

A Cross-Sectional Study on Serum Magnesium in Non-Proliferative Diabetic Retinopathy in North-East India

Pratim Gupta¹

¹ Department of Biochemistry, Assam Medical College and Hospital, Dibrugarh, India

ORIGINAL PAPER

Abstract

Objective: Diabetic Retinopathy in North-Eastern part of India is a public health problem and its management is a challenge in this part of the country. As very few studies have attempted to find any inter-relationship between this public health hazard and minerals the present study attempts to estimate serum magnesium concentration in diabetic patients without retinopathy and diabetics with non-proliferative retinopathy attending retina clinic in a hospital in Assam, India and comment on the levels of serum magnesium in relation to age, sex, duration of diabetes.

Methods: A total of 42 patients coming to the Retina Clinic (conducted 2 times a week) in the Department of Ophthalmology, Assam Medical College, Dibrugarh, Assam, were examined for Serum Magnesium by Calmagite Method, along with Fasting Plasma Glucose and 2Hour-Post Prandial Plasma Glucose, at Advanced Clinical Biochemistry Laboratory under the Department of Biochemistry, Assam Medical College, Dibrugarh.

Results: Serum magnesium of (2.52 ± 0.15) mg/dl (1.04 ± 0.06 mmol/L) in patients without retinopathy; and serum magnesium of (2.32 ± 0.11) mg/dl (0.95 ± 0.05 mmol/L) in those with retinopathy was observed. The difference was found to be statistically significant ($p < 0.001$).

Conclusions: Lower magnesium levels may trigger endothelial cell dysfunction and thrombogenesis, and cause proinflammatory and pro-fibrogenic response. Lower magnesium levels in patients with non-proliferative Diabetic Retinopathy than Diabetic patients without Retinopathy may be attributed to the longer duration of disease or poorer glycemic

status in those patients. The distinct changes observed in Non-Proliferative Retinopathy may also be attributed to the role of low magnesium in causing pro-inflammatory response.

Keywords: Diabetes Mellitus, Diabetic Retinopathy, Diabetes Complications, Fluorescein Angiography, Magnesium.

Introduction

A study found a high prevalence of Type 2 diabetes among adults in Guwahati, Assam, in northeastern India [1]. The study of the prevalence of diabetes and its complications in the northeastern part of India is still ongoing. Diabetic retinopathy is rapidly becoming an important cause of visual disability in India, as the World Health Organization (WHO) reports an epidemic increase in type 2 diabetes mellitus [2]. The purpose of this study is to see if there is any link between the important trace element magnesium and non-proliferative diabetic retinopathy in patients who come for a retinal examination at a tertiary care center in Assam, India. This could help researchers determine the efficacy of maintaining magnesium levels in the management of Diabetes Mellitus and, as a result, mitigate the dreadful side effects of this public health problem.

I. MATERIAL AND METHODS

A total of 42 patients coming to the Retina Clinic (which is conducted 2 times a week) in the Department of Ophthalmology, Assam Medical College, Dibrugarh, Assam, were examined for serum Magnesium at Advanced

Corresponding author: Dr. Pratim Gupta Dept. of Biochemistry, Assam Medical College & Hospital, Dibrugarh, Assam India-786002
E-mail: pratdbs@gmail.com

Clinical Biochemistry Laboratory under the Department of Biochemistry, Assam Medical College, Dibrugarh.

Inclusion criteria.

Patients with history suggestive of Diabetes mellitus, diagnosed clinically (supported by earlier Blood Glucose concentration, HbA1c%, wherever available); and attending the retina clinic for examination of the retina. Fundoscopic findings, determined by direct and indirect ophthalmoscopy and confirmed by subsequent fundus fluorescein angiography, were considered to diagnose cases of diabetic retinopathy.

