ROLE OF VITAMIN D DEFICIENCY IN HEARING AND VESTIBULAR DISORDERS

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ABSTRACT:

Background: *low serum vitamin D could be a cause of labyrinthine demineralization and in particular otoconial fragility. Vitamin D has a strong immunomodulatory role and regulation the expression of pro-inflammatory mediators. Its deficiency has been associated with increase the inflammatory processes in the inner ear.*

Aim of the work: *Study relation between vitamin D level and audio-vestibular disorders.*

Patients and Methods: *Present study was conducted on 214 subjects divided into two groups; study group included 107 adults who suffered from common audio-vestibular disorders while control group consisted of 107 volunteers with no audio-vestibular abnormalities. All the participants underwent audiological, vestibular evaluation, laboratory measurement of serum 25-hydroxyvitamin D3. Bone mineral density (BMD) was measured in the study group only at lumbar spine (L1–L4), proximal femur and mid ultra 1/3 forearm.*

Results: *Serum 25(OH) D_3 levels were significantly lower in BPPV patients compared to control group. Patients with recurrent episodes of BPPV had significantly more low average serum level of 25(OH) D_3 than patients with a first episode. Presbycusis patients showed lower 25(OH) D_3 level compared to the senior adult controls yet not reach significant level. However, Vitamin D deficiency and low femur & forearm bone mineral density showed inverse correlation with hearing thresholds. Moreover, there was significant inverse correlation between low bone mineral density in Otosclerosis group and mean air, bone conduction hearing thresholds. No association found between vitamin D deficiency and Meniere's disease.*

Conclusions: *The prevalence of vitamin D deficiency is common in patients suffered from BPPV and BPPV associated with presbycusis. Moreover vitamin D deficiency and low bone mineral density is risk factor for age related hearing loss.*

Keywords: *Hearing; vitamin D deficiency; vestibular disorders*

INTRODUCTION:

Vitamin D has recently received significant attention; as it was demonstrated to play a crucial role in acute and chronic diseases[(1)]. There are many risk factors to develop vitamin D insufficiency or deficiency expected from its complex metabolism. The main ones are reduced or restricted sun exposure, reduced cutaneous synthesis, inadequate dietary intake, malabsorption syndrome, chronic renal and liver disease[(2)]. The prevalence of severe vitamin D deficiency in Egyptian population was 30.1% while 36.9% had vitamin D deficiency. Insufficient and sufficient categories represent 15.6% and 17.2% respectively[(3)].

Vitamin D deficiency or its metabolic derivatives may cause disruption of the calcium concentration important to maintain normal hearing and vestibular functions [(4)]. Several studies reported that low vitamin D levels were associated with development and recurrence of benign paroxysmal positional vertigo (BPPV). Nevertheless, recent studies reported that a low vitamin D level was not associated with BPPV occurrence and/or recurrence[(5)]. Considering these inconsistencies, the relationship between BPPV and vitamin D deficiency is debatable.

Recent studies observed that correcting vitamin D deficiency in newly diagnosed cases of Meniere's disease decreased the necessity of the ablative therapy with intratympanic gentamicin. According to their hypothesis, vitamin D supplementation may indeed have a beneficial effect in Meniere's disease if the symptoms are caused by a local postviral autoimmune reaction. Moreover vitamin has a strong immunomodulatory role and regulation of the expression of pro-inflammatory mediators[(6)].

These observations raised the question if vitamin D influences inner ear pathology in general and by what mechanism. Accordingly, this study was conducted to address the role of vitamin D deficiency in different audio-vestibular disorders.

AIM OF THE WORK:

Study relation between vitamin D level and audio-vestibular disorders.

PATIENTS AND METHODS:

Patients:

The present study was conducted on September 2017 to November 2019 on 214 subjects. They were divided into two groups; the study group included 107 adults who suffered from common audio-vestibular disorders while control group consisted of 107 volunteers with no audio-vestibular abnormalities. Both groups were subdivided according to age into adult group (30-59) and senior group (60-70) years old [(7)]. Patients with the following conditions were excluded; history of vitamin D supplement, head trauma, noise exposure, chronic or systemic diseases, neurological and cardiovascular disorders.

Methods:

All the participants in this study underwent audiological, vestibular evaluation and laboratory measurement for measurement of 25-hydroxyvitamin D_3, using a chemiluminescence immunoassay. Bone mineral density (BMD) was measured in the study group only at lumbar spine (L1–L4), proximal femur and mid ultra 1/3 forearm. The approach of interpretation of Dual-Energy X-ray Absorptiometry results of DEXA were categorized into normal, osteopenia and osteoporosis based on lowest T-score of either three sites for each subject**.** [(8)]. Both Dual-energy x-ray absorptiometry and biochemical parameters were assessed within 48 hours of the clinical diagnosis.

