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Assessment of balance after recovery from Covid-19 disease

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ABSTRACT

Objective: To answer the question whether balance related systems have been affected in adults who recovered from Covid-19 disease. This is the first case-control study to assess balance objectively and quantitatively in Covid-19 disease.

Methods: Thirty-seven patients who recovered from Covid-19 disease and 30 healthy controls were compared using Dizziness Handicap Inventory (DHI), Computerized Dynamic Posturography (CDP), Vestibular Evoked Myogenic Potentials(VEMP) and Video Head Impulse Test (v-HIT).

Results: On CDP, the composite and visual general scores of the patients were significantly lower than controls ($p<0.01$). The v-HIT gains of the patients significantly decreased in the vertical semicircular canals compared to controls ($p<0.01$).There was a significant difference between the patients and controls regarding the absence of o-VEMPs ($p<0.01$) while the amplitudes and latencies were similar between the groups ($p>0.05$). Decreased P1/N1 amplitudes and elongated N1 latencies were found on c-VEMP testing ($p<0.05$). Anosmia, taste disorder and gender were not associated with subjective and objective test results ($p>0.05$).

Conclusion: The Covid-19 disease can cause dizziness rather that incapacitating vertigo. Dizziness can be seen in almost one-fifth of the adult covid19 out-patients, which may be due to involvement of vestibular and visual systems,ortheir central connections. The squeals created in the balance related systems may be irreversible as they have persisted after the recovery of the patients. It is also plausible to anticipate more severe condition in the older patients who were treated in the intensive care units. In the long term follow up of the survivors, the need for balance rehabilitation programs should be remembered in order to minimize risks of falling down.

1. Introduction

Since December 2019, the novel type of corona virus (SARS-CoV-2)has been a major world health problem in the form of pandemic [1]. The virus can lead to a spectrum of disorders in the human body depending on the sites of involvement [2,3,12,4–11]. That is,SARS-CoV-2 infections or Covid-19 disease is protean in its symptoms.

Central and peripheral nervous system involvement are also possible [3–5,13], which can occur by direct invasion of the neural tissues or indirectly via inflammatory reactions [6]. It is evident that the virus may gain access to central nervous system through olfactory bulb causing inflammation and de-

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myelination [7]. The neurologic problems can be seen not only in the course of active disease, but they may also be seen in the form of post-neurological problems after recovery from the infection [2,8–12,14,15]. At this point, a thorough assessment of balance related systems is required by using objective test batteries.

Balance integration is critical in human life, and performed in the central nervous system depending on the information coming from the vestibular, ocular and proprioceptive systems. The impact of SARS-CoV-2infections on balance systems has been speculated in the light of a few cases reports and clinical observations [6,7,16]. Accordingly, dizziness seems one of the main balance problems encountered in almost one-third of the patients [4,9–11,14,15]. Despite these facts, balance evaluations in Covid-19 disease have been performed using questionnaires rather than objective measurements. That is, a comprehensive assessment is still lacking [12], which warrants an objective assessment of the balance related systems.

Computerized dynamic posturography (CDP)is used to quantify the relative contributions of sensory systems to postural control in the upright stance under either static or dynamic conditions. It can provide insight into the presence of postural instability, and helps identify which sensory system is involved although it does not provide a topographic diagnosis. The sensory organization test (SOT) protocol of CDP determines which sensory inputs the patient relies upon most to maintain postural stability, and monitor central compensatory state [17]. The SOT assesses the ability of individuals to evaluate and coordinate information from the somatosensory, visual and vestibular systems as well. The individuals are assessed in six conditions (eyes open/close, sway/fix referenced visual surround and sway/fix referenced support surface) at three successive trials in every condition.

Vestibular evoked myogenic potentials (VEMP) allow for the assessment of function and integrity of vestibular pathways in the brainstem as well as detection and localization of central lesions, especially when the lesions are silent [18]. Cervical VEMPs (c-VEMP) can be recorded from the contracted sternocleidomastoid muscle in response and represent the inhibitory vestibulo-collic reflex in response to an acoustic stimulus. The test reflects the functional status of the ipsilateral saccule and inferior vestibular nerve. Ocular VEMPs (o-VEMP) can be recorded from inferior oblique muscle and represent the active vestibulo-ocular reflex in response to an acoustic stimulus. The test reflects the functions of contralateral utricle and superior vestibular nerve.

