



The effect of COVID-19 pandemic on the attendance and clinical outcomes of patients with ophthalmic disease: A mini-review

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ABSTRACT

The outbreak of COVID-19 was followed by a rapid spread leading to its declaration as a pandemic in a short time. The transmission through aerosols and direct contact with infected individuals forced the application of strict safety protocols and rearrangements in the activities of different healthcare systems around the world. Ophthalmology healthcare workers are highly exposed to viral infection and therefore adjustments were made to ensure the safety of patients and health providers by performing only urgent treatments. The suspension and delay in regular follow-up visits and the lower number of patients recorded during the lockdown period due to restrictions and patient anxiety led to severe consequences in the clinical and anatomical outcome affecting the overall prognosis. The current review aims to summarize the effect of the lockdown policies in the number and profile of patients that attended the ophthalmology clinics from different countries and analyze the effect of the pandemic in terms of vision and patient functionality. The effects of the pandemic included a reduction in the number of appointments, cancellations of non-emergency conditions and delays of surgical interventions. These had a negative effect in terms of visual outcomes.

1. Introduction

In December 2019, the outbreak of the novel coronavirus disease (COVID-19) initiated from the city of Wuhan, Hubei province, China and rapidly spread all around the globe. The disease was caused by “severe acute respiratory syndrome coronavirus type 2” (SARS-CoV-2) and manifested as an acute infection of the upper and lower respiratory tract but also affected other systems, including the heart, kidneys, circulatory and nervous system [1–4]. The transmission is primarily airborne through droplets/aerosols of the infected individuals and direct contact [5], while a number of studies indicated the isolation of viral particles from other body fluids such as saliva and tears [6].

The disease is counting nearly 200 million confirmed cases and four million deaths, as of August 2021 [7]. The rapid, uncontrolled transmission along with the unprecedented mortality rates led to the declaration of this situation as a ‘pandemic’ by the World Health Organization (WHO) in March 11, 2020 [8]. The dramatic progression of the pandemic forced governments in many countries to apply lockdown policies and citizens to adopt social distancing rules in order to slow

down the extent of the infection rate [9]. However, restriction strategies led to major consequences in many different aspects, including economy, social life, mental health, education and healthcare provision [9, 10].

The extent of the pandemic brought huge difficulties as far as healthcare is concerned. The extremely high numbers of new and severely infected patients in daily basis along with the restricted number of intensive care unit (ICU) workers rapidly exhausted the system and subsequently led to a number of measures. Hospitals transformed their units ICUs admitting only Covid-19 patients, recruited different specialties and healthcare providers and cut down outpatient clinics and non-emergency surgeries [9].

Meanwhile, practicing ophthalmology in the era of Covid-19 turned out to be a particularly challenging issue. The close proximity between the patient and the doctor during the ophthalmological examination combined with the detection of the virus in the tear film and conjunctival discharge turned to be a dangerous hazard for ophthalmologists [11,12]. Therefore, doctors and medical staff in ophthalmology clinics were strongly advised to adopt strict preventive measures, including eye

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protection and frequent disinfection of equipment in order to eliminate the risk of spread among patients and healthcare providers [13]. In addition, avoidance of all treatments, surgeries and follow-up visits unless urgent was strongly recommended by a number of ophthalmological societies around the world [14]. Finally, there are data suggesting that SARS-CoV-2 may directly affect the retina [15].

These strict lockdown policies had a negative impact in the course of chronic ophthalmic conditions requiring regular follow-up and specific timeframe for treatment. This review analyzes the effect of the pandemic on the attendance rate in ophthalmology clinics around the world and the consequences on the clinical outcome of patients during this period.

2. The effect of the pandemic on the attendance rate

During the lockdown period the number of patients attending regular follow-up visits or receiving intravitreal, laser or surgical treatments was significantly decreased compared to the same period of previous years, as presented in a number of publications from different countries. Furthermore, a significant percentage of patients with retinal disease have diabetes and/or obesity which are known risk factors for Covid-19 and these patients are often hesitant in attending their appointments [16,17].

