



Serum vitamin D and Recurrent Benign Paroxysmal Positional Vertigo

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Abstract:

Vertigo is defined as the subjective perception of rotation or translation without external movement. The subtype benign paroxysmal positional vertigo (BPPV) is the commonest one. Although BPPV has been named benign, some patients suffered recurrences. Vitamin D regulates serum calcium and phosphorus homeostasis and maintaining bone structure. goal of this study To measure the serum levels of 25-hydroxyvitamin D3 (25-OH D3) and calcium total & ionized in patients with BPPV and determine whether there is a difference in the serum levels of vitamin D3 between patients with and without recurrence, Thirty patients with BPPV were divided into 2 groups: non-recurrence (Group I) and recurrence (Group II). Detailed history and clinical examination were performed, and blood samples were collected, and the serum level of 25-OH D3 and calcium total & ionized was assessed and compared in both groups, There was non-significant difference between both groups regarding the affected canal and laterality between both groups. Serum vitamin D, total and ionized calcium levels were lower in recurrence group than non-recurrence group, with non-significant difference between both groups.

Keywords: BPPV, and vitamin D, calcium.

1. Introduction:

Benign paroxysmal positional vertigo (BPPV) is a disease known to cause clinical symptoms when body positions change due to otoconia that has become dislodged from the macula of the utricle or the saccule and has entered the semicircular canal or attached to the cupula. Otoconia consist of the crystals of its main components, calcium carbonate and glycoproteins and are connected to hair cells with protein fibres [1].

The calcium channel proteins that are associated with vitamin D in the epithelium are known to be involved in the calcium metabolism of the vestibular organ, and the interactions between calcium-related diseases and BPPV have been studied [2].

During the formation and maintenance processes of otoconia, calcium flows from the epithelial cells of the utricle and saccule into cells through Ca^{2+} -selective transient receptor potential vanilloid channels involved in active calcium movements. There after, the Ca^{2+} ions are combined with both calcium buffer proteins, which are intracellular-binding proteins discharged from hair cells through sodium-calcium exchangers, and plasma membrane Ca^{2+} -ATPases, which are Ca^{2+} exit pathways existing in

cytosolic membranes. In addition, along with the HCO_3^- discharged through carbonic anhydrase, locally high concentrations of Ca^{2+} and HCO_3^- are formed in the endolymph to constitute CaCO_3 vitreous bodies (crystallite). The CaCO_3 vitreous bodies are induced to form otoconia through the actions of NADPH oxidases and otopetrin-1, which are membrane-bound enzymes. The vitreous bodies formed are combined with otolithic proteins, such as Oc90, Otolin-1, keratan sulphate proteoglycan, and Sc1, so that otoconia can grow. Matured otoconia are attached to the otolithic membranes through anchoring [2].

Recently, along with study results indicating that the vitamin D levels of BPPV patient groups are lower compared to controls, there were case studies indicating that the vitamin D deficiency of patients who chronically suffer recurrences of BPPV was quite severe [3].

Although BPPV has been named a benign disease, a number of BPPV patients suffer recurrences, and BPPV patients show 1-year recurrence rates of approximately 20% and 5-year recurrence rates of approximately 50%. In particular, some patients experience severe

difficulties in their daily lives due to frequent recurrences of BPPV [4].

Vitamin D is mostly synthesized in the skin and is changed into 25-hydroxyvitamin D (25-OH vitamin D) in the liver and into 1,25-dihydroxyvitamin D [1,25 (OH)₂ vitamin D] in the kidney to act on various parts of the human body [5]. Among metabolites, 25-OH vitamin D has the highest serum concentration, and the concentration level is a good indicator of the vitamin D held in vivo [1]. The aim of this study was to measure the serum levels of 25-hydroxyvitamin D₃ (25-OH D₃) and calcium total & ionized in patients with BPPV and determine whether there is a difference in the serum levels of vitamin D₃ between patients with and without recurrence.

