Original Article

Vitamin D, Parathyroid Hormone and Metabolic Syndromes in Morbidly Obese Children

Sana Javaid, Zukhruf Maryam, Maroofa Habib

ABSTRACT

Objective: To observe the association of the parathyroid hormone and vitamin-D with the occurrence of metabolic syndromes in severely obese children.

Study Design: A prospective observational study

Place and Duration of Study: This study was conducted at the Department Pediatric Medicine of Nishtar medical university and hospital, Multan from July, 2018 to December, 2018.

Materials and Methods: Age, BMI, gender, serum vitamin-D, parathyroid hormone level, serum calcium, total cholesterol, HDL, LDL, triglycerides, fasting blood glucose and presence or absence of metabolic syndrome were equated between the two groups of the patients, taking normal or low vitamin-D levels as grouping variable. Then, the comparison was done taking normal or high PTH levels as grouping variable. Chi-square and student t tests were applied accordingly. The dissimilarities were reflected statistically significant if the $p \leq 0.05$.

Results: Out of 58, 37 children had low vitamin-D while 21 children had normal vitamin-D levels. The prevalence of metabolic syndromes was 75.7% and 33.3% in the children with low and normal vitamin-D levels, respectively ($p=0.002$); and differences in serum calcium, PTH, vitamin-D, total cholesterol, HDL, LDL and triglycerides were statistically significant ($p \leq 0.05$). Thirty five children had high PTH levels while 23 children had normal PTH levels. The prevalence of metabolic syndromes was 62.8% 56.5% in the children with high and normal PTH levels, respectively ($p=0.629$); and differences in serum PTH, vitamin-D, HDL and triglycerides were statistically significant ($p \leq 0.05$).

Conclusion: Vitamin-D, but not parathyroid hormone, is considerably associated with the occurrence of the metabolic syndromes in severely obese children.

Key Words: Vitamin-D, parathyroid hormone (PTH), obesity, children, metabolic syndromes.

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INTRODUCTION

Obesity is one of the major health complications all across the world. There has been observed significant increase in obesity among the western population in the past thirty years. It is expected that almost one third of the adult population comprises of obese people [1,2]. Obesity is considered to have significant effect over the health and thought to cause cancer [3] and cardiovascular diseases [4], consequently decreasing the life expectancy. Owing to the obesity, cardiovascular risk factors which include insulin resistance, adiposity, hypertension, dyslipidemias, and glucose intolerance have been increased significantly and these factors are usually termed as metabolic syndromes. Almost 20% of the adult population of the United States is affected with metabolic syndromes and the prevalence is thought to increase with the increase in obesity [5].

Vitamin D plays role in maintaining mineral homeostasis and normal skeletal structure. Provitamin D precursor, transforms to previtamin D3 after absorbing ultraviolet light from the skin, which in turn converted to 25-hydroxyvitamin D3 in liver and then to 1,25-dihroxyvitamin D3 in the kidneys. Diets are also a good source of vitamin D. Serum 25-hydroxyvitamin D is measured to assess the vitamin D status [6]. Vitamin-D are adequate in the people living in sun exposure areas of land [7]. Not only metabolic bone disease is triggered by vitamin D deficiency, but other chronic disorders are also associated with deficiency. The association of vitamin D deficiency has been observed with type-II diabetes mellitus [8, 9] and cardiovascular diseases [10]. Therefore the link of vitamin D deficiency and metabolic syndromes has also been suggested [11, 12]. It is supposed to be due to the non-calcemic functions of vitamin D as vitamin-D receptors are present in most of the cells in the body [13].

Vitamin-D deficiency is observed to be more in the obese population and is assumed to be due to the

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accumulation of vitamin-D in the abundant fat cells. Extent of obesity and vitamin-D levels have the inverse relationship, which is why to establish whether vitamin-D deficiency or the obesity is responsible for the incidence of metabolic syndromes. Inverse association between vitamin-D and metabolic syndromes has been witnessed in various studies [11, 14-17] but some studies have found no significant relationship [18-20]. As there is interplay between parathyroid hormone (PTH) levels and vitamin-D, according to some researches, PTH is also thought to have relationship with the incidence of metabolic syndromes [18, 20] while others have failed to observe any relation [16, 19].

