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A Comparative Study of Serum Magnesium among Type 2 Diabetes Mellitus Patients with and without Diabetic Retinopathy

Dr. Md. Ashiqur Rahman Chowdhury[1*], Dr. Nusaffarin Khan[2], Dr. Abir Bin Sajj[3], Dr. Md. Hasnat Jaki Chowdhury[4], Dr. Md. Iqram - Ul - Azam Khan[5], Dr. Shah Md. Atiqul Haque[6], Dr. Tariq Reza Ali[7]

[1]Indoor Medical Officer, Department of Ophthalmology, Gopalganj Eye Hospital and Training Institute, Gopalganj, Bangladesh
[2]Assistant Professor, Department of Ophthalmology, BIHS General Hospital, Dhaka, Bangladesh
[3]Consultant, Department of Cornea and Refractive Surgery, Vision Eye Hospital, Dhaka, Bangladesh
[4]Resident Surgeon, Department of Ophthalmology, 250 Bed General Hospital, Barguna, Bangladesh
[5]Consultant, Department of Ophthalmology, Dhaka Progressive Lions Eye Hospital, Narsingdi, Bangladesh
[6]Assistant Professor, Department of Anatomy, Mymensingh Medical College, Mymensingh, Bangladesh
[7]Associate Professor, Department of Ophthalmology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh

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***Corresponding author:** Dr. Md. Ashiqur Rahman Chowdhury
Indoor Medical Officer, Department of Ophthalmology, Gopalganj Eye Hospital and Training Institute, Gopalganj, Bangladesh
Email: dr.ashiqurrahman11@gmail.com

Abstract **Original Research Article**

Background: Diabetes mellitus (DM) characterized by metabolic disorders related to high levels of serum glucose is one of the most common diseases associated with magnesium (Mg) depletion in intra and extra cellular compartments. Hypomagnesemia has been related as a cause to insulin resistance also being a consequence of hyperglycemia. When it is chronic, it leads to the development of macro and microvascular complications of diabetes. ***Objective*****:** To compare the serum magnesium status among type 2 diabetes mellitus patients with and without diabetic retinopathy. ***Methods*****:** This analytical study was conducted at Department of Ophthalmology, Bangabandhu Sheikh Mujib Medical University (BSMMU). A total of 76 Type 2 diabetic patients were divided into two groups -with and without diabetic retinopathy. Patients were selected through purposive sampling method after considering the inclusion criteria. After taking informed written consent, comprehensive ocular examination, samples for serum Magnesium and HbA1c were collected. Serum Magnesium was estimated by enzymatic method. ***Results*****:** The age of the respondents was in between 40 to 60 year and the mean age was 49.16± 7.17 year. Majority respondent (58%) was female, 47.4% had DM for >15 year, 81.6% had normal level of Mg and rest 18.4% had hypomagnesemia. Majority respondents (84.2%) belonged to ≥6.5 HbA1c level group, 51.3% respondents had RBS level ≥11.1 mmol/l and 71.1% respondents belonged to overweight/Obese group. Statistically significant relationship was found between age of the respondent and DR (p=0.043), duration of DM and DR (p=0.005), Mg level and DR (p=≤0.001) and BMI and DR (p=0.043). The difference of Mg value between two groups (Diabetic retinopathy and nondiabetic retinopathy) was statistically significant (p=0.002). Statistically significant relationship was found between age of the respondent and Serum Mg Level (p=≤0.001), duration of DM and Serum Mg level (p=0.012) and between BMI and Serum Mg level (p=0.043). ***Conclusion*****:** This study revealed that hypomagnesemia along with duration of diabetes made patients more susceptible to develop diabetic retinopathy.

Keywords: Diabetic retinopathy, Diabetes mellitus.

