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Original Research Article

Prevalence and Predictors of Diabetic Retinopathy in the Population of Punjab: North Indian Diabetic Retinopathy Epidemiology and Molecular Genetic Study (Ni-Dreams)

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ABSTRACT

Background: Diabetic retinopathy (DR), an imperative sequel is posing huge threat of blindness because of substantial prevalence of diabetes in the population of Punjab. In depth understanding of its risk factors is relatively unexplored in this region.
Objective: To identify the prevalence and risk predictors of diabetic retinopathy in the population of Punjab.
Methods: A cross sectional study was conducted in 562 type 2 diabetic subjects of age ≥45 years. Consenting subjects were tested with dilated pupil fundoscopy and categorised into non proliferative (NPDR) and proliferative diabetic retinopathy (PDR) according to modified Airlie House Classification.
Results: Univariate regression analysis revealed advancing age (≥55 years), duration of diabetes (DOD) >10 years, systolic (>120mmHg), diastolic blood pressure (>80mmHG), smoking, sedentary life style, total cholesterol (>200mg/dl), low density lipoproteins (LDL) cholesterol (>150mg/dl) and high density lipoprotein (HDL) cholesterol (< 40 mg/dl) as risk factors. In multivariable logistic regression analysis, age≥65 years, DOD>10 years, SBP>120mmHg, DBP>80mmHg, total cholesterol >200mg/dl, sedentary life style and smoking were observed to be substantial risk variables influencing independently the risk of DR in the population of Punjab.
Conclusion: Higher prevalence of NPDR (33.98%) and PDR (31.50%) existed in the population of Punjab, which is regulated by advancing age (≥65 years), DOD>10 years, SBP>120mmHg, DBP>80mmHg, total cholesterol >200mg/dl, sedentary life style and cigarette smoking.
Key Words: Prevalence of diabetic retinopathy, Risk variables, Predictors, NPDR, PDR

INTRODUCTION

Diabetic retinopathy (DR) is a complication of retina of the eye that results in visual impairment or blindness and is largely influenced due to long term effects of uncontrolled hyperglycemia. It is relatively unnoticed micro-vascular complication in developing countries, especially India, where largest number of type 2 diabetes mellitus (T2DM) patients are living. [1] Only few studies from south and central India have investigated and revealed its prevalence ranging from 7.3 to 65 percent [2-8] with high rural-urban heterogeneity [6] and decadal increase by 2 percent. [7] If its prevalence remains unaltered, then it is estimated that approximately 7 lakh Indians will have proliferative diabetic retinopathy (PDR) and 18 lakh Indians will have severe clinical

macular oedema. [8] In order to understand in depth causes and consequences of diabetic retinopathy, several risk factors have been identified and observed so far. [9,10] However, contrasting regional variations of the prevalence of DR exist in India similar to the prevalences of other diseases like cardiovascular disorders, [11] diabetes [12] and adult celiac disease. [13]

Risk surveillance for diabetic retinopathy and their effective management have helped in markedly reducing the risk of visual acuity and blindness in developed countries. [14] Consequently, epidemiological and public health studies, which address regional trends and identify locally occurring risks and reasons have special role in health care and its cost effective prevention. The current cross sectional study has examined the prevalence and predictors of diabetic retinopathy in the population of Punjab, which will help for the better management and welfare of such subjects.

Assessment and Definition of risk variables

Information regarding demographic variables such as age, education status, marital status, tobacco smoking and alcohol drinking was collected by detailed interview with the subjects. Fasting blood sample was drawn by trained paramedic staff and sent to pathology laboratory for biochemistry tests such as total cholesterol, low density lipoprotein cholesterol, triglyceride levels, high density lipoproteins and glucose levels. Duration of diabetes, medication use, self-reported diseases and previous medical history were recorded from the medical records of the subjects. Socioeconomic status was examined by using an updated version of Kuppuswamy and Pareekh scale and classified the subjects according to per capita per month income in Indian rupees (≤ 10, 000; low income group, 10,000 to 50,000; middle income group and >50,000; high income group). BMI was determined by using Quetelet's equation i.e. BMI= Weight in Kilograms/ Height in meters squared. Physical activity was assessed; whether the subject did aerobic exercise/walked for at least half an hour. Subjects doing it daily were considered to be physically active, otherwise sedentary. For blood pressure determination, two individual tests were conducted and noted down after an interval of three minutes in sitting relaxed position. The mean of these two tests were taken as final value of systolic or diastolic blood pressure.

