VESTIBULAR ASSESSMENT IN POST COVID-19 DIZZY PATIENTS

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ABSTRACT:

Background: *It has been postulated that COVID-19 has a bstantial audiovestibular impact, so further research is needed to sess vestibular system function in post COVID- 19 dizzy patients.*

Aim of the Work: *Assess vestibular system function after recovery om COVID-19 disease.*

Patients and Method: *The present study was conducted on a total sixty subjects in Audiology unit at Hearing and Speech Institute. The idy was performed on two groups: a study group consisted of 30 post OVID-19 patients 15 days post diagnosis and complaining of zziness with mean age of 37.10± 7.95 years and a control group nsisted of 30 normal hearing individuals without previous history of OVID-19 infection. Both study and control groups underwent basic idiological assessment, vestibular evaluation (Arabic version of zziness handicapped inventory "DHI", bedside tests for vestibular id balance impairment, cervical Vestibular Evoked Myogenic otential Test "cVEMP", video Head Impulse Test "vHIT")*

Results: *The majority had normal hearing except for 5 (16.7%) bjects showed high frequency sensorineural hearing loss. The mean r total dizziness handicapped inventory score was 39.07± 13.10. Fourteen patients (46.7%) showed positional nystagmus. Nine patients (30%) showed abnormal vHIT results. cVEMP results showed a significant difference between the two groups in number of absent waves either unilateral or bilateral. COVID-19 affects mainly the peripheral vestibular system.*

Conclusion: *COVID-19 virus could affect peripheral end organ (semicircular canals, saccule, superior and inferior vestibular nerves) but central affection should be considered.*

Keywords: *COVID-19, DHI, bed side vestibular tests, cVEMP, vHIT.*

INTRODUCTION:

Coronavirus disease-19 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-COV-2). The WHO announced a pandemic of this virus in March 2020. It has been shown that, in addition to the most common symptoms of the disease, including fever, dry cough, taste and smell disorders, and general weakness some patients had audio- vestibular symptoms such as tinnitus, dizziness and sudden sensorineural hearing loss [(1)]. Hossam et al. [(2)] found that dizziness was attributed to COVID-19 infection in up to 40% of patients as an acute symptom, but 15% of them showed documented vestibular dysfunction.

Dizziness is a nonspecific sequela of COVID-19, which requires further investigations to detect its leading cause such as, vestibular neuritis, acute labyrinthitis, acute otitis media, or due to stroke following COVID-19 which can be explained by several hypotheses [(3)]. Among those hypotheses are anatomical extensions from the regions of viral loads to the middle ear which enable the SARS-CoV-2 to cause either an inflammatory response due to viral adhesion to angiotensin-converting enzyme 2 ACE2 or virus-mediated immune reaction. Lymphatics, blood vessels, nerves and the meninges in some cases have been proposed as an entry for the virus [(4)]. Direct effect on the mucosal epithelium of the middle and inner ears, leading to hearing and balance related symptoms in COVID-19[(5)].

AIM OF THE WORK

To assess vestibular system function after recovery from COVID-19 disease.

PATIENTS AND METHOD

Study population: The study was conducted on a total of sixty subjects.

The subjects were divided into: **Control group:** thirty normal hearing subjects with no complain of vertigo or COVID-19 infection. Age and gender were matching to the study group. **Study group:** thirty subjects with past history of COVID-19 infection complaining of dizziness.

Criteria for selection:

Inclusion Criteria:

1. Adults aged from 18 to 50 years old.
2. Post COVID-19 subjects diagnosed by PCR, CT chest or specific symptoms 15 days post diagnosis and patients complaining of dizziness which occurred during the attack of COVID- 19 and persisted till the time of evaluation .

Exclusion Criteria:

1. Patients with acute infection of COVID-19
2. History of any balance problems before COVID-19 infection.
3. Patients with systemic diseases known to affect the vestibular system.
4. Patients with cervical complains or history of cervical injury as a contraindication for the video head impulse test.

