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RESEARCH ARTICLE

SERUM MAGNESIUM LEVEL IN TYPE2 DIABETES MELLITUS WITH SPECIAL REFERENCE TO DIABETIC RETINOPATHY

Ahmed R.H[1], Pegu U.R[2], Gogoi T.[3] and Devi B.[4]

1. Post Graduate Trainee, Department Of Medicine, Jorhat Medical College And Hospital, Jorhat, Assam.
2. Associate Profeesor, Department Of Medicine,Jorhat Medical College And Hospital, Jorhat, Assam.
3. Professor and Hod, Department Of Ophthalmology, Jorhat Medical College And Hospital, Jorhat, Assam.
4. Associate Profeesor, Department Of Biochemistry, Jorhat Medical College And Hospital, Jorhat, Assam.

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Abstract

Background: Diabetes mellitus (DM) is a worldwide, growing epidemic, with an estimated 415 million adults globally. Patients with diabetes are at increased risk of death and a triad of serious diabetes-specific complications (neuropathy, nephropathy, and retinopathy) and other associated complications. Magnesium is an intracellular cation and co-enzyme for various reactions of glycolytic pathway. Hence, we evaluated serum magnesium level in type 2 DM with and without diabetic retinopathy.

Materials and methods: The study is carried out on 40 patients of type 2 DM with retinopathy and 40 patients of type 2 DM without retinopathy. All patients are subjected to the detailed history taking, ocular examination, and investigations like serum magnesium, FBS, PPBS, glycated hemoglobin.

Results: The study revealed that there is a significant decrease in serum magnesium level in diabetic patients with retinopathy than without retinopathy (t= -6.297, df= 58 p= <0.001).Similarly Fasting Blood sugar, post prandial blood sugar and duration of diabetes also show significant difference.

Conclusion: As magnesium level decreases in patients with type 2 DM, the prevalence of retinopathy increases. Timely monitoring of serum magnesium levels and glycated hemoglobin as well as appropriate interventions would be beneficial in early detection and treatment of diabetic retinopathy.

Introduction:-

Diabetes mellitus is a serious and rising global issue, ranking it as the 9th leading cause of death around the globe.[1] Type 2 diabetes mellitus is a multi-factorial, chronic, metabolic disorder characterized by persistent hyperglycemia.[2] The prevalence of diabetes for all age-groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030. The diabetes mellitus in urban population in developing countries is projected to double between 2000 and 2030. According to the latest World Health Organization (WHO) report, India has 31.7 million diabetic subjects, and the

Corresponding Author: - DEVI B
Address:- Associate Professor, department of biochemistry, JORHAT MEDICAL COLLEGE AND HOSPITAL, JORHAT, ASSAM.

number is expected to increase to a staggering 79.4 million by 2030.[3] Globally, Type 2 diabetes mellitus contributes to 90% of all diabetes cases.[1]

Diabetic patients are prone for multi-system effects of diabetes mellitus such as retinopathy, nephropathy, neuropathy and cardiovascular diseases. Diabetic retinopathy is among the most common ophthalmic complication of diabetes mellitus, being one of the leading causes of blindness among working age people worldwide.[4] WHO has estimated that diabetic retinopathy is responsible for about 4.8% of the 37 million cases of blindness throughout the world.[5] Globally, it is estimated that about 30% people with diabetes mellitus have diabetic retinopathy.[6]

Chronic hyperglycemia is an important risk factor for the development of microvascular complications in DM. HbA1c has a special affinity for O2 thereby causes tissue anoxia and plays a role in the causation of micro and macroangiopathy. There is a direct relation between the degree of glycemic control and the incidence and progression of retinopathy.[7,8]

Mineral ions play specific roles in our body and one of the important mineral cation is magnesium (Mg), which is a second most common intracellular cation acts as a cofactor in glucose transporting mechanism of the cell membrane of nearly or more than cellular enzymatic systems. Many studies have been shown reduced magnesium concentrations in diabetic adults. Intracellular magnesium is having an important role in insulin action regulation, insulin-mediated glucose uptake, and vascular tone. In diabetic patients, reduced intracellular Mg concentrations results in abnormal tyrosine-kinase activity, post receptorial impairment in insulin action, and insulin resistance worsening.[9]

Magnesium (Mg) deficiency can be rarely seen in healthy persons, but has been reported in 47% of hospitalized patients. Not only patients with diabetes have lower serum Mg levels compared with their counterparts without diabetes, but also the serum Mg levels among the cohort with diabetes had an inverse correlation with the retinopathy. Magnesium depletion has been linked to development of diabetic retinopathy.[10]

The concentrations of magnesium in serum of healthy people are remarkably constant, whereas 25-39% of diabetics have low concentrations of serum magnesium.[11]

Hypomagnesemia has been definitely shown to be associated with increased risk of diabetes mellitus, but its association with retinopathy has been inconclusive. Hence this current study had been undertaken to evaluate the association of serum levels of magnesium with retinopathy in type 2 diabetes and correlation with long term control of diabetes mellitus. Newer insights into the biochemical changes and molecular events that occur in diabetic retinopathy can aid in its presentation and adequate treatment.

