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RESEARCH ARTICLE

VITAMIN D3 LEVELS IN DIABETES MELLITUS AND ITS CORRELATION WITH HbA1C LEVELS.

Gurinder Mohan, RanjeetKaur, NarotamBhalla, GuntasGill.
Department of Medicine, Sri Guru Ram Das Institute of Medical Sciences and Research, Sri Amritsar.

Manuscript Info *Abstract*

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Corresponding Author

Enas Mohamed Attia.

Background- Vitamin D3 is known for its calcium absorption and bone metabolism; but now been recognized as an accessible predictor, risk factor and biomarker of type 2 diabetes mellitus (T2DM).
Aim- The aim of the study is to determine serum vitamin D3 levels in T2DM patients and ascertain its correlation with HbA1c.
Setting and design- This is a cross-sectional study through screening of patients with T2DM attending the OPD/ indoor of SGRDIMSR, Amritsar.
Material and method- With prior informed consent, 100 diabetic patients were examined for complications of diabetes and investigated for HbA1c, serum calcium and vitamin D3 levels in addition to routine investigations. Vitamin D3 levels were determined and relation with HbA1c levels was established.
Results- Among the 100 T2DMpatients, 46% had deficiency, 22% had insufficiency and 32% had sufficiency of vitamin D3. The mean HbA1c value was 7.74 ± 1.63% in vitamin D sufficiency, 9.83 ± 2.02% in insufficiency, and 9.91 ± 2.5% in deficiency making the correlation highly significant ($p < 0.0001$). The fasting plasma glucose levels were significantly higher in deficient group (156.76 mg/dl) as compared to insufficient (147.91mg/dl) and sufficient group (138.28mg/dl). The above observations suggest a highly significant correlation between the two ($p < 0.0001$). There was established a highly significant inverse correlation between vitamin D3 and HbA1c and FPG levels.
Conclusion- Vitamin D3 is a potential risk factor for diabetes mellitus and has a role to play in its pathogenesis. Not only a patient should be screened for serum vitamin D3 levels as a possible risk factor but also as a potential beneficial role of serum vitamin D3 supplementation in improving glycemic status in patients with diabetes mellitus.

Introduction:-

Diabetes mellitus refers to a group of common metabolic disorders that share the phenotype of hyperglycemia.[1]The different types of diabetes mellitus are caused by a complex interplay of genetic and environmental factors. Diabetes is one of the most common, costly and fast-growing chronic diseases around the world. There were more than 371 million people living with diabetes, among which type 2 Diabetes Mellitus (T2DM) accounted for the overwhelming majority.[2] In India alone 41 million individuals are affected by this deadly disease, and this is likely to go up to 70 million by the year 2025.[3] Although adequate knowledge has been acquired on the etiology of diabetes its precise etiopathogenesis is still under discussion. Inflammatory factors, reactive oxygen species and autoimmune reactions have all strongly emerged as the major pathogenic factors for diabetes. Recently, vitamin D has sparked widespread interest in the pathogenesis and prevention of diabetes.

As the major regulator for calcium homeostasis, vitamin D directly or indirectly improves insulin exocytosis via activating calcium-dependent endopeptidases.[7] In peripheral insulin-target tissues, vitamin D3 might directly enhance insulin action through stimulation of the expression of insulin receptors and regulation of insulin-mediated intracellular processes via regulation of the calcium pool.[4] There is evidence to suggest that vitamin D supplementation increases pancreatic insulin release and reduces insulin resistance in people with impaired glucose tolerance and type 2 diabetes mellitus.[5-6]

The aim of the present study is to evaluate the levels of serum vitamin D3 and the relationship between vitamin D3 levels and glycemic control in patients with T2DM. Given the importance of lipids control in diabetes management to protect cardiovascular diseases, the association between serum vitamin D3 and lipid profiles will also be evaluated.

Material and Methods:-

In this cross sectional study, a total of 100 Diabetic patients (as per ADA criteria mentioned below)aged more than 18 years attending the OPD/ Indoor of SGRDIMSAR for routine health check up were enrolled.

