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## Study of Biochemical Parameters in Diabetic Patients with and without Diabetic Retinopathy – A Hospital based study

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### Abstract

**Background:** Diabetic Retinopathy (DR) is a common, potentially blinding and visually disabling complication of diabetes. Early detection of retinopathy and its progression to severity with routine referral for screening by Ophthalmologist can save vision by timely management. **Methods:** This was a hospital based cross-sectional study done to study the association of glycated hemoglobin (HbA1c), fasting and postprandial blood sugar, serum lipid profile, serum creatinine and urine albumin in diabetic patient with and without DR. A total of 50 patients with Diabetic retinopathy and 50 patients without diabetic retinopathy were enrolled in this study. All patients included were Type 2 DM aged 35 years and above. **Results:** The mean HbA1c was  $8.62 \pm 1.5$  and  $5.54 \pm 1.2$ , total cholesterol was  $228.9 \pm 63$  and  $184.9 \pm 39.8$  mg/dl, serum triglyceride was  $226.6 \pm 80.7$  and  $160.8 \pm 45.1$  mg/dl, LDL-C was  $152.3 \pm 49$  and  $127.2 \pm 37$  mg/dl and serum creatinine was  $1.15 \pm 0.45$  and  $0.66 \pm 0.27$  mg/dl in diabetic retinopathy group and no diabetic retinopathy group respectively. There was significant association of elevated HbA1c, serum triglyceride, LDL- C and total cholesterol with diabetic retinopathy in patients with type 2 DM. The mean values of serum lipoproteins were higher in the diabetic retinopathy group. **Conclusion:** Elevated fasting and postprandial blood sugar, glycated hemoglobin, total cholesterol, serum triglyceride, LDL-C, serum creatinine and urine albumin were significantly associated with DR in our study. So, all patients with diabetes mellitus should be screened routinely for serum lipoproteins along with blood sugar profile, as it would help in early detection of diabetic retinopathy.

**Keywords:** Type 2 Diabetes mellitus, Diabetic Retinopathy, Serum Lipoproteins

### Introduction:

Diabetic Retinopathy (DR) is a common, potentially blinding and visually disabling complication of diabetes where the cause of vision loss can be due to diabetic maculopathy or complications of proliferative diabetic retinopathy (PDR).<sup>1</sup> Diabetic patient are 25 times more likely than the general

population to develop vision loss and blindness.<sup>2</sup> Diabetes has emerged as a major global concern. In 2040, the global diabetes prevalence in adults is predicted to rise to 10.4%.<sup>3</sup> In Nepal, the burden of diabetes is increasing rapidly due to increasing urbanization, aging population, rapid increase in obesity, and sedentary lifestyle. As per the recent meta-analysis, the prevalence of diabetes in Nepal was 8.5%.<sup>4</sup>

According to a hospital based study by Thapa et al<sup>5</sup> and Shrestha et al<sup>6</sup> in Nepal, the prevalence

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## ORIGINAL ARTICLE



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of diabetic retinopathy was 38% and 44.7% respectively. Long duration of diabetes, poor glycaemic control, high blood pressure, pregnancy and nephropathy are the known risk factors for diabetic DR.<sup>7</sup> Biochemical parameters being the reflection of the state of control of diabetes are valuable resources in identifying the progression of retinopathy. However, there are little conclusive evidence regarding the association of biochemical parameters especially serum lipid profile with retinopathy in this region. So, the objective of this study was to study the association of glycated hemoglobin (HbA1c), fasting and postprandial blood sugar, serum lipid profile, serum creatinine and urine albumin in diabetic patient with and without DR.

### Methods:

This was a hospital based cross-sectional study conducted at B.P. Koirala Institute of Health Science, Dharan, Nepal. Written Informed consent was obtained from all the patients enrolled in the study. The research was approved by the ethics committee and institutional board of BPKIHS, Dharan, Nepal on 22nd July 2014 (Ref. No.ACd/10/071/072), and has adhered to the tenets of the Declaration of Helsinki.

