

Original Research Article

Evaluation of vitamin D status in suspected cases of metabolic syndrome

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ABSTRACT

Background: Metabolic syndrome is associated with an increased risk of cardiovascular disease and type 2 diabetes mellitus. Vitamin D has been linked to glucose metabolism and insulin regulation. Hence, this study aims to evaluate the association between the serum level of vitamin D and metabolic syndrome. This may help generate additive strategies in the prevention and management of this syndrome. The objective of the study was to compare the levels of serum vitamin D in subjects with metabolic syndrome and subjects without metabolic syndrome.

Methods: A prospective study with 80 subjects was conducted at a tertiary care hospital in Southern India. The sample comprised 40 subjects in the age group of (18-60 years) with metabolic syndrome as cases and 40 subjects without metabolic syndrome in the age groups of (18-60 years) as controls. The presence of any 3 of the following-fasting blood glucose (FBS ≥ 100 mg/dl), triglycerides (TGL ≥ 150 mg/dl) and high-density lipoprotein cholesterol (HDL-C ≤ 40 mg/dl-men, ≤ 50 mg/dl-women) levels, blood pressure ($\geq 130/85$ mmHg or drug treatment) and abdominal waist circumference (>94 cm (37 in) in men and >80 cm (31 in) in women) were used as criteria to screen for the presence (cases) or absence (controls) of metabolic syndrome. Serum vitamin D (25-hydroxy vitamin D) levels were compared between the two groups.

Results: Mann Whitney U test was used to compare the vitamin D levels between the two groups. Significantly ($p=0.05$) lower vitamin D levels were seen in the cases compared to the controls.

Conclusions: Metabolic syndrome is associated with significantly lower serum vitamin D levels. We suggest that further studies with a larger sample size be undertaken to confirm the same.

Keywords: Coronary heart disease, Fasting blood glucose, High density lipoprotein, Metabolic syndrome, Triglycerides, Type 2 diabetes mellitus

INTRODUCTION

Metabolic Syndrome is a cluster of common abnormalities including insulin resistance, impaired glucose tolerance, abdominal obesity, reduced HDL-cholesterol levels, elevated triglycerides and hypertension.^{1,2} In recent years, there has been an increase in the prevalence of metabolic syndrome across the world, particularly in India and other South Asian

countries, resulting in increased morbidity and mortality.³⁻⁵ This condition is associated with endothelial dysfunction and atherosclerosis contributing to an elevated risk of cardiovascular disease and type 2 diabetes mellitus.¹ However, the exact pathogenesis is still uncertain.⁶ Lifestyle changes like physical activity, weight reduction, dietary measures and smoking cessation have been found to play a role in the prevention of metabolic syndrome.^{7,8} The utility of drugs in its

prevention is also being evaluated.⁷ Vitamin D is a fat-soluble vitamin and is regarded as a prohormone. It is necessary for the absorption of dietary calcium from the gut and thus, is essential for the growth, development and maintenance of the skeletal system.⁹ Most experts have defined vitamin D deficiency as 25-hydroxy vitamin D level lower than 20ng/mL and insufficiency as levels between 21-29.99ng/mL. The optimal concentration of 25-hydroxy vitamin D is at least 30ng/mL.^{10,11}

Vitamin D deficiency is associated with rickets in growing children and osteomalacia in adults.¹² In addition, many recent studies have suggested an associated between vitamin D deficiency and the development of non-communicable diseases particularly cardiovascular disease and type 2 diabetes mellitus as well their risk factors of obesity and insulin resistance. Vitamin D is said to play a role in glucose homeostasis and insulin regulation.¹³

Further, the prevalence of hypovitaminosis D has been increasing worldwide, especially in Asian Countries.^{6,14,15} Considering the potential morbidity and mortality associated with metabolic syndrome, there is a need to better understand the contributing factors and pathogenesis of this condition to further improve its management strategies. Since hypovitaminosis D has been linked to the risk factors of metabolic syndrome, through this study we wished to evaluate the relationship between metabolic syndrome and the serum vitamin D levels.

Thus, the objective of our study was to compare the levels of serum vitamin D in subjects with metabolic syndrome and subjects without metabolic syndrome.

METHODS

The study design was a comparative study. The study period was one year from January 2016 to February 2017. The sample size was calculated to be 80 patients. The inclusion criteria were males and females between 18-60 years of age who visited the outpatient department of the tertiary care hospital considered during this study period. The exclusion criteria were those patients who received vitamin D and calcium supplements within 60 days prior to the screening and those patients who were known cases of diabetes mellitus, cardiovascular disease, alcohol abuse, chronic smokers or chronic renal failure.

