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A Comparative Study Of Vitamin D And Liver Function Test Association In Type 1 And Type 2 Diabetes

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Abstract:

Diabetes mellitus is a modern worldwide epidemic. Its complications are a significant causes of morbidity and mortality and the consequences of its explosive growth are an intolerable burden both to the individual and to health care system. This study originated from an interest in vitamin D, which has attained a lot of focus the last couple of decades as a possible multifunctional and important contributor to health and especially in the context of chronic lifestyle-related diseases. Thus, vitamin D deficiency has been associated with osteoporosis, cardiovascular disease, diabetes, cancer, autoimmune diseases and depression. Our vitamin D status is therefore vulnerable to modern lifestyle with less physical activity and outdoor time, at the same time as overweight, contributing to vitamin D deficiency, increases. Many of the same lifestyle choices predispose both for vitamin D deficiency as well as for many diseases associated with vitamin D deficiency. Therefore, there are huge methodological challenges in defining whether vitamin D deficiency has a causal role in the development of these diseases.The present study was conducted as a cross sectional observational study including 60 diabetic patients, with an objective to compare vitamin D and LFT in Type 1 DM and Type II DM.

Findings from this study suggest that vitamin D may play a significant role in both types of diabetes. In this study , the evidence for a potential association is stronger for vitamin D and type 2 diabetes with much less data on type 1 diabetes and The activities of ALP and GGT were significantly higher in Type II DM compared to Type I DM.

Keywords: LFT-(SGOT, SGPT, GGT), Type 1 and 2 diabetes, vitamin D

Introduction:

Diabetes is a syndrome of hyperglycemia an disturbances of carbohydrate, fat and protein metabolism associated with absolute or relative deficiencies in insulin secretion [1]. Diabetes is the commonest metabolic disorder affecting the people all over the world. As per WHO estimates, globally, 422 million adults aged over 18 years were living with diabetes in 2014. Diabetes caused 1.5 million deaths in 2012. Higher-than-optimal blood glucose was responsible for an additional 2.2 million deaths as a result of increased risks of cardiovascular and other diseases, for a total of 3.7 million deaths related to blood glucose levels in 2012 [1]. Associated risk factors such as being overweight or obese are increasing. Diabetes is an important cause of

blindness, kidney failure, lower limb amputation and other long-term consequences that impact significantly on quality of life[1]. This research originated from an interest in the ancient hormone vitamin D, which has attained a lot of focus the last couple of decades as a possible multifunctional and important contributor to health and especially in the context of chronic lifestyle-related diseases. Thus, vitamin D deficiency has been associated with osteoporosis, cardiovascular disease, diabetes, cancer, autoimmune diseases and depression[3]. In general, a person's vitamin D level (measured as 25-hydroxyvitamin D (25(OH)D)) is a product of ultraviolet B (UVB) radiation from the sun, and to a less degree, from food . Our vitamin D status is therefore vulnerable to modern lifestyle with less physical activity and outdoor time, at the same time as overweight, contributing to vitamin D deficiency, increases. Many of the same lifestyle choices predispose both for vitamin D deficiency as well as for many diseases associated with vitamin D deficiency. Therefore, there are huge methodological challenges in defining whether vitamin D deficiency has a causal role in the development of these diseases.

There are various animal studies and clinical trials in patients with newonset of T-1 DM which showed that the improvement of vitamin D level may arrest the deterioration of pancreatic function and improve the levels of C-peptide[4]. There is strong epidemiologic data showing that the population in countries with a high prevalence of T-1DM is commonly vitamin D deficient. Vitamin D supplementation during pregnancy decreased the risk of the development of T-1DM for off spring[6]. Supplementation of vitamin D at an early age also decreases the risk for developing T-1 DM.[7]

