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STUDY OF SERUM MAGNESIUM, HBA1 C AND MICROALBUMINURIA IN DIABETIC RETINOPATHY

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ABSTRACT

Diabetic retinopathy is a sight threatening complication of diabetes mellitus and is one of the leading causes of acquired blindness. There is a series of risk factors related to the development and progression of diabetic retinopathy such as hypomagnesemia, dyslipidemia, duration of diabetes, poor diabetes control. There was a significant increase in the HbA_{1c} and microalbumin were as magnesium is decreased in urine in diabetic patients with retinopathy and also in diabetic patients without retinopathy, when compared to the control group.The severity of diabetic retinopathy in the studied groups was influenced by factors such as duration of diabetes mellitus, good glycemic control, hypomagnesemia and microalbuminuria.

KEY WORDS: **Diabetic retinopathy, HbA_1C, Magnesium, Microalbumin.**

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INTRODUCTION

Diabetes Mellitus is a complex metabolic disease caused by a variable interaction between hereditary and environmental factors. It is one of the most common metabolic diseases in which either the hormone insulin is lacking or the body's cells are insensitive to insulin effects.[1, 2] It is associated with a considerable mortality from a variety of complications, which tend to worsen over time and carries a significant premature mortality risk. Its main features are abnormal insulin secretion, high levels of blood glucose and its complications such as retinopathy, nephropathy, neuropathy and arteriosclerosis.[1, 3] Diabetes Mellitus is one of the main threats to human health in the 21st century. The WHO has estimated that there would increase to 300 million by the year 2025. Increasing urbanization and Industrialization are the chief reasons for the rapid increase in the prevalence of type 2 diabetes mellitus.[4,5] Diabetic retinopathy (DR) is a sight threatening complication of diabetes mellitus and is one of the leading causes of acquired blindness in adults. The chance of loosing the sight is about 25 times higher compared to normal individuals. There are a series of risk factors related to the development and progression of diabetic retinopathy such as duration diabetes mellitus, poor glycemic control, dyslipidemia, hypertension and hypomagnesemia.[1, 2] Hypomagnesemia has long been known to be associated with diabetes mellitus. Magnesium depletion is said to have a negative impact on glucose homeostasis and Insulin sensitivity. This association between diabetes mellitus and magnesium is said to have a wide range of impact on diabetic control and complications.[6,7] Recent improvements in the detection of low urinary levels of albumin have made the consideration of microalbuminuria important in the care of patients with diabetes mellitus. Using microalbuminuria determinations, physicians are now better able to predict which patients are at a greater risk of developing microvascular complications.[8] Chronic hyperglycemia and its associated non-enzymatic glycation plays an important role in the development of microangiopathy. Hyperglycemia leads to the formation of advanced glycation end products, which result in the various vascular complications like myocardial infarction etc.[9] Intensive glycemic control as measured by serum HbA_{1c} levels have been demonstrated in randomised trials to reduce diabetic complications especially microvascular disease. Several studies have been done to study the influence of these individual risk factors on the progression of retinopathy. However, very few studies have been done to study the correlation between all these risk factors in diabetic patients with retinopathy. In this study, an attempt has been made to find the correlation between these risk factors in the onset and progression of diabetic retinopathy.

MATERIALS AND METHODS

The study included 60 Type II Diabetic patients, 30 patients with clinically diagnosed retinopathy and 30 patients without retinopathy. The subjects were selected from the outpatient and inpatient departments of ophthalmology in Hospital. Clinical diagnosis was based on history and fundoscopic findings.The age of patients varied from 30-60 years. The cases were selected on the basis of simple random sampling method. The exclusion criterion included chronic diarrhea, alcoholism, pregnancy, drugs causing hypomagnesemia like diuretics, cisplatin, pentamidine, urinary tract infection, inflammatory conditions like rheumatoid arthritis, myocardial infarction, H/o recent surgery and major trauma. The results were compared with 30 normal healthy randomly selected individuals after obtaining due consent. The controls were age and sex matched. The investigations included serum magnesium, HbA_{1c} in blood and microalbumin in urine. The same were compared with controls.Under all aseptic precautions serum separated was

