Review Paper

COVID-19 Related Eye Manifestations: A Narrative Review

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ABSTRACT

Background: The COVID-19 pandemic has affected human beings in many ways. The presence of SARS-CoV-2 in conjunctival cells and its secretion has been reported in the literature. In addition, there were significant reports of ocular complications that coincide with COVID-19 disease. This study aims to evaluate the COVID-19 symptoms associated with ocular manifestations.

Context: Evidence Acquisition: We conducted a literature search with the keywords of "SARS-CoV-2," "COVID-19," "nCoV-19," "SARS," "MERS," and "severe acute respiratory syndrome coronavirus-2" combined with key terms of "eye," "ocular," "ophthalmologic," "ophthalmic," "conjunctivitis," "conjunctiva," "uveitis," "optic," "retina," "retinitis," "cornea," "scleritis," and "glaucoma" in LitCovid hub, PubMed, Scopus, ISI Web of Sciences, Cochrane, and Embase databases, as well as non-review articles.

Results: The COVID-19 pandemic and its lockdown has drastically changed people's lifestyles and health. The pandemic has also affected medical performance in various fields, including ophthalmology. This study summarized some findings in several areas of ophthalmology, including: 1) The surface of the eye (conjunctivae, cornea), 2) Intraocular manifestations (uveitis, retinitis), 3) Neurological features of the eye, 4) COVID-related ocular coagulopathy (retinal vein occlusion), 5) Ophthalmological follow-up failure due to lockdown, 6) Rare manifestations, and 7) Diagnostic and protective measures. Data collection about the ophthalmological experience was done during this respiratory viral infection pandemic, and the most relevant literature was reviewed.

Conclusions: Data findings showed a wide range of ocular manifestations and complications associated with COVID-19 and its pandemic. Conjunctivitis is the most common ocular manifestation of COVID-19.

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1. Context

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is the etiology of novel coronavirus disease 2019 (COVID-19). The disease first emerged in December 2019, and the World Health Organization (WHO) declared it a pandemic on March 11, 2020. The number of confirmed cases of COVID-19 was more than 122 million by March 21, 2021, and it was associated with more than 2.7 million deaths worldwide (1).

The coronavirus is a single-stranded RNA virus and enters the target cell via binding its spike (S) protein to angiotensin-converting enzyme 2 (ACE2), which is facilitated by type 2 transmembrane serine protease (TMPRSS2). The binding results in substantial structural change in the S protein, which leads to the fusion of viral and host cell membranes and coronavirus entrance (2). Thus, the presentation of ACE2 and TMPRSS2 is essential for viral entry and infection. They may also be associated with the activity of the cysteine proteases cathepsin B and L (CTSB and CTSL). They are widely expressed in the human body (3). The nose, heart, intestine, esophagus, testis, and kidneys are high-risk organs for infection due to the high expression of ACE2 and TMPRSS2 in these organs. Brain, gall bladder, and fallopian tubes may also be sensitive to the COVID-19 infection. ACE2 receptor expression as a mediator of SARS-CoV-2 in the eye is reported in the conjunctiva, limbus, cornea, retina, and aqueous humor. Overall, respiratory, gastrointestinal, and genitourinary systems have the highest risk for COVID-19 infection (4). T cells, along with antigen-presenting cells and macrophages, are the main immune mediator against SARS-CoV-2 (5).

The most common transmission route of this virus is respiratory droplets during direct close contact. Although many people experience asymptomatic infection (6), symptomatic patients show various clinical manifestations within a mean incubation period of 5 days. Most of them have mild manifestations; meanwhile, a considerable percentage of them experience severe or critical conditions (which are reported to be 14% and 5%, respectively). The most frequent symptoms of admitted patients are fever, dry cough and dyspnea, fatigue, nausea, vomiting or diarrhea, and muscle pain. COVID-19 complications consist of dysfunction in various organs, including blood, heart, brain, kidney, and liver. Reverse transcription PCR analysis of respiratory samples is the COVID-19 standard diagnostic method, and the management of the disease consists of supportive treatment as well as antiviral, anti-inflammatory, and immunologic therapy (7).

The presence of SARS-CoV-2 in tear and conjunctival secretion has been reported in the literature. Many reports demonstrated ocular manifestations of COVID-19, especially symptoms associated with the conjunctiva. However, with the promising results of COVID-19 vaccine administration (8, 9), the pandemic is likely to subside soon in many countries. This study aimed to search the available literature regarding the effects of COVID-19 and its pandemic on the eye to show the different aspects of ophthalmologic experience in this era and its respiratory viral pandemic.

