ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACEUTICAL SCIENCES

Published by JK Welfare & Pharmascope Foundation Journal Home Page: www.ijrps.com

Assessment of Drug Utilization Pattern, Prevalence and Risk Factors for the Development of Diabetic Retinopathy among Type 2 Diabetic Patients in a South Indian Tertiary Care Hospital: a cross-sectional observational study

Madhavi Mannam[1], Lavanya Nalluri[1], Ravindrababu Pingili[2], Jaidev Sudagani[3], Naveenbabu Kilaru[*4]

[1]Department of Pharmacy Practice, KVSR Siddhartha College of Pharmaceutical Sciences, Vijayawada-520010, Andhra Pradesh, India
[2]Department of Pharmacology, KVSR Siddhartha College of Pharmaceutical Sciences, Vijayawada-520010, Andhra Pradesh, India
[3]Endocrinologist, Santhi Endocrine and Diabetes Hospital, Vijayawada-520010, Andhra Pradesh, India
[4]Department of Pharmaceutics and Pharmaceutical Biotechnology, KVSR Siddhartha College of Pharmaceutical Sciences, Vijayawada-520010, Andhra Pradesh, India

Article History:

Received on: 05.09.2019
Revised on: 08.12.2019
Accepted on: 15.12.2019

Keywords:

Type 2 diabetes,
Prevalence,
Risk factors,
Diabetic Retinopathy,
Metformin

ABSTRACT

Diabetic retinopathy (DR) is a leading cause of visual impairment and blindness in the working-age population across the globe. The objective of the present study was to assess the drug utilization pattern, risk factors and prevalence of diabetic retinopathy in patients with type 2 diabetes mellitus in a south Indian tertiary care hospital. A cross-sectional observational study was conducted on 745 subjects (386 with diabetic retinopathy and 359 without diabetic retinopathy). Prevalence of diabetic retinopathy was measured and risk factors for the development of diabetic retinopathy were determined by calculating odds ratios using graph-pad prism statistical software and drug utilization pattern was assessed. Retinopathy was significantly higher in the subjects who are married, uneducated, housewives, urban residents, no income group and risk factors were comorbidities HbA1c, high serum creatinine, duration of diabetes (5-10 years and >10 years), physical inactivity, junk foods (weekly once and weekly twice), soft drinks occasionally and tea/ coffee (daily twice). Metformin (38.21%), combination of Insulin Isophane and Insulin Regular (16.75%), Insulin Regular (15.18%), combination of Glimepiride and Metformin (11.51%), Glimepiride (7.85%), combination of Metformin and Vildagliptin (7.85%) were most commonly prescribed antidiabetic drugs to the T2DM patients with retinopathy.

*Corresponding Author

Name: Naveenbabu Kilaru
Phone: +91- 9885589543,
Email: naveenbabukvsr@gmail.com

ISSN: 0975-7538

DOI: https://doi.org/10.26452/ijrps.v11i2.2229

Production and Hosted by

IJRPS | www.ijrps.com

INTRODUCTION

With 387 million people diagnosed with diabetes mellitus worldwide and a prevalence of 8.2% as per the Diabetes atlas 2014, diabetes mellitus has become a global burden (Fernandes *et al.*, 2016; Guariguata *et al.*, 2014). Diabetic retinopathy (DR) is a leading cause of visual impairment and blindness in the working-age population across the globe (Cheung *et al.*, 2010; Klein, 2007). In 2010, of an estimated 285million people worldwide with diabetes, over one-third have signs of DR, and a third

of these are afflicted with vision-threatening diabetic retinopathy (VTDR), defined as severe non-proliferative DR or proliferative DR (PDR) or the presence of diabetic macular edema (DME) (Yau *et al.*, 2012; Lee *et al.*, 2015). Without treatment, 50% of patients with proliferative diabetic retinopathy will become blind within 5 years (Resnikoff *et al.*, 2004; Burgess *et al.*, 2013). The risk factors of DR can be broadly divided into modifiable and non-modifiable factors. The modifiable risk factors include hyperglycemia, hypertension, hyperlipidemia and obesity. In contrast, the duration of diabetes, puberty and pregnancy are the non-modifiable risk factors for DR development and progression (Ting *et al.*, 2016). The overall prevalence of DR and VTDR in T2DM was 34.6% and 10.2%, respectively. With the increasing number of people with diabetes, the number of DR and vision-threatening DR (VTDR), which includes severe non-proliferative DR, proliferative DR (PDR) and diabetic macular edema (DME), has been estimated to rise to 191.0 million and 56.3 million, respectively by 2030.

The World Health Organization (WHO) defines "drug utilization" as the marketing, distribution, prescription and use of the drugs in a society considering its medical, social, and economic consequences (Ashutosh *et al.*, 2017). Drug utilization studies help to assess whether the drug treatment is rational or not and to determine rational drug use, especially in poorer and rural populations (Mandal *et al.*, 2016). This study was conducted with an objective to screen the type 2 diabetes patients in order to determine the prevalence of diabetic retinopathy and to determine the risk factors that are responsible for the development of diabetic retinopathy and to assess the drug utilization pattern.

MATERIALS AND METHODS

For this purpose, a cross-sectional observational study was carried out at the outpatient department of a tertiary care hospital by following the method developed by (Cui *et al.*, 2017). The study was initiated after approval by the Institutes Ethical Review Committee. The protocol approval number was KVSRSCOPS/IEC/PG/231/2017.

Selection of participants

Patients of either sex diagnosed with or without T2DM of any duration (as per ADA guidelines) and willing to participate were included in the study. A total of 745 patients (359 patients with T2DM and 386 patients with diabetic retinopathy) were enrolled in the study.

Inclusion criteria

Patients of either sex diagnosed with type 2 diabetes mellitus of any duration, established as per American Diabetes Association (ADA) guidelines. Patients who are visiting a public endocrine hospital in six months would be recruited.