After obtaining an informed consent, a total of 80 subjects comprising 54 women and 26 men were screened for metabolic syndrome and the sample was then divided into two groups-cases (with metabolic syndrome) and controls (without metabolic syndrome). To classify patients as having metabolic syndrome (cases), the 2009 International Diabetes Federation (IDF) and American Heart Association definition of metabolic syndrome was used as the screening tool. It is defined as the presence of any three of the following criteria¹⁶

- Abdominal waist circumference >94cm (37 in) in men and >80cm (31 in) in women,
- Serum hypertriglyceridemia ≥ 150 mg/dl (1.7mmol/L) or drug treatment for elevated triglycerides,
- Serum high-density lipoprotein (HDL) cholesterol <40mg/dl (1mmol/L) in men and <50mg/dl (1.3mmol/L) in women or drug treatment for low HDL-C,
- Blood pressure $\geq 130/85$ mmHg or drug treatment for elevated blood pressure,
- Fasting glucose ≥ 100 mg/dl (5.6mmol/L) or drug treatment for elevated blood glucose.

The serum vitamin D levels (25-hydroxy vitamin D) of the two groups were then measured using chemiluminescence method by an auto analyser.¹⁷ SPSS-16 was used to analysed the data obtained. A Mann Whitney U test was performed.

RESULTS

Demographics

The sample size was 80 subjects of whom 54 subjects (67.5%) were women and 26 subjects (32.5%) were men. There were 40 subjects in the cases group of whom 24 (60%) were female and 16 (40%) were male. There were 40 subjects in the control group of whom 30 (75%) were female and 10 (25%) were male (Table 1).

Table 1: Gender distribution of the cases and controls.

Gender	Cases (n=40)		Controls (n=40)	
	Number	%	Number	%
Male	16	40%	10	25%
Female	24	60%	30	75%
Total	40		40	

In the cases group (n=40), 2 subjects were between 21-30 years (5%), 5 subjects were between 31-40 years (12.5%), 18 subjects were between 41-50 years (45%) and 15 subjects were between 51-60 years (37.5%). In the control group (n=40), 11 subjects were between 21-30 years (27.5%), 10 subjects were between 31-40 years (25%), 11 subjects were between 41-50 years (27.5%) and 8 subjects were between 51-60 years (20%) (Table 2).

Table 2: Age distribution in the cases and controls.

Age (years)	Cases (n=40)		Controls (n=40)	
	Number	%	Number	%
21-30	2	5%	11	27.5%
31-40	5	12.5%	10	25%
41-50	18	45%	11	27.5%
51-60	15	37.5%	8	20%
Total	40		40	

The outcome variable was the serum vitamin D level. Since the data was not following a normal distribution, the median serum vitamin D levels of the 2 groups were considered. Mann Whitney U test was used to compare

the median serum vitamin D levels of the 2 groups. A p value of ≤ 0.05 was taken to be statistically significant for the study.

Table 3: Comparison of vitamin D levels between the cases and controls.

Group	Number	Median vitamin D (ng/ml)	Interquartile range	Test statistic	P value
Cases	40	9.9	5.03-13.9	2.1#	0.05*
Control	40	12.9	6.9-18.6		

#- Mann Whitney U test statistic. *- statistically significant at $p \leq 0.05$

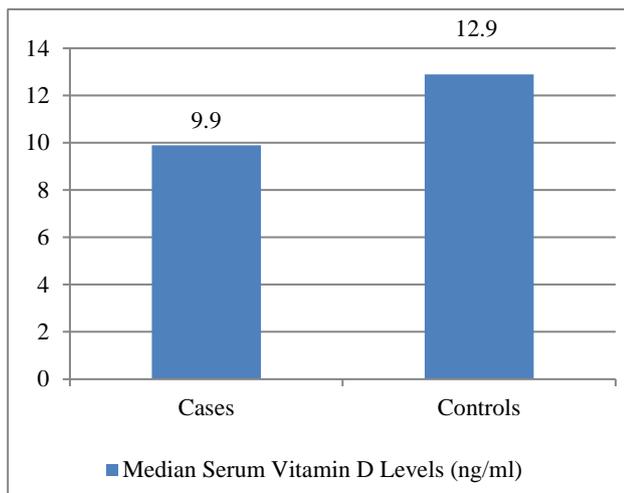


Figure 1: Median serum vitamin D levels in the cases and controls.

