

The study of association of serum parathyroid hormone level with obesity in subjects admitted to a tertiary care centre

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Abstract

Objectives: Obesity has become an ever growing problem of epidemic proportions. Recent researches in this field suggested a possible association of high serum parathyroid hormone level and low vitamin D level with obesity and metabolic syndrome. This study was conducted in Mysore Medical College, Mysore to evaluate association of obesity with high serum PTH level in obese individuals.

Methods: The study was conducted on 100 obese subjects admitted to medical wards who met the required criteria. Subjects were divided into different categories based on anthropometric measurements. Serum parathyroid hormone level was estimated in each group based on early morning sample drawn.

Results: Among 100 subjects studied, 52 were females and 48 were males. Subjects with grade 1 obesity had mean S.PTH value of 54.5pg/ml which was within normal population limit (8.9-82.4). Mean serum PTH in subjects of grade 2 obesity was 77.305, towards the upper limit of normal level (fourth quartile). Among patients with grade 3 obesity, serum PTH level was high with a mean value of 116.42 pg/ml. Pearson's coefficient of analysis for association of S.PTH with waist circumference was 0.652 (less than 1). There was significant positive correlation for level of S.PTH with waist hip ratio (coefficient of correlation 0.530) These findings were statistically significant with a P value < 0.001.

Conclusion: The study shows that there is a significant association of high serum parathyroid hormone level with BMI. This association was most significant among subjects with morbid obesity. Analysis based on waist circumference and waist hip ratio also showed a positive correlation.

Keywords: Body mass index (BMI), Serum parathyroid hormone (PTH), waist hip ratio, waist circumference.

1. Introduction

According to WHO, Overweight and obesity are major risk factors for a number of chronic diseases, including diabetes, cardiovascular diseases and cancer. Once considered a problem only in high income countries, overweight and obesity are now dramatically on the rise in low and middle income countries, particularly in urban settings. Obesity is one of the leading preventable causes of death worldwide [1]. Large scale American and European studies have found that mortality risk is lowest at a BMI of 20–25 kg/m² in non-smokers and at 24–27 kg/m² in current smokers, with risk increasing along with increase in BMI. In Asians risk begins to increase between 22–25 kg/m² [2].

In the United States obesity is estimated to cause 111,909 to 365,000 deaths per year, while 1 million (7.7%) of deaths in Europe are attributed to excess weight. On average, obesity reduces life expectancy by six to seven years [2]. BMI of 30–35 kg/m² reduces life expectancy by two to four years while severe obesity (BMI > 40 kg/m²) reduces life expectancy by ten years [2]. Many low and middle income countries are now facing a "double burden" of disease, particularly in urban settings [3]. Obesity has reached epidemic proportions in India in the 21st century, with morbid obesity affecting 5% of the country's population. This is only the tip of an iceberg and the

incidence is growing. In this context, it is important to understand traditional and non-traditional risk factors that contribute to this disease burden [4].

Association of vitamin D with obesity, Type 2 diabetes and cardiovascular disease (CVD) was extensively studied in the recent past. Many of such studies showed that a low vitamin D level was associated with increase in BMI. Many countries have adopted food fortification with vitamin D3 as a remedy to address vitamin D3 deficiency in general population, especially children [5]. If a low serum vitamin D is associated with obesity, one should expect the same to be true for high serum PTH. Most recently studies are being concentrated on the possible role of serum PTH as a possible mediator between these variables (vitamin D, calcium) and obesity. But most of such studies have been carried out in high income populations in developed countries. Such a study among Indian population, where incidence of obesity and diabetes is on a rise, has not been published yet, making this study needful. Apart from that, estimation of serum PTH hormone level is less expensive compared to that of serum vitamin D. If a significant association is proved between serum PTH and obesity, it can play a platform for further studies whether a reduction in serum parathyroid hormone by specific medication or an increased intake of calcium and vitamin D3 will reduce the risk of obesity.

2. Review of Literature

The term obesity was first used in 1960 by the English physician Dr. Tobias Venner[7]. In 1800, Alphonse Quetelet (1795-1844) in his attempts to define the average man, used data from the heights and weights of the French and Scottish armies to show that most cases fell within the range defined as a person's weight in kilograms divided by the square of the person's height in meters, this was termed later as the "Quetelet index". In 1893 Harvey William Cushing identified that pituitary gland and obesity are related [9].

