Department of Medicine of our facility. All cases were subjected to complete ocular examination after taking demographic and medical history. Diabetic Retinopathy was graded as per ETDRS categories. Biochemical investigations like serum creatinine, serum urea, urine microalbumin levels, Blood sugar (fasting/post prandial), HbA1c were done.

RESULTS: Out of 444 cases, Male to female ratio was 0.88: 1, where majority (54.73%) were aged between 41-60 years. 246 patients who did not suffer from retinopathy were grouped as Group I, while the rest of 198 patients having retinopathy were categorized as Group II. This was further divided into IIA suffering from Very mild to moderate NPDR (58.59%), IIB suffering from Severe to very severe NPDR (29.29%), and those suffering from Proliferative diabetic retinopathy were grouped as IIC (12.12%). A statistical significant association with severity of diabetic retinopathy and duration of diabetes was observed. A statistically significant association between severity of diabetic retinopathy and HbA1c values was found ($p < 0.001$). A statistically significant association between grade of microalbuminuria and severity of diabetic retinopathy was observed ($p < 0.001$). A statistically significant difference in prevalence of diabetic retinopathy in different HbA1c levels with microalbuminuria Grade 0 was found ($p < 0.001$). The difference in proportion of patients suffering from very mild to moderate diabetic retinopathy with duration of diabetes was found to be statistically significant ($p < 0.001$) in grade I microalbuminuria. Difference in proportion of patients suffering from diabetic retinopathy with duration of diabetes was found to be statistically significant in grade II microalbuminuria ($p < 0.001$). In grade III microalbuminuria, this difference was not found to be statistically significant ($p = 0.093$).

CONCLUSION: Microalbuminuria poses a risk for diabetic retinopathy which is affected by duration of diabetes and level of glycemic control. Microalbuminuria of higher grades is a strong predictor for occurrence and severity of diabetic retinopathy.

Key words: Diabetic retinopathy; Microalbuminuria; HbA1C

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INTRODUCTION: Type 2 diabetes is now a common and serious global health problem, which, for most countries, has evolved in association with rapid cultural and social changes, ageing populations, increasing urbanisation, dietary changes, reduced physical activity and other unhealthy lifestyle and behavioural patterns. The risk of developing diabetic retinopathy or other microvascular complications of diabetes depends on both the duration and severity of hyperglycemia. The other microvascular complication associated with diabetes is diabetic nephropathy. Therefore, correlation between microalbuminuria and HbA1C level with diabetic retinopathy has been explored in this study.

MATERIAL AND METHOD: A hospital based cross-sectional study was conducted including 444 consecutive pre diagnosed cases of type II diabetes mellitus attending the Diabetic Clinic of Department of Medicine of our facility. All cases were subjected to complete ocular examination after taking demographic and medical history. Diabetic Retinopathy was graded as per ETDRS categories. Biochemical investigations like serum creatinine, serum urea, urine microalbumin levels, Blood sugar (fasting/post prandial), HbA1c were done.
INTRODUCTION

Type 2 diabetes constitutes about 85 to 95% of all diabetics in high income countries and accounts for an even higher percentage in low- and middle-income countries. Type 2 diabetes is now a common and serious global health problem, which, for most countries, has evolved in association with rapid cultural and social changes, ageing populations, increasing urbanisation, dietary changes, reduced physical activity and other unhealthy lifestyle and behavioural patterns.

Diabetic retinopathy is the most common microvascular complication of diabetes. The risk of developing diabetic retinopathy or other microvascular complications of diabetes depends on both the duration and severity of hyperglycemia.

Most patients with type 1 diabetes develop evidence of retinopathy within 20 years of diagnosis. Retinopathy may begin to develop as early as 7 years before diagnosis of diabetes in patients with type 2 diabetes.

The other microvascular complication associated with diabetes is diabetic nephropathy. Microalbuminuria is defined as albumin excretion of 30-299 mg/24 hours.

The association between two major microvascular complications of diabetes (nephropathy and retinopathy) has been explored and evidence has shown a direct relationship between the two.

It is essential to understand as to which factors are instrumental in bringing about retinal changes among patients of diabetes complicated by microalbuminuria and also it’s correlation with duration and severity of hyperglycaemia.

MATERIAL AND METHODS

A hospital based cross-sectional study was conducted including 444 consecutive pre diagnosed cases of diabetes mellitus type II (defined as a fasting plasma glucose of more than or equal to 126 mg/dl or 2 hour post glucose load plasma glucose of more than or equal to 200 mg/dl or a random plasma glucose of more than or equal to 200 mg/dl in the presence of symptoms of hyperglycemia) attending the Diabetic Clinic of Department of Medicine of our facility. We excluded patients with acute or chronic renal failure, having opaque/hazy ocular media preventing fundus visualisation, having coexisting ocular disorders likely to mask the findings of diabetic retinopathy, those with presence of any of the confounding factors viz fever, acute systemic infections, exercise, high protein intake, accelerated hypertension, congestive heart failure.