then used for the estimation of magnesium 2ml of blood, collected in vacutainers containing EDTA was used for the estimation of HbA_{1c}.The random, midstream urine samples (10ml) were collected in sterile containers without preservative and assayed for microalbumin . The estimation of microalbumin was done after screening the samples by uristix for any protein. Negative samples (negative/trace by uristix) were estimated for microalbumin by immmunoturbidimetric method using RANDOX KIT-MA 2426 in autoanalyzer and urinary creatinine is done . Serum magnesium was estimated by Xylidyl blue method using RANDOX KIT-MG 3880 and HBA1c was estimated by Latex agglutination inhibition method using RANDOX KIT-HA 3830 analysed both in the auto analyzer and For the tests conducted suitable controls were run according to protocols.

RESULTS

SPSS for windows Version-16 (2007) was employed for statistical analysis. In the present study Cross tabs procedure (contingency coefficient test), Descriptive statistics, One-way Anova, Independent samples 't'test, Pearson's correlation The age group was between 30-60 years. The mean age in diabetic patients with retinopathy was 49.53 ± 5.82 yrs, in diabetic patients without retinopathy it was 46.77 ± 6.99 yrs and in controls, it was 45.50 ±6.14 yrs.

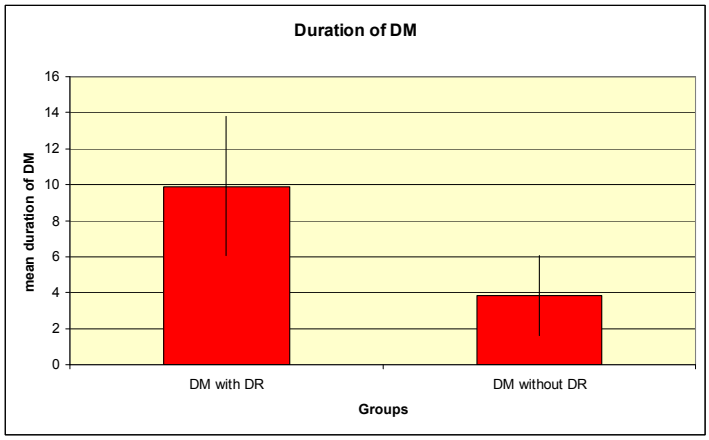
Table No 1
Age distribution in the study groups.

Age in Yrs	Diabetic with retinopathy	Diabetic without retinopathy	Controls
31-40	5	6	4
41-50	16	15	18
51-60	9	8	8

Table No 2
Gender distribution in the study groups.

	Diabetic with retinopathy	Diabetic without Retinopathy	Controls
Males	19	20	15
Females	11	10	15

Figure 1
Bar diagram showing the duration of diabetes mellitus in the diabetic groups



Duration of diabetes mellitus: The mean duration of diabetes mellitus in diabetic patients with retinopathy was 9.90 ± 3.86 yrs and in diabetic patients without retinopathy it was 3.84 ± 2.23yrs.

The duration of diabetes mellitus in diabetic patients with retinopathy was significantly higher when compared to the diabetic patients without retinopathy (P<0.001). The above findings show that as the duration of diabetes mellitus increases, there is increase in the incidence and progression of retinopathy.

