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RESEARCH ARTICLE

Vitamin D Deficiency in Metabolic Syndrome Patients.

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Abstract

Vitamin D has an essential role in calcium metabolism and bone health. Vitamin D3 or cholecalciferol is synthesized from 7-dehydrocholesterol or provitamin D3, by sunlight ultraviolet radiation to the skin. 7-dehydrocholesterol is subsequently hydroxylated in the liver and then in the kidney to produce 1,25-(OH)2D3, the active metabolite that binds to specific receptors (VDR) in target tissues, mainly bone and intestine. Other tissues, such as the immune and cardiovascular system, have also VDR. Vitamin D deficiency can induce rickets in children and osteomalacia and osteoporosis in adults. A possible inverse association between vitamin D levels and the prevalence of metabolic syndrome has been proposed. Vitamin D deficiency increases the risk of type 1 diabetes, insulin resistance, and hypertension, key components of this syndrome.This clinical research study focuses on correlation between Vitamin D and Metabolic syndrome.

Introduction:-

The prevalence of common obesity has become a public health concern in many countries as phenomenological approaches to the understanding of pathogenesis have failed to achieve any long term effect on prevention or treatment.

There is evidence for a central control mechanism which maintains body-weight to a set-point by the regulation of energy intake and energy expenditure through homeostatic pathways. It is suggested that common obesity occurs when the set-point is raised and that accumulation of fat mass functions to increase body size. Larger body size confers a survival advantage in the cold ambient temperatures and food scarcity of the winter climate by reducing surface area to volume ratio and by providing an energy store in the form of fat mass. In addition, it is suggested that the phenotypic metabolic and physiological changes observed as the metabolic syndrome, including hypertension and insulin resistance, could result from a winter metabolism which increases thermogenic capacity. Common obesity and the metabolic syndrome may therefore result from an anomalous adaptive winter response.

The stimulus for the winter response is proposed to be a fall in vitamin D. the synthesis of Vitamin D is dependent upon the absorption of radiation in the ultraviolet-B range of sunlight. At ground level at midlatitudes, UV-B radiation falls in the autumn and becomes negligible in winter. Vitamin D in the form of is the stimulus for the winter consists of an accumulation of fat mass (obesity) and the induction of a winter metabolism (the metabolic syndrome). Vitamin D deficiency can account for the secular trends in the prevalence of obesity and for individual differences in its onset and severity. It may be possible to reverse the increasing prevalence of obesity by improving vitamin D status.

In accord with this hypothesis, many studies have been done across the globe, most of which have found a negative correlation between vitamin D level and BMI. These studies were done in populations belonging to a particular region. In this context there is scarcity of data on Indian population and no such Indian study could be traced.

Present study will provide valuable information regarding relation of vitamin D level with obesity and metabolic syndrome in Indian population.

Aims & objectives:-

1. To determine mean serum 25 OH Vitamin D level in apparently healthy Indian population & to estimate prevalence of vitamin D deficiency in apparently healthy Indian population.
2. To determine mean serum 25 OH vitamin D level in patients suffering from metabolic syndrome & to estimate prevalence of vitamin D deficiency in patients of metabolic syndrome.
3. To determine correlation between metabolic syndrome & vitamin D deficiency.
4. To establish correlation between serum 25 OH vitamin D level and BMI, waist circumference, mean blood pressure, Fasting Blood Sugar, HDL cholesterol & Triglyceride level.

Material & methods:-

Study Design:-

- Cross Sectional, Case Control, Observational study.

Source of cases & controls:-

- Patients from OPD and wards of Hamidia Hospital, their attendants and other healthy volunteers.

Case:-

- One who meets IDF criteria for Metabolic Syndrome and has BMI>30.0

Control:-

- One who meets none of the five parameters of Metabolic Syndrome and has BMI<25.0

Inclusion Criteria:-

1.Willing to participate in study
2. Age between 15 to 65 years.

Exclusion Criteria

1.Suffering from any chronic renal, hepatic, cardiac, gastrointestinal, skeletal, or endocrine disease (except diabetes).
2.Suffering from any acute critical illness.
3.Those on calcium or vitamin D supplementation.