Many studies have been performed to observe the link of vitamin-D and PTH with the incidence of metabolic syndromes in the adult population but the data regarding these associations in the obese children in not available. So, we are conducting this study to observe the association of the PTH levels and vitamin-D concentration with the occurrence of metabolic syndromes in severely obese children of south-east Asian population.

MATERIALS AND METHODS

This prospective observational study was conducted in the department of Pediatric Medicine of Nishtar medical university and hospital, Multan. The duration of the study was July 5, 2018 to December 20, 2018. We included 58 obese children, using non-probability consecutive sampling technique, after calculating the sample size from the reference study [14]. Hospital review board was consulted and ethical approval was obtained before commencing the study. Parents of all the children were informed about the nature and procedure of the study and written consent was taken. Included children were 4 to 13 years old and their BMI was above 30 kg/m2. All the children below 3 years of age, having BMI less than 30 kg/m2, malabsorption syndromes and with developmental delay were not a part of the study.

All patients were kept under strict observation and venous samples were obtained after overnight fasting. Age, weight, gender and height were documented for all the patients. All the blood samples were analyzed for serum levels of PTH, vitamin-D, calcium, total cholesterol, HDL-C, LDL-C, triglyceride and fating blood glucose levels. Evaluation of the patients was done for the diagnosis of metabolic syndromes. Metabolic syndromes were diagnosed if at least derangement in 3 of the following parameters were present; abdominal circumference, fasting blood glucose levels, HDL cholesterol, triglycerides and blood pressure. Normal range for serum vitamin-D was taken as 20-50 ng/ml, and for serum PTH levels was taken as 10-65 pg/ml. BMI of all the patients was calculated from their weight and height.

Age, BMI, gender, serum vitamin-D, serum parathyroid hormone level, serum calcium, total cholesterol, HDL-C, LDL-C, triglycerides, fasting blood sugar levels and the presence or absence of metabolic syndrome were documented for all the patients. All the data was put in SPSS version 23 and analyzed. First, all the variables were compared taking normal or low vitamin-D levels as grouping variable. Then, all the variables were compared taking normal or high parathyroid hormone levels as grouping variable. Pearson chi square test was applied on nominal data and student t test was applied on the continuous data. The dissimilarities were considered statistically significant if the $p \leq 0.05$.

RESULTS

On comparison of the two groups based on the sufficient or poor levels of vitamin-D in the serum, 37 children had low serum vitamin-D while 21 children had normal vitamin-D. The occurrence of metabolic syndromes was 75.7% in the children with low vitamin-D and 33.3% in the children with normal vitamin-D levels (p=0.002). Among the children deficient in vitamin-D, mean age was 7.56±2.47 years, BMI was 37.51±3.48 kg/m2, 22 were males and 15 were females; while among the children with normal vitamin-D, mean age was 8.66±2.27years, BMI was 38.71±4.01 kg/m2, 10 were males and 11 were females (p values 0.092, 0.237 and 0.384, respectively). Mean serum calcium, PTH and vitamin-D levels were 8.1±0.8 mg/dl, 52.97±8.40 ng/ml and 15.19±2.50 ng/ml in the children deficient in vitamin-D; and 8.6±0.6 mg/dl, 45.57±8.67 pg/ml and 34.09±9.19 ng/ml in the children with normal serum vitamin-D (p-value 0.032, 0.002 and <0.001, respectively). Mean serum total cholesterol, HDL, LDL, triglycerides and fasting blood sugar were 156.35±31.47 mg/dl, 34.32±7.19 mg/dl, 110.68±11.93 mg/dl, 161.16±20.81 mg/dl and 93.81±10.9 mg/dl in the children deficient in vitamin-D; while 142.29±21.45 mg/dl, 42.52±6.58 mg/dl, 105.52±14.73 mg/dl, 96.57±27.17 mg/dl and 87.62±13.7 in the children with normal vitamin-D (p-value 0.049, <0.001, 0.180, <0.001 and 0.064, respectively). The difference in serum calcium, PTH, vitamin-D, total cholesterol, HDL, LDL and triglycerides were statistically significant. Table-I

