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Comparative study of serum magnesium levels in patients with type 2 diabetes mellitus with and without retinopathy at tertiary care centre in Bangalore

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Abstract
Background and Objectives: Diabetic retinopathy (D.R.) is the most common cause of loss of vision (acquired blindness) in the world that increases the probability of loss of vision about 25 times higher compared to healthy individuals. Several precipitating factors, such as duration of disease, hypomagnesemia, glycemic control has been implicated in the development and progression of diabetic retinopathy.
Objective
1. Estimating Serum Magnesium concentration in patients with type 2 Diabetes mellitus patients with and without retinopathy.
2. Correlating severity of hypomagnesemia in patients with Diabetic retinopathy and Diabetes mellitus without retinopathy.

Material and Methods: This is an observational study conducted in Dr. B.R Ambedkar Medical College and Hospital, Bengaluru to study hypomagnesemia as an important factor in the early progression of diabetic patients without retinopathy to retinopathy. 30 diabetic patients with retinopathy and 30 diabetic patients without retinopathy were selected for the study in our hospital. There was an increase in the Fasting Blood Sugar (FBS) and HbA1c in diabetic patients with retinopathy when Contrast to diabetic mellitus patients without retinopathy. The increase was statistically significant.
Results: There was a decrease in the magnesium levels in diabetic patients with retinopathy compared to the diabetic patients without retinopathy, and it was statistically significant. The estimation of serum magnesium and HbA1c can help us to predict the onset and progression of diabetic retinopathy.

Keywords: Type 2 diabetes mellitus, hypomagnesemia, retinopathy

Introduction
Diabetes mellitus is a group of metabolic disease characterised by increased levels of glucose in the blood (hyperglycaemia) resulting from defects in insulin secretion, insulin action or both. Related to: An endocrine disorder causes abnormal insulin production, impaired insulin utilization, both abnormal production and impaired utilization. Metabolic abnormalities in carbohydrates, proteins, and lipids resulting from Insulin's importance as an anabolic hormone. Low levels of Insulin to achieve an adequate response or Insulin the resistance of target tissues, mainly adipose tissue, skeletal muscles, and to a lesser extent, the liver, at the level of insulin receptors, signal transduction system and effector enzymes are responsible for these metabolic abnormalities. The severity of the disease depends on the duration of diabetes mellitus. Some patients with type 2 diabetes during the early years of the disease are asymptomatic. Others with marked hyperglycaemia, especially in children with an absolute insulin deficiency may suffer from polyuria, polydipsia, weight loss, polyphagia, and blurred vision. Stupor, coma, and, if not treated, death may occur in uncontrolled diabetes mellitus due to keto acidosis or rare from non ketotic hyper osmolar syndrome [1, 2, 3]. Diabetes mellitus can cause damage to the retina is called Diabetic retinopathy. It is the most important cause of blindness in developed countries [4]. Diabetic retinopathy is caused by up to 80% of those who have had diabetes mellitus for 20 years or more.5 in 90% of new cases could be reduced with adequate treatment with Insulin or oral hypoglycaemic drugs and eye monitoring [2].

The higher chances of developing diabetic retinopathy in a long duration of diabetes mellitus patients [6]. Diabetic retinopathy occurs for 12% of all new blindness cases in the United States each year. Duration of diabetes mellitus, poor glycaemic control, dyslipidaemia, hypertension and hypomagnesaemia are the most important predisposing cause related to the development and progression of diabetic retinopathy [7, 8]. Magnesium (Mg) has a critical role in essential enzymes' actions and is the most abundant cation in the human body [9]. It is claimed that there is an inverse relationship between Mg intake and incidence of diabetes mellitus (D.M.) [10]. Mg deficiency is common in diabetic patients. The incidence of hypomagnesemia varies between 11 and 47.7%. Compared with the standard group, the incidence of Hypomagnesemia in newly diagnosed diabetes is 10.5-fold/, and in patients with previously diagnosed diabetes is 8.5-fold more common

Materials and Method

The study population consists of 60 Patients with Diabetes Mellitus who satisfy the inclusion criteria and presenting to Dr. B.R Ambedkar Medical College, Bangalore from February 2018 to February 2020 were taken up for the study

Type of Study: A hospital-based observational Prospective Study Sampling Criteria

Inclusion Criteria

1. All patients with Type 2 Diabetes Mellitus
2. 2.Patients with diabetes mellitus who are taking oral Hypoglycaemic agents and /or Insulin
3. Patients with Fundus examination showing changes in diabetic retinopathy and without diabetic retinopathy.

