COVID-19 AND AUDIO-VESTIBULAR SYSTEM IN EGYPTIAN ADULT SUBJECTS

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ABSTRACT:

Background: *Despite Audio-vestibular symptoms were reported in several studies, still limited and further investigations are necessary to confirm the effects of COVID - 19 on the audio-vestibular system and estimate their incidence.*

Aim of the study: *This study aimed to highlight the extent of affection of the audio-vestibular system in post COVID 19 Egyptian subjects and to describe the pattern of affection, if any.*

Patients and Method: *A total number of 105 confirmed post COVID-19 subjects, recruited from Ain shams University hospitals compared to 50 normal age and gender matched healthy volunteers with no history of COVID 19 participated as control group. All participants were subjected to: detailed history taking, Otological and otoscopic examination, Pure Tone & speech Audiometry, Acoustic immittancemetry testing and screening bedside tests for vestibular and balance impairment.*

Results: *Thirty-four subjects (32%) had hearing loss. Twenty-nine subjects (28%) had SNHL, 5 subjects (5%) had CHL and 16 cases (15%) had vestibular affection.*

Conclusion: *Post COVID-19 auditory-vestibular affection is to be documented. The majority of affected subjects had bilateral, moderate, high frequency SNHL with sudden onset. BPPV is the most common cause of post COVID-19 vertigo.*

Keywords: *Coronavirus; Covid-19; SARS-CoV-2; hearing loss; vertigo*

INTRODUCTION:

A new sequence of human RNA coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified in December 2019 in Wuhan, China [(1)]**.** The infection started in December 2019 spreading worldwide due to its high contagious human-to-human transmission. In March 2020 the World Health Organization (WHO) declared COVID-19 outbreak as a pandemic disease[(2)]**.**

The clinical symptoms of that disease expected to appear 2-14 days after exposure, according to the incubation period of SARS-CoV-2 virus[(3)]**.** The clinical features range from fever, cough, dyspnea, myalgia, arthralgia, headache, diarrhea, fatigue, anosmia (i.e. loss of the sense of smell) and ageusia (i.e. loss of taste) or even asymptomatic[(4-6)]**.** In more severe cases, this virus could cause pneumonia and could lead to severe acute respiratory distress syndrome (ARDS) and even death[(7)]**.**

Coronaviruses, and beta-coronaviruses that SARS-CoV-2 belongs to, do not limit their presence to the respiratory tract, actually they frequently invade the Central

Nervous System (CNS)[7]**.** The spectrum of neurologic syndromes known to be caused by COVID-19 includes encephalitis, meningitis, demyelination and Guillain-Barre syndrome. Thus, SARS-CoV-2 neurotropism may lead to a wide spectrum of neuropathic effects, potentially including hearing and balance neural networks [8]**.**

Sriwijitalai et al.[9] reported that the disease caused sensorineural hearing loss (SNHL) in an elderly individual. In another study, **Fidan** [10] reported that otalgia, tinnitus and unilateral conductive hearing loss in a patient with COVID-19.

Mao et al [11] in earlier published study from China found dizziness to be the most common neurological manifestation of COVID-19. Dizziness was proposed to occur as a result of the neuroinvasive potential of SARS-CoV-2.

Despite Audio-vestibular symptoms were reported in several studies, still limited and further investigations are necessary to confirm the effects of COVID - 19 on the audio-vestibular system and estimate their incidence. So, this work aimed to investigate the effects of COVID 19 on the audio-vestibular system in Egyptian subjects and to find if there is a specific pattern of affection.

PATIENTS AND METHOD:

Patients:

A total number of 105 subjects confirmed to have SARS-COV-2 virus infection; after recovery. They were recruited from Ain shams University hospitals. A control group consisted of fifty normal healthy volunteers. They were age and gender matched to the study group. They didn't show any history of SARS-COV-2 virus infection, history of any audiological, ENT diseases or any general health problems.

The study was done in Audiology unit, Otolaryngology department, Ain Shams University.

Inclusion criteria included adults 18 – 60 years old. Subjects confirmed to have SARS-COV-2 virus infection either by PCR &/or CT chest &/or lab &/or clinical diagnosis.

Exclusion criteria were subjects with active COVID-19 and non-documented pre COVID-19 audiovestibular complaint.

Ethical considerations: All results are kept in confidentiality to be only accessed by the researchers and informed consent was taken.

