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TO COMPARE PREVALENCE OF VITAMIN D DEFICIENCY IN PATIENTS WITH METABOLIC SYNDROME AND CONTROL POPULATION WITHOUT METABOLIC SYNDOME: A CASE CONTROL STUDY

Medicine

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ABSTRACT

We here by present our case control study done in Noble hospital Hadapsar pune on total 100 patients of age group between 20-50years ,both males and females, with metabolic syndrome(50) and those without metabolic syndrome(50) population ,both IPD and OPD patients coming to noble hospital. In study we found that there is significant vitamin D deficiency in patients with metabolic syndrome population as compared to control population without metabolic syndrome .

KEYWORDS

INTRODUCTION:

There has been increasing interest in recent past about the role of vitamin D in governing non-skeletal functions in the body. Increasing curiosity in subject has resulted in launching number of research activities related to association between vitamin D deficiency and metabolic syndrome. How far this association is strong and to what degree, needs further studies.

It is quite sometime that the physicians have realized that adding vitamin D along with anti-diabetic drugs improve glycemic control in diabetic patients. It has favorable effect on endothelium, peripheral tissues like liver, skeletal muscles, and adipose tissue. Vitamin D receptor is present in many cells of body and thus 1, 25(OH)2D has wide range of biological actions.

Recent studies indicate that, vitamin D deficiency could be risk factor for metabolic syndrome,a highly prevalent health condition in India. If a strong association between these two conditions is proved then, Vitamin D estimation can become a good biological marker to project individual propensity to develop metabolic syndrome.

Conventionally, Vitamin D function is considered for action on skeletal and joint architecture. However in recent times, clinical practice and research has shown multiple non-skeletal function's of vitamin D like,it regulate insulin synthesis and secretion, inhibits renin production, RAAS and angiogenesis[1-2].Vitamin D deficiency leads to adipose tissue pre-maturation and therefore early adipogenesis[3]. Vitamin D also regulates adiposite apoptosis, adipose tissue fat depot location and expansion[4].It also regulates serum triglyceride levels.[5] Vitamin D found to have many more other functions like role in modulation of immune system, leading to beneficial role in prevention and treatment of bronchial asthma and multiple sclerosis. And also happens to be effective role in prevention of colon and breast cancer.It has also found out that ,vitamin D has effective favorable role in autoimmune diseases like rheumatoid arthritis and crohns disease.[6-9].
In Australian adults involving 6537 participants-a prospective study over 5 years, it was reported that; lower vitamin D concentration was associated with increased risk of metabolic syndrome[10]. Majority of studies done in countries outside India showing association of vitamin D deficiency to metabolic syndrome. But in India, there have been not many major studies conducted.

So, our effort in this study is to prove or to disprove a association between the two i.e vitamin D deficiency and metabolic syndrome , which can become a pointer to the further research. More evidence would lead to one step ahead towards a therapeutic use of vitamin D in metabolic syndrome in day to day practice.

No study with control group has been done so far. This is significant lacunae. Therefore, to add credibility, we have taken sample size statistically determined for both diseased and control population.

Hence, this subject was taken up to study prevalence of vitamin D deficiency in patients with metabolic syndrome as per "International Diabetes Foundation (IDF) Criteria "(Harmonising definition) for Metabolic Syndrome and to compare it with control population without metabolic syndrome[11]. Relevant literature has been reviewed and sample size is calculated according to statistical principles.

MATERIAL AND METHODS

STUDY SITE: Noble Hospital, Hadapsar, Pune-411013.

STUDY POPULATION: We included cases of metabolic syndrome and controls without metabolic syndrome from inpatient and outpatient department, satisfying inclusion criteria.

STUDY DESIGN: A CASE CONTROL STUDY .

SAMPLE SIZE: A 50 cases of patients with metabolic syndrome and 48 controls without metabolic syndrome as per inclusion criteria.

STUDY DURATION: DECEMBER 2015 to MARCH 2017.

