



Correlation of severity of diabetic retinopathy with various risk factors

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Abstract:

Objective: To determine correlation of severity of diabetic retinopathy with various risk factors. **Material and Methods:** The study was conducted on a total of 200 diabetic patients. The cases were selected from patients attending OPD of Regional Institute of Ophthalmology, Govt. Medical college, Amritsar over a period of four years. The association of risk factors – duration of diabetes, dyslipidemia, glycemic control, hypertension, role of genetics, anemia, pregnancy, alcohol, hypomagnesemia and smoking with severity of diabetic retinopathy was determined. **Results-** Prevalence of diabetic retinopathy was 43.5% with mild NPDR in 16.5%, moderate NPDR in 9%, severe NPDR in 8.5%, very severe NPDR in 4.5% and PDR in 5%. Severity of diabetic retinopathy is significantly affected by uncontrolled diabetes ($p < 0.001$), longer duration of diabetes ($p < 0.001$), systemic hypertension ($p < 0.001$), hyperlipidemia ($p < 0.001$), anemia ($p < 0.001$) and hypomagnesemia ($p < 0.001$). However effect of pregnancy ($p = 0.358$), alcohol intake ($p = 0.358$) and smoking ($p = 0.851$) was not found to affect prevalence of diabetic retinopathy in our study. **Conclusion:** Severity of diabetic retinopathy is significantly affected by uncontrolled diabetes, duration of diabetes, systemic hypertension, hyperlipidemia, anemia and hypomagnesemia. However effect of pregnancy, alcohol intake and smoking was not found to affect prevalence of diabetic retinopathy in our study

Key words: Diabetes; Hyperlipidemia; Hypertension; Retinopathy; Smoking.

Introduction

Diabetes mellitus is the most common endocrine disorder. A report by International Diabetic Federation (IDF) on the global burden of Diabetes highlighted that-

1. 382 million people have diabetes in 2013; by 2035 this will have risen to 592 million.

2. The greatest number of people with diabetes is between 40-59 years of age and 80% diabetics are in low and middle income countries.

3. 175 million people with diabetes are undiagnosed.

4. More than 79000 children developed Type 1 diabetes in 2013[1].

Diabetic retinopathy has been classified by various methods, but the most commonly accepted classification is according to International Clinical Diabetic Retinopathy Scale which classifies diabetes retinopathy into Non Proliferative (NPDR) and Proliferative Diabetic Retinopathy (PDR) [2].

It is not possible to define which diabetic individual will present with retinopathy. However it is possible to determine the risk factors related to development of retinopathy, such as duration of disease, poor metabolic control, dyslipidemia, hypertension, alcoholism, associated renal disease, anaemia, hypomagnesemia and smoking. Among these, duration of diabetes is proposed to be the most significant risk factor.

Objectives

1. To Correlate severity of diabetic retinopathy with duration and severity of diabetes.
2. To assess the relationship of other risk factors with the grading of diabetic retinopathy.

Material and Methods

200 cases of diabetes attending Out patient department of Ophthalmology and Medicine Department, Govt. Medical College Amritsar were subjected to comprehensive eye examination including Ophthalmoscopy under mydriasis to look for grading of diabetic retinopathy. An informed consent was taken from each case and approval from the ethical committee was obtained.

A detailed clinical history with particular emphasis on various risk factors - age of onset of diabetes mellitus, duration, control of diabetes mellitus, any alcohol intake, smoking, hypertension and pregnancy was taken. A complete general and physical examination and detailed binocular examination was done with particular emphasis on -

Recording of visual acuity, Intraocular pressure ,Slit lamp examination, detailed funduscopy (both direct and indirect) to find out various stages of diabetic retinopathy.

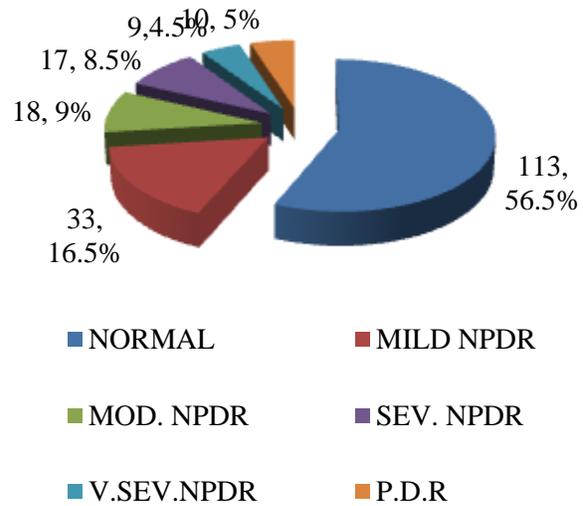
All patients were subjected to routine tests like complete blood count, fasting blood sugar, glycosylated Hb, urine examination, and lipid profile and serum magnesium. All findings were recorded in tabulated form and the data analyzed by using suitable statistical tests.

