The Study of the Association of Serum Parathyroid Hormone Level with Obesity in Patients Admitted to a Tertiary Care Center in Basrah

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Keywords
Obesity · Parathyroid hormone · Vitamin D deficiency

Abstract

\textbf{Background:} Parathyroid hormone (PTH) has been reported to have a positive correlation with insulin resistance and the development of the metabolic syndrome. This study aims to evaluate if there is an association between obesity and serum PTH levels.

\textbf{Methods:} This case-control study was conducted at the Faiha Specialized Diabetes Endocrine and Metabolism Center in Basrah (Southern Iraq) from September 2018 to July 2019. A total of 230 patients were recruited for this study (103 male and 127 female), divided into 2 groups according to the BMI: <30 kg/m\textsuperscript{2} were considered as the control group (83 persons) and ≥30 kg/m\textsuperscript{2} were considered as obese persons (147 persons). The study groups were also subdivided into 3 groups according to the serum level of PTH: <40 pg/mL, 40–65 pg/mL, and >65 pg/mL.

\textbf{Results:} The mean age of the obese and control groups was 44.39 ± 10.64 and 30.12 ± 8.95 years, respectively. About 46.25% of obese were men and 53.75% were women, while 42% of the control group were men and 58% were women. Serum PTH level was significantly higher (p < 0.001) among obese persons with a mean level of 53.21 ± 19.58 pg/mL for obese and 37.63 ± 21.8 pg/mL for control. Vitamin D deficiency was seen in 84.4% of the obese group while in 71.1% of the control group (p value 0.04). Females turned to have higher PTH levels than males in both the obese and the control group (p value <0.001). However, age and the presence of diabetes mellitus were not associated with higher PTH levels (p value 0.155 and 0.6, respectively). \textbf{Conclusion:} Obesity was associated with a higher serum PTH level related to the severity of vitamin D deficiency.

Introduction

Several medical organizations and societies were conflicted about the definition of obesity as a disease or not because the evidence was weak; however, the concept was raised recently to recognize obesity as a chronic disease of public health burden [1]. Overweight and obesity are considered major risk factors for a number of chronic diseases, such as diabetes mellitus, cardiovascular diseases, and cancer [2]. Obesity is one of the leading preventable causes of death worldwide. In the USA, obesity is estimated to be responsible for 111,909–365,000 deaths per year, while 1 million (7.7%) of the deaths in Europe are...
attributed to excess weight. Obesity decreases life expectancy by approximately 6–7 years [3]. A BMI of 30–35 kg/m² decreases life expectancy by 2–4 years; however, obesity of BMI >40 kg/m² decreases life expectancy by 10 years [2]. Overall, obesity is considered a major contributor to metabolic syndrome (MetS) and is linked with insulin resistance [4]. Different types of obesity have been introduced, including metabolically healthy obesity and metabolically obese. Metabolically healthy obesity is defined as obese individuals who lack any metabolic abnormalities or MetS despite the fact of having obesity based on BMI, while metabolically obese is defined by metabolic abnormality or MetS with obesity based on BMI [5].

The link between both vitamin D and parathyroid hormone with MetS has been well established [6] in cross-sectional studies. The relationship between serum 25-hydroxyvitamin D (25-OHD) concentrations and MetS was inversely related as it has been observed in several cohorts [7–9]. The parathyroid hormone which is considered the main regulator of calcium homeostasis along with vitamin D was also noted to have a positive relation with insulin resistance and the development of MetS [9, 10]. If a section D was also noted to have a positive relation with in 

Materials and Methods

The sample size was calculated by the Steven K. Thompson equation:

\[
N = \frac{Nx p(1-p)}{\left( (N-1) \left( d^2 - z^2 \right) \right) + p(1-p)} = 385,
\]

where \( n \) = sample size (?), \( N \) = population size, \( z \) = confidence level at 95% = 1.96, \( d \) = error proportion (0.05), and \( p \) = probability (50%).

Study Design, Place, and Time

The current case-control study was conducted at the Faiha Specialized Diabetes Endocrine and Metabolism Center (FDEMC) in Basrah, Southern Iraq, during the period between September 2018 and July 2019.