Exclusion criteria

Patients with incomplete case reports. Patients having type 1 diabetes mellitus, gestational diabetes and maturity-onset diabetes of the young were excluded from the study.

Data collection

Physicians were requested to report the clinical and biochemical data not exceeding 6 months before the observation. The information regarding demographics (age, sex), socioeconomic and lifestyle characteristics (smoking, alcohol consumption) was collected by interviewing the participant. Biochemical parameters were derived from the latest laboratory investigation reports documented in the clinical records. Socioeconomic status was assessed using the modified Kuppuswamy's scale, which considers the education qualification, occupation of the family head and family income per month of the participant. The diagnosis of diabetic retinopathy was made by an ophthalmologic examination that included fundoscopy or retinal photography and measurement of visual acuity, carried out by an ophthalmologist. All the relevant data were collected in a predesigned paper case record form with the prior consent of the participant. Data were collected from a total of 745 patients (359 patients with T2DM and 386 patients with diabetic retinopathy).

Statistical Analysis

In the descriptive statistical analysis, categorical variables were expressed as numbers and percentages. For categorical variables, the tests of significance analysis, we applied a Chi-Square test or Fisher Exact test. For all analysis, $P<0.05$ was regarded as statistically significant. The odds ratio with 95% confidence intervals was calculated using univariate regression analysis. Data were analyzed using a statistical tool Graph pad prism software (version 5.0).

RESULTS AND DISCUSSION

A total of 745 subjects (359 with type 2 diabetes and 386 with diabetic retinopathy) were included in the study and the clinical characteristics of T2DM were presented in Table 1.

Table 1: Biochemical and clinical characteristics of patients with type 2 diabetes mellitus (N = 359)

Variable	Patients with T2DM N (%)
Gender	
Male	155 (43.2)
Female	204 (56.8)
Age	
0-20 years	0(0.3)
21-40 years	83 (23.2)
41-60 years	217 (60.6)
Above 60 years	57 (15.9)
Marital Status	
Unmarried	16(4.5)
Married	343(95.5)
Education	
Un Educated	131(36.5)
Educated	228(63.5)
BMI (Kg/m2)	
<25 Kg/m2	114(31.8)
>25 Kg/m2	245(68.2)
Body Weight (Kg)	
<50	5(1.3)
50-70	161(45)
>70	192(53.6)
Nature of Work	
Not working anywhere	41(11.4)
Private job	93(25.9)
Govt. job	39(10.8)
Daily labor	38(10.6)
Housewife	148(41.3)
Locality	
Rural	105(29.2)
Urban	254(70.7)
Monthly Income	
No income	170(47.5)
Below 25000	115(32.1)
Above 25000	73(20.4)
Co-morbidities	
No	131(29.4)
HTN	138(30.8)
History of CVDs	7(1.56)
Endocrine diseases	59(13.2)
Other diseases	112(25.1)
HbA1C	
<7	141(44.2)
7-9	109(34.2)
>9	69(21.6)
Fasting Blood Glucose (mg/dL)	
70-80	10(3)
80-120	92(27.6)
121-160	107(32)
161-200	71(21.3)
>200	54(16.2)
Post prandial blood glucose levels (mg/dL)	

Continued on next page

Table 1 continued

90-110	3(1)
111-130	9(3)
131-150	33(10.9)
151-200	165(54.6)
>200	92(30.5)
Random Blood Glucose (mg/dL)	
80-100	0
101-120	0
121-140	0
141-160	2(13.3)
161-200	1(6.7)
>200	12(80)
HDL (mg/dL)	
Not available	54(20.1)
Normal	130(48.3)
Low	55(20.4)
High	30(11.2)
Triglycerides (mg/dL)	
Not available	54(20.5)
Normal	109(41.5)
Low	8(3)
High	92(35)
Total Cholesterol (mg/dL)	
Not available	54(19.6)
Normal	151(54.7)
Low	6(2.2)
High	65(23.6)
LDL (mg/dL)	
Not available	57(20.8)
Normal	163(59.4)
Low	9(3.3)
High	45(16.5)
Urea (mg/dL)	
Not available	72(36.4)
Normal	78(39.4)
Low	0
High	48(24.2)
Serum creatinine (mg/dL)	
Not available	45(12.6)
Normal	305(85.2)
Low	5(1.4)
High	3(0.8)
Duration of T2DM (Years)	
<5	172(47.9)
5-10	111(30.9)
>10	76(21.2)
Following T2DM education	
Yes	282(79.2)
No	74(20.8)

T2DM, Type 2 Diabetes Mellitus; BMI, Body Mass Index; HTN, Hypertension; CVDs, Cardiovascular Diseases; HbA1C, Glycated hemoglobin; HDL, High-DensityLipoproteins; LDL, Low-Density Lipo proteins

Table 2 and Table 3 shows the socio-demographic and lifestyle characteristics of subjects with and without diabetic retinopathy, respectively. The prevalence of diabetic retinopathy was significantly higher in the subjects who are married (98.2%, P=0.0371), uneducated(69.9%)patients, nature of work (housewives 47.6%, P=0.0227), urban residents(60.6% P=0.0037), no income group(65.5%) and risk factors were comorbidities (other diseases 40.41%, P<0.0001, HTN 31.1%, P<0.0001, endocrine diseases 8.57%, P=0.0223, history of CVDs 4.84%, P< 0.0001), no physical activity(63.3%), habit of taking junk foods (weekly once 19.9%, weekly twice13.2%, P<0.0001), soft drinks (occasionally 24.9%, P=0.0073), tea/coffee(daily twice without sugar 38.1%, P=0.0465),HbA1c(7-9% 39.3%, P=0.0018, >9% 31.9%, P<0.0001), high serum creatinine(14.8%, P<0.0001), duration of diabetes (5-10 years 37.8%, > 10 years 37.3%, P<0.0001). Gender, age, BMI, body weight, monthly income, blood glucose levels, food habits, the habit of smoking, alcohol, stress levels are not significantly associated with the development of diabetic retinopathy.

