



Does the SARS-CoV-2 pandemic really increase the frequency of peripheral facial palsy?

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ABSTRACT

Purpose: Publications about increased number of peripheral facial paralysis in the COVID-19 pandemic emerged in the literature. However, these studies comprised of an estimate rather than a broad analysis of exact numbers. In this study, we planned to investigate whether the pandemic really resulted in an increase in facial paralysis cases admitted to the hospital by evaluating the cases who applied to our hospital due to facial paralysis in the COVID-19 pandemic year and in the previous 4 years.

Materials and methods: Patients who applied to our hospital due to facial paralysis between March 2016–February 2017 (Group 1), between March 2017–February 2018 (Group 2), between March 2018–February 2019 (Group 3), between March 2019–February 2020 (Group 4), and between March 2020–February 2021 (Group 5) were investigated and detailed data were noted.

Results: 156, 164, 149, 172 and 157 patients were admitted to the hospital due to peripheral facial paralysis in Group 1, 2, 3, 4, and 5, respectively. Of these patients, 155, 164, 145, 169, and 153 were Bell's palsy, respectively. SARS-CoV-2 RT-PCR test was positive in only 2 of the 153 patients who were diagnosed in the year of the pandemic.

Conclusions: This study showed that the number of peripheral facial paralysis detected during the COVID-19 pandemic was similar to previous years. Very few number of positive SARS-CoV-2 RT-PCR test results may have been found incidentally in Bell's palsy patients. These stating that SARS-CoV-2 causes peripheral facial paralysis should be supported by laboratory studies and postmortem research.

1. Introduction

The new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) resulted in a pandemic with a novel spread rate by infecting thousands of people in a short period of time. The rapid spread of the outbreak occurred because of the infection being contagious during its asymptomatic period and the disease could be starting with common nonspecific upper respiratory tract symptoms such as unproductive cough, sore throat, and postnasal discharge [1]. By affecting the lower respiratory tract, the disease could lead to mortality in the setting of severe respiratory failure.

Several symptoms due to the multisystemic effects of the disease were defined and reports about neurotropism of coronaviruses are

recently being published [1,2]. A variety of peripheral or central neurological symptoms indicating the neurological involvement are defined in the literature. Among the central symptoms dizziness, impaired consciousness, headache, nausea, acute cerebrovascular disease, and seizure; and due to the involvement of peripheral nerves anosmia, ageusia, and vision loss are reported [2].

This coronavirus disease-19 (COVID-19) pandemic period reminded us the term “excess mortality”. This public health term is related with the extraordinarily increased number of expected mortality [3]. In a similar way, there are some reports about the peripheral facial paralysis regarding SARS-CoV-2 infection [4–14]. Thereupon, in this study, we performed an archival research determining the patients who admitted to our hospital with peripheral facial paralysis in the COVID-19

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pandemic year and in the previous four years to reveal whether there was really an increase in the admission rate during the pandemic and to evaluate the patients who had a positive Real-time polymerase chain reaction (RT-PCR) test result for SARS-CoV-2 among those patients who were admitted with this symptom.

2. Material and methods

This retrospective study was conducted in Istanbul Medeniyet University Goztepe Training and Research Hospital Department of Otorhinolaryngology and is approved by Istanbul Medeniyet University Goztepe Training and Research Hospital Clinical Investigation Ethics Committee (Date of decision: April 9, 2020/number: 0188). The hospital archive was investigated and patients who were admitted to the hospital with the complaint of facial paralysis in the years 2016–2017–2018–2019–2020 and 2021 were identified retrospectively. As the first COVID-19 case in Turkey was diagnosed in March 2020, the patients were divided into 5 different groups of those who were diagnosed in between March 2016–February 2017 (1st group), March 2017–February 2018 (2nd group), March 2018–February 2019 (3rd group), March 2019–February 2020 (4th group), and March 2020–February 2021 (5th group); and yearly numbers of patients admitted with facial paralysis were determined. After excluding the known causes such as trauma, Ramsay Hunt syndrome, or chronic otitis media and central facial paralysis, those who were diagnosed with idiopathic peripheral facial paralysis (Bell's palsy) were included in assessment. In order to calculate the incidence of Bell's palsy in our hospital district, the population data of Kadikoy district of Istanbul city in the years 2016–2020 were accessed from Turkey Statistical Institute (TURKSTAT). Incidence data was calculated as the number of new Bell's palsy cases admitted to our hospital divided by the population of the at-risk area. The incidence data of each year were compared with the 2020–2021 value by one-sample *t*-test. The level of significance was accepted as $p < 0.05$. In addition, of the patients who were diagnosed with idiopathic peripheral facial paralysis during the pandemic, results of those who had a RT-PCR test of nasopharyngeal and oropharyngeal swabs for SARS-CoV-2 at the time of diagnosis were noted.