Exclusion Criteria

1. Patients with Chronic Renal Failure
2. Patients on Diuretics
3. Patients with Alcohol Abuse
4. Patients receiving Magnesium supplements such as Laxatives
5. Patients with Malabsorption or Chronic Diarrhoea
6. Patients without informed consent.

Methods

Detailed clinical history through a physical examination with relevant investigations were done in all included patients. A detailed history was taken for all patients, which included a history of 21 1. Increased urination, 2. Increased thirst, 3. Weight loss 4. Blurring of vision 5. Headache 6. Fatigue 7. Itchy skin 8. Pain abdomen 9. Nausea and vomiting 10. Smell of acetone on the breath.

Investigations

1. Fasting blood sugar (FBS)
2. Postprandial blood sugars (PPBS)
3. Serum Magnesium
4. HbA1C
5. Blood urea
6. Serum Creatinine
7. Serum Electrolytes
8. Complete Urine Examination
9. Fundoscopy

Statistical Methods

An Independent t-test, also called the two-sample t-test, was used to correlate gender distribution, FBS, PPBS, HbA1c, duration of diabetes mellitus, and hypomagnesemia diabetes with retinopathy and without retinopathy patients.

Results

The present study analyses the correlation between serum magnesium levels measured in diabetic patients with retinopathy and diabetic patients without retinopathy.

The study was conducted on 30 diabetic patients with retinopathy, 30 diabetic patients without retinopathy who came to the department of General medicine at our hospital.

Table 1: Age Distribution in the study groups

Age Distribution in the study groups					
Age (In Years)			Group		Total
			Diabetic with Retinopathy	Diabetic without Retinopathy	
Age group	31 - 40	Count	4	6	10
		%	13.3%	20.0%	16.7%
	41 - 50	Count	18	13	31
		%	60.0%	43.3%	51.7%
	51 - 60	Count	8	11	19
		%	26.7%	36.7%	31.7%
Total		Count	30	30	60
		%	100.0%	100.0%	100.0%

