

“A Study of Vitamin - D Levels in Metabolic Syndrome And its Association with Complications”

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Abstract: The discovery of pleiotropic functions of Vitamin D has led to several studies associating the sunshine vitamin and several diseases. It is the anti inflammatory and immunomodulatory role of the vitamin that links it with metabolic syndrome. It also has anti-proliferative, anti-angiogenesis, anti-thrombotic functions. In our study we are interested in studying the association between Vitamin D levels and components of metabolic syndrome and its complications like stroke and myocardial infarction. It was interesting to find significant association between low levels of vitamin D and components of metabolic syndrome like hypertension, waist circumference, duration of diabetes, triglyceride levels and total cholesterol levels. There was also inverse relationship between vitamin D and vascular complications of metabolic syndrome like myocardial infarction and stroke. We also found that Vitamin D was not significantly associated with fasting blood glucose levels, HDL and LDL cholesterol levels. We find it would be justified to analyse vitamin D insufficiency in patients with metabolic syndrome and supplementation with this vitamin might be of beneficial value in preventing some of the complications of the disease. But the protective and preventive role of Vitamin D in this disease needs further trials to prove its efficiency.

Keywords: Vitamin D, Metabolic Syndrome.

I. Introduction

Metabolic syndrome consists of a constellation of cardio metabolic disease risk factors. It has been recognized as a global epidemic. Metabolic syndrome is characterised by hyperglycemia especially insulin resistance, central abdominal obesity, dyslipidemia and hypertension. The clinical importance of metabolic syndrome is that it identifies the people at increased long term risk of cardiovascular disease and diabetes mellitus type II. Vitamin D insufficiency has become a common health problem, often unrecognized and untreated. Recently vitamin D, the sunshine vitamin have been reported to be associated with various non skeletal disorders including diabete mellitus, cardiovascular disease and systemic hypertension. Recent research have also linked vitamin D with auto immune diseases, depression and certain types of cancers. The studies have also emphasized on hypovitaminosis D with metabolic syndrome. Metabolic syndrome is a state of low grade systemic inflammation. The immunomodulatory effects and anti inflammatory action of vitamin D links its role with metabolic syndrome. This study aims to analyse the 25-hydroxy vitamin D status in metabolic syndrome patients and also to correlate its level with individual components and complications of metabolic syndrome.

II. Methodology

2.1. Source of data:

Patients diagnosed with metabolic syndrome admitted at Coimbatore medical college hospital over a period of 1 year between August 2014 – July 2015.

2.2. Study design:

Cross sectional study

2.3. Sample size:

100 patients with metabolic syndrome were selected for the study

2.4. Study population:

100 patients with metabolic syndrome patients admitted to Coimbatore medical college hospital during the study period were randomly selected as per inclusion and exclusion criteria. Out of these 62 were men and 38 were women. Written informed consent was obtained from each patient.

2.5. Inclusion criteria:

2.5.1. Patients with metabolic syndrome defined using the national cholesterol education programme, adult treatment panel III (NCEP : ATP III 2001) With three or more of following components

- Central obesity : Waist circumference > 102 cm(male), >88cm(female)
- Hypertriglyceridemia: Triglycerides >150mg/dl or on specific medication
- Low HDL cholesterol: <40mg/dl for men and <50mg/dl for women or specific medication
- Hypertension: Blood pressure > 130mmhg systolic or > 85 mmhg diastolic or specific medication.
- Fasting plasma glucose > 100mg/dl or specific medication or previously diagnosed type II diabetes mellitus

2.5.2 Age above 18 years

2.6. Exclusion criteria:

- Patients with chronic renal failure
- Patients with liver failure
- Patients on treatment with vitamin D
- Malabsorption
- Malignancy
- Infections

2.6. Data collection:

The 100 metabolic syndrome patients were included in the study. Detailed history regarding duration of diabetes, hypertension and complications were recorded. A thorough physical examination such as anthropometry, vitals and systemic examination was conducted. The height and weight were recorded and BMI was calculated based on the formula.

$$BMI = \frac{\text{Weight in kg}}{\text{Height in m}^2}$$

BMI in the range of < 18.5 kg/m² was considered as underweight, 18.5-24.9 was considered as normal, 25-29.9 as overweight, >30 as obese. The waist circumference was measured using a standard measuring tape in cm. waist circumference of > 102 cm in males and > 88 cm in females was considered as abnormal. Investigations such as fasting blood sugar, lipid profile (Triglycerides, HDL, Total cholesterol) were done and findings were recorded.

Serum vitamin D levels were measured and interpreted as follows < 20 ng/ml – deficient, 21-29 ng/ml – insufficient and 30 ng/ml – sufficient

2.7. Statistical method

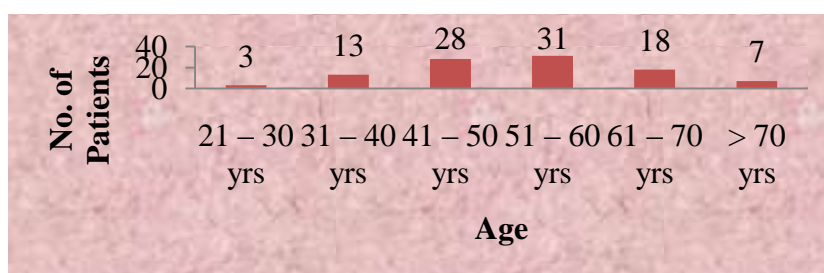
Statistical method analysis was done using chi square test and ANOVA test. Statistical results were considered significant at p < 0.05

III. Results

Table No : 1 - Age Distribution

21 – 30 yrs	3	3%
31 – 40 yrs	13	13%
41 – 50 yrs	28	28%
51 – 60 yrs	31	31%
61 – 70 yrs	18	18%
> 70 yrs	7	7%
Total	100	100%

Chart No : 1 - Age Distribution



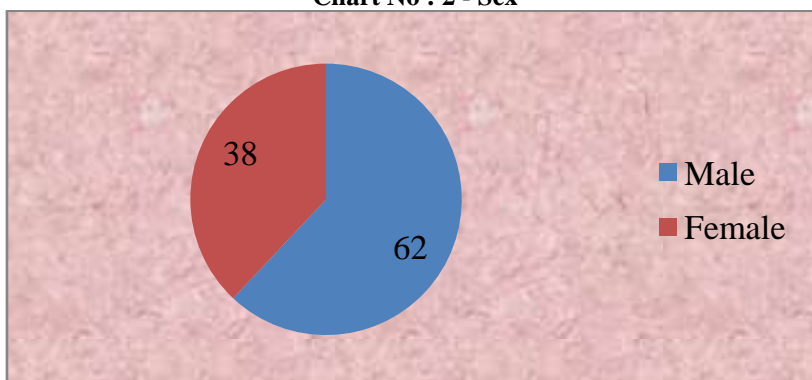
Patients age ranged from 21-80 years. Maximum number of cases were in the age group of 51-60 years (31%) and 28% of cases were in the age group of 41-50 years.