Univariate regression analysis was performed to determine the odds ratios for the modifiable and non modifiable risk factors for T2DM (Table 4). The analysis showed that married (OR,2.526; 95% CI,1.026 to 6.214, P=0.0371), poorly educated (OR,0.2468; 95% CI,0.1818 to 0.3352, P<0.0001), house wives (OR,0.6068; 95% CI,0.3941 to 0.9344, P=0.0227), urban residents (OR, 0.6364; 95% CI, 0.4688-0.8639, P=0.0037) and risk factors were co-morbidities (other diseases (OR,4.650; 95% CI,3.281 to 6.591, P<0.0001), hypertension (OR,2.642; 95% CI,1.868 to 3.736, P<0.0001),Endocrine diseases (OR,1.685;95% CI,1.075 to 2.641, P=0.0223), history of CVD (OR,8.117; 95% CI,3.451 to 19.09, P<0.0001), duration of diabetes (5-10 years (OR, 2.357; 95%CI, 1.659-3.348, P<0.0001 and with duration >10 years (OR, 3.395; 95% CI, 2.336-4.933, P <0.0001), HbA1c (7-9% OR,1.774;95% CI,1.235 to 2.547, P=0.0018; >9% OR, 2.275; 95% CI, 1.529 to 3.386, P<0.0001), high serum creatinine (OR, 11.55; 95% CI, 3.415 to 39.10, P<0.0001), physical inactivity(OR, 0.5558;95%CI, 0.4146 to 0.7450, P<0.0001), junk foods weekly once (OR,3.287; 95% CI, 2.049 to 5.274, P<0.0001) and weekly twice (OR,2.935; 95% CI, 1.709 to 5.038, P<0.0001), soft drinks occasionally (OR,1.642; 95% CI, 1.141 to 2.364, P=0.0073), tea/ coffee(daily twice without sugar OR,1.598; 95% CI, 1.006 to 2.539, P=0.0465).

The drug utilization pattern was assessed and presented the results in Table 5. Metformin (38.21%), combination of Insulin Isophane and Insulin Regular (16.75%), Insulin Regular (15.18%), combination of Glimepiride and Metformin (11.51%), Glimepiride (7.85%), combination of Metformin and Vildagliptin (7.85%) were most commonly prescribed anti-diabetic drugs to the T2DM patients with retinopathy. The present study's results suggested that subjects who are married, uneducated patients, nature of work (housewives), urban residents, no income group and risk factors were comorbidities(other diseases, HTN, endocrine diseases, history of CVDs), no physical activity, habit of taking junk foods (weakly once, weakly twice), soft drinks (occasionally), tea/coffee(daily twice without sugar), poor glycemic control, high serum creatinine, duration of diabetes are major risk factors for the development of retinopathy complication.

Marital status

The present study's results revealed that marital status (98.2%, P=0.0371) was significantly associated and was the major risk factor for diabetic retinopathy (OR, 2.526; 95% CI, 1.026 – 6.214). Therefore, further studies are needed to evaluate the exact impact of marital status on risk for diabetic retinopathy.

Education

Education is one of the risk factors for the development of diabetic retinopathy. (Martinell *et al.*, 2016) conducted a study on Prevalence and risk factors for diabetic retinopathy at diagnosis (DRAD) in patients recently diagnosed with type 2 diabetes (T2D) or latent autoimmune diabetes in the adult (LADA) and concluded that DRAD prevalence in patients recently diagnosed with T2DM or is 12%. Low educational levels and low beta-cell function at diagnosis are risk factors for DRAD (Martinell *et al.*, 2016). The present study's results also supported that educational status was significantly associated with (69.9%, P <0.0001) and a risk factor for the development of diabetic retinopathy.

Nature of work

The present study's results revealed that housewives (47.6%, P=0.0227) were significantly associated and was the major risk factor for diabetic retinopathy (OR, 0.6068; 95% CI, 0.3941-0.9344). Therefore, further studies are needed to evaluate the exact impact of the nature of work on risk for diabetic retinopathy.

Urban residence

The present study's results revealed that urban residents (60.6%, P=0.0037) were significantly associated and was the major risk factor for diabetic retinopathy (OR, 0.6364; 95% CI, 0.4688-0.8639).

Table 2: Socio-demographic characteristics of diabetic patients with (N=254) or without diabetic retinopathy (N= 359)

Variable	Patients with T2DM N (%)	Patients with T2DM and retinopathy N (%)	P-Value
Gender			
Male	155 (43.2)	99 (39)	Ref
Female	204 (56.8)	155 (61)	0.2985
Age			
0-20 years	1 (0.3)	–	Ref
21-40 years	83 (23.2)	20 (7.9)	0.6239
41-60 years	217 (60.6)	152 (59.8)	0.4031
Above 60 years	57 (15.9)	82 (32.3)	0.2328
Marital Status			
Unmarried	16 (4.5)	3 (1.2)	Ref
Married	343 (95.5)	251 (98.8)	0.0211*
Education			
Un Educated	131 (36.5)	155 (61)	Ref
Educated	228 (63.5)	99 (39)	<0.0001***
BMI (Kg/m^2)			
<25 Kg/m^2	114 (31.8)	62 (24.5)	Ref
>/=25 Kg	245 (68.2)	191 (75.5)	0.0511
Body Weight (Kg)			
<50	5 (1.3)	5 (2)	Ref
50-70	161 (45)	112 (44.3)	0.5714
>70	192 (53.7)	136 (53.7)	0.5897
Nature of Work			
Not working anywhere	41 (11.4)	57 (22.5)	Ref
Private job	93 (25.9)	45 (17.7)	<0.0001***
Govt. job	39 (10.8)	14 (5.5)	0.0002***
Daily labour	38 (10.6)	25 (9.8)	0.0221*
Housewife	148 (41.2)	113 (44.4)	0.0120*
Locality			
Rural	105 (29.2)	130 (51.2)	Ref
Urban	254 (70.8)	124 (48.8)	<0.0001***
Monthly Income			
No income	170 (47.5)	148 (58.3)	Ref
Below 25000	115 (32.1)	87 (34.2)	0.4382
Above 25000	73 (20.4)	19 (7.4)	<0.0001***
Co-morbidities			
No	131 (29.4)	37 (8.6)	Ref
HTN	138 (30.8)	161 (37.44)	<0.0001***
History of CVDs	7 (1.56)	34 (7.90)	<0.0001***
Endocrine diseases	59 (13.2)	41 (9.53)	0.0009***
Other diseases	112 (25.1)	157 (36.51)	<0.0001***
Systolic Blood Pressure			