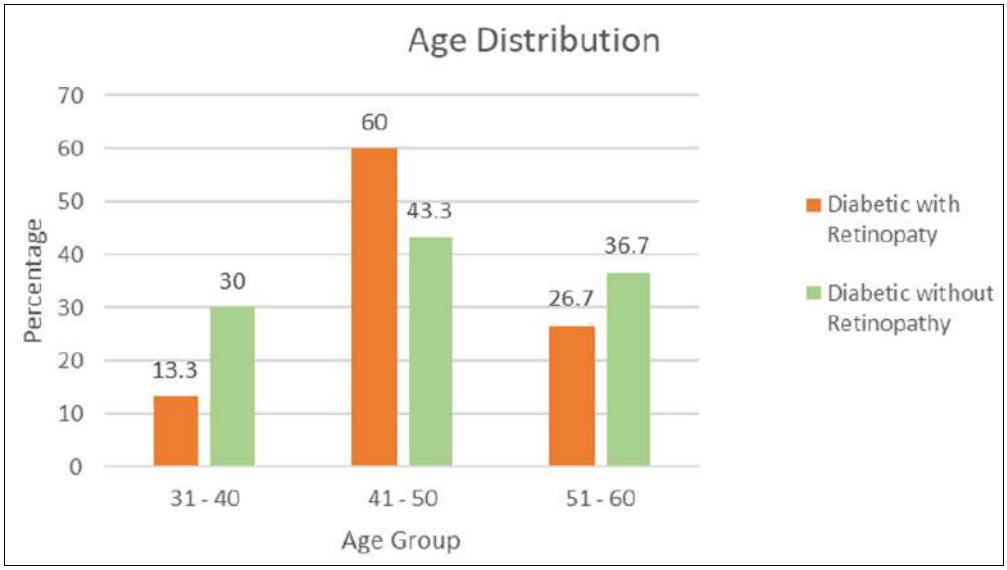

Fig 1: Bar diagram showing age distribution in the study groups

As represented in Table-1 and Fig-1, Out of 60 patients, 13.3% were diabetic with retinopathy, and 20.0% were diabetic without retinopathy in 31-40 years of age group, 60.0% were diabetic with retinopathy, and 43.3% were diabetic without retinopathy in 41-50 years of age group, and 26.7% were diabetic with retinopathy, and 36.7% were diabetic without retinopathy in 51-60 years of age group. The predominant age group was 41-50 years.

Table 2: Gender distribution in the study groups.

Sex Distribution					
			Group		Total
			Diabetic with Retinopathy	Diabetic without Retinopathy	
Sex	Male	Count	20	19	39
		%	66.7%	63.3%	65.0%
	Female	Count	10	11	21
		%	33.3%	36.7%	35.0%
Total		Count	30	30	60
		%	100.0%	100.0%	100.0%

As represented in Table 2, among diabetic patients with retinopathy, 20 patients (66.7%) were males, and ten patients 33.3%) were females. Among the diabetes mellitus patients without retinopathy, 19 patients (63.3%) were males, and 11 patients (36.7%) were females in the study group. Hence diabetic retinopathy was predominantly seen in males.

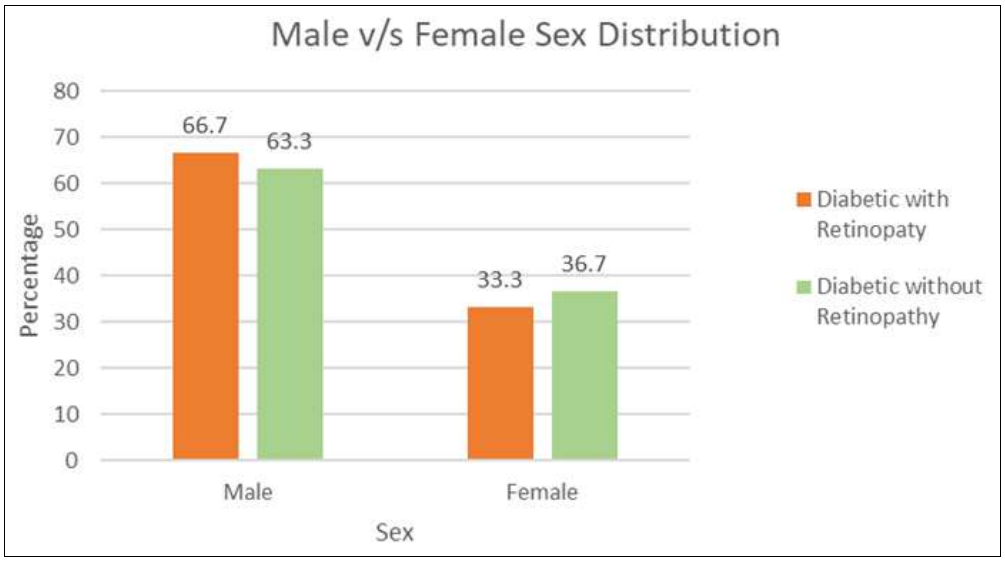

Fig 2: Bar diagram showing gender distribution in the study groups

Figure 2. Shows the gender distribution in the study groups. The above findings show that the incidence of diabetic retinopathy was higher in males when compared to females.