Video head impulse test (v-HIT) detects saccades in response to high-acceleration head movements, and provides information about each semicircular canal by quantifying the vestibule-ocular reflex (VOR) gains. The test reflects the functions of semicircular canals, vestibular and ocular motor nuclei in the brainstem and the extra-ocular muscles.

In this study, we aimed to answer the question whether balance related systems have been affected in adults who recovered from Covid-19 disease. This is the first case-control study to assess balance objectively and quantitatively in Covid-19 disease.

2. Materials and methods

The study was approved by the Ethical Committee of Istanbul Medipol University (507, 25 June 2020) and informed consent was obtained from all patients. The evaluations were conducted at the Istanbul Medipol University Hospital between 1.07-2020-01.01.2021 (Fig. 1). Sample sizes were detected by G*Power Statistical Power Analyses program.

2.1. Patients and controls

Totally, 37 patients (17 males and 20 females with a mean age of 32±11 years) who recovered from Covid-19 disease and 30 healthy age and gender matched controls (15 males and 15 females with a mean age of 28±4 years) were included in the study.

The confirmation of SARS-CoV-2 infection was made by isolation of the virus in the nasal and pharyngeal swabs using polymerase chain reaction test. The patients had mild Covid-19 disease with the symptoms like cough, sub-febrile fever, anosmia, taste disturbance and myalgia. None of them had pulmonary involvement, dyspnea or cytokine storm necessitating hospitalization or intensive care unit facilities.

Thirty of 37 patients were treated with hydroxychloroquine and favipiravir in an out-patient setting, and followed up by the Covid-19 staff of the ministry of health. The remainder did not receive a specific medical treatment. The balance tests of the patients were performed 22 to114 days after their recovery from the disease, which was confirmed by the evaluations of the Covid-19 staff and negative polymerase chain reaction test.

2.2. Balance evaluations

Initially, the participants were evaluated using questionnaires. First, the question was whether they were feeing imbalance in the daily life or not. The answer was classified as “yes” or “no”. Second, they were asked to fill “Dizziness Handicap Inventory” (DHI), which is a multidimensional self-assessment scale created to evaluate the effects of dizziness and balance problems on the quality of life as well as the level of disability of the patients [19].

On SOT test battery of CDP (Natus Smart Balance Manager, California, USA), coordination abilities for somatosensory, visual and vestibular systems were assessed as described previously [20]. There SOT was performed under 6 different conditions, repeated 3 times, and averaged (Fig. 2).

Both c-VEMP and o-VEMP recordings (Interacoustics Eclipse, Denmark, Middelfart) were performed in a standard manner as described previously [21]. In v-HIT testing, VOR gains for each semicircular canal on both sides were tested in response to high-frequency head stimuli (Otometrics ICS Impulse v-HIT, Denmark). Both ears of the patients and controls were tested using VEMPs and v-HIT.

