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Prevalence of SARS-CoV-2 infection in patients presenting for intravitreal injection

Stephan Szegedi [iD] · **Wolfgang Huf** [iD] · **Kata Miháltz** [iD] · **Pia Veronika Vécsei-Marlovits** [iD]

Summary

Aim Due to the coronavirus disease 2019 (COVID-19) pandemic, nosocomial transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is of great concern to clinicians of all specialties. Currently there are no published data available on the prevalence of the infection in ophthalmology patients presenting for intravitreal injection (IVI). The purpose of this retrospective study was to estimate the prevalence of SARS-CoV-2 infection in patients presenting for IVI at our hospital.
Methods Patients presenting for IVI in April 2020 at our hospital who had been screened for SARS-CoV-2 infection using nasopharyngeal and oropharyngeal specimen for real-time reverse transcription polymerase chain reaction analysis were included in a retrospective study. To assess the representativity of this sample for IVI patients, characteristics were compared with patients presenting for IVI during March–April 2019.
Results The study included 279 patients and 319 historic control patients. Of 277 valid test results, one SARS-CoV-2 positive patient was found, resulting in a carrier rate of 0.36% with a 95% Clopper–Pearson confidence interval of 0.01–1.99%. No differences in sex (57.7% vs. 59.9% female, $p = 0.650$), age (77.63 ± 10.29 vs. 77.59 ± 10.94 years, $p = 0.962$), and region of residence were found between groups.
Conclusion The study provides an estimate for the prevalence of SARS-CoV-2 infection in asymptomatic patients presenting for IVI. While these data may be used as a baseline, further research is needed to assess the development of SARS-CoV-2 prevalence in this patient group in order to support risk assessment and infection prevention strategies.

Keywords Coronavirus · COVID-19 · Severe acute respiratory syndrome coronavirus 2 · Ophthalmology · Epidemiology

Prävalenz der SARS-CoV-2-Infektion bei Patienten mit intravitrealer Injektionstherapie

Zusammenfassung

Zielsetzung Durch die „coronavirus disease 2019"-(COVID-19)-Pandemie ist die nosokomiale Übertragung des „severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) von großer Bedeutung für Kliniker aller Fachrichtungen. Derzeit liegen keine Daten zur Prävalenz der Infektion bei ophthalmologischen Patienten vor, die intravitreale Injektionen benötigen. Zielsetzung dieser retrospektiven Studie war die Abschätzung der Prävalenz der Infektion mit SARS-CoV-2 bei Patienten vor intravitrealer Injektion.
Methodik Patienten, die im April 2020 vor intravitrealer Injektion mittels eines naso- und oropharyngealen Abstrichs und reverser Echtzeit-Polymerasekettenreaktion auf SARS-CoV-2 gescreent worden waren, wurden in eine retrospektive Studie einbezogen. Um die Repräsentativität der Stichprobe zu untersuchen, wurden die Charakteristika mit Patienten vor intravitrealer Injektion aus den Monaten März bis April 2019 verglichen.

S. Szegedi (✉) · K. Miháltz · P. V. Vécsei-Marlovits
Department of Ophthalmology, Wiener Gesundheitsverbund, Hietzing Hospital, Wolkersbergenstraße 1, 1130 Vienna, Austria

Karl Landsteiner Institute for Process Optimization and Quality Management in Cataract Surgery, Vienna, Austria
stephan.szegedi@gesundheitsverbund.at

W. Huf
Department of Laboratory Medicine, Wiener Gesundheitsverbund, Hietzing Hospital, Vienna, Austria

Karl Landsteiner Institute for Clinical Risk Management, Vienna, Austria

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Ergebnisse In die Studie wurden 279 Patienten und 319 historische Kontrollpatienten eingeschlossen. Unter 277 validen Testergebnissen wurde ein SARS-CoV-2-positiver Patient gefunden. Die Prävalenz betrug daher 0,36 % mit einem 95 %-Clopper-Pearson-Konfidenzintervall von 0,01–1,99 %. Es wurden keine Unterschiede bei Geschlecht (57,7 vs. 59,9 % weiblich; $p = 0,650$), Alter ($77,63 \pm 10,29$ vs. $77,59 \pm 10,94$ Jahre; $p = 0,962$) und Wohnort zwischen den Gruppen festgestellt.

Schlussfolgerung Die Studie liefert eine Schätzung der Prävalenz der SARS-CoV-2-Infektion bei asymptomatischen Patienten vor intravitrealer Injektion, die als Grundlage für zukünftige Untersuchungen dienen kann. Weitere Untersuchungen sind notwendig, um den Verlauf der Prävalenz von SARS-CoV-2 in dieser Patientengruppe zu bestimmen und somit die Risikoabschätzung und Infektionspräventionsstrategien zu unterstützen.