Inference : Majority of patients were in the 5th and 6th decade.

Table No : 2 - Sex

Sex	No. of Patients	%
Male	62	62%
Female	38	38%
Total	100	100%

Chart No : 2 - Sex

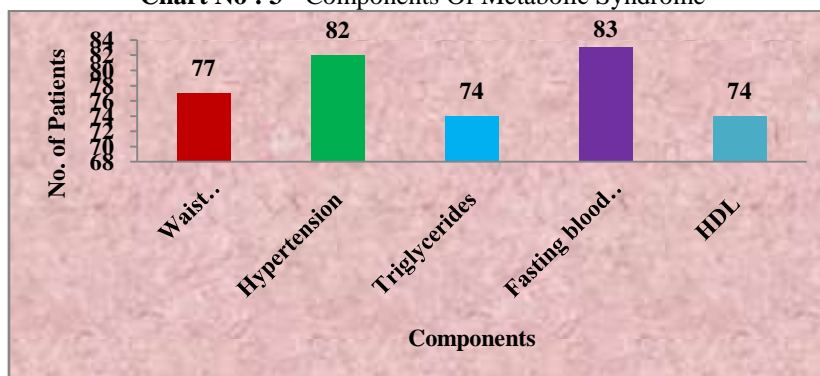


Out of 100 patients, 62 (62%) were males and 38 patients (38%) were females .

Table No : 3 - Components Of Metabolic Syndrome

Waist Circumference	77	77%
Hypertension	82	82%
Triglycerides > 150 mg/dl	74	74%
Fasting blood sugar	83	73%
HDL	74	74%
Total	100	100%

Chart No : 3 - Components Of Metabolic Syndrome

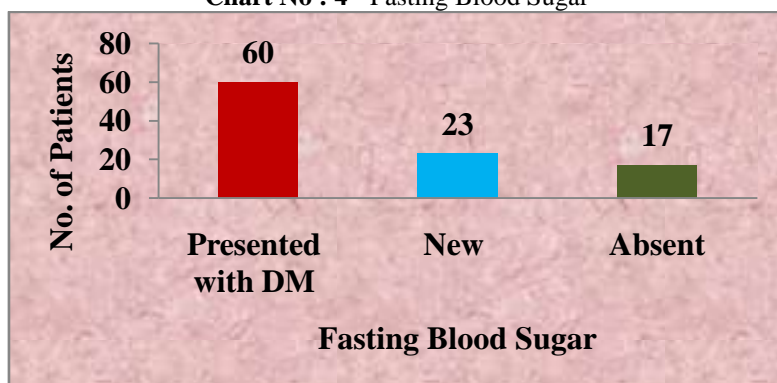


The commonest component of metabolic syndrome was observed to be fasting blood sugar abnormality(83%) followed by hypertension (82%). Waist circumference (77%), low HDL (74%), triglycerides (74%).

Table No : 4 - Fasting Blood Sugar

Presented with DM	60	60%
New	23	23%
Absent	17	17%
Total	100	100%

Chart No : 4 - Fasting Blood Sugar

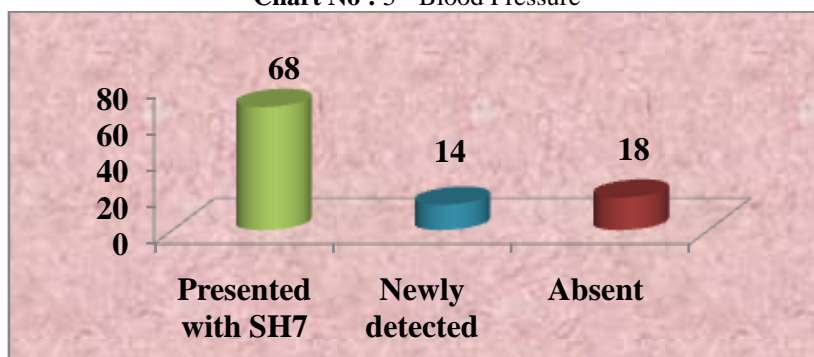


60% of the patients were known diabetic, 23% of patients had fasting blood sugar abnormality and 17% had normal fasting blood sugar levels.

Table No : 5 - Blood Pressure

Presented with SHT	68	68%
Newly detected	14	14%
Absent	18	18%
Total	100	100%

Chart No : 5 - Blood Pressure

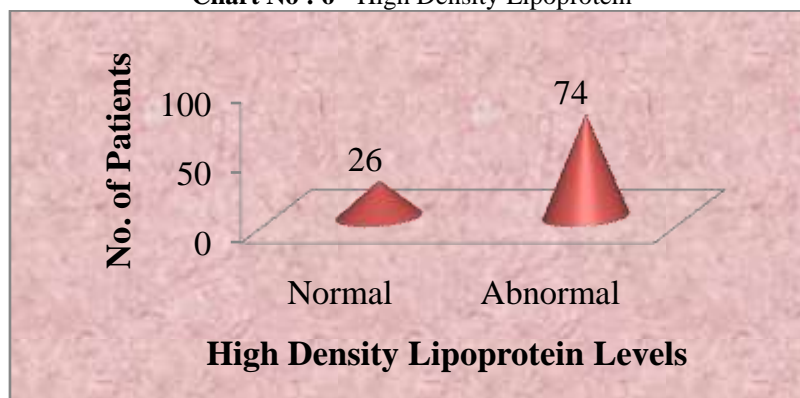


68% of the patients were known hypertensive, 14% were newly detected and 18% of patients had normal blood pressure levels.

