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Study of Vitamin D and Magnesium Levels in Newly Diagnosed Type 2 Diabetes Mellitus Patients in India

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ABSTRACT

Introduction: The global burden of Diabetes Mellitus is huge. This research was undertaken with an aim to study the prevalence of Vitamin D deficiency and Magnesium deficiency and their relation with insulin resistance and insulin secretion defect in newly diagnosed Type 2 DM patients.

Materials and methods: This was a hospital based cross-sectional comparative study on newly diagnosed Type 2 Diabetes Mellitus patients done over 18 months. Data was analysed using SPSS 21.0. Descriptive and Bivariate Analysis were used. P value less than 0.05 was considered significant.

Results: 25-Hydroxy Vitamin D deficiency was found to be more prevalent in new onset Type 2 Diabetes Mellitus group. 19.17% cases had preclinical hypomagnesaemia. We found strong negative co-relationship between HOMA-IR and 25-HydroxyVitD and Mg Level of Cases (R^2 0.4556 and R^2 0.5413 respectively); between HbA1C and 25-HydroxyVitD and Mg Level of Cases (R^2 0.5055 and R^2 0.564 respectively); and between HOMA-B and 25-HydroxyVitD and Mg Level of Cases (R^2 0.2337 and R^2 0.2476 respectively).

Conclusion: 25-Hydroxy Vitamin D levels and Magnesium were found to be significantly low in new onset Type 2 Diabetic Mellitus patients. We recommend screening for Vitamin D and Magnesium levels in newly diagnosed T2DM patients.

Key words: Newly diagnosed type 2 diabetes mellitus, Vitamin D, Magnesium, HOMA-IR, HOMA-B

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INTRODUCTION

Type 2 Diabetes Mellitus is a metabolic disorder characterized by hyperglycaemia which arises due to inability of the body to use insulin properly. Its prevalence is increasing not only in developed nations but also in the developing world. The diabetic population is expected to exceed double by 2030 from 171 million to a remarkable 366 million worldwide with ninety percent being Type 2 Diabetes Mellitus [1,2]. If untreated, Type 2 Diabetes Mellitus can increase the burden of chronic microvascular and macrovascular conditions like retinopathy, nephropathy, neuropathy and cardiovascular disease (CVD) [3].

The global burden of Diabetes Mellitus is huge, with an estimated yearly expenditure touching 673 billion US dollars in 2015, which constituted 12% of global health spending for that year. This is expected to mount to $802 billion by 2040. Approximately three-fourth of the Diabetic population live in low- and middle-income countries (LMICs) [4-6].

India contributes to a major part of the global burden of Type 2 Diabetes Mellitus. India being home to 69.1 million diabetics, ranked second highest after China in terms of the population with Type 2 Diabetes Mellitus in 2015. In India, the prevalence of Diabetes Mellitus ranges between 5–17%, with higher prevalence rates in the southern parts of the country and in urban areas [7,8]. Progressive cultural and social changes like ageing populations, increasing urbanization, dietary changes,

reduced physical activity and unhealthy behaviour contribute to the increasing trends of Diabetes Mellitus. As per recent epidemiological date the rising trend in the incidence of Diabetes Mellitus transcends the affluent class affecting urban India's middle class and working poor equally. Indians are genetically more predisposed to diabetes and have a greater degree of insulin resistance [9].

There are wide variations in the diabetes burden across the Indian states. The India State-Level Disease Burden Initiative as part of the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2016, reported a varied epidemiological transition and prevalence of diabetes among the states of India between 1990 and 2016 [10]. The Crude prevalence of diabetes in adults aged 20 years or older in Bihar in 1990 and 2016 shows an increase in prevalence from <4.5% to 20.0-27.9% [11].

The magnitude of the Type 2 Diabetes Mellitus epidemic with the burden it poses on the individuals and the society at large, stresses on the importance of finding ways to prevent and ameliorate the deleterious effects of this disease [12]. Type 2 Diabetes Mellitus has a multi-factorial pathogenesis with complex interplay between the potential causes. In addition to genetics which predisposes individuals to developing Type 2 Diabetes Mellitus, other factors like physical inactivity, poor nutrition practices and obesity, insulin resistance, deranged fatty acid metabolism, mitochondrial dysfunction and endoplasmic reticulum stress potentiate Type 2 Diabetes Mellitus through complex interactions many of which are unclear and are merely postulated. Moreover increasing evidence suggests that deficiency of Vitamin D and Magnesium may also contribute to the pathogenesis of Type 2 Diabetes Mellitus [13,14].