INTRODUCTION

Diabetic retinopathy is one of the dangerous complications of DM and also is a leading cause of acquired blindness in adults. Several risk factors are related to the development and progression of retinopathy such as the duration of DM, poor glycemic control, dyslipidemia, hypertension and hypomagnesemia [1]. Magnesium is the fourth most abundant cation in the human body Cation [2], it has an atomic mass of 24.32 and an atomic number of 12. Approximately half of the body's magnesium is found in the skeletal system, of which one-third is exchangeable [3]. Magnesium influences the activity of enzymes by (i) binding to ligands such as ATP in ATP-requiring enzymes, (ii) binding to the active site of the enzyme, eg. enolase, pyruvate kinase, pyrophosphatase, (iii) causing a conformational change during the catalytic process,eg. Na+, K+-ATPase, (iv) promoting

the aggregation of multi-enzyme complexes eg. aldehyde dehydrogenase, or (v)a mixture of the above mechanisms, eg. F1-ATPase. Most of the body's Magnesium stores are intracellular, principally within bone. In the extracellular fluid, Magnesium can be ionized (free), bound to anions, or bound to protein. Normal concentrations of extracellular Magnesium and calcium are crucial for normal neuromuscular activity. Intracellular Magnesium forms a key complex with ATP and is an important cofactor for a wide range of enzymes, transporters, and nucleic acids required for normal cellular function, replication, and energy metabolism. Over 300 enzymes are dependent on Magnesium. A possible relationship between DM and hypomagnesemia was first suggested in 1952. DM, or more specifically hyperglycemia, appears to induce magnesium depletion both directly via osmotic diuresis and indirectly by its effect on vitamins, ions, and proteins. It has been reported that the incidence of mild hypomagnesemia in patients with DM may be as high as 25 percent [4]. Ocular structures where Mg is present includes cornea, lens, retina, vitreous body and anterior chamber. Mg provides neurovascular protective effects by mediating through activation of endothelial nitric oxide synthase and inhibition of endothelin-1 eventually result in vasodilatation of retinal vessels. Endothelin-1 has been shown to cause vasoconstriction of retinal vessels and has mitogenic effects on retinal pericytes. Alterations in the pericyte-endothelin interaction ultimately causes early hemodynamic and histopathological abnormalities found in diabetic retinopathy [5]. Hence Magnesium has a protective role to play in preventing DR by inhibiting Endothelin-1. Being a major cofactor for the normal cellular metabolism to produce ATP, Magnesium is found to be involved in regulating the intracellular ionic balance and, thus, maintain the functional and structural integrity of many ocular tissues [6] Magnesium is a cofactor in phosphorylation of glucose, and it helps in carbohydrate metabolism [7]. Many studies have been shown reduced magnesium concentrations in diabetic adults [8]. In diabetic patient's reduced intracellular Mg concentrations results in abnormal tyrosine-kinase activity, post receptorial impairment in insulin action, and insulin resistance worsening [9]. 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 [10]. Hypomagnesaemia linked with diabetic retinopathy was reported in two cross-sectional studies that included both insulin-dependent and non-insulin-dependent patients. In this way, Magnesium depletion has been linked development of diabetic retinopathy [11]. So, we want to determine whether there is any correlation between serum magnesium levels and diabetic retinopathy in Type 2 diabetes patients who are more likely to experience hypomagnesemia. If an association is established, serum magnesium levels may be used as a prognosis indication, a management tool for DR and a probable indicator of the severity of diabetic complications. Studies on this parameter have been done in other areas but very few in our locality. Hence, we conducted this study with the aim to estimate serum magnesium levels in cases of type 2 DM with and without retinopathy and to compare the level of serum magnesium.

