

Trigeminal Neuralgia of COVID-19: Meta-analysis

Waseem Al-Talalwah¹

¹King Saud bin Abdulaziz University for Health Sciences, Riyadh Department of Basic Medical Sciences College of Medicine

Disclose and conflicts of interest: none to be declared by all authors

ABSTRACT

Introduction: trigeminal nerve is fifth cranial nerve carrying face sensation and dividing into ophthalmic, maxillary and mandibular divisions. Trigeminal neuralgia is clinical condition can be presenting in Covid19 patients. The current study reviews the clinical cases of trigeminal neuralgia of covid19 and explains the anatomical mechanism of pain and its radiation as present with associated symptoms. On current studies reviews entire cases covid19 since 2019 up to 2022 presenting with Trigeminal pain. It found to be a very rare reason comparing to the previous reasons such as infection, tumor, thrombosis, vasculitis, autoimmune disease leading to direct or indirect effects on trigeminal nerve demyelination. Knowing the case presentation of covid19 patient presenting with trigeminal neuralgia may lead to prevent further complications and saving patients life. Learning new clinical issues based on understanding the basic medical sciences prepare good safe physicians to raise their level of education resulting in good medical services in future. Pediatricians, internist, radiologist, ophthalmologist, Otorhinolaryngologists and surgeons has to be aware of this clinical presentation to be able to take more precaution and avoid outbreak of covid 19 infection between medical staffs in different regions of hospital such as clinics, wards, emergency rooms and operations.

Keyword: COVID19; Trigeminal neuralgia; Trigeminal nerve; Ophthalmic; Ocular headache; cavernous sinus.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was originally noticed in Wuhan, China in 2019 [Veritti *et al* 2020]. Severe acute respiratory syndrome coronavirus 2 was named as COVID-19 and defined as a pandemic disease on March 11, 2020. [Khalili *et al* 2020]. By March 28, 2022, 21,092,096 people were infected with SARS-CoV-2, 757,727 of whom passed away due to COVID-19 or its adverse health consequences (Worldometer).

Trigeminal nerve is fifth paired cranial nerve exists from pons which is a middle part of brainstem. It carries the face sensation to three sensory nuclei are mesencephalic, principal sensory, spinal nuclei extending through brainstem and into the high cervical spinal cord. Also, it has one motor nucleus motor extending in brainstem to control mastication muscles (Masseter, Temporalis, lateral pterygoids and medial pterygoids in addition to tensor veli palatini, mylohyoid, tensor tympani, and anterior belly of digastric muscles. The trigeminal nerve passes lateral to the cavernous sinus. It divided into ophthalmic, maxillary and mandibular divisions existing the skull via the superior orbital fissure, foramen rotundum and foramen ovale respectively (Huff and Daly 2020). The current study highlights the trigeminal neuralgia present with different clinical features in covid19 and explained the neuroanatomical mechanism of pain and radiations.

Material and Method

The literatures linked to trigeminal nerve involvement and covid19 are attained from PubMed and Google Scholar database. On PubMed there are 252 articles and on google scholar 607. On The entire articles have been published in 2020 found to be almost 9 hundred articles. The entire articles are founded and selected based on the keyword 'trigeminal neuralgia, ocular pain, corona virus and covid19. The articles are selected only in English language. Out of six hundred articles, 7705 Covid19 cases including 728 trigeminal neuralgia cases found to be relevance to the study and were collected from 2020 till 2022. The data is collected and analysis via Statistical Package for the Social Sciences (SPSS).

Result

The current study reviews the 7561 cases of Covid19 that is including 638 trigeminal neuralgia (8.4%). The known cases, there are several reports and research studies which are 638 trigeminal neuralgia cases of Covid19 disease with clear reasons of ophthalmic neuroglia (ocular pain). The unknown cases, 48 cases of trigeminal neuralgia of Covid19 disease without any reasons of affected eye. The trigeminal neuralgia divided into 590 known (7.8%) and 48 unknown cases (0.6%). 638 trigeminal neuralgia found to be known (92.5%) more than unknown reason cases (7.5%).