MATERIALS AND METHODS

The present cross sectional study was conducted from January, 2013 to March, 2018 on type 2 diabetic mellitus (T2DM) subjects attending ophthalmology outpatient departments (OPDs) of G.S Randhawa Eye Hospital and Lasik Centre, Patiala, Rajindra Government Medical College and Hospital (GMCH), Patiala, J.P Eye Hospital, Zirakpur, Dhami Eye Hospital, Ludhiana and Kalia Eye Hospital, Ferozepur. These hospitals provide specialized state of the art facilities to referral cases. A total of 1049 subjects were screened being diagnosed as T2DM according to the diagnostic criteria given by American Diabetes Association (ADA, 2012). [15] Out of these, 487 subjects were excluded depending upon the exclusion criteria as shown in Figure 1. Finally, 562 subjects were qualified for participation in the study. All these eligible participants were examined with dilated pupil fundoscopy and/or fluorescein angiography. Subjects having diabetic retinopathy were confirmed if they had any pronounced lesion comprising microaneurysms, cotton wool spot, hemorrhage, microvasculature derangement, exudates, bleeding from retina or neovascularization. These were categorized on the basis of modified Airlie house classification, [16] whereby level < 10, levels upto 53 and levels>60 were considered as no retinopathy, NPDR and PDR respectively. After confirmation, 191 T2DM patients had NPDR, 177 subjects had PDR and 194 subjects were diagnosed negative for diabetic retinopathy. All the subjects were examined for cognitive

function by using the Mini Mental State Examination (MMSE), a 30 point test given by Folstein *et al.*(1975). [17] It identifies memory, language use, arithmetic and orientation (basic motor skills) of the subjects at a given point of time. It is a validated tool to access cognitive decline and impairment. Score of <23 were confirmed to have 81.3 percent sensitivity and 62 percent specificity. [18] All the participants gave their written consent. The study protocol was approved by Institutional Ethical Committee and strictly adhered to Helsinki Declaration.

Statistical analysis

Data values are given as absolute numbers, mean±SD and percentages in the parenthesis. Descriptive statistics between groups was calculated with chi-square for categorical and student's *t*-test for continuous variables. A linear regression analysis was done (JLM procedure) to examine the association between risk variables and diabetic retinopathy (dependent variable). All those variables which showed linear relationship (P<0.05) with the dependent variable were further included in multivariable (backward stepwise) regression analysis to identify the independent predictors. Insignificant variables were excluded to avoid any noise in the data and collinearity diagnostic was done to determine variance inflation factor (VIF). The significance was checked at 5 percent level however, Bonferroni correction was applied for multiple comparisons.

RESULTS

Current study comprised of 562 T2DM subjects of Punjab whereby, 321 (57.12%) were men and 241 (42.88%) were women. Point prevalence of NPDR and PDR in T2DM patients of Punjab aged 45 years and more appeared to be 33.98 percent and 31.50 percent respectively. In the age range of 55-64 years, lesser number of subjects (32.77%) had PDR in comparison to NPDR (36.13%), however, in subjects with ≥65 years of age, this trend reversed significantly and more number of subjects (38.98%) had PDR than NPDR (33.80%). Similarly subjects having ≤ 10 years of diabetes were more susceptible to NPDR (60.21%) than PDR (33.90%) however, when DOD exceeded 10 years, higher number of subjects (66.10%) had PDR than less severe form of NPDR (39.79%). Almost 34 percent of the subjects were current smokers, where as 44 percent were non-smokers and 22 percent were ex-smokers. Higher number of those subjects had PDR (46.33%) in comparison to NPDR (41.36%) who did not drink alcohol whereas; drinkers had lesser propensity of PDR (27.68%) than their NPDR (31.94%) counterparts (Table 1).