INCLUSION CRITERIA

- A 48 patients in each group
- Aged between 20 and 50 years
- Belonging to both genders
- Already or recently diagnosed cases of metabolic syndrome as per IDF criteria and
- Control population i.e cases other than metabolic syndrome patients, with similar criteria as above will be included in this study.

EXCLUSION CRITERIA

A study will exclude

- Seriously ill ,
- Chronic bed ridden patient's,
- Organ failure(liver, kidney, heart) patients, and
- People already taking vitamin D

METHODOLOGY:

As we are doing comparative study ,we will define cases and controls on the basis of measurement of following parameters. Systolic blood pressure, diastolic blood pressure, mean arterial pressure, fasting plasma glucose ,fasting triglyceride, IDL levels, HbA1C, waist circumference and serum vitamin D3 levels will be measured.

NULL HYPOTHESIS : There is no association between vitamin d deficiency and metabolic Syndrome

HYPOTHESIS: There is a association between vitamin D deficiency

and components of metabolic syndrome.

VITAMIN D DEFICIENCY: It is defined as serum vitamin D3 concentration less than 20ng/ml [By Electro Chemiluminescence (ECL) TECHNOLOGY.]

VITAMIN D INSUFFICIENCY: It is defined as serum vitamin D3 concentration between 20-30 ng/ml.

NORMAL RANGE =30-70 ng/ml

STATISTICAL METHODS:

The data on categorical variables is shown as n (% of cases) and the data on continuous variables is presented as Mean and Standard deviation (SD) across two study groups. The inter-group comparison of categorical variables is done using Chi-square test / Fisher's exact probability test. The statistical significance of inter-group difference of mean of continuous variables is tested using unpaired OR independent sample 't' test. The underlying normality assumption was tested before subjecting the study variables to 't' test. The entire data is entered and cleaned in MS Excel before it's statistical analysis. All the results are shown in tabular as well as graphical format to visualize the statistically significant difference more clearly.

The p-values less than 0.05 are considered to be statistically significant. All the hypotheses are formulated using two tailed alternatives against each null hypothesis (hypothesis of no difference). The entire data is statistically analyzed using Statistical Package for Social Sciences (SPSS ver 16.0, Inc. Chicago, USA) for MS Windows.

ABOUT THE SOFTWARE USED:

We used software called PS: power and sample size calculation software. It is an interactive program for performing power and sample size calculations. The program runs on the Microsoft Windows operating systems (Windows 95 and later). It can be used for studies with dichotomous (the present study), continuous, or survival response measures. The alternative hypothesis of interest may be specified either in terms of differing response rates, means, or survival times, or in terms of relative risks or odds ratios. Studies with dichotomous or continuous outcomes may involve either a matched or independent study design. The program can determine the sample size needed to detect a specified alternative hypothesis with the required power, the power with which a specific alternative hypothesis can be detected with a given sample size, or the specific

OBSERVATIONS

Table 1) The age distribution of the cases studied between two study groups (n=100).

Age Group (years)	Cases Group (n=50)		Control Group (n=50)		P-value (Cases v Controls)
	n	%	n	%	
<30.0	1	2.0	11	22.0	0.004**
30.0 – 39.0	19	38.0	20	40.0	
40.0 – 50.0	30	60.0	19	38.0	
Total	**50**	**100.0**	**50**	**100.0**	

*Values are n (% of cases). P-value by Chi-Square test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001, NS: Statistically Non-Significant.*

Comments:

1) The mean ± standard deviation of age of the patients from Case Group and Control Group 41.3 ± 5.9 years and 36.4 ± 8.1 years respectively.
2) In both the study groups, the majority of patients were in the age group 30.0 to 50.0 years (Case Group – 51 patients and Control Group – 39 patients,).
3) The age distribution did not differ significantly between two study groups (P-value>0.05).

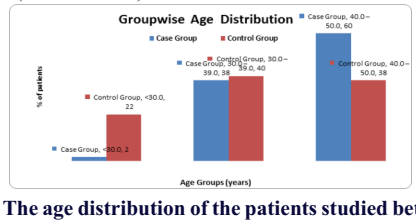

Figure 1) The age distribution of the patients studied between two study groups (n = 100).