Exclusion criteria:

Patients who refused to give consent for the study; patients with retinopathy other than diabetic retinopathy; patients with chronic renal failure; patients on diuretics; patients on hormonal preparations (other than insulin), antacids, anticonvulsants, lithium, cytotoxic drugs, patients having acute/chronic diarrhea or malabsorption states; patients with history of alcohol consumption; patients on mineral and vitamin supplementation; patients with endocrinal dysfunction; patients who are pregnant or lactating; patients who are critically ill or having incapacitating disorder of the locomotor system.

Identical investigations were conducted on diabetic patients without retinopathy.

Estimation of blood glucose (Fasting and Postprandial)[3]

Method used: Glucose Oxidase/Peroxidase Method. (GOD/POD METHOD)

Glucose is oxidized to gluconic acid and hydrogen peroxide in the presence of glucose oxidase. Hydrogen peroxide further reacts with phenol and 4-aminoantipyrine by the catalytic action of peroxidase to form a red colored quinonimines dye complex. Intensity of the color formed is directly proportional to the amount of glucose present in the sample.

Estimation of serum Magnesium :Calmagite method[4]

Principle: Magnesium combines with calmagite in an alkaline medium to form a red coloured complex. Interference of protein and calcium is eliminated by the addition of chelating agent and detergent. Intensity of the colour formed is proportional to the amount of magnesium present in the sample.

II. RESULTS AND DISCUSSIONS

A. Results.

Patients with no diabetic retinopathy had higher levels of mean serum magnesium (2.52 ± 0.15) mg/dl (1.04 ± 0.06 mmol/L) as compared to those with non-proliferative diabetic retinopathy who had mean serum magnesium level (2.32 ± 0.11) mg/dl (0.95

± 0.05 mmol/L) This was found to be statistically significant ($p < 0.001$) (**Figure-1**)

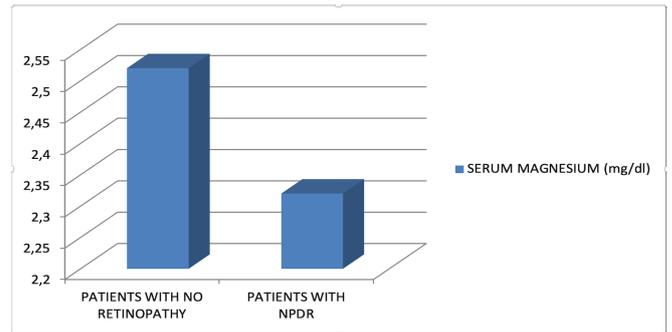


Figure 1. Bar-diagram showing the difference between mean serum magnesium concentrations in patients with no retinopathy and those with NPDR.

The mean fasting plasma glucose levels was 128.43 ± 32.48 mg/dl (7.1 ± 1.8 mmol/L), in patients without retinopathy and 144.86 ± 68.86 mg/dl (8.1 ± 3.8 mmol/L) in those with non-proliferative retinopathy. (**Figure-2**)

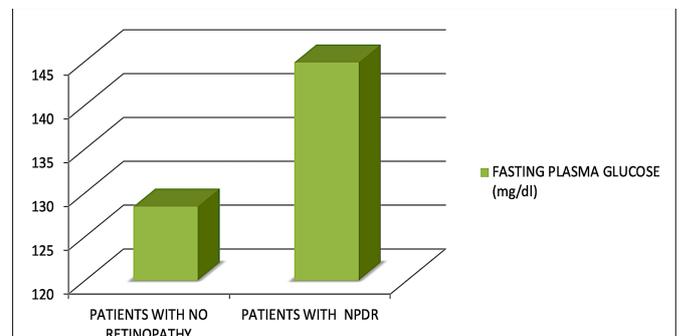
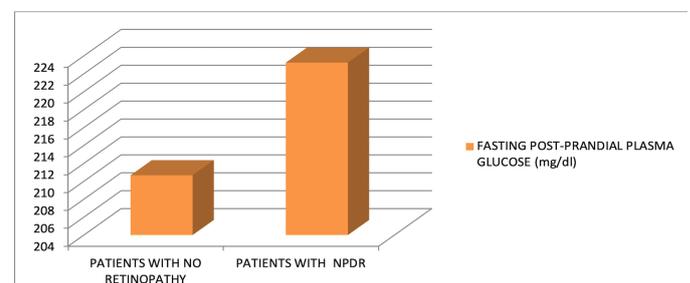


Figure 2. Bar-diagram showing the difference between mean fasting plasma glucose concentrations in patients with no retinopathy and those with NPDR.

