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Original article

Evaluation of Parathyroid Hormone and Vitamin D Levels among Surgery Outpatient Clinic Attendants in Shifa Medical Complex: A Cross-sectional Study

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Abstract

Background: Vitamin D and parathyroid hormone (PTH) play crucial roles in calcium homeostasis and bone metabolism. Understanding their levels and associations in the general population is essential for preventive and therapeutic interventions. ***Methods:*** A cross-sectional study was conducted to evaluate PTH and vitamin D levels among the general population. Data were collected over one year. A convenience sampling method was employed, and demographic information and laboratory results were obtained through standardized questionnaires and blood samples. Descriptive and inferential statistics were used for data analysis. ***Results:*** A total of 390 participants were included, with a predominance of females (65.9%). The mean age was 50.12 years, ranging from 8 to 89 years. Analysis of PTH levels revealed that 68.5% of participants had elevated levels (>65 pg/mL), while 26.4% had normal levels (15-65 pg/mL), and 5.1% had deficient levels (<15 pg/mL). Vitamin D deficiency was prevalent, with 17.2% severely deficient (<10 ng/mL) and 28.5% moderately deficient (10-15 ng/mL). A significant negative correlation was observed between vitamin D and PTH levels ($p < 0.05$), indicating higher PTH levels in individuals with severe vitamin D deficiency. Age was significantly associated with PTH levels ($p < 0.05$), with older individuals (>60 years) exhibiting higher mean PTH levels compared to younger age groups. ***Conclusion:*** This study highlights the high prevalence of vitamin D deficiency and its association with elevated PTH levels in the general population. The findings underscore the importance of monitoring and addressing vitamin D status, particularly in older individuals, to mitigate the risk of secondary hyperparathyroidism and related complications. Further research is needed to explore the underlying mechanisms and inform targeted interventions for optimizing vitamin D and PTH levels in diverse populations.

Keywords: ***Vitamin D, Parathyroid Hormone, Calcium Homeostasis, Cross-sectional, Bone Metabolism***

Introduction

Vitamin D's hormone-like effects, both autocrine and paracrine, are crucial to maintaining a steady blood calcium level [1]. The active form of vitamin D, 1,25(OH)2D3, primarily interacts with the vitamin D receptor (VDR), which is expressed in both the distal and proximal intestines, to enhance calcium absorption from the intestines [2].

More than 90% of the vitamin D content in the blood comes from the skin's own production [1]. Provitamin D3, or 7-dehydrocholesterol, changes into cholecalciferol, the active form of vitamin D3, when exposed to ultraviolet B radiation from the sun. Vitamin D may also be obtained from food sources, such as fish oils and fortified dairy products [3,4]. Despite its perceived lack of biological activity, 25-hydroxyvitamin D (25(OH)D) is generally considered the gold standard for gauging vitamin D status; it is produced when vitamin D3 enters the bloodstream and is then delivered to the liver for conversion. The physiologically active form of vitamin D, known as calcitriol, is produced when the kidneys metabolize 25(OH)D [5].

Recent research has shown that vitamin D's benefits extend beyond only regulating calcium levels in the body. 1,25[OH]2D controls a wide variety of cellular activities, including those of the immune system, the heart, and the interaction between several hormones [4].

Vitamin D insufficiency may be caused by a number of things, including poor diet, lack of sun exposure, malabsorption due to inflammation in the intestines, celiac disease, gastric bypass surgery, and long-term use of corticoids and anticonvulsants [6]. Intestinal calcium absorption is impaired in those with low 25(OH)D status, which causes an increase in parathyroid hormone (PTH) output [7]. Increased blood parathyroid hormone (PTH) concentrations are associated with an increased risk of fractures, abnormalities in mineralization, bone turnover, and loss, particularly in the elderly [8]. Supplementing with calcidiol-containing vitamin D not only improves blood 25OHD, but it also considerably decreases PTH levels, which in turn reduces secondary hyperparathyroidism [9]. The current research suggests a link between vitamin D insufficiency and autoimmune illnesses, neurological disorders, cancer, and poor bone metabolism and quality [10]. Research on various populations has shown that vitamin D insufficiency is likely prevalent in subtropical regions as well as the northern hemisphere, where sunshine exposure is limited [11].