Results

1. Prevalence of diabetic retinopathy was 43.5%, with Mild NPDR was present in 16.5% moderate

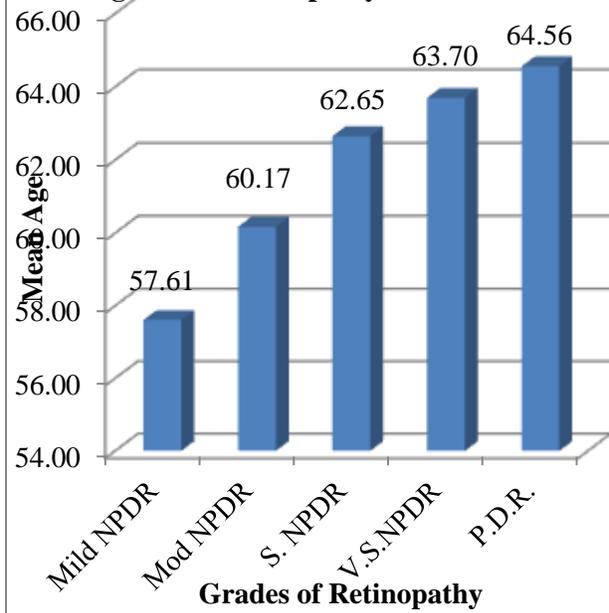
NPDR in 9.0%, severe NPDR in 8.5%, very severe in NPDR 4.5% and PDR 5.0%

Figure 1: Prevalence of grades of retinopathy

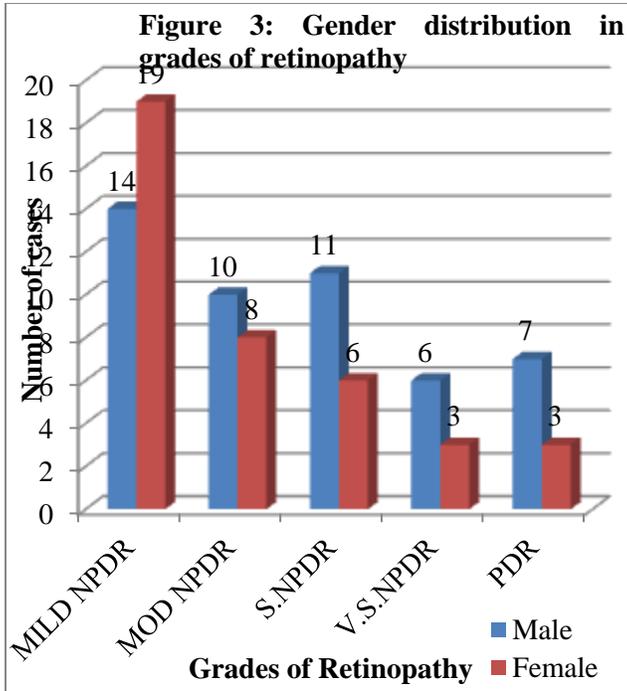


2. The mean age of patients with Mild NPDR, Mod NPDR, S.NPDR, V.S.NPDR and PDR was 57.61+ 11.8, 60.17+ 11.16, 62.65+ 12.16, 63.70 + 13.33 and 64.56 + 9.46 years respectively. Statistical analysis was done and the p value obtained was <0.001.

Figure 2: Mean age according to grades of retinopathy



- The prevalence of family history of diabetes mellitus in study was 58%.
- In our study, 114 males and 86 female (a total of 200 patients) were found to have diabetic retinopathy. In various grades of retinopathy the M: F >1 except in mild NPDR.
- In the study, maculopathy was positive in 40 patients out of which 26 were males and 14 were females and the ratio of M:F in positive maculopathy was 1.8:1.