2. Patients and Methods:

Thirty patients (21 women and 9 men) with a mean age of 44 ± 12.5 years (30–70 years). Cases were collected from Audiology unit, faculty of medicine Beni-Suef University hospital, diagnosed as BPPV based on the criteria of brief episodes of positional vertigo, and characteristic paroxysmal positional nystagmus. The study took place during the period from Feb 2018 to May 2019.

2.1 Inclusion criteria:

The patients who were diagnosed as BPPV based on the criteria of brief episodes of positional vertigo, and characteristic paroxysmal positional nystagmus.

Exclusion criteria:

The patients who had other causes than idiopathic BPPV such as: head trauma, post-operative or Meniere's disease are excluded.

2.2 All patients were subjected to: All BPPV patients were subjected to the following:

1. Full medical history taking: It includes full description of the dizziness complaint regarding frequency, duration, progression and character. Also, precipitating and relieving factor were included. Any accompanying symptoms, medication received, or other diseases were documented, then full general examination and otological examination.

2. Basic audiological evaluation:

- Pure tone audiometry including air and bone conduction: pure-tone audiometry for frequencies ranging from 250Hz to 8 kHz for air and 500Hz to 4kHz for bone conduction thresholds.

- Speech audiometry including Speech Reception Threshold (S.R.T): Using Arabic spondic words and word discrimination score (WDS %), using Arabic phonetically balanced [7].
 - Immitencemetry including tympanometry (single frequency tympanometry) and acoustic reflex threshold: With a probe tone of 226 Hz, tympanic membrane compliance, the middle ear pressure and the static volume, were analyzed and testing of the acoustic reflex threshold for the ipsilateral elicited reflexes using pure tones at frequencies 500,1000,2000,4000 Hz.
3. Vestibular system evaluation using videonystagmography that include:
- (a) Occulography test: smooth pursuit testing, saccade, optokinetic tests.
 - (b) Water caloric test.
 - (c) Positional tests.
 - (d) Positioning tests.
4. Laboratory investigation: Total & Ionized Calcium level.
5. Special investigation: Detection of the serum levels of 25-hydroxyvitamin D3 (25-OHD3) via Enzyme Immunoassay (EIA).

Statistical methodology:

- Analysis of data was done by IBM computer using SPSS (statistical program for social science) as follows;
 - Description of quantitative variables as mean, SD and range.
 - Description of qualitative variables as number and percentage.
 - Unpaired t-test was used to compare quantitative variables, in parametric data (SD < 50 % mean)
- P value > 0.05 insignificant
- P < 0.05 significant

3. Results:

The current study included 30 male and female patients with Benign paroxysmal positional vertigo (BPPV). They all presented to the Audiology unit in the Faculty of Medicine in Beni-Suef University hospital. Their age ranged from 30 to 70 years. Some inclusion and exclusion criteria were taken, and they were age and sex matched. Detailed history and clinical examination were performed. Blood samples were collected, and the serum levels of 25-hydroxyvitamin D3 (25-OH D3) and calcium total & ionized in patients expression levels was assessed and compared in two patients' groups:

Nonrecurrence group (Group I) and Recurrence Group (Group II).

Table (1): Comparative study between groups regarding the gender.

Gender	Non-recurrence Group I		Recurrence Group II		P-value
	%	Count	%	Count	
Male	40 %	6	20 %	3	1
Female	60 %	9	80 %	12	

P-value = 1 (no statistically significant difference)

Table (1): show no statistically significant difference in gender between patients with non-recurrence group I and recurrence group II.

Table (2): Comparative study between groups regarding the affected canal.

CANAL BPPV	Nonrecurrence Group I		Recurrence Group II		P-value
	%	Count	%	Count	
Posterior Canal BPPV	67%	10	67%	10	<0.05
Lateral Canal BPPV	27%	4	20%	3	
Multi Canal BPPV	7%	1	13%	2	

P-value > 0.05 (Non-significant)

Table (2): show non significant difference between both groups as regards the affected canal of the patient.