Method:

All participants were subjected to the following;

1. Detailed history taking: Personal history, complaint, history of present illness, past history of any medical condition, and family history of audiovestibular problem.
2. Otological and otoscopic examination.
3. Pure Tone & speech Audiometry: Pure tone audiometry for frequencies 250-8000 Hz for air conduction using two channel audiometer interacoustics, model AC40, calibrated according to ANSI S.3.6, 1996 and TDH -49 supra-aural headphone. Test was performed in a double walled sound treated room I.A.C. model 1602. The mid-octaves 3000 and 6000 Hz were also tested when indicated and 500-4000 Hz for bone conduction using B 71 bone vibrator for bone conduction threshold. Effective masking using narrow band noise was introduced to the contralateral ear whenever indicated. Speech Audiometry includes: speech reception threshold (SRT) using Arabic spondee words list and supra-threshold speech recognition test (SD%) using Arabic phonetically balanced words for adult at

40 dB (SL) with respect to listener's SRT.

4. Acoustic immittancemetry testing using acoustic immitancemeter otopront.
5. Screening bedside tests for vestibular and balance impairment; a minute screening battery included: I) Vestibule-ocular reflex (VOR) testing: Spontaneous nystagmus, Head thrust test, Head shake test, Dix-hallpike maneuver and Positional tests. II) Vestibule-spinal reflex (VSR) testing included Fukuda stepping test and Modified Clinical Test of Sensory Integration and Balance (mCTSIB). All screening office tests were done using Inter-acoustics Micro-medical Visual Eyes 505 (video goggles) except m-CTSIB and Fukuda stepping tests.

Statistical Analysis:

The collected data were revised, coded, tabulated and introduced to a PC using statistical package for social sciences (IBM SPSS 20.0). Data were presented and suitable analysis was done according to the type of data obtained for each parameter.

RESULTS:

A study group of 105 subjects post COVID compared to control group of 50 normal healthy volunteers. Tables 1&2 show age and gender distribution of both groups.

Table (1) shows mean and standard deviation of age in the control and study groups:

Age	Study (n.=105)		Control (n.=50)		Independent sample t-test	P-value
	Mean	SD	Mean	SD		
	39	12.1	35.7	11.8	-1.613	0.110

Table (2) shows gender distribution in the control and study groups:

Gender	Study (n.=105)		Control (n.=50)		Chi-square	P-value
	n.	%	n.	%		
Male	38	36%	19	38%	0.048	0.827
Female	67	64%	31	62%		

I. Basic audiological evaluation:

1. Pure tone audiometry and speech audiometry:

Thirty-four subjects (32%) had hearing loss. As shown in the diagram twenty-nine subjects (28%) had SNHL, 26 of them (25%) had sudden onset while 3 subjects (3%) discovered accidently with no hearing complaint or any risk factors except COVID-19 infection. Twenty-one subjects had bilateral SNHL while 4 cases had right SNHL and another 4 subjects had left SNHL. The majority of study group subjects had moderate, high frequency SNHL. Five subjects had CHL; 3 of them had moderate CHL and 2 had mild CHL. CHL was unilateral in one case and bilaterally in the rest. Regarding control group, all subjects had normal pure tone audiometry results except one case who had normal hearing up to 2KHz and left mild SNHL at frequencies above.

Table (3) shows the distribution of study group according to side, configuration and degree of sensorineural hearing loss.

SNHL		Number (n.=29)	Percentage %
Configuration	High frequency	17	59%*
	Low frequency	3	10%
	Flat curve	9	31%
Degree of hearing loss	Mild	9	31%
	Moderate	12	41%*
	Moderately sever	4	14%
	Severe	1	3%
	Profound	3	10%

There was statistically significant difference between control and study group subjects in pure tone thresholds at all frequencies (table 4) also there were statistically significant difference between control and study group subjects in SRT and SD % at all frequencies in both ears (table 5).

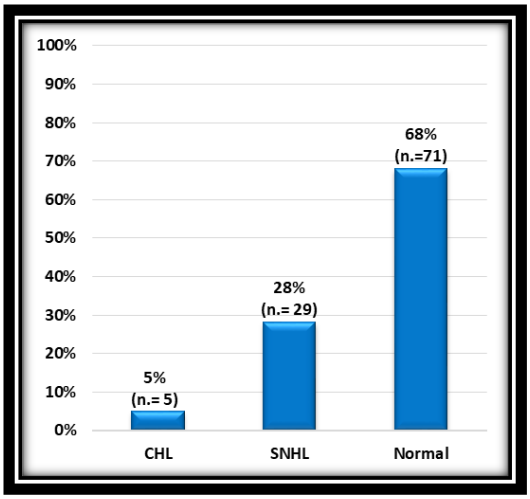

Diagram shows distribution of study group subjects according to results of pure tone audiometry

Table (4) shows Mean, Standard deviation, t and p values of pure tone audiometry thresholds the study group with hearing loss and the control group.