Different labs employ different approaches to test circulation vitamin D levels, and there is currently no consensus on what amounts constitute normal or unhealthy. On the other hand, everyone agrees that 25(OHO)D plasma levels are the gold standard for vitamin D assessment [12]. Levels of 25(OH)D below 20 ng/mL are considered inadequate, levels between 20 and 29 ng/mL are insufficiency, and levels between 30 and 100 ng/mL are sufficiency, but there is some disagreement between experts on the exact numbers that should be used to determine appropriate vitamin D levels [13,14]. The target for high-risk people should be to achieve levels of 25(OH)D over 30 ng/mL, according to the Brazilian Society of Endocrinology and Metabolism (SBEM) [13]. Serum 25(OH)D levels that are low are thought to be linked to elevated parathyroid hormone (PTH) levels and an increased risk of death [15].

Methods

Study Design

This study employed a cross-sectional design to evaluate the levels of parathyroid hormone (PTH) and vitamin D among the general population.

Study Setting

The study was conducted in among people attending a single consultation outpatient surgical clinic at Shifa Medical Complex, Gaza. This study took place during the period from June 2020 to July 2021.

Population

The target population for this study comprised individuals from the general population attending a single consultation outpatient surgical clinic at Shifa Medical Complex, Gaza participants with known hepatic or renal diseases, type 1 diabetes, malignancy and pregnant ladies were not eligible for this study.

Sample and Sampling

A convenience sampling method was utilized to recruit participants for this study. Individuals from all ages were eligible to participate. The sample size was determined based on total number of populations. Participants were recruited through non-probability convenient sampling technique.

Data Collection

Data collection was conducted through face to face interviews and laboratory reports. Participants provided informed consent prior to data collection. Information regarding demographic characteristics and medical laboratory results was obtained through standardized questionnaires. Blood samples were collected from participants for the assessment of PTH and vitamin D levels.

Instruments

The instruments used for data collection included two sections; demographic characteristics and laboratory test results.

Statistical Analysis

Descriptive statistics, such as mean, standard deviation were used to summarize continuous variables, including PTH and vitamin D levels. Categorical variables were summarized using frequencies and percentages. Inferential statistics, such as t-tests, chi-square tests, or correlation analysis, were employed to examine associations between variables of interest. Statistical significance was set at a p-value of <0.05.

Ethical Consideration

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the department of human resources at ministry of health, Gaza. Informed consent was obtained from all participants prior to their inclusion in the study. Participant confidentiality and privacy were maintained throughout the study duration. Data were anonymized and stored securely to protect participant confidentiality.

Results

A total of 390 subjects were included in this study. Of these, 133 (34.1%) were of male and 257 (65.9%) were of female. The mean age was 50.12 (±16.56) range from 8-89 years. Majority (65.9%) of patients were female with female to male ratio of 1.93:1. The results from the analysis of all parathyroid hormone (PTH) test results showed a mean value of 194.58 (±221.15) pg/mL. Most of our subjects 267 (68.5%) had an increased (>65 pg/mL) PTH level followed by 103 (26.4%) who had normal (15-65 pg/mL) levels and 20 (5.1%) who had deficient (<15 pg/mL). Levels of 25OHD were also found to be severe deficiency (<10ng/mL) in 17.2% of sample, followed by 28.5% who had moderate deficiency (10-15ng/mL), 19.5% who had mild deficiency (16-20ng/mL), 22.3% who had insufficient (21-30ng/mL), and 12.3% who had normal (31-100ng/mL) as shown in Table 1.

Table 1: Demographic and clinical characteristics of study subjects

	N	%	Mean±SD
Age (year)			50.12±16.56
0-20	37	9.5	
21-40	38	9.7	
41-60	196	50.3	
>60	119	30.5	
Gender			
Male	133	34.1	
Female	257	65.9	
PTH (pg/ml)			194.58±221.15
Deficient (<15)	20	5.1	
Normal (15-65)	103	26.4	
Increased (>65)	267	68.5	
25OHD (ng/ml)			18.70±11.84
Severe deficiency (<10)	67	17.2	
Moderate deficiency (10-15)	111	28.5	
Mild deficiency (16-20)	76	19.5	
Insufficient (21-30)	87	22.3	
Normal (31-100)	48	12.3	
Increased (>100)	1	0.3	
SD: Standard deviation; PTH: Parathyroid hormone; 25OHD 25-hydroxyvitamin D;			

Table 2: Parathyroid hormone concentration according to vitamin D rang. Values of PTH are presented as mean ± standard deviation.

