Original Article

Impact of COVID-19 on Peripheral Nervous System Disorders

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ABSTRACT

Objective: The objective of this study was to determine the frequency of peripheral nervous system disorders among COVID-19 survivors.

Study Design: Cross-sectional Survey

Place and Duration of Study: This study was conducted at the Department of Rehabilitation and Allied Health Sciences, Riphah International University Lahore Campus from December, 2020 to June, 2021 for a period of 06 months.

Materials and Methods: 144 patients recovered from Covid–19 through non probability convenience sampling were recruited for study. Patients were assessed for pain, smell, taste, balance and two-point discrimination and the ability to identify familiar objects. The data was collected according to the responses after patients approved to provide information. Data was coded in SPSS data sheet which was later analyzed for statistical frequencies and percentages.

Results: Mean age of patients was reported to be 34.5 ± 6.9 years. The mean score patients marked on the VAS scale for their pain was reported to be 4.96 with a standard deviation of 1.77. 42.4% of the 144 patients had complaints of symptoms associated to peripheral nerve involvements thus making a prevalence of 42.4%. Out of 144 patients in total, 39 i.e. 27.1% reported to have a total loss of smell i.e. Anosmia, 42 patients i.e. 29.2% sensed the smell accurately, 45 i.e. 31.3% had a reduced sense of smell whereas 18 patients i.e. 12.5% had an increased sensitivity to the different smells they were asked to sense. 47 patients i.e. 32.6% had ageusia i.e. a total loss of taste they were offered. 36 i.e. 25% had normal taste and accurately comprehended the different flavors they were offered, 41i.e. 28.5% had reduced taste sense i.e. hypoeusia and responded that they could taste but the intensity was lesser than normal.

Conclusion: Majority of the patients had peripheral nerve symptoms, a loss of smell, taste and impaired balance after recovery.

Key Words: COVID-19, Peripheral nerve disorders

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INTRODUCTION

With the outbreak of SARS-CoV-2 in China and ultimately around the globe, it leads to many medical, economic and social problems. In Pakistan, it leads to 3 waves at 3 different times. The government imported the vaccinations and had controlled it to a great extent now. But many of the people i.e. around 38% of the population hadcontracted Coronavirus since its outbreak in Pakistan [(1)]. Many of elder ages could not fight and combat the pathologies it caused and ultimately expired due to different respiratory complications it caused[(2)].

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Others had to combat the systemiccomplications caused by it[(3)]. Other than systemic and respiratory complications, SARS-CoV-2 is also known to produce neurological complications in patients after surviving from it. It was a general observation that people who contracted SARS- CoV-2 and survived from it, usually complained of vestibular symptoms, a generalfatigue in body, myalgia pain in upper and lower limbs especially and numbness inhands and feet [(4)]. This observation led us to conduct this research in order to document the prevalence of neurological symptoms in patients who have survived. Many neurological manifestations have already been documented as a result of Covid-19. These include encephalitis, encephalopathy, meningitis, steroid responsive encephalopathy etc. [(5)]. Few studies have also reported patients having symptoms of hyposmia or complete absence of smell for more than 2 months after being positive for Covid-19 [(6)]. Others had opthalmoparesis, facial muscles weakness and fatigue, symmetrical neuropathy i.e. bilateral pain and numbness in most of the time of day or night, critical illness myopathy, myositis, myalgias and Guillain Barre Syndrome as well. Few patients reported symptoms of rhabdomyolysis as well secondary to Covid 19 [(7)]. The

mechanism of peripheral nervous system involvement is still unclear but few analysts have thought it to be immune mediated. GBS is from long considered to be an immune mediated disease of peripheral nerve sheath or the Schwann cells of nerve [8]. This may be because of the resemblance which the glycoproteins on surface of virus and glycoconjugates of human nervous tissue with each other. The antibodies as a result of this complex starts acting against the glycoconjugates of nerve tissue of humans [9].