A Total of 100 patients were enrolled in this study. Convenient sampling method was used. All patients with Type 2 DM with and without DR aged 35 years and above were included in the study. Patients were categorized as either presence or absence of DR. The patients with DR were classified as per ETDRS classification of Diabetic Retinopathy.<sup>8</sup> Patients with Type 1 DM, Gestational diabetes mellitus, central corneal opacity, cataract obscuring detailed fundus evaluation, vitreous hemorrhage were excluded from the study. Detailed history was taken and all participants underwent a comprehensive ophthalmic examination. HbA1c, fasting and postprandial blood sugar, lipid profile, and serum creatinine and urine albumin were evaluated. All the biochemical parameters except urinary albumin were measure by using the standard commercial assay kits in CobasC311 auto-analyzer, closed system in the biochemistry laboratory of BPKIHS, Dharan.

### Statistical analysis:

All the data were entered in Microsoft Excel spreadsheet 2013 and converted into SPSS (Statistical Package for Social Science) version 17.0 program for statistical analysis. For inferential statistics, X<sup>2</sup> test was used for categorical data, for comparison of mean t test was used and for association between two continuous variable correlations was used.

### Results:

A total of 50 patients with diabetic retinopathy and 50 patients without diabetic retinopathy were enrolled in the study. Out of 50 patients with DR, 28 had mild NPDR, 19 had moderate NPDR, 1 had severe NPDR with CSME and 1 had PDR with CSME.

The mean age was 59.56±10.9 and 54.30±9.7 years in patients with and without DR respectively. There was equal number of male and female in both groups. The mean duration of DM in DR group was 8.20±4.6 years and in no DR group were 4.08±2.7 years. Most of the patients in the DR group were housewives/retired and most of the patients in no DR group were businessmen. Forty two point nine percent of the patients on OHA 42.9% had DR whereas 57.1% had no DR. DR patients on insulin were 87.5% (P=0.002). In those patients with DR, only 22% had positive family history of diabetes while 78% had no family history of diabetes. In DR group, 74% were aware and 26% were not aware of DR as a complication of DM. The mean systolic blood pressure in DR group was 134.40±18.6 mm Hg and in no DR group was 126.60±15.8 mmHg. The mean diastolic blood pressure in DR group was 81.20±9.39 mm Hg and in no DR group was 76.60±10 mm Hg. The mean BMI in the DR group was 25.91±2.8 and in no DR group were 25.05±2.5. Best corrected visual acuity of ≥6/18 was present in 84% of the patients with DR and 16% had visual acuity of <6/18. In the patients without DR, right eye was considered for evaluation and 100% had visual acuity of ≥6/18. The mean CCT in the patients with DR was 533.7±17.9 and in those without DR was 513.9±29.

**ORIGINAL ARTICLE**



The mean fasting blood sugar was  $120 \pm 1$  mg/dl and  $119.86 \pm 63.6$  mg/dl in DR group and no DR group respectively ( $P < 0.001$ ). The mean postprandial blood sugar in the patients was  $272.5 \pm 91.8$  mg/dl and  $192.6 \pm 63.6$  mg/dl in DR group and no DR group respectively ( $P < 0.001$ ). The mean glycated hemoglobin in the patients with DR was  $8.62 \pm 1.5\%$  and in those without DR was  $5.54 \pm 1.2\%$  ( $P < 0.001$ ). (Table 1)

**Table 1: Blood sugar**

Fasting Blood sugar (mg/dl)	Diabetic retinopathy (N)			Odds ratio	95% Confidence Interval		P-value
	Yes	No	Total		Lower	Upper	
$\leq 126$	7 (18.9%)	30 (81.1%)	37 (100%)	0.109	0.041	0.289	$< 0.001$
$> 126$	43 (68.3%)	20 (31.7%)	63 (100%)				
Postprandial blood sugar (mg/dl)							
$\leq 200$	8 (19.5%)	33 (80.5%)	41 (100%)	0.098	0.038	0.255	$< 0.001$
$> 200$	42 (71.2%)	17 (28.8%)	59 (100%)				
HbA1c (%)							
$< 7$	5 (10.6)	42 (89.4%)	47 (100%)	0.021	0.006	0.070	$< 0.001$
$\geq 7$	45 (84.9)	8 (15.1%)	53 (100%)				

The mean level of total cholesterol in the patients with DR was  $228.9 \pm 63$  mg/dl and in those without DR was  $184.9 \pm 39.8$  mg/dl. The mean HDL-C in the patients with DR was  $40.6 \pm 8.0$  mg/dl and in those without DR was  $40.12 \pm 9.5$  mg/dl. The mean serum triglyceride in the patients with DR was  $226.6 \pm 80.7$  mg/dl and in those without DR was  $160.8 \pm 45.1$  mg/dl. The mean LDL-C in the patients with DR was  $152.3 \pm 49.1$  mg/dl and in those without DR was  $127.2 \pm 37.3$  mg/dl.