Table (3): Comparative study between groups regarding the expression of vitamin D levels.

Vitamin D	Nonrecurrence Group I		Recurrence Group II		P-value
	%	Count	%	Count	
Normal VIT D	47%	7	20%	3	0.89
Deficient VIT D	20%	3	20%	3	
Insufficient VIT D	33%	5	60%	9	>0.05

P-value > 0.05 (Non-significant)

Figure (1): Comparative study between groups regarding expression of vitamin D level.

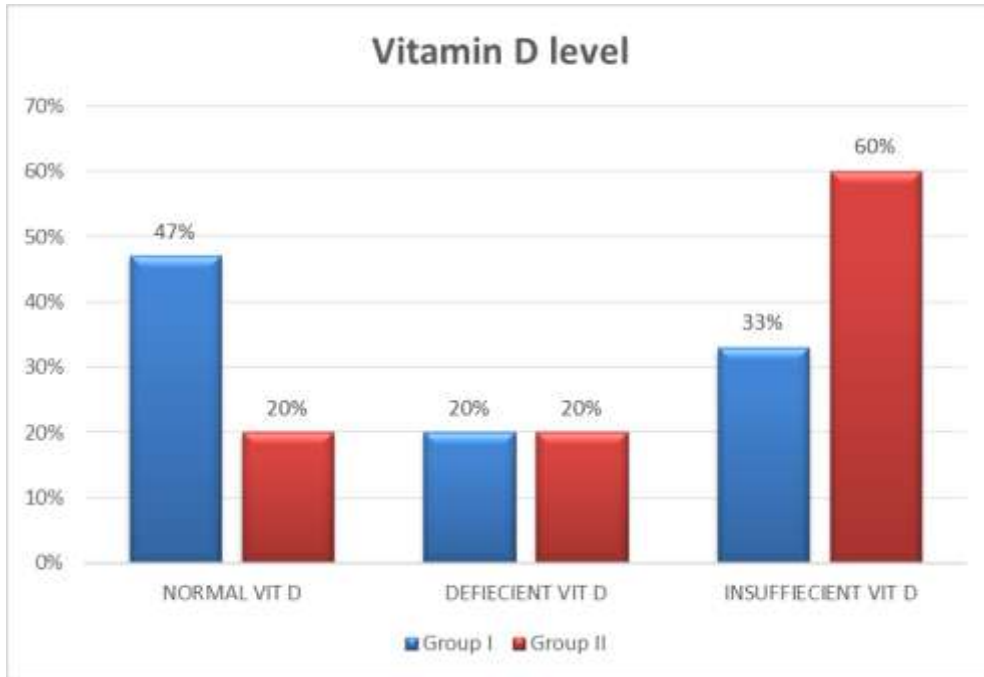


Table (3) and figure (1): show no statistically significant difference in vitamin D expression between patients with non-recurrence group and recurrence group.

Table (4): Comparative study between groups regarding the expression of Calcium.

Ca Level	Nonrecurrence Group I		Recurrence Group II		P-value
	%	Count	%	Count	
Normal Total Ca	100%	15	100%	15	1
Law Total Ca	0%	0	0%	0	> 0.05

P-value > 0.05 (Non-significant)

Table (4): show no significant difference between groups regarding the expression of Calcium.

Table (5): Comparative study between groups regarding the expression of Ionized Calcium.

Ca Level	Nonrecurrence Group I		Recurrence Group II		P-value
	%	Count	%	Count	
Normal Ionized Ca	93%	14	87%	13	1
Low Normal Ionized Ca	7%	1	13%	2	> 0.05

P-value > 0.05 (Non-significant)

Table (5): show no significant difference between groups regarding the expression of Ionized Calcium.