Participants

A total of 230 subjects were recruited for this study (103 male and 127 female), divided into 2 groups according to the BMI: <30 kg/m² was considered as the control group (83 persons) and ≥30 kg/m² was considered as the obese group (147 persons). The obese group was further subdivided into 3 classes (class 1: BMI 30–35 kg/m², class 2: BMI 35–40 kg/m², and class 3: BMI >40 kg/m²). A preformed questionnaire was used to collect the data, and a thorough anthropometric examination with the required investigation was performed for all.

Inclusion Criteria

Inclusion criteria included age between 18 and 60 years.

Exclusion Criteria

Exclusion criteria included chronic kidney disease, age below 18 years or above 60 years, weight loss intervention, all endocrine diseases apart from diabetes, use of drugs (oral contraceptive pills, hormone replacement therapy, vitamin D supplementation, and glucocorticoids), other chronic illnesses apart from diabetes and hypertension, recent surgery, and pregnancy or breastfeeding. Hypertension was defined as BP ≥140/90 on 2 occasions using the standardized method to measure blood pressure [19] or the patient was using antihypertension therapy. Patients who have been previously diagnosed with diabetes or on antihyperglycemic therapy were considered in the diabetes group.

Biochemical Analysis

All subjects were instructed to fast overnight, and a peripheral venous blood sample was collected at 9:00 a.m. Then, all samples were analyzed for fasting plasma glucose, renal function test, and serum calcium using COBAS INTEGRA® 400 plus. 25-OHD level and parathyroid hormone level were measured using Cobas e 411 analyzers.

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Reference Ranges
Serum calcium normal reference range was 8.4–10.4 mg/dL. Serum PTH was 15–65 pg/mL. Serum 25-OHD levels were subdivided into 3 categories as follows: vitamin D sufficiency when serum vitamin D ≥30 ng/mL, vitamin D insufficiency with serum vitamin D 20–30 ng/mL, and vitamin D deficiency with serum vitamin D <20 ng/mL [20].

Statistical Analysis
All data were tabulated using statistical package for the social sciences (version 25). Quantitative data were represented as mean and standard deviation, and the qualitative data were represented as numbers and percentages. Independent Student’s t test was used to compare quantitative data, whereas the χ² test and Fisher’s exact test were used to compare categorical data. A p value of <0.05 was considered to be significant.

Results
The main characteristics of the study population are shown in Table 1. Men among the obese group were 68/147 (46.25%), and women among the obese group were 79/147 (53.75%), while men and women among the control group were 35/83 (42%) and 48/83 (58%), respectively, with no gender differences between both groups. PTH level was significantly higher (p < 0.001) among obese persons with a mean level of PTH of 53.21 ± 19.58 pg/mL for the obese and 37.63 ± 21.8 pg/mL for the control. There was no significant association in the serum calcium level between obese (9.23 ± 0.6 mg/dL) and control (9.20 ± 0.58 mg/dL) groups. The mean plasma glucose level for obese persons was 149.34 ± 79.28 mg/dL, while it was 95.5 ± 43.9 mg/dL for control persons. The p value was <0.001, that is, statistically significant.

The mean 25-OHD level was 13.39 ± 6.99 ng/mL in the obese group versus 15.49 ± 8.53 ng/mL in the control group, and the difference was statistically significant (p value = 0.04). Vitamin D deficiency was seen in 84.4% of the obese group while in 71.1% of the control group (p value 0.04).