Ocular manifestations of COVID-19 in children

Children account for 1% of cases of COVID-19, with a significantly reduced risk of morbidity and mortality (10, 11). Fever and cough are the most common clinical findings among the active COVID-19 children (12). Regarding COVID-19-associated ocular manifestations in children, few studies have been published so far. In a retrospective cross-sectional study of 216 hospitalized children in Wuhan (China) with a laboratory-confirmed COVID-19, nearly one-quarter (49 participants, 22.7%) had ocular manifestations, including conjunctival discharge (27 cases, 55.1%), eye rubbing (19 cases, 38.8%), conjunctival congestion (5 cases, 10.2%), ocular pain (4 cases, 8%), eyelid swelling (4 cases, 8%) and tearing (2 cases, 4%). The median duration of ocular symptoms was 7 days. Cases with systemic symptoms, including fever or cough, were more likely to develop ocular symptoms, which were mild and self-limited (13) (Table 1).

Ocular transmission

Studies have identified the presence of the virus in the tear film and conjunctival secretion through a real-time reverse transcription-polymerase chain reaction (RT-PCR) analysis of SARS-CoV-2 in conjunctival swabs and tear samples of COVID-19 patients. In a study by Wu et al., almost three-fourths of COVID-19 patients had a positive RT-PCR for nasopharyngeal swabs, whereas only 5% showed positive conjunctival samples (14).

Although the rate of PCR positive conjunctival or tear samples is very low, and the virus was detected more in those with ocular involvement, cases of virus detection in COVID-19 patients without any ocular symptoms have been reported (15). So, the virus may spread from the conjunctiva of COVID-19 infected patients with no ocular symptoms. The low rate of positive PCR in con-

junctival swabs seems to be due to low sensitivity of the test, late sampling (sampling after the resolution of ocular symptoms), low volume of conjunctival secretion sample, unsui sampling technique, and washing of the virus by tears (16, 17). Thus, the virus may be present in conjunctiva and tears of COVID-19 patients without a positive PCR. Since SARS-CoV-2 can be transmitted through conjunctival contact, protecting eyes and less hand-to-eye contact is essential in disease prevention.

2. Evidence Acquisition

We conducted a literature search with the keywords of "SARS-CoV-2," "COVID-19," "nCoV-19," "SARS," "MERS," and "severe acute respiratory syndrome coronavirus-2" combined with the "eye," "ocular," "ophthalmologic," "ophthalmic," "conjunctivitis," "conjunctiva," "uveitis," "optic," "retina," "retinitis," "cornea," "scleritis," and "glaucoma" in LitCovid hub, PubMed, Scopus, ISI Web of Sciences, Cochrane, and Embase databases from December 1, 2019, to April 2021 and studied the English non-review articles. We included cross-sectional, case reports, case series, and case-control cohort studies about the ocular manifestations in COVID-19 patients. We excluded research studies such as commentaries, editorials, letters to editors, and reviews.

Two authors independently evaluated the quality of included studies by the Joanna Briggs Institute critical appraisal tool (18). Reviewers resolved the disputes with the judgment of the senior author. Then the findings were summarized in several areas as follows:

1. Ocular surface (conjunctivae, cornea),

2. Intraocular manifestation (uveitis, retinitis),

3. Neuro-ophthalmologic features,

4. COVID-19-related ocular coagulopathy (retinal vein occlusion),

5. Ophthalmologic follow-up failure due to lockdowns,

6. Rare manifestations, and

7. Diagnostic and protective measures.

3. Results

Ocular surface (conjunctiva and cornea)

Conjunctivitis

Conjunctivitis is the most frequent ocular finding in COVID-19. The signs of COVID-19 conjunctivitis, like another viral conjunctivitis, include bilateral conjunctival hyperemia, chemosis, the follicular reaction of the tarsal conjunctiva, watery discharge, eyelid edema, enlarged preauricular lymph nodes, and conjunctival injection. The duration of symptoms is typically 7-14 days (19-23).

COVID-19 conjunctivitis may vary in severity, from mild red-eye or eye irritation to severe tarsal conjunctival hyperemia or hemorrhagic conjunctivitis with pseudomembranous (24). In addition, Guo et al. reported a case of complicated conjunctivitis by relapsing keratoconjunctivitis associated with COVID-19 (25).

