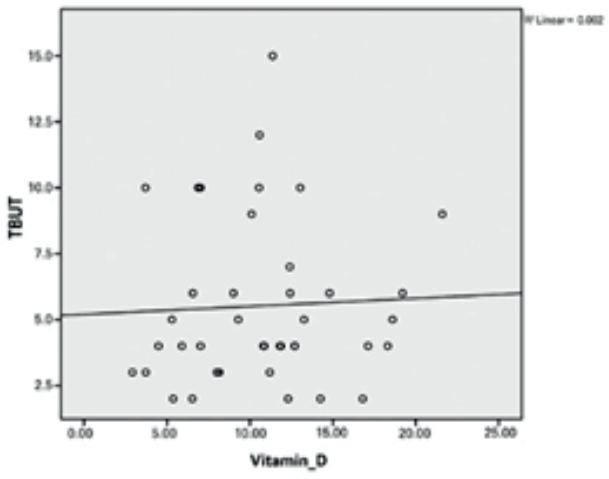
The OSDI score improved throughout the entire study period (all $p<0.001$).

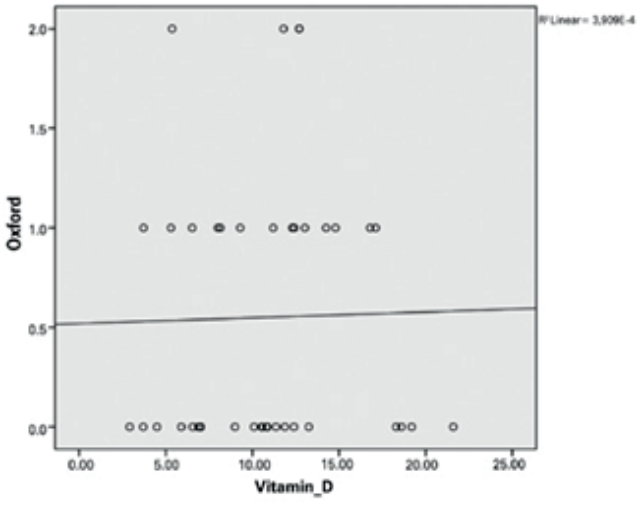
Clinical outcomes of ocular surface in patients treated with vitamin D oral replacement

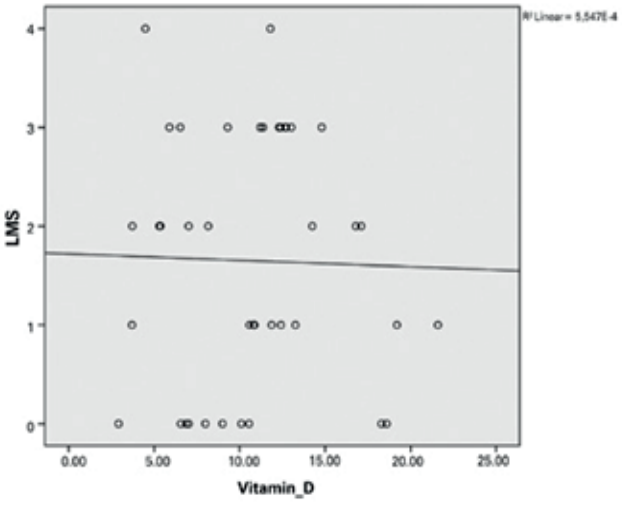


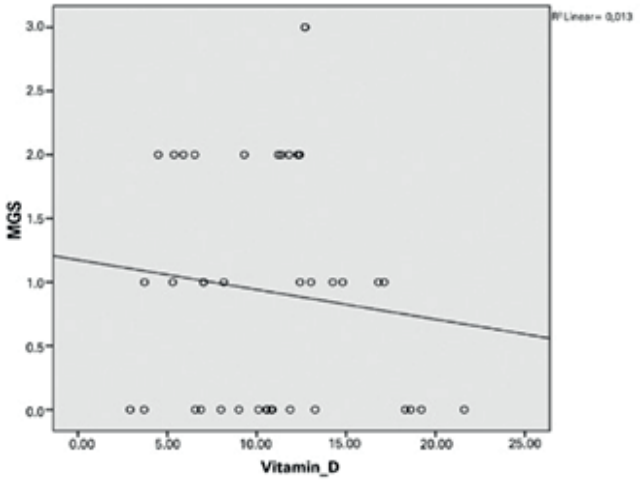












OSDI= Ocular Surface Disease Index; TBUT= tear breakup time; LMS= eyelid margin score; MGS= meibomian gland expressibility score).

Figure 1. Correlation graphs showing the levels of vitamin D and tear function tests.

Table 1. The effects of treatment with vitamin D on ocular surface parameters

	Mean ± SD	After vitamin D supplementation					
	Baseline	8 weeks		12 weeks		24 weeks	
		Mean ± SD	p-value	Mean ± SD	p-value	Mean ± SD	p-value
Eyelid margin score	1.65 ± 1.27	1.60 ± 1.24	0.160	1.33 ± 1.02	0.000*	1.28 ±1.01	0.000*
Meibomian gland expressibility score	0.93 ± 0.94	0.83 ± 0.81	0.044*	0.73 ± 0.78	0.003*	0.70 ± 0.79	0.005*
Oxford grading	0.55 ± 0.68	0.43 ± 0.59	0.058	0.33 ± 0.57	0.002*	0.33 ± 0.57	0.002*
Schirmer I tear secretion test (mm)	13.10 ± 8.01	15.03 ± 7.80	0.002*	16.55 ± 7.26	0.000*	17.33 ± 7.29	0.000*
TBUT (s)	5.53 ± 3.12	6.90 ± 2.72	0.000*	8.30 ± 2.66	0.000*	9.13 ± 3.01	0.000*
Tear osmolarity	307.4 ± 15.4	304.1 ± 11.8	0.000*	303.5 ± 12.1	0.000*	302.7 ± 10.6	0.000*
OSDI score	36.4 ± 22.1	27.40 ± 18.2	0.000*	21.97 ± 13.9	0.000*	19.12 ± 11.9	0.000*

*p<0.05 by paired t-test compared with baselin.TBUT= tear breakup time; OSDI= Ocular Surface Disease Index; SD= standard deviation.

Discussion

In this study, we assessed the ocular surface health of patients with vitamin D deficiency and investigated the effects of treatment with vitamin D on tear function and the ocular surface. The tear function and ocular surface health of these patients showed improvement during the treatment. Vitamin D regulates the levels of calcium and phosphate in the serum, thereby exerting an important effect on bone health. Furthermore, vitamin D deficiency is closely related to certain autoimmune diseases, such as rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, type I diabetes mellitus, and inflammatory bowel diseases.[20,21] Hence, vitamin D supplementation is recommended in the treatment of certain rheumatic diseases.[22] Numerous studies showed an association between vitamin D and inflammatory markers. Vitamin D showed a negative relation with the levels of C-reactive protein and interleukin 6 (IL-6).[23] In another study, vitamin D was suggested to induce the production of IL-10, which inhibits the production of certainproinflammatory cytokines (e.g., IL-1, IL-6, and tumor necrosis factor-α).[24] DES is assumed to be a localized autoimmune disease. Thus, current studies presume that vitamin D plays an important role in DES and ocular surface health, owing to its anti-inflammatory properties.[7,25] In addition, vitamin D induces cathelicidinproduced by corneal and conjunctival epithelial cells and assists corneal and conjunctival wound healing.[26,27] Yin et al. reported the presence of the vitamin D receptor and vitamin D metabolites in corneal epithelial samples.[15] They claimed that 25 $(OH)D^3$ and its active metabolite $1,25(OH)^2D,^3$ enhanced the function of the corneal epithelial barrier. Thus, vitamin D may play a role in the development of DES and wound healing. Yildirim et al. showed that patients with vitamin D deficiency developed DES and showed impaired tear function.[28]

They demonstrated lower scores in the Schirmer I test and TBUT, and higher in the OSDI score in vitamin D deficient patients versus controls. Demirci et al. reported that the TBUT score and Schirmer I test results were significantly lower in patients with vitamin D deficiency versus the control group.[5] Tear osmolarity values, and the OSDI and Oxford grading scores were significantly higher than those reported in the control group. Osmolarity is one of the most objective parameters of DES and contributes to the pathogenesis of ocular surface damage.[7] Osmolarity aggravates tear film instability and negatively affects the ocular surface. In our study, tear osmolarity at baseline was significantly higher than that observed post treatment. However, there was no significant correlation between the levels of vitamin D and osmolarity.