According to the ADA criteria, patients were assigned a diagnosis of Diabetes Mellitus if;

1. HBA1C≥6.5% or
2. Fasting plasma glucose greater than 126 mg/dl ; fasting is defined as no calorie intake for atleast 8 hours, or
3. 2-h plasma glucose>= 200mg/dl during an OGTT.

After taking the formal approval by the ethical committee and informed consent of the patient, detailed history was taken regarding the duration of diabetes, associated symptoms suggestive of micro vascular and macro vascular complications. Complete general physical examination was done with due emphasis on anthropometry (ie BMI, waist circumference and waist/hip ratio). A detailed systemic examination was performed for signs of neuropathy, retinopathy and cardiovascular involvement.
Besides routine hematological and biochemical investigations, electrocardiogram, fasting plasma glucose, lipid profile, serum vitamin D3 levels, and glycosylated hemoglobin levels were measured. Serum 25-hydoxyvitamin D3 levels will be measured using ENZYME IMMUNO ASSAY (ELISA kits).

The criteria used to define vitamin D status are[7]:-

a)	Sufficiency	30-100 ng/ml
b)	Insufficiency	20 to 30 ng/ml
c)	Deficiency	< 20 ng/ml

The serum 25-hydroxy vitamin D3 levels were compared with the fasting plasma glucose and Glycosylated Haemoglobin levels to determine the correlation and results obtained were statistically analysed.

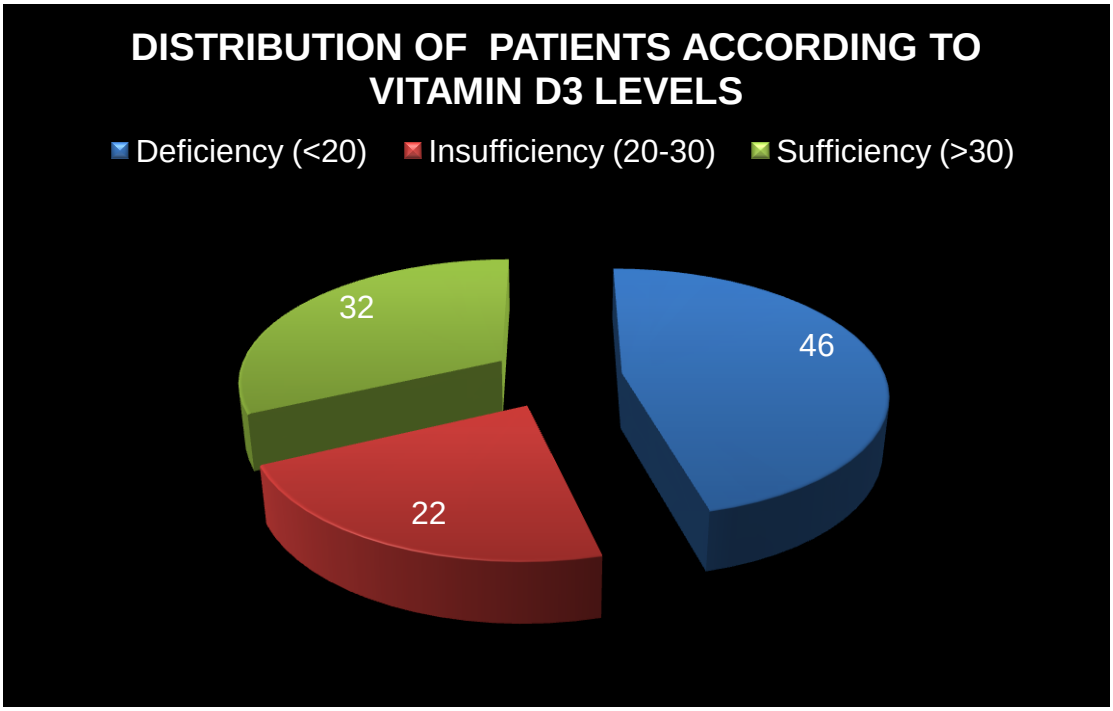
Exclusion criteria:-

1. Age less than 18 years.
2. Patients with chronic renal failure which corresponds to chronic kidney disease stages 3-5 (glomerular filtration rate< 60ml/min per 1.73 m2.)
3. Patients taking calcium supplements.
4. Patients taking Vitamin D supplements.
5. Orthopaedic problems like rickets, osteomalacia, and pregnancy were excluded from the study.