In Italy, the extremely high number of infected patients rapidly exhausted the healthcare system, especially in the northern province of Lombardy [18]. Thus, elective, non-urgent treatments were significantly reduced in the context of prioritizing the management of emergency conditions, as presented by dell' Omo et al. [19]. The authors gathered the number of ophthalmological procedures and intravitreal injections from six ophthalmology departments of different areas in Italy during the first month of the pandemic. The comparison of this number with the corresponding one recorded in the same time period of the previous year showed an extreme reduction of all types of surgical treatments. More specifically, the total number of surgeries was reduced by 76.7%, including elective and emergency treatments while specific centers completely suspended any type of eye treatment during that time. Cataract surgeries were reduced by 97.8% which is translated as 50,000 less surgeries in comparison to 2019 and 93.9% less elective vitreoretinal surgeries including pars plana vitrectomy (PPV) for silicon oil removal and epiretinal membrane (ERM) were performed. Nevertheless, a significant decrease was also recorded in the number of emergency interventions. The number of trabeculectomies and surgeries for rhegmatogenous retinal detachments (RRD) were reduced by 73.7% and 64.2%, respectively. Intravitreal injections of anti-VEGF and dexamethasone were also eliminated by 78.1% for diabetic and retinal vein occlusion (RVO)-related macular edema and 46.2% for choroidal neovascularization (CNV). Another publication from Italy by Borelli et al., presented the decrease of patients attending the outpatient medical retina clinic of a tertiary hospital during the first two months of the pandemic in 2020 [20]. The number of patients examined during that period had a 75.2% reduction, affecting primarily elderly patients suffering from age-related macular degeneration (AMD) (−79.9%), while more than 50% reduction was recorded for intravitreal injections. As in the former study published from Italy, injections for AMD were prioritized (−53.6%) and presented a smaller reduction than those for diabetes, RVO and uveitis (−85.7, −61.9% and −59.6%, respectively).

The Greek healthcare system was also tested through the pandemic. A publication by Chatziralli et al., presented a significant decrease in the number of patients diagnosed with proliferative diabetic retinopathy (PDR) or diabetic macular edema (DME) as compared to the same period in 2019 [21], while the number of diabetic patients managed with intravitreal injections, PPV and panretinal photocoagulation (PRP) was also severely eliminated.

Yeter et al., presented data from Turkey showing that the first lockdown between March to June 2020 brought a statistically significant decrease in the total number of patients examined in the outpatient medical retina clinic (from 2824 ± 34.6 to 854.3 ± 758.4) and in the

number of intravitreal injections performed (from 238.3 ± 50.4 to 47.6 ± 52.4) [22].

Data from Germany showed a 30% reduction in the number of patients visiting the emergency department, while 63.4% decrease was recorded in the number of surgical activities performed during the lockdown based on data collected from different medical centers and hospital of the country [23]. Additionally, emergency admissions including RRD, endophthalmitis, open globe injuries, closed angle glaucoma, penetrating keratoplasties and optic neuritis showed a 34% decrease. Another study from the same group showed that there was a significant reduction in the capacity of clinics by 35.2% combined with staff shortages due to infections, quarantine measures or reassignments to departments in need [24].

Strict lockdown policies led to severe consequences in the number of intravitreal injections performed for the management of several retinal pathologies, including neovascular AMD (nv-AMD), diabetes, retinal vascular occlusions and uveitis. A study published from Israel showed that the number of visits in the medical retina clinics during the first 4 weeks of the lockdown represented only 50% of the actual number of patients examined the same period of the previous year [25]. More specifically, the overall drop of intravitreal injections reached up to 36% within the first four weeks of lockdown compared to the previous year, while nearly the same levels of decrease (33%) were recorded in a study conducted in Portugal from the first semester of 2020 [26]. In the same study, although there was a significant reduction of cataract surgeries, posterior vitrectomies and laser sessions, the application of proper safety measures and re-scheduling of patient visits maintained the provision of ophthalmological healthcare during the first lockdown. In United Kingdom, the management timeframe of chronic retinal entities was guided by the instructions provided by the Royal College of Ophthalmologists suggesting the postponement of intravitreal injections in non-monocular, stable patients during the lockdown period and individual evaluation of the guideline application from each hospital [27]. A publication from the UK showed that even though 2738 patients were scheduled prior to the restrictions for their regular appointment in the medical retina clinic and for anti-VEGF injections within the first four weeks of the lockdown in 2020, only 33% (893 patients) were examined and received treatment during the pandemic [28], while data published from another hospital in London showed that the number of intravitreal injections declined by 17.8% compared to the previous year [29].