In 1972, the modern term "body mass index" (BMI) gained its popularity to a paper published in the Journal of Chronic Diseases by Ancel Keys. This found that BMI to be the best proxy for body fat percentage, In 1988 Syndrome X was named as an insulin resistant metabolic syndrome, in which obesity is a part of the syndrome [10]. In 1994, research on obesity took a decidedly molecular turn with the discovery of the peptide hormone and satiety factor leptin [11]. In 2007, Researchers using genome-wide association studies identified the first obesity-related gene variants in the so-called "fat mass and obesity-associated" (FTO) gene on chromosome 16[12].

3. Materials and methods

3.1 Source of data

- Subjects admitted to medical wards in K.R. Hospital Mysore and who satisfy the inclusion criteria will be studied during a period from January 2014 to January 2015

3.2 Method of collection of data

- A minimum of 100 cases including both male and female who are admitted to medicine wards of KR Hospital and who satisfy the inclusion criteria were selected by simple random sampling. Informed written consent was taken from all the subjects
- A pre structured Performa was used to collect the baseline data.
- Detailed anthropometric examination and required investigation was done in all subjects

3.3 Inclusion Criteria:

- Age between 18yrs and 60 yrs
- BMI more than 30

3.4 Exclusion Criteria:

- Pregnancy
- Breast feeding
- Renal failure
- Age below 18 yrs or above 60
- Previous bariatric surgery
- Known thyroid diseases/post thyroidectomy status

3.5 Anthropometric measurements:

- Weight and height were measured in patients wearing light clothing
- BMI was calculated using the formula $BMI = \text{weight in kg}/(\text{height in meter})^2$
- The waist circumference was measured with a soft measuring tape at the level midway between the lowest rib margin and the iliac crest according to the WHO Guidelines
- Waist hip ratio was calculated as waist measurement divided by hip measurement (W/H) waist measurement was done as mentioned above using a stretch resistant tape. Hip circumference should be measured around the widest portion of the buttocks, with the tape parallel to the floor.

3.6 Biochemical analysis

- After overnight fasting of at least 8 hours, peripheral venous blood was collected in EDTA tubes for serum PTH.
- The sample was analysed using ECLIA method, and level of parathyroid hormone level was assessed.
- Sample for random blood sugar estimation was taken and was analysed using glucose oxidase method.

3.7 Study design

Cross sectional study

Total study time -18 month {January 2014 to July 2015}

Data collection time-1 year {January 2014 to January 2015}

3.8 Statistical analysis

Statistical methods used are descriptive statistics, chi-square test, contingency coefficient analysis and pearsons correlation coefficient analysis.

A probability value <0.05 was considered significant for all analyses.

4. Results

We studied 100 cases of obesity. The result is as follows:

Table 1: Relation between Gender and Obesity Grade

Obesity grade	Gender		Total
	Female	Male	
Obesity grade1	18 34.6%	17 35.4%	35 35%
Obesity grade2	18 34.6%	21 43.8%	39 39%
Obesity grade3	16 30.8%	10 20.8%	26 26%
Total	52 100.0%	48 100.0%	100 100.0%

$\chi^2=1.486 \cdot df=2 \cdot \phi c=.122 \cdot p=.476$

Among 100 subjects studied, 52 were females and 48 were males. Dividing them according to grades of obesity, female population was evenly distributed among 3 grades of obesity. 30% of females had morbid obesity. Among males, majority of subjects were having either grade 1 or 2 obesity. Grade 3 (morbid obesity) was present in only 20% of male subjects.

Table 2: Mean S.PTH Levels in Sex groups:

Serum PTH in sex groups				
Sex	No of patients	Mean	Maximum	Minimum
Female	52	84.931	161	2.8
Male	48	73.531	141	14.6

The mean S.PTH levels in female population (84.9 pg/ml) was higher than that of male population (73.5 pg/ml).

Table 3: Relationship between age and serum PTH

Serum PTH in sex groups				
Age	No of patients	Mean	Maximum	Minimum
20-45yr	78	77.823	132.8	2.8
>45yr	22	82.541	161.0	20.8

The mean serum PTH among subjects in age group 45-60 yrs was higher (82.54ng/ml) compared to subjects in age group 20-45yrs (77.82 ng/ml).