Analysis of the univariate (GLM) full factorial model (Table 2) revealed that diabetic subjects with ≥65 years of age were at 2.5 times higher risk of developing PDR (OR 2.52, 95% CI:1.49-4.27, P<0.001), however, this age did not influence the risk of NPDR (P<0.05). Some variables such as gender, education level, socio-economic status, alcohol drinking, low density lipoprotein, place of residence and neurocognition did not impact the risk of diabetic retinopathy. Duration of diabetes>10 years significantly influenced the risk of both NPDR (OR 1.64, 95% CI: 1.09-2.47, P=0.02) and PDR (OR 1.65, 95% CI: 1.08-2.51, P=0.02). Blood pressure and smoking were found to be significant risk factors whereby, SBP, DBP, smoking and ex-smoking influenced the risk of NPDR and PDR considerably (P<0.01). Subjects having BMI of 23-29.99 $kg.m^{-2}$ and ≥30 $kg.m^{-2}$were at 1.69 to 4.75 times risk of developing NPDR and PDR (P<0.05). Other risk factors that influenced the risk of diabetic retinopathy were total cholesterol>200 mg/dl, triglycerides >150 mg/dl, high density lipoprotein <40 mg/dl (P<0.01).All these univariate risk factors were analysed by multivariable logistic regression analysis (backward stepwise) to discern those variables which independently influenced the risk of NPDR and PDR.

Table 1. General Characteristics of study participants

Characteristics	Diabetic Retinopathy subjects (n=368)		Controls (n=194)	Total (n=562)	P value	
Variables	**Subjects with NPDR (n=191)**	**Subjects with PDR (n=177)**	**Diabetic Subjects without retinopathy (DWR) (n=194)**		**NPDR versus DWR**	**PDR versus DWR**
AGE						
45-54 years	58 (30.37)	50(28.25)	75(38.66)	183(32.56)		
55-64 years	69 (36.13)	58(32.77)	78(40.21)	205(36.48)		
≥65 years	64 (33.50)	69(38.98)	41(21.13)	174(30.96)	0.02	<0.001
Mean Age (years)	56.27±8.76	60.07±11.25	63.96±11.98	59.91±11.63	<0.001	0.003
GENDER						
Men	112(58.64)	101(57.06)	108(55.67)	321(57.18)		
Women	79(41.36)	76(42.94)	86(44.33)	241(42.88)	0.56	0.79
DURATION OF DIABETES						
≤10 years	65(34.03)	60(33.90)	89(45.88)	214(38.08)		
>10 years	126(65.97)	117(66.10)	105(54.12)	348(61.92)	0.02	0.02
GLUCOSE LEVELS (mg/dl)	138.76±36.65	145.80±37.60	130.81±31.20	128.10±31.20	0.035	0.001
BLOOD PRESSURE (mmHg)						
Systolic	132.5±15.47	137.0±12.81	129.4±12.34	127.80±11.64	0.046	<0.001
Diastolic	81.16±12.91	85.20±11.51	84.81±11.17	83.68±11.32	0.006	0.008
EDUCATION LEVEL						
Matriculation	70(36.65)	85(48.02)	82(42.27)	237(42.17)		
Secondary	54(28.27)	39(22.03)	53(27.32)	146(25.98)		
Graduation and above	67(35.08)	53(29.94)	59(30.41)	179(31.85)	0.48	0.42
SOCIO-ECONOMIC STATUS						
High Income	59(30.89)	53(29.94)	54(27.83)	166(29.54)		
Middle Income	72(37.70)	67(37.85)	73(37.63)	212(37.72)		
Low Income	60(31.41)	57(32.20)	67(34.54)	184(32.74)	0.74	0.86
SMOKING STATUS						
Non-Smokers	63(32.98)	70(39.55)	115(59.28)	248(44.13)		
Smokers	92(48.17)	53(29.94)	47(24.23)	192(34.16)		
Ex-Smokers	36(18.85)	54(30.51)	32(16.49)	122(21.71)	<0.001	<0.001
ALCOHOL DRINKING						
Non-Drinkers	79(41.36)	82(46.33)	98(50.51)	259(46.09)		
Drinkers	61(31.94)	49(27.68)	60(30.93)	170(30.25)	0.09	0.23
Ex-Drinkers	51(26.70)	46(25.99)	36(18.56)	133(23.66)		
BODY MASS INDEX ($kg.m^{-2}$)	26.42±4.01	26.91±4.91	25.18±3.98	25.42±3.62	0.005	<0.001
PHYSICAL ACTIVITY						
Active	81(42.41)	75(42.37)	117(60.31)	273(48.58)		
Sedentary	110(57.59)	102(57.63)	77(39.69)	289(51.42)	<0.001	<0.001
LIPID LEVELS (mg/dl)						
Total cholesterol	214.28±35.70	216.58±41.20	209.8±17.23	212.6±20.9	0.14	0.054
Low density lipoproteins	149.2±36.4	154.6±38.9	140±46.5	147.8±39.9	0.048	0.003
Triglycerides	172.10±37.1	196.0±52.1	176.1±45.0	188.3±51.2	0.38	0.07
High density lipoproteins	46.2±3.9	47.8±4.2	45.8±3.6	46.4±5.2	0.002	<0.001
PLACE OF RESIDENCE						
Rural	110(57.59)	99(55.93)	114(58.76)	323(57.47)		
Urban	81(42.41)	78(44.07)	80(41.24)	239(42.53)	0.81	0.58
COGNITION (MMSE Score)						
Normal cognition (>23)	106(55.50)	102(57.63)	113(58.25)	321(57.12)		
Impaired cognition (≤23)	85(44.50)	75(42.37)	81(41.75)	241(42.88)	0.59	0.90
MMSE Score(mean ± SD)	24.76±6.68	22.81±7.14	23.63±4.61	23.68±3.28	0.054	0.18