The median serum vitamin D level in the cases group was 9.9ng/ml with an interquartile range of 5.03-13.9. The median serum vitamin D level in the Control group was 12.9ng/ml with an interquartile range of 6.9-18.6. On comparing the median serum vitamin D levels between the 2 groups a Mann Whitney U statistic of 2.1 was obtained. The p value was 0.05 which was statistically significant (Table 3, Figure 1).

DISCUSSION

In our study, in general, individuals of both the groups had serum vitamin D (25- hydroxy vitamin D) levels that were in the range of vitamin D deficiency. However, there was a statistically significant difference in the levels between the two groups wherein the serum vitamin D levels were significantly lower in those individuals with metabolic syndrome than those without metabolic syndrome. Thus, our study shows that metabolic syndrome is associated with significantly lower serum vitamin D levels.

This result is in concurrence with separate studies done by Ford et al, Reis et al and Boucher BJ respectively which all reported a significant inverse relationship between serum 25-hydroxy vitamin D and metabolic

syndrome.^{18,19,20} Gagnon C et al, found that the serum 25-hydroxy vitamin D level had an inverse association with the waist circumference ($P < 0.001$), triglyceride level ($P < 0.01$), fasting blood glucose ($P < 0.01$) and insulin resistance ($P < 0.001$).²¹ The study also concluded that the risk of metabolic syndrome was higher in those individuals with lower serum vitamin D levels and recommended vitamin D supplementation studies to definitively prove the same. Similar results were found in a study with 126 participants by Maghbooli Z et al which showed a three times increased risk of metabolic syndrome in participants with hypovitaminosis D compared with those with normal vitamin D levels.²²

The findings of our as well as all the above-mentioned studies indicate that vitamin D could play a role in the prevention of metabolic syndrome. This can be explained by the following possible mechanisms- 1) increase in the insulin secretion and sensitivity; 2) stimulation of the expression of the insulin receptors; 3) enhancement of glucose transport into the cells of target tissues and 4) and regulation of intracellular calcium.^{23,24} Vitamin D has also been found to modulate lipolysis.^{25,26} The above mechanisms have been reiterated in animal studies which have shown that vitamin D is essential for insulin secretion. In one such study, insulin secretion was impaired in the vitamin D deficient pancreas, which improved on supplementation with dietary vitamin D. This repletion of vitamin D improved the blood glucose clearance and insulin secretion in vivo, independent of other nutritional factors and the prevailing plasma calcium and phosphorus concentrations.²⁷ Thus, when vitamin D is deficient, insulin regulation and lipid metabolism are affected resulting in the development of metabolic syndrome which in turn increases the cardiovascular morbidity and mortality as well as increases the risk of type 2 diabetes mellitus.^{1,4,5} Considering this important role that vitamin D could be playing, more studies are required to further evaluate the pathogenesis.

As mentioned before, while our study showed that metabolic syndrome was associated with significantly lower serum vitamin D levels, the overall levels of vitamin D across both the groups were in the deficiency range. This could be explained by the very high

prevalence of vitamin D deficiency in India (40-99%).²⁸ There is a possibility that the subjects without metabolic syndrome but with deficient vitamin D levels are at a potential risk of developing one or more of the factors which contribute to metabolic syndrome at a later point in their life, particularly if the serum vitamin D levels decreased further. This is indicated by the significantly lower serum vitamin D levels in the subjects with metabolic syndrome in our study. In order to confirm the same, there is a need for studies evaluating the role of vitamin D supplementation in those with deficient levels in the prevention of metabolic syndrome. If confirmed, supplementation of vitamin D in the deficient individuals could be considered as an important preventive measure in addition to lifestyle modifications for potentially reducing the syndrome associated morbidity and mortality. In addition, due to the high prevalence of vitamin D deficiency across the Indian population strategies like fortification of food with vitamin D could be considered.^{28,29} Some of the drawbacks of our study included the small sample size and that it was a hospital-based study. Hence community-based studies and studies with a larger sample size evaluating the relationship between serum vitamin D levels and metabolic syndrome are required.

CONCLUSION

Metabolic syndrome is associated with lower serum levels of 25-hydroxy vitamin D. There is a high prevalence of vitamin D deficiency in the Indian population. Thus, supplementation of vitamin D in the deficient through diet or medications is necessary for the prevention of metabolic syndrome and potentially cardiovascular disease and type 2 diabetes mellitus.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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