Table 3
Showing mean and S.D of HbA_{1c} (%of total Hb) in the study groups

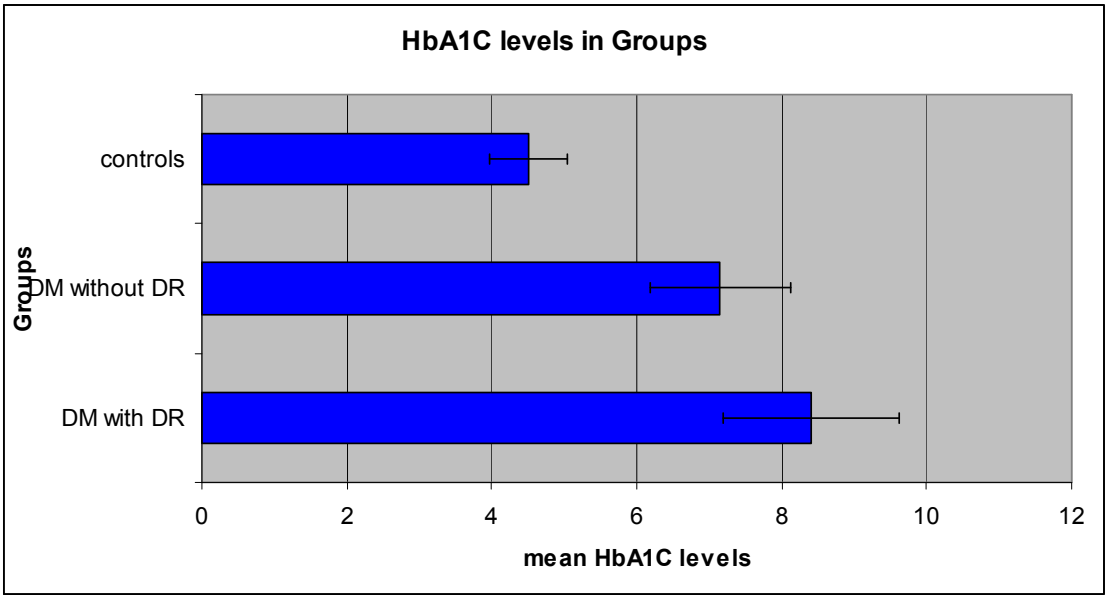
Groups	Mean ±S.D
DM with retinopathy	8.41±1.21
DM without retinopathy	7.15±.97
Controls	4.51±0.53

Table 4
Showing the significant difference in the mean HbA_{1c} values between the study groups

Between groups	t- value	'p' value	Inference
DM with DR & DM without DR	3.468	<0.001	Highly significant
DM with DR & Controls	11.557	<0.001	Highly significant
DM without DR & Controls	10.596	<0.001	Highly significant

As represented in the table no 3 & 4, there was a statistically significant increase in the mean HbA_{1c} values in diabetic patients with retinopathy when compared to the diabetic patients without retinopathy (p<0.001) and the control group (p<0.001). Similarly, there was a significant increase in the mean HbA_{1c} values in diabetic patients without retinopathy when compared to the control group (p<0.001).

Figure 2
Bar diagram showing the mean HbA_{1c} levels in the study groups



The above bar diagram shows that there is a significant increase in the mean HbA_{1c} values in diabetic patients with retinopathy when compared to the diabetic patients without retinopathy and the control group.

Table 5
Showing mean and S.D of serum magnesium (mg/dl) in the study groups

Groups	Mean ±S.D
DM with retinopathy	1.95 ± 0.32
DM without retinopathy	2.01 ± 0.18
Control	2.45 ± 0.21

Table 6
showing the significant difference in the mean magnesium (mg/dl) levels in the study groups

Between groups	t-value	'p' value	Inference
DM with DR & DM without DR	-1.997	<0.05	Significant
DM with DR & Controls	-7.830	<0.001	Highly Significant
DM without DR & Controls	-7.681	<0.001	Highly significant

As represented in table No.5 & 6, there was a statistically significant decrease in the mean magnesium levels in diabetic patients with retinopathy when compared to the diabetic patients without retinopathy (p<0.05) and the control groups (p<0.001). Similarly there was a statistically significant decrease in the mean magnesium levels in diabetic patients without retinopathy when compared to control group (p<0.001

Figure 3
Bar diagram showing the mean magnesium levels in study groups.