Methodology:-

Cases and controls were evaluated for following
1. Body Mass Index
2. Waist Circumference
3. Supine Blood Pressure
4. Serum HDL Cholesterol Level
5. Serum triglyceride Level
6. Serum 25OHVitD Level

Serum 25OHvitD levels were measured by Radio Immuno Assay (RIA).

Analysis of Data:-

Mean serum 25 OH vitamin D level of cases and controls were calculated and the significance of difference of two means calculated by applying unpaired student‘t’ test. Correlation drawn between 25 OH vitamin D level & Body Mass index using PEARSON's correlation coefficient.

Correlation drawn between 25 OH vitamins D level & fasting blood sugar using PEARSON's correlation coefficient. Correlation drawn between 25 OH vitamin D level & serum HDL cholesterol level using PEARSONS correlation coefficient. Correlation drawn between 25PJ vitamin D ;eve; & serum triglyceride level using PEARSONS correlation coefficient.

Observation & results:-

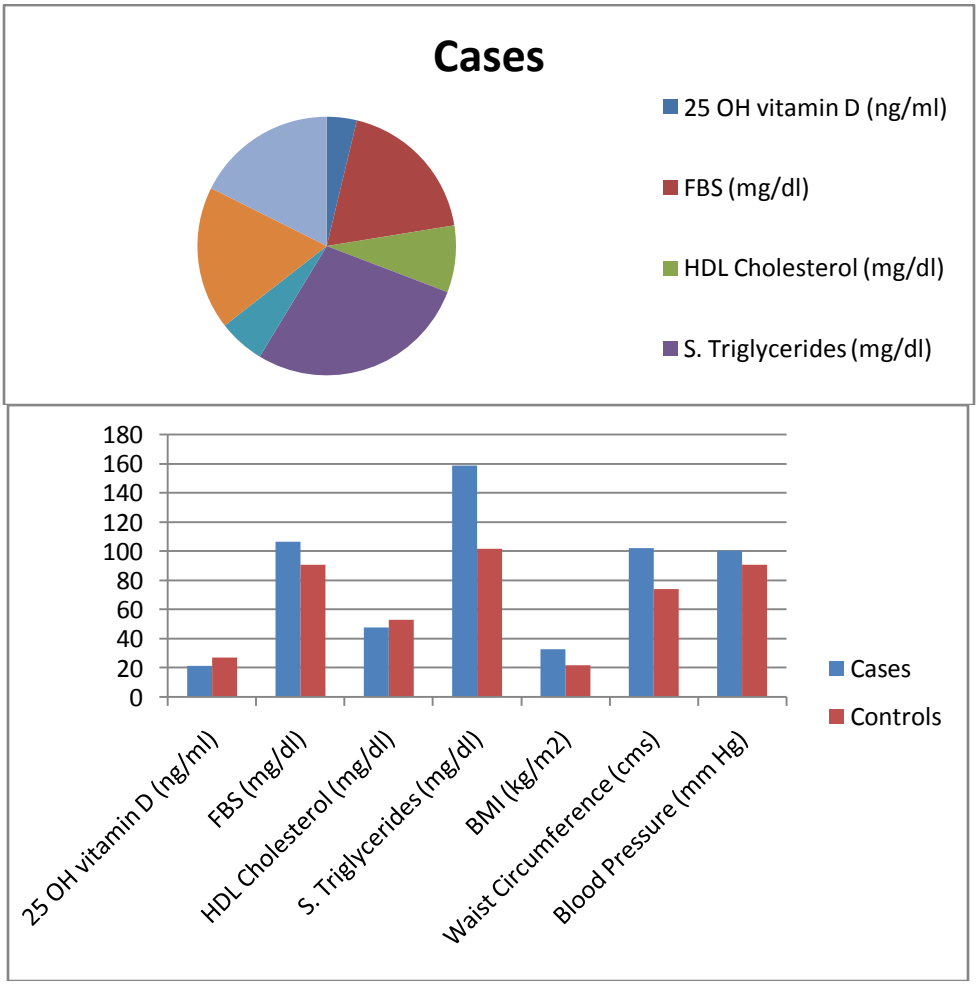
Table – 1Comparison of mean serum 25 OH vitamin D, BMI, waist circumference, mean blood pressure, F.G.S., HDL cholesterol & serum triglyceride level between cases & controls.