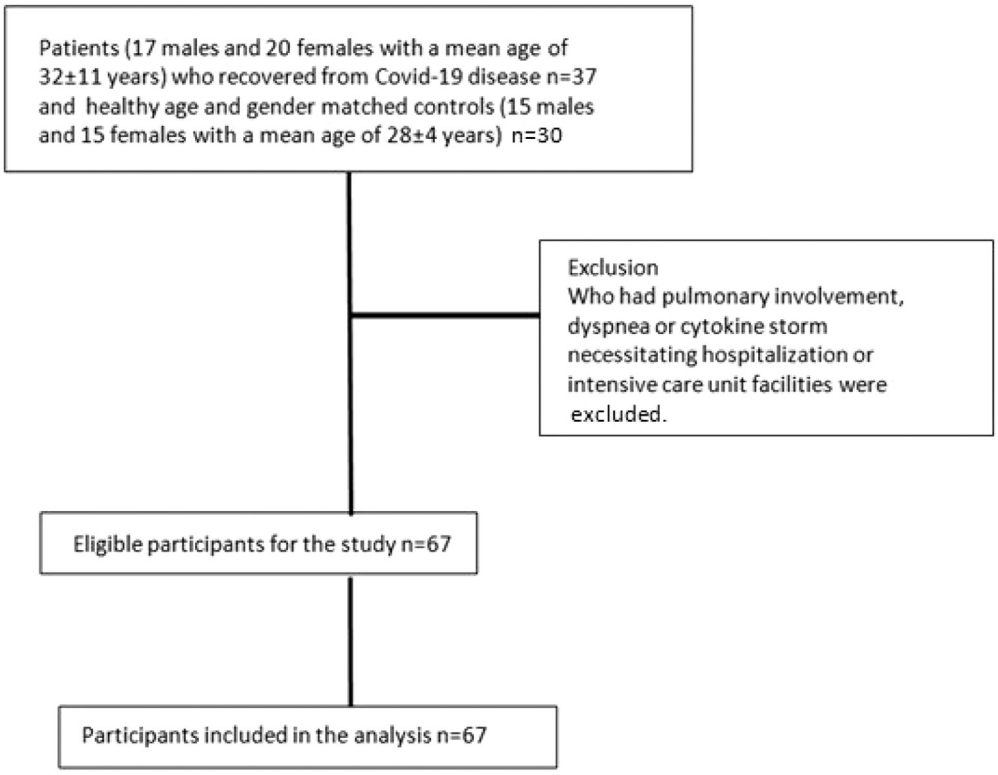
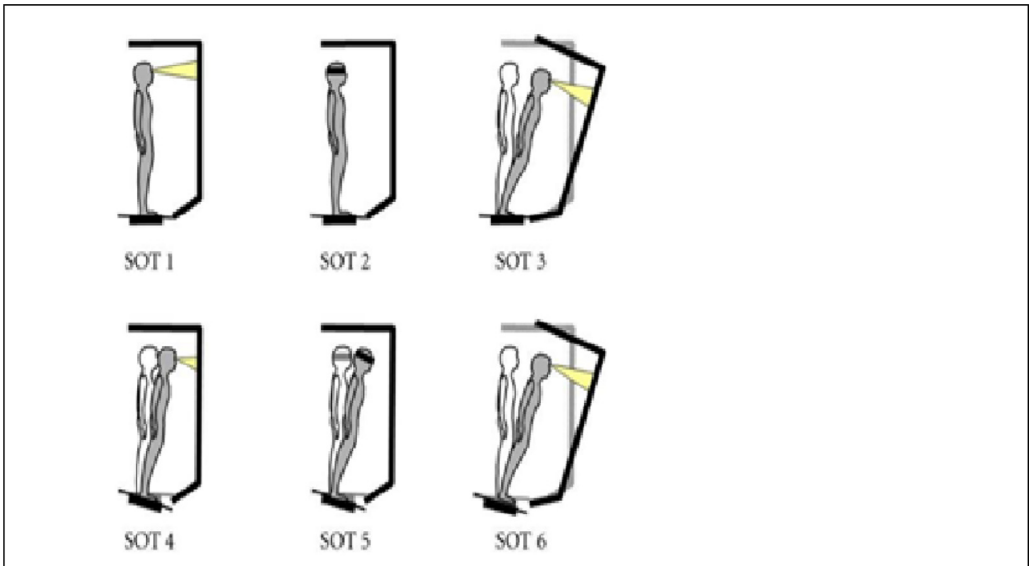


Fig. 1. Flow diagram.



Condition 1. Eyes open, both the platform and the surround remain immobilized

Condition 2. Eyes closed, both the platform and the surround remain immobilized

Condition 3. Eyes open, the platform immobilized and the surround moves

Condition 4. Eyes open, the platform moves and the surround remains fixed

Condition 5. Eyes closed, the platform moves, surround remains fixed

Condition 6. Eyes open, both the platform and the surround remain immobilized

Fig. 2. SOT strategies on CDP test battery.