VItaminD (ng/ml)		PTH (pg/mL) *
Severe deficiency (<10)		308.15±308.82
Moderate deficiency (10-15)		164.26±178.68
Mild deficiency (16-20)		176.19±190.07
Insufficient (21-30)		175.49±198.59
Normal (31-100)		166.22±207.51
*significant correlation (P<0.05)		

From the total 25OHD test results obtained we could find a significant and negative correlation between level of 25OHD and PTH ($p<0.05$). these data suggest that individuals with severe vitamin D deficient show high PTH (308.15pg/mL) while those with normal vitamin D level show lower level of PTH (166.22pg/mL) as shown in table 2. No significant difference were observe between gender of individuals and vitamin D level.

Table 3: Mean and SD of Vitamin D and PTH according to Age group (classification).

Age group	Vitamin D (ng/ml)	PTH (pg/mL)*
1-20	16.25±9.42	140.62±137.17
21-40	21.69±11.31	161.06±152.06
41-60	18.66±11.10	180.17±197.01
>60	17.72±9.91	244.19±282,96
*significant correlation (P<0.05)		

Table 3 summarized the results of comparison of the mean values of Vitamin D and PTH in different age groups, which suggest that individuals >60 years have high mean PTH (244.19±282,96pg/mL) levels. In contrast, those with age group < 20 years have lower mean of PTH (140.62±137.17pg/mL) levels. This relation was statistically significant P<0.05. There is no statistically significant between mean values of Vitamin D in different age groups.

Discussion

Our study, conducted according to the criteria set by the Institute of Medicine (IOM) and the Endocrine Society (ES), revealed a significant prevalence of low levels of vitamin D in different age groups, as compared to other countries. This remained accurate even when compared to different populations. The PTH levels we saw align with the insufficient category, as reported by ES.

Currently, the Endocrine Society considers 25(OH)D levels beyond 30 ng/mL to be appropriate, as long as this quantity ensures enough effectiveness without any danger of toxicity, given that laboratory procedures have varying threshold values [16-17]. In 2011, ES classified readings below 20 ng/mL as insufficient [18] and those between 20 and 30 ng/mL as insufficiency. In their research of population requirements, the IOM established that Vitamin D deficiency is characterized by values below 20 ng/mL [19,20]. They assert that diverse groups should establish their own criteria for determining the appropriateness of using 25(OH)D supplementation. Manson *et al.* [6] suggested a threshold of fewer than 12.5 ng/mL based on their analysis of the data [6]. If Manson's concept were implemented, the prevalence of vitamin D hypovitaminosis in our population would be much lower compared to other equatorial zone countries [2,8]. This discovery implies that latitude and mean insolation, which are two demographic characteristics, have a substantial influence in influencing blood 25(OH)D levels.

There is a scarcity of demographic studies that address this specific problem. In 2007, Unger performed a cross-sectional study in São Paulo, analyzing 603 people aged 18 to 90 years. The author found that 19.3% of the participants had a shortage of 25(OH)D, while 77.4% had insufficient levels of vitamin D. A study done by Scalco *et al.* including 102 non-institutionalized seniors found that a high percentage (87.5%) of them had vitamin D hypovitaminosis [22]. Furthermore, Linhares *et al.* performed a study in Recife, Brazil with 226 children, and no cases of vitamin D inadequacy were detected [23]. The study's standard criteria were derived from those established by the Endocrine Society. The higher occurrence of hypovitaminosis D in the first two studies might be attributed to the comparatively lower average exposure to sunlight in the South-Southeast region of Brazil (22°-33° S), where the studies were carried out [23].