	Cases	**Controls**
25 OH vitamin D (ng/ml)	21.34	26.94
FBS (mg/dl)	106.36	90.64
HDL Cholesterol (mg/dl)	47.64	53
S. Triglycerides (mg/dl)	158.56	101.44
BMI (kg/m^2)	32.988	21.772
Waist Circumference (cms)	101.96	74.04
Blood Pressure (mm Hg)	100.276	90.848

Tabular representation mean serum 25 OH vitamin D was less in cases (21.34 ng/ml) than in control (26.94 ng/ml). Mean FBS, HDL cholesterol, Triglycerides, BMI< Waist circumference & blood pressure in cases was 106.36 mg/dl, 47.64 mg/dl, 158.56 mg/dl, 32.988 kg/m^2, 101.96 cms& 100.276 mm Hg respectively while those in controls was 90.64 mg/dl, 53mg/dl, 101.44 mg/dl, 21.772 kg/m^2, 74.04 cms& 90.848 mm Hg respectively.

Graph – 1

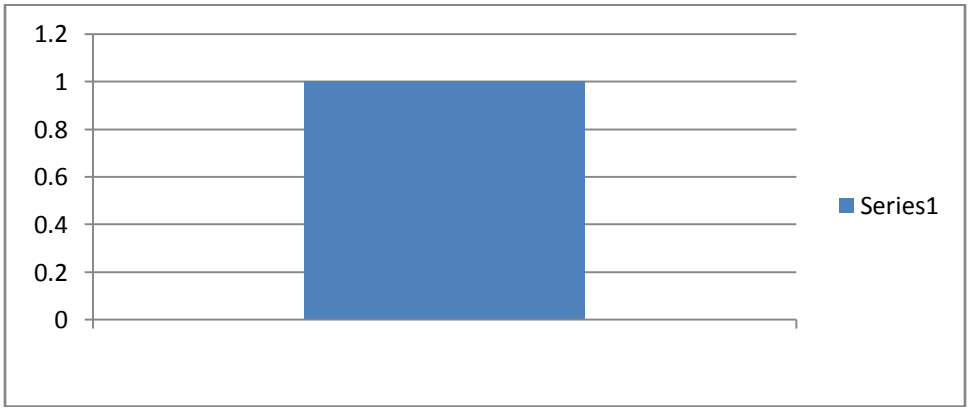
Comparison of mean serum 25 OH vitamin D, BMI< Waist circumference, Mean Blood Pressure, F.B.S., HDL Cholesterol & Serum Triglyceride Level between cases & controls.



Graphic representation-mean serum 25 OH vitamin D was less in cases (21.34 ng/ml) than in controls (26.94 ng/ml). Mean FBS, HDL cholesterol, Triglycerides, BMI< Waist circumference & flood pressure in cases was 106.36 mg/dl, 47.64 mg/dl, 158.56 mg/dl, 32.988 kg/m^2, 101.96 cms& 100.276mm Hg respectively while those in controls was 90.64 mg/dl, 101.44 mg/dl, 21.772 kg/m^2, 74.04cms & 90.848 mm HG respectively.

Table -2Comparison of mean serum 25 OH vitamin D Level between males & females

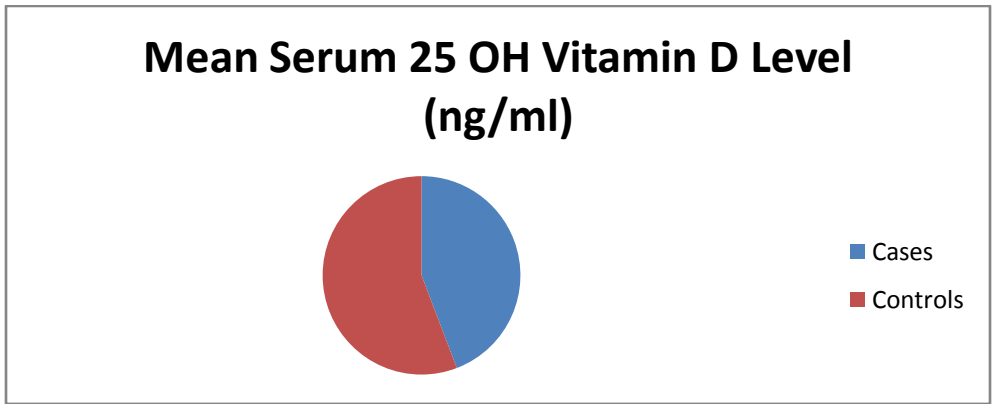
Mean Serum 25 OH vitamin D level between Males & Females (in ng/ml)	
Males	22.26
Females	23.2