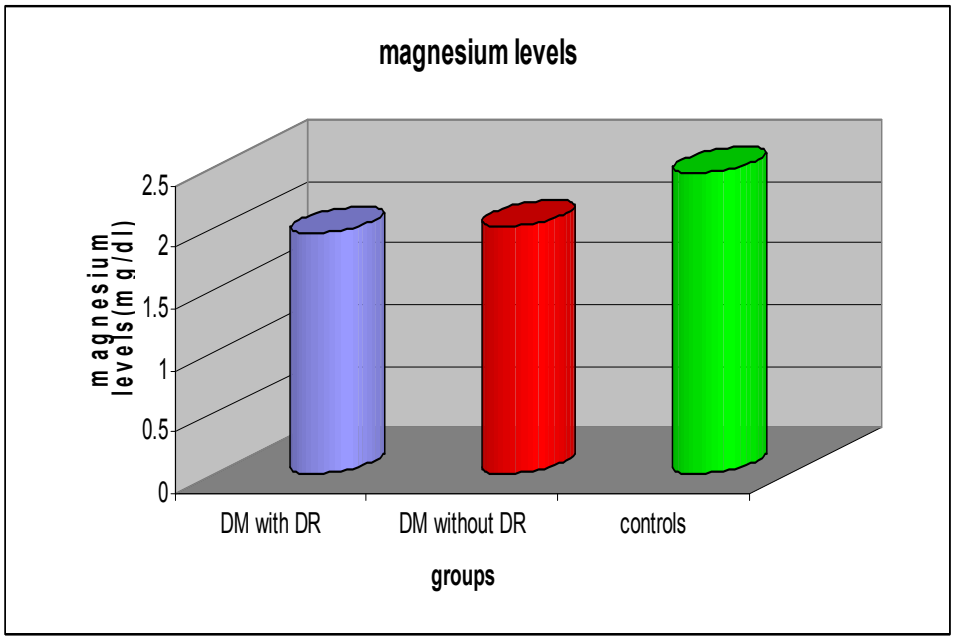


Table 7
showing the mean & S.D. of microalbumin (µg/mg of creatinine) in urine

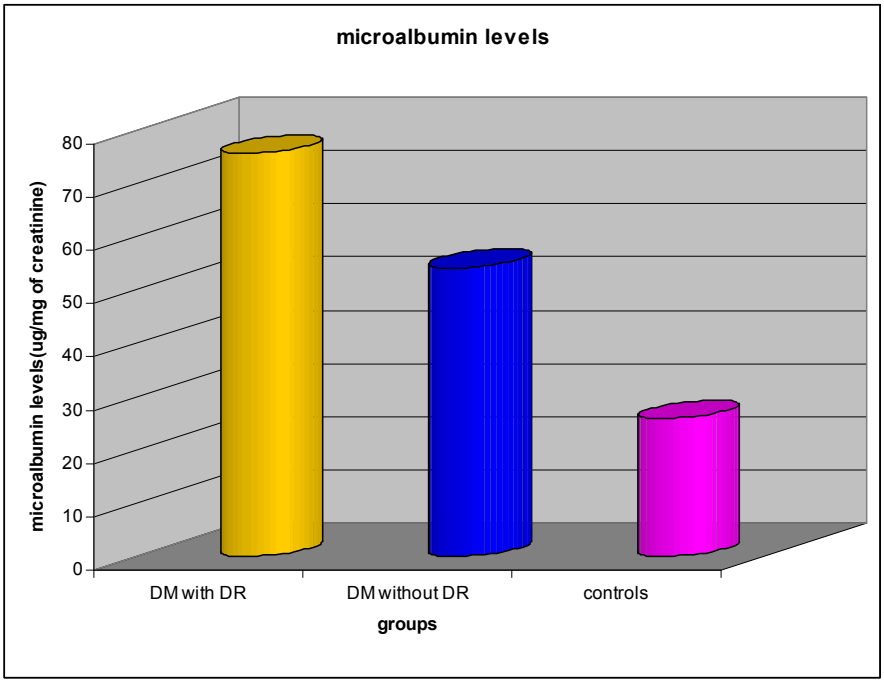
Groups	Mean ±S.D
DM with retinopathy	75.53 ± 45.46
DM without retinopathy	54.12 ± 22.81
Control	25.84 ± 5.13

Table 8
Showing significant difference in the mean microalbumin (µg/mg of creatinine) levels in urine.

Between groups	t-value	'p' value	Inference
DM with DR & DM without DR	2.838	<0.05	Significant
DM with DR & Controls	6.254	<0.001	Highly Significant
DM without DR & Controls	5.932	<0.001	Highly significant

As represented in table No.7 & 8, there was a significant increase in the microalbumin levels in urine in diabetic patients with retinopathy when compared to the diabetic patients without retinopathy (p<0.05) and the controls (p<0.001). Similarly, there was a significant increase in the microalbumin levels in urine in diabetic patients without retinopathy when compared to the controls (p<0.001).