The extra-skeletal effects of Vitamin D have attracted considerable interest in the recent years. Deficiency of Vitamin D is emerging as one of the important nutritional risk factors for development of insulin resistance and Type 2 Diabetes Mellitus. Its association has also been implicated in poor glycaemic control and progression of complications among patients of Type 2 Diabetes Mellitus. In India, despite adequate exposure to sunlight throughout the year, deficiency of Vitamin D among Indians is a well-documented fact. The relationship of Vitamin D and Type 2 Diabetes Mellitus gains paramount importance with the surge in both Type 2 Diabetes Mellitus and hypo-vitaminosis D among Indians. Vitamin D directly stimulates insulin secretion from beta cells of pancreas, increases intracellular calcium levels, which attenuates insulin synthesis, improves insulin sensitivity in peripheral muscle and fats cells and plays important roles in glucose metabolism. Growing evidences suggest an association between vitamin D deficiency and an increased risk of developing Type 2 diabetes [15-17].

Diabetic patients often develop electrolyte disorders with diverse pathophysiology which may increase the morbidity and mortality associated with Type 2 Diabetes Mellitus. These electrolyte disturbances though are more common in decompensated diabetics, in elderly diabetics and diabetic patients with renal impairment but may also be observed in new onset diabetes mellitus subjects. Besides being a frequently encountered electrolyte disorder in diabetic patients, hypomagnesemia has been implicated as a contributory factor in various long term complications of diabetes mellitus. Hypomagnesemia through its association with insulin resistance and carbohydrate intolerance has been associated with worsening diabetes. This insight can pave way for pathophysiology-directed therapy, thus contributing to the avoidance of the several ominous effects associated with hypomagnesemia and its treatment [18].

OBJECTIVES

To study the prevalence of Vitamin D deficiency in new diagnosed Type 2 Diabetes Mellitus patients and its relation with insulin resistance and insulin secretion defect.

To study the prevalence of Magnesium (Mg) deficiency in newly diagnosed Type 2 Diabetes Mellitus patients and its relation with insulin resistance and insulin secretion defect.

MATERIALS AND METHODS

We conducted this hospital based cross-sectional comparative study on newly diagnosed Type 2 Diabetes Mellitus patients over a period of eighteen months from 1st October 2018 to 31st March 2020 in a tertiary care teaching hospital in the State of Bihar in India. This study was undertaken as a part of a thesis project for the Post Graduate Training Program in MD, Biochemistry under the MGM University. The study commenced after obtaining proper Institutional Ethics Committee approval.

The study included newly diagnosed Type 2 Diabetes Mellitus patients between 40-60 years age, of either sex or who were to be started on treatment for Type 2 Diabetes Mellitus. Patients with Type 1 Diabetes Mellitus or other forms of Diabetes; Patients with known history of Type 2 Diabetes Mellitus; Patients with known history of Hypertension; Patients with complications of Type 2 Diabetes Mellitus like Retinopathy, Neuropathy and Nephropathy; Geriatric patients> 60 years who may have associated hypo-vitaminosis D and electrolyte disorders which are age related; Patients with known Vitamin D deficiency; Patients with known electrolyte disorders; Patients who refused to participate in the study were excluded from the study.

Sample size and study group

The required sample size was calculated as 120 cases and 120 controls rounding to the next nearest number, using the formula suggested for case-control studies, and hypothesizing that almost 30% of the study population were diabetics as was evident from the prevalence of newly diagnosed Type 2 Diabetes Mellitus patients in MGM Medical College and LSK Hospital, Kishanganj over

the last couple of years and also the data of India State-Level Disease Burden Initiative as part of the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2016, further assuming the type I error of 5%, study power of 80% (β = 0.20) and the ratio of controls to cases as 1.

A total of 426 patients were screened from the outpatient unit of the Department of Medicine based on inclusion and exclusion criteria. Out of this, 120 patients were enrolled for the study after each one of them went through the Patient Information Sheet and consented by signing the Informed Consent Form in the local language. All the 120 enrolled study participants underwent estimation of Vitamin D levels, Serum Mg, Fasting Blood Sugar, Post Prandial Blood Sugar, Fasting Insulin levels and Glycosylated haemoglobin (HbA1C). The investigations were conducted in the Department of Biochemistry.