Discussion

Trigeminal neuralgia (TN) is unusual illness, which is a chronic neuropathic sharp pain due to spontaneous, and excitation of electric shock-like the distribution of one or more trigeminal nerve's divisions (Bendtsen *et al.* 2019). The lifetime prevalence of trigeminal neuralgia in population-based studies found to be to be about 0.16% to 0.3% (Mueller *et al.* 2011). The incidence rate of Trigeminal neuralgia ranges between 0.0004 and 0.0013% and surges with age (Yadav *et al.* 2017) whereas it found to be to be increasing to 0.07% (Cephalalgia. 2018, Jones *et al.* 2019). The classical trigeminal neuralgia is defined severe sharp one side of face pain involving one or more of trigeminal branches, aggravating by a stimulus without radiating and occurring between second and two minutes to the affected side of the face in Headache Classification Committee of the International Headache Society (Cephalalgia. 2018). The trigeminal nerve innervates the meninges above tentorium therefore the headache is due to referred pain from trigeminal irritation of any Covid-19 infection its branch distributions however it can be a serious sign of cerebral venous thrombosis when the vein dilated and irritate the meninges to because of its coverage of the cerebral veins.

There are several theories explained the mechanism of neuropathy. Covid19 may infect neurons, glial cells (astrocytes and microglia) results in activating innate reaction producing high serum protein S100b, and a higher BBB associated with severity of tissue injury (Aceti *et al.* 2020). As the virus become systemic infection, a huge of inflammatory mediators such as cytokines, chemokines, interleukins, and antibodies will release resulting in the neural damage and consequences (Klein *et al.* 2019). Moreover, Covid19 may penetrate nervous system through trans synaptic neurons, immunological, or meningeal affecting cranial nerve (trigeminal nerves) however the respiratory and enteric routes which circulating the virus to brainstem nuclei so-called a hematogenous route (Paniz-Mondolfi *et al.* 2020, Yashavantha and Jayabaskaran 2020, Deffner *et al.* 2020, Franca *et al.* 2021).

Based on anatomical interpretation of AlDorazi and Altalalwah (2021), the covid19 may lead to vasculitis therefore the trigeminal Neuralgia may result due to vascular compression as the trigeminal nerve passes next to superior cerebellar artery, anterior inferior cerebellar artery, or the superior petrosal veins (Apfelbaum 2000, Hong *et al.* 2011). Moreover, the covid19 invade nose epithelium by its binding to ACE-2 receptors in which the trigeminal nerve sensory branches distribution (Fodouljian *et al.* 2020). Furthermore, the cerebral vein thrombosis occurs in 13 persons per million yearly (Sharouni and Narayanan 2015). The cerebral vein thrombosis includes Cavernous thrombosis occurs in 22–157 per ten million which is more in Female than male (Devasagayam *et*

al. 2016) due to coagulopathy, contraceptive uses, pregnancy and post-partum period, Malignancy, Infection, Mechanical precipitants lumbar puncture. Recently, Covid19 found to be a reason of cerebral vein thrombosis as super infection with fungal or binding with ACE2 producing vasculitis (AlDorazi and Al Talalwah 2021). It has been estimated to have orbital fissure syndrome involving ophthalmoplegia in 30% in post covid19 cavernous sinus thrombosis (Kasimov *et al.*, 2022). For instance, the Cavernous sinus thrombosis is a cerebral vein thrombosis caused by infection through venous system either superficial and deep face veins such as facial veins and air sinuses veins. Based on details description of basic Venus system draining (Standring, 2005), current study describes the pathogenic of covid19 infection transmission to cause cavernous sinus thrombosis through superficial veins transmit face skin infection via superior and inferior ophthalmic veins as well as transmit the skin of scalp infections through supra orbital and supra trochlear veins through to superior ophthalmic veins.

Cavernous sinus thrombosis may occur due to spread of infection from ethmoid by ethmoidal veins or sphenoid sinuses (Zhang and Stringer. 2010) due to cerebral, meningeal and diploic veins and dental procedures (Patel *et al.* 2020) due to the superior and inferior alveolar veins drained into cavernous sinuses. Although, the maxillary sinus infection may occur due to Covid19 infection in which the viruses transmit by venous system in which the maxillary veins drain backward to pterygoid plexus then to cavernous sinuses via emissary veins. As a result, the post COVID19 cavernous thrombosis may compress the trigeminal nerve and produce clinical features by its lateral wall however it may effect more than one neurological cranial deficits presenting dysfunction of extraocular muscle innervated by oculomotor and trochlear nerves as well as the ophthalmic and maxillary divisions of trigeminal nerve. Therefore, physician should examine the eye and other cranial nerve followed by request of computerize tomography CT to exclude or document cavernous thrombosis which ends with blindness. During pandemic, sever covid19 found to be a main reason of mucormycosis infection in 88% affecting 57% PNS involvement (Carlos and Pablo 2021), infraorbital nerve in 64% and maxillary branch of trigeminal nerve in 52% (Bhuskute *et al.* 2022). On the other hand, several trigeminal neuralgia case studies have been reported by (Kaya & Kaya, 2021; Narasimhalu *et al.*, 2021; Santovito and Pinna 2021; Onoda *et al.* 2022). However, three cases beyond of 45 years presented with history of coexistent chronic disease such as diabetes, hypertension with or without hyperlipidemia, scoliosis or brain surgery. The investigation is highly suggested that trigeminal neuropathy is result of consequences of chronic diseases whereas Santovito and Pinna (2021) presented a case believing that the vaccine is main reason inducing the trigeminal neuropathy based on no

other significant finding in history and investigation.

