

Original Article

Assessment of Effect of Nicotine on Severity of Diabetic Retinopathy

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Background : Diabetic Retinopathy (DR) is a microvascular complication of Diabetes, caused by high blood sugar levels that damages the vascular endothelial pericytes. DR is one of the most frequent causes of new cases of blindness among adults. Nicotine is a known risk factor for development of Diabetes and progression of DR. The aim of this study is to find the association of Nicotine with severity of DR.

Materials and Methods : 100 type 2 diabetic patients, between 20 and 75 years of age, visiting the Department of Ophthalmology from July, 2021 to December, 2022, were divided into two Groups : Group 1 included Diabetics consuming nicotine (>2 years) and Group 2 had Diabetics without Nicotine addiction. Best corrected visual acuity was recorded followed by dilated fundus examination to look for DR. Visual acuity and severity of DR were compared in two groups.

Results : The mean LogMar visual acuity in Group 1 was 1.13 and 0.84 in Group 2 ($p < 0.05$). DR changes were found to be more severe in Group 1 as compared to Group 2 ($p = 0.031$). Proliferative DR was more common in nicotine users as compared to non-users ($p = 0.028$). Increased duration of nicotine use resulted more severe DR ($p = 0.0289$).

Conclusion : Nicotine has a deleterious effect on visual acuity and it causes more severe DR. It is recommended that physicians must counsel diabetic patients regarding abstinence from Nicotine besides doing routine Diabetes counselling.

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Key words : Diabetes, Nicotine, Diabetic Retinopathy.

Diabetes is a chronic illness characterized by elevated blood glucose levels, accompanied by disturbed metabolism of fats and proteins.

Over time, a persistently high blood sugar level can damage pericytes of these blood vessels. Diabetic Retinopathy (DR) is a microvascular complication of Diabetes, caused by high blood sugar levels damaging the Retina. With uncontrolled Diabetes, it can cause blindness if left undiagnosed or untreated¹.

Diabetic Retinopathy is one of the frequent cause of new cases of blindness among adults aged 20-74 years². There are many risk factors associated with Diabetes Mellitus (DM) and development of DR such as quality of diabetic control, duration of disease, age of onset and age of patient³. Diabetic retinopathy progresses from mild non-proliferative abnormalities, characterized by increased vascular permeability, to moderate and severe Non-proliferative Diabetic Retinopathy (NPDR), characterized by vascular closure, to Proliferative Diabetic Retinopathy (PDR),

Editor's Comment :

"India has an estimate of 77 million cases of diabetics with an additional 25 million cases being pre-diabetic."

- Diabetes mellitus can lead to various sight threatening complications affecting quality of life.
- There are many risk factors which are modifiable and evaluating them may help live a better life.
- With a rising trend in consumption of tobacco, it is important to understand that nicotine has a deleterious effect on vision as it worsens diabetic retinopathy and may even lead to blindness.
- We as health care providers must counsel every patient and serve for better mankind.

characterized by the growth of new blood vessels on the Retina and posterior surface of the vitreous, haemorrhages and tractional retinal detachment. Macular oedema, characterized by retinal thickening from leaky new blood vessels, can develop at all stages of Retinopathy⁴.

Nicotine consumption is also a very important risk factor associated with various systemic illnesses including Diabetes. Nicotine is a dangerous and highly addictive chemical. It can cause narrowing of the arteries and hardening of the arterial walls, which in turn, decreases the blood flow⁵. Tobacco Optic Neuropathy is another rare disorder of optic nerve function related to the toxic effects of an unidentified constituent of Tobacco⁶.

Generally, awareness of the association between smoking and cancer, cardiovascular diseases and respiratory diseases is higher⁷. A study concluded

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that close to two thirds (64%) of Diabetic patients reported that smoking will not affect the disease and only 10% reported that smoking causes a lot of aggravation of Diabetes⁸. This shows the lack of awareness regarding nicotine and its side effects and its association with diabetes among general population including many health professionals.

The aim of this study is to find the association of nicotine use with severity of Diabetic Retinopathy. To assess this, patients with history of diabetes were selected and analysed for visual acuity and grade of Diabetic Retinopathy and compared with their Nicotine usage.

This study was prompted by the need of evaluating such individuals (both Diabetics and Nicotine users) clinically, in a developing nation like India where the prevalence of Nicotine consumption and Diabetes is high but the resources as well as awareness is quite low so as to assess the risk factors regarding development of Diabetic Retinopathy and thereby counselling the patient to refrain from Nicotine consumption.