The liver helps maintain normal blood glucose concentration in the fasting and post prandial states. Loss of insulin effect on the liver leads to glycogenolysis and an increase in hepatic glucose production. Abnormalities of triglyceride storage and lipolysis in insulin-sensitive tissues such as the liver are an early manifestation of conditions characterized by insulin resistance and are detectable earlier than fasting hyperglycemia. The precise genetic, environmental, and metabolic factors and sequence of events that lead to the underlying insulin resistance,however, is not fully understood.[8] hyperinsulinemia might directly lead to hepatic insulin resistance with associated fatty changes. The excess in free fatty acids found in the insulin-resistant state is known to be directly toxic to hepatocytes. Putative mechanisms include cellmembrane disruption at high concentration, mitochondrial dysfunction, toxin formation, and activation and inhibition of key steps in the regulation of metabolism **[9].** The insulin- resistant state is also characterized by an increase in proinflammatory cytokines such as tumor necrosis factor-_ (TNF-_), which may also contribute to hepatocellular injury. In preliminary studies, an increased frequency of specific TNF- _–promoter polymorphism was found in nonalcoholic steatohepatitis (NASH) patients, suggesting a possible genetic link or predisposition to fatty liver found in insulin-resistant states**.[10]** The present study is planned to study the vitamin D and liver function test and their association in type 1 and type 2 Diabetes cases.[11]

Vitami n D

Vitamin D is a seco-steroid hormone and it is critically important for the development, growth and maintenance of a healthy skeleton from birth until death **[15].** Vitamin D has other roles in human health; it can play a role in decreasing the risk of many chronic illnesses, including cardiovascular disease, diabetes, autoimmune diseases, infectious diseases, and cancer **[16].** The molecular structure of vitamin D is closely allied to that of classic steroid hormones in that it has the same root cyclopentanoperhydrophenanthrene ringstructure.

Vitamin D is a lipophil secosteroid that exists in two forms; ergocalciferol (vitamin D2) and cholecalciferol (vitamin D3). These two forms differ in one double-binding and one methyl group. While vitamin D2 is found in vegetable sources like mushrooms, vitamin D3 can ben found in animal sources like fat fish, cod liver oil, egg yolk and fortified food like dairy products

Importantly, the body itself has the ability to produce vitamin D3, when UVBradiation (wavelength 290-315 nm) reaches preformed 7-dehydrocholesterol in the skin. Previtamin D3 is then formed, which under normal temperature conditions isomerizes to form vitamin D3

Aims And Objective:

1. To study the levels of Vitamin D and its association with type 1 and type 2diabetes cases.

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2. To study the liver function test and its association with type 1 and type 2diabetes cases.

3. To compare the vitamin D and liver function test in type 1 and type 2diabetes cases.

Materials & Methods:

Study Type & Area

A prospective observational study will be conducted at Department of Medicine of a tertiary care centre.

Study Population

All patients of both sexes with type 1 and 2 diabetes coming to our hospital giving informed consent.

Inclusion Criteria

Cases of type 1 and 2 diabetes mellitus on insulin or oral hypoglycemicagent therapy or on diet control.

Exclusion Criteria

1. Age less than 18 years.

2. Patients with chronic renal failure which corresponds to chronic kidney disease stage 3-5 (glomerular filtration rate < 60ml/min per 1.73m^2).

3. Patients taking calcium or vitamin D supplements.

Sampling Technique & Sample Size

A total of 60 patients of type 1 and 2 diabetes mellitus (30 each), with fasting Blood sugar levels ≥126 mg/dl and glycosylated HBA1C levels ≥ 6.5% will be selected using purposive sampling techniques.

Study Methodology

About 5ml of venous blood will be collected from every case for the estimation of biochemical parameters. Fasting blood glucose, postprandial blood glucose and HbA1c will be estimated to diagnose Diabetes Mellitus. For diagnosis of DM, diagnostic criteria provided by the IDF will be used [151]. HbA1c will be estimated by ion exchange resin method colorimetrically and all other parameters were analyzed by HumaStar 300 fully automated analyzer following manufacturers' instructions.The method used for analysis of serum 25-hydroxyvitamin D3 level willbe electrochemiluminescene immunoassay.

Liver enzymes including ALP levels will be estimated by using standard methods as per the guideline provided by the reagent manufacturer (Human GmBh, Germany). ALT and AST will be estimated at 37° C flow cell temperature and normal range for both was considered up to 42 U/L in male and up to 32 U/L in female as provided by SOP [17].

Statistical Analysis

The quantitative data was represented as their mean ± SD (Standard Deviation). The t-test was used for analysing normally distributed quantitative data. Categorical data was analyzed by using chi-square test. The significance threshold of p-value was set at <0.05. All analysis was carried out by using Statistical Package for the Social Sciences (SPSS) software version 21.