Recent studies established the relationship between vitamin D deficiency and Sjögren's syndrome.[7,29] Bang et al. reported lower levels of vitamin D in patients with Sjögren's syndrome.[30] In addition, they revealed a relationship between Sjögren's syndrome activity and the levels of vitamin D. On the contrary, we did not find an association between the levels of vitamin D and TBUT, Schirmer I, Oxford grading scale, MGS, LMS, and tear osmolarity values. However, following vitamin D replacement, all these parameters showed significant improvement. Recently, the mechanisms through which diet, hormones, and habits influence ocular surface health and tear production are a major concern among ophthalmologists. The use of omega-3 fatty acids has been recommended by the American Academy of Ophthalmology Preferred Practice Pattern guidelines for relieving symptoms and signs in DES patients, despite the lack of evidence. Hence, the Dry Eye Assessment and Management (DREAM) trial investigated the mean change in OSDI, conjunctival staining, corneal staining, TBUT, and Schirmer's test scores of patients with DES receiving n-3 fatty acid or olive oil placebo at 6 and 12 months(31). The results did not show improvements in these parameters in patients receiving omega-3 fatty acids or placebo. In addition, patients in the DREAM study were selected according to the following criteria: presence of conjunctival and corneal staining, TBUT<8 s, Schirmer I test 1-7 mm, and OSDI score 25-80. Although osmolarity is an important finding in DES, the investigators did not report changes in this parameter during active omega-3 supplementation.The DEWS II report defined DES as “a multifactorial disease of the ocular surface

characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles".[32] Moreover, this new report emphasized the role of inflammation in DES.

It is established that vitamin D is a fat-soluble vitamin and possesses anti-inflammatory properties. The ocular surface health of the patients in the present study (TBUT, Oxford, LMS, MGS, osmolarity) improved after vitamin D replacement, on account of its anti-inflammatory properties and effects on the function of the epithelial barrier. It is proposed that vitamin D does not affect the secretion capacity of the lacrimal glands. Therefore, the results of the Schirmer I test were approximately within the normal range of values and showed limited improvement after oral replacement.

This study had some limitations, such as the small sample size and lack of a control group. Patients who were not deficient in vitamin D were not included as a control group in this study. Additionally, we did not investigate the presence of inflammatory markers in the patients. Tear osmolarity, OSDI, and other tear function parameters appear to have improved following vitamin D supplementation.

In conclusion, vitamin D replacement appears to improve ocular surface health in patients with vitamin D deficiency. However, further clinical trials with a large sample size and control group are warranted to define the role of vitamin D.

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There are no conflicts of interest.

Original Article

Improving Quality of Living of Low Vision Patients in Patna, India with Living Space Modifications and Using Household Artefacts

Ashwini Kumar

Abstract

Low Vision (LV) is a condition with irreversible visual loss, decreased visual field, glare, and contrast, and decreased ability to perform daily activities, leading to daily challenges and social withdrawal of people who suffer this condition. A study was conducted in Patna to assess the effectiveness of a combination of household environment modification, use of common everyday household artefacts and counselling to improve the quality of life of patients with low vision. A cross-sectional analysis of 140 LV patients attending a Low Vision Clinic in Patna between November 2021 to February 2022 was undertaken with a telephone prospective follow up after few weeks. Household modifications such as better lighting and alignment of furniture were recommended, and a variety of household artefacts were experimented, used and recommended for use by LV patients to improve the quality of their lives. In addition, simple techniques, user training and counselling were undertaken to improve motivation and confidence. On follow up, 138 patients responded and 2 were lost to follow up. Of them, 81% benefitted from the counselling; 16% benefitted from household modifications, 35% benefitted from household artefacts and 36% benefitted from a non-specific mix of household modifications, artefacts and counselling. Patients' satisfaction to the set of interventions were overall very high and the interventions helped in improvement of overall quality of life and ease in doing day to day tasks.

Keywords : low-vision; household modification; household artefacts; counselling

Introduction

Low vision is defined as visual impairment despite treatment, surgery, or standard refractive correction, but with the potential to use the residual vision.

The World Health Organization describes a person with low vision (LV) as one who has an impairment of visual function, even after treatment and/or standard refractive correction, and has a visual acuity (VA) of <6/18 to perception of light (PL), or a visual field of <10° from the point of fixation, but who uses–or is potentially able to use–vision for the planning and/or execution of a task for which vision is essential.[i]

LV is characterized by irreversible visual loss, decreased visual field, glare, and contrast, and decreased ability to perform daily activities such as reading or writing, and some people who suffer from this condition may be socially withdrawn.

The prevalence of LV in a population-based cross-sectional study in India was reported to be 1.05% in the year 2000, with a burden of 10.6 million people requiring LV services. The magnitude of LV is estimated to be 54.5 million in India.

Materials and methods

The aim of the study was to explore the clinical profile of patients requiring Low Vision Aids (LVA) and assess the effectiveness of common everyday household artefacts to improve the quality of life of patients with low vision. As opposed to optical devices such as tele-lens and other more expensive low vision aids, an attempt was made to explore the availability and experiment the use of household artefacts, readily available or modifiable in a patients' household, to improve the quality of life among patients with low vision.

A cross-sectional analysis of LV patients attending a Low Vision Clinic in Patna between November 2021 to February 2022 was undertaken with a telephone prospective follow up after few weeks. A total of 138 patients who were referred to

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the Low Vision Clinic were screened with Snellen's chart. The Snellen chart was used to assess VA for distance and for near vision. For all cases, BCVA was determined after refraction. Color vision, contrast sensitivity and visual field were done, wherever possible.

A semi-structured interview was undertaken to understand their abilities and dis-abilities around their day-to-day activities and tasks (modified Activity of daily living tool). A general interaction helped determined the condition of their residences and living spaces, the availability of household artefacts in the places of their residence and their ability to modify them for their use. Oral informed consent was obtained from the patients who were explained about their condition and supported to use LVAs The study adhered to all ethical protocols.

Household modifications and artefacts were categorised as per place and need to use to improve quality of life in LV patients. This was combined with simple techniques, user training and counselling to improve motivation and confidence. These were as follows:

- Kitchen and cooking: change of wall color along with source and direction of light. Special or modified utensils for safety and user friendliness, techniques for pouring hot and cold beverages differently.
- Outdoor and Indoor field of vision: M training; walking cane; foldable walking cane with alarm.
- Common household activities and finer work: needle threader, torch light; coloured chocolate beads, mobiles with usage of voice commands.
- Writing and reading: Signature guide
- Money related: Cardboard notex for counting money.

Patients were followed up physically or on phone to assess their improvement and overall satisfaction at a five-point scale; the highest point being for most satisfaction.

Results

Of the 140 patients who attended Low Vision Clinic, 110 (79%) were male and 30 (21%) were female. Of the patients 23% were young (first 2 decades), 55% were mid-aged (3rd to 5th decades), 20% were senior citizens (6th and 7th decade) and 2% were elderly (8th decade or older).

On screening with Snellen's chart after best correction of visual acuity (BCVA), 18% had Perception of Light in RE and 14% in LE; and 14% and 22% hand movement in RE and LE, acuity between and including 6/60 and 6/36 was 55% in RE and 41% in LE, visual acuity between and including 6/18 and 6/6 were 13% in RE and 23% in LE.

On enquiry of activities of daily living, difficulties were faced in viewing and using mobile phones (45%), viewing TV (21%), undertaking outdoor tasks (20%), undertaking household work (12%) , undertaking finer work like writing and reading (10%), undertaking kitchen work (14%) and transport, work or occupation related (25%). (Multiple responses were allowed so the percentages will not add to 100%)

During follow up, 138 patients responded and 2 were lost to follow up, and their responses related to living space modifications and household artefacts were as follows (multiple responses):81% benefitted from the counselling; 8% reported improvement through modifications in household lighting, 8% through changes in kitchen ambience and utensil modifications; among artefacts 10% benefitted by using torch light, 25% benefitted from money counting notex, 9% benefitted from use of walking stick or cane, and 36% benefitted from a non-specific mix of household modifications, artefacts and counselling.

Patient satisfaction to the set of interventions were overall very high with 65% rating 5/5, 32% rating 4/5 and 3% rating 3/5, and they reported a general improvement in overall quality of life and ease in doing day to day tasks.