RESULTS:

Table (1): Age distribution in the study and control group:

		Study group	Control group	P
		No. = 107	No. = 107	
Age in years	Mean ± SD	56.23 ± 10.20	54.96 ± 10.44	0.369
	Range	33 – 70	30 – 70	
Age classification	Adult	49 (45.8%)	62 (57.9%)	0.075
	Senior	58 (54.2%)	45 (42.1%)	
Gender	Female	65(60.7%)	60 (56.1%)	0.487
	Male	42 (39.3%)	47 (43.9%)	

Independent t-test, Chi-Square test

This table showed matched study and control group for age and gender.

Table (2): Clinical entities in study group:

Clinical entities	No.	(%)
BPPV	64	(59.8%)
Presbycusis	19	(17.8%)
Presbycusis &BPPV	11	(10.3%)
Endolymphatic hydrops (Ménière's disease)	7	(6.5%)
Clinical otosclerosis	6	(5.6%)

N.B: Vestibular migraine patients were excluded according to study exclusion criteria. During the study period three patients presented with acute (uncompensated) vestibular neuritis they didn't complete all study requirements so they was excluded from this study.

Table (3): Serum 25(OH) D_3 level in study group according to its clinical entities:

		25(OH)D_3			H	P
	N	Mean±SD	Median	Range		
Control [a,d,e,f]	107	17.12 ± 7.82	16.2	5.3 – 36.1	27.0	<0.0001
BPPV [b,c,f]	64	12.48 ± 6.65	10.5	4.1 – 38.7		
Presbycusis & BPPV [c,b,f]	11	10.75 ± 9.38	8.6	3.2 – 38.7		
Presbycusis [d,a,e,f]	19	15.89 ± 5.07	17	7.1 – 23.7		
Endolymphatic hydrops [e,a,d,f]	7	18.16 ± 4.62	19.7	9.66 – 23		
Clinical Ostosclerosis [f,a,b,c,d,e]	6	14.07 ± 4.76	15.45	7.1 – 19.1		

Kruakal-Wallis test, Post hoc test (homogenous groups had the same sympol)

This table showed statistically significant differences between {Control vs. BPPV and BPPV with Presbycusis}. There were no statistically significant differences between {Control vs., Presbycusis, Endolymphatic hydrops or clinical osteosclerosis}.

Table (4): DEXA categories in the study group:

DEXA categories	N=(107)	(%)	T- score Reference level
Normal	30	28%	BMD ≥−1 SD of the mean BMD in a young adult 30 years old of the same sex and ethnicity
Osteopenia	44	41%	BMD <−1 to > −2.5 SD of the mean BMD in a young adult 30 years old of the same sex and ethnicity
Osteoprosis	33	31.8%	BMD ≤ − 2.5 SD of the mean BMD in a young adult 30 years old of the same sex and ethnicity

Bone mineral density (BMD) was measured at lumbar spine (L1–L4), proximal femur and mid ultra 1/3 forearm. Results of DEXA were categorized into normal, osteopenia, osteoporosis based on lowest T-score of either three sites for each subject**.**

Table (5): DEXA categories in study group according to its clinical diagnosis:

	BMD classification						X^2	P
	Normal (N=30)		Osteopenia (N=44)		Osteoprosis (N=33)			
	N	%	N	%	N	%		
BPPV	16	(53.3%)	29	(65.9%)	19	(57.6%)	12.10	0.115
Presbycusis associated with BPPV	3	(10.0%)	2	(4.5%)	6	(18.2%)		
Presbycusis	7	(23.3%)	9	(20.5%)	3	(9.1%)		
Endolymphatic hydrops	4	(13.3%)	2	(4.5%)	1	(3.0%)		
Clinical Ostosclerosis	0	(0.0%)	2	(4.5%)	4	(12.1%)		

Chi-Square test, Fisher's Exact test

This table showed no statistically significant difference between groups according to its DEXA classification. Yet osteoporosis was ranged between 12.1% in clinical otosclerosis up to 57.6% in BPPV.

Presbycusis Category:

19 (17.8%) patients in study group had age related hearing loss (Presbycusis) age ranged 60-70 years old associated with bilateral, symmetrical and slowly progressive hearing loss with no restriction to hearing aid use; 11 (10.3%) of patients have benign paroxysmal positional vertigo disorder associated with age related hearing loss. Both groups were gathered together for depth analysis.

