A Clinical, Biochemical Profile of Type-2 Diabetes in Women with Special Reference to Vitamin-D Status in Obese and Non-Obese

Mamatha B Patil[1*], E Dinesh Ragav[2]

Abstract

Introduction: Type-2 Diabetes is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production. Obese diabetic patients have 13.5% more chances of developing diabetic complications compared to non – obese diabetic patients. Vitamin D has found to be deficient in diabetic patient and it's role in insulin regulation. Obese females are more prone to develop diabetic complications and hypovitaminosis-D.

Materials and Method: Total of 156 female diabetic patients aged 30 to 60 years who are a case of type-2 diabetes mellitus seen in Rajarajeswari Medical College and Hospital were clinically evaluated including anthropometric measurements are done, namely height, weight, waist-hip ratio, tested for vitamin-D levels and other necessary diabetes related investigations were carried out.

Result: Among the studies 156 patients, Mean age of study group: 48.47±9.56 years. Mean duration of diabetes in the study population: ± SD: 5.10±4.36 years mean BMI was 24.97±4.16.Mean waist circumference: 98.93±12.18 cm, Mean Waist-Hip ratio: 0.98±0.08. Mean FBS: 202.73±81.73 mg/dl, Mean PPBS: 280.99±94.14 mg/dl, Mean HbA1C: 9.33±1.83 %. Almost all diabetic females (92.5%) have Vitamin-D deficiency. Mean Vitamin-D levels: 16.19±8.97 ng/ml. Duration of diabetes (P=0.082+, Fisher Exact test), Poor Glycemic control (P<0.001**, Chi-Square test) and increased BMI (P=0.011*, Fisher Exact test) had significant role in causing Vitamin-D deficiency.

Conclusion: Almost all diabetic females were with Waist circumference > 80 cm and Waist-Hip ratio > 0.8. Most of the diabetic patients have poor control of diabetes. Vitamin-D deficiency is found in almost all diabetic female patients (92.5%) and the most probable cause is poor glycemic control and obesity according to this study.

Introduction

Type-2 Diabetes is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production. Diabetes mellitus is one of the most common chronic diseases across the world and number of diabetic patients is on rise. In 2011, there were 366 million people with diabetes globally.[1] On 2010, it was estimated that almost 143 million women in the world have type-2 diabetes.[2] Total of 10.1 million women have type-2 diabetes in America. In India, the total number of diabetes patients are 63.01 million as on 2012.[3] Prevalence of diabetes mellitus in India is 9.01 % as on 2012.[3] Among Indian type-2 diabetic patients, female prevalence accounts for 37.87%.[4] So, the prevalence of women with type-2 diabetes in India is 3.41% as on 2012. The prevalence of women with type-2 diabetes mellitus in Karnataka is 22.04%.[5]

Many people are diagnosed type-2 diabetes in their teens or early 20s. And with advancing age, the risk of getting type-2 diabetes goes up too, especially if you don't change any of the diabetes risk factors like your weight and physical activity level. Women who get type-2 diabetes are at greater risk than men of cardiovascular disease and blindness.

According to the National Family Health Survey (NFHS-3), 15% of women in India are either obese or overweight. Obese diabetic patients have 13.5 % more chances of developing diabetic complications compared to non –obese diabetic patients. This means obesity is associated with higher prevalence of complications. Vitamin D has found to be deficient in diabetic patient and it's role in insulin regulation. Obese females are more prone to develop diabetic complications and hypovitaminosis-D.[6,7]

According to recent data, there may be a connection between vitamin D levels and cardiometabolic diseases: obesity; impaired glucose tolerance and diabetes mellitus type 2; arterial hypertension; and atherogenic dyslipidemia. Although the mechanisms are still unclear. an increased body fat and obesity is associated with low circulating 25(OH)D level.[8]