3. Results

The first analysis revealed that there were 156, 164, 149, 172, and 157 patients in the 1st, 2nd, 3rd, 4th, and 5th group, respectively. Patients who were diagnosed other than Bell's palsy and thus excluded from the study by years are given in Table 1. The number of patients diagnosed with idiopathic peripheral facial paralysis in the 1st, 2nd, 3rd, 4th, and 5th group, respectively, were 155, 164, 145, 169, and 153. In the 5th group, 2 of the patients were tested positive for SARS-CoV-2 while 96 of them were found to be negative. 53 of them did not have a RT-PCR analysis at the time of diagnosis (Table 1).

The number of Bell's palsy cases, the population of the district, and

the incidence of Bell's palsy according to years are given in Table 2. At the end of the comparisons, no significant difference was found in the incidence of idiopathic peripheral facial paralysis between the pandemic year and the previous years ($p = 0.088$) (Table 2).

4. Discussion

In this study, by evaluating the patients who were admitted to our hospital and had a diagnosis of peripheral facial paralysis in the last year spent with the COVID-19 pandemic and in the previous 4 years, it was investigated whether there was an increase in the incidence of Bell's palsy during the pandemic period and seen that no significant difference existed.

The newly emerging SARS-CoV-2 effects on human body, particularly which systems and how it affects, are defined in several studies. SARS-CoV-2 is a virus similar to Severe Acute Respiratory Syndrome Corona Virus (SARS-CoV) and Middle East Respiratory Syndrome Corona Virus (MERS-CoV) in terms of genomic structure [1]. Apart from respiratory symptoms, SARS-CoV and MERS-CoV were reported to involve nerves by developing a neuroinvasive process [15,16]. Eliezer et al. reported a case with total loss of olfactory sensation [17]. On this basis, the ability of SARS-CoV-2 to have neurological involvement and its potential symptoms were discussed [1,2]. In a study conducted in Wuhan, Mao et al. reported patients with central nervous system involvement in more severe cases [1]. In another article, it was argued that failure of respiratory system was not correlated with central involvement [18]. Zhou et al. mentioned the relation of SARS-CoV-2 and viral encephalitis [19]. Some case reports and series stated an association of SARS-CoV-2 infection with Guillain-Barré syndrome [20–26].

In etiology of idiopathic peripheral facial nerve palsy, viral agents are also thought to be responsible. Specifically, Herpes Simplex Virus-1 and Varicella Zoster Virus, which are able to establish latent infection in ganglion cells for long periods of time, are mostly accused [27]. As we know the potential effects of viruses on facial nerve palsy, in these COVID-19 pandemic days we are living, occurrence of peripheral facial paralysis cases and RT-PCR test results turning out to be positive in some

Table 2

The number of Bell's palsy cases, the population of the district, and the incidence of Bell's palsy according to years.

Year	Bell's palsy	Population	Incidence	Mean incidence $\pm$ SD
2016–2017	155	452,302	0.00034490	0.000338372 $\pm$
2017–2018	164	451,453	0.00036327	0.000020809
2018–2019	145	458,638	0.00031615	
2019–2020	169	482,713	0.00035010	
2020–2021	153	481,983	0.00031744	
$p = 0,088$				

SD; Standard deviation.

Table 1

The number of idiopathic and secondary peripheral facial nerve palsies diagnosed according to years and the RT PCR results of idiopathic facial paralysis patients in the pandemic year.

	March 2016–February 2017	March 2017–February 2018	March 2018–February 2019	March 2019–February 2020	March 2020–February 2021
Total number of peripheral facial paralysis cases	156	164	149	172	157
Bell's palsy	155	164	145	169	153
Trauma	–	–	–	2	1
Ramsay Hunt syndrome	–	–	1	–	2
Chronic otitis media	1	–	3	1	1
SARS-CoV-2 RT PCR results in Bell's palsy cases					153
Positive					2
Negative					92
Unknown					59