Method:

All patients were subjected to the following:

Detailed audiological history including presence of hearing loss, tinnitus, discharge, and earache/ ear fullness. Full COVID-19 specific history including method of diagnosis, types of symptoms, symptoms severity, number of attacks, investigations, treatment. Vestibular history by full description of vertiginous attacks if present (onset, course, duration, severity) and any associated or precipitating symptoms. Otological Examination: to exclude any external or middle ear pathologies. Basic audiological evaluation including Pure tone audiometry for frequencies 250-8000 Hz for air conduction and 500-4000 Hz for bone conduction, speech audiometry including speech reception threshold (SRT) using Arabic spondee words for adult [(6)] and speech discrimination scores using adult Arabic phonetically balanced monosyllabic words [(7)]. Acoustic immittancemetry (Tympa-nometry, ipsilateral acoustic reflex threshold at 0.5, 1, 2 and 4 KHz). Vestibular evaluation: Arabic version of dizziness handicapped inventory, bedside tests for vestibular and balance impairment, cervical Vestibular Evoked Myogenic Potential Test (cVEMP), video Head Impulse Test (vHIT).

Ethical Considerations:

The study was conducted in Audiology unit at Hearing and Speech Institute in a period between February 2022 to October 2022after approval of research Ethics Committee number is (00017585) and General Organization for Teaching Hospitals and Institutes (GOTHI) approval number is (IHS00038). The purpose and design of the study were explained to all participants individually and written consent was taken before starting the examination.

Statistical Analysis:

The collected data was revised, coded, tabulated and introduced to a PC using statistical package for social sciences (IBM SPSS) version 23. Data were presented and suitable analysis was done according to the type of data obtained for each parameter.

RESULTS:

The study was performed on two groups: a study group involved 30 post COVID-19 patients complaining of dizziness with mean age of 37.10 years, 33.3% males and 66.7% females and a control group constituted of 30 normal hearing individuals without previous history of COVID-19 infection. Imbalance was noticed to be the most frequent presentation that reported in 22 cases (73.3%) followed by self-rotation in 8 cases (26.7%). Pure tone audiometry showed normal hearing in 25 subjects (83.3%) of the study group, mild high frequency sensorineural hearing loss in 4 (13.3%) subjects, one patient (3.3%) had moderate sensorineural hearing loss in right ear, mild sensorineural hearing loss in left ear. As regards severity of COVID- 19 infection, thirty cases (43.3%) had mild degree of symptoms (asymptomatic or mild symptoms), ten cases (33.3%) had moderate degree (pneumonia with SpO2 equal or more than 90%) while 7 cases (23.3%) had severe degree (severe pneumonia with SpO2 less than 90%) according to WHO [8] classification of COVID-19 severity.

Table (1): Arabic version of dizziness handicapped inventory including functional score (F), emotional score (E), physical score (P) and total score in study group.

Dizziness Handicapped Inventory		Study group (N=30)		
		Mean	±SD	Range
F score		16.07	4.74	6 – 24
E score		12.93	6.32	2 – 24
P score		10.07	4.50	4 – 22
Total score		39.07	13.10	18 – 62
		N		%
Total score	Mild	14		46.7%
	Moderate	13		43.3%
	Severe	3		10.0%

Table 1 showed that 46.7% had mild impairment, 43.3% had moderate impairment while 3 cases (10%) had severe impairment.

Table (2): Relation between severity of COVID and DHI

		Severity of COVID						Test value	P-value
		Mild		Moderate		Severe			
		No.	%	No.	%	No.	%		
Dizziness Handicapped Inventory F score		13	4	16	3	21	4	H =11.6	0.003
Dizziness Handicapped Inventory E score		8	5	14	5	20	3	H =17.3	<0.001
Dizziness Handicapped Inventory P score		7	3	11	3	13	6	H =9.8	0.007
Dizziness Handicapped Inventory Total score		29	8	42	9	55	5	H =18.8	<0.001
Dizziness Handicapped Inventory Total score	Mild	11	84.6%	3	30.0%	0	0.0%	X^2= 22.02	<0.001
	moderate	2	15.4%	7	70.0%	4	57.1%		
	Severe	0	0.0%	0	0.0%	3	42.9%		

Table (2) showed statistically significant relation between severity of COVID and DHI scores.