Statistical analysis

The results of the study observations were tabulated in Microsoft Office Excel 2010, compared and statically analysed through descriptive and bivariate statistics using the statistical software SPSS version 21.0. Continuous data were presented as means and standard deviation (SD). Differences among groups were analysed with unpaired Student's t-test for continuous variables, or using the chi-square test for dichotomous variables. Correlation was established by Bivariate analysis and linear regression analysis using Pearson correlation coefficient and r2value. Multivariate analysis was done between the different variables to arrive at a conclusion. P value less than 0.05 was considered significant.

Criteria of the different parameters in the study

Patients were considered having Type 2 Diabetes Mellitus based on the American Diabetes Association (ADA) guidelines if the patient fulfilled any one of the following criteria (on two occasions in two consecutive days).

- ✓ A fasting blood sugar ≥ 126 mg/dl (7.0 mmol/l).. The definition of "Fasting" was the first test in the morning before breakfast with no calorie intake except water for at least 8 hours.
- ✓ HbA1C ≥ 6.5%
- ✓ 2 hour blood sugar ≥ 200 mg/dl (11.1 mmol/l) after an oral intake of 75 gms glucose dissolved in water.
- ✓ For the purpose of this study, 25-hydroxy vitamin D below 30 ng/ml was considered low [19].
- ✓ Patients with serum Mg concentrations of ≤1.5 mg/dl were considered to have frank hypomagnesemia. While Mg concentrations of ≤1.8 mg/dL were considered as preclinical hypomagnesemia [20].
- ✓ Insulin levels are proportional to blood glucose levels in normal healthy individuals. However, insulin levels are either high or normal in the initial stages of Type 2 Diabetes Mellitus while insulin levels are low in the secondary stage of Type 2 Diabetes Mellitus.
- ✓ Insulin Resistance (IR) and beta-cell function for the purpose of this study was calculated as below using the following simple indices:
- ✓ HOMA-IR: Fasting glucose (mmol/L) ×fasting insulin (μU/mL)/22.5 [21].
- ✓ HOMA-B: 20 × fasting insulin (μU/ml)/fasting glucose (mmol/L) − 3.5 [22,23].
- ✓ Insulin resistance was considered in patients when HOMA-IR was ≥2.6 [24].

Sample collection and processing

A total of 7 ml of venous blood was withdrawn and divided in the Glucose Vial, Clot vial and the EDTA (Ethylenediamine Tetra-Acetic Acid) vial. The EDTA blood sample was used for doing HbA1C assay. Investigations were carried out using standard techniques. Fasting and Post Prandial Plasma Glucose and Serum Magnesium estimation was performed using Standard Colorimetric techniques. Serum Vitamin D level estimation, and Insulin levels were done by ECLIA (Electrochemiilluminiscence immunoassays) method. HbA1C was done by HPLC (high performance liquid chromatography) method.

RESULTS

A total of 426 patients were screened of which 120 patients were enrolled for the study. Thus the prevalence of new onset Type 2 Diabetes Mellitus among the Study Group in the age range of 40-60 years was 28.17%.

The study population included 240 individuals (120 new onset Type 2 Diabetes Mellitus patients [Cases] and 120 non Type 2 Diabetes Mellitus individuals [Controls]).

The Baseline and Demographic characteristics in the Study Group (Cases and Controls) are depicted in Table 1.

There were 65 (54.17%) females and 55 (45.83%) males in the cases (new onset Type 2 Diabetes Mellitus), whereas 62 (51.67%) females and 58 (48.33%) males in controls (without Type 2 Diabetes Mellitus). This is represented in Table 2. Chi square test revealed a P value of 0.241 with 1 degree of freedom. By conventional criteria, this difference is not statistically significant.

The mean age of the cases (new onset Type 2 Diabetes Mellitus) was 51.88 years (+6.05 SD) and the mean age

Table 1: Baseline and demographic characteristics of the study group.

Parameters	Case (Mean ± SD)	Control (Mean ± SD)	t value, df	P Value
Age (years)	51.88 ± 6.05	51.76 ± 6.04	-0.155, 119	0.877
25-Hydroxy VIT D (ng/ml)	27.19 ± 13.17	40.06 ± 21.25	5.330, 119	0.000*
Mg(mg/dL)	1.99 ± 0.18	2.25 ± 0.16	11.783, 119	0.000*

*Statistically significant (unpaired Student's t test) P value (<0.05)

of the controls (individuals without Type 2 Diabetes Mellitus) was 51.76 years (+6.04 SD). By conventional criteria, this difference was not statistically significant as the P value is 0.877. This is depicted in Table 3.