Based on current study reviews, the unknown cases, 48 cases of trigeminal neuralgia of Covid19 disease without any reasons of affected eye which are Bohania *et al* 2021 reported four cases, Vasanthpuram and Badakere (2021), A.C.De.F Ferreira *et al* 2020, Zhang *et al* 2020 and Molina *et al* 2021, Emami and Marolin (2021) and Maksimova *et al* (2022) reported six cases whereas Caggia *et al* 2021 reported ten cases and Kasimov *et al* (2022) reported twenty-eight cases postcovid19 cavernous sinus thrombosis involving ophthalmic division of trigeminal nerve which have no reason of

ocular pain in 0.6% of covid19 cases. Therefore, current study explain that reason of trigeminal neuralgia is due to compression of trigeminal nerve by lateral wall of cavernous sinuses.

According on to Sen *et al* (2021), the ocular pain is presenting feature of COVID-19 disease ranging from 10.3% to 31.2% as Aggarwal *et al* (2020) reported a highest incidence rate whereas Rokohl *et al* (2020) reported lowest rate. On current met analysis study, the ocular pain is presenting feature of COVID-19 disease ranging from 0.8% to 48.6% (Table 1, Figure 1) as Abrishami *et al* (2020) reported a highest incidence

Table 1. The incidence rate of trigeminal neuralgia of known and unknown reasons.

Study	Number trigeminal (ophthalmic) neuralgia cases	Total covid19 cases	Rate
Known reason cases			
Abrishami <i>et al</i> (2020)	69	142	48.6
Aggarwal <i>et al</i> (2020)	68	196	34.2
Atum <i>et al</i> (2020)	10	40	25
Chen <i>et al</i> (2020)	23	535	4.2
Guan <i>et al</i> (2020)	9	1099	0.8
Guemes-Villahoz <i>et al</i> (2020)	35	310	11.3
Hong <i>et al</i> (2020)	15	56	26.8
Karimi <i>et al</i> (2020)	2	43	4.9
Lan <i>et al</i> (2020)	3	81	3.7
Landecho <i>et al</i> (2020)	6	27	22.2
Lee <i>et al</i> (2020)	3	103	2.9
Loffredo <i>et al</i> (2020)	13	1167	1.1
Lomi <i>et al</i> (2020)	8	127	8.7
Ma <i>et al</i> (2020)	4	216	27.3
Marinho <i>et al</i> (2020)	12	12	100
Meduri <i>et al</i> (2020)	3	29	10.3
Öncül <i>et al</i> (2020)	16	197	8.1
Perlman <i>et al</i> 2020	218	2523	8.6
Rokohl <i>et al</i> (2020)	11	108	10.2
Seah <i>et al</i> (2020)	1	17	5.9
Sindhuja <i>et al</i> (2020)	12	127	9.4
Sun <i>et al</i> (2020)	2	102	2
Tostmann <i>et al</i> (2020)	31	91	34.1
Wu <i>et al</i> (2020)	12	38	31.6
Xia <i>et al</i> (2020)	1	30	3.3
Xu <i>et al</i> (2020)	2	30	6.7
Zhou <i>et al</i> (2020)	1	67	1.5
Total study rate of known	590	7513	7.8
Unknown reason cases			
	48	48	0.6
Total study rate of known and unknown	638	7561	8.4