Values are either mean ± SD or numbers with percentages in the parenthesis. P values were calculated by chi square analysis for categorical variables and t-test for continuous variables. NPDR: Non proliferative diabetic retinopathy, PDR: Proliferative diabetic retinopathy. MMSE: Mini Mental State Examination.

Table 2. Disease association analysis for the risk of diabetic retinopathy

Characteristics	**Diabetic Retinopathy Subjects (n=368)**		**Controls (n=194)**	**Disease association analysis**	
	Subjects with NPDR (n=191)	**Subjects with PDR (n=177)**	**Diabetic Subjects without retinopathy (n=194)**	**OR (95% CI), P value†**	**OR (95% CI), P value‡**
AGE					
45-54 years	58 (30.37)	50(28.25)	75(38.66)	Referent	Referent
55-64 years	69 (36.13)	58(32.77)	78(40.21)	1.14(0.71-1.83), 0.58	1.11(0.68-1.83), 0.66
≥65 years	64 (33.50)	69(38.98)	41(21.13)	1.62(0.98-2.68), 0.059	2.52(1.49-4.27), <0.001
GENDER					
Men	112(58.64)	101(57.06)	108(55.67)	Referent	Referent
Women	79(41.36)	76(42.94)	86(44.33)	0.88(0.59-1.33), 0.56	0.94(0.63-1.42), 0.79