Results:-

Of the 100 patients included in the study, 63% were females and 37% were males. 72% patients were from rural area while 28% belonged to urban area. The maximum numbers of patients in our study were in the age group of 46 – 60 years ie 42(42%) patients. The mean age of patients in our study population was 56.85±11.87 years. Body mass index (BMI) was calculated in the population studied. It was found that maximum number of patients 54(54%) were in the pre obese category (BMI 25 – 29.9). 29(29%) patients were obese ie BMI >30 while 10 patients (10%) were in the overweight category (23-24.9) and only 7 patients (7%) had normal BMI. Vitamin D3 levels were measured

in all the patients. We observed that 46(46%) patients had deficient levels of vitamin D(<20ng/ml) while 22(22%) patients had insufficient levels(20-30ng/ml) and 32(32%) patients had sufficient levels of vitamin D(>30ng/ml).

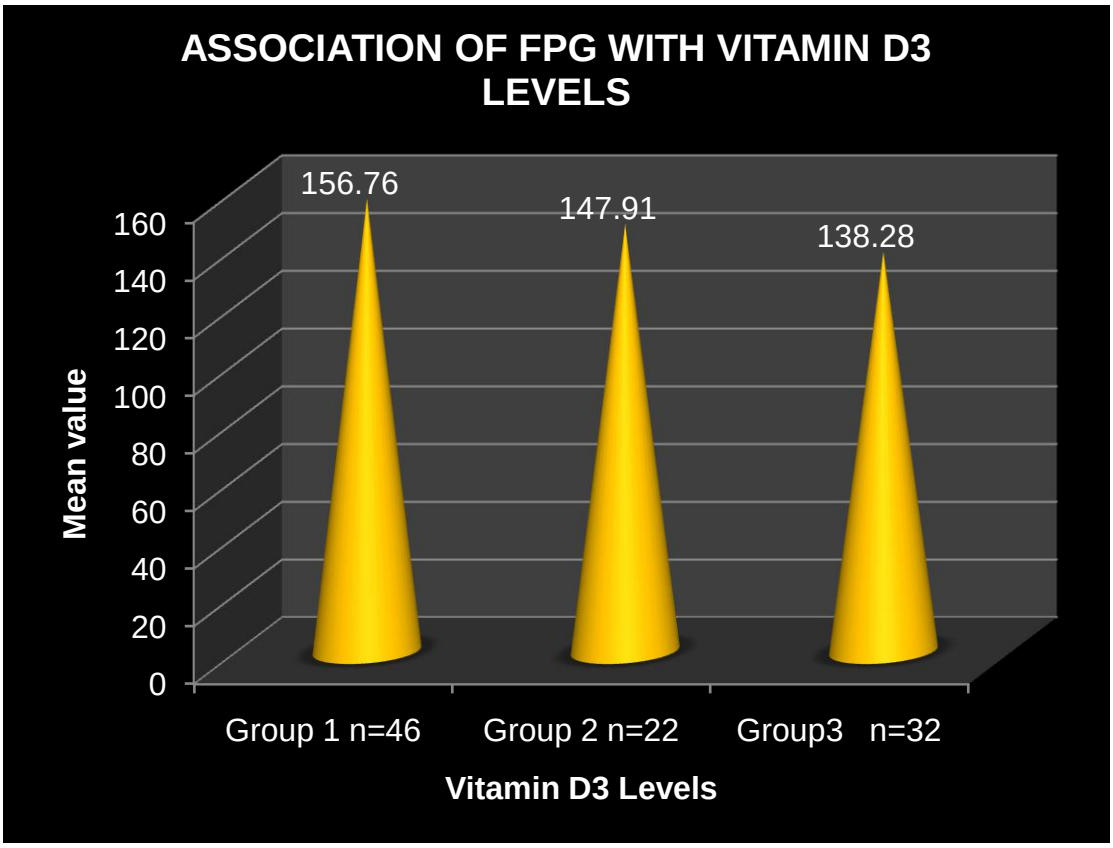


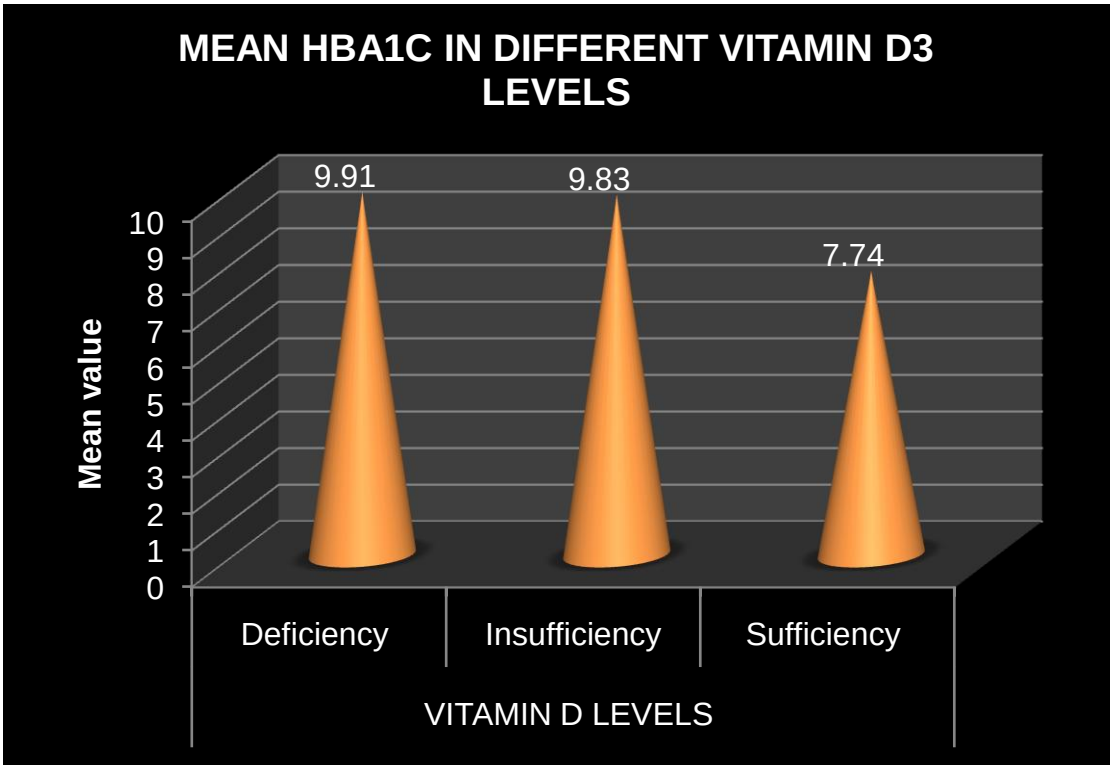