Some studies have also reported that Covid-19 also leads to multiple cranial neuropathies along with all other peripheral complications [10]. They have been reported in about 73% of the total cases infected. Some observational studies have also reported that patients often present with frequent complains of headache, nausea, myalgia, hyposmia, vomiting and dizziness. Others have also reported impaired levels of consciousness in patients of Covid-19[11]. Other possibly of the virus entering into the cerebral circulation is the hematogenous spread of the virus from systemic circulation [12]. Other experiments have also revealed that coronavirus compromises the central and peripheral nervous system as well as the respiratory drive through targeting the neurons located in cardiorespiratory centers [13]. Some animal studies have also reported that the virus affects the brainstem and brain in both patients as well as experimental animals[14]. An experiment following intranasal virus inoculation into the mice revealed that SARS CoV2 enters the central nervous system through the first cranial nerve i.e. olfactory nerve. The viruses were later detected in the central nervous system and not in the pulmonary tissues. Thus suggesting the direct transfer of virus through olfactory nerves [15]. Another possible explanation of this viral load in brain and brainstem after contracting infection is by the direct connection of vagus nerve to ambiguous and solitary nuclei which lie in the brain stem, thus indicating the spread of infection from respiratory tract to the central nervous system [16]. Olfactory nerve is the nerve most specific and the only one which provided us a sense of smell and because this nerve gets affected due to viral infections, the smell of smell too gets affected i.e. either the individuals smells more intense than normal, or lesser than normal [17]. Affected individuals lose their sense of smell completely during the active phases of viral infection [18]. The sense of taste is provided by two cranial nerves. The anterior 1/3rd is supplied by facial nerve whereas the posterior 2/3rd of the tongue is supplied by glossopharyngeal nerve. The nerve sensations are tested by alternativelytesting the taste buds with sugar and salt flavor and asking the respondent to inform about the taste with closed eyes. Patients of Covid-19 complain of altered balance until 3 months of being negative for SARS-CoV-2, reasons of which are yet unclear. In order to assess the patients for balance and their vestibular function,patients were asked to perform Fukuda step test and the angular deviation from the starting point were recorded [19]. The purpose of the current study was to find out effects on sensory changes in peripheral nervous system due to COVID-19.

MATERIALS AND METHODS

The study design was cross-sectional survey. Data was collected from the community of Lahore, Faisalabad, Sialkot, Rawalpindi and Islamabad. The study duration was six months after approval of synopsis i.e. December 2020 to June 2021. Study was conducted on patients who have been positive for Covid – 19 and have recovered from it. Patients were recruited through Non-probability convenient sampling technique. The sample size computed was 144. The online sample calculator was used to calculate the sample. Patients with SARS Cov-2 PCR positive reports from a reliable laboratory i.e. Shaukat Khanum Laboratory and Chughtai Labs, both males and females, age ranging from 18 to 60 were included. Patients with any respiratory complication prior to being positive for Covid-19, Diabetes mellitus, hypersensitive, allergic and with any neurological disorder before being positive for Covid-19 were excluded. Outcome measures were pain, smell, taste, balance- Labyrinthine function, stereognosis, and Two-point discrimination. VAS, NPRS, olfactory nerve test, Facial & Glossopharyngeal Nerve Test, Fukuda Test and Paper clip test for two-point discrimination were used as data collection tool. Patients were recruited according to the inclusion criteria and were asked for their consent after informing them the objective of this study. Patients who consented were included in the study. The research questionnaire including two sections was administered by the researcher herself. The first section of questionnaire included questions about their age, gender, marital status, co-morbidities and duration passed after they had their SARS Cov-2 test negative. Second session included the assessment based on pain score on VAS and NPRS for pain scale, olfactory nerve test for smell along with facial and glossopharyngeal Nerve test for taste. Other complaints of patients were also recorded.

RESULTS

Table No.1: Age of patients

N	Mean	Standard Deviation
144	34.51 years	6.889

Mean age of the patients was reported to be 34.51 ± 6.89 years.

Out of 144 patients, 84 i.e. 58.3% were females and 60 i.e. 41.7% were males. 55 i.e. 38.9% had hypertension, 78 i.e. 54.17% had no other medical problem whereas11 i.e. 7.64% reported to have renal problems (4), cardiac

problems (6) and psoriasis (1).28 i.e. 19.4% were unmarried and 116 i.e. 80.6% were married.

Table No.2: Demographics of patients

Sr. No.	Demographical Variable	Frequency (Percent)
1.	Gender of patients	Females – 84 (58.3%) Males – 60 (41.7%)
2.	Co-morbidities of patients	Hypertension – 55 (38.9%) None – 78 (54.17%) Others – 11 (7.64%)
3.	Marital status of patients	Unmarried – 28 (19.4%) Married – 116 (80.6%)

Table No.3: Duration passed after being negative for COVID -19

	Duration passed after being negative for Covid-19	Frequency (Percent)
1.	1-2 months	41 (28.5%)
2.	2-4 months	42 (29.2%)
3.	4-6 months	35 (24.3%)
4.	More than 6 months	26 (18.1%)

Out of 144 patients included in the study, 41 i.e. 28.5% had their SARS Cov 2 positive 1-2 months earlier and 42 i.e. 29.2% had 2-4 months back. 35 i.e. 24.3% had been positive 4-6 month back and 26 had been negative from more than 6 months' back.