Table 2) The sex distribution of the cases studied between two study groups (n=100).

Sex	Cases Group (n=50)		Control Group (n=50)		P-value (Cases v Controls)
	n	%	n	%	
Male	36	72.0	36	72.0	0.999^{NS}
Female	14	28.0	14	28.0	
Total	**50**	**100.0**	**50**	**100.0**	

*Values are n (% of cases). P-value by Chi-Square test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001, NS: Statistically Non-Significant.*

Comments:

1) In both the study groups, the majority of patients were males (Cases Group – 36 patients and Control Group – 36 patients).
2) The sex distribution did not differ significantly between two study groups (P-value>0.05).
3) The male to female sex ratio in both the study groups is 2.57 : 1.00.

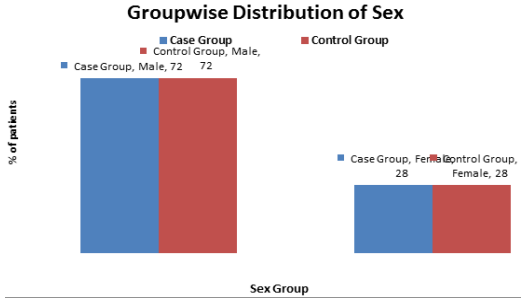

Figure 2) The sex distribution of the cases studied between two study groups (n=100).

Table 3) The distribution of the cases studied according to co-morbidity between two study groups (n=100).

Co-Morbidity	Cases Group (n=50)		Control Group (n=50)	
	n	%	n	%
Nil	19	38.0	50	100.0
T2DM	6	12.0	0	0.0
HTN	4	8.0	0	0.0
T2DM + HTN	5	10.0	0	0.0
Dyslipidemia	1	2.0	0	0.0
T2DM + Dyslipidemia	1	2.0	0	0.0
T2DM + HTN + Dyslipidemia	9	18.0	0	0.0
Hypothyroidism	3	6.0	0	0.0
T2DM + Hypothyroidism	2	4.0	0	0.0
Total	**50**	**100.0**	**50**	**100.0**

Values are n (% of cases).

Comments:

1) In Case Group, 19 patients did not have any co-morbidity, 6 cases (12.0%) had T2DM, 4 cases (8.0%) had HTN, 5 cases (10.0%) had both T2DM + HTN, 1 case (2.0%) had Dyslipidemia, 1 case (2.0%) had T2Dm + Dyslipidemia, 9 cases (18.0%) had T2Dm + HTN + Dyslipidemia, 3 cases (6.0%) had Hypothyrodism and 2 cases (4.0%) had T2Dm = Hypothyroidism.
2) In Control Group of 50 cases studied, none had any co-morbidity.

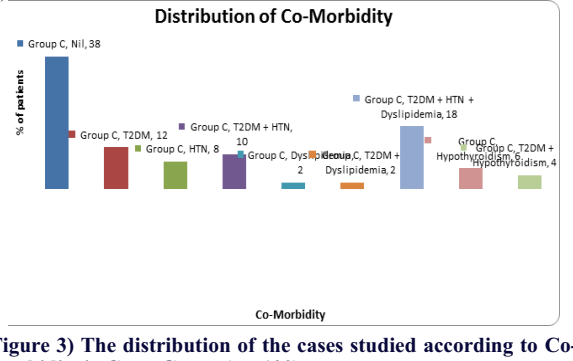

Figure 3) The distribution of the cases studied according to Co-morbidity in Cases Group (n = 100).

Table 4) The distribution of mean height, weight, BMI and waist circumference of the cases studied between two study groups (n=100).

	Cases Group (n=50)		Control Group (n=50)		P-value (Cases v Controls)
Parameters	Mean	SD	Mean	SD	
Height (cm)	164.0	9.1	164.9	5.1	0.519NS
Weight (kg)	76.9	13.3	61.0	6.0	0.001***
BMI (kg/m2)	28.5	4.6	22.4	1.5	0.001***
Waist Circumference (cm)	101.2	12.0	81.5	3.3	0.001***

Values are Mean and standard deviation (SD). P-value by unpaired t test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001, NS: Statistically Non-Significant.