Table No : 6 - High Density Lipoprotein

Normal	26	26%
Abnormal	74	74%
Total	100	100%

Chart No : 6 - High Density Lipoprotein

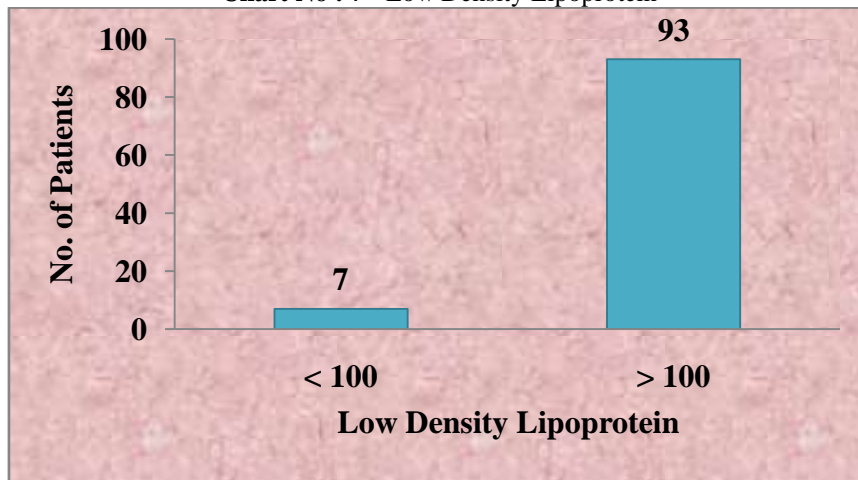


74% of patients had abnormal High Density Lipoprotein cholesterol levels and 26% of patients had normal High Density Lipoprotein levels.

Table No : 7 - Low Density Lipoprotein

< 100	7	7%
> 100	93	93%
Total	100	100%

Chart No : 7 - Low Density Lipoprotein

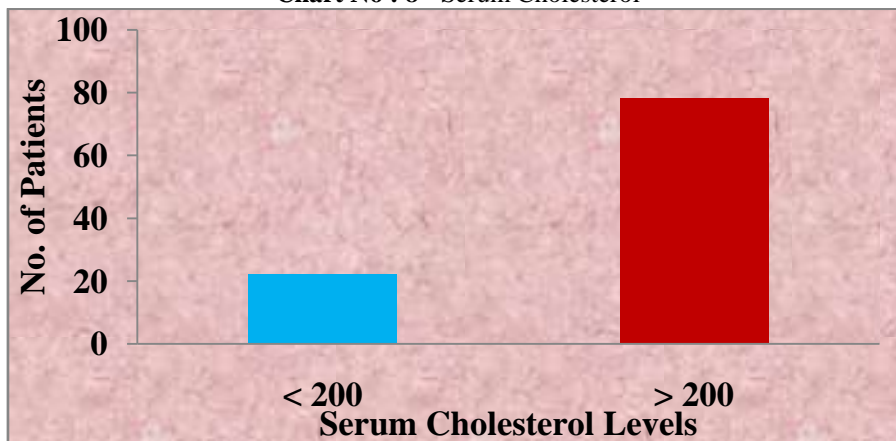


93% of patients had abnormal Low Density Lipoprotein levels > 100 mg/dl and 7% of patients had normal Low Density Lipoprotein levels.

Table No : 8 - Serum Cholesterol

< 200	22	22%
>200	78	78%
Total	100	100%

Chart No : 8 - Serum Cholesterol

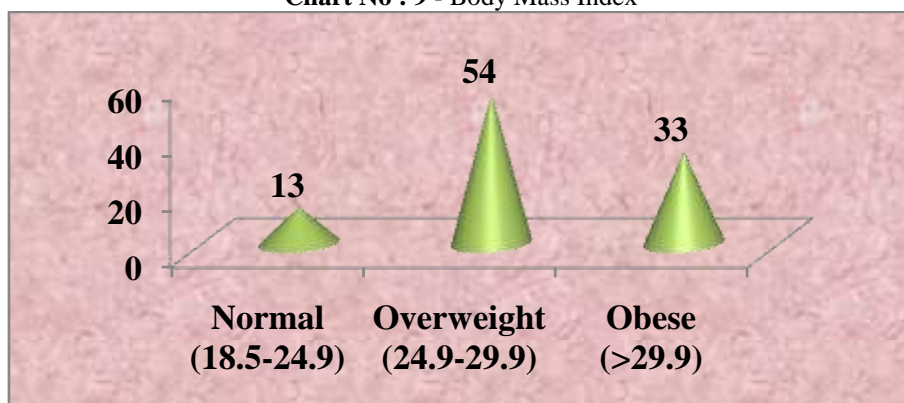


78% of patients had total cholesterol more than 200 mg/dl and 22% had < 200 mg/dl.

Table No : 9 - Body Mass Index

Normal (18.5-24.9)	13	13%
Overweight (24.9-29.9)	54	54%
Obese (>29.9)	33	33%
Total	100	100%

Chart No : 9 - Body Mass Index

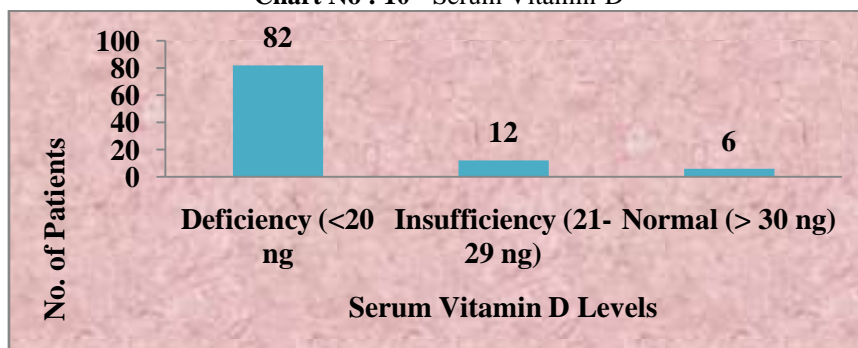


13% of patients were of normal weight, 54% of them were overweight and 33% were obese.