Table 1. Study characteristics of 230 persons involved in the study

|                          | Obese   | Control | p values |
|--------------------------|---------|---------|----------|
| Gender, n (%)            |         |         |          |
| Men                      | 68 (46.25) | 35 (42) | 0.54     |
| Women                    | 79 (53.75) | 48 (58) |          |
| Age                      |         |         |          |
| Mean ± SD, years         | 44.39±10.64 | 30.12±8.9 |          |
| <40 years, n (%)         | 54 (36.7) | 70 (84.3) | <0.0001  |
| ≥40 years, n (%)         | 93 (63.3) | 13 (15.7) |          |
| Systolic blood pressure, mean ± SD, mm Hg | 137.59±17.25 | 118.98±11.08 | <0.0001  |
| Diastolic blood pressure, mean ± SD, mm Hg | 83.52±12.55 | 76.02±9.99 | <0.0001  |
| BMI, mean ± SD, kg/m²   | 35.99±5.35 | 24.46±3.11 | <0.0001  |
| Serum parathyroid hormone level |         |         |          |
| Mean ± SD, pg/mL         | 53.21±19.58 | 37.63±21.8 | <0.0001  |
| Normal PTH 15–65 pg/mL, n (%) | 40 (27.2) | 59 (71.1) |          |
| *Upper limit ≥40 pg/mL, n (%) | 73 (49.7) | 14 (16.9) | <0.0001  |
| **Hyperparathyroidism, n (%) | 34 (23.1) | 10 (12) |          |
| Serum calcium, mean ± SD | 9.23 ±0.64  | 9.20±0.58  | 0.73      |
| Fasting plasma glucose, mean ± SD, mg/dL | 149.34±79.28 | 95.51±43.98 | <0.0001  |
| Vitamin D level, mean ± SD, ng/mL | 13.39±6.99 | 15.49±8.53 | 0.04      |
| Vitamin D sufficiency, 25(OH)D ≥30 ng/mL, n (%) | 6 (4.1) | 4 (4.8) |          |
| Vitamin D insufficiency, 25(OH)D = 20–30 ng/mL, n (%) | 17 (11.6) | 20 (24.1) | 0.04      |
| Vitamin D deficiency, 25(OH)D <20 ng/mL, n (%) | 124 (84.4) | 55 (71.1) |          |

* Upper limit PTH level ≥40 pg/mL. ** Hyperparathyroidism = rise of the serum PTH level above the upper limit of normal (65 pg/mL).
Table 2. Variables affecting parathyroid hormone levels among obese and control

| Variables                        | Obese | p value | Control | p value |
|----------------------------------|-------|---------|---------|---------|
|                                 | <40   | 40–65   | >65     | <40   | 40–65   | >65     |
| Gender, n (%)                    |       |         |         |       |         |         |
| Males                            | 27 (40)| 31 (45) | 10 (15) | 0.0001| 28 (80) | 4 (11)  | 3 (9)   | 0.127  |
| Females                          | 13 (16)| 41 (52) | 25 (32) |         | 31 (65) | 10 (21) | 7 (14)  |         |
| Age, n (%)                        |       |         |         |       |         |         |         |         |
| <40 years                        | 16 (30)| 25 (46) | 13 (24) | 0.478 | 52 (74) | 11 (16) | 7 (10)  | 0.225  |
| ≥40 years                        | 24 (26)| 47 (50) | 22 (24) |         | 7 (54)  | 3 (23)  | 3 (23)  |         |
| Diabetes mellitus, n (%)         |       |         |         |       |         |         |         |         |
| Yes                              | 19 (31)| 33 (53) | 10 (16) | 0.162 | 4 (67)  | 2 (33)  | 0 (0)   | 0.541  |
| No                               | 21 (25)| 39 (46) | 25 (29) |         | 55 (71) | 12 (16) | 10 (13) |         |

Table 3. The effect of different age groups on PTH in the obese and control

| Age group | Obese |       |       |       | Control |       |       |       |
|-----------|-------|-------|-------|-------|---------|-------|-------|-------|
|           | <40, n (%) | 40–65, n (%) | >65, n (%) |       | <40, n (%) | 40–65, n (%) | >65, n (%) |       |
| <20 years | 0 (0) | 0 (0) | 2 (6) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |       |
| 21–30 years | 3 (7) | 9 (12.5) | 4 (11) | 3 (5) | 0 (0) | 1 (10) |       |
| 31–40 years | 13 (33) | 16 (22) | 7 (20) | 49 (83) | 11 (79) | 6 (60) |       |
| 41–50 years | 18 (45) | 38 (53) | 16 (46) | 1 (2) | 0 (0) | 3 (60) |       |
| 51–60 years | 6 (15) | 9 (12.5) | 6 (17) | 6 (10) | 3 (21) | 0 (0) |       |
| Subtotal | 40 (27) | 72 (49) | 35 (24) | 59 (71) | 14 (17) | 10 (12) |       |
| Total | 147 (64) |       |       | 83 (36) |       |       |       |
| p value | 0.419 |       |       | 0.469 |       |       |       |