Table 4: S.PTH relationship with Diabetes Mellitus:

Serum PTH		N	Minimum	Maximum	Mean	t- statistics	P-value
Diabetes Mellitus	No	79	2.8	141	77.280	1.5790	0.11754
	Yes	21	20.8	161	91.806		

Mean of S.PTH is higher in group with diabetes (91.80) compared to group with no diabetes (77.28). Since the P-value is greater than 0.05, the mean of S.PTH among both the groups of diabetes is statistically not significant.

Table 5: Comparing waist circumference between obesity grades

Comparison of waist circumference between obesity grades								
Obesity grade	Waist circum	Mean	Median	Standard deviation	Minimum	Maximum	F-value	P value
1	35	90.90	92.4	4.545	80.6	96.5	92.18	0.001
2	39	96.83	98	4.008	86.4	102.3		
3	26	105.45	104.85	3.735	98.8	113.2		

There is proportional increase in waist circumference as BMI increases. The association was statistically significant with P value= 0.001.

Table 6: S.PTH relationship with Hypertension:

S.PTH		N	Minimum	Maximum	Mean	T-statistics	P-value
Hypertension	No	85	2.8	141	75.98	2.067	0.141
	Yes	15	25	161	92.51		

Mean of S.PTH is different among both the groups. Since the P-value is greater than 0.05, the difference in mean of S.PTH among both the groups is not statistically significant.

Table 7: Comparison of waist hip ratio (WHR) between obesity grades

Obesity grade	WHR	Mean	Median	Standard deviation	Minimum	Maximum	F value	P value
1	35	0.921	0.91	0.063	0.81	1.02	43.55	0.001
2	39	1.004	0.98	0.111	0.84	1.4		
3	26	1.21	1.25	0.182	0.96	1.5		

Increase in waist hip ratio was proportional to the increase in BMI. This association was statistically significant since P value is less than 0.05.

Table 8: Correlation analysis of S.PTH with Waist circumference and W/H ratio

Correlation analysis of S.PTH with Waist circumference and W/H ratio:		
		Result
Waist circumference	Pearson correlation	0.652
	P value	0.0001
Waist hip ratio	Pearson correlation	0.530
	P- value	0.0001

A correlation coefficient of less than 1 indicates positive correlation and more than 1 indicates negative correlation. Here, S.PTH has significant positive correlation with Waist Circumference and W/H ratio. This correlation was statistically significant as P value was less than P=0.05 at 95% CI.

5. Discussion

Among 100 subjects studied, 52 were females and 48 were males. Most of the subjects were 25-50 yrs of age (76%). These subjects were categorised into 3 groups based on grades of obesity. Among subjects, 35% had grade 1 obesity, 39% had grade 2 obesity and 26% had grade 3 obesity. Proportions of subjects with grade 3 obesity (morbid obesity) were more common in female sex (30%) compared to males (20%). Similarly, proportions of subjects with morbid obesity were more in older age group (50-60 years). Higher proportion of morbid obesity in female sex and elderly subjects could be partly due to more physical inactivity in this subset of population. Mean S.PTH level in female gender (84.9) was higher than that of male gender (73.5). Gender difference in the mean level of S.PTH could be due to hormonal factors. Females in the peri /post menopausal age group have more incidences of osteoporosis and thus a secondary rise in serum parathyroid hormone level.

25% of subjects participated in the study had diabetes mellitus. There was statistically significant association between prevalence of type 2 diabetes and BMI. Higher grades of obesity were associated with greater prevalence of diabetes in study population. (p=0.007). Among diabetic subjects 52% had morbid obesity, while only 19% of non diabetic subjects had morbid obesity. A recent study by Gupta *et al* on "The prevalence of type 2 diabetes in south India" showed that 12.5 % of general populations were diabetic. A study by ICMR also showed similar prevalence of diabetes [6]. According to our study, prevalence of diabetes among obese people is double that of normal population in this region. It is known that obesity can cause insulin resistance and is associated with impairment in glucose tolerance.

Among 100 subjects, 15 subjects had systemic hypertension. Among subjects with hypertension, 46.7% were morbidly obese while 33.3 % had grade 2 obesity.