Table No : 10 - Serum Vitamin-D

Deficiency (<20)	82	82.0%
Insufficiency (21-29)	12	12.0%
Normal (> 30)	6	6.0%
Total	100	100%

Chart No : 10 - Serum Vitamin-D

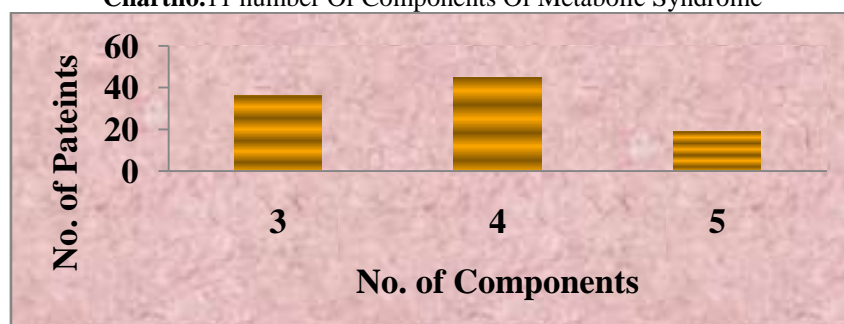


82% of patients had deficient (<20 ng/dl) vitamin D levels, 12% of patients had insufficient levels (21-29 ng/dl) and 6% of patients had sufficient (> 30 ng/dl) levels of vitamin D.

Table no.11 Number of components of metabolic syndrome

3	35	35%
4	46	46%
5	19	19%
Total	100	100%

Chartno.11 number Of Components Of Metabolic Syndrome

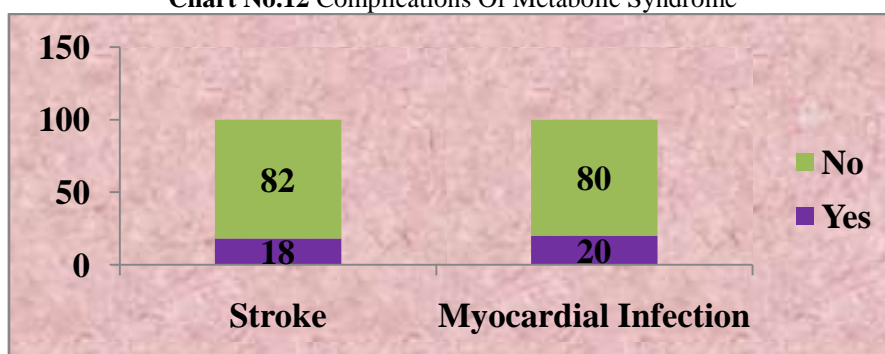


In the present study, 46% patients had metabolic syndrome with four components and 35% had 3 components and 19% had 5 components of metabolic syndrome.

Table No.12 Complications Of Metabolic Syndrome

Complications		No. of Patients	%
Stroke	Yes	18	18%
	No	82	82%
Myocardial Infection	Yes	20	20%
	No	80	80%

Chart No.12 Complications Of Metabolic Syndrome



In the present study, 18 patients had stroke and 20 patients had myocardial infarction.

Table:13 Correlation Of Vitamin D Levels With Age

Age		VITAMIN D		
		Mean	S.D	No.
Age	21-30 YRS	22.33	6.03	3
	31-40 YRS	17.92	7.16	13
	41-50 YRS	17.18	5.81	28
	51-60 YRS	15.00	5.76	31
	61-70 YRS	12.61	5.74	18
	71-80 YRS	15.43	7.46	7
Total		15.81	6.30	100

Anova For Vitamin D

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	443.701	5	88.740	2.393	<0.05
Within Groups	3,485.689	94	37.082		
Total	3,929.390	99			

We observed vitamin D levels were less in age group of 5th, 6th & 7th decade. ANOVA test shows that there is significant difference in the mean vitamin D levels with age groups. There is significant decrease in vitamin D levels with increasing age.

Table : 14 - Correlation Of Vitamin D With Gender

		VITAMIN D		
		Mean	S.D	No.
Gender	Male	16.48	6.65	62
	Female	14.71	5.59	38
Total		15.81	6.30	100

t-test for Equality of Means

t	df	Sig.
1.372	98	Ns

The mean vitamin D levels among men was 16.48 ng/ml and among women was 14.71. We observed that there is no significant difference in vitamin D levels among men and women in our study.

Table : 15 - Bmi

BMI		VITAMIN D						TOTAL	
		Deficient (<=20)		Insufficient (21-29)		Sufficient (>=30)		No.	%
		No.	%	No.	%	No.	%		
BMI	Normal (18.5-24.9)	7	53.8	4	30.8	2	15.4	13	100.0
	Overweight (24.9-29.9)	45	83.3	7	13.0	2	3.7	54	100.0
	Obese (>29.9)	30	90.9	1	3.0	2	6.1	33	100.0
TOTAL		82	82.0	12	12.0	6	6.0	100	100.0

Chi-Square Test

	Value	df	Sig.	P value
Chi-Square	10.041	4	.040	P<0.05

Table no : 16

Correlation of vitamin d levels with duration of diabetes mellitus

		VITAMIN D		
		Mean	S.D	No.
Diabetes mellitus-Duration	1-5 YRS	17.29	6.78	21
	6-10 YRS	14.00	5.35	27
	>10 YRS	12.42	3.80	12
Total		14.83	5.87	60

Anova For Vitamin D

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	215.131	2	107.565	3.367	<0.05
Within Groups	1,821.202	57	31.951		
Total	2,036.333	59			

ANOVA test shows that there is significant decrease in vitamin D levels with increase in duration of diabetes mellitus. (p<0.05)

Table No : 17 Correlation Of Vitamin D With Duration Of Hypertension

		VITAMIN D		
		Mean	S.D	No.
SYSTEMIC HYPERTENSION-Duration	1-5 YRS	16.13	6.11	40
	6-10 YRS	13.76	5.47	21
	>10 YRS	14.00	6.81	7
Total		15.18	6.01	68

Anova For Vitamin D

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	87.698	2	43.849	1.222	Ns
Within Groups	2,332.185	65	35.880		
Total	2,419.882	67			

ANOVA test shows there is no significant association between vitamin D levels and duration of hypertension.