Table 4. PTH levels according to the 25(OH)D status among obese and control

| Variable                        | PTH levels |       |       |       |       |       |       |
|---------------------------------|------------|-------|-------|-------|-------|-------|-------|
|                                 | mean ± SD pg/mL | <40 pg/mL, n (%) | 40–65 pg/mL, n (%) | >65 pg/mL, n (%) |       |       |       |
| Vitamin D sufficiency           |            |       |       |       |       |       |       |
| Obese                           | 34.0±5.1 | 3 (50) | 3 (50) | 0 |       |       |       |
| Control                         | 30.5±11.9| 3 (75) | 1 (25) | 0 |       |       |       |
| p value                         | 0.5 |       | 0.4 |       |       |       |       |
| Vitamin D insufficiency         |            |       |       |       |       |       |       |
| Obese                           | 47.8±17.5| 6 (35.3) | 8 (47.1) | 3 (17.6) |       |       |       |
| Control                         | 39.3±22.1| 14 (70) | 3 (15.0) | 3 (15.0) |       |       |       |
| p value                         | 0.2 |       | 0.07 |       |       |       |       |
| Vitamin D deficiency            |            |       |       |       |       |       |       |
| Obese                           | 54.8±19.7| 31 (25.0) | 62 (50.0) | 31 (25.0) |       |       |       |
| Control                         | 37.5±22.3| 42 (71.2) | 10 (16.9) | 7 (11.9) |       |       |       |
| p value                         | <0.0001 |       | <0.0001 |       |       |       |       |
Serum Parathyroid Hormone Level with Obesity

Table 3 and Figure 1 show that those with sufficient and insufficient 25-OHD have no significant differences in PTH level between obese people and controls, while in vitamin D deficiency patients, the PTH level was significantly higher in obese than the control group ($p$ value $<0.0001$). In the control group (nonobese) despite vitamin D deficiency, they had significantly lower serum PTH levels. Of the total number of patients, 145 (60.4) were obese, and of them 77.8% had their PTH in the high normal of overt increase PTH compared to 71.25% of the control group having their PTH below 40 pg/mL (Table 4).

**Discussion/Conclusion**

Obesity is a chronic complex and degenerative disease which will affect one out of 5 adults in 2025 [21]. The WHO (2016) stated that 13% of the population was suffering from obesity and 39% was overweight, and it is considered as a major reversible cause of morbidity worldwide, so identifying variables that can be associated with or causing it has a great impact on the global health. This study tries to assess the relationship between obesity and serum PTH levels.

Although the mean age in the obese group is higher than that of the control (44.39 ± 10.64 and 30.12 ± 8.9) and their mean serum PTH is higher than that of the control, the effect of age on serum level of PTH in both groups was nonsignificant ($<0.861$ and $<0.571$). Vishnu et al. [11] reported that serum PTH can be elevated in the elderly due to physical inactivity. This study also showed that gender is an important variable as it revealed that females were associated with a higher level of serum PTH compared to males which is possible due to hormonal influences.

Serum PTH level was positively associated with BMI, and this finding was stated in a study by Bolland et al. [17] comparing BMI to PTH in both obese and nonobese adults and concluded that fat mass significantly affects serum PTH independent of the relationship between vitamin D and parathyroid hormone. The number of patients with serum levels of PTH from 40 to 65 pg/mL increased from 16.9% in the control group to 49.7% in the obese. A similar finding was also documented by a previous study on 196 people which noted a higher serum PTH level in obese versus nonobese [22].