MATERIALS AND METHODS

The present study was conducted after approval from the Institutional Ethical Committee (IEC NO: SAIMS/IEC/2021/189) and in adherence to the tenets of declaration of Helsinki. It is an observational study of 100 cases which was conducted over a period of 1.5 years starting from July, 2021 to December, 2022.

A clinical history was obtained from patients presenting to the Ophthalmology out-patient department at a Tertiary Care Centre with regard to their status of DM and Nicotine use. Patients with age between 20-75 years with known history of Diabetes Mellitus type 2 with and without history of nicotine consumption were included in the study. Patients were selected on the basis of history of duration of type 2 diabetes of 5-10 years with random blood sugar less than 150 mg/dl, only patients with HbA1c less than 8 gm% were included confirmed by respective blood tests. Exclusion criteria consisted of patients with any systemic co-morbidity other than diabetes mellitus type 2, patients on insulin therapy, patients with any other ocular co-morbidity apart from Diabetic Retinopathy and patients who had already quit nicotine. Total 100 patients were selected which were divided into two groups. Group 1 consisted of 50 patients with additional history of Nicotine consumption of at least 2 years. The second group included 50 diabetic patients with no history of consumption or exposure to nicotine. Nicotine users were considered to be patients with any habitual use

of tobacco plant leaf and form of nicotine was products for a minimum of two years. Commonly used form of nicotine was smoke inhalation of cigarettes, bidi and cigars, as well as consumed in smokeless way as in products that were either sniffed or chewed.

Best corrected visual acuity was assessed using Snellen's alphabet chart (converted into LogMar values for the purpose of statistical analysis) and preliminary torch light examination was done followed by detailed anterior segment examination using slit lamp bio microscopy and detailed fundus examination by indirect Ophthalmoscope.

On indirect Ophthalmoscopy clinical features of diabetic patients were noted and classified for objective diagnosis by Early Treatment Diabetic Retinopathy System (ETDRS) Classification⁹.

Data thus obtained was subjected to statistical analysis, chi square test and p value less than 0.05 was considered significant.

OBSERVATIONS AND RESULTS

Our study included patients lying in age group 20-74 years. We found that Group 1 consisted of Diabetic patients who were nicotine consumers and had significantly higher number of Males (76%) than Females (24%) while vice versa in group 2 with 60% female preponderance.

Table 1 shows the distribution of grades of diabetic retinopathy in Group 1 and Group 2. Changes of diabetic retinopathy were present in both groups with a significantly higher number of proliferative Diabetic Retinopathy in nicotine users (85.7 %) as compared to non- users (Figs 1-3).

Visual acuity measured was converted to LogMar values for the purpose of statistical analysis. Mean LogMar value for visual acuity in Group 1 was 1.13 and in Group 2 was 0.84. The difference of visual acuity was significant in both Groups. The visual acuity was significantly lower in Group 1.

Table 2 compares the visual acuity with fundus changes in the nicotine users. There were no Diabetic Retinopathy changes in fundus of nicotine users with visual acuity between 6/6 and 6/12. There was significant deterioration of vision as the fundus changes progressed. Thirty percent of nicotine users with history of diabetes having no signs of clinical

Fundus changes	Group 1	Group 2	P value
None	16 (32%)	15 (30%)	
Mild NPDR	7 (14%)	15 (30%)	
Moderate NPDR	8 (16%)	8(16%)	0.031
Severe NPDR	7 (14 %)	10 (20%)	
PDR	12 (24%)	2 (4%)	



Fig 1 — Showing Moderate to severe Non-proliferative Diabetic Retinopathy Changes

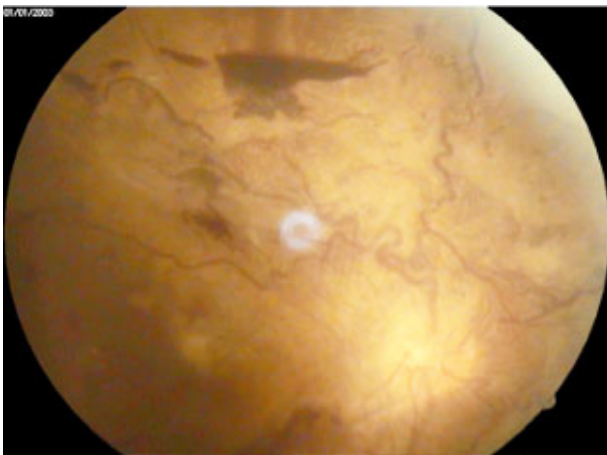


Fig 2 — Showing Proliferative Diabetic Retinopathy Changes

diabetic retinopathy had visual acuity 6/6-6/12. Sixteen percent of Group 1 patients had visual acuity between 6/12- 6/60, out of these 16%, 25% had mild NPDR changes, while 6.25% each belonged to patients with no changes, moderate NPDR, severe NPDR and PDR changes. Twenty two percent of Group 1 patients had visual acuity less than 6/60-1/60 among which 27.27% patients had mild NPDR changes, 36.36 % had moderate NPDR changes while severe NPDR and PDR changes were 18.18% each. Total 32% of