In all the subjects included in the study demographic details and medical history was noted. A detailed history about the ocular symptoms, if any, and various confounding factors was recorded on a preset proforma. All the patients were subjected to a thorough systemic and local examination. Thorough ocular evaluation was done on all selected patients both clinically as well as with the help of diagnostic instruments. Visual Acuity was measured using Snellen’s charts. Both uncorrected and best corrected visual acuities were noted. Anterior segment examination by diffusce torch light and slit lamp examination was done to look for any other associated pathology and other manifestations of diabetes like neovascularization of iris, diabetic cataract.

Fundus examination-included, Direct ophthalmoscopy done by Heinz ophthalmoscope to visualize central fundus mainly the posterior pole (including the optic disc and macula) where the earliest diabetic changes occur. Indirect ophthalmoscopy was done to visualize the fundus up to periphery. The more peripheral parts of the fundus were visualised to rule out any other pathology and retinal detachments. Examination using +90D Lens was done using binocular slit lamp microscope. Amsler Grid Examination was done to evaluate 20 degrees of the visual field around central fixation point. Any areas of missing/ faint or distorted lines or disappearance of central dot on the amsler grid chart was recorded. Application Tonometry was done using a Goldmann tonometer. Fundus Fluorescein Angiography was performed using Carl Zeiss fundus camera. Seven-field stereo photography using Standardized 7-field stereo photography was performed using the Carl Zeiss fundus camera.

The grading of Diabetic Retinopathy adhered to the ETDRS levels. Optical coherence tomography (OCT) was performed. Dilatation of the pupil was done prior to OCT scanning to optimize image quality. Macular thickness in present study; was measured using Cirrus500 Zeiss Spectral Domain Optical Coherence Tomography. All the patients were advised to undergo biochemical investigations which were Blood sugar (fasting/PP), HbA1c, Urinary albumin to creatinine ratio.

RESULTS

Out of 444, study subjects included in the study 208 (46.85%) were males and rest 236 (53.15%) were females. Male to female ratio was 0.88:1. Majority of patients (54.73%) were aged 41-60 years, followed by 61-80 (29.28%) and 20-40 years (15.09%). Only 4 (0.90%) patients were aged > 80 years (Table 1).

246 patients who did not suffer from retinopathy were grouped as Group I, while the rest of 198 patients having retinopathy were categorized as Group II. This was further divided into IIA suffering from Very mild to moderate NPDR (58.59%), IIB suffering from Severe to very severe NPDR (29.29%), those suffering from Proliferative diabetic retinopathy were grouped as IIC (12.12%).

A statistical significant association with severity of retinopathy and duration of diabetes was observed (Table 2).

Patients having HbA1c value ≤ 7.0% i.e. Good control had low prevalence of retinopathy (22.7%) as compared to patients having HbA1c values between 7.1-8.5% (64.6%) and poor control (HbA1c values >8.5%) (94.0%). Proliferative diabetic retinopathy was found in higher proportion of patients with poor control (36.0%) as compared to fair control (3.4%) and good control (0.4%) of HbA1c values. A statistically significant association between severity of retinopathy and HbA1c values was found (p < 0.001) (Table 3).

Majority of patients (89.3%) of Grade0 microalbuminuria (<2.5 mg/mmol) had no retinopathy. It was found that higher the level of microalbuminuria more is the severity of retinopathy. Proportion of Severe to very severe retinopathy and proliferative diabetic retinopathy were higher in higher grade of microalbuminuria (Grade II and Grade III). A statistically significant association between microalbuminuria grade and severity of retinopathy was observed (p < 0.001) (Table 4).

On trivariate analysis of severity of retinopathy, HbA1C level and microalbuminuria, it was found that in cases of microalbuminuria Grade 0, 134 patients had good controlled diabetes, out of which 130 (97.01%) had no retinopathy. While of 52 patients with fair controlled diabetes 36 (69.23%) had no retinopathy. A statistically significant difference in prevalence of retinopathy in different HbA1c levels in Microalbuminuria Grade 0 was found (p < 0.001).

In microalbuminuria grade I, as the duration of diabetes increases
there was a simultaneous increase in number of patients in grade II. The difference in proportion of patients suffering from very mildmoderate retinopathy with duration of diabetes was found to be statistically significant (p < 0.001).

In microalbuminuria grade II, higher proportion of patients with shorter duration of diabetes had either no retinopathy or mild-moderate degree of retinopathy as compared to longer duration of diabetes of whom higher proportion were suffering from severe retinopathy. Difference in proportion of patients suffering from retinopathy with duration of diabetes was found to be statistically significant (p < 0.001).