Table 2 to be continued…					
DURATION OF DIABETES					
≤10 years	65(34.03)	60(33.90)	89(45.88)	Referent	Referent
>10 years	126(65.97)	117(66.10)	105(54.12)	1.64(1.09-2.47), 0.02	1.65(1.08-2.51), 0.02
BLOOD PRESSURE (mmHg):SBP					
≤120	82(42.93)	57(32.20)	135(69.59)	Referent	Referent
>120	109(57.07)	120(67.80)	59(30.41)	3.04(2.00-4.62), <0.001	4.82(3.10-7.47), <0.001
BLOOD PRESSURE (mmHg):DBP					
≤80	69(36.13)	52(29.38)	143(73.71)	Referent	Referent
>80	122(63.87)	125(70.62)	51(26.29)	4.96(3.21-7.66), <0.001	6.74(4.28-10.62), <0.001
EDUCATION LEVEL					
Matriculation	70(36.65)	85(48.02)	82(42.27)	Referent	Referent
Secondary	54(28.27)	39(22.03)	53(27.32)	1.19(0.73-1.96), 0.48	0.71(0.42-1.18), 0.19
Graduation and above	67(35.08)	53(29.94)	59(30.41)	1.33(0.83-2.14), 0.24	0.87(0.54-1.40), 0.56
SOCIO-ECONOMIC STATUS					
High Income	59(30.89)	53(29.94)	54(27.83)	Referent	Referent
Middle Income	72(37.70)	67(37.85)	73(37.63)	0.90(0.55-1.48), 0.68	0.93(0.56-1.55), 0.79
Low Income	60(31.41)	57(32.20)	67(34.54)	0.82(0.49-1.36), 0.44	0.87(0.51-1.45), 0.59
SMOKING STATUS					
Non-Smokers	63(32.98)	70(39.55)	115(59.28)	Referent	Referent
Smokers	92(48.17)	53(29.94)	47(24.23)	3.57(2.24-5.69), <0.001	1.85(1.13-3.03), 0.01
Ex-Smokers	36(18.85)	54(30.51)	32(16.49)	2.05(1.16-3.62), 0.01	2.77(1.63-4.70), <0.001
ALCOHOL DRINKING					
Non-Drinkers	79(41.36)	82(46.33)	98(50.51)	Referent	Referent
Drinkers	61(31.94)	49(27.68)	60(30.93)	1.38(0.88-2.18), 0.16	0.98(0.60-1.57), 0.92
Ex-Drinkers	51(26.70)	46(25.99)	36(18.56)	1.55(0.91-2.63), 0.10	1.53(0.90-2.58), 0.11
BODY MASS INDEX (kg.m^{-2})					
<23	53(27.75)	37(20.90)	87(44.85)	Referent	Referent
23-29.99	65(34.03)	51(28.81)	63(32.47)	1.69(1.04-2.75), 0.03	1.90(1.12-3.24), 0.02
≥30	73(38.22)	89(50.28)	44(22.68)	2.72(1.64-4.52), <0.001	4.75(2.81-8.06), <0.001
PHYSICAL ACTIVITY					
Active	81(42.41)	75(42.37)	117(60.31)	Referent	Referent
Sedentary	110(57.59)	102(57.63)	77(39.69)	2.06(1.37-3.09), <0.001	2.07(1.36-3.12), <0.001
LIPID LEVELS (mg/dl)					
Total cholesterol					
≤200	84(43.98)	48(27.12)	112(57.73)	Referent	Referent
>200	107(56.02)	129(72.88)	82(42.27)	1.74(1.66-2.60), 0.007	3.67(2.37-5.68), <0.001
Low density lipoproteins					
≤100	86(45.03)	97(54.80)	102(52.58)	Referent	Referent
>100	105(54.97)	80(45.20)	92(47.42)	1.35(0.91-2.02), 0.14	0.91(0.61-1.38), 0.67
Triglycerides					
≤150	93(48.69)	58(32.77)	127(65.46)	Referent	Referent
>150	98(51.31)	119(67.23)	67(34.54)	1.99(1.32-3.01), <0.001	3.89(2.53-5.99), <0.001
High density lipoproteins					
≥40	88(46.07)	79(44.63)	117(60.31)	Referent	Referent
<40	103(53.93)	98(55.37)	77(39.69)	1.78(1.19-2.66), 0.005	1.88(1.24-2.85), 0.003
PLACE OF RESIDENCE					
Urban	81(42.41)	78(44.07)	80(41.24)	Referent	Referent
Rural	110(57.59)	99(55.93)	114(58.76)	0.95(0.63-1.43), 0.81	0.89(0.59-1.34), 0.58
COGNITION (MMSE score)					
Normal (<23)	106(55.50)	102(57.63)	113(58.25)	Referent	Referent
Impaired (≥23)	85(44.50)	75(42.37)	81(41.75)	1.12(0.74-1.67), 0.58	1.02(0.68-1.55), 0.90

†Comparison between subjects with NPDR and diabetic subjects without retinopathy. ‡Comparison between subjects with PDR and diabetic subjects without retinopathy. NPDR: Non proliferative diabetic retinopathy, PDR: Proliferative diabetic retinopathy, OR: Odds ratio, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MMSE: Mini Mental State Examination.