Aims And Objectives:-

1) To estimate the serum magnesium levels in type2 diabetes mellitus with special reference to diabetic retinopathy.
2)To evaluate the relationship of serum magnesium levels with severity of diabetic retinopathy

Materials And Methods:-

It was a Observational Cross Sectional Study conducted in the Department of Medicine and Ophthalmology , Jorhat Medical College and Hospital (JMCH), Jorhat for a period of one year i.e. 1st July 2020 – 30th June 2021 . About 80patients were studied during this period of study. Consecutive sampling was done, cases were selected taking into account both inclusion and exclusion criteria.

Inclusion Criteria:
Patients with diagnosed case of Type 2 DM as per ADA guidelines, 2020 who admitted in JMCH. Patients/ Legally Acceptable Representative (LAR) who gave informed consent for the study.

Exclusion Criteria:
Patient age < 30 years and who had other types of diabetes: Type1 DM, MODY, LADA, Gestational Diabetes Mellitus. Other causes of retinopathy: Hypertensive, lupus retinopathy, sickle cell retinopathy. Malabsorption syndrome patients. Chronic renal failure patients. Patient on magnesium supplements, loop diuretics, steroid,

alcoholism. Acute myocardial infarction within 6 months. Pregnant women with hypertension, proteinuria and preeclampsia. Media opacity prevented visualization of the posterior segment.

Ethical Permission
obtained from Institutional Ethics Committee(H), Jorhat Medical College and Hospital. **Written informed consent** which is validated in the local language obtained from the participants prior to collection of data. Data have been collected in a predesigned, pre tested structured Proforma.

Patient's examination was performed as per the proforma after informed consent was taken from all subjects and details of procedure, involving detailed history taking, complete ocular examination including determination of visual acuity, fundus examination. Fundus Fluorescien Angiography (FFA)/ Optical Coherence Tomography (OCT) was performed only when clinically necessary. Subjects were divided into two groups diabetic with and without retinopathy. Based on the ETDRS classification, DR patients were graded according to their severity of retinopathy. Blood sample was used to assess HbA1C levels, serum electrolytes including serum magnesium and blood sugar level.HbA1C levels were determined in all patients by high performance liquid chromatography technique and serum magnesium was determined by colorimetric method. In case of patients with asymmetric fundus findings the eye with a more severe grade of diabetic retinopathy was taken into consideration.

Statistical analysis:
IBM SPSS 23.0 used to analyse data using student independent t and ANOVA test. Differences between groups were evaluated and considered statistically significant at $p < 0.05$.

Results And Observations:-

During the study period in one year (2020 -2021), those who met the inclusion and exclusion criteria were included in the study. A total of 80 Patients analyzed in the study. Among 80 type 2 diabetics, 5%[4] were in between 30-<40years; 18.75%[15] were in between 40-<50 years; 33.75% [27] were in between 50-<60 years; 31.25% [25] were in between 60-<70 years and 11.25% [9] were ≥70 years. Among 80 type 2 diabetics, 56.25% [45] were male and 43.75% [35] were female.

Hypomagnesemia was (serum magnesium <1.7 mg/dl) found in maximum, 47.5% (19) among diabetic retinopathy patients and 7.5%(3) among group without diabetic retinopathy. Mean ±SD of serum magnesium were 1.81±0.24 and 2.14±0.23 among diabetic retinopathy and without diabetic retinopathy group respectively. Results found to be statistically significant (p value < 0.001).

Table 1:- Serum magnesium level in diabetes patients with and without Diabetic retinopathy.

Group	Serum magnesium level			p value
	<1.7mg/dl	≥1.7 mg/dl	Mean ±SD	
With DR (n=40)	19	21	1.81±0 .24	< 0.001
Without DR (n=40)	03	37	2.14 ±0 .23	

Among 80 type 2 diabetes patients, mean FBS±SD value found to be 227±42.40 and 178.73±46.89 mg/dl in diabetic retinopathy and without diabetic retinopathy respectively and found to be statistically significant between groups (p value <0.001).

Similarly, mean PPBS±SD value found to be 292.05±48.69 and 244.03±55.05 among diabetic retinopathy and without diabetic retinopathy group respectively. Higher FBS and PPBS values found in diabetic retinopathy group.

Among 40 diabetic retinopathy patients, maximum 35% [14] were presented in moderate NPDR stage and minimum 7.5% [3] were presented in PDR stage

Among 40 diabetic retinopathy patients, serum magnesium minimum [1.50±0.17] in proliferative diabetic retinopathy and maximum [1.97±0.14] in mild non proliferative diabetic retinopathy. With progression of diabetic retinopathy serum magnesium level decrease p value found to be 0.012 which statistically significant.