Vitamin D is a secosteroid which is converted into its active form via 1 α-hydroxylase enzyme. Though kidney is the classical site for 1 α-hydroxylase activity, it is also expressed in other tissues such as endothelial and vascular smooth muscle cell. Besides, vitamin D receptor (VDR) is present in more than 30 different tissues including pancreas, myocardium, lymphocytes, *etc*. The widespread distribution of VDR signifies important role of vitamin D in humans. While vitamin D is critical for calcium homeostasis, current studies also highlight role of vitamin D deficiency (VDD) in diseases other than the metabolic bone disorders.[9]

The potential mechanisms of beneficial effect of vitamin D in type 2 DM include (*i*) improved b-cell function via direct effect of vitamin D or by increase in the intracellular ionized calcium which therefore would result in enhanced insulin release, (*ii*)

[1]Professor, Department of General Medicine, Rajarajeswari Medical College and Hospital, Mysore Road, Kambipura, Bengaluru, Karnataka; [2]Assistant Professor, Department of General Medicine, Shri Sathya Sai Medical College and Research Institute, Ammapettai, Nellikuppam, Tamil Nadu; *Corresponding Author
Received: 09.07.2017; Accepted: 14.08.2018

Table 1: Comparison of clinical variables according to Vitamin-D levels of patients studied

Variables	Vitamin D (ng/dl)			Total	P value
	<20	20-30	30-100		
Age in years	48.11±9.72	49.19±8.76	51.50±10.10	48.47±9.56	0.571
Duration	4.91±4.20	4.81±3.08	8.88±8.13	5.10±4.36	0.041*
BMI (kg/m²)	25.43±4.05	23.75±4.64	22.18±1.60	24.97±4.16	0.024*
Waist Circumference	99.12±12.63	100.22±9.38	91.75±12.52	98.93±12.18	0.212
HIP Circumference	101.58±12.64	98.56±5.42	91.5±11.51	100.54±11.85	0.041*
Waist Hip Ratio	0.98±0.08	1.01±0.09	0.98±0.09	0.98±0.08	0.125

ANOVA test

Table 2: Duration of DM in years in relation to Vitamin-D levels of patients studied

Duration of DM (yrs)	Vitamin D (ng/dl)			Total
	<20	20-30	30-100	
<5	61(50.4%)	13(48.1%)	2(25%)	76(48.7%)
5-10	53(43.8%)	13(48.1%)	3(37.5%)	69(44.2%)
11-15	4(3.3%)	1(3.7%)	1(12.5%)	6(3.8%)
>15	3(2.5%)	0(0%)	2(25%)	5(3.2%)
Total	121(100%)	27(100%)	8(100%)	156(100%)

P=0.082+, Significant, Fisher Exact test; Vitamin-D levels are inversely proportional to duration of diabetes

Table 3: Vitamin D (ng/ml) levels in relation to BMI distribution of patients studied

Vitamin D (ng/ml)	BMI (kg/m²)						Total
	<18.5	18.5-24.9	25-29.9	30-34.9	35-39.9	40 and above	
<20	2(100%)	59(66.3%)	41(93.2%)	16(94.1%)	3(100%)	0(0%)	121(77.6%)
20-30	0(0%)	22(24.7%)	3(6.8%)	1(5.9%)	0(0%)	1(100%)	27(17.3%)
30-100	0(0%)	8(9%)	0(0%)	0(0%)	0(0%)	0(0%)	8(5.1%)
Total	2(100%)	89(100%)	44(100%)	17(100%)	3(100%)	1(100%)	156(100%)

P=0.011*, Significant, Fisher Exact test; Vitamin-D levels are inversely proportional to BMI.

increased insulin sensitivity related to expression of insulin receptor or via calcium dependent pathways in target cells leading to increase in the glucose utilization, and (*iii*) inhibition of b-cells apoptosis due to VDR transcription factor mediated inhibition of cytotoxic cytogene expression.[10]

With the above idea, this study is done estimating vitamin D levels in serum of type-2 diabetic females and its correlation with obese and non-obese female patients.