of them reminded the idea of SARS-CoV-2 leading to this pathology and articles, most of which were case reports and series, were published about the issue [4–7,9–11,14]. In the beginning of the outbreak when the pandemic spread to our country, after one of the five patients admitted to our clinic with peripheral facial paralysis had a positive RT-PCR test, we reported that to WHO and presented it in the Turkish National Otorhinolaryngology and Head & Neck Surgery Virtual Congress of 2020 [28]. Consideration of every possible symptom during the pandemic period is of utmost importance to break the chain of spread. Knowing the sensibility of the issue, publishing reports in this regard is rather unexceptional. However, as the time progresses, further developments and accumulation of observational knowledge could lead to changes in the preliminary arguments. This is what suits for the nature of scientific progress: First suspecting, then searching for the truth. In the first month of the pandemic, when five idiopathic peripheral facial paralysis patients admitted to our clinic successively in this short time of period and the RT-PCR test of one of those patients who admitted with peripheral facial paralysis but no other symptoms resulted positive, with the idea of contributing to the control of the pandemic we thought that one of the first and the only sign of SARS-CoV-2 infection could be peripheral facial paralysis although the positivity rate was only one in five patients. After the acute period of the pandemic, however, as we observed there was actually no apparent difference in the number of facial paralysis patients compared to previous years, we decided to review the data of the last 5 years and the SARS-CoV-2 RT-PCR test results of the patients admitted in the last year with peripheral facial paralysis. As a result, we found 155 patients in between 2016–2017, 164 patients in between 2017–2018, 145 patients in between 2018–2019, 169 patients in between 2019–2020, and 153 patients in between 2020–2021 which was the pandemic period were admitted to our clinic with idiopathic peripheral facial paralysis (Table 1). As is seen from the results, there was no increase in the number of cases in the pandemic year. Thus, the results do not validate the arguments set up in the first few months of the pandemic stating that there was an increase in the number of peripheral facial paralysis cases. When the SARS-CoV-2 RT-PCR test results of those patients were analysed, of the 98 patients who were tested during their paralysis, 2 had a positive result whereas the remaining patients resulted negative. That result is unable to support the thesis that SARS-CoV-2 virus leads to facial paralysis. Clarifying the issue could only be possible by performing postmortem studies in COVID-19 patients who developed facial paralysis and became exitus.

Evidence-based and certain results showing the effects of virus on nerves can be obtained from autopsy, for sure. As for SARS-CoV-2, certain involvement can be revealed by determining the presence of SARS-CoV-2 in the nervous system or demonstrating it by autopsy. In literature, it was reported that brain tissue was hyperemic and edematous and some neurons were degenerated in autopsy findings of patients infected with SARS-CoV-2 [29]. Although these findings lead to an expectation of involvement of the cranial nerves as well, demonstrating the involvement of the facial nerve by the virus in similar studies that will be performed on patients died from SARS-CoV-2 infection could enlighten the subject.

In this disease which has become a pandemic by infecting millions and causing the death of hundreds of thousands of people, it would certainly be crucial in terms of public health to recognize every potential symptom in order to break the chain of transmission. Every new symptom revealed has to be evidence-based, though. In the beginning of the pandemic, reporting of every newly encountered symptom alerts clinicians to pay attention to the issue and thus could decrease the spread rate of the disease by taking measures. However, absolute data could be acquired by concentrating on the subject after the end of the acute period. Through the detection of a positive SARS-CoV-2 RT-PCR test result in an idiopathic peripheral facial paralysis patient during our clinical observation in the early period of the pandemic, we had a first impression of an increase in the number of peripheral facial paralysis patients during this infectious period, which turned out to be inaccurate

after the collection of yearly data. We revealed that the number of patients did not increase compared to the previous years and the RT-PCR tests resulted negative in 98% of them.

5. Conclusions

COVID-19 patients could also present with nonspecific symptoms other than the commonly known symptoms. One of these nonspecific symptoms could be idiopathic peripheral facial paralysis. In opposition to the case reports and series regarding this and reports stating an increased frequency of these patients during this period, in our study it is seen that during the pandemic year there was no increase in the number of patients with idiopathic peripheral facial paralysis admitted to our clinic and 98% of those patients had a negative SARS-CoV-2 RT-PCR test result. To clarify the subject, postmortem studies on patients who developed idiopathic peripheral facial paralysis and died from COVID-19 in the same time period are needed.

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Statement of human rights

The study has been approved by the Ethical Committee of the Istanbul Medeniyet University, Goztepe Training and Research Hospital (4 April 2020; 2020/0188) and has been performed according to the ethical standards of the Helsinki Declaration.

Informed consent

NA

We declare that all authors have contributed to read and approved the final manuscript for submission.