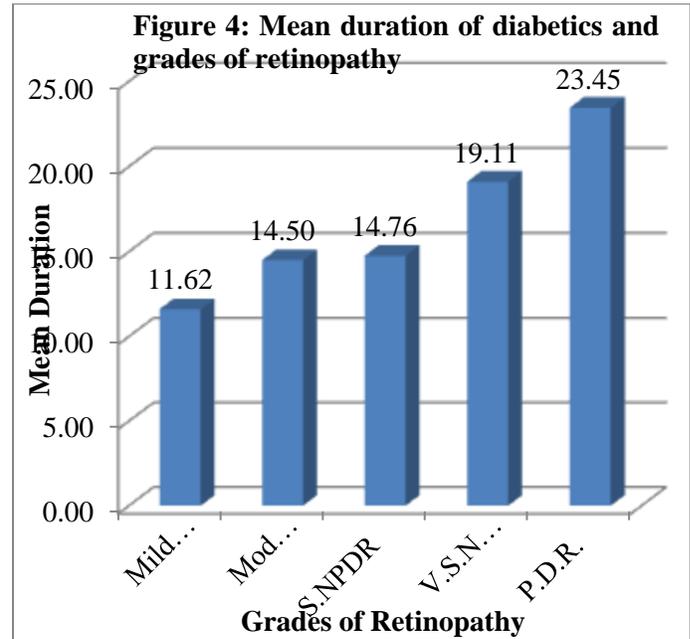
6. The mean duration of diabetes in patients with Mild NPDR, Moderate NPDR, Severe NPDR, very severe NPDR and PDR was 11.62 ± 4.41 , 14.50 ± 7.17 , 14.76 ± 6.45 , 19.11 ± 8.22 and 23.45 ± 10.13 with a p- value of <0.001 This showed that with increased duration of diabetes, there is significant progression of grade of diabetic retinopathy.

7. The mean FBS was 166.12 ± 43.96 , 192.33 ± 57.32 , 206.67 ± 98.85 , 211.88 ± 41.67 and 218.60 ± 70.20 in patients mild NPDR, Mod NPDR, S.NDR, V.S. NPDR and PDR respectively.

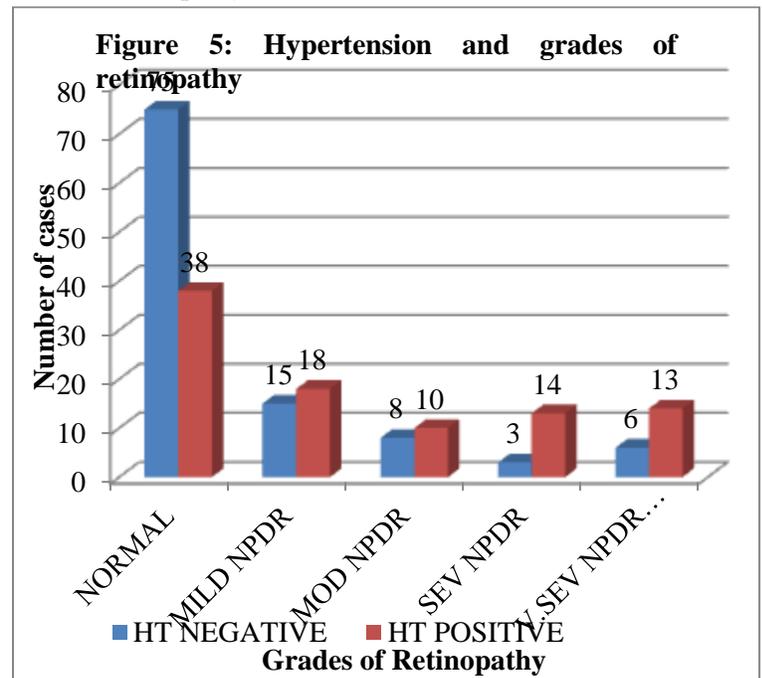
Statistical test was applied and the p value obtained was <0.001 i.e. as the mean level of FBS increases, the severity of diabetic retinopathy also increases.