The results of bed side tests showed presence of positional nystagmus were the commonest VOR findings seen in 14 patients (46.7%) and 3 patients (10%) presented with positive Dix Hall pike test. Out of 14 patients who presented with abnormal positional test, two patients showed horizontal nystagmus after head shaking test, and seven patients showed abnormal vHIT results. Two patients showed gaze evoked nystagmus and one of them presented with abnormal smooth pursuit and saccade tests and MRI is recommended for this patient to exclude any central origin of nystagmus.

Table (3): Comparison between study group and control group regarding vHIT gain of each canal.

Variable	Study group (N=30)		Control group (N=30)		Test value•	P-value
	Mean	SD	Mean	SD		
Rt lateral canal gain	0.98	0.15	1.03	0.09	-1.360	0.179
Lt lateral canal gain	0.94	0.17	0.99	0.10	-2.190	0.033
Rt anterior canal gain	0.80	0.11	0.84	0.06	-2.036	0.046
Lt anterior canal gain	0.78	0.12	0.83	0.04	-2.382	0.021
Rt posterior canal gain	0.79	0.11	0.82	0.06	-2.620	0.011
Lt posterior canal gain	0.80	.09	0.81	0.05	-1.210	0.231

Table (3): showed a significant decline of (left lateral, right anterior, left anterior and right posterior) canal gain in study group compared to control group.

Table (4): Comparison between study group and control group regarding overt and covert saccades.

Variable	Study group (N=30)		Control group (N=30)		Test value	P-value
	No.	%	No.	%		
Rt lateral covert saccade	3	10.0%	0	0.0%	X^2= 1.404	0.237 FE
Rt lateral canal overt saccade	0	0.0%	0	0.0%	-	-
Lt lateral covert saccade	2	6.7%	0	0.0%	X^2= 0.268	0.612 FE
Lt lateral canal overt saccade	1	3.3%	0	0.0%	X^2= 1.017	0.500 FE
Rt anterior covert saccade	3	10.0%	0	0.0%	X^2= 2.411	0.112 FE
Rt anterior canal overt saccade	0	0.0%	0	0.0%	-	-
Lt anterior covert saccade	2	6.7%	0	0.0%	X^2= 0.517	0.492 FE
Lt anterior canal overt saccade	0	0.0%	0	0.0%	-	-
Rt posterior covert saccade	1	3.3%	0	0.0%	X^2= 1.017	0.500 FE
Rt posterior canal overt saccade	1	3.3%	0	0.0%	X^2= 1.017	0.500 FE
Lt posterior covert saccade	1	3.3%	0	0.0%	X^2= 0.0	1.00 FE
Lt posterior canal overt saccade	1	3.3%	0	0.0%	X^2= 0.0	1.00 FE

Table (4): showed non-significant difference all 6 semicircular canals covert and overt saccade in study group compared to control group.

VSR tests result showed 6 cases (20%) showed exaggerated sway in Modified CTSIB test "condition 4". Six cases (20%) deviated greater than 45 degrees in fukuda stepping test. One patient presented with abnormal Romberg test.

Table (5): Qualitative comparison between study patients and controls regarding cVEMP.

cVEMP		Study group (N=30)			Control group (N=30)			Independent t-test	
		Mean	±SD	Range	Mean	±SD	Range	Test value	P-value
Right ear	P1 latency	14.60	2.36	11.7 - 19.33	13.66	1.43	11.33 - 16.00	1.584	0.119
	N1 latency	24.50	1.88	22.3 - 29.00	23.82	1.66	20.33 - 26.67	2.173	0.034
	N1-P1 latency	9.97	1.35	7.66 - 12.34	9.31	1.75	6.33 - 13.66	0.211	0.834
	N1-P1 amplitude	45.42	16.24	16.5 - 81.23	85.43	16.7	20.52 - 142.43	0.863	0.392
Left ear	P1 latency	14.90	2.09	11.0 - 19.00	13.57	1.58	11.00 - 16.67	2.620	0.011
	N1 latency	24.32	2.18	20.3 - 27.33	23.56	1.37	20.67 - 26.00	1.487	0.143
	N1-P1 latency	9.43	2.04	7.00 - 15.33	9.99	1.54	7.66 - 13.33	-1.126	0.265
	N1-P1 amplitude	49.23	15.60	27.8 - 77.40	79.45	16.3	20.44 - 129.2	1.389	0.171

Table (5): showed a significant difference between the two groups in the percentage of wave identification either unilateral or bilateral.