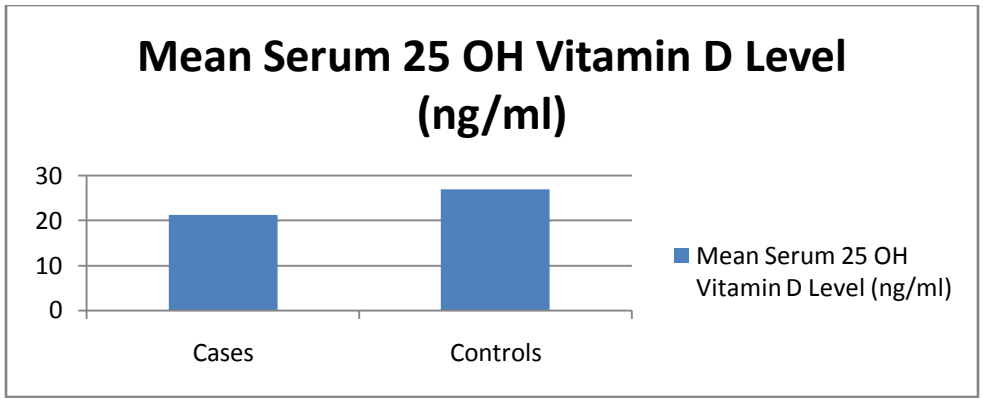


Mean serum 25 OH vitamin D level in males was 22.26 ng/ml and in females was 23.2 ng/ml. The difference was not statistically significant.3

Table -3Comparison of mean serum 25 OH vitamin D in cases & controls

Study Group	Mean Serum 25 OH Vitamin D Level (ng/ml)
Cases	21.34
Controls	26.94





Mean serum 25 OH vit D level in cases (21.34 ng/ml) was less than those in controls (26.94 ng/ml). The significance of difference between both means was calculated using students unpaired 't' test. 't' value was 2.02 which was significant at 5% level but was not significant at 1% level (0.05>p<0.01).

Table – 4

Comparison of 25 OH vitamin D deficiency in cases & control

Study Group	No.(%) of subjects deficient in 25 OH Vitamin D
Cases	11 (44%)
Controls	6 (24%)

11 cases out of 25 (44%) and 6 controls out of 25(24%) were 25 OH vitamin D deficient. This categorical data was assessed by chi-square test, which was not statistically significant (p>0.01)

Inverse relation between serum 25 OH vit D & serum triglyceride level. PEARSONS correlation coefficient between serum 25 OH vit D & serum triglyceride level was -0.3824 and p>0.01.

Direct relation between serum 25 OH vit D & serum HDL cholesterol level. PEARSONS correlation coefficient between serum 25 OH vit D & serum HDL cholesterol level was 0.2266 and p>0.01.

Inverse relation between serum 25 OH vit D & FBS. PEARSONS correlation coefficient between serum 25 OH vit D & FBS is -0.3854 and p<0.01.

Inverse relation between serum 25 OH vitamin D & waist circumference. PEARSONS correlation coefficient between serum 25 OH vit D & waist circumference was -0.54 and p<0.01.

Inverse relation between serum 25 OH vitamin D &BMI. PEARSONS correlation coefficient between serum 25 OH vit D &BMI was -0.56 and p<0.01.

Inverse relation between serum 25 OH vitamin D &Mean Supine B.P. PEARSONS correlation coefficient between serum 25 OH vit D &Mean Supine B.P. was -0.3838 and p<0.01.

Discussion:-

For the last two to three decadesvitamin D deficiency has been associated with obesity and metabolic syndrome. Many studies have been done to establish association between vitamin D levels and occurrence of obesity/metabolic syndrome. According to a publication 22 years back[168]. Body weight increases with higher latitude with lower altitude ad in winter. Different explanations exist for all three associations but vitamin D provides a parsimonious explanation as vitamin D decreases with higher latitude, lower altitude and with winter. In a south Carolina study[169] all obese subjects had vitamin D levels (<2.2 ng/ml) lower than non obese subjects (>8ng/ml). These two studies suggested a inverse relation between vitamin D level and obesity but no causal relationship was explained and no insight into the pathogenesis was made. However, these landmark publications set the stage for further studies to establish this apparent relationship between vitamin D level and obesity.