Results:

Table 1. Baseline characteristics of type 1 DM

Baseline characteristics(N=30)	Mean ±**SD**
Age (years)	36.93 ± **6.37**
FBS	176.07 ± **48.77**
PPBS	222.17 ±**66.74**

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HbA1C	10.13 ± **1.78**
Vitamin-D	25.72 ± **13.74**
Cpep	0.52 ± **0.29**
Total Bilirubin	1.03 ± **0.46**
SGOT	50.13 ± **38.95**
SGPT	49.60 ± **34.55**
ALP	107.70 ±**61.61**
GGT	43.73 ± **18.10**
Duration of illness	3 ± **1.4**

Table 2. Baseline characteristic of type 2 DM

Baseline characteristics(N=30)	Mean ±**SD**
Age (years)	62.07 ± **12.32**
FBS	177.77 ± **49.47**
PPBS	217.13 ± **66.46**
HbA1C	9.79 ± **3.37**
Vitamin-D	16.37 ± **13.46**
Cpep	2.62 ± **2.26**
Total Bilirubin	0.81 ± **0.47**
SGOT	59.20 ± **65.77**
SGPT	40.97 ± **24.94**
ALP	159.47 ± **69.99**
GGT	60.43 ± **33.33**
Duration of illness	10.4 ± **4.45**

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Table 3.Distribution of study participants according to age

Age (Years)	Numbers	Percentage
≤30	5	8.3
31-40	17	28.3
41-50	13	21.7
>50	25	41.7
Total	60	100.0

Table 3. Shows that in age <30 years 8.3 % patients ,age 31-40 years 28.3 % patients , age 41-50 years 21.7 % patients , >50 years 41.7 % patients

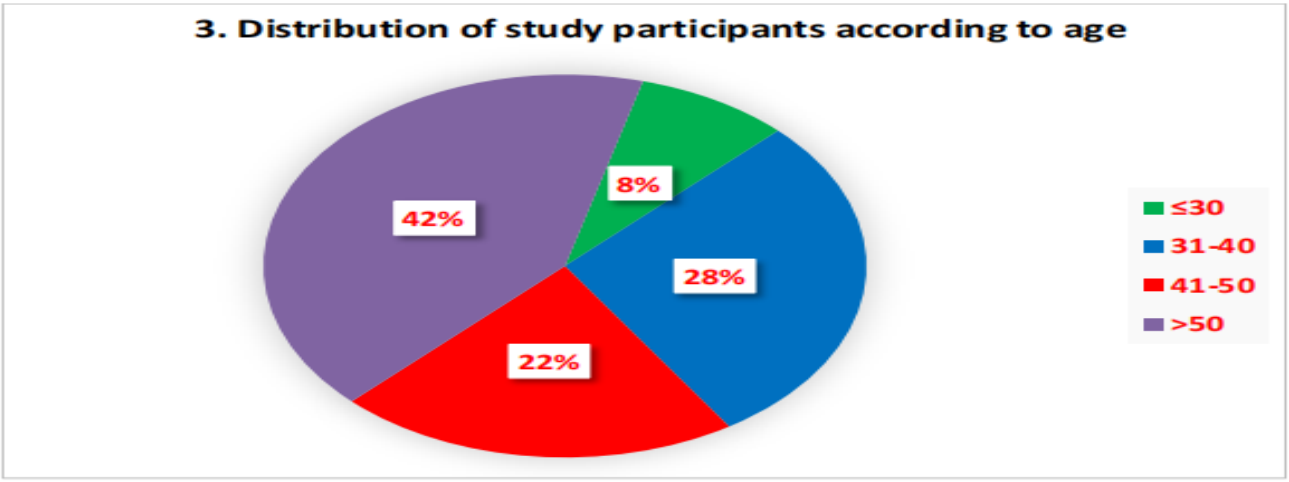

Table 4: Distribution of participants according to gender

Gender	Numbers	Percentage
Male	33	55.0
Female	27	45.0
Total	60	100.0

Table 4 shows that in this study 55 % were male and 27% females.