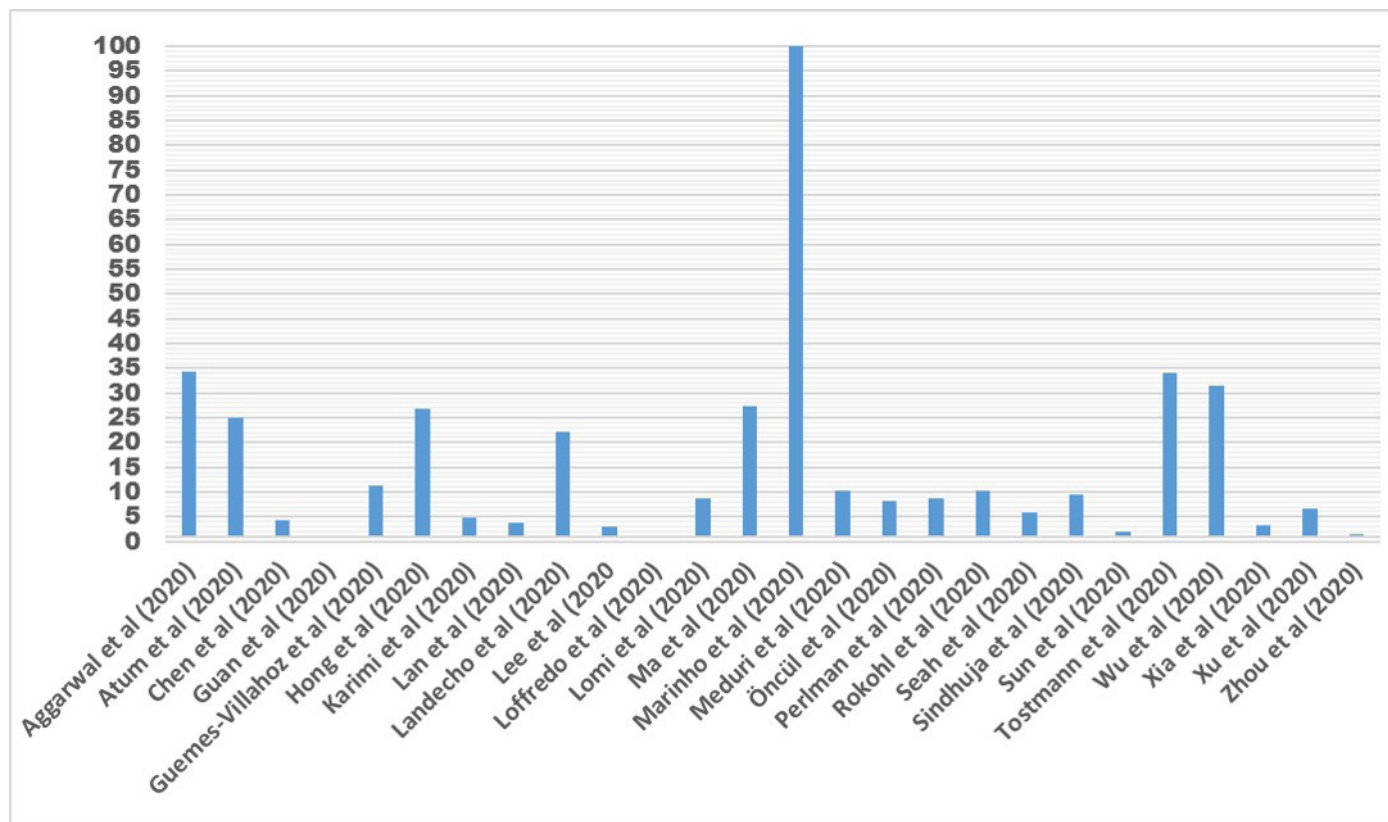


Figure 1. The incidence rate of trigeminal neuralgia

rate whereas Guan *et al* (2020) reported lowest rate. However, Nasiri *et al* (2021) according to meta-analysis found the ocular pain in COVID-19 cases due eye condition found to be 7.8%. Based on current meta-analysis study, the ocular pain due eye condition found to be 7.8% (Table 1). Further, meta-analysis result of current study, the incidence of trigeminal neuralgia including known and unknown reason of eye condition based on history and clinical examination is 8.4% (Table 1). Therefore, the trigeminal neuralgia is a manifestation of covid19 disease. The physician should be aware of trigeminal neuralgia to isolate patient to prevent spread of infection. Further, ophthalmologist must to be careful in examination of patient presenting with trigeminal neuralgia using personal protective equipment to avoid spread of infection. This study to

alert administration of health to prevent outbreak of covid19 between staffs and patients.

Acknowledgments

I would like to thank Professor Roger Soames who support me by encouraging and inspiring instead of despairing me or providing obstacles. I would take opportunity to acknowledge people who stress me to produce positive side and to expand my research vision as long as increase their efforts to make the challenge more difficult in my profession. Finally, I would like to thank my mum (Mariam Abdulhay Al Abdalnabi) for her support entire her life when she passed away on Friday (23-7-2021) due to outbreak infection in hospital and entire medical employees who served her well.