Table (6): Quantitative comparison between study group and control group regarding cVEMP.

Variables		Study group (N=30)		Control group (N=30)		Chi- Square test	
		No.	%	No.	%	Test value (X2)	P-value
cVEMP	present wave	22	73.3%	30	100.0%	9.231	0.026
	Absent unilateral (Rt. ear)	2	6.7%	0	0.0%		
	Absent unilateral (Lt. ear)	2	6.7%	0	0.0%		
	Absent bilateral wave	4	13.3%	0	0.0%		

Table (6): showed that there was a significant difference between the two groups in N1 latency in right ear and P1 latency in left ear. While non-significant difference was observed between them regarding other parameters.

Table (7): Number and percentage of cVEMP latencies shift in study group.

Latency	cVEMP		
	Unilateral		Bilateral
	Right	Left	
Prolonged	2 (8.3%)	2 (8.3%)	1 (5.6%)
Normal	22 (91.7%)	22 (91.7%)	17 (94.4%)
Total	24	24	18

Table (7): showed number and percentage of patients with normal and prolonged latencies in each side in cVEMP test.

DISCUSSION:

COVID-19 disease is a worldwide pandemic associated with more than 767 million infections and more than 6 million deaths [9]. Respiratory and gastrointestinal manifestations were described first but also the virus may cause many audiovestibular disorders including sudden sensorineural hearing loss (SSNHL) and vestibular neuritis (VN)[10].

The age for the inclusion in the study was set from 18 to 50 years, the upper age limit was set to 50 years in order to avoid the risk of age-related comorbidities and changes in the hearing and vestibular system. Female gender (66.7%) was more common than males (33.3%), female-to-male ratio was (2: 1). Eighty percent of subjects in *Hossam et al.* [(2)] study were females versus 20% were males. These gender differences have been hypothesized to be related to the hormonal factor influence [(11)] psychological factors, such as, anxiety, sleep and depressive disorders, were observed more in females [(12)].

By history taking of audiovestibular manifestation for study group, imbalance was noticed to be the most frequent presentation that reported in 22 cases (73.3%) followed by self-rotation in 8 cases (26.7%) then rotation of surrounding in 4 cases (13.3%), lightheadedness was reported in two cases (6.7%) and black out in one case. Four (13.3%) cases reported imbalance and self-rotation. Two (6.7%) cases reported imbalance and lightheadedness. Hearing loss complaint was found in one case in right ear. Two cases had right ear tinnitus while one case had left ear tinnitus.

The majority had normal hearing except for 5 patients (16.67%) showed high frequency sensorineural hearing loss, mild high frequency hearing loss in 4 (13.3%) subjects, one patient (3.3%) had moderate sensorineural hearing loss in right ear, mild sensorineural hearing loss in left ear. The results showed non-significant differences between the two groups in all frequencies examined, the mean thresholds at each frequency were within normal range ≤ 25 dB, that can be attributed to small number of subjects that had hearing affection.

This finding is consistent with other studies reporting higher frequencies affection in post COVID-19 patients. *Tan et al.* [(13)] reported a significant difference was found regarding the mean values of the 4k Hz and 8k Hz in both ears between the study group and control group.

Affection of the auditory system may be due to ischemic damage of the auditory system by causing clot formation in the blood vessels of the auditory structures by binding to the ACE-2 receptor in capillary endothelium to enter the cell. Yong [(14)] added that the ACE-2 receptor is abundant in the brainstem. Hence, the virus may affect the hearing centers in the brainstem.