Continued on next page

Table 2 continued

Variable	Patients with T2DM N (%)	Patients with T2DM and retinopathy N (%)	P-Value
<140 mmHg	259 (72.1)	160 (63)	Ref
>/=140 mmHg	100 (27.9)	94 (37)	0.0164*
Diastolic Blood Pressure			
<90 mmHg	281 (78.3)	203 (79.9)	Ref
>/=90 mmHg	78 (21.7)	51 (20)	0.6219
HbA1C			
<7	141 (44.2)	52 (21.8)	Ref
7-9	109 (34.2)	100 (42)	<0.0001***
>9	69 (21.6)	86 (36.1)	<0.0001***
Fasting Blood Glucose (mg/dL)			
70-80	10 (3)	2 (0.9)	Ref
80-120	92 (27.6)	54 (24)	0.1572
121-160	107 (32)	62 (27.6)	0.1610
161-200	71 (21.3)	41 (18.2)	0.1678
>200	54 (16.2)	66 (29.3)	0.0113*
Post prandial blood glucose levels (mg/dL)			
90-110	3 (1)	1 (0.5)	0.6885
111-130	9 (3)	5 (2.3)	0.9423
131-150	33 (10.9)	12 (5.6)	0.6143
151-200	165 (54.6)	98 (45.4)	0.2834
>200	92 (30.5)	100 (46.3)	Ref
Random Blood Glucose (mg/dL)			
80-100	0	4 (5.2)	0.3259
101-120	0	5 (6.5)	0.2729
121-140	0	2 (2.6)	0.4857
141-160	2 (13.3)	8 (10.4)	0.9807
161-200	1 (6.7)	9 (11.7)	0.4635
>200	12 (80)	49 (63.6)	Ref
HDL (mg/dL)			
Not available	54 (20.1)	84 (37.8)	Ref
Normal	130 (48.3)	73 (32.9)	<0.0001***
Low	55 (20.4)	51 (23)	0.0470*
High	30 (11.2)	14 (6.4)	0.0008***
Triglycerides (mg/dL)			
Not available	54 (20.5)	85 (38.5)	Ref

Continued on next page

Table 2 continued

Variable	Patients with T2DM N (%)	Patients with T2DM and retinopathy N (%)	P-Value
Normal	109 (41.5)	46 (20.8)	<0.0001***
Low	8 (3)	2 (0.9)	0.0108*
High	92 (35)	88 (39.8)	0.0293*
Total Cholesterol (mg/dL)			
Not available	54 (19.6)	82 (36.8)	Ref
Normal	151 (54.7)	78 (35)	<0.0001***
Low	6 (2.2)	1 (0.4)	0.0161*
High	65 (23.6)	62 (27.8)	0.0617
LDL (mg/dL)			
Not available	57 (20.8)	82 (37.1)	Ref
Normal	163 (59.4)	71 (32.2)	<0.0001***
Low	9 (3.3)	4 (1.8)	0.0496*
High	45 (16.5)	64 (28.9)	0.9649
Urea (mg/dL)			
Not available	72 (36.4)	120 (59.1)	Ref
Normal	78 (39.4)	22 (10.8)	<0.0001***
Low	0	0	—–
High	48 (24.2)	61 (30.1)	0.2656
Serum creatinine (mg/dL)			
Not available	45 (12.6)	7 (2.8)	Ref
Normal	305 (85.2)	175 (68.9)	0.0009***
Low	5 (1.4)	0	0.3811
High	3 (0.8)	72 (28.3)	<0.0001***
Duration of T2DM (Years)			
<5	172 (47.9)	59 (23.2)	Ref
5-10	111 (30.9)	101(39.8)	<0.0001***
>10	76 (21.2)	94 (37)	<0.0001***
Following T2DM education			
Yes	282 (79.2)	180 (70.9)	Ref
No	74 (20.8)	74 (29.1)	0.0177*

T2DM, Type 2 Diabetes Mellitus; BMI, Body Mass Index; HTN, Hypertension; CVDs, Cardiovascular Diseases; HbA1C, Glycated hemoglobin; HDL, High-DensityLipoproteins; LDL, Low-Density Lipoproteins

Table 3: Food and lifestyle characteristics of diabetic patients with (N=254) or without diabetic retinopathy (N=359).