On comparison of the two groups based on the PTH levels in the serum, 35 children had high PTH levels while 23 children had normal PTH levels. The prevalence of metabolic syndromes was 62.8% in the children with high PTH levels and 56.5% in the children with normal PTH levels (p=0.629). Among the children with high PTH level, mean age was 8.11±2.29 years, BMI was 37.51±3.58 kg/m2, 21 were males and 14 were females; while among the children with normal PTH level, mean age was 7.74±2.54 years, BMI was 38.61±3.83 kg/m2, 11 were males and 12 were females (p values 0.562, 0.273 and 0.362, respectively). Mean

serum calcium, PTH and vitamin-D levels were 8.4±0.7 mg/dl, 53.34±8.48 ng/ml and 17.03±6.76 ng/ml in the children with high PTH level; and 8.2±0.8 mg/dl, 45.65±8.29 pg/ml and 29.65±11.56 ng/ml in the children with normal serum PTH level (p-value 0.338, 0.001 and <0.001, respectively). Mean serum total cholesterol, HDL, LDL, triglycerides and fasting blood sugar were 154.43±30.69 mg/dl, 35.51±6.91 mg/dl, 108.34±12.43 mg/dl, 157.89±25.34 mg/dl and 92.77±11.45 mg/dl in the children with high PTH level; while 146.43±25.76 mg/dl, 40.01±8.86 mg/dl, 109.52±14.37 mg/dl, 107.17±36.12 mg/dl and 89.74±13.41 in the children with normal vitamin-D (p-value 0.307, 0.035, 0.741, <0.001 and 0.361, respectively). The difference in serum PTH, vitamin-D, HDL and triglycerides were statistically significant. Table-2.

Table No.1: Comparison between patients with normal and deficient vitamin D level

Variable	Patients with vit. D deficiency (n=37)	Patients without vit. D deficiency (n=21)	p-value
Age, years	7.56 ± 2.47	8.66 ± 2.27	0.092
BMI, Kg/m2	37.51 ± 3.48	38.71 ± 4.01	0.237
Gender, male/female	22 / 15	10 / 11	0.384
Serum Calcium , mg/dl	8.1 ± 0.8	8.6 ± 0.6	0.032
Serum PTH, pg/ml	52.97 ± 8.40	45.57 ± 8.67	0.002
Serum Vitamin D, ng/ml	15.19 ± 2.50	34.09 ± 9.19	<0.001
Metabolic syndrome, n (%)	28 (75.7)	7 (33.3)	0.002
Total cholesterol, mg/dl	156.35 ± 31.47	142.29 ± 21.45	0.049
HDL, mg/dl	34.32 ± 7.19	42.52 ± 6.58	<0.001
LDL, mg/dl	110.68 ± 11.93	105.52 ± 14.73	0.180
Triglycerides, mg/dl	161.16 ± 20.81	96.57 ± 27.17	<0.001
Fasting blood sugar, mg/dl	93.81 ± 10.9	87.62 ± 13.7	0.064