Vestibular evaluation:

Arabic version of Dizziness handicapped inventory score:

Dizziness Handicapped Inventory was assessed among study group, the mean for total inventory score was 39.07± 13.10, mild impairment presented in 46.7%, 43.3% had moderate impairment while 10% had severe impairment. In this study, the functional subscale was the most affected in all groups as shown in table (1). Table (2) illustrates that there was significant relation between severity of COVID with Dizziness Handicapped Inventory P score, F score, E score &Total score.

This finding is consistent with a study conducted by *Eğilmez et al.* [(15)] that reported the mean for total inventory score was 35.90 ± 24.30 in the study group and DHI score means were higher in hospitalized patients and those with CT of significant pathology.

Ocular- motor tests finding:

Two patients showed gaze evoked nystagmus, one patient had left beating nystagmus in left gaze and spontaneous left beating nystagmus abolished by fixation which documented as acute vestibular neuritis (duration of dizziness complaint of 2 days), another patient presented with gaze evoked nystagmus (right beating nystagmus in right gaze and left beating nystagmus in left gaze), spontaneous left beating nystagmus diminished by fixation, abnormal saccade and smooth pursuit tests, MRI was recommended for this patient to exclude any central origin of nystagmus. ***Ahmed et al.*** ***[16]*****,** found in their study that neurological manifestations affect 30% of patients with COVID-19, one of those manifestations, balance disorders can affect 18% of patients.

Baig et al. ***[5]*** mentioned that the virus could attach and damage the neuronal tissue by invasion the brain and spinal neurons through the angiotensin converting enzyme-2 receptor (ACE 2) in the glial cells.

VOR finding:

1. Bedside tests for vestibular and balance impairment:

The bed side tests showed 14 patients (46.7%) presented with positional nystagmus, seven patients out of 14 patients who presented with abnormal positional test, showed abnormal vHIT results and two patients showed horizontal nystagmus after head shaking test which revealed uncompensated peripheral vestibular lesion. Three patients (10%) presented with positive Dix Hall pike test. This finding is consistent with ***Abdelrahman and Shafik*** ***[17]*** who found that 65% of patients showed positional nystagmus. In ***Hossam et al.*** ***[2]*** study, positive Dix Hall pike test (12%) and the presence of positional nystagmus were the commonest VOR findings seen. It is believed that the inner ear structures are susceptible to ischemic damage which lead to vestibular affection ***[18]*****.** The sequelae of such manifestations may be attributed to inner ear hypoxia or thrombosis and could explain vestibular dysfunction.

2. vHIT:

Nine patients (30%) showed abnormal vHIT results in the form of abnormal saccade with or without gain reduction table (3). Six semicircular canals were affected. Five patients had a combined canal affection. Moreover, there was a significant decline of left lateral, right anterior, left anterior and right posterior canal gain in study group compared to control group table (4).

Tan et al. ***[12]*** reported lower gains in all semicircular canals of post COVID-19 subjects compared with the control group in vHIT.

The semicircular canals affection may be due to the presence of the ACE2 receptors and transmembrane protease serine 2 (TMPRSS2) in the eustachian tube, the lining epithelium of the middle and inner ears. Thus, these receptors could act as an entry for the SARS-CoV-2 to the vestibule and cause vestibular neuritis ***[19&20]*****.**

In contrast, ***Charpiot et al.*** ***[21]*** also did not find a correlation between COVID-19 and acute peripheral vestibulopathy.

Baig et al. ***[5]*** hypotheses that the virus invades neural tissue directly such as cytomegalovirus, rubella, and adenoviruses by binding to ACE-2 receptors located in the blood vessels endothelium.

VSR finding.

1. Bedside tests for vestibular and balance impairment

Abnormal VSR in the form of deviation > 45º in fukuda stepping test or showed exaggerated sway in modified CTSIB test "condition 4" were seen in 30% of patients.

2. cVEMP

cVEMP results showed a significant difference between the two groups in number of absent waves either unilateral or bilateral table (5).