Variable	Patients with T2DM N (%)	Patients with T2DM and retinopathy N (%)	P-value
Food habits			
Vegetariam	60 (16.7)	37 (14.6)	Ref
Mixed	299 (83.3)	217 (85.4)	0.4732
Physical activity			
No physical activity	176 (49)	165 (64.9)	Ref
Regular exercise	183 (50.9)	89 (35)	<0.0001***
Habit of smoking			
No	320 (89.1)	218 (85.8)	Ref
Yes	22 (6.1)	18 (7.1)	0.5781
Past smoker	17 (4.7)	18 (7.1)	0.2039
The habit of drinking alcohol			
No	304 (85.1)	221 (87)	Ref
Yes	44 (12.3)	25 (9.9)	0.3526
Past alcoholic	9 (2.5)	8 (3.2)	0.6834
The habit of taking junk foods			
No	180 (50.3)	123 (48.6)	Ref
Weekly once	31 (8.7)	16 (6.3)	0.3931
Weekly twice	23 (6.4)	18 (7.1)	0.6860
Weekly thrice and more	28 (7.8)	23 (9.1)	0.5455
Occasionally	96 (26.8)	73 (28.9)	0.5824
The habit of taking fruits /fruit juices			
No	66 (18.5)	62 (24.5)	Ref
Weekly once	27 (7.5)	17 (6.7)	0.2604
Weekly twice	35 (9.8)	22 (8.7)	0.2145
Weekly thrice & more	125 (34.9)	57 (22.4)	0.0023**
Occasionally	105 (29.3)	96 (37.8)	0.9047
The habit of taking soft drinks			
No	272 (76.2)	163 (64.1)	Ref
Weekly once	6 (1.7)	6 (2.4)	0.3773
Weekly twice	5 (1.4)	2 (0.8)	0.6291
Weekly thrice & more	14 (4)	2 (0.8)	0.0417*
Occasionally	60 (16.8)	81 (31.9)	<0.0001***
The habit of taking tea/coffee			
No	55 (15.3)	29 (11.5)	Ref
Daily once without sugar	54 (15)	32 (12.6)	0.7151
Daily twice without sugar	110 (30.6)	107 (42.3)	0.0208*
Daily thrice without sugar	58 (16.2)	35 (13.9)	0.6671
Daily once with sugar	25 (6.9)	16 (6.3)	0.6226
Daily twice with sugar	37 (10.3)	24 (9.5)	0.5518
Daily thrice with sugar	20 (5.6)	10 (4)	0.9061
Situations at working places			
No stress	181 (50.4)	127 (50)	Ref
Stress	178 (49.6)	127 (50)	0.9188

Table 4: Univariate regression analysis of modifiable and non-modifiable risk factors for the developmentof retinopathy in patients with type 2 diabetes mellitus

Variable	OR (95% CI)	P-value
Gender		
Male	1	Ref
Female	1.190 (0.8574 to 1.651)	0.2985
Age		
0-20 years	1	Ref
21-40 years	0.7365 (0.02891 to 18.76)	0.6239
41-60 years	2.103 (0.08505 to 52.02)	0.4031
Above 60 years	4.304 (0.1721 to 107.6)	0.2328
Marital Status		
Unmarried	1	Ref
Married	3.903 (1.125 to 13.54)	0.0211*
Education		
Uneducated Educated	1	Ref
	0.3670 (0.2635 to 0.5112)	<0.0001***
BMI (Kg/m2)		
<25 Kg/m2	1	Ref
>/=25 Kg/m2	1.433 (0.9974 to 2.060)	0.0511
Body Weight (Kg)		
<50	1	Ref
50-70	0.6957 (0.1967 to 2.460)	0.5714
>70	0.7083 (0.2011 to 2.495)	0.5897
Nature of Work		
Not working anywhere	1	Ref
Private job	0.3480 (0.2035 to 0.5952)	<0.0001***
Govt. job	0.2582 (0.1243 to 0.5363)	0.0002***
Daily labour	0.4732 (0.2483 to 0.9020)	0.0221*
Housewife	0.5492 (0.3432 to 0.8789)	0.0120*
Locality		
Rural	1	Ref
Urban	0.3943 (0.2820 to 0.5513)	<0.0001***
Monthly Income		
No income	1	Ref
Below 25000	0.8690 (0.6092 to 1.240)	0.4382
Above 25000	0.2990 (0.1723 to 0.5187)	<0.0001***
Co-morbidities		
No	1	Ref
HTN	4.131 (2.687 to 6.350)	<0.0001***
History of CVDs	17.20 (7.049 to 41.95)	<0.0001***
Endocrine diseases	2.460 (1.433 to 4.224)	0.0009***
Other diseases	4.963 (3.202 to 7.692)	<0.0001***
Systolic Blood Pressure		
<140 mmHg	1	Ref
>140 mmHg	1.522 (1.079 to 2.146)	0.0164*
Diastolic Blood Pressure		
<90mmHg	1	Ref
>90mmHg	0.9051 (0.6088 to 1.346)	0.6219
HbA1C		
<7	1	Ref
7-9	2.488 (1.638 to 3.779)	<0.0001***
>9	3.380 (2.157 to 5.295)	<0.0001***

Continued on next page

Table 4 continued

Variable	OR (95% CI)	P-value
Fasting Blood Glucose (mg/dL)		
70-80	1	Ref
81-120	2.935 (0.6196 to 13.90)	0.1572
121-160	2.897 (0.6146 to 13.66)	0.1610
161-200	2.887 (0.6028 to 13.83)	0.1678
>200	6.111 (1.283 to 29.10)	0.0113*
Post prandial blood glucose levels (mg/dL)		
90-110	1	Ref
111-130	1.667 (0.1349 to 20.59)	0.6885
131-150	1.091 (0.1032 to 11.53)	0.9423
151-200	1.782 (0.1827 to 17.38)	0.6143
>200	3.261 (0.3331 to 31.92)	0.2834
Random Blood Glucose (mg/dL)		
80-100	2.273 (0.1146 to 45.09)	0.3259
101-120	2.778 (0.1437 to 53.69)	0.2729
121-140	1.263 (0.05689 to 28.02)	0.4857
141-160	0.9796 (0.1837 to 5.222)	0.9807
161-200	2.204 (0.2540 to 19.13)	0.4635
>200	1	Ref
HDL (mg/dL)		
Not available	1	Ref
Normal	0.3610 (0.2310 to 0.5640)	<0.0001***
Low	0.5961 (0.3572 to 0.9947)	0.0470*
High	0.3000 (0.1459 to 0.6168)	0.0008***
Triglycerides (mg/dL)		
Not available	1	Ref
Normal	0.2681 (0.1651 to 0.4354)	<0.0001***
Low	0.1588 (0.03249 to0.7765)	0.0108*
High	0.6077 (0.3878 to 0.9523)	0.0293*
Total Cholesterol (mg/dL)		
Not available	1	Ref
Normal	0.3402 (0.2193 to 0.5277)	<0.0001***
Low	0.1098 (0.01285 to0.9377)	0.0161*
High	0.6281 (0.3852 to 1.024)	0.0617
LDL (mg/dL)		
Not available	1	Ref
Normal	0.3028 (0.1954 to 0.4693)	<0.0001***
Low	0.3089 (0.09070 to 1.052)	0.0496*
High	0.9886 (0.5939 to 1.646)	0.9649
Urea (mg/dL)		
Not available	1	Ref
Normal	0.1692 (0.09703 to 0.2951)	<0.0001***
Low		
High	0.7625 (0.4728 to 1.230)	0.2656
Serum creatinine (mg/dL)		
Not available	1	Ref
Normal	3.689 (1.628 to 8.358)	0.0009***
Low	0.5515 (0.02754 to 11.05)	0.3811
High	154.3 (37.92 to 627.7)	<0.0001***
Duration of T2DM (Years)		