Conjunctivitis is also one of the symptoms of the multi-system inflammatory syndrome in children (MIS-C) following COVID-19 in children (26). However, cases of conjunctivitis with Kawasaki-like and toxic shock syndromes in adults have also been reported (27, 28).

A possible correlation may exist between the severity of COVID-19 systemic infection and conjunctival involvement. This involvement may predict poorer prognosis as it is associated with higher white blood cell counts, especially neutrophils, and higher levels of procalcitonin, C-reactive protein (CRP), and lactate dehydrogenase which are biomarkers of disease severity (20, 29). The pathogenic mechanism of conjunctival infection was an area of ongoing debate. The presence of ACE2 receptor (which is responsible for virus binding and internalization) on the ocular surface is controversial. Zhou et al. demonstrated ACE2 expression on the ocular surface, especially on the superficial conjunctival and corneal epithelium though many studies did not find a significant conjunctival ACE2 expression (30, 31). The expression of ACE2 on the surface of endothelial cells was reported in many studies, so transient vasculitis may be a possible mechanism of conjunctival involvement (32).

Some reports show that conjunctivitis may be the initial sign and symptom of the disease. Also, it could be the only disease manifestation. This atypical presentation necessitates high levels of precaution in dealing with patients with conjunctivitis, such as applying eye protection for healthcare staff and using telemedicine to manage complaints like red-eye during pandemics (33-37).

Treatment of COVID-19 conjunctivitis mostly includes symptomatic treatment and decreased contact with others. However, topical antivirals such as ribavirin and ganciclovir were reported to be helpful in some studies (38).

Intraocular manifestation

Lauermann et al. analyzed different ocular tissues of a patient passed on due to COVID-19 pneumonia. They demonstrated no tissue tropism for SARS-CoV-2 among intraocular tissues (39). However, there are several reports of intraocular findings associated with COVID-19.

Uvea

A case report describes simultaneous unilateral acute anterior uveitis (presented by blurred vision, photophobia, and immune precipitates on the capsule of the lens) and bilateral follicular conjunctivitis in a 30-year-old woman with coexisting fever and impaired taste, which was concurrent with a positive PCR for SARS-CoV-2 (40).

Retina

Retinal involvement was reported in several different forms in COVID-19. Marinho et al. reported retinal changes, mainly hyperreflective lesions at the level of ganglion cell and inner plexiform layers, in 12 patients in the examination 10-30 days after COVID-19's first symptoms, with a normal Optical coherence tomography (OCT) angiography and ganglion cell complex analysis. They also observed cotton wool spots and retinal pinpoint hemorrhages in 4 patients. However, no visual acuity loss or intraocular inflammation were found (41). Regarding this study, Demetrios et al. stated that the retinal changes might be unrelated to COVID-19, and the retinal OCT findings may merely represent normal retinal vessels (42).

There was a reported case of bilateral retinal hemorrhage followed by a diagnosis of COVID-19 in a 59-year-old female patient who presented with 7 days history of blurred vision and mild respiratory symptoms that progressed to severe respiratory distress within several days. Fundal examination showed small intra-retinal hemorrhage and venous dilation. One month after COVID-19 resolution, there was an improvement in fundus examination and no sign of vasculitis, diabetic retinopathy, or delayed arteriovenous filling in fluorescein angiography (43).

Retinal vascular occlusion may be another form of retinal involvement in COVID-19. Cases of retinal vein occlusion occur secondary to COVID-19, even in young and healthy adults, with the proposed mechanism of hypercoagulability due to severe inflammatory response to SARS-CoV-2 (44-48). A case of paracentral acute middle maculopathy after central retinal artery occlusion due to COVID-19 has also been noted in a case report (49).

Neuro-ophthalmologic features

COVID-19 is associated with some neuro-ophthalmic manifestations in the literature. These manifestations include cranial nerves palsies, nystagmus, optic neuritis, and visual field defects (50).

Optic neuritis

Cases of optic neuritis have been noted in COVID 19 patients, concomitant with or days to weeks after COVID-19 classical findings. This neuritis is associated with a fruitful response to systemic methylprednisolone (51-53).