The mean serum creatinine in the patients with DR was  $1.56 \pm 0.43$  mg/dl and in those without DR was  $0.78 \pm 0.22$  mg/dl. In the patients with serum creatinine level  $> 1.2$  mg/dl (male) and  $> 1$  md/dl (female), DR was seen in 91.8% of the patients ( $P < 0.001$ ). In the patients with albuminuria, 78.2% (43) had DR ( $P < 0.001$ ). (Table 2)

**Table 2: Lipid profile, serum creatinine and urine albumin**

Total Cholesterol (mg/dl)	Diabetic retinopathy (N)			Odds ratio	95% Confidence Interval		P-value
	Yes	No	Total		Lower	Upper	
$\leq 200$	13 (24.1%)	41 (75.9%)	54 (100%)	0.077	0.030	0.201	$< 0.001$
$> 200$	37 (80.4%)	9 (19.6%)	46 (100%)				
HDL-C (mg/dl)							
$< 40$	27 (48.2%)	29 (51.8%)	56 (100%)	0.850	0.386	1.874	0.687
$> 40$	23 (52.3%)	21 (47.7%)	44 (100%)				
Serum Triglyceride (mg/dl)							
$\leq 150$	7 (25.9%)	20 (74.1%)	27 (100%)	0.244	0.092	0.650	0.003
$> 150$	43 (58.9%)	30 (41.1%)	73 (100%)				
LDL-C (mg/dl)							
$< 160$	24 (38.1%)	39 (61.9%)	63 (100%)	0.260	0.109	0.621	0.002
$\geq 160$	26 (70.3%)	11 (29.7%)	37 (100%)				

ORIGINAL ARTICLE



Serum creatinine (mg/dl)	Diabetic retinopathy (N)			Odds ratio	95% Confidence Interval		P-value
	Yes	No	Total		Lower	Upper	
≤ 1.2 (male); ≤ 1 (Female)	5 (9.8%)	46 (90.2%)	51 (100%)	0.010	0.002	0.038	<0.001
>1.2 (male); >1 (Female)	45 (91.8%)	4 (8.2%)	49 (100%)				
Urine Albumin							
No albuminuria	7 (15.6%)	38 (84.4%)	45 (100%)	0.051	0.018	0.144	<0.001
Albuminuria	43 (78.2%)	12 (21.8%)	55 (100%)				

**Correlation:**

In this study, 51.1% with poor HbA1c control had mild NPDR. (Table 3)

**Table 3: Relation of Glycated Hemoglobin with Stages of Diabetic retinopathy**

Stage of diabetic retinopathy	Glycated hemoglobin %	
	Good control <7%	Poor control ≥7%
Mild NPDR	5 (100%)	23 (51.1%)
Moderate NPDR	0	19 (42.2%)
Severe NPDR with CSME	0	1 (4.4%)
PDR with CSME	0	2 (2.2%)
Total	5 (100%)	45 (100%)

Serum triglyceride and serum creatinine showed low degree of positive correlations with abnormal HbA1c ≥7%. (Table 4)

**Table 4: Correlation between abnormal HbA1C and serum lipoproteins in patients with Diabetic Retinopathy**

Blood Parameters	Karl-Pearson correlation coefficient r	P-value
S. Triglyceride	0.055	0.707
T. Cholesterol	- 0.041	0.779
HDL-C	- 0.132	0.361
LDL-C	- 0.163	0.259
S. creatinine	0.166	0.25

**Discussion:**

In our study, there was significant association of fasting blood sugar with DR (P<0.001). Among the patients with DR, 68.3% had fasting blood sugar of >126 mg/dl. El Hadd et.al<sup>9</sup> showed that a high fasting capillary glucose level was significantly related to occurrence of retinopathy (P=0.002). The fasting capillary glucose level in patients with DR was 9.8mmol/l and with no DR was 8.5mmol/l. Samatha et al<sup>10</sup> found that there was significant increase in fasting blood sugar in patients with DR (P<0.001).

There was significant association of postprandial blood sugar with DR in our study (P<0.001). Among the patients with DR, 71.2% had postprandial blood sugar of >200mg/dl. El Bab et al<sup>11</sup> showed that the patients with DR had significantly higher postprandial glucose.