Continued on next page

Table 4 continued

Variable	OR (95% CI)	P-value
<5	1	Ref
5-10	2.653 (1.778 to 3.958)	<0.0001***
>10	3.606 (2.362 to 5.504)	<0.0001***
Following T2DM education		
Yes	1	Ref
No	1.567 (1.079 to 2.274)	0.0177*
Food habits		
Vegetarian	1	Ref
Mixed	1.177 (0.7538 to 1.838)	0.4732
Physical activity		
No physical activity	1	Ref
Regular exercise	0.5188 (0.3727 to 0.7220)	<0.0001***
Habit of smoking		
No	1	Ref
Yes	1.201 (0.6292 to 2.292)	0.5781
Past smoker	1.554 (0.7835 to 3.083)	0.2039
The habit of drinking alcohol		
No	1	Ref
Yes	0.7816 (0.4643 to 1.316)	0.3526
Past alcoholic	1.223 (0.4643 to 3.220)	0.6834
The habit of taking junk foods		
No	1	Ref
Weekly once	0.7553 (0.3960 to 1.440)	0.3931
Weekly twice	1.145 (0.5930 to 2.212)	0.6860
Weekly thrice and more	1.202 (0.6614 to 2.185)	0.5455
Occasionally	1.113 (0.7601 to 1.629)	0.5824
The habit of taking fruits /fruit juices		
No	1	Ref
Weekly once	0.6703 (0.3332 to 1.348)	0.2604
Weekly twice	0.6691 (0.3542 to 1.264)	0.2145
Weekly thrice & more	0.4854 (0.3042 to 0.7746)	0.0023**
Occasionally	0.9733 (0.6245 to 1.517)	0.9047
The habit of taking soft drinks		
No	1	Ref
Weekly once	1.669 (0.5292 to 5.262)	0.3773
Weekly twice	0.6675 (0.1280 to 3.481)	0.6291
Weekly thrice & more	0.2384 (0.05348 to 1.063)	0.0417*
Occasionally	2.253 (1.531 to 3.315)	<0.0001***
The habit of taking tea/coffee		
No	1	Ref
Daily once without sugar	1.124 (0.6001 to 2.105)	0.7151
Daily twice without sugar	1.845 (1.094 to 3.112)	0.0208*
Daily thrice without sugar	1.144 (0.6186 to 2.117)	0.6671
Daily once with sugar	1.214 (0.5607 to 2.627)	0.6226
Daily twice with sugar	1.230 (0.6214 to 2.435)	0.5518
Daily thrice with sugar	0.9483 (0.3923 to 2.292)	0.9061
Situations at working places		
No stress	1	Ref
Stress	1.017 (0.7373 to 1.402)	0.9188

T2DM, Type 2 Diabetes Mellitus; BMI, Body Mass Index; HTN, Hypertension; CVDs, Cardiovascular Diseases; HbA1C, Glycated hemoglobin; HDL, High-Density Lipoproteins; LDL, Low-Density Lipoproteins

Therefore, further studies are needed to evaluate the exact impact of urban residence on risk for diabetic retinopathy.

Monthly income

The present study's results revealed that monthly income (P<0.0001) was significantly associated and was the major risk factor for diabetic retinopathy (OR, 0.1841; 95% CI, 0.1082 - 0.3133). Therefore, further studies are needed to evaluate the exact impact of monthly income on risk for diabetic retinopathy.

Comorbidities

Hypertension (P < 0.0001) was positively associated with diabetic retinopathy. (Yau *et al.*, 2012) conducted a study to examine the global prevalence and major risk factors for diabetic retinopathy (DR) and gave a conclusion that DR has the potential to be the leading cause of visual impairment and blindness worldwide and also concluded that poorer glycemic and blood pressure control are strongly associated with DR (Yau *et al.*, 2012). Another study conducted by (Al-Rubeaan *et al.*, 2015) also concluded that hypertension was the most significant risk factor. The present study's results are also supported that hypertension (30.1%, P < 0.0001) was a risk factor for diabetic retinopathy (OR, 2.642; 95% CI, 1.868-3.736).

Physical inactivity

The present study's results revealed that physical inactivity (63.3%, P <0.0001) was significantly associated and was the major risk factor for diabetic retinopathy. Therefore, further studies are needed to evaluate the exact impact of physical inactivity on risk for diabetic retinopathy.

Junk foods

The present study's results revealed that habit of taking junk foods weakly once (19.9%, P <0.0001), weakly twice (13.2 %, P<0.0001) was significantly associated and was the major risk factor for diabetic retinopathy (weekly once OR, 3.287; 95%CI, 2.049 – 5.274 and weekly twice OR, 2.935; 95%CI, 1.709 –5.038). Therefore, further studies are needed to evaluate the exact impact of the habit of taking junk foods on risk for diabetic retinopathy.