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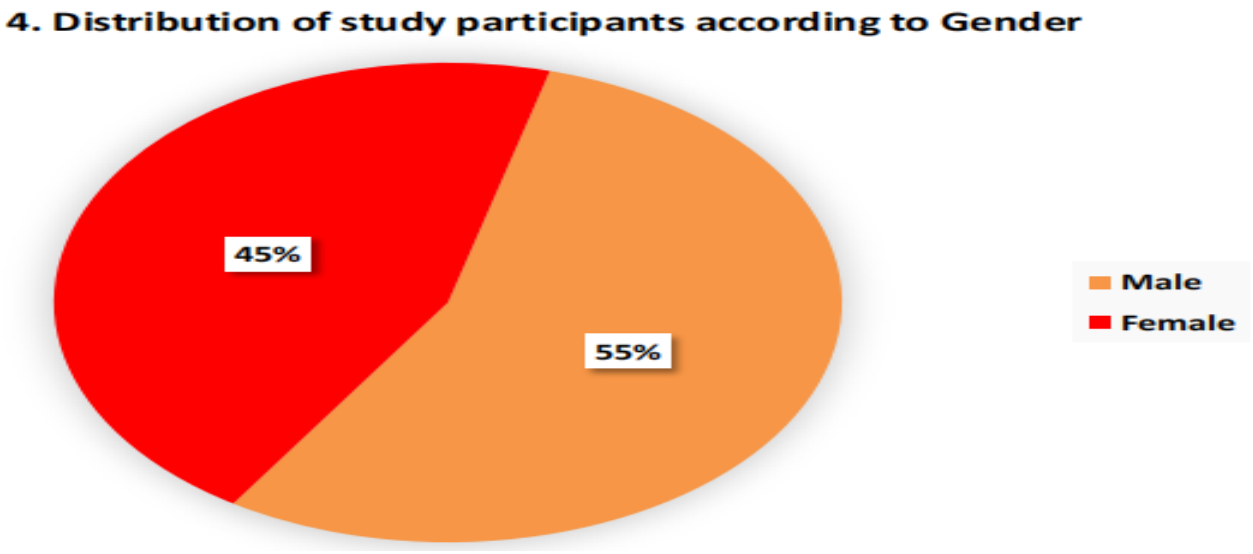

Table 5. Age wise distribution of study participants in type-I & type-II Diabetes Mellitus cases

Age (Years)	Type-I DM (n=30)		Type-II DM (n=30)	
	Numbers	Percentage	Numbers	Percentage
≤30	5	16.7%	0	0.0%
31-40	16	53.3%	1	3.3%
41-50	9	30.0%	4	13.3%
>50	0	0.0%	25	83.3%
Total	30	100.0%	30	100.0%

Table 5. Shows that in age group <30 years 16.7% patients were type 1 DM and 0% were type 2 DM , age group 31-40 years 53.3 % were type 1 DM and3.3 % type 2 DM , age group 41-50 years 30 % were type 1 DM and 13.3 % type 2 DM , age group >50 years 0% were type 1 DM and 25% were type 2 DM

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5. Age wise distribution of study participants intype-I & type-II Diabetes Mellitus cases