Furthermore, we observed that males exhibited higher levels of 25(OH)D. The body region that exhibits greater efficiency in absorbing 25(OH)D, so more exposure to sunlight in that location may be the underlying cause. Our findings corroborate the correctness of the conclusions made by Al-Ghamdi [24] and Kiani *et al.* [25]. A study conducted in Saudi Arabia examined a sample of 150 individuals and discovered that ladies had lower levels of vitamin D compared to men. This difference may be attributed to the clothing choices of females. Due to the scorching heat, men in the Amazon often choose for shorts and a t-shirt, which exposes a larger portion of their chests. Testosterone levels may serve as an additional potential explanation for the observed impact. There is a suggested link between testosterone and higher levels of 25(OH)D, as proposed by studies [26-29]. Araujo *et al.* discovered a correlation between gender and vitamin D levels, with males exhibiting higher levels compared to women. This finding supports the notion that hormones have an influence on vitamin D levels [30]. Insufficient empirical data exists on a possible mechanism that might explain this correlation.

Additionally, another research revealed that there is a drop in blood 25(OH)D concentrations when body mass index (BMI) increases. This suggests that there is a correlation between low vitamin D levels and obesity [31]. Some of the proposed mechanisms that might explain this phenomenon include reduced exposure to sunlight, changes in the activation of vitamin D, and an increase in the storage of vitamin D in adipose tissue [18,32,33]. Obese individuals have lower levels of cutaneous synthesis of vitamin D3 from 7-dehydrocholesterol due to reduced exposure to solar UV radiation [33]. Due to the absence of frequent sunbathing among the obese participants in the study, the researchers discovered a higher likelihood of hypovitaminosis among them. They previously wore clothing that covered a large portion of their bodies, which has led to speculation that their insufficient levels of vitamin D may be due to inadequate exposure to sunlight [33].

In research conducted in São Paulo, Eloi *et al.* [34] used the same evidence-based methodology to investigate patients throughout a wide age range, from 2 to 95 years. The study revealed that 33.9% of the patients had vitamin D concentrations < 20 ng/mL, with higher levels seen during the summer (38.4% vs. 23.3%). The study found that those living in rural areas had higher levels of vitamin D. This corroborates the findings of a recent meta-analysis carried out in African countries [2]. However, the topic still generates significant controversy. A research done in China by Fang *et al.* [35] with a sample size of 1814 participants revealed that those living in urban areas had somewhat higher levels of vitamin D compared to those residing in rural areas. Nevertheless, the researchers observed that these results are in conflict with other similar studies done in Asia [36-39]. Similarly, rural individuals in an Indian research study had lower levels of 25(OH)D, although obtaining enough sun exposure [40]. According to KimLi *et al.* [41], skin exposure was shown to be the primary factor in explaining the difference in 25(OH)D levels. Nevertheless, it is imperative that we examine this issue with more scrutiny.

The covariates included in the regression model from [31] had little predictive power, as they were only able to account for 5.4% of the variance in 25(OH)D levels. Exploring the impact of genetic variations on the functioning of the vitamin D receptor (VDR) is an important hypothesis that might provide insights into these findings. Based on specific references [42-45], the diversity in 25(OH)D levels is likely to be significantly impacted by genetic variation across people. Nissen [46] found that changes in blood vitamin D levels are associated with polymorphisms in the GC and CYP2R1 genes. Nissen analyzed a total of twenty-five different genetic variants in seven genes. In a similar vein, Husain *et al.* [47] discovered that African-Americans had lower levels of 25(OH)D relative to European-Americans, even when considering individuals with similar lifestyles and demographic backgrounds. Both study findings indicate that genetic and ethnic variables might influence vitamin D levels. Ethnic analysis in Brazil is complex due to the country's significant intermixing of different racial and ethnic groups. This might explain the difference between the worldwide occurrence of hypovitaminosis D and the findings of our investigation.

In this study, the researchers analyzed the ROC curve to identify the appropriate cut-off value of 26 ng/mL for the PTH response to vitamin D insufficiency. This value is associated with an increased risk of bone loss. It suggests that those with vitamin D levels below 26 ng/mL may get more advantages from taking supplements, since many people in this group do not exhibit any symptoms. This statistic provides more proof that this demographic requires further attention in clinical treatment, since it falls below the threshold specified by ES guidelines. There is a need to improve the approach used to measure Vitamin D. Liquid chromatography-mass spectrometry is the most dependable technique for measuring 25(OH)D. Despite its difficulty, expense, and limited availability, this test has the advantages of sample adaptability and high specificity [48]. The automated immunoassay has gained widespread use in clinical practice and is considered the benchmark due to its simplicity, speed, and cost-effectiveness [48,49]. The use of the automated immunoassay played a pivotal role in our research, aiming to generate outcomes that might have therapeutic implications.