Discussion and conclusion

Patients with low vision suffer from a complex set of problems ranging from loss of confidence, hesitancy, fear and overall visual and physical inabilities and challenges to live their day to day lives. While they can be from any age range, most difficulties are faced during the productive years of their lives; and in general men access low vision aid clinics more than women. A holistic approach to therapy using a mix of counselling, modification of household ambience and use of household artefacts have a combined result of improving overall patient satisfaction and quality of life.

The author concludes that humble counselling, individual training and use of simple household artefacts, based on specific needs and opportunities, can do miracles in low vision patients who had no hope of living normal and productive lives. The holistic intervention set encompasses the patients home and work spheres of lives, and intervenes across a wide range of daily tasks and accomplishments; and brings an overall improvement in the quality of daily living.

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Ocular Surface Squamous Neoplasia (OSSN)

Chandana Chakraborti, Dew Francis

Abstract

Ocular surface squamous neoplasia (OSSN) is the most common malignancy of the ocular surface and is represented in a wide range of histologic diagnosis ranging from mild epithelial dysplasia to invasive squamous cell carcinoma(SCC). OSSN mimic many simple lesions and have a potential for causing ocular and systemic morbidity and mortality. Although surgical excision is the gold standard for OSSN treatment. Conservative medical treatment with topical chemotherapeutic agents, including Interferon-α2b, mitomycin C, and 5- fluorouracilis steadily gaining popularity. Through this article we have tried to make a comprehensive review on this distinct clinical entity.

Keywords : Ocular surface neoplasia; squamous cell carcinoma; excision biopsy; immunomodulation

Introduction

"Ocular Surface Squamous Neoplasia" the term was first proposed by Lee and Hirst in 1995.[1] It represents a rare spectrum of disease ranging from mild dysplasia to invasive SCC of ocular surface. involving the conjunctiva and cornea occurring mostly in the interpalpebral area mainly at the limbus. The varied malignancies include conjunctival intraepithelial neoplasia (CIN), corneal epithelial dysplasia, Squamous cell carcinoma(SCC), mucoepidermoid carcinoma.[2] The clinical presentation ranges from an ocular mass, excessive irritation, congestion, prominent feeder vessels, and reduced vision.[3] Diagnosis rest on histopathological evaluation of the excised mass and imaging to ruleout infiltrative lesions. High index of clinical suspicion, prompt diagnosis, meticulous management and regular followup postsurgical excision results in excellent outcome. This review describes etiology, risk factors, clinical features, investigations, imaging modalities, treatment options of OSSN.

Incidence

- OSSN is rare, primarily occurs in elderly males. Average age of occurence has been noted to be 60 years(20-80yrs).
- Incidence is between 0.13 to 1.9/100000(8)high incidence in people who liveclose to equator.
- OSSN is the 3rd most common ocular tumour after melanoma and lymphoma.
- People with HIV infection and Xeroderma pigmentosa have onset of OSSN at a younger age with more aggressive course.

Riskfactors And Pathogenesis

- UV B Radiation - people chronically exposed to direct solar light and people doing outdoor occupations are at risk. UB B radiation leads to DNA damage and formation of pyrimidine dimers, p53 mutation that causes conjunctival OSSN[4]
- People with fair skin
- Light iris colour
- People living within 30 degree of the equator.
- Male gender(4)
- Smoking(1)
- Chronic trauma or inflammation
- Exposure to petroleum products
- Use of topical Voriconazole
- HIV (1&2)- young age, severe course, worse prognosis, bilaterality, increased risk of recurrence.
- HPV(16&18) -HPV induced inhibition of the tumour suppressor protein p53 along with sunlight exposure cause UV radiation related DNA damage lead to triggering of the neoplastic transformation of the cell lineage.[3]
- Hepatitis B &C Infections[5]
- Immunosuppression- post organ transplantation/ NHL/ asthma / eczema / atopic diseases.

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The risk factors trigger malignant transformation of the epithelial cells of cornea and conjunctiva.

Clinical Features

- Usual presentation is unilateral vascularized limbal mass located in the inter-palpebral fissure.
- It can also present as a bilateral/ multifocal yellowish pink lesion with dilated tortuous feeder vessels and keratinized plaques[1]
- Signs and symptoms: red eye, ocular irritation, diminution of vision due to astigmatism or involvement of visual axis
- Necrotizing scleritis with severe pain and visual loss in advanced cases.[3]

Clinical features of OSSN

Figure 1a : OSSN with surface keratin and feeder vessels

Figure 1b:A case of recurrent pigmented OSSN

Figure 1c: Corneal OSSN in a case of Xeroderma pigmentosa

Classification

According to morphology

Conjunctival lesions
Nodular, noduloulcerative, gelatinous, leukoplakic, placoid, papillary

Corneal lesions
Preinvasive lesions with mottled ground glass sheet appearance with fimbriated borders
Avascular lesions which are slow growing and prone to recurrence

According to the severity

- **Benign OSSN:** pseudoepitheliomatous hyperplasia, benign hereditary intraepithelial dyskeratosis, papilloma.
- **Pre invasive OSSN:** conjunctival / corneal intraepithelial neoplasms grades.[1-3]
- **Invasive OSSN:** squamous cell carcinoma, mucoepidermoid carcinoma.[3]

Diagnosis

1. Gold standard for the diagnosis of OSSN is histopathological evaluation following an incisional orexcisional biopsy.[6]
2. Impression cytology/exfoliative cytology- identify superficial dysplastic lesions, assess only superficial tissue unable to detect the depth of involvement.
3. HR-OCT- noninvasive, detection of treatment response and subclinical recurrence.
4. Ultrasound Bio-Microscopy (UBM): for detecting the infiltration of adjacent structures due to its higher

penetration and capability to achieve better resolution of the posterior margin of the lesions.[3]

5. Confocal microscopy: reveals cellular details but there is limited field of view[5]

Treatment

Surgical Resection- conjunctival lesions removal carried out following the shield's "no touch" technique to avoid seeding and to get large macroscopically tumour free margins (4mm) followed by cryotherapy to the conjunctival and limbal margins in a freeze and thaw technique.[3]

Corneal components are removed through alcohol kerato-epitheliectomy leaving at least 2 mm tumor free margins

Scleral invasion treated with partial lamellar sclerectomy

Enucleation /orbital exenteration cases with intraocular or periocular invasion

Risk : Extensive surgical excision of limbal OSSN (>6 clock hours) can cause limbal stemcell deficiency. Prevention is by use of intraoperative limbal epithelial transplantation.

The removal of large conjunctival tissue may lead to scarring andsymblepharon despite use of cryopreserved amniotic membrane graft.[6]

Medical

Medical therapy is considered superior to invasive approaches in the treatment of subclinical and microscopic diseases[2]

1. **Topical chemotherapy**
   - **Mitomycin -c (MMC)(0.02%)**
     MOA: Antimetabolite that alkylates DNA and disrupts production of RNA
     Route : topical
     Disadvantage: ocular pain, limbal stem cell loss, punctal stenosis.[4]
   - **2.5-flurouracil(5-FU)**
     MOA: block DNA synthesis by acting as a pyrimidine analog after incorporation into RNA
     Disadvantage: ocular irritation and conjunctivitis.[7]

2. **Topical or local immunomodulation with interferon alpha-2b:**
   MOA: antiproliferative and cytotoxic
   Route : subconjunctival injection or topical eyedrop (1 million IU/ml)
   Disadvantage: costly,need refrigeration.

3. **Topical antiviral medications-cidofovir**

4. **Photodynamic therapy**

Prognosis

Overall OSSN has a good or fair prognosis with less tendency of metastasis and low mortality

Metastasis is mainly regional or distant metastasis is intracranial[4]

Recurrence risk of upto 39% after treatment is reported

And upto 43% with surgery or topical agents treatment[1]

Recurrence occurs more frequently within first 6 months after resection.

Recurrence depends on

- Involvement of surgical margins
- Presence of feeder vessels
- HIV infection status
- Histopathologic grades
- Availability of adjunctive therapy (cryotherapy, immunotherapy, chemotherapy)

A recurrent OSSN can grow rapidly and more invasive and needs to be treated with aggressive medical surgical or combination therapy.[1]

Differential Diagnosis

- Actinic keratosis
- Benign intraepithelial dyskeratosis
- Conjunctival haemangioma
- Keratoacanthoma
- Conjunctival malignant melanoma / nevi
- Pannus
- Pinguecula
- Pterygium
- Pseudoepitheliomatous hyperplasia
- Pyogenic granuloma
- Conjunctival/ tarsal cyst[8]

Conclusion

OSSN is a curable malignancy with a low mortality rate but remains as a major economic and medical burden in the pre-equatorial countries.[2] The improvements in the noninvasive techniques of diagnosis and treatment leads to reduction in mortality. But understaging and misdiagnosis often lead to loss of vision. Surgical removal with or without cryotherapy is still considered the traditional treatment for OSSN.[1] If there is positive margin or incomplete excision local or topical interferon alpha 2b is most effective to minimize recurrence.

