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## RESEARCH ARTICLE

### A COMPARATIVE STUDY OF GLYCOSYLATED H<sub>A</sub>EMOGLOBIN, MAGNESIUM AND LIPID PROFILE IN DIABETIC PATIENTS WITH AND WITHOUT RETINOPATHY

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#### ABSTRACT

Diabetic retinopathy is the most frequent cause of new cases of blindness among adults aged 20–74 years. Patients with diabetic retinopathy (DR) are 25 times more likely to become blind than non-diabetics. Every person with diabetes is at risk of developing DR. More than 75% of people who have diabetes for more than 20 years will have some form of DR. Diabetic retinopathy is the result of damage to the tiny blood vessels that nourish the retina. They leak blood and other fluids that cause swelling of retinal tissue and clouding of vision. Present study was conducted in SMS Medical College and Hospital, Jaipur, including 100 diabetic which were further categorized into two groups i.e. 50 diabetic patients without retinopathy (Group 2), and 50 diabetics with retinopathy (Group 3). Results obtained were compared with 50 age and sex matched healthy controls (Group 1). Fasting blood samples collected using aseptic technique were subjected to analyze level of Fasting blood sugar, HbA1c, Serum Magnesium and serum Total cholesterol, Triglycerides, LDL-cholesterol and HDL-cholesterol in all the groups. Serum magnesium level in diabetic retinopathy was found to be significantly lowered than in Group 2 and I. Significantly Increased HbA1c was observed in diabetic retinopathy as compared to Group 1 and 2. Results obtained in our study showed increased cholesterol/HDL cholesterol ratio, hypercholesterolemia, hypomagnesimia, hypertriglyceridemia, elevated LDL-cholesterol lipoprotein fraction and significantly decreased HDL-cholesterol lipoprotein fraction in subjects with diabetic retinopathy which are responsible for micro vascular changes that the diabetic retinopathy patients have. From this study this is concluded that good glycemic control and lipid-modifying therapy arrests the development and progression of DR and decreases the visual loss.

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## INTRODUCTION

Diabetic retinopathy can be defined as the alteration of microvascular system of retina due to prolonged hyperglycaemia (Gaede et al., 1999). Diabetic retinopathy is a leading cause of blindness among working-age adult population (Fong et al., 2004). Approximately 20–40% of adults with type 2 diabetes have some signs of retinopathy and about 8% have more severe vision-threatening retinopathy (Kempner et al., 2004). Several risk factors are associated with the development of diabetic retinopathy including hyperglycemia, arterial hypertension and elevated serum lipids, obesity and other cardiovascular risk factors (Rema et al., 2006). Impaired auto regulation in the microvasculature arising from high intracellular glucose concentration is a key initiating factor in diabetic retinopathy

(Alder et al., 2007). Magnesium depletion has been linked to the development of retinopathy (Ceriello et al., 1982; Wada et al., 1983). The severity of retinopathy is related to the longer duration of diabetes and the high levels of glycosylated haemoglobin. The incidence of retinopathy was significantly increased with the duration of the diabetes mellitus and it was associated with a poor glycaemic control (Wada et al., 1983). Individuals with elevated total serum cholesterol, low-density lipoprotein (LDL) cholesterol or triglyceride levels are more likely to have or develop retinal hard exudates which can be associated with risk of vision loss independent of the extent of macular oedema (Ucgun et al., 2007). So, in the present study, an attempt is made to evaluate level of biochemical parameters i.e Fasting blood sugar, Post prandial blood sugar, Magnesium, Lipid profile, and Glycosylated haemoglobin [HbA1c] in healthy controls and clinically proven diabetics with and without complications of retinopathy and their correlations with each other if any exist. The extent of the degeneration

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during the course of the disease along with various patterns it adopts can be defined through this study.

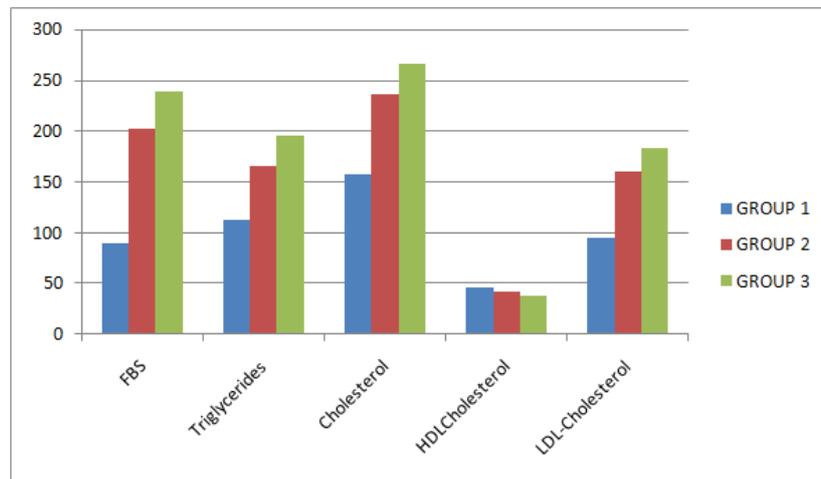
**MATERIALS AND METHODS**

A Hospital based case-control study was planned, including 50 patients of clinically proven diabetic without retinopathy (Group 2), 50 diabetic with retinopathy (Group 3) and 50 age and sex matched controls (Group 1) attending OPD/IPD Ophthalmology and Medicine OPD of S.M.S.