References

1. Abrishami M, Tohidinezhad F, Daneshvar R, Omidtabrizi A, Amiri M, Sedaghat A, *et al.* 2020) Ocular Manifestations of Hospitalized Patients with COVID-19 in Northeast of Iran. *Ocul Immunol Inflamm.* vol. 28, pp.739-44.
2. A. C. De Ferreiraa A, Romao T, Macedoa Y, Pupea C, Nascimento O. 2020. Case Study: COVID-19 and herpes zoster co-infection presenting with trigeminal neuropathy. *European Academy of Neurology.* Vol. 27 no. 9, pp.1748-1750.
3. Aceti A., Margarucci L.M., Scaramucci E., Orsini M., Salerno G., Di Sante G., Gianfranceschi G., Di Liddo R., Valeriani F., Ria F., Simmaco M., Parnigotto P.P., Vitali M., Romano Spica V., Michetti F., 2020. Serum s100B protein as a marker of severity in COVID-19 patients. *Sci Rep.* 10:18665. [PMC free article] [PubMed] [Google Scholar].
4. Aggarwal K, Agarwal A, Jaiswal N, Dahiya N, Ahuja A, Mahajan S, *et al.*, 2020. Ocular surface manifestations of coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis. *PLoS One.* vol.15:e0241661.
5. Al-Talalwah W., Al Dorzi, S., 2021. New Clinical Anatomical Interpretation of COVID-19 Pandemic Infection. *Int. J. Morphol.*, vol. 39 no. 2, pp. 635-637.
6. Apfelbaum RI., 2000. Neurovascular decompression: The procedure of choice? *Clin Neurosurg.* vol. 46, pp.473-498.
7. Bohania N, Ish P, Nune A, Lyengar K.P., 2021. Cranial neuropathy in COVID-19: a case series and review of literature. *Le Infezioni in Medicina*, no. 4, pp. 609-613. doi:10.53854/liim-2904-15.
8. Atum M., Boz A. A. E., Çakır B. *et al.*, 2020. "Evaluation of conjunctival