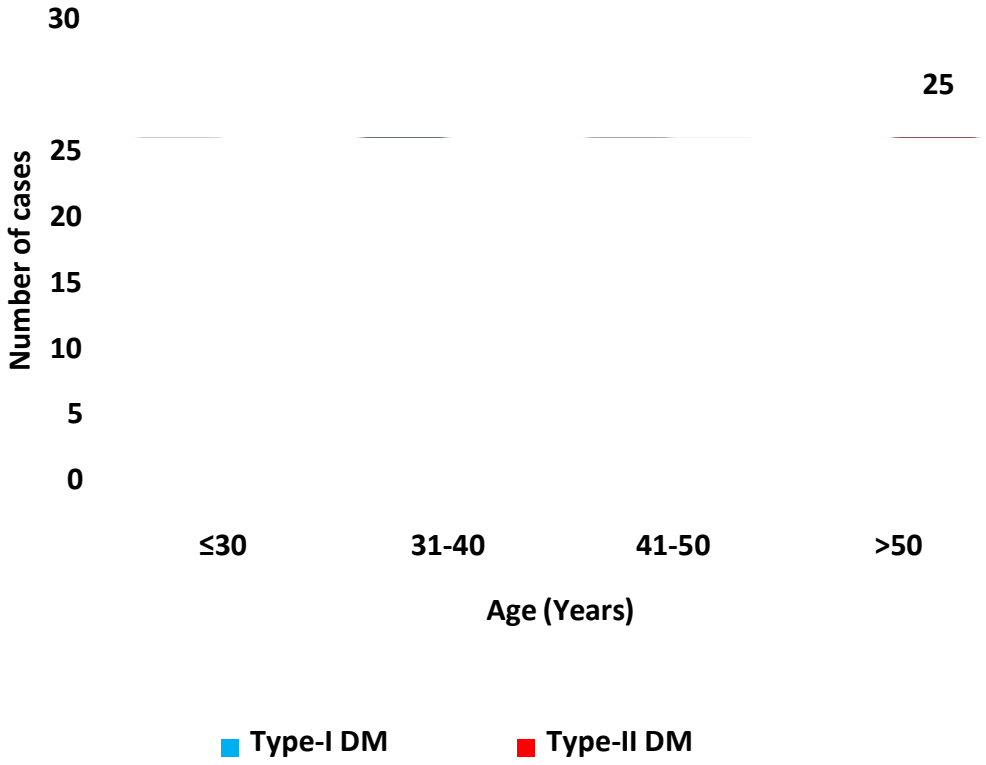

Table 6.Gender wise distribution of study participants in type-I & type-IIDiabetes Mellitus cases

Gender	Type-I DM (n=30)		Type-II DM (n=30)	
	Numbers	Percentage	Numbers	Percentage
Male	19	63.30%	14	46.70%
Female	11	36.70%	16	53.30%
Total	30	100.00%	30	100.00%

Number of cases

Table 6. Shows that in type 1 DM group 63.3 % were male and 46.7% were female whereas in type 2 DM group 36.7% were male and 53.3 % were female

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Table 7Age and gender wise distribution of study participants in type-I & type-II Diabetes Mellitus cases

Age (Years)	Type-I DM (n=30)			Type-II DM (n=30)			
	Male	Female	Total	Male	Female		
	Numbers (%)	Numbers (%)	Numbers (%)	Numbers (%)	Numbers (%)	%age	%age
≤30	3 (10	2 (6.7)	5	0 (0)	0 (0)	0.00%	0.00%
31-40	12 (40)	4 (13.3)	16	0 (0)	1 (3.3)	6.30%	3.30%
41-50	4 (13.3)	5 (16.7)	9	1 (3.3)	3 (10	18.80%	13.30%
>50	0 (0)	0 (0)	0 (0)	13 (43.3)	12 (40)	75.00%	83.30%
Total	19 (63.3)	11 (36.7)	30 (100)	14 (46.7)	16 (46.7)	100.00%	100.00%

Table 7 shows that in Type 1DM in age group <30 3% were males and 2 % females , age group 31-40 12 % males and 4% females , age group 41-50 4% males and 5 % females whereas in Type 2 DM in age group 41-50 years 1 % males and 3 % females , age group >50 years 13% males and 12% females.

Number of cases

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Table 8 :Association of HbA1c level with type-I & type-II DiabetesMellitus cases

HbA1c	Type-I DM (n=30)		Type-II DM (n=30)		Total		P Value
	Numbers	%age	Numbers	%age	Numbers	%age	
<6.5	0	0.00%	2	6.70%	2	3.30 %	0.15
≥6.5	30	100.00%	28	93.30%	58	96.70%	
Total	30	100.00%	30	100.00%	60	100.00%	

Table 8 shows that in type 1 DM patients 100 % have HbA1c levels ≥6.5 , in type 2 DM 6.7% patients have HbA1c levels <6.5 % and 93.3 % patients had HbA1c levels≥6.5

Table 9. Association of C-Pep level with type-I & type-II Diabetes Mellituscases

C-Pep	Type-I DM (n=30)		Type-II DM (n=30)		Total		P Value
	Numbers	%age	Numbers	%age	Numbers	%age	
<1	30	100.0%	1	3.4%	31	52.5%	<0.001*
1-4	0	0.0%	27	89.7%	26	44.1%	
>4	0	0.0%	2	6.9%	2	3.4%	
Total	30	100.00	30	100.00	60	100	

Table 9. Shows that in type 1 DM 100 % patients had C-PEPTIDE <1 , in type2 DM 3.4% patients had C-PEPTIDE <1 , 89.7% C-PEPTIDE 1-4 and 6.9% had C-PEPTIDE >4. All these findings were statistically significant.