The latencies of N1 and P1 were delayed in study group but there was a significant difference between the two groups in N1 latency in right ear and P1 latency in left ear. While non-significant increase was observed between them regarding other latencies table (6). Four patients had unilateral prolonged latency shift, while one patient had bilateral prolonged latency shift table (7). Three cases in study group showed interaural amplitude asymmetry with no statistically significant difference between study and control groups. Most of patients presented with VSR abnormality (either in MCTSIB or fukuda test) showed cVEMP abnormality documented by absent response, prolonged wave latency or inter- aural amplitude asymmetry.

Absent cVEMP response or reduced amplitudes are commonly found in vestibular nerve disturbances, prolonged latencies of P13 may be found in central disturbances *(22)*. The deterioration saccular vestibular functions could be due to the generalized damage of the viral infection on the labyrinthine hair cells, as detected by absent cVEMP response *(23)*

Tan et al. (12) reported a significant difference was found regarding the latencies of VEMPs P13 & N23 of the left ear between the COVID-19 positive and control groups.

Moreover, in *Mustafa& Taya* (22) study, they found a highly significant (p< 0.001) difference was found between the control group and the study groups regarding the latencies of VEMPs P13 & N23 measurements.

Conclusion:

The study showed there is significant association between severity of COVID-19 and DHI score. COVID-19 virus could affect peripheral vestibular end organ (semicircular canals, saccule, superior and inferior vestibular nerves). Central affection should be considered.

Conflicts of Interest:

The authors state that the publishing of this paper is free of any conflicts of interest.

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التقييم الدهليزى لدى مرضى الدوار بعد كوفيد 19

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المقدمة: لقد تم الافتراض بأن كوفيد-19 له تأثير كبير على الجهاز السمعى و الدهليزي، لذلك هناك حاجة إلى مزيد من البحث لتقييم وظيفة الجهاز الدهليزي لدى مرضى الدوار بعد كوفيد-19.

الهدف من العمل: تقييم وظيفة الجهاز الدهليزي بعد التعافي من مرض كوفيد-19.

المرضي وطريقة البحث: أجريت هذه الدراسة على إجمالي ستين شخصًا في وحدة السمع بمعهد السمع والكلام. وقد أجريت الدراسة على مجموعتين: مجموعة دراسة تتكون من30 مريضا بعد الإصابة بفيروس كورونا-19 بعد 15 يوما من التشخيص ويشكون من الدوار, بمتوسط عمر 37.10 ± 7.95 سنة، وتتكون المجموعة الضابطة من 30 فردًا يتمتعون بسمع طبيعي وليس لديهم تاريخ سابق للإصابة بكوفيد-19. خضعت كل من مجموعتي الدراسة واالمجموعة الضابطة للتقييم السمعي الأساسي، والتقييم الدهليزي (استبيان تحديد درجة الإعاقة لمرضى الدوار باللغة العربية ، اختبارات الإتزان المكتبية السريرية، أختبار تصوير الفيديو لدفعات الرأس, الجهود المثارة العضلية لجهاز الاتزان "العنقى")

النتائج: أظهر قياس السمع ذو النغمات النقية فقدان السمع الحسي العصبي عالي التردد في 5 أشخاص (16.7%) من مجموعة الدراسة. كان متوسط إجمالي درجة الاعاقة لمرضى الدوار 39.07 ± 13.10، أظهر أربعة عشر مريضا (46.7٪) رأرأة موضعية. أظهر تسعة مرضى (30٪) أختبار تصوير الفيديو لدفعات الرأس نتائج غير طبيعية. يوجد فرق ذو دلالة احصائية بين مجموعة الدراسة والمجموعة الضابطة فى عدد الموجات المتغيبة فى استجابة الجهود المثارة العضلية لجهاز الاتزان العنقية سواء فى اذن واحدة او الاذنين. يؤثر كوفيد-19 بشكل رئيسي على الجهاز الدهليزي الطرفى ولكن من الممكن حدوث تأثر عللى الجهاز الدهليزى المركزى.

الخلاصة: من الممكن أن يؤثر فيروس كوفيد-19 على الجهاز الدهليزى الطرفى (القنوات نصف الدائرية، والكييس، والأعصاب الدهليزية العلوية والسفلية) ولكن التاثير على الجهاز الدهليزى المركزى يجب ان يؤخذ بعين الاعتبار.