- swab PCR results in patients with SARS-CoV-2 infection," *Ocular Immunology and Inflammation*, vol. 28, no. 5, pp. 745–748.
9. Bendtsen L., Zakrzewska J.M., Abbott J., Braschinsky M., Stefano G. Di, Donnet A., *et al.*, 2019. European academy of neurology guideline on trigeminal neuralgia. *Eur. J. Neurol.*, 26 pp. 831–849.
 10. Bhuskute G, Keshri AK, Mathialagan A, Dubey A, Baghel S, Singh N, Jaiswal AK, Srivastava A, Manogaran R, Behari S, Kumar R., 2022. Changing Spectrum of Invasive Fungal Infections of Anterior Skull Base. *J Neurol Surg B Skull Base*. vol. 83 no. S 01, pp. S1–S270. DOI: 10.1055/s-0042-1743908.
 11. Caggia E, Bongiorno J, Ventura M, Lingenti V, Maci V. 2021. Trigeminal neuralgia post COVID-19: Preliminary report and clinical consideration. *Journal of the Neurological Sciences*. vol. 429 no. 119882, pp. 112. DOI: <https://doi.org/10.1016/j.jns.2021.119882>.
 12. Carlos Duran J, Pablo Duran J. Post COVID-19 neurological syndrome: 2021. A prospective study at 3600 m above sea level in La Paz Bolivia. *J Neurol Sci*. vol. 429 no. 119820. doi:10.1016/j.jns.2021.119820
 13. Arnold, M. 2018. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalgia, vol. 38 no. 1, pp. 1–211. Sage Publications 10.1177/0333102417738202
 14. Devasagayam S, Wyatt B, Leyden J, Kleinig T., 2016. Cerebral Venous Sinus Thrombosis Incidence Is Higher Than Previously Thought: A Retrospective Population-Based Study. *Stroke*. 2016. vol. 47 no. 9, pp.2180–2
 15. Chen L, Liu M, Zhang Z, *et al.* 2020. Ocular manifestations of a hospitalised patient with confirmed 2019 novel coronavirus disease. *Br J Ophthalmol*. vol. 104 no. 6, pp. 748–751.
 16. Deffner F., Scharr M., Klingenstein S., Klingenstein M., Milazzo A., Scherer S., Wagner A., Hirt B., Mack A.F., Neckel P.H. 2020. Histological evidence for the enteric nervous system and the choroid plexus as alternative routes of neuroinvasion by SARS-CoV2. *Front Neuroanat*. vol. 14:596439. [PMC free article] [PubMed] [Google Scholar]
 17. Emami S, Margolin E., 2021 .Diplopia, Ptosis, and Drooling in an 80-Year-Old Woman. *JAMA Ophthalmol*. vol. 139 no. 12, pp.1317–1318.
 18. Fodoulian L, Tuberosa J, Rossier D, Boillat M, Kan C, Pauli V. 2020. SARS-CoV-2 receptors and entry genes are expressed in the human olfactory neuroepithelium and brain. *IScience*, vol. 23, pp. 101839. doi:10.1016/j.isci.2020.101839.
 19. Franca R.A., Uggá L., Guadagno E., Russo D., Del Basso De Caro M. 2021. Neuroinvasive potential of SARS-CoV2 with neuroradiological and neuropathological findings: is the brain a target or a victim? *APMIS*. vol. 129, pp. 37–54.
 20. Guan WJ, Ni ZY, Hu Y, *et al.* 2020. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. vol. 382 no. 18, pp. 1708–20.
 21. Guemes-Villaloz N, Burgos-Blasco B, Arribi-Vilela A, *et al.* 2020. SARS-CoV-2 RNA detection in tears and conjunctival secretions of COVID-19 patients with conjunctivitis. *J Infect*. vol. 81 no. 3, pp. 452–482.
 22. Hong N, Yu W, Xia J, Shen Y, Yap M, Han W. 2020. Evaluation of ocular symptoms and tropism of SARS-CoV-2 in patients confirmed with COVID-19. *Acta Ophthalmol*. vol. 98, pp. e649– e55. doi: 10.1111/aos.14445. PubMed PMID: 32336042; PubMed Central PMCID: PMC7267628.
 23. Hong W, Zheng X, Wu Z, Li X, Wang X, Li Y, Zhang W, Zhong J, Hua X, Li S. 2011. Clinical features and surgical treatment of trigeminal neuralgia caused solely by venous compression. *Acta Neurochir* vol. 153, pp. 1037–1042.
 24. Huff T, Daly DT. 2020. Neuroanatomy, Cranial Nerve 5 (Trigeminal) [Updated 2020 Jul 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.
 25. Jones MR, Urits I, Ehrhardt KP, *et al.* 2019. A comprehensive review of trigeminal neuralgia. *Curr Pain Headache Rep*. vol. 23, pp.74.
 26. Karimi, A. Arabi, T. Shahraki , Safi S. 2020. "Detection of severe acute respiratory syndrome Coronavirus-2 in the tears of patients with Coronavirus disease 2019," *Eye*, vol. 34, no. 7, pp. 1220–1223,
 27. Kasimov, Ulugbek K.; Abdullaev, Ulugbek P. Boboev, Kakhramon X.; and Sultanova, Diyora U. 2022. Analysis of the results of treatment of 93 patients with post-covid thromboses of the cavernous sinus in the conditions of the department of purulent surgery. *Central Asian Journal of Medicine*, Vol. 1. at <https://uzjournals.edu.uz/tma/vol2022/iss1/2>