Table No.4: Two-point discrimination interpretation

Interpretation	Frequency	Percent
Normal	131	91.0%
Fair	7	4.9%
Poor	6	4.2%
Protective	0	0.00%
Anesthesia	0	0.00%

Amongst 144 patients who were tested for their two-point discrimination, 131 i.e. 91.0% responded accurately i.e. they pointed to both the points touched at 2 mm to 5 mm, 7 i.e. 4.9% responded when both points were touched at a distance of 6 – 10 mm, 6 patients i.e. 4.2% responded with a distance of 11 mm to 15 mm. None of the patients fell into the protective and anesthetic category.

Table No.5: Interpretation of Fukuda Step Test for Balance

Interpretation of Fukuda step test	Frequency	Percent
Abnormal deviation to intact side	9	6.3%
Abnormal deviation to affected side	0	0.00%
Normal	135	93.8%

Patients under study were asked to perform Fukuda step test. The test was once demonstrated by the research administrator and was later asked to follow the instruction. Deviations of the patients were reported and thus, 135 i.e. 93.8% reported to have normal balance i.e. vestibular function whereas 9 patients i.e. 6.3% showed abnormal deviation and thus involvement of the vestibular system was reported.

DISCUSSION

The results of this study has shown that many of the patients who have had survived Covid-19 and came out negative for SARS CoV-2 showed features of peripheral neuropathy. Most of them had sensations of tingling and numbness in their distal extremities along with pain in their muscles of upper and lower limb. This resulted in higher scores of patients at LANSS scale. This showed that peripheral neuropathy had a higher prevalence of development after Covid 19. The results of this study were found to be consistent with a study from Mazya et al, the results of which showed that several neurological issues and complications arise because of the prone positioning among patients of Covid 19. The positioning recommended to treat ventilation perfusion matching and enhance drainage of secretions lead to increased intracranial pressure, median, radial as well as sciatic nerve injury. Brachial plexus damage was also reported among patients of Covid – 19.[20]

The same results were also observed by a study of Malik et al who studied 83 hospitalized patients and concluded the presence of nerve injuries in 14.5% of total patients. They also concluded that amongst these patients only one patient did not have a history of prone lying. 76.2 % of these had peripheral nerve injuries in the upper limb, ulnar nerve being the most common followed by radial nerve. Most commonly injured nerve from the lower limb was reported to be sciatic nerve. These findings were related to the finding of EMG studies of the same patients. According to the EMG findings, the patients had nerve injuries of Axonotmesis stage of injury.[21]

Zhang Y et al in their study concluded that Covid 19 leads to multiple cranial nerve involvement amongst which olfactory nerve is the most common one. Anosmia i.e. complete absence of the sense of smell was found to be present in about 73% of those infected with Covid 19. This study was a case study of a 35-year-old Covid 19 patient having right paralysis along with olfactory disturbance and an almost loss of sense of taste on same side of tongue while the sense of sweeter was preserved. The patient had complete loss of smell as he could not sense the smell of coffee and shampoo. The involvement of nerves started within 5 days of respiratory symptoms and it got resolve d in duration of more than 6 weeks [22].

Munro et al concluded in a self-reporting survey that patients recovered from Covid-19 had auditory

complications as well. They followed 138 adult individuals who experienced severe complications of Covid-19 and documented their symptoms 8 weeks after they were discharged from hospital. 13.2% of the total patients reported to have tinnitus and hearing difficulties after they had recovered from Covid-19. This study did not study the effects of Covid-19 on hearing due to which the results remain uncertain and the hearing tests should also have been conducted.

The results were found to be different from a study of Mao et al in which they concluded that the patients had problem identifying familiar objects when placed at palms of their hand and two-pint discrimination. Nerve pain was also found in these patients. Moreover, few patients amongst these had complaints of skeletal muscle injury which was ensured by the reports of Creatine Kinase elevation[23]. Our results did not show much disturbances in two-point discrimination. The patients were also able to identify keys, coin, paper clip and pen cap was placed on their palms. However, pain was found to be around 4-5 on the scale of VAS and NPRS[24].

CONCLUSION

Survivors of Covid – 19 have a higher rate of smell and taste abnormalities even after having negative results for their SARS CoV-2 PCR. Moreover, peripheral neuropathy was also observed considerably among these patients. These positive finding suggest a significant involvement of peripheral nervous system due to the viral invasion. This gives us an impression that Coronavirus influences both the central as well as peripheral nervous system.

Author's Contribution:

Concept & Design of Study:	Amena Batool
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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