Declaration of competing interest

The authors declare that they have no conflict of interest.

References

- [1] Li YC, Bai WZ, Hashikawa T. Response to commentary on “The neuroinvasive potential of SARS-CoV-2 may play a role in the respiratory failure of COVID-19 patients”. *J Med Virol* 2020;92(7):707–9. <https://doi.org/10.1002/jmv.25824>.
- [2] Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan. *China JAMA Neurol* 2020;77(6):1–9. <https://doi.org/10.1001/jamaneurol.2020.1127>.
- [3] Weinberger DM, Chen J, Cohen T, Crawford FW, Mostashari F, Olson D, et al. Estimation of excess deaths associated with the COVID-19 pandemic in the United States, March to May 2020 [published online July 01, 2020]. *JAMA Intern Med*. 2020;e203391. doi:<https://doi.org/10.1001/jamainternmed.2020.3391>.
- [4] Casas E, Barbosa A, Rubio-García E, Cebrián J, Díaz-Pérez C, de la Fuente E, et al. Parálisis facial periférica aislada en un paciente con COVID-19 [Isolated peripheral facial paralysis in a patient with COVID-19]. *Rev Neurol*. 2020;71(1):40–1. doi:[10.33588/rn.7101.2020229](https://doi.org/10.33588/rn.7101.2020229).
- [5] Homma Y, Watanabe M, Inoue K, Moritaka T. Coronavirus disease-19 pneumonia with facial nerve palsy and olfactory disturbance. *Intern Med* 2020;59(14):1773–5. <https://doi.org/10.2169/internalmedicine.5014-20>.
- [6] Ribeiro BNF, Marchiori E. Facial palsy as a neurological complication of SARS-CoV-2. *Arq Neuropsiquiatr* 2020;78(10):667. <https://doi.org/10.1590/0004-282X20200127>.
- [7] Lima MA, Silva MTT, Soares CN, Coutinho R, Oliveira HS, Afonso L, et al. Peripheral facial nerve palsy associated with COVID-19. *J Neurovirol* 2020;26(6):941–4. <https://doi.org/10.1007/s13365-020-00912-6>.
- [8] Codeluppi L, Venturelli F, Rossi J, Fasano A, Toschi G, Pacillo F, et al. Facial palsy during the COVID-19 pandemic. *Brain Behav* 2021;11(1):e01939. <https://doi.org/10.1002/brb3.1939>.
- [9] Figueiredo R, Falcão V, Pinto MJ, Ramalho C. Peripheral facial paralysis as presenting symptom of COVID-19 in a pregnant woman. *BMJ Case Rep* 2020;13(8):e237146. <https://doi.org/10.1136/bcr-2020-237146>.