 28. Khalili M, Karamouzian M, Nasiri N, Javadi S, Mirzazadeh A, Sharifi H. 2020. Epidemiological characteristics of COVID-19: a systematic review and meta-analysis. . vol. 148, pp. e130.
 29. Klein R.S., Garber C., Funck K.E., Salimi H., Soung A., Kanmogne M., Manivasagam S., Agner S., Cain M. 2019. Neuroinflammation during RNA viral infections. *Annu Rev Immunol*. vol. 37, pp. 73–95.
 30. Kaya A, Kaya SY. 2022. A case of trigeminal neuralgia developing after a COVID-19 vaccination. *J Neurovirol*. 28, pp. 81–182.
 31. Lan QQ, Zeng SM, Liao X, *et al.* 2020. A special on epidemic prevention and control: screening for novel coronavirus related conjunctivitis among the patients with coronavirus disease 2019. *Zhonghua Yan Ke Za Zhi*, vol. 56 no. 6, pp. 433–437.
 32. Landecho MF, Yuste JR, Gañdara E, *et al.* 2020. COVID-19 retinal microangiopathy as an in vivo biomarker of systemic vascular disease? *J Intern Med*. <https://doi.org/10.1111/joim.13156>.
 33. Lee YH, Kim YC, Shin JP. 2020. Characteristics of Ocular Manifestations of Patients with Coronavirus Disease 2019 in Daegu Province, Korea. *J Korean Med Sci*; vol. 35pp. e322. doi: 10.3346/jkms.2020.35.e322. PubMed PMID: 32893523; PubMed Central PMCID: PMC7476796
 34. Loffredo L, Pacella F, Pacella E, Tiscione G, Oliva A, Violi F. 2020. Conjunctivitis and COVID-19: a metaanalysis. *J Med Virol*. vol. 92 no. 9, pp. 1413–1414
 35. Lomi N, Sindhuja K, Asif M, Tandon R. 2020. Clinical profile and prevalence of conjunctivitis in mild COVID-19 patients in a tertiary care COVID-19 hospital: a retrospective cross-sectional study. *Indian J Ophthalmol*. vol. 68 no. 8, pp. 1546.
 36. Ma N, Li P, Wang X, *et al.* 2020. Ocular Manifestations and Clinical Characteristics of Children With Laboratory-Confirmed COVID-19 in Wuhan, China. *JAMA Ophthalmol*. vol. 138 no. 10, pp. 1079–1086.
 37. Maksimova M.Yu, Grusha Ya.O. , Fettser E. I. (2022) COVID-19 associated multiple cranial neuropathies. *Неврология, нейропсихиатрия, психосоматика*. vol. 14 no. 1, pp. 99–103.
 38. Marinho PM, Marcos AA, Romano AC, Nascimento H, Belfort R. 2020. Retinal findings in patients with COVID-19. *Lancet*. vol. 395 no. 10237, pp.1610. [https://doi.org/10.1016/s0140-6736\(20\)31014-x](https://doi.org/10.1016/s0140-6736(20)31014-x).
 39. Meduri A., Oliverio G. W., Mancuso G. *et al.*, 2020. "Ocular surface manifestation of COVID-19 and tear film analysis," *Scientific Reports*, vol. 10, no. 1, Article ID 20178,
 40. Molina-Gil J, González-Fernández L, García-Cabo C. 2021 Trigeminal neuralgia as the sole neurological manifestation of COVID-19: A case report. *Headache*. vol. 61 no. 3, pp. 560–562. doi: 10.1111/head.14075. Epub PMID: 33749854; PMCID: PMC8251254.
 41. Mueller D, Obermann M, Yoon MS, Poitz F, Hansen N, Slomke MA, Dommes P, Gizewski E, Diener HC, Katsarava Z. 2011. Prevalence of trigeminal neuralgia and persistent idiopathic facial pain: a population-based study. *Cephalgia*. vol. 31 no. 15, pp. 1542–8.
 42. Narasimhalu K, Lee WC, Salkade PR, De Silva DA. 2021. Trigeminal and cervical radiculitis after tozinameran vaccination against COVID-19. *BMJ Case Rep*. vol. 14 no. 6, pp. e242344.
 43. Nasiri, N., Sharifi, H., Bazrafshan, A., Noori, A., Karamouzian, M., & Sharifi, A. 2021. Ocular Manifestations of COVID-19: A Systematic Review and Meta-analysis. *Journal of ophthalmic & vision research*, vol. 16 no. 1, pp. 103–112.
 44. Öncül H., Öncül F. Y., Alakus M. F., Çağlayan M., Dag U., 2021. "Ocular findings in patients with coronavirus disease 2019 (COVID-19) in an outbreak hospital," *Journal of Medical Virology*. vol. 93 pp.1326–1322
 45. Onoda K, Fujiwara R, Wakamiya T, Michiwaki Y, Tanaka T, Shimoji K, Suehiro E, Yamane F, Kawashima M, Matsuno A. 2022. Trigeminal neuropathy after tozinameran vaccination against COVID-19 in postmicrovascular decompression for trigeminal neuralgia: illustrative case. *J Neurosurg Case Lessons* vol. 3 no. 16:CASE22101, DOI: 10.3171/CASE22101
 46. Zhang J, Stringer, MD 2010. Ophthalmic and facial veins are not valveless. *Clin Exp Ophthalmol*. vol. 38 no. 5, pp.502–10.
 47. Paniz-Mondolfi A., Bryce C., Grimes Z. 2020. Central Nervous System involvement by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). *J Med Virol*. vol. 92, pp. 699–702.
 48. Patel A, Kaur H, Zess I, Michael JS, Savio J, Rudramurthy S, *et al.* 2020. A multicentre observational study on the epidemiology,