Comments:

1) The distribution of mean height did not differ significantly between two study groups (P-value>0.05).
2) The distribution of mean weight is significantly higher among the Case Group compared to Control Group (P-value<0.001).
3) The distribution of mean BMI is significantly higher among the Case Group compared to Control Group (P-value<0.001).
4) The distribution of mean waist circumference is significantly higher among the Case Group compared to Control Group (P-value<0.001).

Table 5) The inter-group comparison of Mean Vitamin D3 levels (n=100).

Vitamin D3 (ng/mL)	Cases Group (n=50)		Control Group (n=50)		P-value (Cases v Controls)
	Mean	SD	Mean	SD	
Vitamin D3	13.33	7.47	22.83	17.50	0.001***

Values are Mean and Standard Deviation. P-values for Inter-group comparisons by independent sample t test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001, NS: Statistically Non-Significant.

Comments (Inter-Group Comparisons):

1) The distribution of mean Vitamin D3 is significantly higher in Control Group compared to Case Group (P-value<0.001).

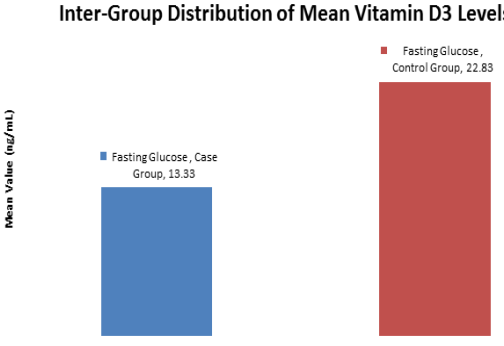

Figure 8) The inter-group comparison of Mean Vitamin D3 levels (n=100).

Table 6) The inter-group comparison of levels of vitamin D3 (n=100).

Vitamin D3 Levels (ng/mL)	Cases Group (n=50)		Control Group (n=50)		P-value (Cases v Controls)
	n	%	n	%	
Less than 5.00	8	16.0	7	14.0	0.010**
5.00 – 10.99	15	30.0	7	14.0	
11.00 – 15.99	7	14.0	10	20.0	
16.00 – 19.99	10	20.0	3	6.0	
20.00 – 29.99	8	16.0	9	18.0	
More than 30.0	2	4.0	14	28.0	
Total	**50**	**100.0**	**50**	**100.0**	

Values are n (% of cases). P-value by Chi-Square test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001, NS: Statistically Non-Significant.

Comments:

1) In Case Group of 50 cases studied, 40 cases (80.0%) had vitamin D3 levels less than 20.0 ng/mL.
2) In Control Group of 50 cases studied, 27 cases (54.0%) had vitamin D3 levels less than 20.0 ng/mL.

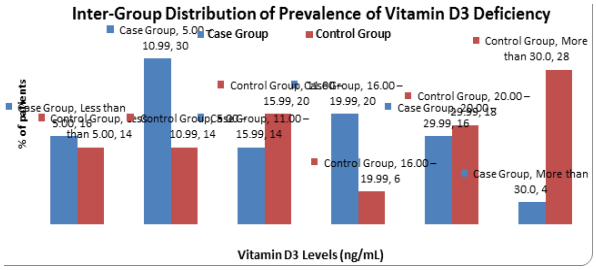

Figure 9) The inter-group comparison of levels of vitamin D3 (n=100).

RESULTS

The age distribution did not differ significantly between two study groups (P-value>0.05).The sex distribution did not differ significantly between two study groups (P-value>0.05).The male to female sex ratio in both the study groups is 2.57 : 1.00.

The distribution of mean Vitamin D3 is significantly higher in Control Group compared to Case Group (P-value<0.001).