It was observed that the mean serum vitamin D3 levels were lower in females 25.73 ± 14.74 as compared to males 29.55 ± 20.01, which was statistically significant (p<0.027). In our study the mean serum vitamin D3 levels in patients with urban background was 21.64 ± 9.48 ng/ml which was lower than a mean serum vitamin D3 of 21.64 ± 9.48 in urban population.

For further statistical analysis of various parameters, patients were divided into three groups depending upon the vitamin D levels.

Group 1 Deficient ie serum vitamin D3 <20ng/ml n = 46
Group 2 Insufficient ie serum vitamin D3 20 – 30 ng/ml n = 22
Group 3 Sufficient ie serum vitamin D3 >30ng/ml n = 32

Correlation between BMI and serum vitamin D3 levels was studied. Mean BMI in group 1 was 27.44 ± 4.43, while group 2 was having mean of 30.63 ± 6.56 and mean BMI in group 3 was 28.84 ± 1.90. The correlation between them was statistically insignificant (p<0.225). In our study, serum vitamin D3 level showed a significant negative correlation to fasting plasma glucose (FPG). In group 1, mean FPG level were 156.76±30.18 mg/dl, in group 2 mean FPG was 147.91±31.14 while it was lowest in group 3 138.28 ± 24.24 mg/dl. The observations were suggestive of a highly significant correlation between the two (p < 0.0001 r -0.360).