Table 3: Duration of diabetes mellitus

Duration of D.M. (Years)					
Group		**N**	**Mean**	**Standard Deviation**	**P-Value**
Duration of D.M. (years)	Diabetic with Retinopathy	30	8.83	3.93	0.003
	Diabetic without Retinopathy	30	3.60	1.71	

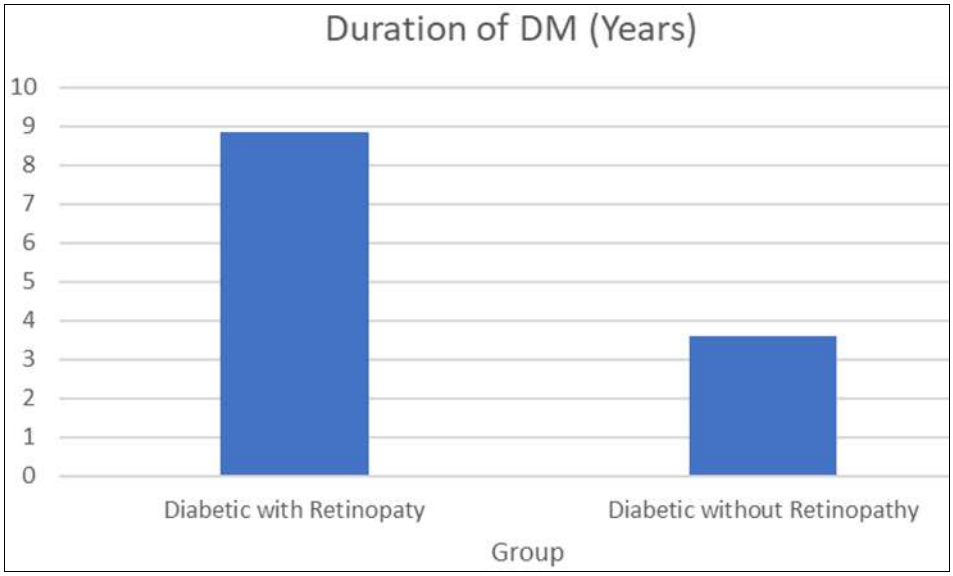

Fig 3: Bar diagram showing the duration of diabetes mellitus in the study group

As represented in Table-3 and fig 3, the mean duration of diabetes mellitus in diabetic patients with retinopathy was 8.83±3.93 years; and in diabetic patients without retinopathy, it was 3.36±1.171 years. There was an increase in diabetes mellitus in diabetic patients with retinopathy compared to diabetic patients without retinopathy. P-value is 0.003, which is significant. The increase was statistically significant.

Table 4: Showing mean and standard deviation of FBS (mg/dl) in the study groups

FBS (mg/dl)					
Group		**N**	**Mean**	**Standard Deviation**	**P-Value**
FBS (mg/dl)	Diabetic with Retinopathy	30	178.57	41.68	0.002
	Diabetic without Retinopathy	30	133.10	17.84	