MATERIALS & METHOD

This was a cross-sectional study was conducted in the Department of Ophthalmology, Bangabandhu Sheikh Mujib Medical University (BSMMU) from July 2021 to August 2022. The study population comprised of 76 type 2 diabetic patients in total. Group 1 consisted of 38 patients with diabetic retinopathy and in group 2 there were 38 without diabetic retinopathy. Patients were in the age group older than 40 years either admitted or attending OPD at the department of Ophthalmology of BSMMU, Dhaka were included in this study. Purposive type of sampling technique was applied to enroll the patients. Sample was collected through non probability sampling method from patients who presented with T2DM with or without having DR. All patients had comprehensive ocular examination consisting of best corrected visual acuity using Snellen chart, Slit lamp biomicroscopy and Fundoscopic examination with direct ophthalmoscope and indirect ophthalmoscopy. BMI was calculated by dividing body weight by height squared (kg/m^2). Laboratory data including RBS, HbA1c and serum Magnesium were investigated. The questionnaires were completed for individual patients during the course of the study to generate data. During sampling, with all aseptic precautions venipuncture at the antecubital vein was done and 6 ml blood was drawn for serum Magnesium and estimation of glycemic status. The samples were divided into three halves (2 ml each portion) introduced into three separate tubes. The samples were sent immediately after collection to the laboratory for analysis. Hence sample preservation was not required. The serum level of Magnesium was determined with automated analyzer Atellica or Beckman Coulter- AU 680 via Enzymatic (kinetic) method. Magnesium present in the sample acts as a cofactor in an enzymatic reaction with Isocitrate dehydrogenase. The rate of increase in absorption at 340 nm, due to the formation of NADPH, is directly proportional to the Magnesium concentration. All data was processed by using SPSS program version 24. Results was described in frequencies or mean ± SD unless otherwise mentioned. All quantitative variables were estimated using measures mean and standard deviation. The summarized data was presented in the table and chart. Between groups, analysis was done by chi square, fisher's exact test and independent sample test. p value < 0.05 was considered as statistically significant.

RESULTS

Table I: Distribution of the respondent by age (N=76)

Age	Frequency	Percentage
≤45 Yrs.	28	36.8
46-55 Yrs.	32	42.1
>55 Yrs.	16	21.1
Total	76	100
Minimum age 40 year Maximum age 60 year Mean age 49.16 ± 7.17 year		

Table I show the distribution of respondents by age. The age of the respondents was in between 40 to 60 year and the mean age 49.16 ± 7.17-year year. Maximum (42.1%) respondents belonged to 46-55-year age group. 36.8% respondents belonged to ≤45, and rest 21.1% belonged to >55-year age group.

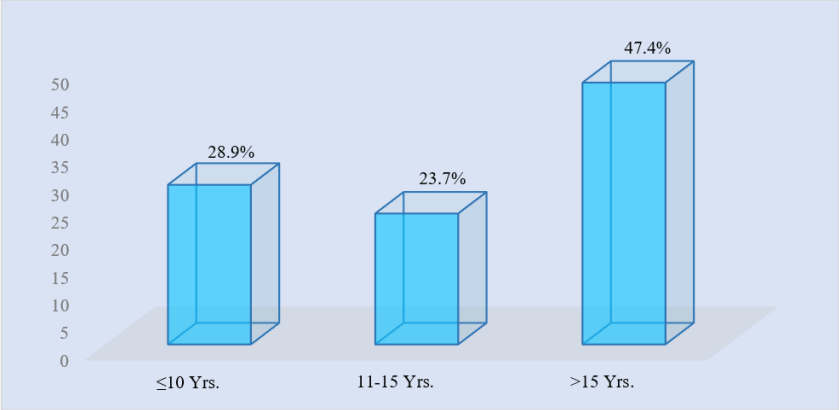

Figure 1: Column chart showed distribution of the respondent by duration of DM (In years) (N=76)

Figure 2 shows distribution of the respondent by duration of DM (In year**)**. Majority respondents (47.4%) had DM for >15 year. 28.9% respondent had DM for ≤10 year and 23.7% respondents had DM for 11-15 year.