Vitamin D insufficiency is widespread in certain places worldwide. In a study conducted by Filgueiras *et al.* [50], it was shown that 91.3% of the 378 youngsters had inadequate vitamin D intake. Peters *et al.* [51] performed tests on 136 teens and Cembranel *et al.* [52] conducted investigations on 1051 patients aged 22 to 63 years. The studies found that 85.1% and 100% of the participants, respectively, did not meet the recommended daily intake of vitamin D. Despite the continued presence of deficiency, a 2013 National Dietary Survey conducted with elderly individuals in Brazil revealed that our region had greater levels of vitamin D intake compared to other areas in the country [53]. This may result in a lower occurrence of vitamin D deficiency.

Skin pigmentation may also affect vitamin D levels. Libon *et al.* [54] found that fair-skinned people had higher levels of vitamin D compared to black-skinned individuals following a single full-body exposure to UVB. The research included individuals with Fitzpatrick skin types II, III, and VI. According to Xiang *et al.* [55], individuals with pigmented skin have a lower rate of vitamin D production. The proportion of Black Brazilians in Brazil's northern area is barely 6.5% [56-57]. This might have influenced our results as well.

Conclusion

In this cross-sectional study assessing parathyroid hormone (PTH) and vitamin D levels among participants, we found significant trends in their distribution and correlation with demographic factors. A majority of the participants were female, with a notable female-to-male ratio. Analysis of PTH levels revealed a substantial proportion of individuals with elevated levels, while a significant portion exhibited vitamin D deficiency. We observed a significant negative correlation between vitamin D and PTH levels, with severe vitamin D deficiency associated with higher PTH levels. Additionally, there was a statistically significant association between age and PTH levels, with older individuals showing higher mean PTH levels compared to younger age groups. These findings emphasize the importance of monitoring PTH and vitamin D levels, particularly in older populations, and highlight the potential impact of vitamin D deficiency on PTH regulation. Further research is needed to better understand these relationships and their implications for clinical practice and public health.

This study has several limitations. The cross-sectional design precludes establishing causality between vitamin D and PTH levels. Conducted at a single outpatient surgical clinic, the findings may not be generalizable to the broader population of Gaza or other regions. The use of convenience sampling introduces selection bias, as participants who attend the clinic might differ systematically from those who do not. Excluding individuals with known hepatic or renal diseases, type 1 diabetes, malignancy, and pregnant women further limits the generalizability. Additionally, the reliance on self-reported data and face-to-face interviews may result in response bias. Lastly, the study did not control for potential confounding factors such as dietary intake, sun exposure, and physical activity, which could influence vitamin D and PTH levels.

Further Studies

For future studies, it is recommended to employ a longitudinal design to better assess causality between vitamin D and PTH levels. Expanding the study to include multiple healthcare settings across different regions would enhance the generalizability of the findings. Using random sampling methods and including a more diverse population, including those with hepatic or renal diseases, type 1 diabetes, malignancy, and pregnant women, would provide a more comprehensive understanding. Additionally, controlling for confounding factors such as dietary intake, sun exposure, and physical activity is crucial. Incorporating objective measures, such as wearable devices for monitoring sun exposure, and conducting follow-up assessments over time could yield more robust and reliable data.

List of Abbreviations

PTH: Parathyroid Hormone
VDR: Vitamin D Receptor
SBEM: Brazilian Society of Endocrinology and Metabolism
SD: Standard Deviation
IOM: Institute of Medicine (IOM)
ES: Endocrine Society
BMI: Body Mass Index
ROC: Receiving Operator Curve

Declaration

Ethical Approval and Consent to Participate

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the department of human resources at ministry of health, Gaza. Informed consent was obtained from all participants prior to their inclusion in the study. Participant confidentiality and privacy were maintained throughout the study duration. Data were anonymized and stored securely to protect participant confidentiality.

Consent for Publication

Author has consented for publication

Availability of Data

Data and other supporting documents are available upon reasonable request.

Competing Interest

Author has no competing interest.

Funding

None

Author's Contribution

Study conceptualization, data collection, data analysis, manuscript writing were all done by KA.

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