ASSOCIATION OF FPG WITH VITAMIN D3 LEVELS
Mean value
160
140
120
100
80
60
40
20
0
156.76
147.91
138.28
Group 1 n=46
Group 2 n=22
Group3 n=32
Vitamin D3 Levels


MEAN HBA1C IN DIFFERENT VITAMIN D3 LEVELS
Mean value
10
9
8
7
6
5
4
3
2
1
0
9.91
9.83
7.74
Deficiency
Insufficiency
Sufficiency
VITAMIN D LEVELS

Recently serum vitamin D3 has been associated with prevalence of coronary artery disease independent of other cardiovascular risk factors. The mean serum vitamin D3 levels in CAD patients were lower ie. 25.96±13.54ng/ml as compared to patients with no evidence of CAD ie 27.54±17.93ng/ml. However these observations were not statistically significant (p < .689).

HbA1c levels were determined in all patients and its correlation with serum vitamin D3 levels was studied. The mean HbA1c in group 1 was 9.91 ± 2.5%, 9.83 ± 2.02% in group 2 while group 3 had mean HbA1c of 7.74 ± 1.63%. There was a negative correlation established between serum vitamin D3 and HbA1c levels for the population as a whole making it highly significant (p <0.0001 r -0.356).

Discussion:-

We observed that 46(46%) patients had deficient levels of serum vitamin D3 (<20ng/ml) while 22(22%) patients had insufficient levels (20-30ng/ml) and 32(32%) patients had sufficient levels of serum vitamin D3 (>30ng/ml). Mansour Al-Zaharani[8] concluded that more than half of 248 patients ie 148 (59.8%) patients were deficient in serum vitamin D3, 96(38.6%) patients had insufficient serum vitamin D3 levels while only 4(1.6%) patients had sufficient serum vitamin D3 level.

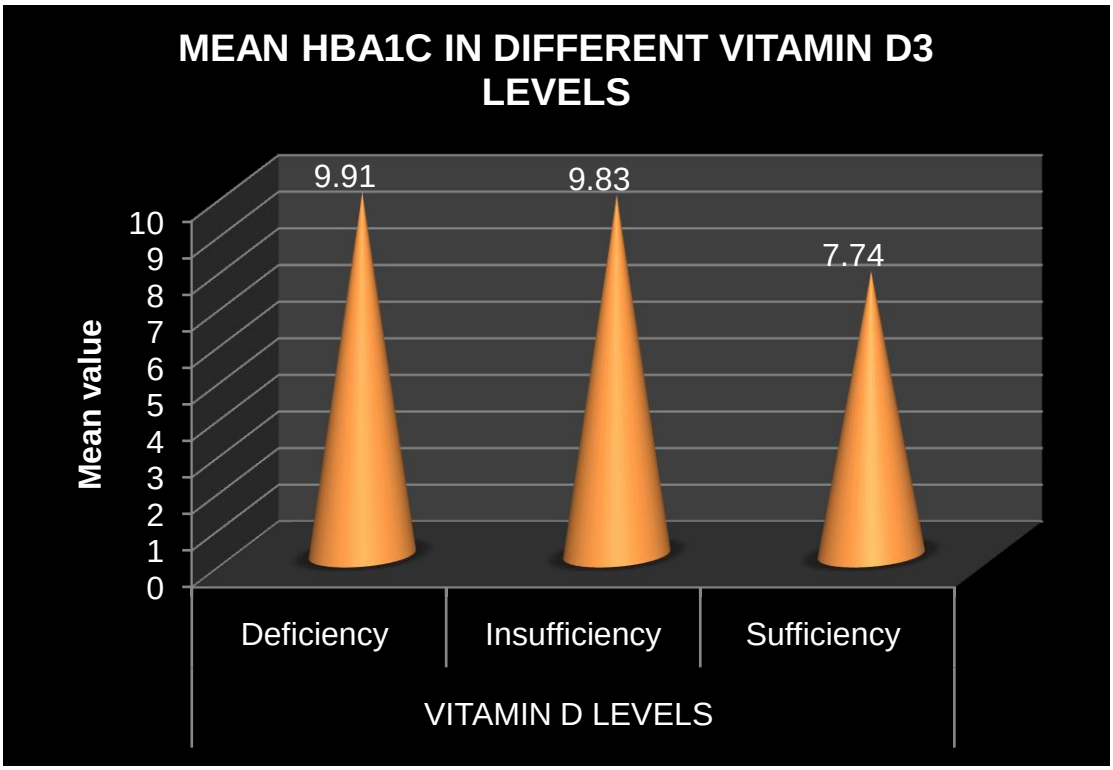
The mean serum vitamin D3 value in our study was 27.14±16.89 ng/ml while in a study done by Shanthi B et al.[9] the mean serum vitamin D3 was 18.49 ±3.497ng/ml and 12.90 ± 0.4 ng/ml in a Korean study done by Yu JR et al. [10]