Collinearity statistics was done to determine variance inflation factor which revealed (VIF=2.20) that there was no interaction between independent variables and the model was free from multicollinearity. In the multivariable regression analysis (Table 3), DOD ≥ 10 years showed independent effect that added 2.02 fold risk (OR 2.02 95%CI:1.06-4.73, P=0.036) of developing NPDR. Tobacco smoking appeared to be the most risky independent predictor (OR 13.08 95%CI:4.77-35.86, P<0.001). Other variables that showed significant risk for NPDR were TC>200mg/dl (OR 1.74 95%CI: 1.03-2.49, P=0.034),

SBP>80mmHg (OR 2.45 95%CI: 1.17-5.12, P=0.009), DBP>120mmHg (OR 2.11 95%CI:1.32-4.92, P=0.22) and sedentary life style (OR 3.71 95%CI:1.52-9.31, P=0.001). Risk variables that independently influenced the risk of PDR were observed to be Age≥65 years (OR 3.92 95%CI: 2.65-6.10, P<0.001), DOD≥10years (OR 2.32 95%CI:1.06-5.07, P=0.025), TC>200mg/dl (OR 4.44 95%CI:2.52-7.45, P<0.001), SBP>80mmHG (OR 2.35 95%CI:1.37-5.89, P=0.005) and sedentary life style (OR 5.34 95%CI:2.25-8.29, P<0.001). The smokers were at 14.12 times higher risk (OR 14.12 95%CI:5.36-37.19, P<0.001) of developing PDR than those who did not smoke. Age≥65 years appeared to be insignificant (P>0.05) factor whereas DBP>120mmHg lost its significance in this mode.

Table 3. Multivariable backward stepwise regression analysis to determine factors independently associated with diabetic retinopathy.

Non proliferative diabetic retinopathy				
Variables	β ± SE	OR	95% CI	P
Age ≥ 65 years	0.52±0.22	1.74	1.03-2.49	0.034
DOD ≥10 years	0.83±0.40	2.02	1.06-4.73	0.036
SBP > 80mmHg	0.92±0.39	2.45	1.17-5.12	0.009
DBP > 120mmHg	0.89±0.26	2.11	1.32-4.92	0.022
Sedentary life style	1.43±0.21	3.71	1.52-9.31	0.001
Smoking	2.57±0.14	13.08	4.77-35.86	<0.001
Proliferative diabetic retinopathy				
Variables	β ± SE	OR	95% CI	P
Age ≥ 65 years	1.43±0.33	3.92	2.65-6.10	<0.001
DOD ≥10 years	0.84±0.44	2.32	1.13-5.07	0.025
TC >200mg/dl	1.52±0.28	4.44	2.52-7.45	<0.001
SBP > 80mmHg	0.93±0.21	2.35	1.37-5.89	0.005
Sedentary life style	1.89±0.24	5.34	2.25-8.29	<0.001
Smoking	2.65±0.50	14.12	5.36-37.19	<0.001

DOD: duration of diabetes, DBP: diastolic blood pressure, SBP: systolic blood pressure, TC: total cholesterol.

DISCUSSION

The present cross sectional study observed a prevalence of NPDR and PDR to be 33.98% and 31.50% respectively in the region of Punjab. Several studies have reported the prevalence of DR in India, which ranged from 7.3% to 65%. [3,6,8,19-27] The reason for such incongruent prevalence is primarily due to different classifications of diabetic retinopathy, different sample size, partial inclusion/exclusion criteria and unadjusted effects of the risk variables. A nationwide population based multicentric cross sectional study on the diabetic subjects has concluded that the prevalence of diabetic retinopathy in India is 21.7%. [3]

Present study has revealed that advancing age from 55 years is a significant marker whereby, the risk of having diabetic retinopathy increases significantly after every 10 year of age, which is consistent with other studies. [24,25] Present study has exposed that one unit increase after 65 years of age increases 0.52 times (0.52±0.22) the risk of NPDR and 1.43 times (1.43±0.33) the risk of PDR.