From across the Atlantic, Sethi et al. reported a 62% decline in the retina clinic appointments with significant reduction in the average duration of patient examination and 88% reduction of in-person visits during the first two months of the lockdown, as shown from data collected in Boston. Interestingly, there was a shift in the percentage of visits in the medical retina clinic from 18% in 2019 to 57% in 2020 out of the total number of patients referred to the ophthalmology department with significant decrease in the examination time aiming to minimize the exposure to the virus. Additionally, telemedicine was a strategy employed in order to monitor patients while keeping a safety distance, with these appointments accounting for 77% of visits during that period [30]. Additionally, the Wills Eye Hospital of Philadelphia collected data from the retina clinic from January to May 2020 and showed a severe reduction in new and follow-up visits, anti-VEGF injections and retinal imaging including optical coherence tomography (OCT), fluorescein angiography (FA) and indocyanine green angiography (ICG) [31].

3. The effect of the pandemic on patient outcomes

A major challenge during the pandemic was the proper management of patients suffering from chronic retinal diseases while preventing viral transmission among patients and healthcare providers. Therefore, each country and institution adopted different algorithms and guidelines for urgent and elective surgical procedures, follow-up visits, intravitreal treatments, laser and imaging sessions. Restricted accessibility to

healthcare units, social distancing and elevated anxiety level of patients led to significant delays in treatment protocols. A number of publications investigated the impact of restriction policies in the clinical outcome of patients suffering from several ocular conditions.

In chronic retinal conditions, including nv-AMD, PDR, DME and RVO the postponement of the specific timeframe of intravitreal injections may lead to severe and irreversible impairment of vision. Due to the fact that AMD patients represent a larger proportion among other retinal entities, the effect of the pandemic on nv-AMD patients was more intensively investigated. In Italy, Borelli et al. showed that delays in the regular follow-up visits and intravitreal treatments in patients with nv-AMD due to the pandemic restrictions led to a worse clinical and anatomic outcome [32]. More specifically, there was compromise in best corrected visual acuity (BCVA) while imaging data through OCT showed increased levels of macular neovascularization, including exudates and presence of intra- and/or subretinal fluid. The statistical analysis that followed highlighted the direct relation between time intervals in follow-up visits and BCVA in patients with nv-AMD.

In Greece, Chatziralli et al. showed that in a cohort of diabetic patients there was statistically significant decrease in BCVA and elevated central retinal thickness (CRT) when comparing the last visit before and the first visit after the lockdown [21]. Moreover, in 30% of patients with severe non-PDR and 8.3% with quiescent PDR progression to active PDR was diagnosed.

Yeter et al. gathered data from the medical retina clinic of a Turkish hospital and showed that the delay in treatment for patients with nv-AMD led to worsening of BCVA and increased CRT in OCT examination, which was improved immediately after returning to a regular program with the injection timeframe [22]. Although the exudative elements and the neovascularization seemed to regress when the injections initiated after lockdown, BCVA did not show the same improvement. Another study conducted in Turkey involved patients of a retina clinic which maintained the scheduled intravitreal injections during the lockdown taking all the necessary precautions to avoid viral transmission [33]. Patients were divided in two groups based on their adherence to their regular visit or the intravitreal injections and clinical examination after the lockdown revealed a statistically significant decrease in BCVA and severe compromise in the OCT images with signs of active neovascularization in the group that skipped their injection during the restriction period. The profile of patients that adhered to their appointments included younger age and worse BCVA, as examined at the last time before the lockdown. A possible explanation given by the authors is the fact that elderly patients decided to avoid hospital facilities due to anxiety and additionally that those with improved BCVA considered that skipping their injections would not severely affect their vision.