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Malarial Retinopathy : Falcinotsofan-see!

Yogya Reddy, Syed Faraaz Hussain, Jesmine Alex, Purva

Abstract

Pregnancy and puerperium period are associated with various ocular changes which can both be physiological and pathological. Pregnancy is known to worsen few conditions whereas, has protective effect on few others. Sometimes it is difficult to diagnose and treat such conditions because of the contraindications and risks associated. However, timely treatment is of utmost importance to prevent serious late complications and permanent visual loss . We report a case of a 21 yr old female in immediate puerperium who presented with sudden bilateral visual loss. Patient was diagnosed as a case of probable VKH and treated with high dose steroids immediately. Patient is being regularly followed up and shows excellent prognosis.

Keywords : VKH; Pregnancy; Puerperium; Uveitis

Introduction

Pregnancy and peurperium associated with transient or rarely permanent ocular changes ranging from a simple change in the refractive error to something as frightening as a cortical blindness.[1] The ocular effects of pregnancy may be divided into physiologic changes, pathologic conditions or modifications of pre-existing conditions. These are believed to be due to hormonal changes, changes in cardiac output and other physiologic changes that occur in the body during pregnancy. Few retinal conditions like eclampsia and pre eclampsia associated retinopathy and central serous chorioretinopathy, PIH induced chorioretinitis e.t.c, are considered unique to pregnancy.[2,3]

Moreover, postpartum optic neuropathies of variable etiologies like demyelinating disease, chiasmal ischaemia, adenohypophysitis are also reported previously.[4]

However, the diagnosis of pregnancy and post partum related visual loss can sometimes be challenging considering the vast spectrum of conditions resulting in the same. This is even intensified by the risks and contra-indications associated with invasive investigations like FFA and also by the patient's and relative's hesitation.

Here we report a case of a 21 year old mother in day 2 post operative period of emergency caeserian section, who presented with sudden bilateral visual loss after the delivery. On thorough examination She was eventually diagnosed as a case of probable VKH. She treated with high dose steroids. Currently she is being regularly followed up and shows excellent prognosis.

Case report

A 21 year post partum female on day 2 of emergency LSCS which done in view of induction of labour, presented with a 2 day history of bilateral blurring of vision along with appearance of black spots bilaterally.

Her distant visual acuity was Finger counting at 2m in both the eyes with a near vision of less than N.36. She had metamorphopsia on Amsler's grid with no appreciation of any plate on Ishihara's colour vision chart in both eyes. Extra ocular muscle movements in both eyes was full, free and painless in all gazes. Anterior chamber of both eyes showed +1 reaction. Anterior segment was otherwise unremarkable in both eyes. However, fundus examination disclosed temporally pale disc bilaterally with attenuated and tortuous blood vessels, multiple hypopigmented spots suggestive of choroiditis with multiple exudative retinal detachments with macular folds and edema in both eyes. [**Fig.1**] Patient was followed up with non invasive investigation like OCT which was suggestive of Subretinal fluid accumulation with septae along with outer nuclear layer showing multiple cystic spaces and choroiditis. [**Fig.2**] USG B-Scan showed choroidal thickening in both eyes. Patient refused to undergo FFA. Despite absence of auditory complaints, she was found to have bilateral sensorineural deafness on clinical testing which

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was later confirmed on Pure tone audiometry. Her general examination was normal. A team of specialists, involving physician, neurophysician, dermatologist, otorhinolaryngologist was consulted. Blood pressure monitoring, Haemoglobin, Complete blood count , MRI Brain with venogram was done. Patient was followed up with all the reports which happened to be normal. On basis of clinical findings, she was diagnosed as a case of "Probable VKH with multiple exudative retinal detachment with macular edema". After due cleareance patient was started on oral high dose steroids tapered gradually. At 1 monthly follow up patient showed excellent prognosis with distant visual acuity of 6/9 in both eyes and near visual acuity of N6 with normal colour vision and amsler's grid. Both eyes were quiet and fundus showed flat retina and normal optic disc with mild pigmentary changes at macula [**Fig.3**]. On OCT, retina appeared to be re attached with absorption of SRF. However, Mild foveal thinning was noticed.[**Fig.4**] Patient is currently on low dose steroids and being followed up regularly.

However foveal thinning is noticed at this stage. Currently patient is on tapering dosage of steroids and being routinely followeed up to monitor the progression of the disease and any possible complications because of steroids.

Abbreviations:VKH-Vogt Koyanagi Harada syndrome. SRF-Sub Retinal

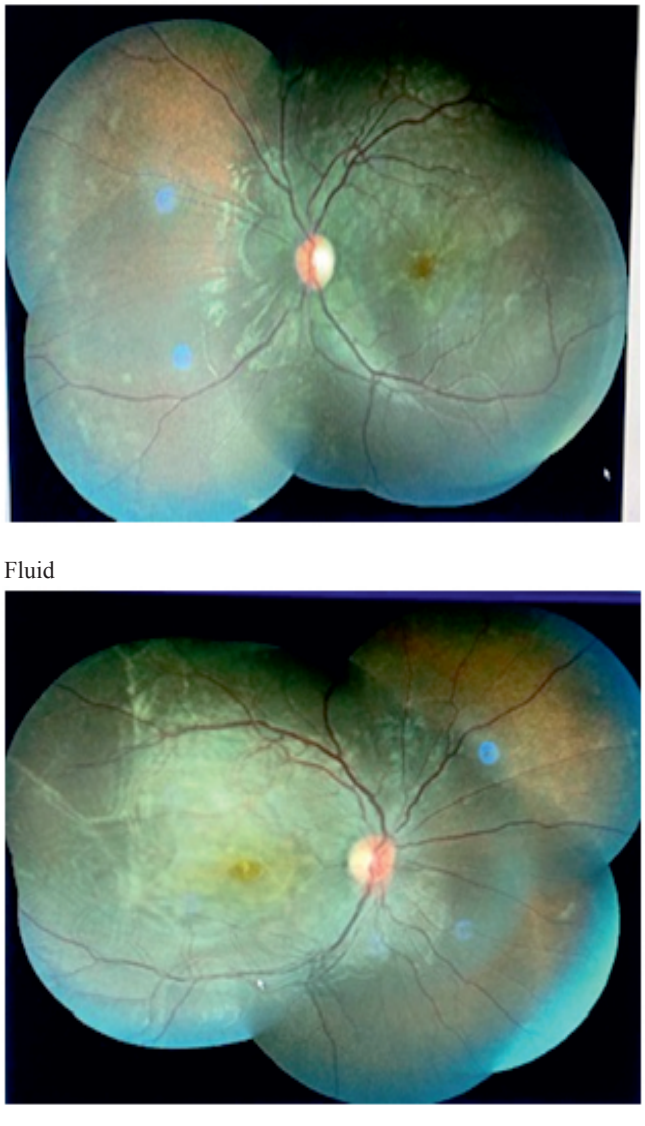

Figure 1: Fundus photo disclosed temporally pale disc bilaterally with attenuated and tortuous blood vessels, multiple hypopigmented spots suggestive of choroiditis with multiple exudative retinal detachments with macular folds and edema in both eyes.