2.3. Statistics

One-way analysis of variance was used to compare categorized variables. Independent samples-t was used to compare the data of the patients and controls. Pearson's correlation, chi square or fisher's exact tests were used to assess correlations and non-parameters.

3. Results

3.1. Questionnaires

According to first questionnaire, 8 of 37 patients (21.6%) declared the presence of imbalance in their daily lives while there was no complaint of imbalance in the controls ($p<0.01$). Of 8 patients with a complaint of imbalance, 4 (20%) were females and 7 (23.5%) were males, which was not significantly different ($p>0.05$).

According to DHI, the mean score of the patients were 16.1±23.3 while controls scored as zero ($p<0.01$). Among the patients, the DHI scores of males and female were 7.2±11 and 23.8±28, respectively. The DHI scores of female patients were significantly higher than male patients ($p=0.02$). There was no correlation between the DHI scores and the complaint of imbalance ($p>0.05$).

3.2. Balance tests

On, CDP, the mean composite scores of the patients and controls were 74.8±9.6 and 79.8±5.9, respectively. The composite scores of patients were significantly lower than controls ($p<0.01$). The visual general scores of the patients were significantly lower than controls ($p<0.01$) whereas no significant difference was found between the groups regarding the general somatosensory, vestibular and preference values ($p>0.05$) (Fig. 3).

On v-HIT, a decrease in the gains of the vertical semicircular canals was found in the patients compared to controls ($p<0.01$) whereas no significant difference between the patients and controls regarding the gains of lateral semicircular canals ($p>0.05$) (Fig. 4).

The o-VEMPS could be obtained in all controls. An o-VEMP could not be obtained in 14(18.9%) ears of 11 (29.7%) patients, which were significantly different than controls ($p<0.01$). The o-VEMPs were absent bilaterally in 3 (8.1%) and unilaterally in 8 (21.6%) patients. The latencies of N1 and P1 waves were 8.7 ± 7.3 and 13.9± 2.8 in the patients, respectively. The corresponding latencies were 9.5 ± 5.2 and 4.2± 2.8 in the controls, which were not significantly different between the groups ($p>0.05$). There was a significant decrease in the P1/N1 amplitudes of o-VEMPs in the patients compared to controls ($p<0.05$) (Fig. 5).

The c-VEMPS could be obtained in all controls. A c-VEMP could not be obtained in 6 (8.1%) ears of 4 (10.8%) patients, which were significantly different than controls ($p<0.01$). The c-VEMPs were absent bilaterally in 2 (5.4%) and unilaterally 2 (5.4%) patients. The latencies of N1 and P1 waves were 23.0 ± 3.1and 15.8 ± 3.1 in the patients, respectively. The corresponding latencies were 15.0 ± 2.2and 21.8 ± 2.6 in the controls, which were not significantly different between the groups ($p>0.05$). There was a significant decrease in the P1/N1 amplitudes of c-VEMPs in the patients compared to controls ($p<0.05$) (Fig. 6).

3.3. Impact of smell disorder, gender and medical treatment

Of the patients 21(56.8%) and 22 (59.5%) had smell and taste disorder. There was a significant a correlation between the presence of taste and smell disorders ($p<0.01$). The presence of anosmia or taste disorder, and gender were not associated with the complaint of imbalance, and results of DHI, CDP, VEMPs and v-HIT ($p>0.05$).

There was no relationship between the commencement of medical treatment and the complaint of imbalance described by the patients ($p>0.05$). The mean DHI scores of the patients who were treated with and without medications were 15.3±22.3 and 26±38.3, respectively, which were not significantly different($p>0.05$). There was no significant relation between the medical treatment, and VEMP and v-HIT results ($p>0.05$). There was no relation between the CDP results and commencement of medical treatment except for composite and vestibular general scores, which were significantly higher in the patients who received medical treatment (Table 1).