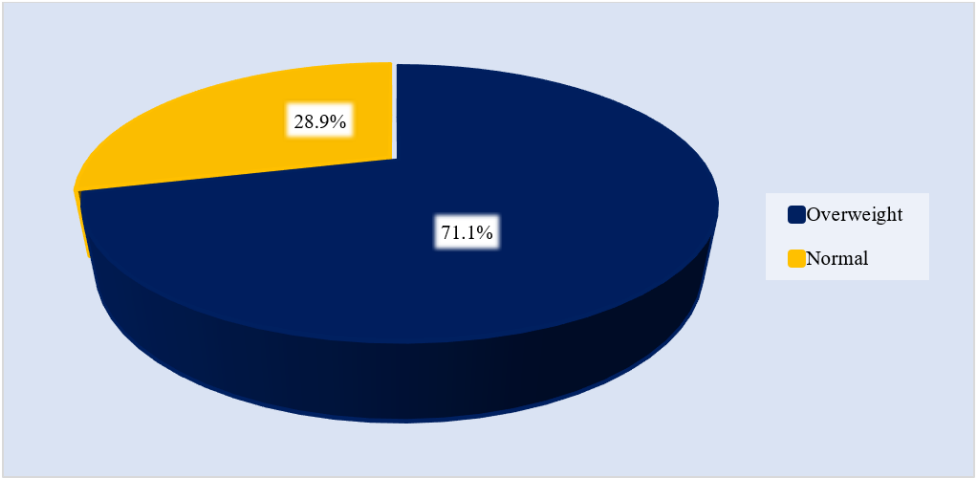

Figure 2: Pie chart showed distribution of the respondent by level of BMI (N=76)

Figure 5 shows distribution of respondents by level of BMI. Majority (71.1%) respondents belonged to overweight/Obese group. Rest 28.9% belonged to normal group.

Table II: Relationship between Mg level and DR (N=76)

Level of Mg	Presence of DR		Total	p value
	DR	Non-DR		
Hypomagnesemia	14 (36.8%)	0 (44.7%)	14	≤0.001(χ^2 test)
Normal	24 (63.2%)	38 (100%)	62	
Total	38	38	76	

Table II shows relationship between Mg level and DR. Statistically significant relationship was found between Mg level and DR (p=≤0.001)

Table III: Relationship between Mg level and DR (N=76)

Presence of DR	Mean value of Mg(mg/dl)	Standard Deviation	p value
DR	1.84	0.39	0.002
Non-DR	2.07	0.21	

Table III shows relationship between DR and serum Mg level of the respondent. Mean value of Mg for DR group was found lower than non-DR group. Mean Mg value for DR and non-DR group was 1.84±0.39 (mg/dl) and 2.07±0.21(mg/dl) respectively. Independent sample t test showed the difference of Mg value between two groups was statistically significant (p=0.002)

Table IV: Relationship between age of the respondent and Serum Mg Level (N=76)

Age (In Year)	Mg level		Total	p value
	Hypomagnesemia	Normal		
≤45 Yrs.	0 (26.3%)	28 (45.2%)	28	≤0.001(χ^2 test)
46-55 Yrs.	6 (42.9%)	26 (41.9%)	32	
>55 Yrs.	8 (57.1%)	8 (12.9%)	16	
Total	14	62	76	

Table IV shows relationship between age of the respondent and Serum Mg Level. Statistically significant relationship was found between age of the respondent and Serum Mg Level (p=≤0.001)

Table V: Relationship between sex of the respondent and Serum Mg Level (N=76)

Sex	Mg level		Total	p value
	Hypomagnesemia	Normal		
Male	6 (42.9%)	26 (41.9%)	32	0.95(χ^2 test)
Female	8 (57.1%)	36 (58.1%)	44	
Total	14	62	76	

Table V shows relationship between sex of the respondent and Serum Mg Level. Statistically significant relationship was not found between sex of the respondent and Serum Mg Level (p=0.95)

Table VI: Relationship between duration of DM and Serum Mg level (N=76)

Duration of DM (years)	Mg level		Total	p value
	Hypomagnesemia	Normal		
≤10 Yrs.	0 (0%)	22 (35.5%)	22	0.012 (Fisher's Exact Test)
11-15 Yrs.	6 (42.9%)	12 (19.4%)	18	
>15 Yrs.	8 (57.1%)	28 (45.2%)	36	
Total	14	62	76	

Table VI shows relationship between duration of DM and Serum Mg level. Statistically significant relationship was found between duration of DM and Serum Mg level (p=0.012)