Naravane et al. investigated the impact of the pandemic restrictions in the clinical and anatomical outcome of patients requiring intravitreal injections in a medical retina clinic in Minnesota, USA [34]. In this study, the authors investigated the difference in the clinical and imaging course of patients that postponed their intravitreal treatments and of those with no lapse in their regular follow-up visit and treatment. As expected, patients with nv-AMD and DME who delayed their visit longer than two weeks apart from their scheduled appointment presented a greater decrease in BCVA. As far as OCT imaging is concerned, DME seemed to present worse outcome in patients that skipped their regular visits while in nv-AMD patients there was no statistically significant difference in the CRT compared to the group of patients with better adherence to the timeframe of their visits.

The effect of the pandemic on nv-AMD and polypoidal choroidal vasculopathy (PCV) was investigated by Zhao et al. in Peking [35]. The authors showed that the participants with an average 4-month delay in the examination or treatment for nv-AMD and PCV had worse BCVA and increased possibility for developing sub-macular scarring. On the other hand, patients with nv-AMD or PCV that were adherent to their regular appointments showed decreased levels of intra- and subretinal fluid,

confirming the necessity for regular follow-up and management.

The negative effect of Covid-19 outbreak in patients receiving anti-VEGF treatment was also investigated in several ophthalmology departments in China. Yang et al. reported that interruption in intravitreal injections for longer than 4.5 months led to statistically significant compromise of the clinical outcome of patients with nv-AMD, DME and RVO. In their analysis, they showed decreased BCVA and statistically significant elevation of CRT, while a small number of patients developed neovascularization on the optic disc, elsewhere or neovascular glaucoma [36].

A publication from Jordan by Saleh et al. showed that by taking all the necessary measures to prevent infection, the scheduled intravitreal therapies were not cancelled during the pandemic but there was a mean 6.2 weeks delay for patients with nv-AMD, PDR and/or DME and RVO [37]. Despite this fact, clinical examination in the first visit after quarantine revealed significant decrease in BCVA and a worse anatomical outcome in OCT, with increased CRT and choroidal neovascularization. In the same study, questionnaires given to the participants asking about the effect of the pandemic on their vision showed that 36.3% noticed worsening and 91.6% declared that the postponement in their injections strikingly affected their life quality.

Several institutions applied a triage system in retina clinics in order to optimize the access to treatment while avoiding viral contamination amongst patients and healthcare workers. In the university hospital of Zurich, patients referred to the medical retina clinic were categorized in three groups according to the short-term vision prognosis if left without treatment; those with expected irreversible vision loss within 1–2 months, those within 3 months and finally those expected with irreversible vision loss in more than 3 months [38]. The first group was scheduled for immediate examination and the second one for a delayed visit. For the patients that their vision was not threatened within the next three months their appointments were cancelled and put on a waiting list for assessment after the termination of the lockdown. This strategy managed to maintain sufficient clinical status for patients with retinal diseases requiring anti-VEGF therapies and also gained patients' satisfaction and sense of safety given by the organized system of triage that was organized and applied in the facility.

In the UK, guidelines indicated the prioritization of intravitreal injections for nv-AMD and diabetic patients, but not for RVO [27]. Data published by Stone et al. from Newcastle confirmed the importance of prioritizing these two entities for scheduling anti-VEGF treatments during the pandemic. Their results showed that the delay in injections led to statistically significant lower BCVA in patients with nv-AMD while the increase of CRT was statistically significant in nv-AMD and diabetic patients only, but not for RVO [39].

Finally, remote monitoring of patients with the use of telemedicine seems to offer many advantages and implementation of such practices in ophthalmology along with the continuation of vaccination programs worldwide and the ongoing research for effective medical treatments, will help minimize the above mentioned effects of the pandemic in the management and outcomes of patients with ophthalmic disease [40–42].

4. Conclusion

Strict measures taken during the first pandemic included restrictions in accessibility in healthcare provision thus leading to suspension and delay of the diagnosis and management of ophthalmologic conditions worldwide. The effects of the pandemic included diminished number of patients visiting ophthalmic departments along with delays and cancellations of non-emergency conditions as well as decreased number of non-surgical interventions. More studies are required in order to investigate the long-term effects of the pandemic on the prognosis of ocular diseases.

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CRediT authorship contribution statement

Maria Syriga: Conceptualization, Methodology, Investigation, Writing – original draft. **Irene Karampela:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Maria Dalamaga:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Michael Karampelas:** Supervision, Project administration.

Declaration of competing interest

The authors report no conflict of interest.

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