In Case Group 80.0% patients had vitamin D3 levels less than 20.0 ng/mL.In Control Group 54.0% patients had vitamin D3 levels less than 20.0 ng/mL.The distribution of mean total cholesterol is significantly higher in Case Group compared to Control Group (P-value<0.05).The distribution of mean triglycerides is significantly higher in Case Group compared to Control Group (P-value<0.01).

The distribution of mean HDL cholesterol is significantly higher in Case Group compared to Control Group (P-value<0.001).The distribution of mean LDL cholesterol is significantly higher in Control Group compared to Case Group (P-value<0.05).

DISCUSSION

As per recent observations in clinical practice and available studies, we came to the point, that a lot of attention is needed over the association of various non skeletal functions and syndromes with vitamin D deficiency. Available studies suggest that Vitamin D deficiency might play a role in metabolic syndrome and its components. After completing the study we found that Vitamin D deficiency is more prevalent in metabolic syndrome group as compared to the control population.

In the study we have taken 100 participants (50 cases and 50 controls), both male and female of socio-economically active age group of 20-50 years in order to avoid any confounding bias. Feature of this study is a young productive age group, who are found to have low vitamin D levels to a large extent, irrespective of whether they have metabolic syndrome or not. To be more precise, metabolic syndrome group has 80% Vitamin D deficiency as compared to 54% in the control group. It is significant to note that 54% of apparently healthy young population (control group) is deficient in vitamin D.Average serum vitamin D3 level in the control group is only 22.83ng/ml. By definition, it can be called as insufficiency of vitamin D levels. Upon this finding one wonders, whether one has to redefine the actual set normal values of Vitamin D levels.

In our study cases had significantly high levels of triglycerides, total cholesterols and HDL as compared to control group. But control population had more LDL cholesterol as compared to cases.Similar studies carried out in other countries, although they did not have any control group, are cross sectional studies. Their results also indicate that Vitamin D deficiency prevalence in their general population varies between 38.4% to 66%. So these findings are consistent with our control group results. Thus this phenomenon of Vitamin D deficiency, with or without manifestations, seems to be a global health issue.

A COMPARATIVE ANALYSIS WITH AVAILABLE STUDIES

SR.NO	STUDY	COUNTRY	POPULATION	NO.OF POPULATIN	SEX RATIO OF PARTICIPANTS(MALE/FEMALES)	TYPE OF STUDY	PREVALENCE
1	YIN et al. (2012)	CHINA	URBAN	601	448/153 (35-60YRS OLD)	CROSS-SECTIONAL STUDY	66%
2	VASMEHJANI et al (2014)	IRAN	URBAN	156	0/156 (28-76YRS OLD)	CROSS-SECTIONAL STUDY	54.5%
3	CHON et al (2013)	KOREA	URBAN	4364	0/4364 (POSTMEN OPAUSAL	CROSS-SECTIONAL STUDY	62.1%
4	MING MOY et al(2011)	MALAYSIA	URBAN	380	160/220 (MEAN AGE OF 48.55YRS)	CROSS-SECTIONAL STUDY	38.4%
5	NEIL THOMAS et al. LURIC STUDY(2012)	GERMANY	URBAN	1801	1204/597 (53-71YRS)	PROSPECTIVE COHORT STUDY	65%
6	CURRENT STUDY	INDIA (PUNE)	URBAN (HOPSITAL)	50/50	(20-50YRS)	Case control STUDY	80%/54 %

YIN et al conducted cross-sectional study on 601 urban Chinese population in year 2012 showing 66% prevalence of vitamin D deficiency ,which are consistent with our study[16].

VASMEHJANI et al have done cross-sectional study on 156 Iranian patients (womens) in 2014 showing 54.5% prevalence of vitamin D deficiency ,which is comparable to our study[15].

CHON et al has done cross-sectional study on 4364 postmenopausal womens in year 2013 in Korea showing 62% prevalence of vitamin D deficiency which is consistent with our study[14].

MING MOY et al has done cross-sectional study on 380 urban Malaysian population in year 2011 ,showing 38.4% prevalence of vitamin D deficiency which is less as compared to our study[13].