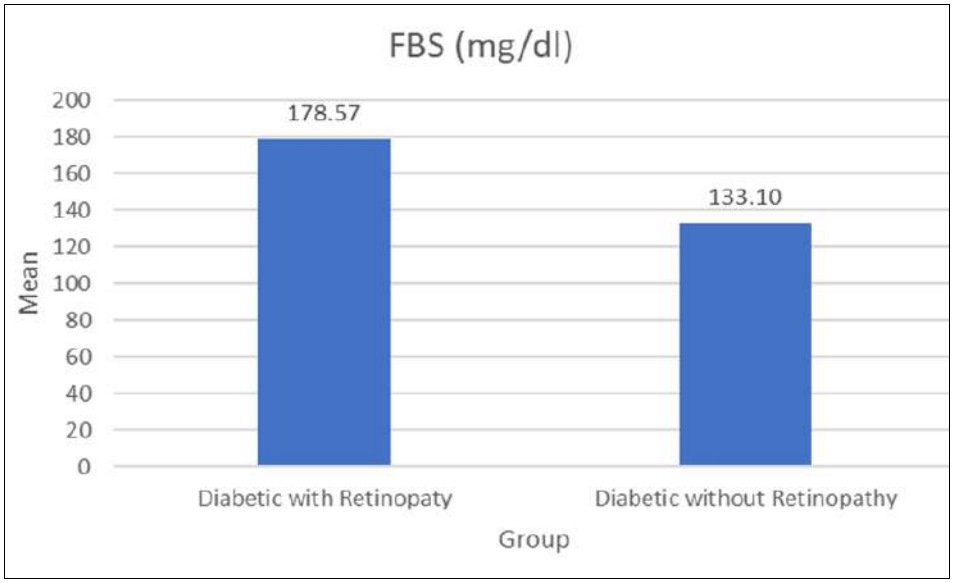

Fig 4: Bar diagram showing the mean FBS values (mg /dl) in the study groups

As represented in Table-4 and Fig-4, the mean FBS levels in diabetic patients with retinopathy was 178.57±41.68 mg/dl; and in diabetic patients without retinopathy, it was 133±17.84. There was an increase in FBS in diabetic patients with retinopathy compared to diabetic patients without retinopathy. P-value is 0.002, which is significant. The increase was statistically significant.

Table 5: Showing mean and standard deviation of PPBS (mg/dl) in the study group

PPBS (mg/dl)					
Group		N	Mean	Standard Deviation	P-Value
PPBS(mg/dl)	Diabetic with Retinopathy	30	247.93	59.23	0.002
	Diabetic without Retinopathy	30	175.53	19.76	

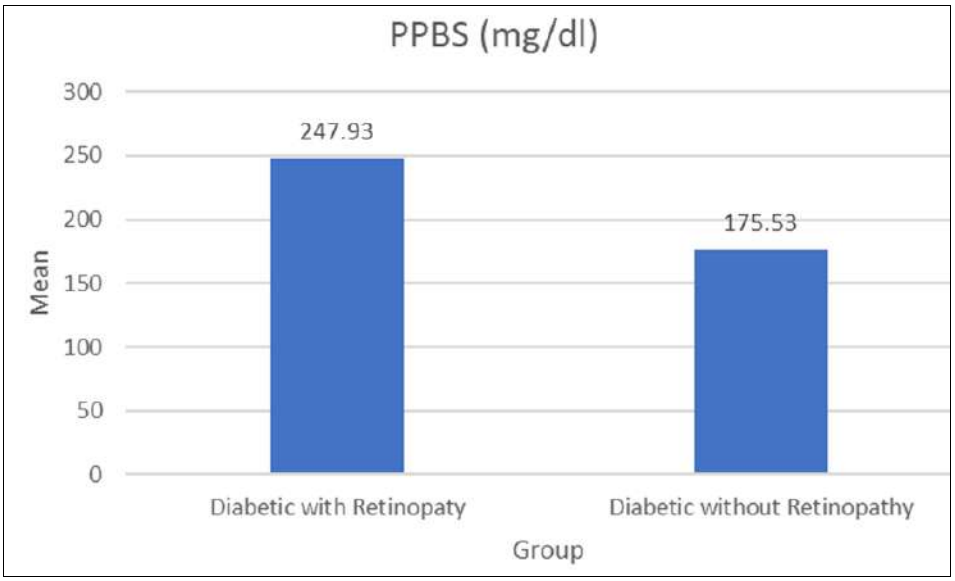

Fig 5: Bar diagram showing the mean PPBS values (mg /dl) in the study groups

As represented in Table-5 and Fig-5, the mean PPBS level in diabetic patients with retinopathy was 247.93±59.23 mg/dl; and in diabetic patients without retinopathy, it was 175.53±19.76. There was an increase in PPBS in diabetic patients compared to diabetic patients without retinopathy. P-value is with retinopathy 0.002, which is significant. The increase was statistically significant.

