A multivariate analysis approach on identifying of influencing factors and the chance of development of diabetic eye disease among diabetes in a diabetic Centre of Southwestern Malabar region of India

Amitha Prasad1, Senthivel Vasudevan2

1Biostatistician Technician, IQVIA, World Trade Center Kochi (Brigarde), 7th floor, Tower A, Info Park SEZ, Info Park Phase-1 Campus, Kakkanad, Kochi, Kerala, India. 2Assistant Professor of Statistics (Biostatistics and Epidemiology), Department of Pharmacy Practice, College of Pharmacy, King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia.

Abstract

**Background:** Diabetic Retinopathy is a non-communicable disease and metabolic disorder. It is a public health problem in Worldwide. In this paper, finding influencing factors and how much probability to development of DR among known T2DM patients.

**Materials and Methods:** This was a hospital-based cross-sectional and observational study among T2DM patients, with and without DR in the diabetes clinic with sample of one hundred and fifty patients. Statistical analysis used chi-square and binary logistic regression analysis was used to identify correlates of DR after controlling of confounders.

**Results:** In this present study, one hundred and fifty DM patients were included and in that, 39 (26%) patients had DR. Smoking habit was strongly associated with development of DR (AOR=15.39, p=0.002), patients had history of hypertension was associated with DR (AOR=1.10, p=0.016), medication, in that insulin users were strongly associated with DR (AOR=5.72, p=0.002), duration of diabetes mellitus with >10 years was associated with DR (AOR=1.18, p=0.001), total cholesterol with abnormal was 5-fold more increase in risk with the development of DR (AOR=5.86, p=0.065) but not significant, high hba1c with >6.5% was associated with the progression of DR (AOR=1.34, p=0.035), and fasting blood sugar with abnormal was associated with the progression of DR (AOR=1.01, p=0.027) except age but, showed positive association in bivariate with DR. The probability of developing DR in a known T2DM patient was 98%.

**Conclusion:** From this study, we revealed that influencing variables were hba1c, smoking habit, intake of tablet/insulin, duration of DM, history of hypertension and fasting blood sugar. The chance/probability of developing retinopathy was very high among known diabetes patients those who had longer duration of DM. Hence, we have recommended a periodic eye screening is mandatory in T2DM patients.

**Keywords:** diabetes mellitus, diabetic retinopathy, influencing factors, probability, multivariate analysis

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**Introduction**

Diabetes Mellitus (DM) is called otherwise by the word “Diabetes”. DM is a non-communicable disease [1]. DM is the public health problem in Worldwide. It is classified into two major types namely Type I DM, Type II DM [2]. Diabetic Retinopathy (DR) is a non-communicable and metabolic disorder. It is the complication of DM. DR is also called as “eye threatening disease”. DR affects the minor blood vessels in the retina. It is a public health problem in both developing and developing countries. Overall, in India there are 65 million people with DM, and it would be projected to increase to 134 million in coming year 2045. [3] If the body glucose level is not maintaining correctly for a long period, then it leads to last stage vision loss [4]. The prevalence of DR was 27% in between 2015 – 2019 based on Worldwide and in that Proliferative DR (PDR) was 1.4% [5].

The prevalence of DR is more in male gender, urban area had more prevalence and 22.18% patients had DR. [6] Even though the literacy rate is high in Kerala, but the prevalence of DM is 16.3% also very high and vision threatening was seen in 39.5% population. So many studies were done with small sample size, and some studies were done with larger sample size. [7] DR progression was associated with older age, male sex, hyperglycaemia (higher HbA1c) and with not smoking. [8] There was no separate paper related to find probability of developing or progressing DR in DM patients. That’s why, we did this study with a reasonable sample size. The main aims of this study was to identify the influencing factors of DR among T2DM patients and to estimate the probability of developing of DR among known T2DM patients.

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Materials and Methods:

A hospital-based cross-sectional and observational study was conducted with one hundred and fifty known DM patients by simple random sampling method were recruited and included in this study. Data were collected from the Diabetic Centre patients in Amrita Institute of Medical Sciences, Kochi, Kerala. This study was done in between February and March 2018.

Selection of variables and allocation for the data analysis: In our present study, we have considered the variables as binary variables for the purpose of data analysis.