Novi et al. described a case of bilateral visual acuity and field loss and afferent pupillary defect associated with a sensory deficit and was diagnosed as acute disseminated encephalomyelitis after a 2-week flu-like illness accompanied by anosmia and ageusia (54).

Cranial nerves palsies

Cases of ocular motility disorders due to cranial nerves palsy have been seen in COVID-19 patients, either isolated nerve palsy or as a part of Miller Fisher syndrome (MFS) (55-59). Gutiérrez-Ortiz et al. reported 2 cases of COVID-19 patients with polyneuritis cranialis and MFS presenting with ocular dysmotility, ageusia, areflexia, etc., which achieved complete neurologic resolution with IV immunoglobulin and acetaminophen (60).

Nystagmus

Nystagmus was seen in a few cases with more severe forms of the disease, mostly as a part of encephalopathy. It was concurrent with ataxia and myoclonus, and cerebral lesions compatible with post-infectious immune-mediated rhombencephalitis were found on brain MRI (61, 62).

COVID-19-related ocular coagulopathy

COVID-19 induces coagulation abnormalities and thrombotic events that are relatively common in this disease, especially in more severe forms (63). Some published complications of COVID-19, such as central retinal vein occlusion (RVO), are assumed to be related to this subject. Besides, other cases have been de-

scribed regarding this matter. Khurram et al. described a highly morbid patient with COVID-19 pneumonitis and saddle pulmonary embolus with superior ophthalmic vein thrombosis. The condition responded well to low molecular weight heparin therapy (64). Padhy et al. reported a case of paracentral acute middle maculopathy (PAMM) 2 weeks after positive PCR and radiological analysis for SARS-CoV-2 infection, which was associated with an increased D-dimer (65).

Ophthalmologic follow-up failure due to lockdowns

Regarding the effects of the COVID-19 lockdown on eye health, it is worth mentioning that the standard care for some eye diseases may be difficult during the COVID-19 pandemic. The American Academy of Ophthalmology (AAO) recommended that ophthalmologists cease non-urgent services. Also, AAO provided a list of urgent and emergent procedures required to solve potential sight-threatening conditions, such procedures that are mostly related to retinal, glaucoma, orbital, and oncology eye diseases (66). The disorders are categorized as A) retinal diseases, B) amblyopia treatment, C) orbital, and D) glaucoma follow-up.

Retinal diseases

Retinopathy of prematurity (ROP) is one of the most common diseases in premature infants worldwide. Screening premature infants prone to ROP according to standard protocols and timely treatment significantly reduces blindness and low vision in these children (67). The overall incidence of ROP may be affected by COVID-19, and it might increase in neonates with an infected mother due to the high cytokine release resulting from COVID-19 (68).

Unfortunately, due to cities' lockdown and parents' fear of medical centers during the COVID-19 pandemic, there is a decrease in referrals of these infants for regular periodic examinations, thereby increasing the chances of eye complications in them. It is essential to inform and encourage parents to refer premature infants promptly and to accurately track the date of the examination with the help of medical assistants. To reduce the possibility of transmitting the virus to the infant through the conjunctiva, strict observance of COVID-19 protocols, including using a sterile speculum, preferably disposable ones, is strongly recommended. If treatment is needed, retinal laser photocoagulation should be used instead of intravitreal anti-VEGF injection (due to less need for frequent follow-up after surgery) except in special cases. Finally, the need for telemedicine and retinal imaging facilities such as RetCam, especially in remote areas, seems more reasonable (69, 70). Intravitreal injection is a well-known procedure in various chorioretinal disorders and is probably the most common procedure performed in ophthalmology (71).

Even though there are many guidelines for performing routine procedures (72), unfortunately, limited guidelines are available for managing intravitreal injections during the COVID-19 pandemic. Since most candidates for intravitreal injections have concomitant comorbidities, such as diabetes, hypertension, and old age, they are prone to severe complications if they develop the COVID-19 infection. It is worthwhile to take special precautions for these patients, including increasing the interval between injections as much as possible (using treat-and-extend or as needed strategies), avoiding more invasive procedures such as fluorescein or indocyanine green angiography, and replacing them with OCT-angiography as much as possible, limiting the number of patients per session in the operating room and strictly following COVID-19 protocols (73-75). One of the essential precautions during the pandemic is wearing face masks. There is a report about the increased incidence of endophthalmitis during intravitreal injections, especially because of a gap between the mask and the nose in different face masks. Thus, it is suggested to tighten the mask during the procedure (76).