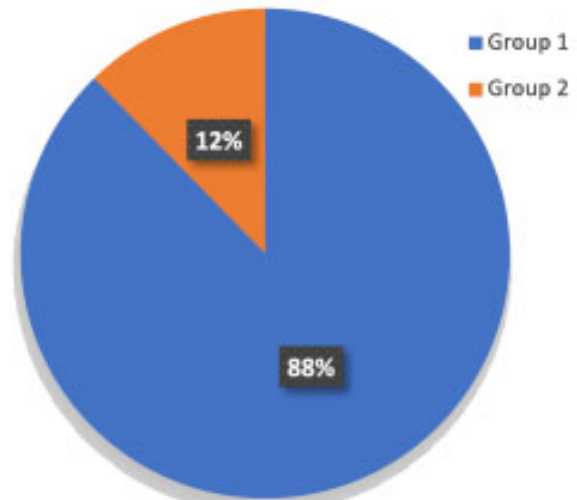


Fig 3 — Shows majority of Proliferative Diabetic Retinopathy Patients belonged to Group 1.

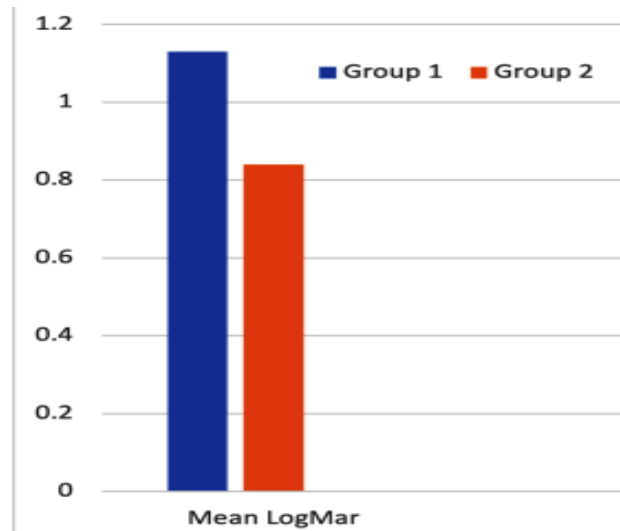


Fig 4 — Shows significant mean LogMar value to be higher in Group 1 signifying deterioration of visual acuity in Group 1

patients in Group 1 had visual acuity less than 1/60. 18.75 % of patients with visual acuity less than 1/60 had Moderate NPDR changes while 25 % and 56.25% of patients had severe NPDR and PDR respectively.

It is important to note that 75% of patients having PDR changes in Group 1 had visual acuity less than 1/60 (Fig 5).

Table 3 compares the fundus changes with respect to duration of Nicotine use. There is significant progression of Diabetic Retinopathy with increase in duration of nicotine use. The proliferative changes in Diabetic Retinopathy increases as duration of Nicotine consumption increases. However, there is no association of duration

Visual acuity in nicotine users	None	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	Total
6/6-6/12	15	-	-	-	-	15 (30%)
<6/12- 6/60	1	4	1	1	1	8 (16%)
<6/60- 1/60	-	3	4	2	2	11 (22%)
<1/60	-	-	3	4	9	16 (32%)
Total	16 (32%)	7 (14%)	8(16%)	7 (14%)	12 (24%)	50(100%)

Duration of Nicotine use (years)	None	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	Total	p value
<10	10	-	4	2	-	16 (32%)	0.014
11-20	2	3	1	1	1	8 (16%)	
21-30	1	2	1	2	2	8 (16%)	
31-40	3	1	2	1	3	10 (20%)	
41-50	-	1	-	1	6	8 (16%)	
Total	16 (32%)	7 (14%)	8(16%)	7(14%)	12 (24%)	50 (100%)	

According to Global Adult Tobacco Survey (GATS) 2016- 17, the prevalence of smoking tobacco use was 10.38% and smokeless tobacco use was 21.38% in India. Of all adults, 28.6% currently consume tobacco either in smoke or smokeless form, including 42.4% of men and 14.2% of women⁹. Similarly, in our study we found male pre-ponderance in Group 1 with nicotine users.