Figure 4
Bar diagram showing microalbumin levels in urine in the study groups



The above bar diagram shows that there is a significant increase in the mean microalbuminuria levels in diabetic patients with retinopathy when compared to the diabetic patients without retinopathy and the control groups.

DISCUSSION

Diabetic Retinopathy is a sight threatening complication of diabetes mellitus and is one of the leading causes of acquired blindness. It is due to microangiopathy affecting the retinal arterioles, capillaries and venules. Damage is caused by both microvascular leakage and microvascular occlusion. A series of risk factors have been related to the development and progression of retinopathy in diabetic patients. Our findings are comparable with the study done by M Rema et.al., who have proposed that duration of diabetes mellitus is probably the strongest predictor for the development of retinopathy. Studies have also shown that for every 5-year increase in the duration of diabetes mellitus, the risk of diabetic retinopathy increases by 1.89 times.[10]Studies done by Farhan K H et.al., have also shown that duration of diabetes mellitus can increase the risk for the development of diabetic retinopathy.[11] We have observed increased HbA_{1c} levels in diabetic patients with retinopathy and in diabetic patients without retinopathy.[6] Studies have also shown that in patients with type 2 diabetes mellitus, every 1%increase in HbA_{1c} would result in an increase in the microvascular complications by 37%. [12]K G Santos et.al., have demonstrated a significant increase in HbA_{1c} levels in diabetic patients with retinopathy.[13] The findings of the present study and the previous studies show that hyperglycemia, as indicated by the increase in the HbA_{1c} levels, is a potent predictor of progression of diabetic retinopathy. The possible mechanism is hyperglycemia leads to glycation of virtually all proteins, resulting in the formation of advanced glycation end products. These advanced glycation end products induce cross linking of collagen and other extracellular matrix proteins in many tissues including arterial vessel walls.[14] Hyperglycemia-induced vascular injury leads to increased glucose flux through the polyol pathway, resulting in cellular damage, thereby resulting in the various micro vascular and macro vascular complications.[15]

HbA_{1c} is also shown to have a special affinity for oxygen thereby causes tissue anoxia and plays a role in causation of micro and macroangiopathy.[6] The interaction of advanced glycation end products and their receptors have been implicated as mediators of micro vascular permeability, ischemia & angiogenesis.[15] In the present study, the mean serum magnesium levels in diabetic patients with retinopathy were There was a statistically significant decrease in the magnesium levels in the diabetic groups compared to the control group. Our findings agree with the study done by Hatwal et.al., Ishrat kareem et.al., who have shown that Hypomagnesemia is a risk factor for the development of retinopathy.[16] have shown the presence of hypomagnesemia in diabetic retinopathy.[6,17] The exact cause of hypomagnesemia in diabetes mellitus in not known. Poor dietary intake, impaired absorption of magnesium, increased urinary loss due to hyperglycemia and osmotic diuresis may be the contributory factors. Magnesium is necessary for several enzymes that play an important role in glucose metabolism. Magnesium depletion is said to reduce the insulin sensitivity, there by increasing the risk of secondary complications.[18]

Hence it is important to monitor the plasma magnesium levels in diabetic patients with complications. Magnesium supplementation may help to reduce the progression of retinopathy in these patients.[19, 20] In the present study, the mean microalbumin levels in urine, in diabetic patients with retinopathy There was a significant increase in the microalbumin levels in urine in diabetic patients when compared to the control group. Cruickshanks et.al., MC Boelter et.al found an association between microalbuminuria and retinopathy in diabetic patients and have

suggested the influence of nephropathy in retinal disease.[21, 22] Possible reason for this is microalbuminuria is strongly related to the degree of hyperglycemia, which leads to the formation of advanced glycation end products. These advanced glycation end products result in the various micro vascular complications.[15, 23] Further, Retinopathy and microalbuminuria could be due to generalized microangiopathy. K.G Santos et.al., have shown that duration of diabetes mellitus, glycosylated hemoglobin and albumin excretion rate were independently related to diabetic retinopathy.[13] Studies have suggested that increased capillary permeability, microangiopathy and retinal ischemia are probably due to the combined effects of various risk factors.[24] Early diagnosis and prompt treatment in these patients can reduce the onset and progression of retinopathy. Further studies with oral magnesium supplementation in different stages of diabetic retinopathy can be interesting.

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