- [10] Goh Y, Beh DLL, Makmur A, Somani J, Chan ACY. Pearls & Oy-sters: facial nerve palsy in COVID-19 infection. *Neurology*. 2020;95(8):364–7. <https://doi.org/10.1212/WNL.00000000000009863>.
- [11] Theophanous C, Santoro JD, Itani R. Bell's palsy in a pediatric patient with hyper IgM syndrome and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). *Brain Dev* 2021;43(2):357–9. <https://doi.org/10.1016/j.braindev.2020.08.017>.
- [12] Islamoglu Y, Celik B, Kiris M. Facial paralysis as the only symptom of COVID-19: a prospective study. *Am J Otolaryngol* 2021;42(4):102956. <https://doi.org/10.1016/j.amjoto.2021.102956>.
- [13] Brisca G, Garbarino F, Carta S, Palmieri A, Vandone M, Severino M, et al. Increased childhood peripheral facial palsy in the emergency department during COVID-19 pandemic. *Pediatr Emerg Care* 2020;36(10):e595–6. <https://doi.org/10.1097/PEC.0000000000002231>.
- [14] Cabrera Muras A, Carmona-Abellán MM, Collía Fernández A, Uterga Valiente JM, Antón Méndez L, García-Moncó JC. Bilateral facial nerve palsy associated with COVID-19 and Epstein-Barr virus co-infection. *Eur J Neurol* 2021;28(1):358–60. <https://doi.org/10.1111/ene.14561>.
- [15] Glass WG, Subbarao K, Murphy B, Murphy PM. Mechanisms of host defense following severe acute respiratory syndrome-coronavirus (SARS-CoV) pulmonary infection of mice. *J Immunol* 2004;173(6):4030–9. <https://doi.org/10.4049/jimmunol.173.6.4030>.
- [16] Li K, Wohlford-Lenane C, Perlman S, Zhao J, Jewell AK, Reznikov LR, et al. Middle East respiratory syndrome coronavirus causes multiple organ damage and lethal disease in mice transgenic for human dipeptidyl peptidase 4. *J Infect Dis* 2016;213(5):712–22. <https://doi.org/10.1093/infdis/jiv499>.
- [17] Eliezer M, Hautefort C, Hamel AL, Verillaud B, Herman P, Houdart E, et al. Sudden and complete olfactory loss function as a possible symptom of COVID-19 [published online ahead of print, 2020 Apr 8]. *JAMA Otolaryngol Head Neck Surg*. 2020; <https://doi.org/10.1001/jamaoto.2020.0832>. doi:<https://doi.org/10.1001/jamaoto.2020.0832>.
- [18] Turtle L. Respiratory failure alone does not suggest central nervous system invasion by SARS-CoV-2. *J Med Virol* 2020;92(7):705–6. <https://doi.org/10.1002/jmv.25828>.
- [19] Zhou L, Zhang M, Wang J, Gao J. Sars-Cov-2: underestimated damage to nervous system [published online ahead of print. Mar 24. *Travel Med Infect Dis* 2020;2020: 101642. <https://doi.org/10.1016/j.tmaid.2020.101642>.
- [20] Zhao H, Shen D, Zhou H, Liu J, Chen S. Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? *Lancet Neurol* 2020;19(5):383–4. [https://doi.org/10.1016/S1474-4422\(20\)30109-5](https://doi.org/10.1016/S1474-4422(20)30109-5).
- [21] Toscano G, Palmerini F, Ravaglia S, Ruiz L, Invernizzi P, Cuzzoni MG, et al. Guillain-Barré syndrome associated with SARS-CoV-2. *N Engl J Med* 2020;382(26): 2574–6. <https://doi.org/10.1056/NEJMc2009191>.
- [22] Scheidl E, Canseco DD, Hadji-Naumov A, Bereznai B. Guillain-Barré syndrome during SARS-CoV-2 pandemic: a case report and review of recent literature. *J Peripher Nerv Syst* 2020;25(2):204–7. <https://doi.org/10.1111/jns.12382>.
- [23] Virani A, Rabold E, Hanson T, Haag A, Elrufay R, Cheema T, et al. Guillain-Barré syndrome associated with SARS-CoV-2 infection. *IDCases*. 2020;20:e00771. <https://doi.org/10.1016/j.idcr.2020.e00771>.
- [24] Bigaut K, Mallaret M, Baloglu S, Nemoz B, Morand P, Baicry F, et al. Guillain-Barré syndrome related to SARS-CoV-2 infection. *Neurol Neuroimmunol Neuroinflamm* 2020;7(5):e785. <https://doi.org/10.1212/NXI.0000000000000785>.
- [25] Velayos Galán A, Del Saz Saucedo P, Peinado Postigo F, Botia Paniagua E. Guillain-Barré syndrome associated with SARS-CoV-2 infection. *Neurologia*. 2020;35(4): 268–9. English, Spanish. doi:<https://doi.org/10.1016/j.nrl.2020.04.007>.
- [26] De Sanctis P, Doneddu PE, Viganò L, Selmi C, Nobile-Orazio E. Guillain-Barré syndrome associated with SARS-CoV-2 infection. A systematic review. *Eur J Neurol* 2020;27(11):2361–70. <https://doi.org/10.1111/ene.14462>.
- [27] Zhang W, Xu L, Luo T, Wu F, Zhao B, Li X. The etiology of Bell's palsy: a review. *J Neurol* 2020;267(7):1896–905.
- [28] Mutlu A, Kalcioğlu MT, Cag Y, Gunduz AY, Bakici B, Yilmaz U. Periferik Fasyal Paralizi İçin Yeni Bir Olası Etiyoloji: SARS-CoV-2. Proceedings of the Turkish National Otolaryngology Head and Neck Surgery Virtual Congress 2020; 2020 November 26–28; p. 128. Available from: <https://tkbonline.serenaslive.com/Home/PosterDetail/61>; 2020 [accessed 5 March 2021].
- [29] National Health Commission of the People's Republic of China. Diagnosis and treatment of the novel coronavirus pneumonia (Trial version 7) [D], Available from: <http://www.nhc.gov.cn/yzygj/s7653p/202003/46c9294a7dfe4cef80dc7f5912eb1989/files/ce3e6945832a438eaae415350a8ce964.pdf>; 2020 [accessed 3 March, 2020].