Amblyopia follow-up

Amblyopia, the most common cause of monocular visual loss in children, is another ophthalmologic disease needing close follow-up to prevent permanent vision loss (77). Specific recommendations to evaluate patients at risk of developing amblyopia during the pandemic are not available. Parenteral home screening and using telemedicine with proper referrals are recommended in this matter (67).

Orbital disease

Graves' disease is the most common cause of hyperthyroidism, with more than 1% prevalence in the general population. Graves' orbitopathy (GO) or thyroid eye disease (TED) is its most frequent extrathyroidal manifestation, affecting about 25%-30% of the patients with Graves' disease. One of the important complications, especially for patients with hyperthyroidism and Grave's disease, is orbitopathy, known as TED (78).

The COVID-19 pandemic affects the management of endocrine and metabolic disorders, including diabetes

mellitus, obesity, adrenal insufficiency, Graves' hyperthyroidism, and orbitopathy. While there is no definite evidence that Graves' disease per se or its treatment increases the risk of COVID-19 infection, patients with Graves' disease may be more prone to present with symptomatic forms of COVID-19 infection. There are no available guidelines for treating these patients in the COVID-19 era. Steroid elicits immunosuppression, which is a risk factor for COVID-19 infection. On the other hand, severe, vision-threatening forms of GO do require aggressive steroid treatment to avoid irreversible loss of vision. If TED is not severe, systemic treatment should be postponed, and topical treatments can be used. In patients who are already under intravenous steroids, it might be to continue this treatment, provided that the hospital offers a clear separation and different paths between COVID-19 areas and COVID-free areas. Alternatively, and preferably to avoid unnecessary visits to the hospital, these patients might be shifted to oral glucocorticoid therapy at home (79).

Glaucoma

We could not find any reported case of increased intraocular pressure or open or closed-angle glaucoma caused by COVID-19. However, there were some reports of drug interactions between medications used in glaucoma patients and COVID-19 treatment drugs. Topical timolol maleate is a non-selective beta-adrenergic antagonist commonly used to treat open/angle glaucoma. In a study by Pratt et al., the risk of bradycardia increased significantly in the 31–180 days after the start of timolol, which increased the hospitalization rate in certain cases. There is evidence suggesting that the use of hydroxychloroquine together with a β-blocker would increase the bioavailability of the latter and potentially further increase its side effects (80). Chellakumar et al. reported COVID-19 patients who developed bilateral acute angle-closure glaucoma (AACG) following heparin therapy. Anticoagulants were also reported to cause AACG in predisposed eyes, which is something to be considered due to the high frequency of thrombotic events in COVID-19 patients and the common use of heparin in these patients (81).

Myopia progression

Lockdown was also found as a reason for myopia progression among children and teenagers. It is associated with reversible and irreversible eye problems, consisting of accommodation spasms and structural changes, respectively (82, 83). Some studies proved that lockdown might also lead to higher digital eye strain due to higher usage of digital devices for e-learning and work. Using preventive measures such as the 20-20-20 rule, less screen time, and rewetting drops is recommended in this era (84).

Rare manifestations

Few reports of other ocular manifestations in COVID-19 patients were also published. Otaif et al. reported a case of episcleritis 3 days before classical findings of COVID-19, which was associated with a positive nasopharyngeal swab PCR for COVID-19 (85). Cases of multifocal choroiditis, dacryoadenitis, and panuveitis have also been described in this matter (86-88). However, because of the scarcity of these reports, they might be coincidental or at least in part attributed to patients' comorbidities. More investigation is recommended to find out whether there is a correlation or it is just a coincidence.

Diagnostic and protective measures

COVID-19 treatment-related ophthalmopathy

Several drugs used to manage COVID-19 may have ocular adverse effects, such as uveitis due to some antivirals, chloroquine-related retinopathy and optic neuritis, or vision loss by some antibodies (20).

Face mask and hand sanitizer ocular manifestations

Considering the effects of the COVID-19 pandemic on the eyes, a study noted that inappropriate use of hand sanitizer might have ocular complications, especially in children (89). Wearing a face mask was a cause of eye irritation and dry eye, which should be considered and managed correctly, especially for those who have worn the mask for a long time. Eye irritation may also be associated with a higher risk of getting infected with COVID-19 through the eyes (90, 91).