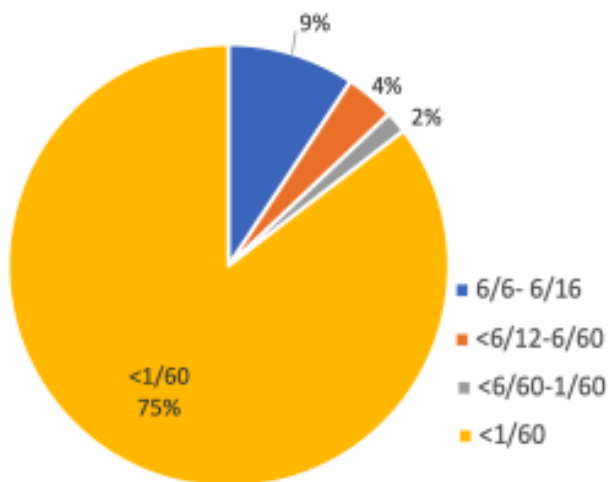


Fig 5 — Shows distribution of visual acuity among patients with proliferative diabetic retinopathy in Group 1

of Nicotine use in patients with no Diabetic Retinopathy changes. The severity of Diabetic Retinopathy increases as the duration of nicotine use increases (p value <0.05).

DISCUSSION

In India, there are estimated 77 million people above the age of 18 years who are suffering from diabetes (type 2) and nearly 25 million are prediabetics⁸. Diabetic Retinopathy is an important cause of blindness and occurs as a result of long-term cumulative damage to the small blood vessels in the Retina. Apart from good control over modifiable risk factors of Diabetes, there are various non-modifiable risk factors responsible for the progression of Diabetic Retinopathy like duration, age of onset and current age of patient⁸. The present study correlated group 1 and 2 on the basis of duration of diabetes and HbA1c less than 8 gm%, thereby removing such confounding factors.

Nicotine has long known to be a major risk factor for many systemic co-morbidities viz cardio vascular diseases, cerebro-vascular accidents, among which is severity of diabetic retinopathy. Our study had similar observations, 87.5% of patients with proliferative Diabetic Retinopathy were Nicotine users.

In Stockholm diabetes intervention study, smoking habits were correlated with the progression of Retinopathy and the total number of complications, deteriorating overall health of diabetic smokers during the 5-years study period. The patients who smoked had a three-fold increase of the risk of progression of retinopathy compared with the non-smokers, independent of blood glucose control¹⁰. Similarly, the present study suggests clinical changes of proliferative Diabetic Retinopathy to be more in nicotine users as compared to Diabetics. These findings also support the pathophysiological changes of Nicotine on Retina.

Nicotine has vasoconstrictive effect which is mediated through sympathetic activation which in turn reduces retinal blood flow and the ability of retinal vessels to autoregulate to hyperoxia. Smoking reduces oxygen carrying capacity of blood which when associated with decreased retinal blood flow leads to hypoxia. Hypoxia is major factor contributing to worsening of Diabetic Retinopathy¹¹. On the contrary, study by Yanagi, *et al*/conclude that smoking is associated with wider retinal calibre in Japanese women, which may be vasodilation in response to long term hypoxia, however these changes are reversible on long term cessation of smoking¹². Author could find limited evidence of reversibility of parafoveal microvasculature changes after nicotine abstinence, so, it is highly recommended area for further research considering the prevalence of Nicotine consumption in India.

Another effect of Nicotine consumption is Toxic Optic Neuropathy. In our study we found no cases with such changes in the fundus of patients clinically, though imaging or Electrophysiological tests can be of help to diagnose sub clinical cases¹³.

The effect of Nicotine on visual acuity and severity of Diabetic Retinopathy is found to be significant (p<0.05). India being a developing nation has high prevalence of both Diabetics and Nicotine users. As per National Family Health Survey (NFHS-5) the Tobacco users in India are more in working group population. The visual impairment caused by the

combined effect of diabetes and nicotine poses socio-economical burden on the society due to loss of jobs and deficit in manpower. Meta-analysis by Pan, *et al* has contributed to the growing evidence that both active and passive smoking are significant modifiable factors for risk of type 2 diabetes¹⁴. Prevention is always a better strategy than to cure the illness. Although risk of continued damage due to diabetes remains high in the short-term after smoking cessation, it decreases substantially among abstinent in the long run¹⁵.

The limitation of the study is small sample size and non-quantified Nicotine usage and no use of OCT and OCT-A was done.

CONCLUSION

Nicotine has a deleterious effect on visual acuity and it causes more severe DR. Due to high burden of Diabetics in India as well as high prevalence of nicotine consumption especially among young population, it is recommended that physicians must counsel Diabetic patients regarding abstinence from Nicotine besides doing routine Diabetes counselling.

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