Schlüsselwörter Coronavirus · COVID-19 · „Severe acute respiratory syndrome coronavirus 2" · Ophthalmologie · Epidemiologie

Introduction

Coronavirus disease 2019 (COVID-19) is a highly infectious respiratory disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Symptoms include dysosmia, dysgeusia, fever, cough, sore throat, dyspnea, fatigue, and conjunctivitis. The course of the disease ranges from asymptomatic or paucisymptomatic infection to severe pneumonia, respiratory failure, and death. Risk factors associated with severe courses of the disease are old age and preexisting illnesses such as obesity, cardiovascular disease, pulmonary disease, hepatic disease, diabetes, neoplastic disease, and immunocompromising illnesses [1–4]. Transmission of SARS-CoV-2 seems to be predominately mediated by direct contact and respiratory droplets [5, 6].

An outbreak of COVID-19 was recognized in Wuhan, China, in December 2019 [7] and was declared a "Public Health Emergency of International Concern" by the World Health Organization (WHO) in January 2020 [8]. On February 25, 2020, the first patients in Austria tested positive for SARS-CoV-2. The outbreak was characterized as a pandemic by the WHO on March 11, 2020 [9].

Until that date, 319 Austrian patients had tested positive for the virus [10]. At the time of writing, approximately 110,000 patients in Austria have tested positive for SARS-CoV-2 [10].

While the laboratory diagnosis of SARS-CoV-2 infection is usually made from specimens obtained via nasopharyngeal (NP) and/or oropharyngeal (OP) swabs, virus particles have been detected via polymerase chain reaction (PCR) in conjunctival swabs [11, 12], feces [13], and blood [14].

Due to a large proportion of asymptomatic infections including older patients [15, 16], hospitals and doctor's offices are faced with potentially infectious patients in emergency and ambulatory care, where definitive PCR diagnosis may not be practical or feasible.

To reduce the possibility of nosocomial transmission, a reduction of non-emergency outpatient care and non-urgent ophthalmologic interventions has been advised internationally [17]. Infection control measures, including increased personal protective equipment for healthcare workers, have been recommended even for the treatment of asymptomatic ophthalmology patients [18–20].

During the COVID-19 pandemic, patients at our hospital are screened for SARS-CoV-2 before surgery, including intravitreal injections (IVIs), at our institution. The aim of the present retrospective study was to estimate the prevalence of SARS-CoV-2 infection in patients presenting for IVI at our hospital.

To date, there are no data available on the prevalence of SARS-CoV-2 infection in ophthalmology patients in general or in patients receiving IVIs—typically patients with macular degeneration, diabetic retinopathy, or retinal vascular occlusions.

Patients, materials and methods

All elective IVIs at our hospital were suspended from March 16, 2020 to April 14, 2020. Subsequently, patients were invited to resume their treatment and follow-up regimen according to medical urgency. Urgency was determined using a combination of prognosis, visual acuity, past need for IVIs, and visual acuity of the partner eye. Decisions were made on a case-by-case basis by the ophthalmologist in charge.

On the day of their appointment, patients were able to use private or public transport to the hospital. Before entering the hospital, patients were required to answer questions regarding COVID-19 symptoms and have their tympanic temperature taken. Only asymptomatic non-suspect patients were allowed to enter our department for an appointment. Patients receiving an indication for IVI at the follow-up visit underwent the procedure on the same day.

Patients presenting with suitable cloth face coverings or surgical masks were allowed to wear these, patients presenting without or with inadequate cloth face coverings were given a surgical mask. Personnel in close contact with the patient wore filtering facepiece (FFP) 2 certified respirators, surgical gowns, surgical caps, and eye protection. All other personnel wore surgical masks. Whenever possible, an interpersonal distance of 1.5 m was observed.

Before IVI, NP and OP specimens from every patient were collected using swabs. After the collection of swabs, both NP and OP swabs were agitated in a transport medium tube and pressed against the inner side of the tube to wash out the specimen.

Samples were processed using the Abbott RealTime SARS-CoV-2 assay (Abbott Molecular, Des Plaines, IL, USA). The targets for this real-time reverse transcription (rRT) PCR test are SARS-CoV-2 RdRp and N genes. Samples were prepared using the provided reagents and internal control ribonucleic acid (RNA) sequences were added for each specimen. Additionally, positive and negative controls were processed for each run. The assay's limit of detection is 100 virus copies per milliliter with a detection rate of 95.2% according to the manufacturer's specifications. A clinical performance evaluation of negative NP specimen spiked with SARS-CoV-2 RNA sequences is reported as positive percent agreement 100% (confidence interval [CI] 94–100%), negative percent agreement 100% (CI 88.8–100%; [21]).

All patients presenting for IVI during the period April 14–30, 2020 were included in this retrospective study. The case definition for SARS-CoV-2 published by the Austrian Federal Ministry of Social Affairs, Health, Care and Consumer Protection was applied, which defines a "confirmed case" as "[...] persons who have been confirmed as positive for SARS-CoV-2 in a direct laboratory test, regardless of the symptoms" [22].

Additionally, we included all patients receiving IVI at our hospital from March 1, 2019 to April 30, 2019, in order to assess the representativity of the screening sample. Patients present in both samples were excluded from the 2019 sample to avoid overlap.