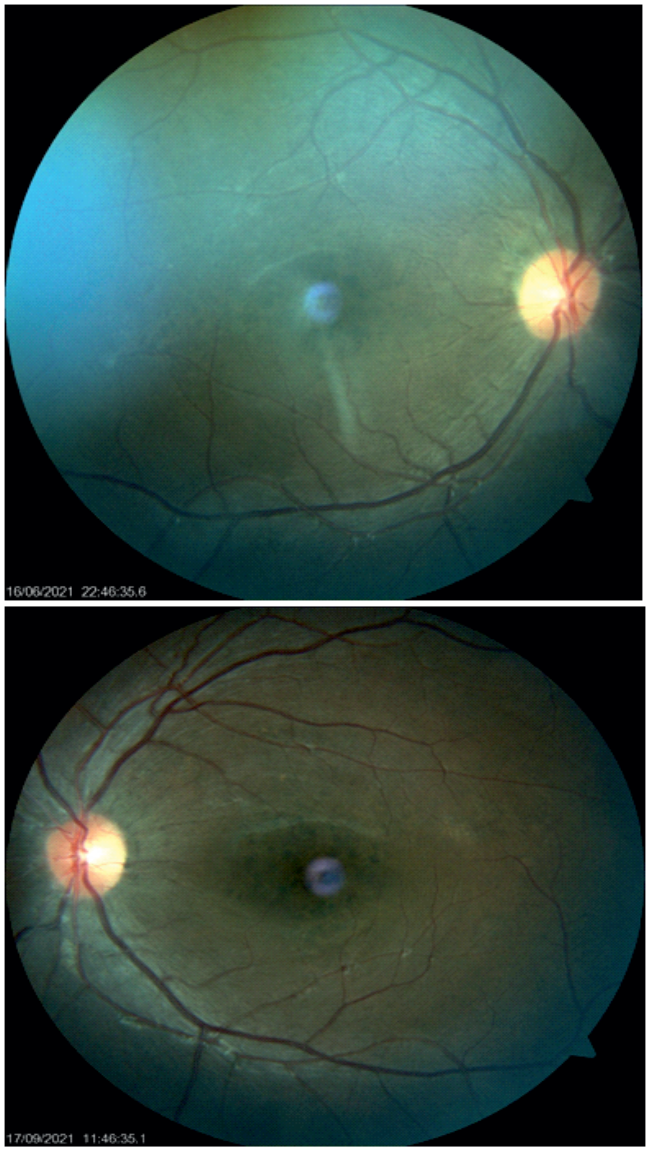

Figure 3: Fundus photo of both eyes were quiet and fundus showed flat retina and normal optic disc with mild pigmentary changes at macula on follow up.

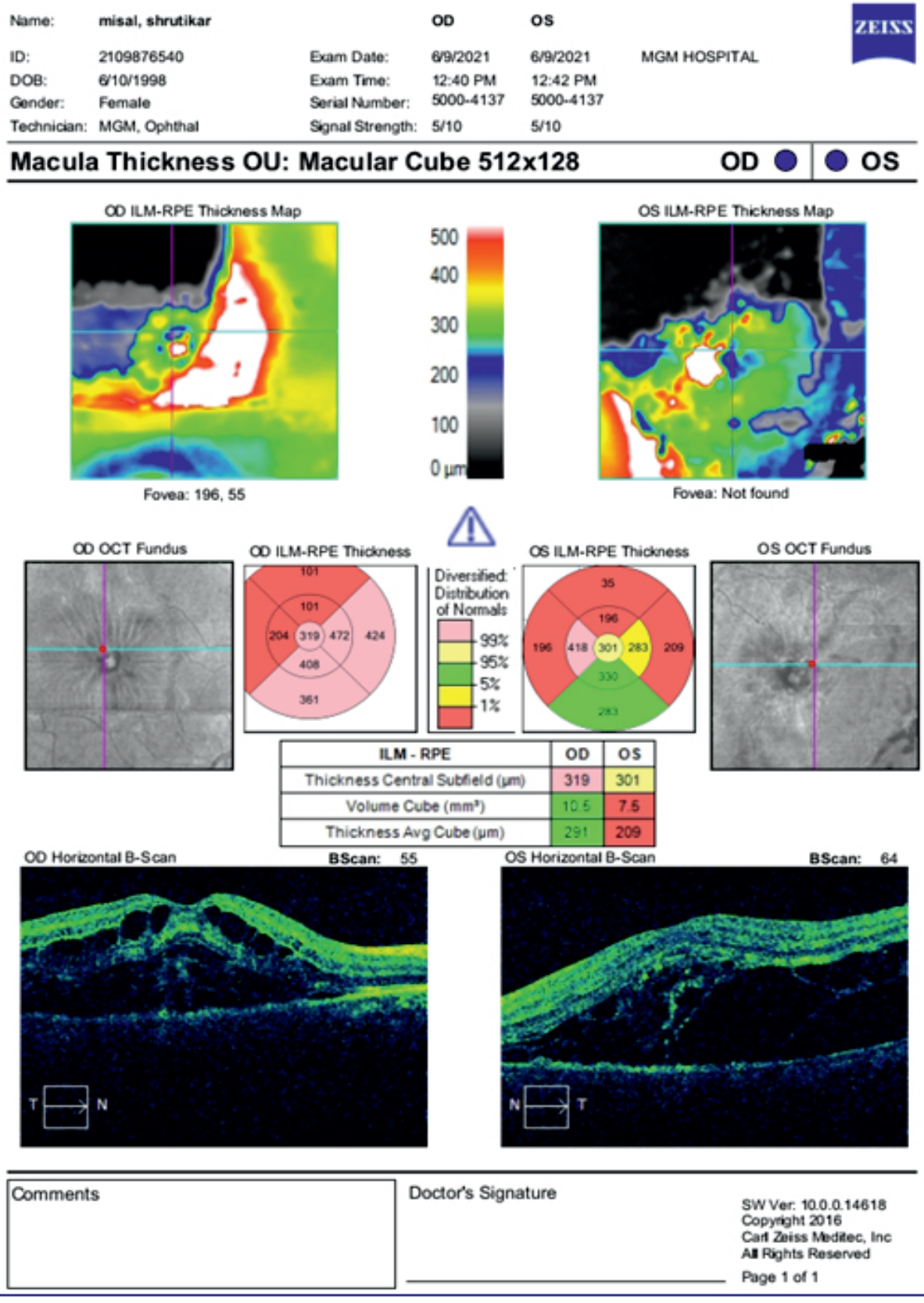

Figure 2: OCT showing Subretinal fluid accumulation with septae along with outer nuclear layer showing multiple cystic spaces and choroiditis.

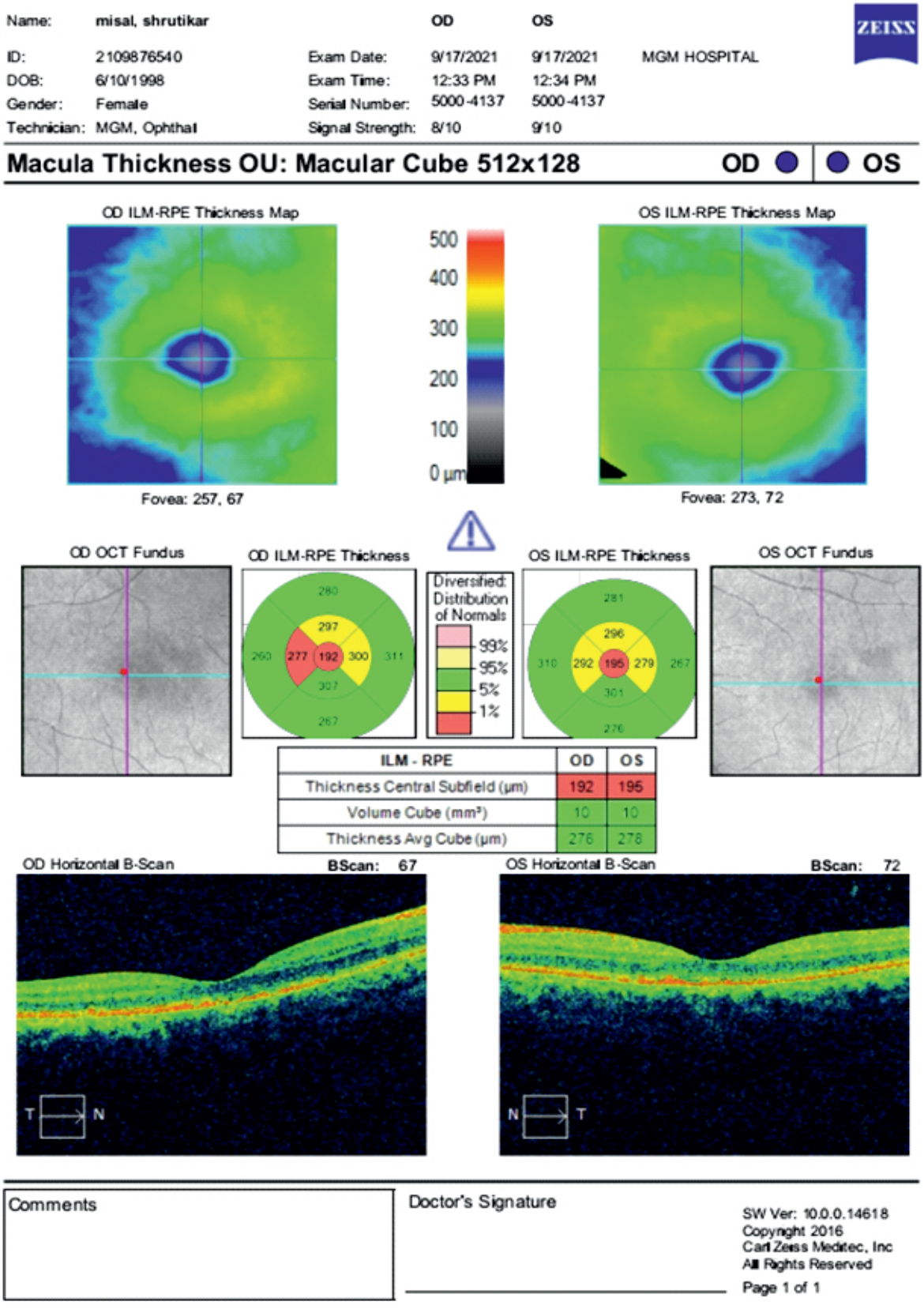

Figure 4: OCT showing re-attached with absorption of SRF with mild foveal thinning on follow up.