NEIL THOMAS et al have done prospective cohort study on 1801 urban German population in year 2012 showing 65% prevalence iof vitamin D deficiency which iss consistent with our study[12].

Difference in results from different studies is may be due to other factors affecting lipid level like diet, exercise, sun exposure and genetic predisposition, which were not considered in present study.So, vitamin D deficiency in patients with metabolic syndrome is established,therefore it should be identified at earliest and treated effectively in all metabolic syndrome patients, which will improve overall prognosis.The main redeeming feature of our study is unique, in the sense that we have 2 groups – cases (metabolic syndrome) and controls (without metabolic syndrome). Such a type of study has not been found to be conducted elsewhere in the world.

However such a case control study on a larger population of a big sample size becomes essential to draw any definitive conclusion, which will reveal how much really in percentage vitamin D deficiency prevails in the community. It also will reveal other determinants and variables of vitamin D deficiency, like for example- differences in race, age group, life style, lack of sun exposure and diet.

It is worthwhile to conduct a large population study with a control group to assess whether vitamin D deficiency is really a strong determinant of metabolic syndrome in an individual person. If this strong association is proved over a period of time then vitamin D estimation can be considered as a good biological marker to project individual propensity or probability to development of metabolic syndrome.

It can also put vitamin D as an adjuvant therapy to a variety of components of metabolic syndrome, for example- most of our physicians like to add vitamin D supplements in patients with diabetes mellitus. According to medical literature and text books it has been recommended to be useful in allergic conditions like bronchial asthma, multiple sclerosis and most of the other disorders like Alzheimer's disease.

More research and studies on a larger population is essential on this subject because we should not be in enthusiasm to neglect on insufficient data and recommend a vitamin D supplementation for every patient of metabolic syndrome.

The result of present case control study on prevalence of vitamin D deficiency in patients with metabolic syndrome and control population without metabolic syndrome showed that,there is significant vitamin D deficiency in patients with metabolic syndrome(cases) as compared to control population without metabolic syndrome.Cases with metabolic syndrome found to have 80% prevalence of vitamin D deficiency as compared to 50% in control population.

SUMMARY & CONCLUSIONS

In the recent past, there has been an increased interest in vitamin D associated syndromes. Today no conclusive pointer between vitamin D deficiency and metabolic syndrome has been established, even though our study shows otherwise.It was found that, there is significant vitamin D deficiency in patients with metabolic syndrome as compared to control population without metabolic syndrome.

Mean vitamin D levels were low in cases with metabolic syndrome as compared to control population without metabolic syndrome.It is important to ascertain, how strong is the association between vitamin D deficiency and metabolic syndrome and whether we can recommend vitamin D as an adjuvant therapy in metabolic syndrome.

Conventionally Vitamin D function has been associated with skeletal and joint architecture. However many metabolic conditions can be indirectly attributed to Vitamin D deficiency. Thus more research in the future will reveal the degree of strength of our hypothesis or will dismiss our contention.As on today we cannot strongly recommend on the available evidence, "Vitamin D as an adjuvant or an empirical therapy for all cases of metabolic syndrome"

LIMITATIONS

Study was conducted on smaller group of patients, so results cannot be generalized even though our results were statistically significant .Other risk factors for vitamin D deficiency like diet, lack of exercise, lack of sun exposure, skin colour complexion ,location in relation to altitude were not considered in this study.

RECOMMANDATIONS

As results of this study were significant, similar case control study can be conducted on larger group metabolic syndrome patients and control population. As high prevalence of vitamin D deficiency was seen in metabolic syndrome patients in present study, it is recommended to measure vitamin D levels in each of metabolic syndrome patient.Patients with metabolic syndrome are at high risk for cardiovascular diseases & hence treatment for deficient vitamin D levels should be initiated in all metabolic syndrome patients and such patients should be periodically screened for any cardiovascular pathology .

Many more cohort studies, Randomised control trials with larger sample size are needed to establish causal relationship.Normal or abnormal values of vitamin D need to be redefined.

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