8. The mean Glycosylated Hemoglobin level of patients with Mild NPDR, Mod NPDR, S.NPDR V.S. NPDR and was 8.74 ± 1.57 , 9.48 ± 1.10 , 9.59 ± 1.40 , 9.98 ± 1.61 and 9.91 ± 1.44 respectively statistical analysis was done using the ANOVA test. For the data, the calculated p-value was $p < 0.001$

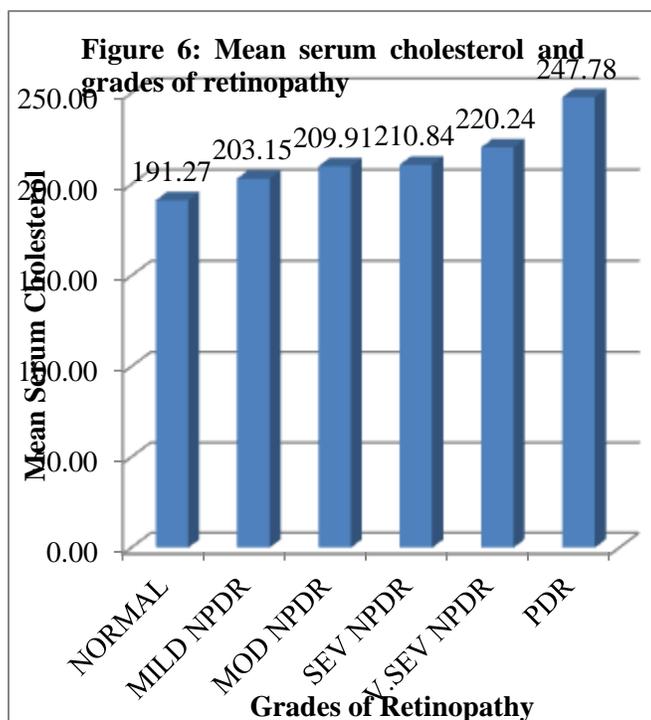
indicating that as the mean Glycosylated hemoglobin level of patients increases the severity of retinopathy increases.



7. Prevalence of hypertension in our study was 46.5%. The relative prevalence rate (%) in the group (V.S.NPDR and PDR) was on higher side as compared to other groups giving an indication that hypertension has a correlation with the severity of diabetic retinopathy.



8. The mean Cholesterol level of patients with Mild NPDR, Mod NPDR, S.NPDR V.S NPDR and PDR was 203.15 ± 33.26 , 209.91 ± 43.97 , 210.84 ± 51.86 , 220.24 ± 63.99 and 247.78 ± 61.59 respectively statistical analysis was done using the ANOVA test. For the data, the calculated p-value was $p < 0.001$ indicating that as the mean cholesterol level of patients increase, the severity of retinopathy increases.



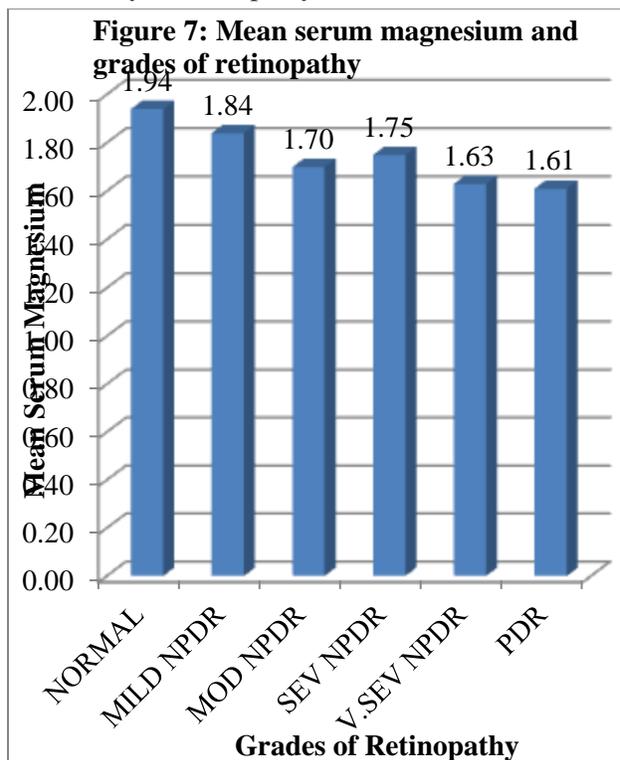
11. The mean Triglyceride level of patients with Mild NPDR, Mod NPDR, S.NPDR V.S NPDR and PDR was 157.94 ± 44.40 , 158.72 ± 47.58 , 190.47 ± 67.50 , 172.44 ± 58.07 and 174.50 ± 39.52 respectively statistical analysis was done using the ANOVA test. For the data, the calculated p-value was $p < 0.001$ indicating that as the mean Triglyceride level of patients increase, the severity of retinopathy increases.