Discussion

Pregnancy is known to cause depression of cellular immunity which is reversed during the post partum period. These changes in the cellular immunity during pregnancy can influence the course VKH, as the pathological mechanism of the condition is believed to be cellular autoimmune response to melanocyte containing tissues. The primary organs affected are eyes, ears and CNS with latter involvement of skin. The clinical findings are bilateral panuveitis with serous retinal detachment, pleocytosis in the cerebrospinal fluid (CSF), headache, hearing loss, alopecia, poliosis, and vitiligo depending on the stage of the disease.

However, immunological influence of pregnancy on VKH has not been clarified yet.[5]

Various cases have been reported of patients with VKH in pregnancy.[6,7]

The cases reported previously, majorly showed two patterns. One is where known cases had gone into remission during pregnancy with later recurrences and the others developed VKH during pregnancy and were treated. Various treatment modalities are also proposed including topical and steroids depending on the trimester of pregnancy.[7]

Inspite of steroids being considered as a safe option for VKH in pregnancy, a cases of alleged fetal death and complications in infants have been reported raising a contraversy.[8,9]

This makes alternatives like immunomodulators pertinent.

In a study on the course of noninfectious uveitis during pregnancy and the postpartum period Rabiah and Vitale et al. stated that uveitis exacerbations are commoner in first 4 months of pregnancy and 6 months of post partum period than in later trimesters of pregnancy. They proposed that exacerbations of uveitis are commoner in VKH patients than in Behcet's patients. They also stated that VKH causes flare in first trimester more commonly and Behcents tend to flare up more during the post partum period which is paradoxical in the current case.[10]

We treated our patient with high dose steroids which is considered safe in post partum period.[11]

Neverthless, the long term course of the disease and side effects needs to be monitored.

On thorough review of literature, we found that cases of VKH during post partum period are rarely reported.

Henceforth there is a need to enrich the literature on the current condition.

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There are no conflicts of interest.

Case Report

Optical Coherence Tomography Angiography a Rescue Tool in a Case of Solitary Peripapillary Pigment Epithelial Detachment

Ashwini D Patil, Sachin V Mahuli

Abstract

Background : SD-OCT and OCTA are the new diagnostic modalities in suspected cases of polyp related activity where angiography cannot be done. OCTA can guide in diagnosing and monitoring response to treatment. Materials and Methods : A study of polypoidal choroidal vasculopathy (PCV) was done in a hypertensive patient with a history of transient ischaemic attack and on blood thinners. On fundus examination, solitary peripapillary pigment epithelial detachment (PED) and overlying neurosensory detachment (NSD) temporal to disc seen. SD-OCT and OCTA was done since the patient was unfit for angiographic procedure. It revealed peripapillary polyp and abnormal vascular network (AVN). 3 loading doses of intravitreal brolucizumab injection was given. Results : SD-OCT showed complete resolution of PED and NSD but there was outer retinal defect. OCTA showed mild regression of polyp and AVN following treatment. Conclusion : With the help of SD-OCT and OCTA, we could diagnose this case as peripapillary polyps and AVN and treated early with intravitreal anti VEGF injections there by preventing blinding complications secondary to polyps.

Key words : OCT Angiography; Solitary Peripapillary PED

Risk Factors

55 year old south asian female presented with complaints of seeing black shadow in the right eye for 3 days. She was a known case of hypertension and on treatment with blood thinners for 5 years, she also had an episode of transient ischaemic attack 4 years ago. Her best corrected visual acuity was 6/6 snellen in both eyes. Right eye anterior segment examination was normal,fundus examination revealed solitary peripapillary pigment epithelial detachment (PED) and overlying neurosensory detachment (NSD) temporal to disc(Fig 1), disc was healthy, no signs of inflammation noted, rest fundus examination was not remarkable and examination of left eye was normal. Patient could not get fitness for angiographic procedure for invastigating the cause, hence we did spectral domain optical coherence tomography (SD-OCT) and OCTA, automated segmentation was done, this confirmed above findings (Fig 2.A), it revealed localised pachychorid features (Fig 2.B). OCTA showed multiple polyps (Fig 2.C1&C2) and abnormal vascular network in avascular complex (AVC) (Fig 2 D1&D2) and an area of choroidal ischaemia (Fig 2 E1&E2). Based on above features peripapillary polyps and AVN was made and advised 3 loading doses of intravitreal brolucizumab injection 6mg in 0.05ml. Following loading doses patient was asymptomatic, vision was 6/6 snellen , SD-OCT (Fig 3A) showed complete resolution of PED and NSD but there was outer retinal defect, OCTA showed mild regression of polyps (Fig 3 B1&B2), mild regression of AVN (Fig 3 C1&C2), choroidal area showed the presence of seigrist streak area with feeder vessel for polyps and AVN (Fig 3 D1&D2). Since there was no complete regression of polyps and AVN and patient being asymptomatic has been advised injection brolucizumab on treat and extend basis.

Discussion

Polypoidal choroidal vasculopathy(PCV) develops when there occurs aneurysmal dilatation of the terminal ends of the vascular network between RPE and BM. Alternatively, the polyps may develop in the absence of CNV due to chronic choroidal venous hypertension.[1] Based on OCT[2,3] PCV can be suspected if there is any one of following features.

1. Thumb like polyp/ sharp peaked polyp.
2. Tomographic notch in PED.
3. Hypo reflective lumen surrounded by hyper reflective ring attached to undersurface of PED.
4. Double layer sign: presence of two hyper reflective lines on SD OCT.

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The presence of normal/increasesss thicknesss (pachychoroid) on ED-OCT provides supportive evidence of PCV and can be used to differentiate from AMD, in which choroid is thin.[4] According to Giridhar Anantharaman et al the updated treatment protocol for peripapillary polyp is the thermal laser photocoagulation with anti VEGF. Since we could not perform invasive angiography procedure could not do laser photocoagulation, hence we gave 3 loading doses of anti VEGF injections and we could see good response in the form of resolution of exudation from polyps and AVN, though complete regression was not seen and patient being asymptomatic decided to go ahead with intravitreal anti VEGF injection alone as treat and extend regimen.

Conclusion

With the help of SD-OCT and OCTA, we could diagnose this case as peripapillary polyps and AVN and treated early with intravitreal anti VEGF injections there by preventing blinding complications secondary to polyps. We also could monitor the activity of polyps and AVN and their response to treatment. Hence, in all those cases where we suspect polyp related activity and angiography cannot be done, OCTA can guide us in diagnosing the condition and also monitoring response to the given treatment.

FIG 1: Fundus photo showing peripapillary PED with blue arrow and NSD with arrow head.