Frequencies (Hz)		Study group			Control group		Independent sample t-test	P-value
		Mean	± SD	Range	Mean	± SD		
Right	250	23	11	5-60	19	4	2.313	0.023
	500	23	12	5-55	17	4	3.288	0.001
	1k	23	14	5-60	14	4	4.308	0.000
	2k	26	16	5-70	14	3	5.366	0.000
	4k	32	20	5-80	14	6	5.828	0.000
	8k	37	21	5-85	14	4	7.745	0.000
Left	250	32	22	10-120	17	5	4.001	0.000
	500	34	22	10-120	16	4	4.907	0.000
	1k	32	26	5-120	14	5	4.982	0.000
	2k	34	25	5-120	13	4	5.789	0.000
	4k	42	26	10-120	16	5	6.746	0.000
	8k	48	26	10-120	14	6	8.808	0.000

Table (5): Mean, Standard deviation, t and p values of speech audiometry thresholds in study group subjects with hearing loss and the control group.

Variables		Group				Independent sample t-test	P. value
		Study group		Controls			
		Mean	± SD	Mean	± SD		
Right	SRT	24	11	14	4	5.422	0.000
	WRS %	89	11	97	3.5	-4.783	0.000
Left	SRT	35	25	15	4	5.294	0.000
	WRS %	78	27	97	3	-4.826	0.000

2. Tympanometry test results:

Table (6) shows the different types of tympanogram seen in the ears of the study group subjects.

Tymanogram	Ears (n.=210)	
	Number	Percentage %
A	178	85%
B	9	4%
C	16	8%
As	4	2%
Ad	3	1%

Table (6) showed that abnormal tympanogram was seen in 8%, 4% in the form of type (C), (B) respectively. Interestingly, all subjects (n.= 5) with earache had type (B) tympanogram.

II. Analysis of vestibular office tests results:

Vestibulo-ocular reflex office tests were done in 98 subjects (7 subjects were excluded due to; congenital nystagmus in one subject, cervical disc in five subjects and recent vertebral surgery in one subject). Vestibulo-spinal reflex office tests were done in 99 subjects (6 subjects were excluded due to; hemiplegia in two subjects, one subject was on a wheel chair and three subjects were using assessing walking stick). Forty-two subjects complained of post COVID dizziness, and 16 of them (15%) had positive findings in one or more vestibular office tests.

Table (7): Distribution of COVID-19 subjects according to vestibular office tests findings

		abnormal		Normal	
		n.	%	n.	%
VOR (n.=98)	Spontaneous nystagmus	0	0%	98	100%
	Positional nystagmus	5	5%	93	95%
	HST	1	1%	97	99%
	HTT	4	4%	94	96%
	Dix Hallpike	12	12%	86	88%
VSR (n.=99)	Fukuda stepping	3	3%	96	97%
	mCTSIB	5	5%	94	95%

Table (7) showed signs of uncompensated peripheral vestibular lesion for further investigations to confirm site and degree of vestibular lesion. Also, BPPV was found the most common post COVID-19 vestibular disorder in the study group.

Table (8): Number of COVID-19 subjects and controls according to vestibular office tests using fisher exact test

			Control group		Study group		Fisher exact	P-value
			n.	%	n.	%		
VOR (n.=98)	Spontaneous nystagmus		0	0%	0	0%	NA	NA
	BPPV (Dix Hallpike) right		0	0%	7	7%	6.229	0.029*
	BPPV (Dix Hallpike) left		0	0%	5	5%	6.229	0.029*
	Positional right	rt beating nystagmus	0	0%	1	1%	1.588	0.703
		lt beating nystagmus	0	0%	3	3%		
	Positional central	rt beating nystagmus	0	0%	1	1%	1.588	0.703
		lt beating nystagmus	0	0%	3	3%		
	Positional left	rt beating nystagmus	0	0%	1	1%	2.160	0.401
		lt beating nystagmus	0	0%	4	4%		
	HST		0	0%	1	1%	0.514	1.000
	HTT	rt beating nystagmus	0	0%	1	1%	2.098	0.300
		lt beating nystagmus	0	0%	3	3%		
VSR (n.=99)	Fukuda stepping		0	0%	3	3%	2.484	0.551
	mCTSIB1		0	0%	0	0%	NA	NA
	mCTSIB2		0	0%	0	0%	NA	NA
	mCTSIB3		0	0%	0	0%	NA	NA
	mCTSIB4		0	0%	5	5%	4.175	0.169

Table (8) showed that there were statistically significant differences between the two groups regarding Dix Hallpike right and left (p=0.029).