4. Discussion

The impact of SARS-CoV-2 infections on the central and peripheral nervous systems have been debated. The information about audio-vestibular effects of the infection is controversial as well [12]. Balance problems have been reported in Covid-19 disease despite the fact that there is no objective data based on case control studies. In our study, almost 20% of the patients complained of balance problems, which was mainly in the form of dizziness, which is an important neuro-otological problems [22]. However, none of the patients described an incapacitating peripheral vertigo.

Dizziness may result from a variety of reasons in the body and can impact on the daily activities as well as quality of life. It would be expected for the people to feel dizziness or similar balance problems in the course of fearful pandemic, especially when that they are infected by the virus. In addition to that Covid-19 disease may also have long term effects like neurodegenerative and neuropsychiatric diseases [8,23]. That is, the patients may have delayed morbidities or sequels even after recovery from the viral disease.

The patients included in our study were otherwise healthy young adults who were treated in an out-patient setting. The reason for this sort of selection was the patient compliance for the balance test procedures. In addition to that the findings in this groups might represent more severe balance problems in the older patients who needed intensive care facilities.

The CDP results helped us to disclose the involvement of gait control systems in general. Specific vestibular test result suggested the presence of sequels at different severities in the peripheral vestibular system, vestibular nuclei in the brainstem, or extra-ocular muscles or in their connections [24].

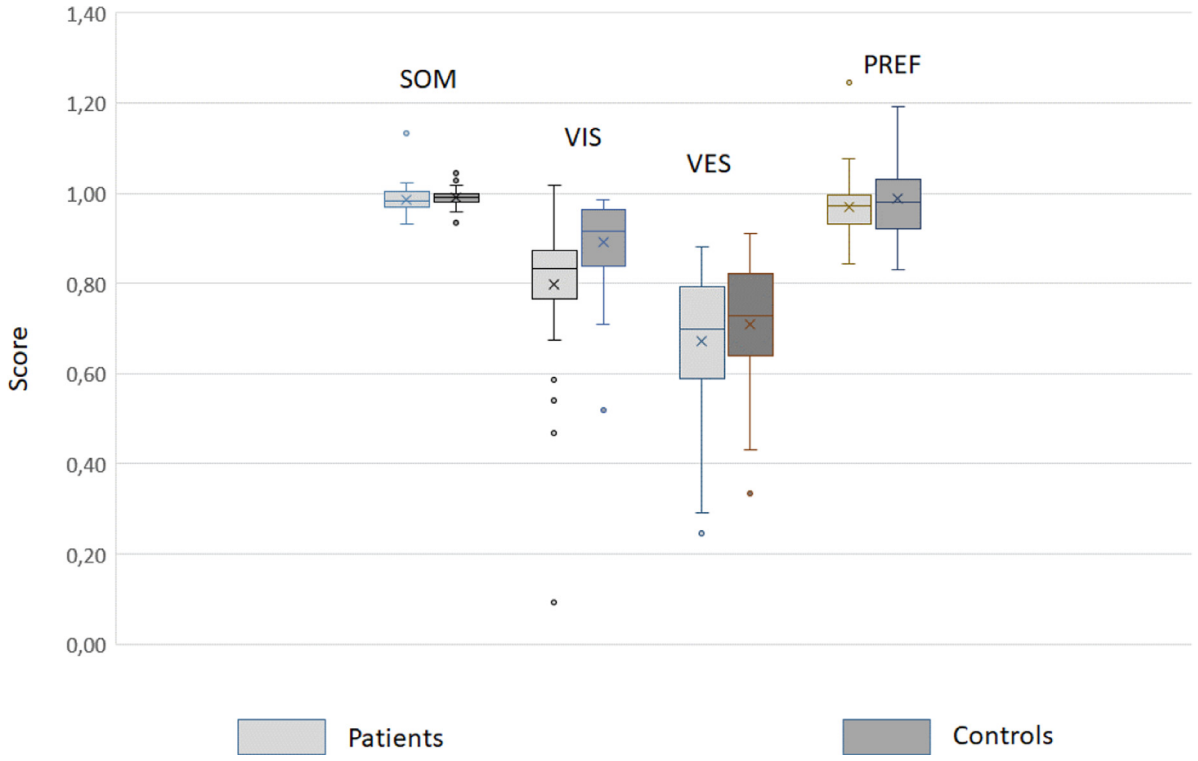


Fig. 3. SOT results of CDP.