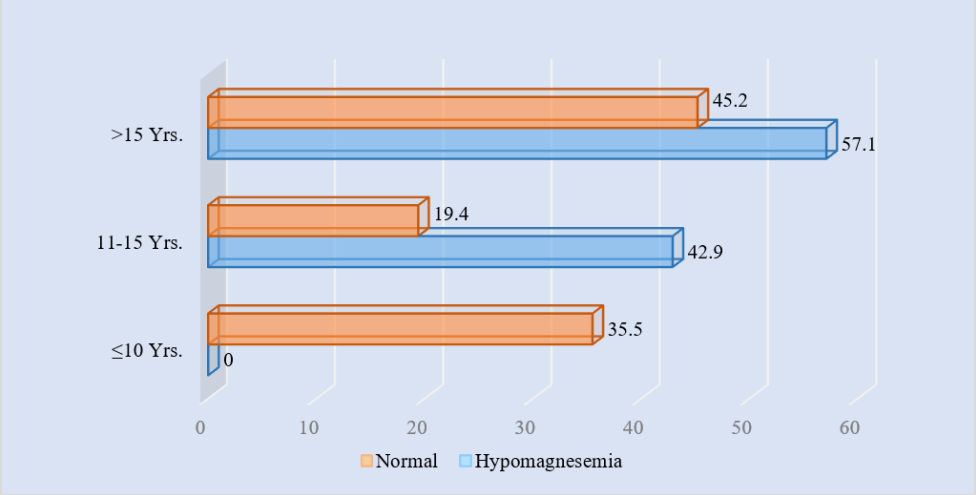

Figure 3: Bar chart showed relationship between duration of DM and Serum Mg level (N=76)

Table VII: Relationship between HbA1c level and Serum Mg level (N=76)

HbA1c level	Mg level		Total	p value
	Hypomagnesemia	Normal		
<6.5	2 (14.3%)	10 (16.1%)	12	0.864(Fisher's Exact Test)
≥6.5	12 (85.7%)	52 (83.9%)	64	
Total	14	62	76	

Table VII shows relationship between HbA1c level and Serum Mg level. Statistically significant relationship was not found between HbA1c level and Serum Mg level (p=0.864).

Table VIII: Relationship between BMI and Serum Mg level (N=76)

BMI	Mg level		Total	p value
	Hypomagnesemia	Normal		
Normal	2 (14.3%)	20 (32.3%)	22	0.043(χ^2 test)
Overweight/Obese	12 (85.7%)	42 (67.7%)	54	
Total	14	62	76	

Table VIII shows relationship between BMI and Serum Mg level. Statistically significant relationship was found between BMI and Serum Mg level (p=0.043)

DISCUSSION

Diabetes Mellitus has imposed a massive economic burden on emerging on Bangladesh. Related comorbidity, expensive medicines, tests and increased out-of-pocket costs have made it more difficult for primary health care practitioners. As a result, research emphasis should be directed at avoiding or delaying complications through cost-effective therapies. We emphasized on magnesium levels in connection to glycemic control and retinopathy in this investigation. The age of the respondents was in between 40 to 60 year and the mean age 49.16± 7.17 years. Statistically significant relationship was found between age of the respondent and diabetic retinopathy (p=0.043). In previous study it was found that increasing age was associated with diabetic retinopathy [12]. Statistically significant relationship was found between age of the respondent and Serum Mg Level (p=≤0.001). Statistically significant relationship was found between duration of DM and DR (p=0.005). In another study, direct link was also found between the duration of DM and DR [13]. Mean value of RBS for DR group was found higher than non DR group. Independent sample t test showed the difference of RBS value between two groups was not statistically significant (p=0.583). Singh *et al.*, suggested that relationship between RBS value and diabetic retinopathy was statistically significant [14]. Statistically significant relationship was also