The mean post-prandial plasma glucose levels was 210.67 ± 77.09 mg/dl (11.7 ± 4.3 mmol/L) in patients with no retinopathy and 223.24 ± 118.53 mg/dl (12.4 ± 6.6 mmol/L) in those with non-proliferative retinopathy (**Figure-3**)



post-prandial plasma glucose concentrations in patients with no retinopathy and those with NDPR.

Most patients (20 out of 21) with Non-Proliferative Diabetic Retinopathy are in the age group of 40-60 years. (**Table-1**)

Table 1: Distribution of patients in terms of age

AGE (IN YEARS)	PATIENTS WITH NO RETINOPATHY	PATIENTS WITH NPDR
<30	1	0
31-40	2	1
41-50	7	6
51-60	4	8
>60	7	6
TOTAL	21	21

There is a male preponderance (16 out of 21) amongst patients with Non-Proliferative Diabetic Retinopathy(**Table-2**)

Table 2: Distribution of patients in terms of gender

GENDER	PATIENTS WITH NR	PATIENTS WITH NPDR
FEMALES	8	5
MALES	13	16
TOTAL	21	21

13 out of 21 diabetic patients have had the disease for more than years while 14 out of 21 diabetic patients without retinopathy have had the disease for less than five years, giving an Odd's ratio of 3.25 (95% CI=0.92-11.5, $p>0.05$) (**Table-3**)

Table 3. Distribution of patients in terms of duration since the diagnosis of diabetes mellitus.

DURATION SINCE DIAGNOSIS OF DIABETES MELLITUS	PATIENTS WITH NO RETINOPATHY	PATIENTS WITH NPDR
<5 YRS	14	8
5-10 YRS	7	11
>10 YRS	0	2
TOTAL	21	21

B. Discussion.

McNair et al found that diabetic subjects with severe retinopathy had significantly lower serum magnesium than diabetic subjects without evidence of that complication [5]. The authors had suggested the hypomagnesaemia to be an additional risk factor in the development and progress of diabetic

retinopathy. In another study conducted by Hatwal et al [6], the workers have opined that serum Magnesium levels in diabetics with retinopathy is significantly lower than in controls, and the workers have opined that patients who have a more severe degree of retinopathy have the lowest magnesium concentration. As in the present study, BonakdaranShokoofeh et alin 2012 found the fasting blood glucose levels to be higher (187.28 ± 84.24 mg/dl) in patients with Diabetic retinopathy than in Diabetics without retinopathy(163.3 ± 59.14 mg/dl) indicating poor glycemic control in patients with Retinopathy [7]. In a similar study in Tripura, India in 2014, Arindam Datta et al [8] found the post prandial blood glucose to be (210 ± 55.3) mg/dl in diabetic patients without retinopathy and (270 ± 53.1 mg/dl) in patients with diabetic retinopathy which corroborates with findings of the present study. Regarding the increased prevalence of Diabetic Retinopathy in males, evidence was forwarded by Raman R et al [9] who had also reported a higher prevalence of Diabetic retinopathy among males. In the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), the widest and most prolonged population based ophthalmologic survey, reported that higher prevalence of Diabetic Retinopathy was associated with longer duration of diabetes [10] which supports the finding of a longer duration of Diabetes in patients with non-proliferative Diabetic Retinopathy in the present study.