Precautions in ophthalmologic practice

We highly suggest using telemedicine during the pandemic. However, when it comes to medical appointments, like in other clinics, all patients in ophthalmologic clinics should be asked about COVID-19-related symptoms, temperature screening should be applied, and suspected cases should be isolated and referred to COVID-19 referral centers for further evaluation. The waiting and consultation time should be less, and the number of patients at the clinic should be minimal (92). A 2-m distance should be maintained between the patients and the windows. Also, the doors should be opened 6-12 times per hour. Disinfectant solutions in

Table 1. Some of the best studies regarding COVID-19 ocular manifestations

Author(s)	Total No.	Number of Patients With Ocular Manifestations	Ophthalmologic Manifestations (Number of Patients)	Number of Patients With Positive RT-PCR on Tear/Conjunctival Swab	Ref.
Lechien et al.	1420	-	Conjunctivitis (9), vision loss (6)	-	(94)
Guan et al.	1099	9	Conjunctival congestion (9)	-	(21)
Chen et al.	535	-	Conjunctival congestion (27), secretion (52), foreign body sensation (63), blurred vision (68), dry eye (112), itching (53), photophobia (16), and tearing (55)	-	(22)
Wu et al.	38	12	Conjunctivitis (12) symptoms, such as conjunctival hyperemia, chemosis, epiphora, or increased secretions	2	(14)
Zhang et al.	72	2	Conjunctivitis (2)	9	(95)
Xia et al.	30	1	Conjunctivitis (1)	1	(20)
Öncül et al.	359	16	Conjunctival hyperemia (9), epiphora (5), secretion (6), photophobia (4), chemosis (2), vitreous hemorrhage (1), subconjunctival hemorrhage (5)	-	(96)
Abrishami et al.	142	92	Conjunctival hyperemia (44), chemosis (22)	-	(97)
Ma et al.	216, children	49	Conjunctival discharge (27), eye rubbing (19), and conjunctival congestion (5)	-	(13)
Ceran et al.	93	20	Hyperemia (20), photophobia (15), epiphora (9), increased secretion (6), chemosis (3), follicular conjunctivitis (2), and episcleritis (2)	-	(98)
Cavalleri et al.	172	45	The most frequent manifestations were bilateral conjunctival hyperemia, epiphora, and foreign body sensation, followed by itching, lid swelling, and mucopurulent discharge. Forty patients had features consistent with conjunctivitis during hospitalization.	0 from 22 patients accepted sampling	(99)
Valente et al.	27	4	Mild viral conjunctivitis (4)	3	(100)
Deng et al.	114	0	-	0	(101)
Zhou et al.	121	8	Itching (5), redness (3), tearing (3), discharge (2), and foreign body sensation (2)	One patient with ocular symptoms and 2 patients without any ocular symptom	(102)
Sindhuja et al.	127	11	Conjunctival congestion (8), ocular burning sensation (1), watery eyes (1), and hordeolum externum (1)	Not done	(103)

RT-PCR: Rreal-time reverse transcription-polymerase chain reaction.

the waiting room and soap in the washing closet should be available to all patients (93).

4. Conclusion

A wide range of ocular manifestations and complications have been reported during the COVID-19 pandemic. While conjunctivitis is the most common ocular manifestation of COVID-19, several other ocular complications, especially retinal involvement, have been reported. It is unclear whether there is a correlation or a coincidence, so further research is recommended. COVID-19 also affects eye health in many ways. Locking up and not following up is an obstacle to properly managing retinal diseases and myopia in children. Because of the pervasive effects of pandemics such as COVID-19 on eye health, new guidelines must be applied in various areas of ophthalmology. Precautions should be taken at high levels, and COVID-19 should be remembered in diagnosing and managing various ocular manifestations.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles are considered in this article. The participants were informed of the purpose of the research and its implementation stages. They were also assured about the confidentiality of their information and were free to leave the study whenever they wished, and if desired, the research results would be available to them.

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Authors' contributions

Conceptualization and Supervision: Abdolreza Medghalchi and Yousef Alizadeh; Methodology: Reza Soltani-Moghaddam; Ebrahim Azaripour; Investigation, Writing – original draft, and Writing – review & editing: All authors; Data collection: Amirhossein Tamimi; Data analysis: Abdolreza Medghalchi and Hasan Behboodi.

Conflicts of interest

The authors declared no conflict of interest.

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