Table 6: Mean and standard deviation of Serum magnesium levels in the study group

Sr. Magnesium (mg/dl)					
Group		N	Mean	Standard Deviation	P-Value
Sr. magnesium(mg/dl)	Diabetic with Retinopathy	30	1.75	0.16	0.001
	Diabetic without Retinopathy	30	2.02	0.17	

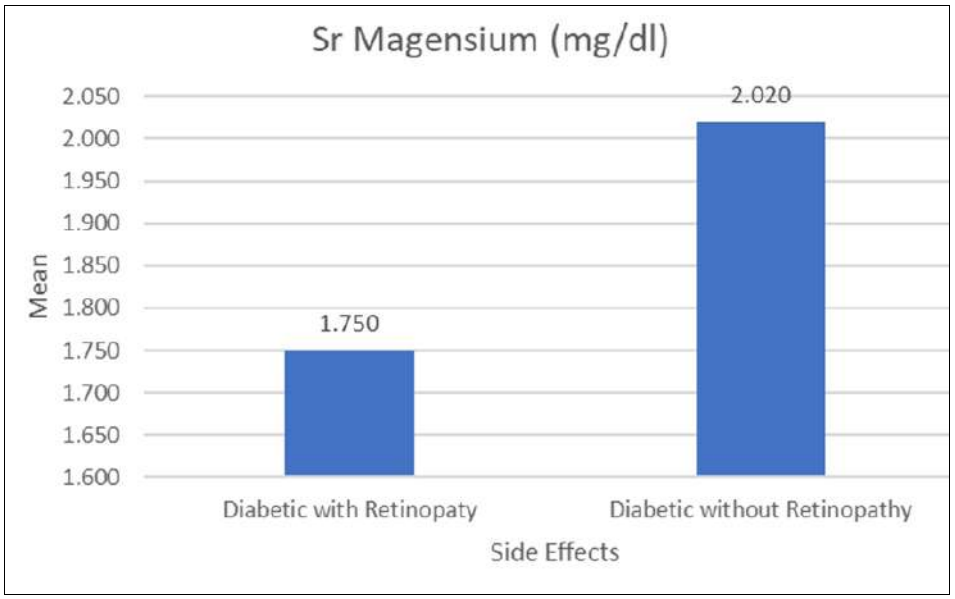

Fig 6: Bar diagram showing the mean magnesium levels (% mg/dl) in the study groups.

As represented in table No 6 and Fig-6, the mean serum magnesium levels in diabetic patients with retinopathy was 1.75±0.16 mg/dl, and in diabetic patients without retinopathy was 2.02±0.17mg/dl. There was a decrease in serum magnesium levels in diabetic patients with retinopathy compared to diabetic patients without retinopathy. P-value is 0.001, which is significant. The decrease was statistically significant. The above bar diagram shows that there is a significant decrease in the mean magnesium levels in diabetic patients with retinopathy when compared to diabetic patients without retinopathy**.** The exact cause of hypomagnesemia in diabetes mellitus is not known. Inadequate dietary intake, impaired absorption of magnesium, increased urinary loss due to hyperglycemia, and osmotic diuresis may be contributory factors. Magnesium depletion is also said to increase the risk of secondary complications.

Table 7: Showing HbA1c group * Group cross tabulation

HbA1C group * Group Cross tabulation					
			Group		Total
			Diabetic with Retinopathy	Diabetic without Retinopathy	
HbA1C group	3 -6.9	Count	5	13	18
		%	16.7%	43.3%	30.0%
	7 -10.9	Count	25	16	41
		%	83.3%	53.3%	68.3%
	11 -14.9	Count	0	1	1
		%	0.0%	3.3%	1.7%
Total		Count	30	30	60
		%	100.0%	100.0%	100.0%