Gender (X1): Male = 0, Female = 1,
Age (X2): ≤50 years = 0, >50 years = 1,
Educational status(X3): School = 0, College = 1,
Family history of Diabetes Mellitus (X4): No = 0, Yes = 1,
Alcohol consumption (X5): No = 0, Yes = 1,
History of hypertension (X6): No = 0, Yes = 1,
Medication (X7): Tablet Users = 0, Insulin Users = 1,
Duration of Diabetes Mellitus (X8): <10 years = 0, ≥10 years = 1,
Body Mass Index classification (X9): Normal = 0, Over Weight = 1,
Total cholesterol (X10): Normal = 0, Abnormal = 1,
HbA1c (X12): ≤6.5% = 0, >6.5% = 1, and Fasting blood sugar (X11): Normal = 0, Abnormal = 1 as shown in Table 1.

For the analysis, I have taken the variables were converted as binary variables. We have found the association between dichotomous variables (gender, educational status, family history of DM, smoking habit, history of hypertension, medication, BMI classification, total cholesterol, and fasting blood sugar) and found mean comparison between continuous variables (age, duration of diabetes mellitus, and HbA1c), with and without variables by using Chi-Square test.

To find out the odds ratio (Probability of developing DR in a DM patient) as follows:

\[ Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \ldots + \beta_d X_d + \ldots + \beta_n X_n \ldots \ldots \ldots \ (1) \]

Find the value of Y and substitute in \( e^Y \), and then

\[ P \quad \frac{\text{------------}}{1 - P} = e^Y \quad \ldots \ldots \ldots \ (2) \]

and find the value of P.

This P – value is the probability of developing DR in a DM patient.

Inclusion Criteria: T2DM patients with aged ≥30 years those who have been lived permanently in area in and around Kochi area.

Exclusion Criteria: Patients those who had other chronic diseases and other communicable and non-communicable diseases.

Statistical analysis: All data were entered and managed by using Microsoft Excel 2010 [Microsoft Office 360, Microsoft Ltd., USA] and data were analyzed by using SPSS 20.0 version for windows [IBM SPSS Ltd., Chicago IL, USA].

Descriptive Statistics: Quantitative variables were expressed as mean and standard deviation, and qualitative variables were expressed as frequency, and proportions. Bivariate analysis: Chi-Square test was used to compare dichotomous variables.

Multivariate Logistic Regression (MLR) Analysis: Binary Logistic Regression equation \( Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \ldots + \beta_n X_n \) with backward conditional analysis was used to find the influencing factors in the development of DR among known T2DM patients. [9] The statistically significant (p<0.05) variables were identified from bivariate analysis and variables had p-value <0.20 were identified and included in the final Binary Logistic Regression analysis. [10] The level of significant was fixed as p<0.05.

Ethical Consideration: This study was done with prior permissions were obtained from both the institutions before conducted. Patients’ data were obtained from the medical records and some information from the patients directly. Patients’ data were confidential and preserved by the AIMS institutions, Kochi, Kerala. Ethical approval from the Institutional Review Board/Ethics Committee had been obtained and informed all the details about the study and had got the oral consents were taken from all participants at the time of study period.

Results:

In our present study, two hundred T2DM patients as per inclusion and exclusion criteria with aged thirty years and above were recruited and included. In that, 39 (26%) patients had DR and 111 (74%) patients were not having DR. The average age of the participants was 58.2 ± 10.5 (31–87) years. The other variables were presented in Table 1.

In bivariate analysis, the variables duration of diabetes mellitus, medication, duration of hypertension, smoking habit, HbA1c, and FBS were showed statistically significant with and without DR with p<0.05. So, these variables were influencing with the development of DR among known T2DM patients.

In this study, we have used Binary Logistic Regression (BLR) Analysis with backward conditional analysis to predict the influencing factor to develop the diabetic retinopathy among known T2DM patients. From the multivariate logistic regression analysis, the results were obtained and in that, Hosmer-Lemeshow test was showed a goodness of fit with Chi-Square value of 2.891 and p-value was 0.941 (p>0.05). Hence, we have concluded that the selection of prediction variables was very much suitable to the final model binary logistic regression model was a good fit and the substitute variables.