Statistical analysis was performed using R (version 3.5.3, R Foundation for Statistical Computing, Austria; [23]). Unpaired t tests were used to compare continuous variables, Pearson's chi-squared test was used to compare categorical variables between groups. A p value <0.05 was considered significant. Binomial proportion CIs were calculated according to Clopper–Pearson as implemented in binom (function binom.confint; [24]).

Results

In this study, 279 IVI screening patients and 319 IVI historic control patients were included. The characteristics of both groups are summarized in Table 1.

Of 279 screened patients, we obtained 277 valid PCR results. For two patients, PCR results could not be obtained. In one case, contamination of the specimen prevented PCR, in the other case, no laboratory records were found. Among the remaining 277 valid tests, we detected one SARS-CoV-2 positive asymptomatic patient, constituting a carrier rate of 0.36% with a 95% Clopper–Pearson CI of 0.01–1.99%. The PCR-positive asymptomatic patient initially tested as negative on the day of the procedure in our hospital, but the PCR test result was positive 1 day later in an NP swab taken as a preventative measure at the patient's retirement home. Another 2 days later, he again received a negative PCR test result. In the 3 weeks following the positive test result, the patient did not develop symptoms.

The comparison of the screened group and historical control group showed good representativity of the sample, with no differences in sex (57.7% vs. 59.9% female, $p = 0.650$), age (77.63 ± 10.29 vs. 77.59 ± 10.94 years, $p = 0.962$), and region of residence (see Table 1). Although the most frequent International Statistical Classification of Diseases and Related Health Problems—10th revision (ICD-10) diagnosis in both groups was H35.3, "degeneration of macula and posterior pole," relatively fewer patients with the diagnoses H34.8 "other retinal vascular occlusions" and H36.0 "diabetic retinopathy" were present in the screening sample.

Discussion

Our study provides an estimate of the prevalence of PCR-positive SARS-CoV-2 infection in asymptomatic patients presenting for IVI at our hospital. To our knowledge, this is the first estimate of the prevalence in ophthalmology patients presenting for IVI.

Table 1 Patient characteristics

		Control	Screening	p
n	–	319	279	–
Age, years, mean (SD)	–	77.59 (10.94)	77.63 (10.29)	0.962
Sex (%)	Male	128 (40.1)	118 (42.3)	0.650
	Female	191 (59.9)	161 (57.7)	–
Diagnosis (%)	H34.8	47 (14.7)	25 (9.0)	0.001
	H35.3	217 (68.0)	228 (81.7)	–
	H36.0	55 (17.2)	26 (9.3)	–
Region of residence (%)	Burgenland	7 (2.2)	6 (2.2)	0.845
	Lower Austria	109 (34.2)	105 (37.6)	–
	Styria	2 (0.6)	2 (0.7)	–
	Vienna	201 (63.0)	166 (59.5)	–

ICD-10 diagnoses are: *H34.8* other retinal vascular occlusions, *H35.3* degeneration of macula and posterior pole, *H36.0* diabetic retinopathy

From comparison of the screened patient sample with a sample taken from 2019, it can be reasonably inferred that the sample is representative of our IVI patient clientele. The lower percentage of patients with diabetic retinopathy and vascular occlusion seems to be a direct result of the clinical grading of medical urgency for these patients.

A study designed to provide an estimate for the prevalence of SARS-CoV-2 infection in the Austrian population performed PCR tests in a representative random sample of 1544 persons during April 1–6, 2020. The authors estimated a prevalence of 0.33% of the weighted sample (95% CI 0.12–0.77%; [25]).

A subsequent study estimated an upper limit of SARS-CoV-2 prevalence of 0.15% (95% CI) in the Austrian population based on a sample of 1432 persons tested via PCR during April 21–24, 2020 [26].

In contrast to nation-wide surveys [25, 26], the sample in our study represents a less heterogeneous group, consisting of asymptomatic patients with chronic ophthalmologic disease and higher age.

Limitations

Several limitations need to be considered when interpreting these results. Although commercially available rRT PCR assays for SARS-CoV-2 are validated under controlled laboratory conditions, the real-world sensitivity and specificity of a test depend on preanalytical procedures such as sampling, handling, transportation and storage of specimen, the analytical procedures, including purity of the test reagents [27] and the load of viral RNA in NP and OP secretions, which varies during the course of the disease. The predictive value of a diagnostic test is influenced by its sensitivity and specificity as well as by the pre-test probability for presence of the disease [28, 29]. For an asymptomatic individual, the pre-test probability largely depends on the prevalence of the disease in the population [29]. While the analytical specificity of the assay used in this study has been reported to be 100% [21, 30], sample mix-up and technical errors including reagent contamination [27] can lead to false-positive results.

Finally, as a result of the retrospective design of the study, we did not question patients regarding their adherence to stay-at-home orders or their household situation (e.g., living with their children).

Conclusion

Despite these limitations, the results presented here may be used as a baseline for further studies of SARS-CoV-2 prevalence in ophthalmology patients. The study provides data for risk assessment and infection prevention strategies during a pandemic that forces healthcare providers to balance infection prevention and continuing treatment of chronic illnesses.

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