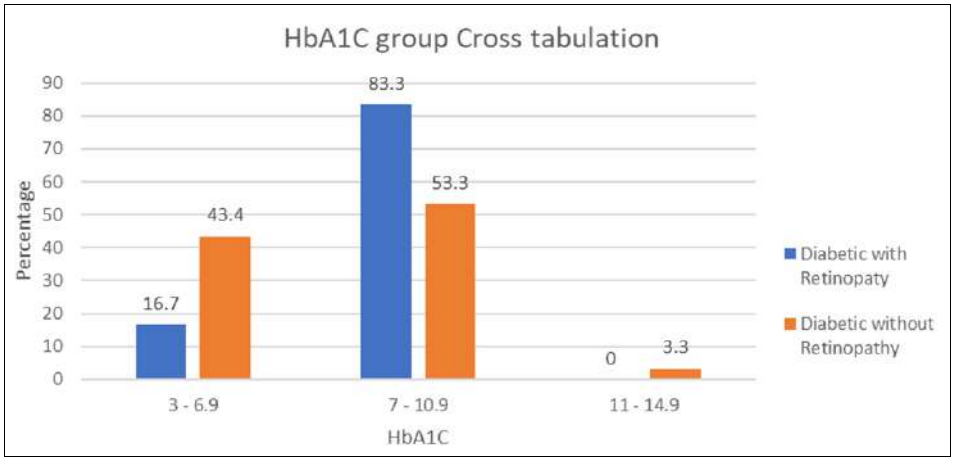

Fig 7: Bar diagram showing HbA1C Group* Group cross tabulation.

As represented in the above table-8, Fig-8, Out of 30 patients with diabetic retinopathy, the HbA1C levels in 5 patients (16.7%) is 3-6.9% and in 25 patients is 7-10.9%. Out of 30 diabetes patients without retinopathy, the HbA1C levels in 13 patients (43.3%) is 3-6.9%, in 16 patients (53.3%) is 7-10.9% and in one patient (3.3%) is 11-14.9%. Most of the diabetic patients with and without retinopathy had between 7-10.9%.

Discussion

Diabetes mellitus is a group of metabolic disease characterized by increased levels of glucose in the blood (hyperglycemia) resulting from defects in insulin secretion, insulin action or both. Hyperglycemia-induced vascular damage leads to increased glucose flux via the polyol pathway, causing cellular damage, resulting in various macrovascular and microvascular complications. Our study revealed lower levels of serum magnesium in diabetes mellitus patients without retinopathy. Moreover, patients who had retinopathy were found to have the lowest serum magnesium levels (Mg). Hypomagnesemia's exact cause is unknown, but an increased urinary excretion of magnesium (Mg) may contribute. Some studies revealed that hyperglycemia contributes to hypomagnesemia by causing depression in the net tubular reabsorption of magnesium. [12]

In the present study, the mean serum magnesium levels in diabetic patients with retinopathy is 1.75±0.16mg/dl, in diabetic patients without retinopathy, it is 2.02±0.17mg/dl. So there was a statistically significant decrease in the Mg (Magnesium) levels in diabetic patients without retinopathy when compared to patients without retinopathy.

The present study found a significant correlation with this study. The mean serum magnesium level is 1.75±0.16 mg/dl. The mean FBS level in diabetic patients with retinopathy is 178.57±41.68 mg/dl; in diabetic patients, without retinopathy, it is 37 133±17.84.P-value is 0.002, which is significant. The mean PPBS level in diabetic patients with retinopathy is 247.93±59.23 mg/dl; in diabetic patients without retinopathy, it is 175.53±19.76. P-value is 0.002, which is significant. The mean HbA1c levels in diabetic patients with retinopathy is 8.01±1.48%, and in diabetic patients without retinopathy, it is 6.40±1.14%. Intracellular magnesium plays a crucial role in regulating insulin action, vascular tone, Insulin-mediated glucose uptake. Reduced intracellular Mg concentrations result in a post-receptor impairment in insulin action, defective tyrosine-kinase activity, and worsening insulin resistance in

diabetic patients. P.Mc Nair *et al* have found definitive hypomagnesemia in diabetic patients with retinopathy. Low magnesium levels have frequently been demonstrated in patients with type 2 Diabetes mellitus. Magnesium deficiency appears to have a negative effect on glucose homeostasis and insulin sensitivity in patients with type 2 diabetes. Magnesium depletion is said to reduce insulin sensitivity, thereby they are increasing the risk of secondary complications. Hence it is crucial to monitor the plasma magnesium levels in diabetic patients with complications. Magnesium supplementation may help to reduce the progression of retinopathy in these patients. Studies have suggested that microangiopathy and increased capillary permeability, and retinal ischaemia is probably due to the combined effects of various risk factors. Early diagnosis and advance treatment in these patients can reduce the onset and progression of retinopathy. Further studies with oral magnesium supplementation indifferent stages of diabetic retinopathy can be interesting.