Table no : 18 correlation of vitamin d levels with waist circumference:

		VITAMIN D						TOTAL	
		Deficient (<=20)		Insufficient (21-29)		Sufficient (>=30)		No.	%
		No.	%	No.	%	No.	%		
WC	Abnormal	65	84.4	10	13.0	2	2.6	77	100.0
	Normal	17	73.9	2	8.7	4	17.4	23	100.0
TOTAL		82	82.0	12	12.0	6	6.0	100	100.0

Chi-Square Test

	Value	df	Sig.
Chi-Square	6.970	2	<0.05

When levels of vitamin D were compared with waist circumference, most of the patients with abnormal waist circumference had deficient levels(84.4%),10 patients(13%) had insufficient levels and only 2 patients(2.6%) had sufficient levels.(p<0.05,significant)

Table No : 19 Correlation Of Vitamin D Levels With Fasting Blood Sugar

		VITAMIN D						TOTAL	
		Deficient (<=20)		Insufficient (21-29)		Sufficient (>=30)		No.	%
		No.	%	No.	%	No.	%		
FBS	Abnormal (>100)	71	85.5	6	8.4	5	6.0	83	100.0

	Normal (<=100)	11	64.7	6	29.4	1	5.9	17	100.0
TOTAL		82	82.0	12	12.0	6	6.0	100	100.0

Chi-Square Test

	Value	df	Sig.
Chi-Square	5.922	2	Ns

When levels of vitamin D were compared with, Fasting blood sugar, most of the patients with fasting sugar abnormality had deficient levels(85.5%),6 patients(8.4%) had insufficient levels and only 5 patients(6%) had sufficient levels.(p>0.05,insignificant)

Table no : 20 correlation of vitamin d levels with elevated blood pressure:

		VITAMIN D						TOTAL	
		Deficient (<=20)		Insufficient (21-29)		Sufficient (>=30)		No.	%
		No.	%	No.	%	No.	%		
Systemic Hypertension	Abnormal (>100)	71	86.6	6	7.3	5	6.1	82	100.0
	Normal (<=100)	11	61.1	6	33.3	1	5.6	18	100.0
TOTAL		82	82.0	12	12.0	6	6.0	100	100.0

Chi-Square Test

	Value	df	Sig.
Chi-Square	9.501	2	<0.01

When levels of vitamin D were compared with, blood pressure, most of the patients with elevated blood pressure had deficient levels(86.6%),6 patients(7.3%) had insufficient levels and only 5 patients(6.1%) had sufficient levels.(p<0.01,significant)

Table no : 21 correlation of vitamin d levels with triglycerides:

		VITAMIN D						TOTAL	
		Deficient (<=20)		Insufficient (21-29)		Sufficient (>=30)		No.	%
		No.	%	No.	%	No.	%		
TGL	Abnormal (>=150)	65	87.8	5	6.8	4	5.4	74	100.0
	Normal (<150)	17	65.4	7	26.9	2	7.7	26	100.0
TOTAL		82	82.0	12	12.0	6	6.0	100	100.0

Chi-Square Tests

	Value	df	Sig.	P value
Pearson Chi-Square	7.871 ^a	2	.020	P < 0.05

Out of 82 patients with deficient vitamin D Levels,65 patients (87.8%) had >150 mg/dl,17 patients (65.4%) had <150 mg/dl. Among 12 patients with insufficient levels,5(6.8%) had abnormal triglycerides and7 (26.9%) had normal triglyceride levels. Out of 6 patients with sufficient levels,4 patients(5.4%) had triglycerides >150 mg/dl and2 (7.7%) had levels <150 mg/dl.(p<0.05).

Table No : 22 Correlation Of Vitamin D Levels With Hdl

		VITAMIN D						TOTAL	
		Deficient (<=20)		Insufficient (21-29)		Sufficient (>=30)		No.	%
		No.	%	No.	%	No.	%		
HDL	Abnormal	59	79.7	10	13.5	5	6.8	74	100.0
	Normal	23	88.5	2	7.7	1	3.8	26	100.0
TOTAL		82	82.0	12	12.0	6	6.0	100	100.0

Chi-Square Test

	Value	df	Sig.	P value
Chi-Square	.994	2	Ns	P > 0.05

Out of 82 patients with deficient vitamin D Levels,59 patients (79.7%) had abnormal HDL values,23 patients (88.5%) had normal levels. Among 12 patients with insufficient levels,10(13.5%) had abnormal HDL

and 2 (7.7%) had normal HDL level. Out of 6 patients with sufficient levels, 5 patients (6.8%) had abnormal HDL and 1 (3.8%) had normal HDL. ($p > 0.05$).

Table No : 23 Correlation Of Vitamin D Levels With Ldl

		VITAMIN D						TOTAL	
		Deficient (<=20)		Insufficient (21-29)		Sufficient (>=30)		No.	%
		No.	%	No.	%	No.	%		
LDL	Abnormal (>=100)	76	81.7	11	11.8	6	6.5	93	100.0
	Normal (<100)	6	85.7	1	14.3			7	100.0
TOTAL		82	82.0	12	12.0	6	6.0	100	100.0

chi-square test

	Value	df	Sig.
Chi-Square	.497	2	Ns

Out of 82 patients with deficient vitamin D Levels, 76 patients (81.7%) had abnormal LDL values, 6 patients (85.7%) had normal levels. Among 12 patients with insufficient levels, 11 (11.8%) had abnormal LDL and 1 (14.3%) had normal LDL level. Out of 6 patients with sufficient levels, all 6 had patients (6.5%) had abnormal HDL. ($p > 0.05$).

Table No : 24 Correlation Of Vitamin D Levels With Total Cholesterol

		VITAMIN D						TOTAL	
		Deficient (<=20)		Insufficient (21-29)		Sufficient (>=30)		No.	%
		No.	%	No.	%	No.	%		
TC	Abnormal (>=200)	67	85.9	6	7.7	5	6.4	78	100.0
	Normal (<200)	15	68.2	6	27.3	1	4.5	22	100.0
TOTAL		82	82.0	12	12.0	6	6.0	100	100.0

Chi-Square Test

	Value	df	Sig.	P value
Chi-Square	6.239 ^a	2	*	P < 0.05

Out of 82 patients with deficient vitamin D Levels, 67 patients (85.9%) had abnormal total cholesterol values, 15 patients (68.2%) had normal levels. Among 12 patients with insufficient levels, 6 (7.7%) had abnormal total cholesterol and 6 (27.3%) had normal total cholesterol level. Out of 6 patients with sufficient levels, 5 patients (6.4%) had abnormal HDL and 1 (4.5%) had normal levels. ($p < 0.05$).