found between Blood glucose level and Serum magnesium which was in line with the study conducted by other study [15]. HbA1c is formed through the nonenzymatic binding of circulating glucose to hemoglobin. Higher levels of glucose in the blood contribute to more binding and consequent higher levels of HbA1c. Since the life span of an RBC is 120 days, HbA1c reflects average plasma glucose over the past few months. Statistically significant relationship was not found between HbA1c level and DR (p=0.529) and also statistically significant relationship was not found between HbA1c level and Serum Mg level (p=0.864). While another report shows a direct relationship between HbA1c level and hypomagnesemia [15]. Again autonomic neuropathy which is a common side effect of DM results into reduced absorption of Magnesium from the intestine. Hypomagnesemia has been observed to occur more frequently in persons with type 2 diabetes than in those having diabetes [16]. In this study, while evaluating serum magnesium with retinopathy, we found mean value serum Mg among DR patients was lower than non-DR patients and the difference was statistically significant (p =0.002). Similar findings have been observed that serum magnesium levels significantly lower in patients with diabetic retinopathy compared with diabetics without complications [17,18]. Increased endothelial cell destruction creates microaneurysms, which leak and cause maculopathy [19]. Through enhanced platelet aggregation and vascular calcifications, low Mg levels may induce endothelial cell failure and thrombogenesis [20]. Low Mg levels may also trigger a proinflammatory and profibrogenic response, because Mg is required for DNA synthesis and repair, Mg shortage may interfere with proper cell growth and apoptosis control. This would explain why hypomagnesemia was more prevalent in the diabetic retinopathy group [20]. There was significant difference of BMI between diabetic retinopathy and non-diabetic retinopathy in our study (P = 0.017). A statistically significant association was also discovered between the respondent's BMI and serum magnesium. On the other hand, found significant link between BMI and hypomagnesemia (OR - 1.05, P = 0.04) and a high association between T2DM, which was an independent risk factor for hypomagnesemia (OR - 3.77, P = 0.001) [21]. T2DM is the primary cause of low serum magnesium levels in overweight diabetics. In obese people, hypomagnesemia may worsen insulin resistance. This may predispose individuals to metabolic issues associated with diabetes. Statistically significant relationship was not found between sex of the respondent and serum magnesium level. Significant relationship was also not found between sex of the respondent and Diabetic Retinopathy. On the basis of the overall analysis of the data it can be concurred that age had link with the serum Magnesium level. Serum Magnesium level was found to reduce with the increasing duration of DM. Diabetic Retinopathy can be treated with oral magnesium supplements and diabetes management. Magnesium supplements are inexpensive and widely available, making this the most financially viable alternative for patients from low-income families.

CONCLUSION

It can be concluded from this study that with the reduction of the serum Magnesium level the chances of developing diabetic Retinopathy increases. Patients without DR were predominantly found to have normal magnesium concentration. Hypomagnesaemia is likely among patients with type 2 diabetes mellitus. Long term complications especially retinopathy may have hypomagnesemia as a contributing factor. Hence it is prudent that serum magnesium levels should be carefully monitored in diabetic patients. Future studies on the role of magnesium supplementation in type 2 diabetes to prevent diabetic retinopathy in Bangladeshi population are recommended.

LIMITATIONS

The study design being analytical cross section, hence couldn't identify the causal relation between the exposure and outcome also the relationship of serum magnesium with the different stages of diabetic retinopathy was not studied.

RECOMMENDATIONS

Multicentre study can be done to bring out actual scenario, carry out research on the effects of Insulin, oral hypoglycemic agents and lifestyle modification on serum Magnesium in type 2 diabetic patients and conduct Interventional studies on DR and non-DR patients following oral Magnesium supplementation in our country.

REFERENCES

1. Corrêa, Z.M.D.S., Freitas, A.M. and Marcon, I.M., 2003. Risk factors related to the severity of diabetic retinopathy. Arquivos Brasileiros de Oftalmologia, 66(6), pp.739-743.
2. Elin, R.J., 1987. Assessment of magnesium status. Clinical chemistry, 33(11), pp.1965-1970.
3. Levine, B.S. and Coburn, J.W., 1984. Magnesium, the mimic/antagonist of calcium. N EnglJ Med, 310, pp. 1253-5
4. Winter, R.J., Harris, C.J., Phillips, L.S. and Green, O.C., 1979. Diabetic ketoacidosis: induction of hypocalcemia and hypomagnesemia by phosphate therapy. The American journal of medicine, 67(5), pp.897-900.
5. Lam, H.C., Lee, J.K., Lu, C.C., Chu, C.H., Chuang, M.J. and Wang, M.C., 2003. Role of endothelin in diabetic retinopathy. Current vascular pharmacology, 1(3), pp.243-250.
6. Ajith TA. Possible therapeutic effect of magnesium in ocular diseases. Journal of basic and clinical