III. CONCLUSION

Lower serum magnesium concentration in patients with diabetic retinopathy may be a cause or an effect. Urinary excretion of Magnesium, especially in patients with unsatisfactory metabolic control, which is a hallmark of patients with diabetic retinopathy suggests the lower magnesium concentration could, in fact, be an effect of the disease. Measurement of this important trace elements in diabetic patients and its replenishment in deficient states, by means of oral supplementation could be a possible deterrent to the progression of Diabetic Retinopathy. It may be suggested that age of patients, sex of patients, plasma glucose levels, duration since the diagnosis of diabetes mellitus could play a significant role in alterations of serum magnesium. This study is one of the very few attempts in the north-eastern part of the Indian Sub-Continent to suggest that measuring Magnesium in patients with Diabetes Mellitus, routinely may help in throwing light on progression of retinopathy.

Acknowledgements. The authors would like to thank Late Professor Rohini Kanta Goswami, Ex-HOD, Department of Biochemistry, Assam Medical College, Dibrugarh, Assam, India and Dr Jawahar Jyoti Kuli Ex-HOD, Department of

Ophthalmology, Assam Medical College, Dibrugarh, Assam, India, DBT-India

Conflict of interest. The authors declare that they have no conflicts of interest.

Funding. This research was supported by MD/MS Thesis Grant for North-Eastern Students by DBT-India

Ethical statement. This research was reviewed and approved by the Ethics Committee of Assam Medical College and Hospital. Informed consent was obtained from all participants.

REFERENCES

1. Shah S, Saikia M, Burman N, Snehalata C, Ramachandran A. High Prevalence Of Type 2 Diabetes In Urban Population In North Eastern India. *INT J DIAB DEV COUNTRIES*. 1999;19:144-147.
2. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care*. 2004;27(5):1047-1053. doi:10.2337/diacare.27.5.1047
3. Trinder P. Determination of Glucose in Blood Using Glucose Oxidase with an Alternative Oxygen Acceptor. *Annals of Clinical Biochemistry*. 1969;6(1):24-27. doi:10.1177/000456326900600108
4. Makino T. A sensitive, direct colorimetric assay of serum copper using 5-Br-PSAA. *ClinChimActa*. 1989;185(1):7-16. doi:10.1016/0009-8981(89)90125-3.
5. McNair P, Christiansen C, Madsbad S, et al. Hypomagnesemia, a risk factor in diabetic retinopathy. *Diabetes*. 1978;27(11):1075-1077. doi:10.2337/diab.27.11.1075
6. Hatwal A, Gujral AS, Bhatia RP, Agrawal JK, Bajpai HS. Association of hypomagnesemia with diabetic retinopathy. *ActaOphthalmol (Copenh)*. 1989;67(6):714-716. doi:10.1111/j.1755-3768.1989.tb04407.x
7. Shokoofeh B, Nasser S, Abrishami M, Haleh R (2012) Serum Prolactin Level and Diabetic Retinopathy in Type 2 Diabetes. *J Diabetes Metab* 3:173.
8. ArindamDatta, Amar Kanti Chakma, DebasisDatta. "Prevalence of Diabetic Retinopathy in Type-2 Diabetes Mellitus patients in Tripura". *Journal of Evolution of Medical and Dental Sciences* 2014; Vol. 3, Issue 01, January 06; Page: 136-146.
9. Raman R, Ganesan S, Pal SS, Kulothungan V, Sharma T. Prevalence and risk factors for diabetic retinopathy in rural India. *SankaraNethralaya Diabetic Retinopathy Epidemiology and Molecular Genetic Study III (SN-DREAMS III), report no 2. BMJ Open Diabetes Res Care*. 2014;2(1):e000005. Published 2014 Jun 6. doi:10.1136/bmjdr-2013-000005.
10. Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin epidemiologic study of diabetic retinopathy. III. Prevalence and risk of diabetic retinopathy when age at diagnosis is 30 or more years. *Arch Ophthalmol*. 1984;102(4):527-532. doi:10.1001/archophth.1984.01040030405011.