As depicted in Table 4, among the Cases, 25-Hydroxy Vitamin D was normal in 34.17% (41) out of which 36.92% (24) were females while 30.91% (17) were males while among the Controls, 25-Hydroxy Vitamin D was normal in 47.5% (57) out of which 38.71% (24) were females while 56.9% (33) were males. 25-Hydroxy Vitamin D was low in 65.83% (79) of the cases out of which 63.08% (41) were females while 69.09% (38) were males while among the controls 25-Hydroxy Vitamin D was low in 52.5% (63) out of which 61.29% (38) were females while 43.10% (25) were males.

Mean of 25-hydroxy Vitamin D for the Cases is 27.19 ng/ml (+13.17 SD) while the mean among Controls is 40.06 ng/ml (+21.25 SD). This difference is statistically significant with a P value of 0.009.

As depicted in Table 5, among the Cases, Mg level was normal in 80.83% (97) out of which 51.55% (50) were females while 48.45% (47) were males, 19.17% (23)

Table 2: Gender distribution of the study group.

Gender	Case		Control		P Value
	NO.	%	NO.	%	
Male	55	45.83	58	48.33	0.241
Female	65	54.17	62	51.67	
Total	120	100	120	100	

Table 3: Age distribution among cases and controls.

Age in years	Cases		Control		P Value
	No.	%	No	%	
40-44	21	17.5	17	14.17	0.877
45-49	16	13.33	26	21.67	
50-54	39	32.5	32	26.66	
≥55	44	36.67	45	37.5	
TOTAL	120	100	120	100	
Mean ± SD	51.88 ± 6.05		51.76 ± 6.04		

Table 4: Distribution of serum 25-Hydroxy Vitamin D level of the study group.

	Case					Control					P Value
	Male	Percentage	Female	Percentage	Total	Male	Percentage	Female	Percentage	Total	
Normal (≥30 ng/ml)	17	30.91%	24	36.92%	41 (34.17%)	33	56.90%	24	38.71%	57 (47.5%)	0
Low (<30 ng/ml)	38	69.09%	41	63.08%	79 (65.83%)	25	43.10%	38	61.29%	63 (52.5%)	
Total	55	100%	65	100%	120 (100%)	58	100%	62	100%	120 (100%)	

Table 5: Distribution of serum magnesium (Mg) level of the study group.

	Cases			Controls			P Value
	Male	Female	Total	Male	Female	Total	
Normal (≥1.8 mg/dl)	47 (48.45%)	50(51.55%)	97(80.83%)	58(48.33%)	62(51.67%)	120	0
Preclinical hypomagnesaemia (<1.8 md/dl but >1.5 mg/dl)	08 (34.78%)	15(65.22%)	23(19.17%)	0	0	0	
Frank hypomagnesaemia (≤ 1.5 mg/dl)	0	0	0	0	0	0	
Total	55(45.83%)	65(54.17%)	120 (100%)	58(48.33%)	62(51.67%)	120	

Table 6: Multivariate analysis with HbA1C, HOMA-IR and HOMA-B and Age, Sex, 25-hydroxy vitamin D and Mg level.

Variable	Determinants	P Value
HbA1C	Age	0.74
	Sex	0.105
	25-Hydroxy VITD level	0.000*
	Mg level	0.000*
HOMA-IR	Age	0.877
	Sex	0.257
	25-Hydroxy VITD level	0.000*
	Mg level	0.143
HOMA-B	Age	0.363
	Sex	0.589
	25-Hydroxy VITD level	0.001*
	Mg level	0.032*

*Statistically significant P value (<0.05)

cases had preclinical hypomagnesemia of which 65.22% (15) was a female while 34.78% (08) were males, while there were no cases of frank hypomagnesemia. Among the Controls, Mg level was normal all 100% (120) out of which 51.67% (62) were females while 48.33% (58) were males.

Mean of level of Mg for the Cases is 1.99 mg/dl (+0.18 SD) while that among Controls was 2.25 mg/dl (+0.16 SD). This difference was statistically significant with a P value of 0.000.

In Figure 1a, the Scatter Plot shows a strong negative co-relationship between HOMA-IR and 25-HydroxyVitD Level of Cases. The R2 value is 0.4556. This was statistically significant with a P value of 0.000.