Objectives of the Study

1. To study the clinical, biochemical profile of type-2 diabetic women.
2. To study the vitamin-D status in obese and non-obese types-2 diabetic women.

Materials and Method

Total of 156 female diabetic patients aged 30 to 60 years who are a case of type-2 diabetes mellitus seen in Rajarajeswari medical college and hospital were clinically evaluated including anthropometric measurements including height, weight, waist-hip ratio, tested for vitamin-D levels and other necessary diabetes related investigations were carried out. Exclusion criteria such as (1) Patients who are case of type-1 diabetes. (2) Patients for whom hysterectomy has been done. (3) Patients who are case of any carcinoma (including breast, colon). (4) Patients with known renal disease, Crohn's disease, cystic fibrosis, celiac disease, malabsorption syndrome. (5) Patients who have gestational diabetes mellitus. (6) Patients with history of steroid intake and oral contraceptive pills for more than 6 months. (7) Patients who are on calcium supplements. (8) Patients who are on vitamin D supplements.

Serum Vitamin D is estimated by 'ARCHITECT 25-OH Assay kit'.

Statistical Methods: Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made, Assumptions: 1. Dependent variables should be normally distributed, 2.Samples drawn from the population should be random, Cases of the samples should be independent

Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc9.0.1 ,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.Pearson correlation, Chi-square/ Fisher Exact test, Analysis of variance (ANOVA) were done.

Ethical Issues

Approval was taken from Institutional Ethical Committee. A written consent was taken from each study subject. Those who were illiterate, thumb impression were taken in front of a witness. All information collected was kept confidential.

Results

Present study was done on 156 female diabetic patients in sub-urban locality. The mean age of the studied patients was (Mean ± SD: 48.47±9.56 cm), the mean duration of diabetes being Mean ± SD: 5.10±4.36 yrs. 65 patients were having BMI > 25. Mean waist circumference (Mean ± SD: 98.93±12.18 cm). Mean Hip circumference (Mean ± SD: 100.54±11.85 cm). Mean waist-Hip ratio (Mean ± SD: 0.98±0.08). Mean FBS (202.73±81.73 mg/dl). Mean PPBS (280.99±94.14 mg/dl). Mean HbA1C (Mean ± SD: 9.33±1.83 %). Duration of diabetes has no relation to BMI (P=0.409, Not significant, Fisher Exact test). Duration of diabetes has no relation to glycemic control (P=0.107, Not significant, Chi-Square test). The mean Vitamin-D levels in the observed patients were (Mean ± SD: 16.19±8.97).

Discussion

We studied 156 diabetic female patients admitted in medicine ward of our hospital. 74.3 % patients were in the age group more than 40 years. "The Eluru survey" in a rural Indian population on 1987 demonstrated similar result showing that the prevalence of known diabetes was 6.1% in all subjects aged 40 or over and rose to 13.3% in the age group 50-59 years.[11]

Most of the patients had normal BMI (57.1 %) and rest of them had BMI more than 25 (41.6 %). Ashwin Kamath et al, Int J Biol Med Res. 2011 showed that 23.3% of diabetic patients had normal BMI and 59.9% of them had BMI > 25.[12]

Majority of patients (94.2 %) have waist circumference of more than 80 cm. 93.6 % had a Hip circumference of more than 80 cm. All patients

Table 4: Vitamin D (ng/ml) levels in relation to HbA1c distribution of patients studied

Vitamin D (ng/dl)	HbA1c		Total
	Good control	Poor Control	
<20	5(35.7%)	116(81.7%)	121(77.6%)
20-30	4(28.6%)	23(16.2%)	27(17.3%)
30-100	5(35.7%)	3(2.1%)	8(5.1%)
Total	14(100%)	142(100%)	156(100%)

P<0.001**, Significant, Chi-Square test; Vitamin-D levels are inversely proportional to HBA1C levels