4. Discussion:

BPPV is a vestibular end-organ disorder, characterized by a transitory spinning sensation typically lasting less than a minute that is precipitated by positional changes of the head with respect to gravity. A wide spectrum of symptom severity exists, ranging from mild dizziness to vertiginous episodes, severe enough to cause nausea and vomiting, and significantly impair daily functioning. The disorder is prone to spontaneous remissions and recurrences, and it can affect one or more of the 3 semicircular canals simultaneously, both unilaterally or bilaterally [8]. The majority of cases arise from the posterior canal (80–90%), with horizontal canal cases accounting for 10–20%, and superior canal cases being more rare at 3% [9].

The present study was conducted on 30 patients, selected from the Audiology unit,

Faculty of medicine, Bani-Suef University hospital, who diagnosed as BPPV based on

brief episodes of positional vertigo, and characteristic paroxysmal positional nystagmus with exclusion of patients who refuse to continue testing. Serum levels of 25 hydroxyvitamin D3 (25-OH D3) and serum calcium, total & ionized was assessed and compared in two patients' groups: Nonrecurrence group (Group I) and Recurrence Group (Group II). No relationship was established between these values and the disease recurrence rate. Demographic features of studied group showed that the age of patients ranged from 30 to 68 years with mean age of 47.97 years and standard deviation of 10.34. Regarding sex, almost third (30%) were males and two thirds (70%) were females. In

our study we found that type of BPPV did not affect the recurrence rate. Posterior canal BPPV for non-recurrence group was (67 %) and (92 %) for recurrence group, (27 %) and (20 %) respectively for lateral canal BPPV, (7 %) and (13 %) respectively for Multi canal BPPV, with non-significant difference (p value > 0.05). Comparison between both groups regarding unilateral or bilateral BPPV, unilateral BPPV was found in (93 %) of non-recurrence group (group I) and in (87 %) of recurrence group (group II), (7 %) and (13 %) respectively for Bilateral BPPV, with non-significant difference (p value > 0.05) Consistent with our study, Rhim in 2019 stated that locations and types of semicircular canals did not affect the recurrence rate of BPPV [10]. Soto-Varela and his colleagues reported same results [11].

While Talaat and his coworkers reported that the prevalence of horizontal canal BPPV (HC-BPPV) during the relapses was 30%, which was higher than previously reported in the literature [12] There was no statistically significant difference ($p = 1$) in gender between patients with non-recurrence (group I) and recurrence (group II). Where male percentage is (40%, 20% respectively), female percentage is (60%, 80% respectively). Rhim, found that the number of women was higher in the recurrence group ($P=0.051$), but the difference was not statistically significant [10] The levels of vitamin D in non-recurrence

(group I) ranged from 10.5 to 33.5, with mean value of (24.93 ± 6.89). While in recurrence (group II), it ranged from 5.5 to 32.1, with mean value of (21.34 ± 7.82). In our study we did not find relation between serum vitamin D level and recurrence of BPPV. There was no statistically significant difference ($p = 0.89$) in vitamin D levels between patients with non-recurrence group and recurrence group. Where Normal Vitamin D percentage is (47%, 20% respectively), Deficient Vitamin D percentage is (20%, 27% respectively), and Insufficient Vitamin D percentage is (33%, 60% respectively). Unlike our results, Ding and his colleagues in their study that was conducted on 174 patients with BPPV and 348 controls, found that serum levels of vitamin D were lower in the recurrence of BPPV than in the de novo BPPV and suggested that low vitamin D may be a risk factor for BPPV and recurrent BPPV. This correlation between vitamin D deficiency and BPPV was stronger in women than in men [13].