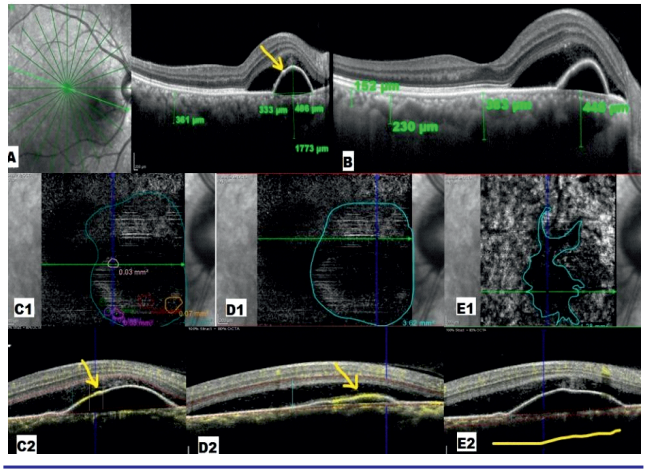

FIG 2. Pre injection images: A)SD-OCT- B scan, radial scan along the maximum height of notched PED(yellow arrow) and NSD. B) Localised pachychoroid features under PED and NSD. C1 and C2) Enface OCTA of avascular complex(OPL-BM) in PED area showing multiple hyper-reflective dots encircled with circles suggestive of polyps and yellow arrow marking polyp in corresponding notched PED in the OCTA B scan respectively. D1 and D2) Enface OCTA of avascular complex showing abnormal vascualr network within blue outlined area and corresponingly vascular flow seen under shallow irrgeular PED marked with yellow arrow in OCTA B scan respectively. E1 and E2) Enface OCTA of choroidal area(60µ from BM-140µ from BM) under PED showing hypovascular area within blue outlined area and low vascular flow signal in corresponding OCTA B scan marked with yellow line area suggestive of seigrist streak.

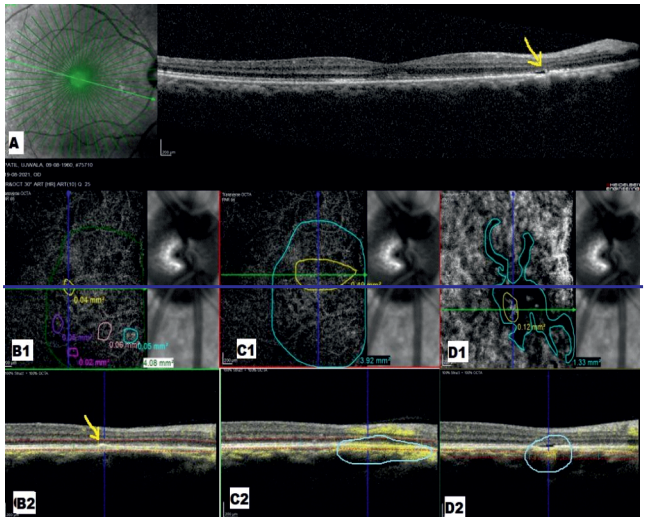

FIG 3. Images taken following 3 loading doses of Brolucizumab injection: A) SD-OCT B scan , radial scan along the previous PED and NSD area shows a small outer retinal defect marked with yellow arrow. B1 and B2) En face OCTA of avascular complex(OPL-BM) shows slightly regressed polyps in encircled areas and corresponding OCTA B scan shows small PED marked with yellow arrow respectively. C1 and C2) En face OCTA of avascular complex showing slightly regressed abnormal vascular network within blue outlined area and corresponding OCTA B scan shows vascular flow signal in RPE and BM layers outlined with blue colour respectively. D1,D2) En face OCTA of choroidal area(60µ fromBM-140µ from BM) shows hypovascular area marked in blue outline with hyper reflective dot area encircled in yellow colour and corresponding OCTA B scan shows low vascular signal and localised vascular flow marked in blue outline suggestive of feeder vessel for AVN and polyps in seigrist streak also we can see a small outer retinal defect overlying the feeder vessel may be a point of entry of AVN into VC.

OPL- outer plexiform layer, BM- Bruch's membrane, RPE- retinal pigment epithelium, AVN- abnormal vascular network, AVC- avascular complex.

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Pseudophakic Bullous Keratopathy Secondary to Anterior Chamber Fixation of Single Piece PMMA Posterior Chamber Intraocular Lens

Raikar Shreya U, Nayak Shinkre Noopur D, Toprani Alpesh N

Abstract

A 70 year old male presented with a 3 months history of symptoms suggestive of Pseudophakic bullous keratopathy (PBK) with diminution of vision since 3 years in the left eye. Examination revealed a hazy edematous cornea with presence of a single piece PMMA PCIOL implanted in the anterior chamber with a superior peripheral iridectomy and vision of light perception and IOP of 32 mm Hg in the left eye. Patient was initially managed medically with systemic and topical Anti Glaucoma medications and PCIOL explantation with anterior vitrectomy was performed, once target IOP was achieved. 3 weeks post-op, vision was light perception and IOP was 12mmHg in the left eye. Fundus examination revealed optic atrophy. Whereas implantation of PCIOL in anterior chamber can be a cause for PBK, in this case, however, it was a vitreous blob blocking the PI and causing the secondary glaucoma and PBK with the anterior chamber fixation of PCIOL playing a contributory factor in the development of PBK.

Keywords : Pseudophakic bullous keratopathy; posterior chamber intraocular lens (PCIOL); Anterior chamber fixation; Raised IOP; Corneal edema; Optic atrophy

Introduction

Pseudophakic bullous refers to the development of irreversible corneal edema after cataract surgery and intraocular lens implantation due to endothelial trauma,followed by progressive stromal and epithelial edema. The epithelial edema leads to formation of bullae, hence the name bullous keratopathy. Insertion of anterior chamber intraocular lens is one of the most common causes for developing PBK in the long run.

Case Report

A 70 year old male presented to our OPD with chief complains of photophobia, redness, watering, ocular pain and discomfort of the left eye since 3 months. He gave a gradual history of DOV in the left eye since 3 years. Patient underwent left eye cataract surgery 15 years back. No H/o any systemic illness.

On examination in the right eye BCVA was 6/6 , N6 and IOP was 16mm Hg and left eye vision was PL + and IOP was 32 mm Hg by GAT. Anterior segment examination revealed Right eye was within normal limits (**Fig 1**) while left eye there was circumciliary congestion , corneal was hazy due to corneal edema, presence of a single piece PMMA PCIOL in the anterior chamber with a superior peripheral iridectomy at 12 o'clock, pupil was round and non reactive (**Fig 2**). Fundus examination of RE was within normal limits and LE view was hazy.

Fig1 : Right eye

Fig2 : Left eye–corneal edema with PCIOL in anterior chamber

BCL was inserted in the left eye and patient was medically managed initially with Tablet Acetazolamide SR 250mg QID for 3 days, Moxifloxacin – prednisolone eye drops QID, Homatropine eye drops BD, Brimonidine –Timolol eye drops BD and Sodium chloride 5% eye drops five times. After 7 days of treatment his Left eye cornea had cleared and IOP was 20 mm Hg (**Fig 3**).

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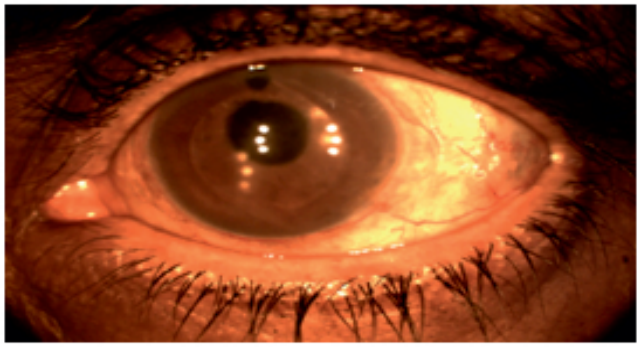

Fig 3 : Clear cornea after medical management

He was planned for IOL explantation of the left eye under peribulbar under guarded visual prognosis. On table it was seen that a vitreous blob was blocking the superior PI. IOL was explanted through the corneo – sclera tunnel with a 6mm sclera incision followed by anterior vitrectomy with planned surgical aphakia. Immediate post operative his vision was PL + and IOP was 22mm Hg (**Fig 4**). At 3 wks post operative his vision was PL +, IOP was 12 mm Hg, cornea was clear (**Fig 5**) and fundus examination showed a pale disc suggestive of optic atrophy due to raised IOP.