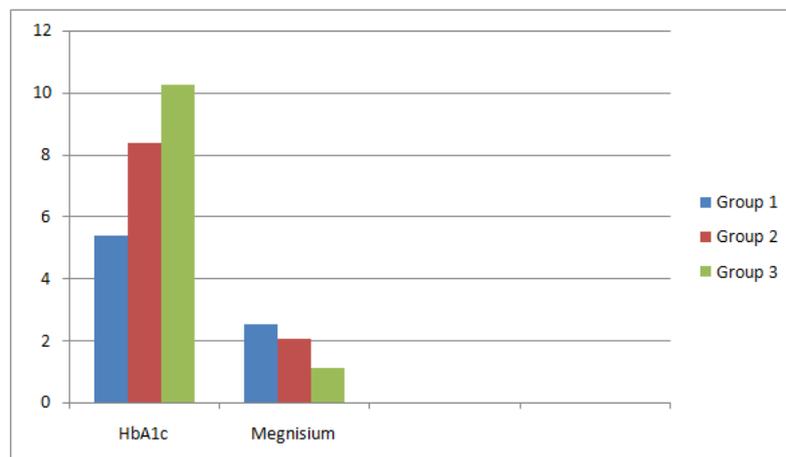
Hospital, Jaipur from Nov 2013 to Dec 2014. The Patients age ranged from 20 to 60 years. Diabetic retinopathy was established in clinically confirmed cases of diabetes using ophthalmoscopic examination and fundus photography. Subjects with alcoholism, smoking, hypertension, diarrhea, use of diuretics, reduced renal function were excluded. Pregnant, lactating women and seriously ill patients were also excluded. A written informed consent was taken from all patients fulfilling the inclusion criteria. This was followed by detailed history and examination, the finding of which was recorded in a pre-designed case record Form.

**Table 1. Mean ± SD of Fasting blood sugar, Glycated haemoglobin, Magnesium, Triglycerides, cholesterol: HDL ratio, LDL-cholesterol in Different groups**

Groups	Normal control (Group 1)	DM without Retinopathy (Group 2)	DM with Retinopathy (Group 3)
FBS (mg/dl)	89.30±20.54	201.77±44.09	238.33±66.66
HbA1c	5.40±0.61	8.39±1.14	10.24±1.81
Magnesium (mg/dl)	2.50±0.40	2.03±0.34	1.1±0.47
Triglycerides (mg/dl)	112.33±48.44	166.23±64.16	195.33±37.15
Cholesterol (mg/dl)	158.10±33.96	236.77±43.71	265.70±52.48
HDL Cholesterol (mg/dl)	45.60±6.51	42.57±3.29	38.13±4.75
Cholesterol/ HDL – ratio	3.46	5.56	6.96
LDL-Cholesterol (mg/dl)	95.43±36.02	159.83±40.57	183.57±46.56
VLDL (mg/dl)	22.27±9.81	34.37±12.86	40.50±7.47



**Fig.1. Comparison of Mean Levels of Fasting blood sugar and serum lipids (mg/dl) between Different Groups**



**Fig.2. Comparison of Mean Levels of HbA1c and serum magnesium (mg/dl) between Different Groups**

## Procedure

About 10 ml of blood samples were collected by venipuncture into labeled dry test tubes. After collection blood samples were allowed to coagulate after which they were centrifuged at 3000 rpm for 5 minutes to obtain sera. For HbA1c about 10 ml of blood samples were collected by venipuncture into labeled EDTA test tubes. Blood glucose, HbA1c, triglyceride, total cholesterol, and high density cholesterol (HDL) were analysed. Magnesium was estimated by Arsenazo method, Glucose by Glucose oxidase – Peroxidase method [Barham and Trinder, 1972], cholesterol by Cholesterol Oxidase – Peroxidase method [Allain *et al.*, 1974] and triglycerides by Trinders Glycerol Phosphate Oxidase-Peroxidase method [Bucolo and David, 1973] and LDL cholesterol by calculated using Friedewald Formula [Friedewald *et al.*, 1972]. Statistical Analysis was done by using SPSS 19.0 and Microsoft excel.