DISCUSSION:

The damaging effect of COVID-19 infection on the inner ear is a new finding which is yet to be explored. Pure tone audiometry and impedance audiometry are two important investigations for auditory assessment among patients with COVID-19 infection[12]. More than 1 in 10 COVID-19 adults report a change in their hearing status, when questioned eight weeks after discharge from hospital[13].

Basic audiological evaluation showed that more than third of the studied cases had SNHL with various degrees of severity of SNHL from mild to total deafness. The majority of study group subjects had bilateral, moderate, high frequency SNHL of sudden onset. While subjects with conductive hearing loss were most probably due to otitis media with effusion as they had bilateral type B tympanograms.

Similarly, in **Aarabi et al.,**[14] study, post COVID hearing loss varied from moderate to severe SSNHL in 10% of the studied cases. In **Almufarrij & Munro** [15] systemic review that included a total number of 28 patients 14 (50%) patients reported to have sudden onset SNHL and 9 subjects (32%) had CHL. Additionally, **Jeong et al.,** [16] in his study that was performed on 10 subjects with confirmed post COVID SNHL, he reported that audiometric data showed that all patients experienced SNHL ranging from mild to profound.

In agreement, in the study of **Basoz et al.,**[17]**,** both air and bone pure tone audiometry of the patient group were found significantly higher than the control group ($p < 0.05$). When the speech tests of the participants were examined, the SRTs of the

patient group were significantly higher (p = 0.000), while a significant decrease was not obtained in the speech discrimination scores (p = 0.804).

Similarly, **Sousa et al.** [18] study point to a pure-tone loss beginning at 1000 Hz and extending through 2000, 3000, 4000 and 8000 Hz when compared to controls. However, **Daikhes et al.**[19] **and Dror et al.** [20] did not find a significant difference in audiometric thresholds between COVID-19 cases and controls**.**

The exact pathophysiology of SSNHL post COVID is still unknown. Inflammation of the auditory pathway, including cochlear nerve, cochlea, and perilymphatic tissue, as well as cross-reaction between the antigens in the inner ear and virus have all been linked in causing SSNHL. Additionally, indirect virus transmission from cerebrospinal fluid to the inner ear structures can also explain the cause behind SSNHL[21]**.**

As regards vestibular clinic office evaluation, the results showed significant differences between the two groups regarding Dix Hallpike right and left (p=0.029) reflecting presence of BPPV as the cause of dizziness. Similarly, **picciotti et al.** [22] studied the vestibular findings of eight patients affected by COVID-19 infection and vertigo and showed that BPPV was found in all the patients. They hypothesized that BPPV in COVID-19 infections can be related to drugs, prolonged bed rest and direct damage by a viral infection on the peripheral vestibular system and in particular on the otolithic membrane due to the cytopathic effect of the virus and to the inflammatory response. **Maslovara and Kosec**[23] also reported 2 cases presented with BPPV post COVID.

In agreement, **Li et al.,** [24] noted that the etiological distribution of dizziness/ vertigo in 2020 was different from that of the corresponding period in 2019 before COVID-19 pandemic. BPPV and psychogenic/PPPD were more abundant, and vascular vertigo was less frequent. Given the high incidence of BPPV and psychogenic/PPPD in the neurological clinic, clinicians should pay attention to the identification of these two causes, as well as the emotional disorders as a triggering factor that are likely to be caused by the epidemic.

While **Abdelrahman and Shafik**[25] found that two-thirds of the patients with a history of either mild or moderate degree COVID-19 had an asymmetrical caloric response and most of the patients showed positional nystagmus. They also reported that there was a significant difference between the incidence in severe versus mild and moderate degrees reflecting a significant association between the severity of the disease and the caloric asymmetry. They concluded that COVID-19 infection has a significant effect on the peripheral vestibular system and superior vestibular nerve.