In a meta-analysis reviewing 7 published articles that investigated the difference between the recurrence and non-recurrence of BPPV, there was a significant difference in the vitamin D levels between the two groups which indicated that vitamin D plays a role in the recurrent nature of BPPV. Several studies implemented vitamin D supplementation therapy in an effort to reduce the recurrence rates of BPPV patients with vitamin D

deficiency [14]. Rhim in his retrospective study on 332 patients, 279 non recurrent and 53 patients with recurrent BPPV, divided them into groups with different vitamin D serum concentrations and the recurrence rates of the groups were compared. when the patients were divided into a group with vitamin D concentrations lower than 10 ng/mL and a group with none lower than 10 ng/mL then the recurrence rates were compared, the recurrence rate of the group with vitamin D concentrations lower than 10 ng/mL was statistically significantly higher ($P=0.040$). In addition, when the patients were divided into a group with vitamin D concentrations lower than 15 ng/mL and a group with none lower than 15 ng/mL and the recurrence rates were compared, the recurrence rate of the group with vitamin D concentrations lower than 15 ng/mL was statistically significantly higher ($P=0.017$) [14].

Furthermore, Buki et al. in 2013 reported that when vitamin D supplementation therapy was implemented on four vitamin D deficiency patients with histories of chronically recurrent severe vertigo, the recurrence decreased. Talaat et al., reported that after vitamin D supplementation therapy was implemented on 28 posterior semicircular canal BPPV patients with vitamin D deficiency for three months, its recurrence significantly decreased compared to the control group for the follow-up period of 18 months [12]. In consistent with our results

Isik and his coworkers found a lower mean vitamin D level in the patient group compared to the control group; however, such a difference was not statistically significant, unlike the literature ($p=0.992$). In total, 64 patients diagnosed with BPPV were included in the study; 41 of them (64.1%) had not experienced similar symptoms before, 16 of them (25%) had an attack previously but did not have the diagnosis, and seven of them (10.9%) were diagnosed with BPPV previously. To determine the effect of vitamin D levels on recurrence, the patient group was divided into two subgroups: those with the first vertigo attack and those with recurrent complaints; however, no significant difference was found in vitamin D levels between these subgroups ($p=0.345$) [15] Similarly, Jeong and his colleagues in their study on 100 patient reported that decreased vitamin D only showed a significant relationship with BPPV occurrence, but the vitamin D level did not differ between the de novo and recurrent groups [16]. Our results may have resulted from the fact that vitamin D deficiency is increasing among the Egyptian population although Egypt is sunny country this may be due to many factors, uses of topical sunscreen, most women prefer to wear scarf and another cover the face, atmospheric pollution, and increased skin pigmentation in some peoples, insufficient intake of food containing vitamin D, and there is no fortification of food by vitamin D. Besides age, seasonal factors,

gender, skin color, dressing habits, food habits, using supplements, hormonal factors,

Due to the effects of vitamin D on the Ca metabolism, we examined the relationship between the recurrence of BPPV and serum ionized Ca, but could not establish any link. The levels of ionized Calcium was non-significant between the two groups, with p value (< 0.051) there was no statistically significant difference ($p = 1$) in Ionized Calcium levels between patients with non-recurrence group and recurrence group. Where Normal Ionized Calcium percentage is (93%, 7% respectively), Low normal ionized Calcium is (87%, 13% respectively) while the total Calcium level among the two groups was in the normal level. The levels of Ionized Calcium in non-recurrence group ranged from 8.5 to 10.2, with mean value of (9.46 ± 0.55) . While in recurrence group, it ranged from 8.4 to 10.2, with mean value of (9.33 ± 0.52) . Parham and his coworkers in their pilot study on 29 subjects evaluated this relationship and could not find any significant relation between Ca levels and recurrent BPPV [18]. Additionally, Isik and his colleagues could not establish any significant relationship Ca levels and recurrence of BPPV, possibly because the total Ca levels are affected by several factors other than vitamin D [15].

5. Conclusion and Recommendations:

preexisting metabolic disorders and body mass index, influence vitamin D levels [17].

A statistically significant difference was not found in vitamin D, ionized or total Ca levels between the patients diagnosed with first time BPPV and the recurrence group, this may be because the vitamin D deficiency is very common even in healthy individuals in the Egyptian population. We suggest further statistical investigations to determine average serum levels of vitamin D in patients with BPPV and its effect on the recurrence rate among Egyptian population.

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