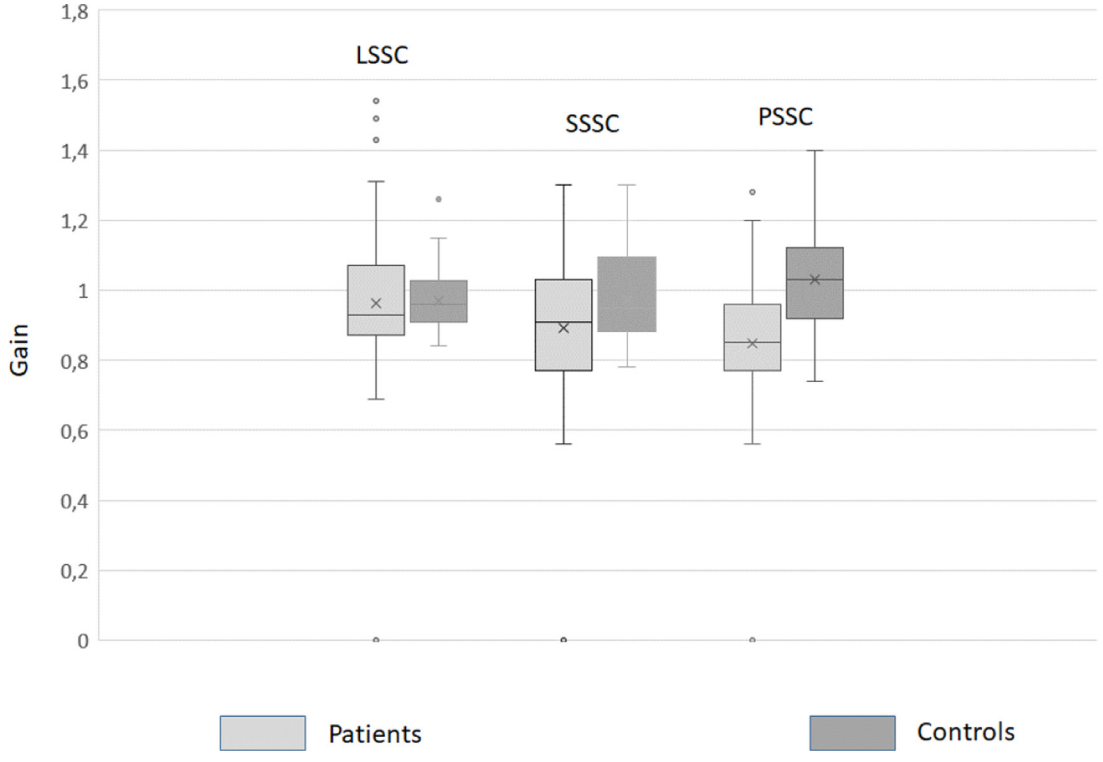


Fig. 4. v-HIT gains of the semicircular canals.

The otolith function is evaluated with VEMPs in response to a high intensity acoustic stimulus [25]. Unilateral or bilateral absence of o-VEMPs may indicate either utricle dysfunction or a disorder in the superior vestibular nerve, extraocular muscles or their central connections. Also, decreased P1/N1 (c-VEMP) amplitudes encountered in one–third of the patients could betoken these dysfunctions or disorders, too. Likewise, absence of c-VEMPs in almost ten percent of the patients and decreased amplitudes may suggest the involvement of saccule, inferior vestibular nerve or their central connections. There-