Table No.2: Comparison between patients with normal and high serum PTH level

Variable	Patients with high PTH levels (n=35)	Patients with normal PTH levels (n=23)	p-value
Age, years	8.11 ± 2.29	7.74 ± 2.54	0.562
BMI, Kg/m2	37.51 ± 3.58	38.61 ± 3.83	0.273
Gender, male/female	21 / 14	11 / 12	0.362
Serum Calcium , mg/dl	8.4 ± 0.7	8.2 ± 0.8	0.338
Serum PTH, pg/ml	53.34 ± 8.48	45.65 ± 8.29	0.001
Serum Vitamin D, ng/ml	17.03 ± 6.76	29.65 ± 11.56	<0.001
Metabolic syndrome, n (%)	22 (62.8)	13 (56.5)	0.629
Total cholesterol, mg/dl	154.43 ± 30.69	146.43 ± 25.76	0.307
HDL, mg/dl	35.51 ± 6.91	40.01 ± 8.86	0.035
LDL, mg/dl	108.34 ± 12.43	109.52 ± 14.37	0.741
Triglycerides, mg/dl	157.89 ± 25.34	107.17 ± 36.12	<0.001
Fasting blood sugar, mg/dl	92.77 ± 11.45	89.74 ± 13.41	0.361

DISCUSSION

We observed in this study that the occurrence of the metabolic syndromes was considerably high among the children who had low levels of vitamin-D. On the other hand, the occurrence of metabolic syndromes was not significantly dissimilar in the children who had higher levels of parathyroid hormone. Among the children who had low serum vitamin-D, there was significantly high levels of parathyroid hormone. Children with raised levels of parathyroid hormone had significantly low levels of serum vitamin-D. We observed significantly higher levels of total cholesterol, serum LDL-C, and serum triglycerides in the children who were deficient in vitamin-D. These children also had significantly lower levels of serum calcium and serum high density lipoproteins. However, the difference in the fasting blood glucose levels was not observed to be significantly different. Considering higher levels of serum parathyroid hormone, there were considerably low level of serum vitamin-D and serum high density lipoproteins, but significantly higher levels of serum triglycerides. However, there were no significant differences were observed in serum calcium levels, serum total cholesterol and serum low density lipoproteins, and fasting blood glucose levels in the children who had higher serum parathyroid hormone level. The prevalence of metabolic derangements were found to be significantly more based on the decreased

levels of serum vitamin-D rather than based on higher levels of serum parathyroid hormones.

Previously studies have been directed on the adult obese persons to observe the correlation of parathyroid hormone and vitamin-D with the occurrence of metabolic syndromes. Ford ES et al. [11]performed the study on 8421 adult patients and they observed that there lies an inverse relationship of serum vitamin-D levels and the occurrence of the metabolic syndromes. Lower levels of vitamin-D tend to promote the prevalence of the metabolic syndromes. Botella-Carretero JI et al. [14] conducted similar study and found that vitamin-D deficiency is associated with the increased prevalence of the metabolic syndromes. Hyppönen E et al. [15] observed that the prevalence of the metabolic syndromes was low in the presence of higher serum vitamin-D levels. Reis JP et al. [16] observes an inverse relationship of prevalence of metabolic syndrome with vitamin-D but no relation with serum parathyroid hormone could be established. Lu L et al. [17]performed a study on the Chinese population and observed the similar results.

Reis JP et al. [18] conducted a study on elderly population and observed linear relation of serum PTH with the occurrence of the metabolic syndromes. They observed no association of vitamin-D with the prevalence of the metabolic syndromes. Rueda S et al. [19] observed effect of parathyroid hormone or vitamin-D over the prevalence of the metabolic syndromes. Hjelmesæth J et al. [20]performed a study on Caucasian adult population and concluded that parathyroid hormone level was the only significant predictor of the occurrence of the metabolic syndrome but vitamin-D had no significant relation.

CONCLUSION

Vitamin-D is significantly linked with the prevalence of the metabolic syndromes in severely obese children but parathyroid hormone level has no significant predictive value of the occurrence of metabolic syndromes.

Author's Contribution:

Concept & Design of Study:	Sana Javaid
Drafting:	Zukhruf Maryam
Data Analysis:	Maroofa Habib
Revisiting Critically:	Sana Javaid, Zukhruf Maryam
Final Approval of version:	Sana Javaid

Conflict of Interest: The study has no conflict of interest to declare by any author.

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