Duration of diabetes seems to be intransigent parameter, which increases the risk of DR in many populations. [28-30] Wong *et al.* have analysed that the risk of diabetic retinopathy increases by 1.07 times with every year passing after the diagnosis of diabetes. [10] A recent study suggests that duration of diabetes after five years is significantly associated with the risk of DR in more than half of the patients (P<0.001). Duration of diabetes is observed to be very risky (OR 6.01, 95% CI 2.63-13.75, P<0.05) in Chennai and rural population of Tamil Nadu. [6,24] In the present study also duration of diabetes >10 years emerges as significant variable which is independently associated and doubles the risk for both NPDR and PDR.

A strong correlation between hypertension and diabetic retinopathy is evident from the perspective that unnecessarily increased blood flow to the

retinal capillaries may damage endothelium of the eye in the subjects having diabetes. [31] It is also validated that aggressive control of blood pressure in T2DM subjects attenuates the risk of blindness, requirement of photocoagulation and progression of diabetic retinopathy. [32] A study has reported that 74.3% of subjects with diabetic retinopathy had coexisting hypertension hence, showing strong association (P<0.001). [25] Higher SBP (>120mmHG) and DBP (>80mmHg) have also been reported to be a significant marker for the risk of diabetic retinopathy by some studies. [6,9] According to the Wisconsin Epidemiological Study of Diabetic Retinopathy(WESDR), [33] DBP is observed as an independent predictor for the progression of NPDR to PDR over 14 years of follow up, irrespective of diabetes mellitus, glycosylated haemoglobin or gross proteinuria. Present study concludes that both SBP>120 mmHg and DBP>80 mmHg increases the risk of NPDR by 2.45 and 2.11 times respectively however, the expression of DBP for the risk of PDR has lost its significance. Every unit increase of SBP>120 mmHg increases the development of PDR by 0.93±0.21 (β±SE) in the present analysis.

Inverse correlation of physical activity and development of diabetic retinopathy [34] and direct relationship of sedentary lifestyle with the risk of diabetic retinopathy [35] has been identified. Plausibly the effect of urbanization, high trans fat rich diet and sedentary behaviour encourages the glucose load in the retinal microvasculature whereby, increased fat deposition enhances the vascular pressure of the eye. Consequently, the chances of retinal bleeding haemorrhage and macular edema increases. Present study reveals that sedentary lifestyle is an independent and strong risk variable, which increases approximately four fold risk of NPDR and fivefold risk of PDR.

It is still controversial that whether smoking enhances the risk of diabetic retinopathy. Smoking is reported as a significant risk for diabetic retinopathy in WESDR, [36] whereas it has been observed as protective in United Kingdom Prospective Diabetes Study (UKPDS). [9] Lately, it is reported that 90% of the smokers have diabetic retinopathy and this association is found to be significant (P<0.001) in Indian population. [25] Other studies also corroborate the fact that smoking adds substantial risk to the development of DR in multivariable analysis. [24,37] Present study has observed cigarette smoking to be the strongest independent risk factor which exacerbates the risk of NPDR by 13 times and PDR by 14 times after adjusting the effect of other affiliated risk factors. The reason for its vigorous contribution for the development of diabetic retinopathy lies in the fact that approximately 12 percent of the world's smokers reside in India [38] and highest number of diabetics in India further impinges upon the deteriorating risk statistics of microvascular complications such as diabetic retinopathy. Secondly, it is well known that cigarette smoking is associated with retinal membrane degradation, whereby nicotine is the major toxic substance which activates the nicotine cholinergic receptors present in pigmented epithelium of the retina. [39]

In conclusion present study exposes that 33.98 percent and 31.50 percent T2DM subjects over the age of 45 years have NPDR and PDR respectively. Age≥65 years, DOD>10 years, SBP>120mmHg, DBP>80mmHg, total cholesterol >200mg/dl, sedentary life style and cigarette smoking are substantial risk variables, which independently influence the risk of DR in the population of Punjab.

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