In Figure 1b, the Scatter Plot shows a strong negative co-relationship between HOMA-IR and Mg Level of Cases. The R2 value is 0.5413. This was statistically significant with a P value of 0.000.ween

In Figure 2a, the Scatter Plot shows a strong negative co-relationship between HbA1C and 25-HydroxyVitD of Cases. The R2 value is 0.5055. This was statistically significant with a P value of 0.000.

In Figure 2b, the Scatter Plot shows a strong negative co-relationship between HbA1C and Mg Level of Cases. The R2 value is 0.564. This was statistically significant with

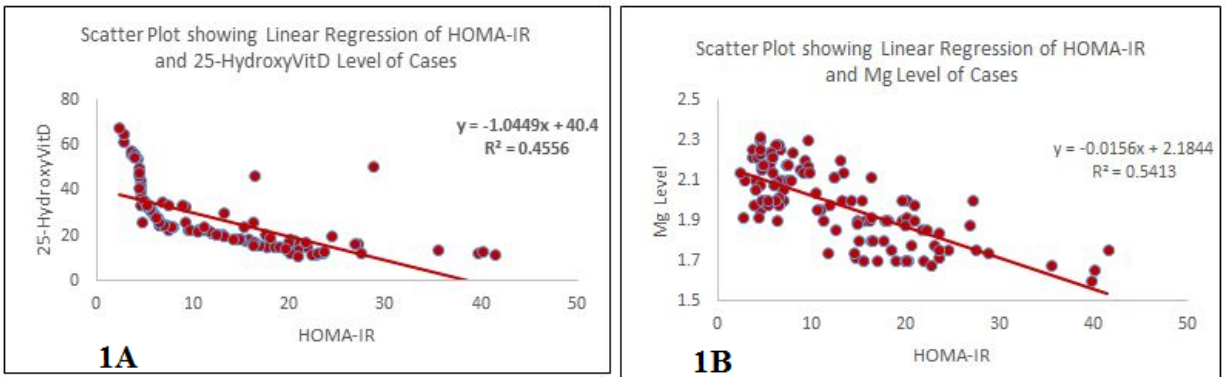
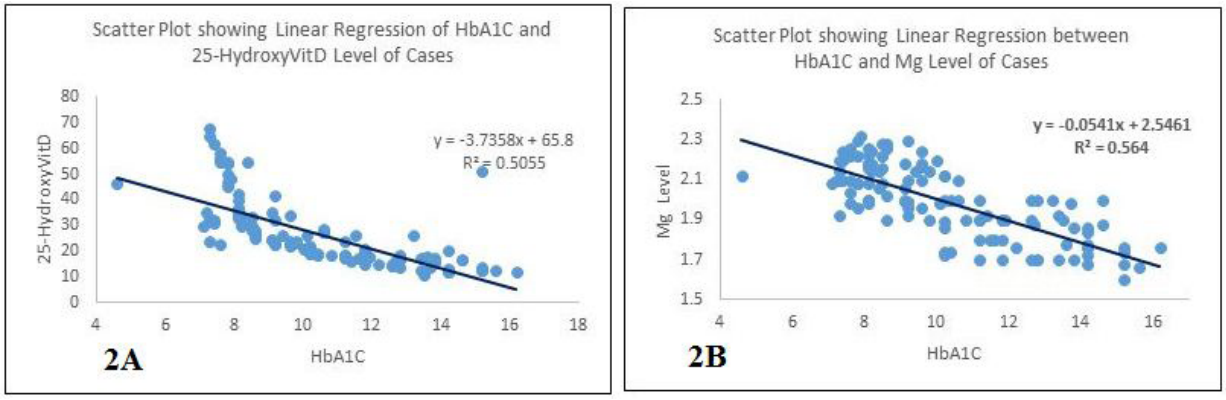
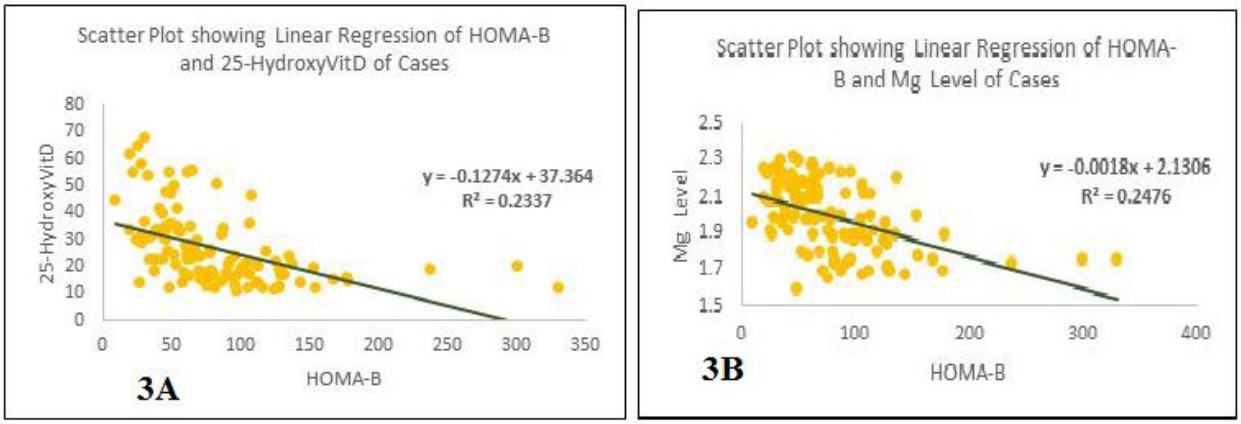