Numberofcases

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Table 10. Comparison of LFT among type-I & type-II Diabetes Mellitus cases

Parameters	Type-I DM (n=30)	Type-II DM (n=30)	P Value
	Mean ± SD	Mean ± SD	
Total Bilirubin	1.02 ± 0.46	0.806 ± 0.47	0.05
SGOT	50.13 ± 38.95	58.16 ± 65.95	0.05
SGPT	49.6 ± 34.55	37.83 ± 21.65	0.05
ALP	107.70 ± 61.62	159.47 ± 69.99	0.001
GGT	43.73 ± 18.10	60.43 ± 33.33	0.001

Table 10. Shows that mean T.B is higher in type 1 DM as compared to type 2 DM , mean SGOT is higher in type 2 DM as compared to TYPE 1 DM , MeanSGPT is higher in type 1 DM compared to type 2 DM , mean ALP is higher intype 2 DM compared to type 1 DM , mean GGT is higher in type 2 DM compared to type 1 DM

Table 11. Comparison of Vit-D and LFT among Type-I and Type-IIDM

Parameters	Type-I DM (n=30)	Type-II DM (n=30)	P Value
	Mean ± SD	Mean ± SD	
Vitamin-D	25.72 ± 13.74	16.36 ± 13.46	0.010**
Total Bilirubin	1.02 ± 0.46	0.806 ± 0.47	0.072
SGOT	50.13 ± 38.95	58.16 ± 65.95	0.568
SGPT	49.6 ± 34.55	37.83 ± 21.65	0.119
ALP	107.7 ± 61.62	159.4 ± 69.99	0.004*
GGT	43.73 ± 18.10	60.43 ± 33.33	0.019**
* Highly Significant at 1% level of significance			
** Significant at 5% level of significance			

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Table no. 11- This table shows significant difference of vitamin D with p value in type 1 and type 2 dibetes and significant difference of ALP with p value 0.004 in type 1 and type 2 diabetes and also shows significant difference of GGT with p value 0.0019 in type 1 and type 2 diabetes

Discussion:

The study entitled "A COMPARATIVE STUDY OF VITAMIN D AND LIVER FUNCTION TEST ASSOCIATION IN TYPE 1 AND TYPE 2

Diabetes " was conducted as a cross sectional observational study in the department of Medicine in Shri Guru Ram Rai Instituteof Medical and Health Sciences (SGRRIM & HS) with the aim to compare the Vitamin D and LFT in patient suffering from type1 and type 2 DM.

It included all consecutive subjects suffering from Type1 and type 2 DM and satisfied the inclusion and exclusion criteria of the study .The subjects were categorized into 2 groups:

Group A included subjects, suffering from type 1 diabetes whereas Group Bincluded subjects suffering from type 2 diabetes both these groups were carefully matched for age, sex and the mean duration of illness .

This study was planned with background that there is a significant inverse association between serum vitamin D3 and presence of diabetes. vitamin D3 level are reported to alter the glycemic control and there is evidence to suggest that altered vitamin D3 and calcium homeostasis may play a role in the development of DM. Although the major and most well-known function of vitamin D3 is to maintain calcium and phosphorus homeostasis and promote bone mineralization, despite of this Vitamin D3 also improves insulin secretion and reduces insulin resistance thus ultimately helps to poor the diabetic complications.

Insulin resistance, the main cause of hyperglycemia and compensatory hyperinsulinaemia is the predominant cause of liver damage in diabetic patient. As liver is the primary organ susceptible to the effect of hyperglycemia induced oxidative stress. In this study it is observed that the number of cases having vitamin D deficiency were significantly higher in Type 2 DM as compared to Type 1 DM, with a significant p value . These findings are in agreement with, Amit, et al. (2014) who observed that there is significant relationship between reduced levels of vitamin D and calcium with type 2 diabetes. The role of vitamin D and calcium homeostasis has long been established and non-skeletal action especially in pancreatic beta cell function, insulini resistance and Type 1 diabetes.[18,19,20]

Subramanian et al., 2011 conclude that severe vitamin D deficiency in asian indians with T2DM compared with the non diabetic patient[21,22].

Taheri et al. (2012) conducted a cross-sectional study on 200 subjects (100 type 2 diabetics and 100 healthycontrols). Concentration of 25(OH) D, calcium,phosphorous, parathyroid hormone (PTH), fasting blood glucose,HbA1c, serum insulin, homeostasis model assessment of insulin resistance (HOMA-IR) was determined in the fasting samples. Anthropometric measurements including body mass index (BMI) were also measured.Eighty-five percent of type 2 diabetics and 79% of healthy subjects were suffering from vitamin D deficiencyor insufficiency. Serum concentration of 25(OH) D (22.08 ± 15.20 ng/ml) (r =0.11, P = 0.04) and calcium(8.94 ± 0.59 mg/dl) (r = −2.25, P = 0.04) has significant statistically with BMI in type 2 diabetic patients[23].

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