In contrast, **Gallus et al**.,[26] suggested that no clinically relevant signs of vestibular impairment can be found in former Covid-19 patients through performing vHIT as a screening and diagnostic test for vestibular loss. Their study hypothesized that whether a transitory vestibular loss with subsequent full recovery is present in patients with COVID-19. Chern et al.,[27] reported a case of bilateral SSNHL, aural fullness, and vertigo in a patient with bilateral intralabyrinthine hemorrhage and documented SARS-CoV-2 infection on IgG serology testing.

The exact cause of the reported vestibular symptoms, remains unknown, but mild vestibular symptoms such as dizziness and imbalance might simply be the result of the profound asthenia and fatigue often experienced by COVID-19 patients. It has been shown that the inner ear structures are particularly susceptible to ischemia and vascular damage, which can lead to both hearing and balance dysfunction. Several

cardiovascular manifestations, including a coagulation abnormality, have been reported in COVID-19 patients[11]**.** The sequelae of such manifestations may result in inner ear thrombosis or hypoxia, and could explain vestibular affection.

Conclusion:

The present study findings indicate that Sars-Cov2 may have deleterious effects on cochlear hair cell functions, despite the patient being asymptomatic and therefore, all patients with SSNHL and/or acute vestibular disease should be screened for COVID-19. The majority of affected subjects had bilateral, moderate, high frequency SNHL with sudden onset. BPPV is the most common cause of post COVID-19 vertigo.

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

Recommendations:

To include history of COVID-19 infection in the history of audiological evaluation. Also to evaluate the different parts of vestibular system through objective evaluation using VNG, VEMP.

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كوفيد ١٩ وعلاقته بجهاز السمع والإتزان في المرضى المصريين البالغين

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وحدة السمعيات قسم الانف والاذن والحنجرة كلية الطب جامعة عين شمس**

المقدمة: اشارت دراسات قليلة مؤخرًا لظهور أعراض لامراض في الجهاز السمعي والاتزان لدى مرضي كوفيد – ١٩ في بعض الدراسات. وجدت الابحاث أن المرضى المصابين بمرض كوفيد – ١٩ قد يعانون من أعراض مثل ضعف السمع , الطنين ,الم بالأذن و الدوار.ولكن التفاصيل لم توصف على نحو جيد. ولم يتم الإبلاغ عن نسبة حدوث ذلك بشكل واضح حتى الآن، حيث تركز الانتباه على الأعراض الخطيرة التي تهدد الحياة.

الأهداف: وتهدف هذه الدراسة إلى تسليط الضوء على مدى اصابة جهاز السمع والاتزان في لدي المصريين المصابين الذين تم تشخيصهم من قبل و وصف نمط الاصابة لاي أعراض تم العثور عليه .

المرضي والمنهجية : شارك مجموعه ١٠٥ أشخاصًا مؤكدين الاصابة بمرض الكورونا ، من عيادة السمعيات مع واحدة أو أكثر من الشكاوى المتعلقة بالسمع والاتزان وتمت مقارنتهم بـ ٥٠ من المتطوعين الأصحاء المتطابقين مع العمر والجنس وليس لديهم تاريخ لـلاصابة بمرض الكورونا كمجموعة ضابطة. خضع جميع المشاركين إلى: تسجيل تاريخ مفصّل للحالة لامراض السمع والاتزان يتضمن والتقييم السمعي الاساسي بما في ذلك:- قياس السمع بالنغمات النقية (التوصيل الهوائي والتوصيل العظمي)، اختبار تفسير الكلام باللغة العربية و قياس ضغط الاذن بالاضافة الي اختبارات الاتزان المكتبية السريرية.

النتائج: أربعة وثلاثون شخصًا (٣٢٪) يعانون من ضعف السمع. تسعة وعشرون شخصًا (٢٨٪) لديهم ضعف سمع حسي عصبي ، 5أشخاص (٥٪) لديهم ضعف سمع توصيلي و ١٦ حالة (١٥٪) لديهم امراض خاصة بجهاز الاتزان.

الخلاصة: يجب توثيق التأثير السمعي الدهليزي بعد الاصابة باالكورونا. غالبية الأشخاص المصابين كان لديهم ضعف سمع حسي عصبي فجائي بالاذنين ، متوسط الشدة ، بالترددات العليا. ويعتبر دوار الوضعة الانتيابي الحميد هو السبب الأكثر شيوعًا لدوار ما بعد الاصابة بالكورونا.