Figure 1A and 1B: Scatter plots showing linear regression between HOMA-IR and 25-Hydroxy Vitamin D Level and Mg level of cases.



Figures 2A and 2B : Scatter plots showing the linear relationship between HbA1C and 25-Hydroxy Vitamin D level and mg level of cases.



Figures 3A and 3B: Scatter plots showing linear relationship between HOMA-B and 25-Hydroxy Vitamin D Level and Mg level of cases.

a P value of 0.000.

In Figure 3a, the Scatter Plot shows a strong negative co-relationship between HOMA-B and 25-HydroxyVitD of Cases. The R2 value is 0.2337. This was statistically significant with a P value of 0.000.

In Figure 3b, the Scatter Plot shows a strong negative co-relationship between HOMA-B and Mg Level of Cases. The R2 value is 0.2476.This was statistically significant with a P value of 0.000.

In the Multivariate Model as depicted in Table 6, Age, Sex, 25-HYDROXY VITD and Mg level were found to be statistically significant with HbA1C; Age, Sex and 25-HYDROXY VITD were found to be statistically significant with HOMA-IR while Age, Sex, 25-HYDROXY VITD and Mg level were found to be statistically significant with HOMA-B.

DISCUSSION

Demographics

We enrolled 240 participants in our study who were divided into two groups of CASE (having new onset Type 2 Diabetes Mellitus) and CONTROL (non-diabetic individuals) with each group containing 120 participants. The mean age of the Cases was 51.88 years (+6.05 SD) while that of the Controls was 51.76 years (+6.04 SD). In the Cases the distribution of males and females was 45.83% (55) and 54.17% (65) respectively whereas in Controls it was 48.33% (58) and 51.67% (62) respectively with P value of 0.241.

Prevalence of new onset Type 2 diabetes mellitus

As per the Diabetes Atlas 2019, the prevalence of Diabetes in India is 8.9%. The prevalence of Diabetes Mellitus in India ranges from 5–17%, with higher levels found in the southern parts of the country and in urban areas [7,8]. As per the India State-Level Disease Burden done as a part of the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2016, the crude prevalence of diabetes in adults aged 20 years or older in Bihar in 2016 shows a rate of 20.0-27.9%. 11 In our study we found that the prevalence of new onset Diabetes Mellitus in the age group of 40-60 years was 28.17%.

25-hydroxy vitamin D and new onset Type 2 diabetes mellitus

In our study, 25-Hydroxy Vitamin D deficiency was found to be more prevalent in new onset Type 2 Diabetes Mellitus group with the prevalence of 65.83% (79) with MEAN ± SD being 27.19 +13.17 whereas in the Control group 25-Hydroxy Vitamin D deficiency accounted for 52.5% (63) with MEAN ± SD 40.06+21.25 (P value 0.000). We did not find any case of severe Vitamin D deficiency (<5 ng/dl). This may be due to the adequate exposure to sunlight due to the rural and agricultural practices in this part of the country. Our findings were similar to a study by Laway et al. conducted among the North Indian population with new onset Type 2 Diabetes Mellitus on the pattern of 25-Hydroxy Vitamin D status. In this study, the overall 25-Hydroxy Vitamin D, was lower (mean ± SD, 18.81 ± 15.18 ng/ml) in patients with Type 2 Diabetes Mellitus as compared to healthy controls (28.46 ± 18.89 ng/ml) (P=0.00) with 81% of Type 2 Diabetes Mellitus patients having either 25-Hydroxy Vitamin D deficiency or insufficiency compared to 67% of healthy control subjects, taking a cut of 25-Hydroxy Vitamin D as 30 ng/ml. Severe Vitamin D deficiency (< 5 ng/ml) was seen in 16.2% of patients with diabetes and 2.5% of control subjects. Levels of 25-Hydroxy Vitamin D had a negative correlation with HbA1c and fasting plasma glucose [25]. In another study by Daga et al. 25-Hydroxy Vitamin D deficiency was seen in 91.1% of the subjects with diabetes, and 58.5% of the healthy controls. Mean ± SD 25-Hydroxy Vitamin D was significantly low, 7.88 ± 1.20 ng/mL in subjects with diabetes against 16.64 ± 7.83 ng/mL in controls [26].