Table No : 25 Correlation Of Vitamin D Levels With Number Of Components

		VITAMIN D						TOTAL	
		Deficient (<=20)		Insufficient (21-29)		Sufficient (>=30)		No.	%
		No.	%	No.	%	No.	%		
No. of comp	3.00	20	57.1	10	28.6	5	14.3	35	100.0
	4.00	43	93.5	2	4.3	1	2.2	46	100.0
	5.00	19	100.0					19	100.0
TOTAL		82	82.0	12	12.0	6	6.0	100	100.0

Chi-Square Test

	Value	df	Sig.	P value
Chi-Square	22.928 ^a	4	**	P < 0.01

In patients with 3 components of metabolic syndrome, 20 (57.1%) patients had deficient vitamin D levels, 10 (28.6%) had insufficient levels and 5 (14.3%) had sufficient levels. In patients with 4 components of metabolic syndrome, 43 (93.5%) patients had deficient vitamin D levels, 2 (4.3%) had insufficient levels and 1 (2.2%) had sufficient levels. In patients with all 5 components of metabolic syndrome (19) all had deficient levels. ($p < 0.01$)

Table No : 26 Correlation Of Vitamin D Levels With Stroke

		VITAMIN D		
		Mean	S.D	No.
Stroke	No	17.01	6.28	82
	Yes	10.33	2.11	18
Total		15.81	6.30	100

t-test for Equality of Means

t	df	Sig.
4.441	98	<0.01

T test shows there is significant decrease in vitamin D levels in patients who developed stroke when compared to those without stroke.(p<0.01)

Table no : 27correlation of vitamin d levels with myocardial infarction:

		VITAMIN D		
		Mean	S.D	No.
MI	No	16.98	6.44	80
	Yes	11.15	2.37	20
Total		15.81	6.30	100

t-test for Equality of Means

T	df	Sig.
3.964	98	<0.05

IV. Discussion

4.1. Vitamin d and its functions :

Vitamin D was first identified and characterized in 1923 by Goldbatt and Soames [1]. There are five forms of vitamin D. (D1-D5). The major form vitamin D2 (ergocalciferol) is obtained from ergosterol. The sources of vitaminD2 are plants and invertebrates which synthesis vitaminD2 in responses to sunlight. They are not synthesized by vertebrates. Vitamin D3 (cholecalciferol) is obtained from dehydrocholesterol. It is synthesized in skin when 7-Dehydrocholesterol reacts with ultraviolet (UV) radiation to form vitamin D3.In humans the major source, about 80-90% of vitamin D comes from skin on exposure to sunlight and the dietary source of vitamin D is only 10-20% [2]. Vitamin D performs wide range of biological functions in the body through Vitamin D receptors which are expressed in tissues including skeletal muscles, vascular smooth muscles, osteoblasts, endothelium, cardiomyocytes, activated macrophages and pancreatic beta cells. Vitamin D regulates calcium and phosphorous homeostasis. It enhances calcium and phosphorus absorption in the gut and promotes bone mobilization [3]. In addition to calcium homeostasis, VDR also stimulate insulin production and modulate immune function [4] including inhibiting angiogenesis, inhibiting renin production and stimulating macrophage eathelicidin production [5].

Serum concentration of 25 –hydroxy vitamin D reflects the vitamin D status and has longer half life than calcitriol. 1, 25-OH vitamin D levels in the circulation may be normal or elevated in vitamin D deficient patients and hence it should not be used to determine vitamin D status .IOM (Institute Of Medicine) and the Endocrine society have defined vitamin D deficiency as 25-hydroxy vitamin D less than 20 ng/ml [6,7].Vitamin D insufficiency has been defined as 25-hydroxy vitamin D of 21-29 ng/ml and concentrations of >30 ng/ml is considered to be sufficient. Excess vitamin D concentration is also undesirable [8]. The upper limit of vitamin D is about 80 ng/ml. Serum vitamin D concentration of > 200 ng/ml is considered potentially toxic [9].Vitamin D can be measured using the following techniques.

1. Immunoassay technique-Radioimmunoassay (RIA) and Chemiluminescence immunoassay
2. Chromatography techniques-High pressure liquid chromatography (HPLC) and liquid chromatography coupled with tandem mass spectrometry (LC- MS).

Vitamin D insufficiency occurs because of inadequate exposure to sunlight. It is common among elderly, hospitalized and institutionalized persons . In addition to this, other factors related to vitamin D deficiency include dark skin colour, increased distance from equator, winter season, clothing, sunscreen, air pollution, smoking, malabsorption, obesity, diseases of renal, liver and some drugs [10]. Vitamin D deficiency in children causes rickets and growth retardation. In adults, it will precipitate osteopenia and osteoporosis. In recent decades, numerous studies have demonstrated the association between vitamin D deficiency with many diseases including diabetes mellitus, systemic hypertension, dyslipidemia, cerebrovascular diseases, cardiovascular disorders, metabolicsyndrome, cancer, infections, chronic kidney disease, tuberculosis and autoimmune disorders [11].

The American academy of paediatrics recommends 400 IU as minimum requirement of vitamin D for all infants and children. The National osteoporosis foundation recommends 400 IU -800 IU daily for adults under the age of 50 years and 800-1000 IU daily for adults older than 50 years. The North American menopause society recommends 700-800 IU daily for women at risk of deficiency due to low sun exposure. Guidelines from the osteoporosis society of Canada recommended vitamin D 400 IU per day for people upto the age of 50 years and 800 IU/day for people over 50 years [12].

Vitamin D is sequestered in subcutaneous fat and hence in obese persons vitamin D stores are less available to become biologically active. Thus there is decreased bioavailability of vitamin D in obesity. Besides this, obese individuals may have sedentary life style and less outdoor activities and thus impaired skin production of vitamin D [13]. Vitamin D deficiency is associated with stroke and the size of infarct. Neuro protective role of vitamin D also has been reported [14]. Vitamin D is associated with several other diseases like peripheral vascular disease, renal diseases, cancer, autoimmune diseases, tuberculosis and cardiovascular diseases including cardiac failure, myocardial infarction. Recently hypovitaminosis D has been recognized as a potential risk factor for cardiovascular events like myocardial infarction, stroke and congestive cardiac failure.. Low serum vitamin D levels are linked with diminished coronary flow, endothelial dysfunction, higher coronary artery calcium scores and increased vascular stiffness and increased mean platelet volume [15]. Vitamin D has cardioprotective role in post myocardial infarction patients via antiapoptotic, anti-inflammatory and antifibrotic mechanisms [16]. Serum vitamin D levels are inversely correlated with TGL (Triglycerides) and VLDL (Very low density lipoprotein) levels. Lipid profile abnormality in vitamin D deficiency occurs because of peripheral insulin resistance. Vitamin D deficiency also increases oxidation of LDL and free radicals. Vitamin D has suppressive effect on serum parathyroid hormone (PTH) concentration. Low PTH causes increased peripheral clearance of TGLs and thus reducing serum TGL levels [17].