In present study patients of metabolic syndrome had lower serum 25 OH vitamin D levels than healthy controls the difference was statistically significant at 5% level 44% of patients of metabolic syndrome were vitamin D deficient as compared t 24% of healthy controls. These results were similar to previous studies of **Reis et al[79], Lu et al[80]& Kim et al[81].**

Serum 25 OH vitamin D had inverse correlation with BMI-The correlation coefficient was -0.56 and the associationwas statistically significant at 1% level. This similar to finds of two precious studies done in Norway by **Kamycheva et al[94]&Lagunova et al[95]**.

Serum 25 OH vitamin D had inverse correlation with waist circumference. The correlation coefficient was -0.54 and the association was statistically significant at 1% level. This correlates well with the study done by **Elizondo et al[96]**.

Serum 25 OH vitamin D had inverse correlation with FBS, mean B.P. and serum triglyceride level & a direct correlation with HDL cholesterol. The pearsons correlation coefficient was -0.3854, -0.3838, -0.3824 & 0.2266 respectively. The association of FBS, mean B.P. and serum triglyceride level with serum 25 OH vitamin D level was significant at 1% level which correlates well with the studies of **kamycheva et al[94]&Lagunova et al[95]**. The correlation between HDL cholesterol & serum 25 OH vitamin D level could not reach statistical significance which contrasts with the study of **kamycheva et al[94]&Lagunova et al[95]**, the reason for this contrast could be s small study group of present study (which results in a lower 't' value for a particular correlation coefficient).

Present study suggests that 24% of apparently healthy Indian people have lower than reference serum 25 OH vitamin D level while 40% of patients of metabolic syndrome have vitamin D deficiency, however the study group is too small to draw inference for a vast country like India & these findings need confirmation by large scale study involving various population groups across the country. Whether this incidentally detected deficiency is clinically significant or not, can't be said at this time & weather it should be corrected by vitamin D supplementation is not clear but probably it warrants a low threshold for checking serum vitamin D levels, should the clinical situation suggests vitamin D deficiency. Further prospective studies are needed to make situation clearer.

Serum 25 OH vitamin D levels were significantly low in patients of metabolic syndrome. This observation is consistent with previous studies done elsewhere. Weather it is low 25 OH vitamin D level contributing to metabolic syndrome or is it the other way round is not clear. To establish a cause and effect relationship, further prospective studies are required.

If prospective studies reveals that vitamin D deficiency is causally related to obesity and metabolic syndrome, then it might be possible to reduce the prevalence of obesity and metabolic syndrome globally by vitamin D supplementation.

Summary & conclusion:-

In present study, patients of metabolic syndrome were found to have lower levels of 25 OH vitamin D levels than healthy population (mean serum level 21.34 ng/ml for cases & 26.94 ng/ml for controls, 44% of cases had vitamin deficiency as compared to 24% in controls). Serum 25 OH vitamin D level correlates inversely with BMI, waist circumference, FBS, serum triglyceride levels & mean supine B.P. The correlation of 25 OH vitamin D with waist circumference, BMI, FBS, Mean supine BP and serum triglycerides was statistically significant level. About 24% of healthy apparently healthy Indian population has lower than reference range 25 OH vitamin D level in this study while 40% of patients of metabolic syndrome had vitamin D deficiency the difference was not significant statistically, probably because of small study group.

Because of small study number of subjects included in this study, it is difficult to draw inference for a large population like India. Thus, a large study involving various population groups around the country is required to estimate true prevalence of vitamin D deficiency in India. If further studies reveal similar figures, then it might be possible to diagnose a large number of persons with subclinical vitamin D deficiency. Weather these persons with subclinical vitamin D deficiency will benefit from vitamin D supplement requires interventional prospective studies.

It is thus concluded that vitamin D deficiency is associated with obesity & metabolic syndrome. However, a cause & effect relation cannot be established in this study & whether or not vitamin D supplementation can help reducing weight loss requires large randomized prospective studies.

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