Serum PTH level has been well linked to obesity and deposition of fat through several mechanisms such as by a decrease in the activity of the enzyme lipoprotein in mature fat cells [23]. Another theory suggests the effect of adipokine on PTH [24] and the positive relation between leptin and PTH [25]. One study showed that hyperparathyroidism in morbid obesity is decreased with weight reduction [26].

This study shows that the mean level of PTH was 46.97 pg/mL among patients with BMI <35 kg/m$^2$, and the mean level of PTH was 60.28 pg/mL among obese with BMI >35 kg/m$^2$, which means that there is a positive correlation between serum PTH level and obesity level as it rises with the increase in the degree of obesity. This finding was consistent with findings of a previous study by Vishnu et al. [11] who stated that PTH levels increase with the increasing body weight depending on waist circumference and waist-hip ratio.

Regarding vitamin D level and its association with obesity and serum PTH level, it was shown that vitamin D deficiency was significant among obese compared to the control group. In addition to this finding, the current study showed that the relationship between obesity and hyper-PTH was significant among severely deficient vitamin D persons.

It is well known that hypovitaminosis D is associated with secondary hyperparathyroidism [27]. Many theories have explained the cause of hypovitaminosis D among obese patients to the sequestration of vitamin D by fat, rendering it less available [14, 18]. Another theory suggested the limited exposure to sunlight among obese people due to less outdoor physical activity and associated osteoarthritis [28].

It is worthy to mention that this study recognized that the majority (80% [183/230]) of the studied individuals
(cases and controls) were vitamin D deficient with no obvious cause for this finding. In addition, it was found that serum PTH level was significantly elevated among obese individuals with vitamin D deficiency compared to controls with vitamin D deficiency.

This finding explains that obesity has an indirect role in the elevation of PTH due to decrease in vitamin D, but in those patients with normal vitamin D, PTH hormone was elevated though statistically nonsignificant which may be explained by the small sample size. It has been shown that obesity is the main determinant for increase in serum PTH level in the absence of known causative factors (serum calcium and renal function).

**Conclusion**

Obesity was associated with a higher serum PTH level related to the severity of vitamin D deficiency. Further studies are needed to evaluate obesity as a cause of high PTH and vice versa.

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**References**

1. Kyle TK, Dhurandhar EJ, Allison DB. Regarding obesity as a disease: evolving policies and their implications. Endocrinol Metab Clin North Am. 2016;45(3):511.
2. Barnes LA, Opitz JM, Gilbert-Barness E. Obesity: genetic, molecular, and environmental aspects. Am J Med Genet A. 2007;143a(24):3016–34.
3. Haslam DW, James WPT. Obesity. Lancet. 2005;366(9492):1197–209.
4. Gallagher EJ, LeRoith D, Karnieli E. The metabolic syndrome: from insulin resistance to obesity and diabetes. Endocrinol Metab Clin. 2008;37(3):559–vii.
5. Geetha L, Deepa M, Anjana RM, Mohan V. Prevalence and clinical profile of metabolic obesity and phenotypic obesity in Asian Indians. J Diabetes Sci Technol. 2011;5(2):439–46.
6. Ford ES, Zhao G, Li C, Pearson WS. Serum concentrations of vitamin D and parathyroid hormone and prevalent metabolic syndrome among adults in the United States. J Diabetes. 2009;1(4):296–303.
7. Ford ES, Ajani UA, McGuire LC, Liu S. Concentrations of serum vitamin D and the metabolic syndrome among U.S. adults. Diabetes care. 2005;28(5):1228–30.
8. Kim J. Association between serum vitamin D, parathyroid hormone and metabolic syndrome in middle-aged and older Korean adults. Eur J Clin Nutr. 2015;69(4):425–30.
9. Reis JP, von Mühlen D, Miller ER 3rd. Relation of 25-hydroxyvitamin D and parathyroid hormone levels with metabolic syndrome among US adults. Eur J Endocrinol. 2008;159(1):41–8.
10. Reis JP, von Mühlen D, Kritz-Silverstein D, Wingard DL, Barrett-Connor E. Vitamin D, parathyroid hormone levels, and the prevalence of metabolic syndrome in community-dwelling older adults. Diabetes care. 2007;30(6):1549–55.
11. Vishnu KSI, Harishkiran NE. The study of association of serum parathyroid hormone level with obesity in subjects admitted to a tertiary care centre. Int J Biomed Res. 2018;9(1):40–4.
12. Holick MF. The vitamin D epidemic and its health consequences. J Nutr. 2005;135(11):2739s–48s.
13. Bilezikian JP, Marcus R, Levine MA, Marcocci C, Potts JT, Silverberg SJ. Preface to the third edition. 3rd ed. In: Bilezikian JP, editor. The parathyroids. San Diego: Academic Press; 2015. p. xix. Available from:
14. Wortsman J, Matsuoka LY, Chen TC, Lu Z, Holick MF. Decreased bioavailability of vitamin D in obesity. Am J Clin Nutr. 2000;72(3):690–3.
15. Snijder MB, van Dam RM, Visser M, Deeg DJ, Dekker JM, Bouter LM, et al. Adiposity in relation to vitamin D status and parathyroid hormone levels: a population-based study in older men and women. J Clin Endocrinol Metab. 2005;90(7):4119–23.
16. Shirazi L, Almquist M, Malm J, Wifålt E, Manjer J. Determinants of serum levels of vitamin D: a study of life-style, menopausal status, dietary intake, serum calcium, and PTH. BMC Womens Health. 2013;13:33.
17 Bolland MJ, Grey AB, Ames RW, Horne AM, Gamble GD, Reid IR. Fat mass is an important predictor of parathyroid hormone levels in postmenopausal women. Bone. 2006;38(3):317–21.