The role of vitamin D in Diabetes is initially suggested by seasonal variation in glycemic control in diabetic patients with worse in winter, that may be due to vitamin D deficiency as a result of reduced sunlight in winter. Vitamin D deficiency inhibits the insulin secretion from pancreas and its turnover which leads to impaired glucose tolerance [18]. Insulin resistance is regarded as precursor in development of Diabetes Mellitus. Vitamin D stimulates the expression of insulin receptors and hence enhances insulin mediated glucose transport. It also enhance insulin action indirectly by regulating the extracellular calcium levels [19]. Vitamin D suppresses the expression of renin. Vitamin D also have direct effects on vascular structure by its antiproliferative property on smooth muscle cells of vessel. A study by Forman et.al reported an increase in the relative risk of hypertension in vitamin D insufficient subjects [20].

4.2. Metabolic syndrome :

Metabolic syndrome previously known as syndrome X or insulin resistant Syndrome is a constellations of factors that link obesity, hypertension, Insulin resistance (IR), Type II DM and cardio vascular disease [11].

IDF (international diabetes foundation) criteria for diagnosis of metabolic syndrome [21]

Central obesity defined as waist circumference :

MEN	WOMEN	ETHNICITY
>94 cm	>80 cm	Europoid, subsaharahafrican, eastern and middle eastern.
>90 cm	>80 cm	South Asian, Chinese, and ethnic south and central American.
>85 cm	>90 cm	Japanese

Plus atleast two of the following:

- Fasting triglycerides > 150 mg/dl or specific medication.
- HDL cholesterol < 40 mg/dl in men and <50 mg/dl in women or on specific medication.
- Blood pressure >130 mm of Hg systole or >85 mm of Hg diastolic or previous diagnosis or specific medication
- Fasting plasma glucose >100 mg/dl or previously diagnosed type 2 diabetes mellitus.

Of the numerous metabolic syndrome definitions, the NCEP-ATP III is commonly used in research. According to this definition, the presence of atleast 3 of the following five confirms having metabolic syndrome for adults.

NCEP: ATP (National Cholesterol Education Programme : Adult Treatment Panel) III 2001 criteria for metabolic syndrome: [22]

- Central obesity - defined as waist circumference of >102 cm in males >88 cm in females.
- Hypertriglyceridemia – defined as serum triglyceride levels of >150 mg>dl or on specific medication.

- Low HDL cholesterol defined as <40 mg/dl in males and <50 mg/dl in females or specific medication
- Hypertension defined as blood pressure >130 mm of Hg systolic or >85 mm of Hg diastolic or on specific medication
- Fasting blood glucose >100mg/dl or on specific medication or previously diagnosed type 2 diabetes mellitus.

4.2.1. Pathophysiology of metabolic syndrome:

Metabolic syndrome is characterized by several abnormalities including impaired glucose tolerance, blood lipid derangements and prothrombotic and pro-inflammatory states. Adipose tissue dysfunction plays major role in pathogenesis of obesity and insulin resistance. Enlargement of adipose tissue and macrophage infiltration of the adipose tissue leads to cytokine release and favours insulin resistance. Insulin resistance seems to be the major mediator of metabolic syndrome. A number of studies suggested obesity visceral obesity as the culprit in metabolic syndrome. The visceral fat secretes inflammatory adipokines and all components of Renin angiotensin system (RAS). The RAS regulates BP and excessive RAS stimulation lead to hypertension. The RAS is upregulated in obesity [23,24,25]. The adipocytokines secreted by adipose tissue are leptin, resistin, IL-6, plasminogen activator inhibitor-1, TNF alpha. Increased concentrations of TNF alpha and IL-6 stimulates production of acute phase protein, C reactive Protein (CRP) in liver. High concentration of CRP indicate systemic inflammation and contribute to atherosclerotic plaque development [26]. Hence increase in adiposity triggers cascade of events including RAS activation and increased secretion of pro-inflammatory adipocytokine leading to insulin resistance, atherogenic dyslipidemia. Other factors like oxidative stress, hereditary and life style factors also contribute development to metabolic syndrome. The risk factors include overweight/obesity, sedentary lifestyle, ageing, diabetic mellitus and lipodystrophy. The family history also a role in pathogenesis of metabolic syndrome. No particular gene has been implicated yet, which suggest that environment place substantial influence [27].

4.2.2. Others disorders associated with metabolic syndrome:

Non alcoholic fatty liver disease (NAFLD), hyperuricemia, polycystic ovarian Syndrome (PCOS), obstructive sleep apnoea syndrome are some other conditions associated with metabolic syndrome [22].

4.2.3. Complications of metabolic syndrome :

Cardiovascular complications are mainly associated with metabolic syndrome. They include coronary artery disease, atrial fibrillation, heart failure, ischemic stroke, veno thromboembolic disease. NAFLD is another important condition associated with metabolic syndrome. Breast carcinoma is also linked to metabolic syndrome because of plasminogen activator inhibitor-1 cycle dysregulation. Studies have suggested that cancers of colon, kidney, gallbladder, prostate gland are also linked with metabolic syndrome recent studies shows association of metabolic syndrome and psoriasis. When there is increase in number of components of metabolic syndrome, the risk of recurrent preeclampsia is also increased. Accelerated cognitive aging is also associated with metabolic syndrome [28].