Significant association of glycated hemoglobin with DR was shown in our study (P<0.001). Among the patients with DR, 84.9% had poor control (≥7%) of HbA1c. In a study by Shakya et al<sup>12</sup> the mean glycated hemoglobin was significantly higher in the DR group (7.7±1.5%) compared to no diabetic retinopathy group (6.9±1.1%) (P=0.004). Various other studies also showed significant association of poor glycemic control with DR.<sup>13,14,15,16</sup>

In our study, there was significant association of elevated total cholesterol with DR (P<0.001). Among the patients with DR, 80.4% had total cholesterol >200mg/dl. Samatha et al<sup>10</sup> showed

## ORIGINAL ARTICLE



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significance association of elevated total cholesterol with DR. The mean total cholesterol in patients with DR was  $187.53 \pm 57$  mg/dl and in those without DR was  $167.79 \pm 29$  mg/dl.

However, there was no significant association of HDL-C with DR in our study ( $P=0.687$ ). However, El Bab et al<sup>11</sup> found that there was significant change of HDL-C from  $2.66 \pm 0.3$  mmol/L and  $2.55 \pm 0.21$  mmol/L for no DR and DR patients, respectively ( $P < 0.05$ ).

Our study showed significant association of serum triglyceride with DR ( $P=0.003$ ). Among the patients with DR, 58.9% had serum triglyceride  $> 150$  mg/dl. Shakya et al<sup>12</sup> showed that the serum triglyceride value was higher in the group with DR but was statistically not significant ( $P=0.56$ ). Serum triglyceride had low degree of positive correlation with HbA1c value. Similarly, Dayanand et al<sup>17</sup> and Mohan R et al<sup>18</sup> showed that hypertriglyceridemia was significantly associated with DR ( $P < 0.05$ ).

Our study also showed significant association of LDL-C with DR ( $p=0.002$ ). Among the patients with DR, 70.3% had LDL-C  $\geq 160$  mg/dl. Samatha et al<sup>10</sup> however did not showed significant association of LDL-C with DR.

In our study, there was significant association of elevated serum creatinine with DR ( $P < 0.001$ ). Studies done by Cai et al<sup>15</sup> and EL Haddad et al<sup>9</sup> also showed significant association of elevated serum creatinine with DR.

There was significant association of urine albumin with DR in our study ( $P < 0.001$ ). Among the patients with DR, 78.2% had albuminuria. Cai et al<sup>15</sup> showed significant difference in urine albumin in patients with and without DR ( $P < 0.001$ ). Raman et al<sup>19</sup>, Klein et al<sup>20</sup> and Shammari et al<sup>21</sup> showed that microalbuminuria was significantly associated with DR.

In our study, serum triglyceride level and total cholesterol had a low degree of positive correlation with HbA1c level. Similar to our study, Shakya et al<sup>12</sup> showed a low degree of positive correlation of serum triglyceride with HbA1c.

### Limitation and Recommendation:

The limitations of our study were convenient sampling method and small sample size. A study with large sample size would be more conclusive.

As our study showed positive association of higher serum lipoprotein with diabetic retinopathy, it is recommended that all patients with diabetes mellitus should be screened routinely for serum lipoproteins along with blood sugar profile, as it would help in early detection of diabetic retinopathy and thereby help in prevention of ocular complications.

### Conclusion:

In our study, elevated fasting and postprandial blood sugar, glycated hemoglobin, total cholesterol, serum triglyceride, LDL-C, serum creatinine and urine albumin were significantly associated with DR.

### List of abbreviations:

DM Diabetes Mellitus, DR Diabetic Retinopathy, LDL-C Low density lipoprotein cholesterol, HDL-C High density lipoprotein cholesterol, HbA1c Glycated hemoglobin  
ETDRS Early Treatment Diabetic Retinopathy Study, PDR Proliferative diabetic retinopathy, NPDR Non-proliferative diabetic retinopathy, CSME Clinically significant macular edema, CCT Central corneal thickness.

### Disclosure:

The authors declare no conflict of interest.

### Authors' contributions:

IJ conceptualized, collected data, analyzed and wrote the manuscript. PL, BPB, RM, ML supervised and guided throughout from the beginning of the study and critically reviewed the manuscript. All authors read and approved the final manuscript.

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