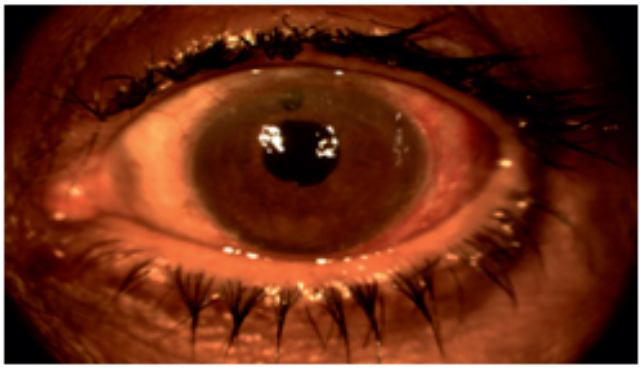

Fig 4 : Immediate post op

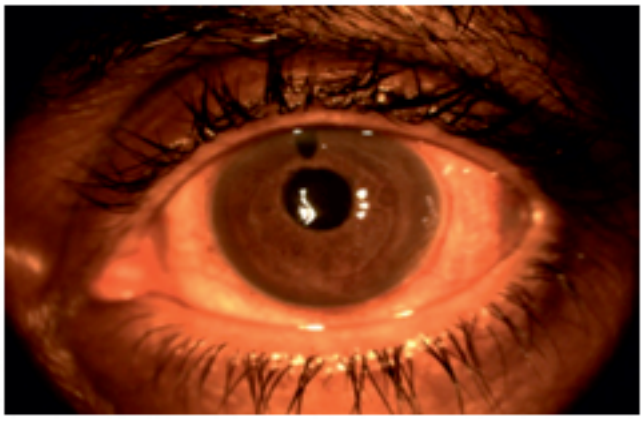

Fig 5 : 3 wks post op. Impression of PCIOL on iris

Discussion

Kelman Multiflex ACIOLs design is for 4 point angle fixation with anterior vault for adequate pupillary clearance while the single piece PMMA PCIOLS have rounded haptics for in the bag/ sulcus placement and haptics angulated anteriorly for pupillary clearance and close contact with PC. PCIOLs in AC can cause fibrosis of the angle structures leading to glaucoma and forward angulation of PCIOL can cause corneal problems. Hence placement of PCIOLs in anterior chamber causes blockage to the aqueous outflow along with pupillary block causing raised IOP. In this case, the culprit was the vitreous blob, blocking the PI and causing a rise in IOP thereby leading to corneal decompensation and PBK. However, the presence of Single piece PMMA PCIOL in the AC also contributed in the decompensation of the cornea, in the long run.

Conclusion

Implantation of PCIOL in anterior chamber is not recommended due to its complications in the long run. Hence use of ACIOLs or sutured/glued SFIOLs is preferable in cases where there is no capsular support to place the IOL.

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CMV Retinitis in Association with HIV: a Case Report and Review of Literature

Preeti Singh, Santosh Kashyap, Swapan Samanta

Abstract

CMV retinitis is the commonest (46%) ocular opportunistic infection in AIDS patients. A 41 years old female presented with gradual painless diminution of vision in both eyes for 15 days with history of vomiting, abdominal pain, glossitis and angular cheilitis. She had history of HAART for 1 month. On fundus examination there were soft exudates superior to disc with hemorrhages in the right eye while in left eye there were soft exudates, hemorrhages and areas of retinal necrosis in macula. The first reported case of CMV retinitis in HIV patient from Raigarh District, Chhattisgarh.

Keywords : CMV retinitis; AIDS

Introduction

CMV Retinitis has been the most common opportunistic ocular infection in AIDS patients representing about 90% cases of all infectious retinitis in this patient population leading to varying degree of visual loss.[1]

Opportunistic infections like CMV retinitis occur typically with a significantly reduced CD4 T-cell counts<50 cells/mm3.[2]

Case report

A 41 years old female came to OPD with gradual painless diminution of vision in both eyes for 15 days (**Fig 1**). The patient had history of abdominal pain, vomiting for 5 days and had history of glossitis and angular cheilitis for which she was taking treatment. Shewas on HAART for 1 month. His presenting visual acuity in the right eye and left eye was 6/18 and counting finger 2 meter respectively not improving with glasses. The intraocular pressure was 18 mmHg in both eyes taken with non contacttonometer. The pupillary reaction was normal and anterior segment was unremarkable on slitlamp biomicroscopy. On fundus examination, there were hemorrhages over disc extending superiorly and soft exudates in the right eye while in left eye, soft exudates, hemorrhages and areas of retinal necrosis in macula with cherry red spot like pictureseen (**Fig 1: a &b**). The overlying vitreous and peripheral retina was normal.

We provisionally diagnosed this case as HIV associated CMV retinitis because of its fundus picture and association with systemic involvement.

Patient was then started on oral gancyclovirfluconazole, topical nepafenac in both eyes andadmitted to medicine ward for management.

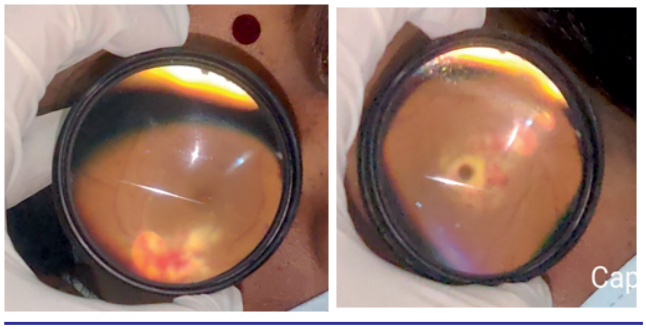

Figure1a:Hemorrhages over disc extending superiorly and soft exudates in the right eye

Figure1b:Soft exudates ,hemorrhages and areas of retinal necrosis in macula with cherry red spot like picture at macula

Discussion

CMV retinitis is the commonest (46%) ocular opportunistic infection in AIDS patients.[3] In Chhattishgarh though there are no such definite publication on the pattern of ocular complication amongst the HIV patient as well as the prevalence of CMV Retinitis in HIV affected individuals, but

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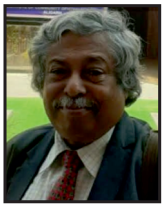

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as per the discussion with RIO, Raipur, Chhattisgarh, there is a monthly attendance of at leastone new case in this apex centre of the state (personal communication).

It occurs in three different clinical forms. First is the classical form also called the pizza or cottage cheese with ketchup retinopathy which is characterized by confluent areas of retinal necrosis with hemorrhages in the posterior pole. The second form is characterized by granular peripheral retinal lesions with little or no hemorrhages. The third form is called frosted branch angiitis, which is characterized by marked vascular sheathing. Loss of vision in CMV retinitis can occur due to the direct involvement of macula or optic nerve, RD, and also due to immune recovery uveitis. Widespread use of HAART has caused a change in the natural history of CMV retinitis, leading to marked reduction in the incidence of this condition.

Conclusion

To our knowledge this is the first case reported in Raigarh, Chhattisgarh.

Proper diagnosis and effective treatment can keep a good visual outcome. Unfortunately everything depends upon regular follow up which is not up to the mark in Raigarh due to the lack knowledge and attitude towards positive eye health care.

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INDIAN JOURNAL OF COMMUNITY OPHTHALMOLOGY (IJCO)

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Sample references:
1. For journal articles:

Koranyi G, Seregard S, Kopp ED. Cut and paste: a no suture, small incision approach to pterygium surgery. Br J Ophthalmol. 2004; 88: 911-4.
Panda A, Kumar S, Kumar A, Bansal R, Bhartiya S. Fibrin glue in ophthalmology. Indian J Ophthalmol. 2009; 57: 371.
Kurian A, Reghunadhan I, Nair KG. Autologous blood versus fibrin glue for conjunctival autograft adherence in sutureless pterygium surgery: a randomised controlled trial. Br J Ophthalmol. 2015; 99: 464-70.
Koranyi G, Seregard S, Kopp ED. The cut-and-paste method for primary pterygium surgery: long-term follow-up. Acta Ophthalmol. 2005;83:298-301.
Malik KP, Goel R, Gupta A, Gupta SK, Kamal S, Malik VK, et al. Efficacy of suture-less and glue free limbal conjunctival autograft for primary pterygium surgery. Nepal J Ophthalmol. 2012;4:230-5.

2. Reference to a book
Authored book (all chapters written by same authors)
Parija SC. Textbook of Medical Parasitology. 3rd ed. New Delhi: All India Publishers and Distributors. 2008. page 32-3.
Chapters in an edited/compiled book
Nesheim M C. Ascariasis and human nutrition. In Ascariasis and its prevention and control, D. W. T. Crompton, M. C. Nesbemi, and Z. S. Pawlowski (eds.). London: Taylor and Francis. 1989: page 87–100.

3. Internet resource
FDA data on TECNIS® Toric 1-Piece IOL [Internet]. [cited 2020 Apr 7]; Available from: https://www.accessdata.fda.gov/cdrh_docs/pdf/P980040S039c.pdf
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