In microalbuminuria grade III, though difference in proportion of patients with retinopathy and duration of diabetes was found but this difference was not found to be statistically significant (p = 0.093) (Table 5).

**DISCUSSION**

The number of people with type 2 DM is estimated to double by 2030[3]. Diabetes is a disease that is strongly associated with both microvascular and macrovascular complications, including retinopathy, nephropathy, and neuropathy (microvascular) and ischemic heart disease, peripheral vascular disease, and cerebrovascular disease (macrovascular), resulting in organ and tissue damage in approximately one third to one half of people with diabetes[3]. Among different microvascular complications, diabetic retinopathy is the most common. Microalbuminuria is a nephrotic disorder which if remains untreated progresses to proteinuria and overt diabetic nephropathy. It has been reported that as many as 7% of patients with type 2 diabetes already have microalbuminuria at the time they are diagnosed with diabetes[7]. Thus microalbuminuria is a microvascular complications that is often accompanied with the diagnosis of type 2 diagnosis and in effect may have a crucial role in determining the future course of disease and per se complications associated with it. In turn a reverse relationship between diabetic retinopathy and microalbuminuria has also been reported in type 1 diabetes[10]. Thus a bidirectional relationship between two entities is reported and indicates an increased risk of one disorder when the other is present.

Despite this observed relationship, not all type II diabetic cases with microalbuminuria have retinopathy. Thus it becomes important to understand as to which factors among type II diabetic cases with microalbuminuria trigger diabetic retinopathy and how the course of

### Table 1 Age and Sex Distribution in study group.

|       | No. of Cases | Percentage |
|-------|--------------|------------|
| Sex   |              |            |
| Male  | 208          | 46.85      |
| Female| 236          | 53.15      |
| Age Group (Years) |       |            |
| < 20-40| 67          | 15.09      |
| 21-40 | 243          | 54.73      |
| 41-60 | 243          | 54.73      |
| > 60  | 4            | 0.9        |

\(\chi^2 = 186.470 \text{ (df = 9)}; p < 0.001.\)

### Table 2 Group distribution of cases based on severity of diabetic retinopathy (n=444) and correlation with duration of diabetes mellitus.

| Group Distribution | Group I (No Retinopathy) (n = 246) | Group IIA (Very Mild To Moderate) (n = 116) | Group IIB (Severe To Very Severe) (n = 58) | Group IIC (Proliferative Diabetic Retinopathy) (n = 24) |
|--------------------|-----------------------------------|-------------------------------------------|------------------------------------------|-----------------------------------------------------|
| NO.                | % NO.                             | %                                        | NO.                                      | %                                                  |
| 246                | 55.41                             | 116                                      | 26.13                                    | 58                                                  |
| NO.                | % NO.                             | %                                        | NO.                                      | %                                                  |
| < 10 years (n = 208)| 162                              | 77.9                                     | 30                                       | 14.4                                                |
| 10-20 years (n = 131)| 71                              | 54.2                                     | 20                                       | 15.3                                                |
| 21-40 years (n = 75)| 7                                | 9.3                                      | 42                                       | 56                                                  |
| > 40 years (n = 30)| 6                                 | 20                                       | 24                                       | 80                                                  |

\(\chi^2 = 186.470 \text{ (df = 9)}; p < 0.001.\)

### Table 3 Correlation of severity of retinopathy and HbA1c.

| HbA1c                          | Group I (No Retinopathy) (n = 246) | Group IIA (Very Mild To Moderate) (n = 116) | Group IIB (Severe To Very Severe) (n = 58) | Group IIC (Proliferative Diabetic Retinopathy) (n = 24) |
|--------------------------------|-----------------------------------|-------------------------------------------|------------------------------------------|-----------------------------------------------------|
| NO.                            | % NO.                             | %                                        | NO.                                      | %                                                  |
| Good control (<=7.0%) (n = 247)| 191                              | 77.3                                     | 51                                       | 20.6                                                |
| Fair control (7.1-8.5%) (n = 147)| 52                              | 35.4                                     | 50                                       | 34                                                  |
| Poor control (>8.5%) (n = 50) | 3                                 | 6                                        | 15                                       | 30                                                  |

\(\chi^2 = 215.651 \text{ (df = 6)}; p < 0.001.\)