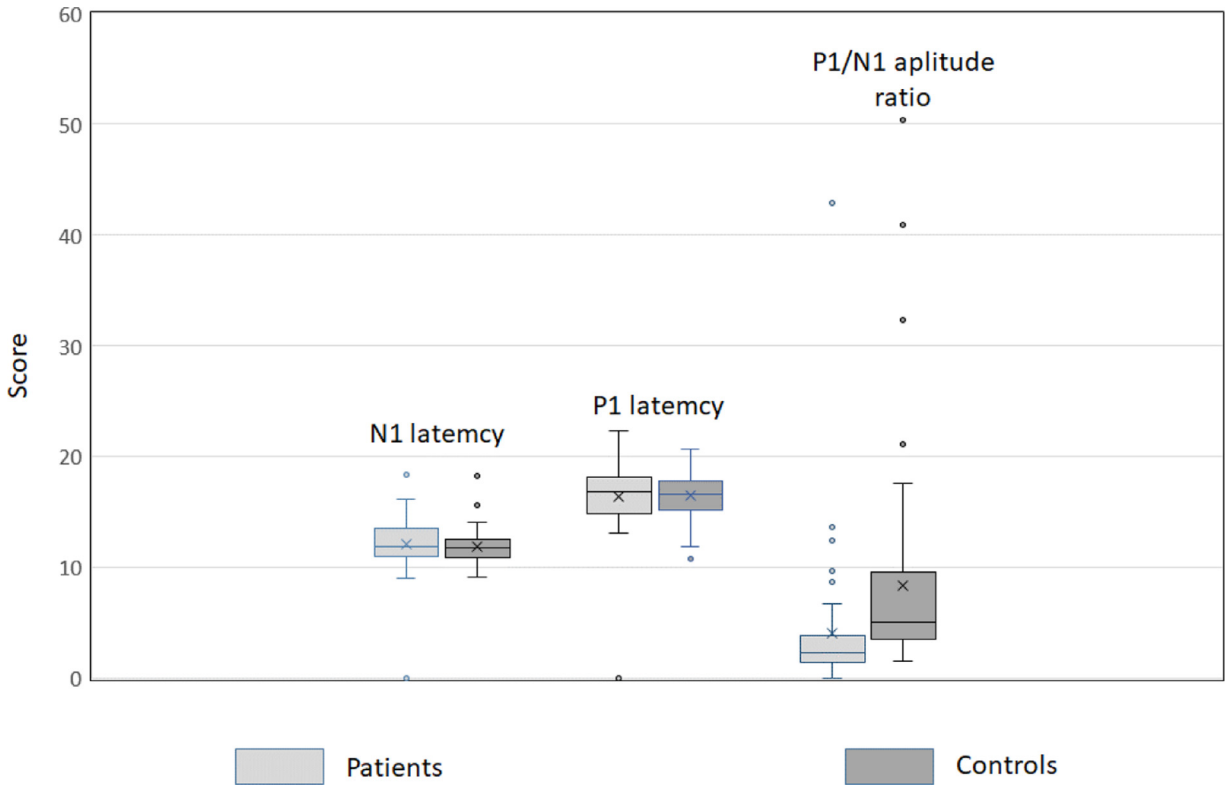


Fig. 5. o-VEMP latencies and amplitudes.