Soft drinks

The present study's results revealed that the habit of taking soft drinks occasionally (24.9%, P = 0.0073) was significantly associated and was the major risk factor for diabetic retinopathy (OR, 1.642;95%CI, 1.141-2.364). Therefore, further studies are needed to evaluate the exact impact of the habit of taking soft drinks on risk for diabetic retinopathy.

The habit of taking tea/coffee

The present study's results revealed that the habit of taking tea/coffee twice without sugar (38.1%, P=0.0465) was significantly associated and was the major risk factor for diabetic retinopathy (OR, 1.598; 95%CI, 1.006-2.539). Therefore, further studies are needed to evaluate the exact impact of the habit of taking tea/coffee on risk for diabetic retinopathy.

HbA1c

Poor glycemic control was significantly associated with the development of diabetic retinopathy. Joanne et al., conducted a study to examine the global prevalence and major risk factors for diabetic retinopathy (DR) and gave a conclusion that DR has the potential to be the leading cause of visual impairment and blindness worldwide and also concluded that poorer glycemic and blood pressure control are strongly associated with DR [15]. In the present study, it was significant that poor glycemic control (7-9% (39.3%, P=0.0018, >9% (31.9%, P<0.0001) was a risk factor for development of diabetic retinopathy (7-9% (OR, 1.774; 95%CI, 1.235-2.547) and> 9% (OR, 2.275; 95% CI, 1.529-3.386)). Other relevant studies were conducted by Donghyun et al. and Khalid et al. concluded that poor glycemic control was significantly associated with the development of diabetic retinopathy (Al-Rubeaan *et al.*, 2015; Jee *et al.*, 2013).

Serum creatinine

The present study's results revealed that high serum creatinine levels (14.8%, P <0.0001) was significantly associated and was the major risk factor for diabetic retinopathy (OR, 11.55; 95%CI, 3.415-39.10). Therefore, further studies are needed to evaluate the exact impact of serum creatinine on risk for diabetic retinopathy.

Duration of T2DM

Joanne et al., 2015 conducted a study to examine the global prevalence and major risk factors for diabetic retinopathy (DR) and gave a conclusion that DR has the potential to be the leading cause of visual impairment and blindness worldwide and also concluded that longer diabetes duration was the significant risk factor. In the present study, it was significant that long-standing diabetes (5-10 years (37.8%, P<0.0001 and with duration >10 years (37.3%, P <0.0001)) was a risk factor for development of diabetic retinopathy (5-10 years (OR, 2.357; 95%CI, 1.659-3.348) and with duration >10 years (OR, 3.395; 95%CI, 2.336-4.933). Other relevant studies were conducted by Donghyun et al., Sadiq et al., Khalid et al., Rajiv et al., they also concluded that long-standing diabetes was significantly associated

Table 5: Medication given for the patients with diabetic retinopathy

S. No	Generic Name of Drugs	N (%)
1	Metformin	72 (47.05)
2	Glimepiride + Metformin	47 (30.71)
3	Insulin Isophane + Regular Insulin	45 (29.41)
4	Teneligliptin	16 (10.45)
5	Insulin Regular	15 (9.80)
6	Glimepiride	10 (6.53)
7	Pioglitazone	10 (6.53)
8	Gliclazide + Metformin	8 (5.22)
9	Insulin Glargine	7 (4.57)
10	Gliclazide	6 (3.92)
11	Sitagliptin + Metformin	4 (2.61)
12	Teneligliptin + Metformin	4 (2.61)
13	Metformin + Voglibose	4 (2.61)
14	Insulin Aspart	4 (2.61)
15	Glipizide + Metformin	3 (1.96)
16	Glibenclamide + Metformin	3 (1.96)
17	Metformin + Vildagliptin	3 (1.96)
18	Lantus Insulin	2 (1.30)
19	Glimepiride + Metformin + Voglibose	2 (1.30)
20	Glimepiride + Metformin + Pioglitazone	2 (1.30)
21	Sitagliptin	2 (1.30)
22	Acarbose	1 (0.65)
23	Linagliptin	1 (0.65)
24	Voglibose	1 (0.65)
25	Dapagliflozin	1 (0.65)
26	Empagliflozin	1 (0.65)

with the development of diabetic retinopathy (Hussain *et al.*, 2013; Raman *et al.*, 2014).

Drug utilization pattern

Sekhar et al. conducted a prospective observational study, including 181 patients for 6 months in Bankura Sammilani Medical College and gave a conclusion that metformin was the commonest drug used; glimepiride and metformin combination was the commonest combination therapy (Resnikoff *et al.*, 2004). Our present study's results revealed that Metformin, a combination of Insulin Isophane and Insulin Regular, a combination of Glimepiride and Metformin, Glimepiride, a combination of Metformin and Vildagliptin were most commonly prescribed anti-diabetic drugs to the T2DM patients with retinopathy.

CONCLUSION

Subjects who are married, uneducated patients, nature of work (housewives), rural residents, no income group and risk factors were comorbidities(other diseases, HTN, endocrine diseases, history of CVDs), no physical activity, habit of taking junk foods (weakly once, weakly twice), soft drinks (occasionally), tea/coffee(daily twice without sugar), HbA1c(7-9%, >9%), high serum creatinine, duration of diabetes (5-10 years, > 10 years) were significant risk factors for development of retinopathy. Metformin, a combination of Insulin Isophane and Insulin Regular, a combination of Glimepiride and Metformin, Glimepiride, a combination of Metformin and Vildagliptin were most commonly prescribed anti-diabetic drugs to the T2DM patients with retinopathy.

Key findings

1. The prevalence of diabetic retinopathy was found to be 31.28%.
2. Retinopathy prevalence was higher in females compared to males (P=0.2608).
3. The prevalence of retinopathy was significantly higher in the subjects who are married (98.2%,

P=0.0371) compared to unmarried.