Table 5: Pearson correlation between Vitamin-D levels and clinical variables

Pearson Correlation	R value	P value
Vitamin D (ng/ml) **vs** Age in years	0.245	0.002**
Vitamin D (ng/ml) **vs** BMI (kg/m^2)	-0.304	<0.001**
Vitamin D (ng/ml) **vs** Waist Circumference	-0.251	0.002**
Vitamin D (ng/ml) **vs** HIP Circumference	-0.337	<0.001**
Vitamin D (ng/ml) **vs** Waist Hip Ratio	0.017	0.836

Inference: As per Pearson correlation, Vitamin-D levels have significant correlation to Age, BMI, Waist Circumference, Hip Circumference. But, Vitamin-D levels are not in correlation with Waist-Hip ratio.

Table 6: Pearson correlation between Vitamin-D levels and sugar parameters variables

Pearson Correlation	r value	P value
Vitamin D (ng/ml) **vs** FBS (mg/dl)	-0.336	<0.001**
Vitamin D (ng/ml) **vs** PPBS (mg/dl)	-0.365	<0.001**
Vitamin D (ng/ml) **vs** HbA1c	-0.390	<0.001**

Inference: Vitamin-D levels have significant Pearson correlation to sugar control.

(100 %) had a Waist-Hip ratio (Table 6) >0.8. According to Kamath et al,[12] 86.6% of diabetic patients had waist circumference of > 80 cm and Chamukuttan et al,[13] demonstrates that Asian Indians have higher upper body adiposity and higher visceral fat for a given BMI when compared with the Western population. BMI for an urban Indian is 23 kg/m^2, and cut off values for Waist Circumference were 80 cm for women, and for Waist-Hip Ratio were 0.81 for women.[13]

Among the evaluated patients , 94.9 % (n=148) of them had Vitamin-D insufficiency and 77.6 % (n=121) of them had Vitamin-D deficiency (< 20 ng/ml). Similarly, in Alhumaidi et al, deficiency of Vitamin-D with levels less than 20 ng/mL in 76.6% of the patients with type-2 diabetes.[14]

The duration of diabetes in relation to Vitamin-D levels shows, suggestive significance with p value = 0.82 (Table 2). But, duration of diabetes does not necessarily be related to Vitamin-D levels of a patient, as the complications related to diabetes are not only influenced by duration of diabetes, but also by the compliance of treatment and apt glycemic control. The above result have also been demonstrated by Shaikhet et al, that in multivariate analysis, age, duration of diabetes did not show any impact on Vitamin D deficiency or insufficiency.[15]

Vitamin-D in relation to patients distributed as per their BMI showed moderate significance (p= 0.011) in our study (Table 3). This means as the BMI increases in patients, the corresponding Vitamin-D levels in them are low.

Vitamin-D levels in relation to glycemic status of a given patient (Table 4) showed strong clinical significance (p = 0.001). This finding could infer that glycemic control in a given diabetic patients is one of the most important factor in determining Vitamin-D levels. Better the glycemic control, the more the Vitamin-D level in a given patient. Or, it could be also interpreted that the patients having poor glycemic control would need the addition of Vitamin-D supplements due to more probability of Vitamin-D deficiency in them.

According to Pearson's correlation (Table 5), almost all the clinical variables except Waist-Hip ratio were of strong clinical significance (p < 0.001) with Vitamin-D levels in this study. The sugar parameter variables (Table 6) were also of strong significance in correlation with Vitamin-D levels. Similar results were also demonstrated by McGill et al. In that study, low serum vitamin D3 was inversely related to weight and BMI, large waist and raised HbA1c.[16]

Wortsman et al, decreased bioavailability of vitamin D in obesity, observed that blood vitamin D3 concentrations increased in both the obese and non-obese subjects after exposure to an identical amount of UV-B irradiation. Moreover, the obese subjects had a larger body surface area of exposure and therefore would be expected to produce more vitamin D3, resulting in higher blood vitamin D3 concentrations, than would the non-obese control subjects. However, the increase in blood vitamin D3 concentrations was 57% less in the obese than in the nonobese subjects 24 hour after the exposure.[17]