There is positive correlation but this correlation was not statistically significant in this sample (p=0.151). In the present study we found that obesity was associated with higher levels of serum parathyroid hormone. This association was true for BMI, Waist circumference as well as Waist/Hip ratio. Comparing S.PTH with BMI, Subjects with grade 1 obesity had mean S.PTH value of 54.5pg/ml which was within normal population limit (8.9-82.4). Mean serum PTH in subjects of grade 2 obesity was 77.305, towards the upper limit of normal level (fourth quartile). Among patients with grade 3 obesity, serum PTH level was high with a mean value of 116.42 pg/ml. There is an increase in serum PTH level as the obesity grade increases and this increase is most significant in people with grade 3 obesity. These findings were statistically significant with a P value < 0.001. This observation was consistent with many similar studies conducted among subjects of different races and regions.

A study published in clinical endocrinology journal of American association of endocrinology in 2010 by Anna *et al* on "Relationship of vitamin D and parathyroid hormone with obesity and body composition in African Americans" found an association of low 25-hydroxyvitamin D and raised parathyroid hormone with greater adiposity, body mass index, and waist and hip circumferences in overweight adult African Americans. They suggested various mechanisms for possible association. They suggested that both depressed 25-OH D and reactive rises in PTH were consequences of obesity

The 5th Tromsø study was a large population based study by Elena Kamycheva, Johan Sundsfjord and Rolf Jorde published in 2004 in European journal of endocrinology, with an objective to study whether serum parathyroid hormone (PTH) and serum calcium are associated with body mass index (BMI), and their predicting role in obesity. Serum calcium and PTH were measured in a subset of 3447 men and 4507 women [7].

The highest quartile of serum PTH (4.20 pmol/l) was a significant predictor for obesity (P 0.001) in both genders, adjusted for age, physical activity and serum calcium. Obesity rates were higher in those with PTH levels in the highest quartile compared with those in the lower quartiles, which resulted in a relative risk of 1.40 (95% confidence interval (C.I.) 1.20–1.60) for men and 1.48 (95% C.I. 1.31–1.67) for women. Thus they concluded that Serum PTH, adjusted for age, physical activity and serum calcium, is positively associated with BMI in both sexes, and serum PTH is an independent predictor of obesity [7].

Thus an association between high S.PTH and obesity is significant but further studies would be needed to ascertain whether it is obesity causing secondary elevation of S.PTH or elevation of PTH contribute to the pathogenesis of obesity. WHO has suggested that waist circumference and waist hip ratio are reliable indicators of central obesity and insulin resistance, particularly among Asian population, where tendency for central adiposity is significantly greater. So we correlated serum PTH level with both waist circumference and waist hip ratio using Pearson correlation. Coefficient of analysis for S.PTH with waist circumference was 0.652 (less than 1) indicating a positive correlation. Thus, increase in serum PTH was correlated with higher waist circumference. This was statistically significant with p value of <0.05. There was significant positive correlation of level of S.PTH with waist hip ratio also (coefficient of correlation 0.530). This was statistically significant, since P value was <0.05.

6. Conclusions

Proportion of subjects having morbid obesity was more among females (30%) compared to males (20%).

Incidence of diabetes and hypertension were more among patients with morbid obesity compared to patients with lower grades of obesity.

There was significant association of indicators of obesity (BMI, waist circumference, waist hip ratio) with serum level of PTH. This association was statistically significant (P = <0.0001) this association was strongest in patients with morbid obesity (mean S.PTH value 116.4, which was higher than normal limits).

There was no statistically significant correlation between S.PTH and diabetes or hypertension. However, in this respect it must be strongly emphasized that we have only demonstrated a statistical association between serum PTH and BMI, which does not necessarily imply a cause-and-effect relationship. Though it was concluded that high serum PTH was associated with morbid obesity, it could not be determined from the study whether it is the primary cause or a secondary response to low serum vitamin D3 in subjects with obesity as many studies suggested. To find the cause and effect relationship, further study which includes measurement of S. calcium, serum vitamin D3

should be under taken. If proven by further studies, supplementation of vitamin D3 or food fortification with vitamin D3 along with good calcium intake could have probable health benefits in subjects with obesity.

Conflict of interest: There is no conflict of interest.

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