- risk factors, treatment and outcomes of mucormycosis in India. *Clin Microbiol Infect.* vol. 26, pp. 944 - e9.;
49. Perlman A, Vodonos Zilberg A, Bak P, Dreyfuss M, Leventer-Roberts M, Vurembrand Y, et al. 2020. Characteristics and Symptoms of App Users Seeking COVID-19-Related Digital Health Information and Remote Services: Retrospective Cohort Study. *J Med Internet Res.* vol. 22, pp. e23197. doi: 10.2196/23197. PubMed PMID: 32961527; PubMed Central PMCID: PMC7609191.
50. Rokohl AC, Loreck N, Wawer Matos PA, Zwingelberg S, Augustin M, Dewald F, et al. 2020. More than loss of taste and smell: burning watering eyes in coronavirus disease 2019. *Clin Microbiol Infect.* vol. 26, pp. 1560. doi: 10.1016/j.cmi.2020.08.018. PubMed PMID: 32835793; PubMed Central PMCID: PMC7442009.
51. Standring, S. 2005. *Gray's Anatomy*. 39th ed. London, Elsevier, Churchill Livingstone, pp.687.
52. Santovito LS, Pinna G. 2021. Acute reduction of visual acuity and visual field after Pfizer-BioNTech COVID-19 vaccine 2nd dose: a case report. *Inflamm Res.* vol. 4, pp.1-3. doi:10.1007/s00011-021- 01476-9.
53. Seah I, Anderson DE, Kang A, et al. 2020. Assessing viral shedding and infectivity of tears in coronavirus disease 2019 (COVID-19) patients. *Ophthalmology.* vol. 127 no. 7, pp. 977-9.
54. Sen M, Honavar SG, Sharma N, Sachdev MS. COVID-19 and Eye: 2021. A Review of Ophthalmic Manifestations of COVID-19. 2013. *Indian J Ophthalmol.* vol. 69, pp488-509.
55. Sharouni H., Narayanan P. 2015. *Iranian Red Crescent Medical Center, 3rd edition (beta version)*. vol. 3317. No 1. pp. 629-808.
56. Sindhuja K., Lomi N., Asif M. I., Tandon R., "Clinical profile and prevalence of conjunctivitis in mild COVID-19 patients in a 2020. tertiary care COVID-19 hospital: a retrospective cross-sectional study," *Indian Journal of Ophthalmology*, vol. 68, no. 8, pp. 1546-1550.
57. Sun X, Zhang X, Chen X, et al. 2020. The infection evidence of SARS-COV-2 in ocular surface: a single-center cross-sectional study. *medRxiv.* 10.1101/2020.02.26.20027938.
58. Tostmann A, Bradley J, Bousema T, Yiek W-K, Holwerda M, Bleeker-Rovers C, et al. 2020. Strong associations and moderate predictive value of early symptoms for SARS-CoV-2 test positivity among healthcare workers, the Netherlands, March 2020. *Euro Surveill.* vol. 25. <https://doi.org/10.2807/1560-7917.ES.2020.25.16.2000508> PMID: 32347200.
59. Vasanthpuram VH, Badakere A. 2021. Internuclear ophthalmoplegia as a presenting feature in a COVID-19-positive patient. *BMJ Case Rep.* vol.14:e241873.doi:10.1136/bcr-2021-241873
60. Worldometer. COVID-19 coronavirus pandemic [Internet]. Worldometer; 2020. Available from: <https://www.worldometers.info/coronavirus/>
61. Wu P, Duan F, Luo C, et al. 2020. Characteristics of ocular findings of patients with coronavirus disease 2019 (COVID-19) in Hubei Province, China. *JAMA Ophthalmol.* vol. 138 no. 5, pp. 575-578.
62. Xia J, Tong J, Liu M, Shen Y, Guo D. 2020. Evaluation of coronavirus in tears and conjunctival secretions of patients with SARS-CoV-2 infection. *J Med Virol.* <https://doi.org/10.1002/jmv.25725> PMID:32100876
63. Xu li, Zhang X, Song W, Sun B, Mu J, Dong X, et al. 2020. Conjunctival polymerase chain reaction-tests of 2019 novel coronavirus in patients in Shenyang, China. *medRxiv.* 2020.02.23.20024935. <https://doi.org/10.1101/2020.02.23.20024935>
64. Yadav YR, Nishtha Y, Sonjjay P, Vijay P, Shailendra R, Yatin K. 2017. Trigeminal Neuralgia. *Asian J Neurosurg.* vol.12 no. 4, pp. 585-597.
65. Yashavantha Rao H.C., Jayabaskaran C. 2020. The emergence of a novel coronavirus (SARS-CoV-2) disease and their neuroinvasive propensity may affect in COVID-19 patients. *J Med Virol.* vol. 92, pp. 786-790.
66. Zhang Q, Shan KS, Abdollahi S, Nace T. 2020. Anosmia and Ageusia as the Only Indicators of Coronavirus Disease 2019 (COVID-19). *Cureus.* vol. 12 no. 5, pp. e7918. Published 2020 May 1. doi:10.7759/cureus.7918
67. Zhou Y, Zeng Y, Tong Y, Chen C. 2020. Ophthalmologic evidence against the interpersonal transmission of 2019 novel coronavirus through conjunctiva. *medRxiv.* 10.1101/2020.02.11.20021956.

Received: September 18, 2022

Accepted: July 20, 2022

Corresponding author

Waseem Al-Talalwah

E-mail: altalalwah@ksau-hs.edu.sa