In a study by Kumar PS, 25-Hydroxy Vitamin D deficiency was observed in 52.5% of the patients. However, in this study 25-Hydroxy Vitamin D levels were not associated with markers of glycaemic control or insulin resistance. This study concluded that hypo-vitaminosis D was observed in more than half of the patients with type 2 diabetes suggesting a potential for vitamin D supplementation in type 2 DM patients [27].

On Bivariate and Linear Regression analysis, there was a strong negative co-relationship between HOMA-IR, HbA1C, HOMA-B and 25-Hydroxy Vitamin D levels with Pearson co-relation coefficient of -0.675,-0.711 and -0.483 respectively which is statistically significant with a P value of 0.000 while R2 of 0.4556, 0.5055 and 0.2337 respectively.

Studies postulated that Vitamin D deficiency is related to insulin secretion, insulin resistance, and β-cell dysfunction in the pancreas and that secretion of pancreatic insulin is inhibited by vitamin D deficiency in the diabetic animal model.15-17

Thus, suboptimal vitamin D status has emerged as a potential contributor to the pathophysiology of Type 2 Diabetes Mellitus, with several lines of evidence supporting a role for vitamin D in pancreatic b-cell function and insulin sensitivity [28].

However, there are studies on the contrary which reveal that low 25-Hydroxy Vitamin D levels are not associated with the risk for Type 2 Diabetes Mellitus [29] and that the association between 25-Hydroxy Vitamin D concentrations and Type 2 Diabetes Mellitus is not causal [30]. According to a recent meta-analysis vitamin D supplementation administered for glycaemic control and insulin resistance in patients with diabetes is not recommended, although doses of vitamin D supplementation may have been suboptimal; almost all trials included in the meta-analysis used vitamin D doses of at least 2000 IU/d [31]. Results from other studies also concluded that vitamin D supplementation at doses of 400 to 800 IU/d, with or without calcium, does not prevent new-onset Type 2 Diabetes Mellitus [32].

A review article by Mitri et al. [28] and Hassan et al. [33] summarized that although the role of vitamin D in helping to control blood glucose is not clear, vitamin D status appears to play a role in the development and treatment of diabetes. We conclude that Vitamin D deficiency is common in patients with new onset Type 2 Diabetes Mellitus and recommend the need for routine assay of Vitamin D in new onset Type 2 Diabetes mellitus patients.

Magnesium and new onset Type 2 diabetes mellitus

In our study, among the Cases, 19.17% (23) cases had preclinical hypomagnesemia while there were no cases of frank hypomagnesemia. Among the Controls, there were no cases of preclinical or frank hypomagnesemia. MEAN of level of Mg2 for the Cases is 1.99 mg/dl (+0.18) while that among Controls was 2.25 mg/dl (+0.16). This difference was statistically significant with a P value of 0.000. Bivariate and Logistic Regression analysis revealed a significantly negative correlation between HOMA-IR, HbA1C, HOMA-B and Mg2+ levels with Pearson co-relation coefficient of -0.736, -0.751 and -0.498 and R2 of 0.5413, 0.564 and 0.2476. The P value was 0.000, 0.000 and 0.000 respectively.

A study by Arpaci et al. reported a mean magnesium level of 1.97 ± 0.25 (1.13 to 3.0) mg / dl. Analysis of this study revealed a weak negative correlation between serum Mg and HbA1c levels (r =-0.110, p=0.004). The study concluded that Mg deficiency is common in diabetics. This study postulated a vicious cycle with low Mg levels affecting glycaemic regulation and also poor glycaemic regulation affecting serum Mg levels [34].