Table (6): Description hearing level in presbycusis patients:

Hearing level (Tested ears N= 60 ears)	No.	%	Pure Tone Average (500-4000Hz)	
			Mean±SD	Range
Mild hearing loss (26-40dBHL)	22	36.7%	33.75 ±3.37	28.75 - 38.75
Moderate hearing loss (41-55dBHL)	35	58.3%	44.94 ±3.50	41.25 - 51.25
Moderately severe hearing loss (56-70dBHL)	3	5.0%	56.25 ± 0.0	56.25 - 56.25

The mean hearing loss is calculated separately for each ear. Degree of hearing loss based on average of four frequencies (500 Hz, 1000 Hz, 2000 Hz and 4000 Hz) hearing thresholds[9].

Table (7): Correlation between tested pure tone frequencies and serum 25 (OH)D_3 (ng/mL) level, BMD of each site in presbycusis:

Tested pure tone Frequencies (Tested ears N= 60 ears)	Pure tone average	
	r	P-value
25 (OH)D_3 (ng/mL)	-0.513**	<0.0001
Spine BMD (L1-L4) (gm/cm²)	-0.021	0.876
Femur BMD (Total hip) (gm/cm²)	-0.300*	0.020
Forearm BMD (Mid ultra1/3) (gm/cm²)	-0.437**	0.0001

Spearman correlation coefficient

This table showed inverse correlation between serum 25 (OH)D_3, Femur, Forearm bone mineral density and pure tone average

Otosclerosis &Endolymphatic hydrops categories:

Table (8): Correlation between tested pure tone frequencies and serum 25 (OH)D_3 (ng/mL) level in Clinical otosclerosis and Endolymphatic hydrops (affected ears) patients:

		25 (OH)D_3 (ng/mL)		Spine BMD (L1-L4) (gm/cm²)		Femur BMD (Total hip) (gm/cm²)		Forearm BMD (Mid ultra1/3) (gm/cm²)	
		r	P-value	r	P-value	r	P-value	r	P-value
Clinical otosclerosis	Pure tone average (Air conduction)	-0.058	0.859	-0.026	0.937	-0.706	0.010	-0.662	0.019
	Pure tone average (Bone conduction)	0.174	0.589	-0.162	0.615	-0.783	0.003	-0.426	0.167
Meniere's disease	Pure tone average (Air conduction)	0.144	0.76	-0.51	0.243	0.127	0.785	0.181	0.696

Spearman correlation:

This table showed no correlation between Serum 25 (OH)D_3 (ng/mL) and mean air, bone conduction hearing threshold in otosclerosis or endolymphatic hydrops patients. In otosclerosis there was inverse correlation between femur, forearm bone mineral densities and mean air conduction hearing threshold. In Meniere's disease there was no correlation between bone mineral density and mean pure tone average hearing threshold.

DISCUSSION:

This study was designed the role of vitamin D deficiency in different audio-vestibular disorders. The relationship between decreasing levels of 25(OH) D_3 and BPPV was demonstrated in the current study. Serum 25(OH) D_3 levels were significantly lower in BPPV and BPPV with presbycusis patients compared to control group with [12.48±6.65 ng/ml, 10.75±9.38 versus 17.12±7.82 ng/ml] ***(Table 3).*** Vitamin D has been suggested to have a role in the pathogenesis of BPPV as it affects the calcium carbonate crystals (otoconia) in their aspect, size and density. It was proposed that otoconia had lost their relatively fine stony appearance and formed giant crystals that lost its attachment on the otoconial membrane**[10&11].**

The present study also investigated the relation between vitamin D status, BMD, and hearing loss among senior adults. Current study demonstrated that vitamin D deficiency and decreased femur, forearm bone mineral density have inverse correlation with hearing thresholds ***(Table 7).*** This findings agree with previous studies as they reported that total 25(OH)D <20 ng/mL and decrease in femoral neck bone mineral density may be a potential risk factor for age-related hearing loss[12].

The bone of the cochlear capsule is lamellar bone with few haversian canals and vascular elements, and thus consists of maximally compact bone tissue**[13].** Earlier radiological studies showed increased sclerosis of otic capsule in few patients with osteoporosis**[14]**. There is a similarity of femoral neck and radius bony structure to the petrous temporal bone **[15].** Therefore, demineralization of femur neck would reflect demineralization of the petrous temporal bone which possibly leads to sensorineural hearing loss.