It was observed that the mean serum vitamin D3 levels were lower in females 25.73 ± 14.74 as compared to males 29.55 ± 20.01 that was statistically significant (p<0.027). These findings were consistent with study done by HavilahPoluret al.[11] where the mean serum vitamin D3 levels were found to be lower in women (36.5 ± 6.23) than in men (48.2 ± 3.56) p<0.0001. In our study the mean serum vitamin D3 levels in patients with rural background was 29.29 ± 18.62 ng/ml which was higher than a mean serum vitamin D3 of 21.64 ± 9.48 in urban population. The correlation was statistically significant.(p<0.041) Similar findings were cited by Bachhel R et al. ninety-six (94.12%) urban subjects displayed insufficient levels as compared to 81.25% rural subjects(P< 0.05).[12] It could perhaps be attributed to a greater exposure to sunlight in the rural as compared to urban areas.

Serum vitamin D3 level showed a significant negative correlation to fasting plasma glucose (FPG). In group 1, mean FPG level were 156.76±30.18 mg/dl, in group 2 mean FPG was 147.91±31.14 while it was lowest in group 3 138.28 ± 24.24 mg/dl. The observations were suggestive of a highly significant correlation between the two (p 0.0001 r -0.360). Similar findings were also cited by VijethaShenoy et al. with mean FPG values of 98.51±11.05, 95.54±9.01 and 91.72±8.64 mg/dl in group 1, 2 and 3 respectively.[13]

The mean serum vitamin D3 levels in CAD patients were lower ie. 25.96±13.54ng/ml as compared to patients with no evidence of CAD ie 27.54±17.93ng/ml. However these observations were not statistically significant (p .689). In a study conducted by Maryam shojaeifard et al. in Tehran, lower levels of serum vitamin D3 was found in those with more severe coronary artery disease (normal coronary condition 26.78 ± 17.07, one-vessel 17.70 ± 14.31 ng/ml, two-vessel 17.49 ± 16.10 ng/ml, and three-vessel 16.04 ± 12.17 ng/ml, p 0.029).[14]

We observed that mean HbA1c in group 1 was 9.91 ± 2.5%, 9.83 ± 2.02% in group 2 while group 3 had mean HbA1c of 7.74 ± 1.63%. There was a negative correlation established between serum vitamin D3 and HbA1c levels for the population as a whole making it highly significant (p 0.0001 r -0.356). HavilahPoluret al.[11] also concluded similar findings in the two groups of normal serum vitamin D3 and low serum vitamin D3 levels. The mean values were 5.72±1.102 and 7.315± 0.924 respectively.In a study by Hyponnen and Power, participants with HbA1c more than 7% had lower 25 hydroxy vitamin D levels (36.9nmol/l) compared to the total population under study (52.7nmol/l).[15]



Conclusion:-

We conclude that there exists a strong association of serum vitamin D3 and diabetes mellitus. Lower levels of serum vitamin D3 can predispose to poor glycemic control and further potentiate complications of diabetes mellitus. Not only a patient should be screened for serum vitamin D3 levels as a possible risk factor but also as a potential beneficial role of serum vitamin D3 supplementation in improving glycemic status in patients with diabetes mellitus.

Conflict of Interest: The authors declare no conflict of interest.

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