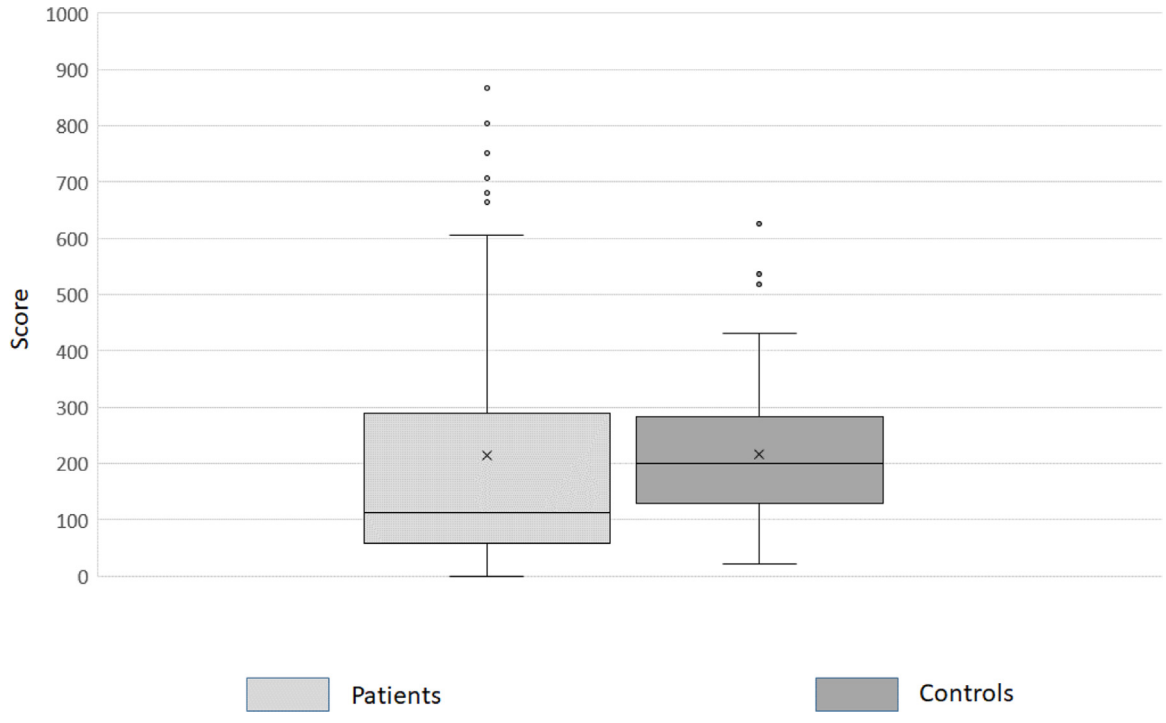


Fig. 6. c-VEMP amplitudes.

fore, it is plausible to say that the viral disease may impact on balance related systems at different levels and severities.

It is known that a sudden impact on the peripheral vestibular organ or statokinetic system can lead to true vertigo attacks. However, the patients in our series described dizziness rather than true vertigo attacks. This may indicate that the impact of viral disease happens in a progressive manner, thereby allowing for central compensation. Likewise, an impairment in the vestibular reflex pathways is possible in the course of acquired immune deficiency syndrome (AIDS) in addition

Table 1. SOT versus commencement of medical treatment in the patients.

Parameter	Treated without medical treatment	Treated with medical treatment	P
Composite	57.6 ± 14.5	76.2 ± 7.6	0.02
Somatosensory	0.99 ± 0.01	0.98 ± 0.03	>0.05
Visual	0.53 ± 0.4	0.82 ± 0.12	>0.05
Vestibular	0.42 ± 0.19	0.69 ± 0.14	0.02
Preference	0.91 ± 0.07	0.98 ± 0.07	>0.05

to other systemic problems caused by the virus [26]. This impairment in AIDS could be attributed to involvement of dopaminergic systemin the central nervous system [27,28].

Anosmia and taste disturbance were seen in almost sixty percent of our patients. These disturbances may occur due to circulatory problems, cytokine reactions or invasion of the central nervous system through circulation or olfactory bulb. Smell and taste problems were not associated with the subjective and objective test results. It seems mechanisms associated with neurotological problems and anosmia might be different.

It would be possible for the medications to cause balance problems as a result of adverse effects [15]. However, there was no correlation between the commencement of medical treatment and subjective and objective balance test results except for the composite and vestibular parameters of CDP. Since the balance test results of the controls and patients were also different, we might consider the additional impact of medical treatment on gait control, which is due possibly to the effects of medicines on the central nervous system rather than vestibular apparatus.

5. Conclusion

The Covid-19 disease can cause dizziness rather that incapacitating vertigo. Dizziness can be seen in almost one-fifth of the adult covid19 out-patients, which may be due to involvement of vestibular and visual systems, or their central connections. The squeals created in the balance related systems may be irreversible as they have persisted after the recovery of the patients. It is also plausible to anticipate more severe condition in the older patients who were treated in the intensive care units. In the long term follow up of the survivors, the need for balance rehabilitation programs should be remembered in order to minimize risks of falling down.

Declaration of Competing Interest

No potential conflict of interest was reported by the authors.

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