4.2.4. Treatment:

Lifestyle modifications and weight reduction are the initial steps in the management of metabolic syndrome. Diets rich in fruits, vegetables, cereal grains and fish should be encouraged. Diet enriched in saturated fats, trans fatty acids and cholesterol should be restricted. Regular moderate intensity physical activity for at least 30 minutes for at least 5 days per week should be followed. In spite of lifestyle intervention, weight loss drugs may be needed in some patients. They can be absorption inhibitors and appetite suppressors. Appetite suppressants include sibutramine and phentermine. Orlistat inhibits absorption of fat in about 30%. Bariatric surgery may be an option in metabolic syndrome patients with BMI > 40kg/m² and > 35kg/m² with other comorbidities. Statins are used to lower LDL cholesterol. Ezetimibe can be used as a second option which reduces 15-20% LDL cholesterol. Cholestyramine and colestipol are the bile acid sequestrants that can be tried but they often increase triglyceride levels and hence, should be used with caution in metabolic syndrome patients. Nicotinic acid also lowers LDL cholesterol by less than 20%. Fibrates like fenofibrate and gemfibrozil can be tried when both triglycerides and LDL cholesterol are elevated. Nicotinic acid is the only available drug with predictable HDL cholesterol raising properties. ACE inhibitors or Angiotensin II receptor blockers are recommended for patients with metabolic syndrome and without diabetes mellitus as they reduce the incidence of new onset diabetes mellitus. Aggressive glycemic control is essential as it helps in modification of triglyceride levels and HDL cholesterol levels. Metformin can be used for hyperglycemia in metabolic syndrome patients and some literature says that it helps to reverse certain pathologic changes in metabolic syndrome. Aspirin can be given for primary prevention of cardiovascular complications [29].

4.3. Vitamin D and metabolic syndrome:

Vitamin D influences several components of metabolic syndrome like hypertension, hyperglycemia, insulin resistance and hyperlipidemia. The immunomodulatory effect of vitamin D and its inverse association with inflammation suggest that role of vitamin D in metabolic syndrome. Metabolic syndrome is usually associated with low grade systemic inflammation and oxidative stress. These two factors are believed to have important role in development of metabolic syndrome itself and its future adverse effects. Vitamin D by its anti-inflammatory and oxidative stress attenuating effect suggested to play a vital role in pathogenesis of metabolic syndrome. Insulin resistance being a major underlying mechanism in metabolic syndrome, most epidemiological studies have demonstrated that serum 25 (OH)D and VDR polymorphism are associated with insulin sensitivity. NHANES study 2003-2004 studies have demonstrated that serum vitamin D levels are significantly negatively correlated with metabolic syndrome and also with each of its individual components. Some studies suggested that maintaining optimal level of vitamin D may provide protective effects against metabolic syndrome and its sequel. In a study done by Ling Lu, et al, middle aged and elderly Chinese individuals demonstrated that low vitamin D levels are significantly associated with increased risk of having metabolic syndrome and adverse values for individual metabolic components. However no data is currently available on effects of vitamin D supplementation and prevalence and treatment of metabolic syndrome in vitamin D deficient patients. Vitamin D levels also predict all cause and cardiovascular mortality in patients with metabolic syndrome. It was evidenced by prospective cohort study done in 1801 metabolic patients who underwent elective coronary angiography between 1997 and 2000. Mortality was tracked for a median of 7.7 years. The results was that there was 75% reduction in the hazard ratio in the patients with optimal vitamin D levels compared to those with severe deficiency. This study also demonstrated serum level dependent reduction in cardiovascular mortality [30,31,32,33].

4.4. Current study and previous studies :

In our study there is significant decrease in vitamin D levels with increasing age similar to the study done by Dalgard C et al [34], where they observed significant low levels of vitamin D with increasing age. With regard to gender, there is no significant difference in vitamin D levels similar to the observation by Ford ES et al [35]. There is significant decrease in vitamin D levels with increase in duration of diabetes. This is contrast to the study done by Braun TR et al [36] where they observed no relation between duration of diabetes and vitamin D levels.

Vitamin D levels were not significantly associated with fasting blood glucose levels in our study. Many cross sectional studies with subjects of varying age groups in non diabetic and diabetic states metabolic syndrome have demonstrated significant association between insulin resistance and low serum vitamin D levels. In a study done by Afsaneh Talari et al [37] where they noted significant reduction in fasting plasma glucose after increased intake of vitamin D. In this study 100 diabetic patients received 50000 units of vitamin D3 orally per week for about 8 weeks. They also showed significant improvement in serum insulin, HOMA- IR after treatment. Thus suggesting that vitamin D supplementation may reduce IR in diabetes. In a cross sectional study done by Hala Ahmadieh et al [38] 136 diabetic patients participated. They noted that vitamin D is negatively correlated with BMI and age but not with duration of diabetes. They showed that low vitamin D levels were highly prevalent in diabetic patients, similar to those observed in our study here.

In our study, waist circumference was negatively correlated with vitamin D levels. We observed significant association between hypertension and vitamin D levels. It is similar to the study done by Chon SJ et al [39] where blood pressure is negatively correlated with vitamin D levels. In our study among the lipid profiles, triglycerides and total cholesterol were significantly inversely correlated with serum levels of vitamin D. This is similar to observed by the study done by Kedam, Durgaprasr et al [33] where they showed significant inverse relation of vitamin D with triglycerides.

In our study 38 patients developed cardiovascular complications of metabolic syndrome in the form of stroke and myocardial infarction. Stroke occurred in 18 patients and myocardial infarction occurred in 20 patients. They are significantly associated with low vitamin D levels. This is similar to those observed in the cohort study done by Wang and colleagues [40]. They studied 1739 Framingham offspring participants without any prior history of cardiovascular disease. They finally concluded that low vitamin D levels were significantly associated with increased incidence of cardiovascular events during the follow up for mean of 5.4 years.

V. Conclusion

The present study was conducted to estimate serum vitamin D levels among metabolic syndrome patients admitted in Coimbatore medical college hospital and to study the possible association of vitamin D levels with various factors. The study included 100 metabolic syndrome patients with no factors significantly altering the vitamin D levels. Vitamin D levels were significantly low among metabolic syndrome patients and there was significant association with duration of diabetes, hypertension, abnormal waist circumference,

triglyceride and total cholesterol levels. However we did not find significant association between vitamin D levels and other factors like fasting blood sugar , HDL and LDL cholesterol levels. At the same time, vitamin D levels were significantly low in patients with complications of metabolic syndrome like myocardial infarction and stroke compared to those without complications. Thus it may be useful in clinical practice to measure vitamin D levels in patients with metabolic syndrome and it can be used to predict complications of metabolic syndrome like myocardial infarction and stroke. Further studies are needed to assess the preventive role of Vitamin D in metabolic syndrome and its complications.

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