4. The prevalence of retinopathy was significantly higher in the subjects who are poorly educated (69.9%, P<0.0001) when compared to educated.

5. The prevalence of retinopathy was significantly higher in the subjects who are not doing any work when compared to others.

6. The major comorbidities for the development of retinopathy complications include hypertension (P<0.0001), history of cardiovascular diseases (P<0.0001), endocrine diseases (P=0.0223) and other diseases (P<0.0001).

7. Locality, physical inactivity, socioeconomic status, food habits, soft drinks, junk foods, the habit of taking tea/coffee are significantly associated with the development of retinopathy complications.

8. Poor glycemic control, serum creatinine levels are significantly associated with the development of retinopathy complications.

9. Duration of diabetes (>10years, 37.3% P<0.0001, 5-10 years 37.8% P<0.0001) was significantly associated with the development of retinopathy complications.

10. Metformin, a combination of Insulin Isophane and Insulin Regular, a combination of Glimepiride and Metformin, Glimepiride, a combination of Metformin and Vildagliptin were most commonly prescribed anti-diabetic drugs to the T2DM patients with retinopathy.

REFERENCES

Al-Rubeaan, K., El-Asrar, A., Youssef, A. M., Subhani, A. M., Ahmad, S. N., Al-Sharqawi, N. A., Ibrahim, A. H. 2015. Diabetic retinopathy and its risk factors in a society with a type 2 diabetes epidemic: a Saudi National Diabetes Registry-based study. *Acta Ophthalmologica*, 93(2):140–147.

Ashutosh, K., Ipseeta, R., Sandeep, R. 2017. Assessment of Prescription Pattern of Antidiabetic Drugs in the Outpatient Department of a Tertiary Care Hospital. *International Journal of Clinical Endocrinology and Metabolism*, 3(1):1–007.

Burgess, P. I., Maccormick, I. J. C., Harding, S. P., Bastawrous, A., Beare, N. A. V., Garner, P. 2013. Epidemiology of diabetic retinopathy and maculopathy in Africa: a systematic review. *Diabetic Medicine*, 30(4):399–412.

Cheung, N., Mitchell, P., Wong, T. Y. 2010. Diabetic retinopathy. *The Lancet*, 376(9735):124–136.

Cui, J., Ren, J.-P., Chen, D.-N., Xin, Z., Yuan, M.-X., Xu, J., You, Q.-S. 2017. Prevalence and associated factors of diabetic retinopathy in Beijing, China: a cross-sectional study. *BMJ Open*, 7(8):e015473.

Fernandes, J. D. R., Ogurtsova, K., Linnenkamp, U., Guariguata, L., Seuring, T., Zhang, P., Makaroff, L. E. 2016. IDF Diabetes Atlas estimates of 2014 global health expenditures on diabetes. *Diabetes Research and Clinical Practice*, 117:48–54.

Guariguata, L., Whiting, D. R., Hambleton, I., Beagley, J., Linnenkamp, U., Shaw, J. E. 2014. Global estimates of diabetes prevalence for 2013 and projections for 2035. *Diabetes Research and Clinical Practice*, 103(2):137–149.

Hussain, S., Qamar, M. R., Iqbal, M. A., Ahmed, A., Ullah, E. 2013. Risk factors of retinopathy in type 2 diabetes mellitus at a tertiary care hospital. *Bahawalpur Pakistan. Pakistan Journal of Medical Sciences*, 29(2):563–569.

Jee, D., Lee, W. K., Kang, S. 2013. Prevalence and risk factors for diabetic retinopathy: the Korea National Health and Nutrition Examination Survey. *Investigative ophthalmology & visual science*, 54(10):6827–6833.

Klein, B. E. K. 2007. Overview of Epidemiologic Studies of Diabetic Retinopathy. *Ophthalmic Epidemiology*, 14(4):179–183.

Lee, R., Wong, T. Y., Sabanayagam, C. 2015. Epidemiology of diabetic retinopathy, diabetic macular edema and related vision loss. *Eye and Vision*, 2(1):17.

Mandal, S., Maiti, T., Kr, A., Das, A., Das, A., Mandal, B., Sarkar, S. M. S. 2016. Drug utilization study in patients with type 2 diabetes mellitus attending the diabetes clinic of a tertiary care hospital in rural Bengal. *IJBCP*, 5(4):1647.

Martinell, M., Dorkhan, M., Stålhammar, J., Storm, P., Groop, L., Gustavsson, C. 2016. Prevalence and risk factors for diabetic retinopathy at diagnosis (DRAD) in patients recently diagnosed with type 2 diabetes (T2D) or latent autoimmune diabetes in the adult (LADA). *Journal of Diabetes and Its Complications*, 30(8):1456–1461.

Raman, R., Ganesan, S., Pal, S. S., Kulothungan, V., Sharma, T. 2014. Prevalence and risk factors for diabetic retinopathy in rural India. Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetic Study III (SN-DREAMS III), report no 2. *BMJ Open Diabetes Research & Care*, 2(1):e000005.

Resnikoff, S., Pascolini, D., Etya'ale, D., Kocur, I.,

Pararajasegaram, R., Pokharel, G., Mariotti, S. 2004. Global data on visual impairment in the year 2002. *Bulletin of the World Health Organization*, 82:844–851.

Ting, D. S. W., Cheung, G. C. M., Wong, T. Y. 2016. Diabetic retinopathy: global prevalence, major risk factors, screening practices and public health challenges: a review. *Clinical & Experimental Ophthalmology*, 44(4):260–277.

Yau, J. W. Y., Rogers, S. L., Kawasaki, R., Lamoureux, E. L., Kowalski, J. W., Bek, T., Wong, T. Y. 2012. Global Prevalence and Major Risk Factors of Diabetic Retinopathy. *Diabetes Care*, 35(3):556–564.