Diabetic retinopathy (D.R.) is one of the leading causes of blindness in the world. The decrease in visual acuity in diabetic retinopathy (D.R.) is either associated with maculopathy and its proliferative complications. Hypomagnesemia has been noticed to occur at an increased frequency in patients with type 2 diabetes compared with diabetes without diabetes mellitus [13]. Increased endothelial cell damage can cause microaneurysm and leakage of which causes maculopathy. Low magnesium levels may promote endothelial cell dysfunction and thrombogenesis by increased platelet aggregation and vascular calcifications. Low magnesium levels can cause induction of proinflammatory and profibrogenic response and reduce protective enzymes against oxidative stress. Moreover, magnesium deficiency may interfere with normal cell growth and apoptosis regulation because magnesium is crucial in DNA synthesis and repair.

Prophylactic supplementation with oral magnesium (Mg) may help avoid or ameliorate such complications as hypertension, arrhythmias, and sudden cardiac death [14].

Cellular magnesium deficiency can alter membrane-bound sodium potassium ATPase activity, which is involved in the maintenance of gradients of sodium, potassium, and glucose transport. The almost universal involvement of magnesium in various cellular processes critical to glucose metabolism, insulin action, and cardiovascular functions has been well-appreciated. Our observations revealed a definite lowering of serum magnesium in diabetic patients, especially in patients with complications. These observations correlate well with the previous studies [15]. In this study, it was observed that the mean serum magnesium level was statistically significantly low (P)

We also noted that in subjects with diabetes mellitus complications, serum magnesium levels were much lower than in people with diabetes without complications (p <0.001).

The reasons for the high prevalence of magnesium (Mg) deficiency in diabetes are not exact. Still, they may include increased urinary loss, lower dietary intake, or impaired absorption of magnesium than healthy individuals [16]. The Study by United Kingdom Prospective Diabetes (UKPDS 35) concluded that, while the risk of diabetes mellitus complications was strongly associated with hyperglycemia, each 1% reduction in HbA1c value reduced any endpoint related to diabetes mellitus by 21% and microvascular complications by 37% [17]. The American Diabetes Association (ADA) has determined the level of glycated hemoglobin (HbA1c) for the prediction of diabetic retinopathy (D.R.) to be 6.5 percent and this threshold have been committed by a further 2013 study by Cho *et al*. [18] This study supported the judicious use of glycated hemoglobin (HbA1c) for the diagnosis of diabetes mellitus and the detection of diabetic retinopathy.

Conclusion

Depends on the results of our study and data available from the literature, it can be incriminating that hypomagnesemia, glycated hemoglobin (HbA1c), and Fasting Blood Sugar (FBS) is involved in the development of diabetic retinopathy. Many studies, as we have seen in the review of literature, have shown that elevated HbA1c levels are found to be the potent predictors of progression of diabetic retinopathy. Hyperglycemia precipitate the formation of advanced glycation end products, which result in various microvascular complications like diabetic retinopathy. Magnesium (Mg) depletion is said to have a negative impact on insulin sensitivity and Glucose homeostasis in diabetes mellitus patients as well as on the development and progression of complications such as retinopathy. From the results of my study, it can be concluded that estimation of HbA1c and serum magnesium can help us predict the onset and progression of diabetic retinopathy. Advanced diagnosis and treatment of the complications of diabetes mellitus, such as retinopathy, can improve the quality of life and increase the life expectancy

Conflict of Interest

Not available

Financial Support

Not available

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