### Table 4 correlation of severity of retinopathy and microalbuminuria.

| Microalbuminuria grade | Group I (no microalbuminuria) (n = 246) | Group IIA (very mild to moderate) (n = 116) | Group IIB (severe to very severe) (n = 58) | Group IIC (Proliferative diabetic retinopathy) (n = 24) |
|------------------------|-----------------------------------------|-------------------------------------------|------------------------------------------|-----------------------------------------------------|
| NO.                    | % NO.                                   | %                                        | NO.                                      | %                                                  |
| Grade 0 (n = 187)      | 167                                     | 89.3                                     | 18                                       | 9.6                                                |
| Grade I (n = 154) (25-12.5 mg/mmol) | 73                              | 47.4                                     | 68                                       | 44.2                                                |
| Grade II (n = 77) (>12.5-25 mg/mmol) | 6                                | 7.8                                      | 30                                       | 39                                                  |
| Grade III (n = 26) (>25 mg/mmol) | 0                                 | 0                                        | 0                                        | 0                                                   |

\(\chi^2 = 329.435 \text{ (df = 9)}; p < 0.001.\)
In the present study, majority of diabetic retinopathy patients had very mild to moderate non-proliferative diabetic retinopathy (58.58%) followed by severe to very severe non-proliferative diabetic retinopathy (29.29%). Only 24 (12.12%) cases had proliferative diabetic retinopathy. In different cross-sectional studies, prevalence of different grades of retinopathy have been shown to be of similar order with prevalence of lower grades of retinopathy being higher compared to higher grades or proliferative retinopathy.[15-18]

Given this physiologic relationship between hyperglycemia and diabetic retinopathy, it is important to evaluate the role of glycemic control on prevalence of diabetic retinopathy. In present study we found that patients having a good glycemic control (HbA1c < 7%) had lower prevalence of diabetic retinopathy (22.7%) as compared to those having poor control (HbA1c > 7%) (72.08%). It was also observed that only 1 (0.4%) patient having HbA1c levels < 7% had proliferative diabetic retinopathy as compared to 5/147 (3.4%) of those having HbA1c level between 7.1-8.5% and 18/50 (36%) of those having HbA1c level > 8.5%. Similar to results of present study, Manaviat et al (2004)[19] also found a significant association between HbA1c, level and diabetic retinopathy. A similar association was also observed in other studies as well.[16-18]

The present study witnessed a significant linear relationship between grade of microalbuminuria and severity of diabetic retinopathy. A similar relation between severity of diabetic retinopathy and grade of albuminuria has been shown by Manaviat et al (2004)[19]. Highest grade of microalbuminuria indicates a higher level of microvascular impairment. In another study Mohan et al. (2011)[20] showed a highly significant correlation of occurrence and severity of diabetic retinopathy with albumin levels in both univariate and multivariate assessments. Similar associations were also shown by other workers.[20-23]

On performing a trivariate analysis, independent role of both microalbuminuria and level of HbA1c was observed, prevalence as well as severity of diabetic retinopathy increases with decreasing glycemic control and increasing albumin levels (except for Grade III microalbuminuria). A similar observation was also made by Mohan et al (2011)[20] who observed that both glycemic control as well as albumin level have independent association with occurrence as well as severity of diabetic retinopathy.

On multivariate analysis, we found that duration of diabetes, microalbuminuria and HbA1c levels were independent significant predictors of diabetic retinopathy.

The present study provided a deep insight into the relationship among type 2 diabetes mellitus, microalbuminuria and diabetic retinopathy. It was observed that higher grades of microalbuminuria, are responsible for occurrence of diabetic retinopathy and have significant predictive role in prediction of severity of diabetic retinopathy too. As the present study was limited by time, a better understanding of this relationship could be gathered with the help of longitudinal clinical trials among the new onset type 2 diabetic patients.

CONCLUSION

The findings in present study endorse the view that microalbuminuria poses a risk for diabetic retinopathy which is affected by duration of diabetes and level of glycemic control. At higher grades (grade II and III) of microalbuminuria, albumin levels themselves become a strong predictor for occurrence and severity of diabetic retinopathy.

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Table 5 Trivariate analysis of severity of retinopathy, microalbuminuria and HbA1c.

| HbA1c          | No retinopathy (n = 246) | Very mild-moderate (n = 116) | Severe - very severe (n = 58) | Proliferative diabetic retinopathy (n = 24) | Statistically significant |
|---------------|--------------------------|------------------------------|------------------------------|---------------------------------------------|--------------------------|
|               | No. | %  | No. | %  | No. | %  | No. | %  | χ² | p     |
| Good control  | 130 | 97.1 | 4 | 2.99 | 0 | 0 | 0 | 0 | 30.842 | < 0.001 |
| Fair control  | 36 | 69.23 | 14 | 32.76 | 2 | 3.85 | 0 | 0 | 26.634 | < 0.001 |
| Poor control  | 1 | 100 | 0 | 0 | 0 | 0 | 0 | 0 | 57.441 | < 0.001 |

χ² = 329.433 (df = 9); p < 0.001.
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