Conclusion

Type-2 diabetes mellitus places a huge burden over the world affecting 387 million people around the world as of 2014. It is expected to increase by 205 million people by 2035. Diabetes has many complications as the age progresses and in every year a new complication, new mode of treatment is being found and this process is constantly evolving. Vitamin-D is currently the topic of interest for many experts in the field of medicine and its various functions is being found in ongoing researches. Vitamin-D deficiency is found in almost all diabetic female patients and the most probable cause for it according to this study is poor glycemic control and obesity. So, life style modification, prompt glycemic control and early Vitamin-D supplementation is necessary for every diabetic patients.

Acknowledgement

I take this opportunity to thank all the patients who have participated in my study who have been an integral part in the completion of my article.

References

1. Mohan V, Shah S, Saboo S. Current Glycemic Status and Diabetes Related Complications Among Type 2 Diabetes Patients in India: Data from the A1chieve Study. *J Assoc Physicians India* 2013; 61.
2. Sicree R, Shaw J, Zimmet P. Baker IDI Heart and Diabetes Institute. The global burden, IDF Diabetes Atlas fourth edition, 2009.
3. Comparative prevalence % WHO standard, International diabetes federation ATLAS, 5th edition, 2012 update
4. Brahmkshatriya PP, Mehta AA, Saboo BD, et al. Characterist and prevalence of latent autoimmune diabetic in adults. International Scholarly Research Network. ISRN Pharmacology. Volume 2012, Article ID 580202, 8 pages.
5. Zaman FA, Pal R, Zaman GS, et al. Glucose indices, frank and undetected diabetes in relation to hypertension and anthropometry in a south Indian rural population. *Indian Journal of Public Health* 2011; 55:34-7.
6. Wortsman J, Matsuoka LY, Chen TC, et al. Decreased bioavailability of vitamin D in obesity. *Am J Clin Nutr* 2000; 72:690–3.
7. Hu J. Women and Diabetes: A Global Perspective. *Women's Health, Issues Care* 2013, 2:1
8. Grineva EN, Karonova T, Micheeva E, et al. Vitamin D deficiency is a risk factor for obesity and diabetes type 2 in women at late reproductive age. *Aging* 2013; 5:7.
9. Goswami R, Mishra SK, Kochupillai N. Prevalence and potential significance of vitamin D deficiency in Asian Indians. *Indian J Med Res* 2008; 127:229-238.
10. Pittas AG, Lau J, Hu FB, et al. The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. *J*

Clin Endocrinol Metab 2007; 92:2017-29.

11. Rao PV, Ushabala P, Seshiah V, et al The Eluru survey: prevalence of known diabetes in a rural Indian population. *Diabetes Res Clin Pract* 1989; 7:29-31.
12. Kamath A, Shivaprakash G, Adhikari P, et al. Body mass index and Waist circumference in Type 2 Diabetes mellitus patients attending a diabetes clinic. *Int J Biol Med Res* 2011; 2:636-638.
13. Snehalatha C. Cutoff Values for Normal Anthropometric Variables in Asian Indian Adults. *Diabetes Care* 2003; 26:1380–1384.
14. Alhumaidia M, Agha AB, Dewish MC. Vitamin D Deficiency in Patients with Type-2 Diabetes Mellitus in Southern Region of Saudi Arabia; MAEDICA. *J Clin Med* 2013; 8:231-236.
15. Sheikh IA, Masood N, Memon S, et al. Serum Vitamin D Level in Type 2 Diabetic Patients. *Professional Med J* 2014; 21:992-7.
16. McGill A, Stewart JM, Lithander FE, et al. Relationships of low serum vitamin D3 with anthropometry and markers of the metabolic syndrome and diabetes in overweight and obesity. *Nutrition Journal* 2008; 7:4.
17. Wortsman J, Matsuoka LY, Chen TC, et al. Decreased bioavailability of vitamin D in obesity. *Am J Clin Nutr* 2003; 77:1342.