12. The mean LDL level of patients with Mild NPDR, Mod NPDR, S.NPDR and PDR was 117.61 ± 32.49 , 113.61 ± 24.82 , 116.11 ± 33.45 , 119.11 ± 19.114 and 136.30 ± 31.63 respectively. Statistical analysis was done using the ANOVA test. The calculated p-value was $p < 0.001$ indicating that as the mean LDL level of patients increase, the severity of retinopathy increases.

13. The mean HDL level of patients with Mild NPDR, Mod NPDR, S.NPDR V.S NPDR and PDR was 53.1 ± 16.48 , 49.61 ± 12.73 , 48.44 ± 11.72 , 47.59 ± 10.48 and 46.89 ± 10.02 respectively. Statistical analysis was done using the ANOVA test. The calculated p-value was $p < 0.001$ indicating that as the mean HDL level of patients decrease, the severity of retinopathy increases.

14. The mean Haemoglobin level of patients with Mild NPDR, Mod NPDR, S.NPDR V.S NPDR and PDR was 9.66 ± 1.55 , 9.63 ± 1.50 , 9.35 ± 1.31 , 9.29 ± 1.22 and 9.16 ± 1.45 respectively. Statistical analysis was done using the ANOVA test. The calculated p-value was $p < 0.001$ indicating that as the mean hemoglobin level of patients decrease the severity of retinopathy increases.

15. The mean Magnesium level of patients with Mild NPDR, Mod NPDR, S.NPDR V.S NPDR and PDR was 1.84 ± 0.1659 , 1.70 ± 0.2029 , 1.75 ± 0.2373 , 1.63 ± 0.1414 and 1.61 ± 0.1410 respectively. Statistical analysis was done using the ANOVA test. The calculated p-value was $p < 0.001$ indicating that as the mean magnesium level of patients decrease, the severity of retinopathy increases.



16. Out of 17 diabetic pregnant patients, 8 had no diabetic retinopathy, 7 had mild NPDR, 1 had moderate NPDR and 1 had severe NPDR. To know the relation of pregnancy and Diabetic Retinopathy, statistical analysis was done using chi square test p-value obtained was 0.358 indicating that there is no

relationship between pregnancy and diabetic retinopathy.

17. In our study, out of 39 alcoholic patients, 20 had no retinopathy, 6 had mild NPDR, moderate and severe NPDR was present in 4 each, 3 patients had very severe NPDR and only 2 had PDR. To know the co-relation between alcohol and diabetic retinopathy chi-square test was applied on data and p-value obtained was 0.358 which was not significant, this depicts that there is no relation between alcohol intake and diabetic retinopathy.

18. Out of 25 patients who smoked, Mild NPDR, Moderate NPDR, severe NPDR, Very severe NPDR and PDR was seen in 13,3,3,3,2,1 patients respectively. The statistical analysis between smoking and diabetic retinopathy was done with chi square test and p-value obtained was 0.851 which is not significant indicating that there is no relation between smoking and diabetic retinopathy.

19. Thus in our study of 200 diabetic patients, severity of diabetic retinopathy is significantly affected by uncontrolled diabetes, duration of diabetes, systemic hypertension, hyperlipidemia, anemia and hypomagnesaemia.

20. However pregnancy, alcohol intake and smoking were not found to affect prevalence of diabetic retinopathy in our study.

Discussion

Prevalence of diabetic retinopathy in our study is 43.5% with mild NPDR, moderate NPDR, severe NPDR, very severe NPDR and PDR 16.5%, 9.0%, 8.5%, 4.5% and 5.0% respectively. Various population-based studies in the past were done with different prevalence rates

	No. of patients	Age in years	Prevalence %
Present Study	200	≥ 25	43.5%
WESDR, Southern Wisconsin ³	1313	≥40	50.3%
Los Angeles Latino Eye Study, California ⁴	1217	≥40	46.9%
Liverpool Diabetic Eye Study, UK ⁵	395	13-92	33.6
Taiwan Taipei Republic of China ⁶	11,478	≥40	35
Chennai Urban rural eye study CURES ⁷ study Chennai	1529	≥ 20	20.6

Age and sex distribution

A total of 114 males and 86 females (200 patients) with a sex ratio of 1.32: 1 was seen in our study. In various grades of retinopathy the M: F ratio was >1 except in very mild NPDR. Ghafour IM et al and Sjolie AK also reported that the prevalence of retinopathy is more in males than in females [8,9]. However Kehn et al found a higher incidence of diabetic retinopathy in females [10].