In support, tendency for osteoporosis was observed to be more prevalent in otosclerosis patients and no case showed normal BMD ***(Table 5).*** Important notice that the mean 25(OH)D3 level was lower in Otosclerosis group ***(Table 3)*** yet the difference from control was not statistically significant. There was significant inverse correlation of bone mineral density measured at femur neck, forearm to air conduction hearing thresholds ***(Table 8).*** It had previously reported an association between otosclerosis and three polymorphic markers within the collagen 1A1 gene

(COL1A1) [16]. A similar association has been reported for the same marker COL1A1 and osteoporosis [17,18]**.** It might play a role in the pathogenesis of both otosclerosis and osteoporosis**.** The limited numbers of patients in current study hinder appropriate demonstration of vitamin D role in otosclerosis.

In Meniere's disease the literature covers only a few studies on vitamin D. However in the present study small number of participants constitutes the main limitation. Mean $25(OH)D_3$ level in Meniere's disease patients was 18.16 ± 4.62 ng/mL and 17.12 ± 7.82 ng/mL in control group with no statistically significant difference ***(Table 3).*** In addition, there was no correlation between vitamin D or bone mineral density and mean pure tone average hearing threshold in affected ears in Meniere's disease ***(Table 8)***

On the other hand, recent study found a lower serum vitamin D level in Meniere's disease with a significant difference than control group and he hypothesized that vitamin D might be a protective factor in Meniere's disease. Data of the current work failed to report any association of vitamin D deficiency with occurrence or degree of hearing loss and this could be possibly explained by for small patient number [19].

Conclusions:

The prevalence of vitamin D deficiency is common in patients suffered from BPPV and BPPV associated with presbycusis. Moreover vitamin D deficiency and low bone mineral density is risk factor for age related hearing loss.

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دور نقص فيتامين (د) على السمع واضطرابات الاتزان

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الخلفيه: نقص فيتامين د٣ قد يسبب اضطراب تركيز الكالسيوم في السوائل الأساسية والأنسجة العصبية في الأذن الداخلية. أيونات الكالسيوم تنظم جوانب عديدة ومتنوعة من فسيولوجيا السمع و الاتزان بالإضافة إلى ذلك نقص فيتامين (د) يساهم في هشاشة العظام يؤدي إلى التغيرات التكسية في العظام الصخريه للاذن الداخليه.

الهدف من الدراسه: دراسه علاقه فيتامين (د) على امراض السمع واضطرابات الاتزان

المرضي و طرق العلاج: أجريت الدراسة الحالية على ٢١٤ شخصاً مقسمة إلى مجموعتين. تضمنت مجموعة الدراسة ١٠٧ بالغين عانوا من اضطرابات سمع و اتزان بينما تألفت المجموعة الاخري من ١٠٧ متطوعين لا يعانوا من اضطرابات سمع و اتزان. خضع جميع المشاركين لتقييم سمعي ، اختبارات توازن ، قياس نسبه فيامين د في الدم وقياس الكثافة المعدنية للعظام في مجموعة الدراسة فقط في العمود الفقري القطني وعظم الفخذ القريب والجزء الأوسط من الساعد.

النتائج: هذه الدراسه أكدت وجود ارتباطات قوية بين مستويات فيتامين (د) والدوار الحركي الحميد. نقص نسبه فيتامين د قد تؤدى الى حدوث الدوار الحركي الحميد كما تبين انخفاض فيتامين (د) وانخفاض كثافة المعادن العظام وخاصة في عظم الفخذ والساعد يمكن أن يكون خطرا محتملا لفقدان السمع المرتبطة بالعمر بسبب التشابه بين عظم الفخذ و العظام الصخريه للاذن الداخليه. تطرح هذه الدراسة علاقة تصلب عظم الأذن وهشاشة العظام حيث كان الميل إلى هشاشة العظام أكثر انتشارا في مرضى تصلب عظم الأذن مع وجود ارتباط عكسي بين كثافة المعادن في العظام التي تم الحصول عليها من عنق الفخذ والساعد و درجه فقدان السمع.

لم تظهر الدراسة الحالية أي ارتباط بين مستويات فيتامين (د) أو انخفاض كثافة العظام مع الأستجابة العضلية المثارة لجهاز الإتزان. وعلاوة على ذلك، فشل هذا العمل في التحقق من وجود ارتباط بين نقص فيتامين (د) مع حدوث مرض مينيير ودرجة فقدان السمع.

الاستنتاجات: انتشار نقص فيتامين (د) شائع في المرضى الذين يعانون من حدوث الدوار الحركي الحميد. علاوة على ذلك ، فإن نقص فيتامين د وانخفاض كثافة المعادن في العظام هو عامل خطر لفقدان السمع المرتبط بالعمر.