Group	Serum Magnesium[Mean± SD]	P value

Mild NPDR	**1.97±0.14**	**0.012**
Moderate NPDR	**1.82±0.28**	
Severe NPDR	**1.76±0.25**	
Very severe NPDR	**1.65±0.06**	
PDR	**1.50±0.17**	

Table 2:- mean± SD serum magnesium level in different stages of diabetic retinopathy

Discussion:-

The present study was carried out to estimate serum magnesium level in type 2 diabetes mellitus with special reference to diabetic retinopathy. 80 numbers of type 2 diabetes mellitus patients were included in the study, after fulfilling inclusion and exclusion criterias, who were admitted in the department of Medicine and Ophthalmology, JMCH. The study population was equally divided into two groups based on diabetic retinopathy status.

In the present study, maximum 33.75% [27] found in 50-<60 years age group followed by 31.25%[25] in 60-<70 years age group in type 2 diabetes patients. Similar results also documented in the study **Singh C et al.** [12] and **Bagzai DS et al.**[13]

In present study, out of 80 diabetic patients, 45 (56.25%) were males and 43.25%) were females with a male to female ratio of 1.28:1. It showed male predominance.The present study results were strongly supported by **Singh C et al.** who reported 57.88% males and 42.12% females among 330 diabetic patients [90]. Similar observations also documented in the study **Bagzai DS et al** [35] and **Reddy et al.**[14]

In present study, Hypomagnesia was to be found 47.5%(19) among diabetic retinopathy patients and 7.5%(3) among diabetes without retinopathy group. Mean ±SD of serum magnesium were 1.81±0.24 and 2.14±0.23 among diabetic patients with retinopathy and diabetics without retinopathy group respectively (p value <0.001). **Amer et al.**[15] found similar results of serum magnesium level 1.727±0.423 and 1.930±0.151 among diabetic patients with retinopathy and diabetics without retinopathy group respectively (p value 0.028). Significant differences also observed in the study **Haddad NS et al.** [16] and **Hatwal A et al.** [17]

In the present study, among 80 diabetic patients, mean FBS±SD was **227±42.40** mg/dl and **178.73±46.89** mg/dl in diabetic retinopathy and diabetics without diabetic retinopathy group respectively (p value <0.001).Similarly mean PPBS±SD was found to be **292.05±48.69** mg/dl and **244.03±55.05** mg/dl among diabetic retinopathy and diabetics without retinopathy group respectively. Results were consistent with **Parasar V et al**[18] who found that both fasting and postprandial blood sugars were higher in the subjects with DR as compared to the subjects with no DR. The values were statistically significant for FBS with p=0.001 (p<0.05) and PPBS with p=0.009 (p<0.05). Similarly **Kauser MM et al.** found that serum FBS was197.90±47.61 and 191.60± 46.47 in diabetic retinopathy and without retinopathy respectively (p value <0.001).[19]

In present study, among 40 diabetic retinopathy patients, **12 (30%)** belonged to mild NPDR, **14 (35%)** belonged to moderate NPDR, **7 (17.5%)** belonged to severe NPDR , **4 (10%)** belonged to severe NPDR and **3 (7.5%)** belonged to PDR. i.e non proliferative were more than proliferative diabetic retinopathy.This is similar to the study conducted by **Agarwal et al.** [20] and **Hegde SS et al.** [21]

In present study, among 40 diabetic retinopathy patients, mean±SD serum magnesium level in mild NPDR , moderate NPDR, severe NPDR, very severe NPDR and PDR were **1.97±0.14**, **1.82±0.28**, **1.76±0.25**, **1.65±0.06**and **1.50±0.17** respectively. Results were statistically significant among different stages of diabetic retinopathy (p value 0.012). **Amer et al.**[15] showed mean values of serum magnesium decreases with severity of diabetic retinopathy, with a highly significant difference (p value= 0.001). The results were in accordance with present study .Similarly, **Haddad NS et al.**[16]study showed that there were significant differences in the level of serum magnesium among different stages of retinopathy and differences correlate negatively with advancing stages of retinopathy (p value =0.001).

Limitations Of The Study:

Sample size was small and the study was done in a single centre and hence the study population may not be adequately represented. Magnesium is predominantly intracellular and intracellular magnesium is most important in

insulin secretion and action. But the magnesium levels measured are from venous sample. Dietary patterns between subject groups were not taken into consideration.

Conclusion:-

In the type 2 diabetes patients, it was found that the disease is more prevalent in male population and in **50**-<**60** year age group. Hypomagnesaemia was likely among patients with type 2 diabetes mellitus. Long term complications especially retinopathy might have hypomagnesemia as a contributing factor. Severity of diabetic retinopathy increased in patients with lower value of serum magnesium. Hence it is prudent that serum magnesium levels are carefully monitored in diabetic patients.

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