A review article by Phuong Chi T et al. reported incidence of hypomagnesemia in patients with Type 2 Diabetes Mellitus, implicated contributing factors, and associated complications. As per this article 13.5 to 47.7% patients with Type 2 Diabetes Mellitus had hypomagnesemia. The article inferred that the increased incidence of hypomagnesemia among patients with Type 2 Diabetes Mellitus presumably is multifactorial and in view of the current evidence suggesting adverse outcomes associated with hypomagnesemia, this study recommended routine monitoring of magnesium in diabetic patient population and treating hypomagnesemia whenever possible. Although no study has ever documented an optimal serum Mg concentration in patients with diabetes, this article by Phuong Chi T et al. speculated that a level between 2.0 and 2.5 mg/dl may be favorable [35].

Ghattaura et al. reported that Type 2 Diabetes Mellitus is the main factor for low serum magnesium levels in overweight diabetics. Hypomagnesemia may aggravate insulin resistance in overweight subjects which can predispose them to metabolic complications of Diabetes Mellitus [36].

In a review article Gommers et al. mentioned that hypomagnesemia (serum Mg <0.7 mmol/L) has been strongly associated with Type 2 Diabetes Mellitus. Clinical studies demonstrate that Type 2 Diabetes Mellitus patients with hypomagnesemia have reduced pancreatic β-cell activity and are more insulin resistant. Moreover, dietary Mg2+ supplementation for patients with Type 2 Diabetes Mellitus improves glucose metabolism and insulin sensitivity [37].

Reddy S et al. reported a negative correlation between serum Mg and HbA1c levels (r =-0.110, p =0.004). The study concluded hypomagnesemia and HbA1c levels are more in uncontrolled Type 2 Diabetes Mellitus patients compared to controlled diabetic and non-diabetic patients. If serum magnesium is low, increased dietary intake of magnesium should be recommended [38].

Chronic Mg deficit is proposed to cause post-receptorial insulin resistance and consequent reduced glucose utilization in the cells leading to worsening of the already reduced insulin sensitivity in Type 2 Diabetes Mellitus. Further Mg deficiency and reduced insulin sensitivity may be through presence of oxidative stress and/or inflammation [39].

CONCLUSION

The study concluded Serum 25-Hydroxy Vitamin D was low in 65.83% of the Cases while it was low in 52.5% of the Controls. 25-Hydroxy Vitamin D is significantly negatively correlated with HbA1C, HOMA-IR and HOMA-B. 25-Hydroxy Vitamin D levels were found to be significantly low in new onset Type 2 Diabetic Mellitus patients and thereby can be considered a determinant for the development and worsening of glycaemic status in new onset Type 2 Diabetes Mellitus patients.

The prevalence rate of pre-clinical hypomagnesemia among the Cases was 19.17% while there were no cases of pre-clinical hypomagnesemia among the Controls. Serum Magnesium level was significantly negatively correlated with HbA1C, HOMA-IR and HOMA-B and can be considered a significant determinant for the development and worsening of glycaemic status in new onset Type 2 Diabetes Mellitus patients.

The study thus recommends routine screening of Vitamin D and Magnesium levels in newly diagnosed Type 2 Diabetes Mellitus patients.

LIMITATIONS

The sample size being small it was difficult to extrapolate the findings of this study and generalize them. Moreover, as the study was done in a multispecialty tertiary care medical college in Kishanganj, Bihar, the generalisability of the study to other populations may not hold true. The study was a cross sectional study. Thus, prospective studies to test associations concretely could not be done. As the study was cross sectional, the effect of correction of Vitamin D deficiency on insulin resistance and β cell secretion defect could not be demonstrated. Follow up could not be done regarding improvement on the status of Magnesium levels after glycaemic control and treatment of insulin resistance.

CONFLICT OF INTEREST

The authors declare there is no conflict of interest in this study.

AUTHOR CONTRIBUTIONS

MB collected patient samples and research data along with doing the laboratory investigations and also helped the other two authors in data analysis and interpretation and writing the paper. MM wrote the paper. GS did the data analysis and data interpretation. All the authors participated in the final revision of the manuscript and approved the final version.

ETHICS COMMITTEE AND CONSENT TO PARTICIPATE

The study was commenced after approval of the Institutional Ethics Committee of MGM Medical College and LSK Hospital, Kishanganj, Bihar, India. The study participants were enrolled only after they read and understood the Patient Information Sheet containing all the necessary information on the study and signing the Informed Consent in the local Language.

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