## RESULTS

The Mean  $\pm$ SD of fasting blood sugar was found to be higher in group 3 ( $238.33 \pm 66.66$ ) as compared to Group 2 ( $201.77 \pm 44.09$ ) and Group 1 ( $89.30 \pm 20.54$ ) and they were highly significant. The Mean  $\pm$ SD of Glycated haemoglobin (HbA1c) as shown was found to be higher in group 3 ( $10.24 \pm 1.81$ ) as compared to Group 2 ( $8.39 \pm 1.14$ ) and Group 1 ( $5.40 \pm 0.61$ ) and they were highly significant. The Mean  $\pm$ SD of Magnesium was found to be higher in Group 1 ( $2.50 \pm 0.40$ ) as compared to Group 2 ( $2.03 \pm 0.34$ ) and group 3 ( $1.1 \pm 0.47$ ). The patients in Group 3 has hypomagnesemia ( $p < 0.01$ ) compared to group 2. The mean  $\pm$  SD of TG, CHOL, LDL and VLDL as shown was found to be higher in group 3 ( $195.33 \pm 37.15$ ,  $265.70 \pm 52.48$ ,  $183.57 \pm 46.56$ ,  $40.50 \pm 7.47$ ) as compared to Group 2 ( $166.23 \pm 64.16$ ,  $236.77 \pm 43.71$ ,  $159.83 \pm 40.57$ ,  $34.37 \pm 12.86$ ) and group 1 ( $112.33 \pm 48.44$ ,  $158.10 \pm 33.96$ ,  $95.43 \pm 36.02$ ,  $22.27 \pm 9.81$ ) respectively and they were highly significant. Significantly low level of HDL- cholesterol in diabetic retinopathy patients ( $38.13 \pm 4.75$ ) as compared to diabetic without retinopathy ( $42.57 \pm 3.29$ ) and healthy controls ( $45.60 \pm 6.51$ ) was observed. The significant observation was that increased cholesterol and decreased HDL-cholesterol observed with increased cholesterol/HDL-cholesterol ratio (6.9).

## DISCUSSION

Hyperglycemia-induced changes are consequence of formation of advanced glycation end (AGE) products, sorbitol and reactive oxygen species that cause DR. The mean level Mean  $\pm$ SD of fasting blood sugar was found to be higher in Group 3 as compared to Group 2 and Group 1 and they are highly significant. These findings were in agreement with Wang *et al.* (2011). Hypomagnesemia was observed in diabetic retinopathy patients. These observation are similar to other workers (Ceriello *et al.*, 1982; Wada *et al.*, 1983; McNair *et al.*, 1978). Magnesium is involved in insulin secretion, critical cofactor of many enzymes in carbohydrate metabolism, and the activity of membrane bound sodium-potassium ATPase (Grofton and Borter, 1992) which maintain the gradients of sodium, potassium and glucose transport. Low levels of

magnesium reduced insulin secretion by the pancreas is reported (Durlach *et al.*, 1983). Glycosylated Haemoglobin (HbA1c) levels correlate well with glycemic levels over the previous six to ten weeks. HbA1c results from post translational changes in the haemoglobin molecule, and Glycosylation of haemoglobin takes place under physiological condition by a reaction between glucose and N terminal valine of Beta chain of Hb molecules. The mean  $\pm$  SD of Glycated haemoglobin (HbA1c) was found to be higher in group 3 as compared to Group II and Group I and they are highly significant. These findings are agreement with the observation of the Rema *et al.* (2000), in this observation she found a linear trend in the prevalence of retinopathy with increase in quartiles of HbA1c ( $p > 0.001$ ) from 8.1 % to 31.7 %. The Mean  $\pm$ SD of serum lipids such as cholesterol, triglycerides, LDL cholesterol and VLDL were found to be higher in Group 3 as compared to Group 2 and Group 1 and they are highly significant (0.0000). But observation of Nargis *et al.* had significant p value (Nargis *et al.*, 2012). These findings of CHOL are akin with Nargis *et al.* (2012). The highly significant result of HDL is agreement of Jayalakshmi *et al.* (2012), Bilijanamil *et al.* (2004), Timothy *et al.* (2004) and Lyons *et al.* (2004) And observation of Nargis *et al.* (2012) had significant p value. These results were reported because the peroxidation of lipids in lipoproteins in the vascular wall leads to local production of reactive carbonyl species that mediate recruitment of macrophages, cellular activation and proliferation, and also chemical modification of vascular proteins by advanced lipoxidation end-products which affect both the structure and function of the vascular wall (Baynes and Thorpe, 2000) Consequently, it was proposed that, hyperlipidemia might contribute to DR and ME by endothelial dysfunction and breakdown of the blood retinal barrier leading to exudation of serum lipids and lipoproteins (Benarous *et al.*, 2011). Hence, this study has been a step forward to find relation of multiple metabolic factors with diabetic retinopathy and raises a fundamental issue of need of further research in this direction which can help in better understanding of this disease and in developing new therapeutic strategies in treatment of diabetic retinopathy patients.

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