physiology and pharmacology. 2020 Mar 26;31(2):20190107.
7. Farid SM, Abulfaraj TG. Trace mineral status related to levels of glycated hemoglobin of type 2 diabetic subjects in Jeddah, Saudi Arabia. Medical journal of Islamic World Academy of sciences. 2013 Apr;21(2):47-56.
8. Maltezos E, Papazoglou D, Exiara T, Kambouromiti G, Antonoglou C. Serum magnesium levels in non-diabetic offspring of patients with Type 2 diabetes mellitus. Diabetes, nutrition & metabolism. 2004 Feb 1;17(1):12-6.
9. Johansson G, Danielson BG, Ljunghall S, Wibell L. Evidence for a distur~ d magn~ sium metabOlism in diabetes mellitus*.
10. Hatwal A, Gujral AS, Bhatia RP, Agrawal JK, Bajpai HS. Association of hypomagnesemia with diabetic retinopathy. Acta Ophthalmologica. 1989 Dec;67(6):714-6.
11. Lott JA, Turner K. Evaluation of Trinder's glucose oxidase method for measuring glucose in serum and urine. Clinical chemistry. 1975 Nov 1;21(12):1754-60.
12. Muqit MM, Kourgialis N, Jackson-deGraffenried M, Talukder Z, Khetran ER, Rahman A, Chan WO, Chowdury FA, Nag D, Ahmad J, Friedman DS. Trends in diabetic retinopathy, visual acuity, and treatment outcomes for patients living with Diabetes in a Fundus photograph–based Diabetic Retinopathy Screening Program in Bangladesh. JAMA network open. 2019 Nov 1;2(11):e1916285-.
13. Shaikh MA, Gillani S. Frequency of diabetic retinopathy in patients after ten years of diagnosis of type 2 diabetes mellitus. Journal of Ayub Medical College Abbottabad. 2010 Sep 1;22(3):158-60.
14. Singh TP, Jolly A, Singh H, Singh G, Kaur D, Kaur N. Study of relation between Serum Magnesium Levels and Vascular Complications in Patients of Type 2 Diabetes Mellitus. International Journal of Research in Health and Allied Sciences. 2019;5(1):54-8.
15. Kumar P, Bhargava S, Agarwal PK, Garg A, Khosla A. Association of serum magnesium with type 2 diabetes mellitus and diabetic retinopathy. Journal of family medicine and primary care. 2019 May 1;8(5):1671-7.
16. Pham PC, Pham PM, Pham SV, Miller JM, Pham PT. Hypomagnesemia in patients with type 2 diabetes. Clinical journal of the American Society of Nephrology. 2007 Mar 1;2(2):366-73.
17. Kundu D, Osta M, Mandal T, Bandyopadhyay U, Ray D, Gautam D. Serum magnesium levels in patients with diabetic retinopathy. Journal of natural science, biology, and medicine. 2013 Jan;4(1):113.
18. Kauser, M.M., Afreen, A. and Kasi, J., 2014. Study of serum magnesium levels in diabetic retinopathy. J Res Med Den Sci, 2(3), pp.19-22.r
19. Rayssiguier Y. Role of magnesium and potassium in the pathogenesis of arteriosclerosis. Magnesium. 1984 Jan 1;3(4-6):226-38.
20. van den Oever IA, Raterman HG, Nurmohamed MT, Simsek S. Endothelial dysfunction, inflammation, and apoptosis in diabetes mellitus. Mediators of inflammation. 2010 Oct;2010.
21. Ghattaura N, Murphy C, Valen P. High prevalence of hypomagnesemia and its relation to BMI, type 2 diabetes, and clinical disease measures in a VA outpatient rheumatology clinic population. InARTHRITIS & RHEUMATOLOGY 2015 Oct 1 (Vol. 67). 111 RIVER ST, HOBOKEN 07030-5774, NJ USA: WILEY-BLACKWELL.