Duration of diabetes and diabetic retinopathy

Our study showed that with increased duration of diabetes, the severity of retinopathy increases. The patients with proliferative diabetic retinopathy were found to have a longer duration of diabetes than those with NPDR. In Chennai rural epidemiologic study (CURES) 41.8% patients had diabetic retinopathy after 15 years of diabetes and severity of retinopathy increased proportionately with longer duration of diabetes [7]. The studies by Dandona et al and Bender et al have also shown that duration of diabetes is the best predictor for retinopathy [11,12].

Fasting blood sugar and diabetic retinopathy

In our study the mean fasting sugar was 166.12±43.96, 192.33± 57.32, 206.67±98.85, 211.88±41.67 and 218±70.20 for mild NPDR, Moderate NPDR, Severe NPDR, Very severe NPDR and PDR respectively. The highly significant value (p< .001) in our study shows that the severity of retinopathy and maculopathy increases as the level of FBS increases. Randomized clinical trials have confirmed the predictive value of poor glycemic control compared with good glycemic control in determining the risk of retinopathy. The South Indian NIDDM study showed that FBS as well as postprandial blood sugar were higher in subjects with retinopathy than those without retinopathy [13].

Hypertension and diabetic retinopathy

The prevalence of hypertension in our study was 46.5%. The relative % in the group (Severe, Very Severe. NPDR and PDR) was 70% i.e. on the higher side as compared to other groups shows that hypertension has a correlation with the severity of diabetic retinopathy. Klein R, Klein BEK, Moss SE. epidemiologic studies have also suggested a relationship between blood pressure elevation and retinopathy progression [14]. IN UKPDS trial, tight blood pressure control was shown to cause 34% reduction of retinopathy [15].

Serum lipids and diabetic retinopathy

The p value (<0.001) obtained in our study was highly significant i.e. as the mean cholesterol

level, the mean triglyceride level, mean LDL level increases, the severity of retinopathy increases. The Dornan et al, ETDRS, WESDR and CURES eye study group also found a statistically significant association between elevated Serum cholesterol and the severity of retinal hard exudates in patients with diabetic retinopathy [16-18,7].

Anaemia and diabetic retinopathy

Our study shows p-value <0.001 which depicts that there is a significant relationship between anaemia and diabetic retinopathy. David et al in Early Treatment of Diabetic Retinopathy study evaluated the effect of moderate levels of anemia by hematocrit measurements. Shorb et al reported that diabetic patients with severe iron deficiency anemia rapidly progressed to severe proliferative retinopathy [19,20].

Detection of anemia and its treatment is important in the management of diabetic retinopathy. In those patients who had both anemia (Hb-10g/dl) and diabetes mellitus, Friedman and associates reported that treatment with erythropoietin was correlated with substantial resolution of macular hard exudates [21].

Hypomagnesemia & diabetic retinopathy

Hypomagnesemia may induce or worsen existing diabetes by altering cellular glucose transport, reduce pancreatic insulin secretion, defective post receptor insulin signaling, or altered receptor interactions. In our study the mean magnesium level, p- value (<0.001.) was highly significant. It shows that as the mean magnesium level decreases severity of retinopathy increases [22-24].

Pregnancy and diabetic retinopathy

Statistical analysis was done using chi-square test and p value obtained was 0.358 which shows that there is no significant relationship between pregnancy and diabetic retinopathy and its progression.

Alcohol and diabetic retinopathy

Alcohol consumption may be an important independent factor associated predicatively with sight threatening diabetic retinopathy. Young et al reported heavy alcohol consumption to be a risk factor for development of diabetic retinopathy. In contrast, WESDR and MOSS et al showed no significant association with incidence or progression of retinopathy with alcohol intake [25-27].

In our study, statistical analysis was done with Chi square test p- value = 0.898 which shows that there is

no relationship between alcohol intake and the severity of diabetic retinopathy.

Smoking and diabetic retinopathy

There are few studies, which show relationship between smoking and diabetic retinopathy. Zuphen Study indicates that cigarette smoking plays a role in development of diabetic retinopathy. According to MOSS et al there is no relation between smoking and diabetic retinopathy. According to our study p- value=0.851 indicates that there was no relationship between smoking and the severity of diabetic retinopathy [28, 29].

Conclusion

In our study of 200 diabetic patients, severity of diabetic retinopathy is significantly affected by uncontrolled diabetes, duration of diabetes, systemic hypertension, hyperlipidemia, anemia and hypomagnesemia. However, pregnancy, alcohol intake and smoking were not found to affect prevalence of diabetic retinopathy in our study.

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