18 Blum M, Dolnikowski G, Seyoum E, Harris SS, Booth SL, Peterson J, et al. Vitamin D (3) in fat tissue. Endocrine. 2008;33(1):90–4.

19 Unger T, Borghi C, Charchar F, Khan NA, Poult ER, Prabhakaran D, et al. International society of hypertension global hypertension practice guidelines. Hypertension. 2020;75(6):1334–57.

20 Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2011;96(7):1911–30.

21 Mohammed MS, Sendra S, Lloret J, Bosch I. Systems and WBANs for controlling obesity. J Healthcare Eng. 2018;2018:1564748.

22 Adam MA, Untch BR, Danko ME, Stinnett S, Dixit D, Koh J, et al. Severe obesity is associated with symptomatic presentation, higher parathyroid hormone levels, and increased gland weight in primary hyperparathyroidism. J Clin Endocrinol Metab. 2010;95(11):4917–24.

23 Querfeld U, Hoffmann MM, Klaus G, Eifinger F, Ackerschott M, Michalk D, et al. Antagonistic effects of vitamin D and parathyroid hormone on lipoprotein lipase in cultured adipocytes. J Am Soc Nephrol. 1999;10(10):2158–64.

24 Maetani M, Maskarinec G, Franke AA, Cooney RV. Association of leptin, 25-hydroxyvitamin D, and parathyroid hormone in women. Nutr Cancer. 2009;61(2):225–31.

25 Matsunuma A, Kawane T, Maeda T, Hamada S, Horiuchi N. Leptin corrects increased gene expression of renal 25-hydroxyvitamin D3-1 alpha-hydroxylase and -24-hydroxylase in leptin-deficient, ob/ob mice. Endocrinology. 2004;145(3):1367–75.

26 Andersen T, McNair P, Hyldestrup L, Fogh-Andersen N, Nielsen TT, Astrup A, et al. Secondary hyperparathyroidism of morbid obesity regresses during weight reduction. Metabol Clin Experimental. 1988;37(5):425–8.

27 Chapuy MC, Preziosi P, Maamer M, Arnaud S, Galan P, Hercberg S, et al. Prevalence of vitamin D insufficiency in an adult normal population. Osteopor Int. 1997;7(5):439–43.

28 Stein EM, Strain G, Sinha N, Ortiz D, Pomp A, Dakin G, et al. Vitamin D insufficiency prior to bariatric surgery: risk factors and a pilot treatment study. Clinical Endocrinol. 2009;71(2):176–83.