The history of hypertension wasn’t significant in the bivariate analysis but included in the final BLR analysis. The history of hypertension wasn’t significant in the bivariate analysis but included in the final BLR analysis.
Table 1: Distribution of basic and clinical characteristics of with and without Diabetic Retinopathy among Type 2 Diabetes Mellitus patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>No. of Patients</th>
<th>Diabetic Retinopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>With DR</td>
</tr>
<tr>
<td>Gender (X_1) Male</td>
<td>85 (56.7)</td>
<td>20 (23.5)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>65 (43.3)</td>
</tr>
<tr>
<td>Age groups (in years) (X_2) ≤50</td>
<td>34 (22.7)</td>
<td>60.38</td>
</tr>
<tr>
<td></td>
<td>&gt;50</td>
<td>116 (77.3)</td>
</tr>
<tr>
<td>Educational Status (X_3) School</td>
<td>91 (60.7)</td>
<td>23 (25.3)</td>
</tr>
<tr>
<td></td>
<td>College</td>
<td>59 (39.3)</td>
</tr>
<tr>
<td>Family History of DM (X_4) Yes</td>
<td>47 (31.3)</td>
<td>9 (19.1)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>103 (68.7)</td>
</tr>
<tr>
<td>Alcohol Consumption (X_5) Yes</td>
<td>127 (84.7)</td>
<td>32 (25.2)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>23 (15.3)</td>
</tr>
<tr>
<td>Smoking Habit (X_6) Yes</td>
<td>136 (90.7)</td>
<td>33 (24.3)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>14 (9.3)</td>
</tr>
<tr>
<td>History of hypertension (X_7) Yes</td>
<td>55 (36.7)</td>
<td>8 (14.5)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>95 (63.3)</td>
</tr>
<tr>
<td>Medication (X_8) Tablet Users</td>
<td>93 (62.0)</td>
<td>11 (11.8)</td>
</tr>
<tr>
<td></td>
<td>Insulin Users</td>
<td>57 (16.0)</td>
</tr>
<tr>
<td>Duration of DM Mean (SD) (X_9) ≤10 years</td>
<td>64 (42.7)</td>
<td>16.62</td>
</tr>
<tr>
<td></td>
<td>≥10 years</td>
<td>86 (57.3)</td>
</tr>
<tr>
<td>BMI Classifications (X_{10}) 18.5–24.9 (Normal)</td>
<td>68 (45.3)</td>
<td>17 (24.6)</td>
</tr>
<tr>
<td></td>
<td>25.0–29.9 (Over Weight)</td>
<td>82 (54.7)</td>
</tr>
<tr>
<td>Total Cholesterol (X_{11}) Normal</td>
<td>123 (82.0)</td>
<td>36 (29.3)</td>
</tr>
<tr>
<td></td>
<td>Abnormal</td>
<td>27 (18.0)</td>
</tr>
<tr>
<td>HbA1C (in %) Mean (SD) (X_{12}) ≤6.5</td>
<td>30 (20.0)</td>
<td>8.94</td>
</tr>
<tr>
<td></td>
<td>&gt; 6.5</td>
<td>120 (80.0)</td>
</tr>
<tr>
<td>Fasting Blood Sugar (X_{13})</td>
<td>Normal</td>
<td>14 (10.4)</td>
</tr>
<tr>
<td></td>
<td>Abnormal</td>
<td>121 (89.6)</td>
</tr>
</tbody>
</table>

In the third step of backward elimination only, the variables smoking habit, β-regression value=0.002, Adjusted Odds Ratio, [AOR:15.39; 95%CI: (2.66–89.18); p=0.002], (p<0.05), was 15-times more risk than non-smokers. History of hypertension, β-regression value=0.013, [AOR:1.10; 95%CI: (1.02–1.18); p=0.016], (p<0.05) with hypertension 10% increase in the risk of development of DR. Medication, β-regression value=0.009, [AOR= 5.72; 95%CI: (1.93–16.91); p=0.002], (p<0.05). The risk was five times more in insulin users than tablet users.

Duration of diabetes mellitus, β-regression value=0.085, [AOR:1.18; 95%CI: (1.07–1.31); p=0.001]. The risk was 18% more those who had DM ≥10 years (p<0.05). Total cholesterol, β-regression value=0.001, [AOR:5.86; 95%CI: (0.89–38.41); p=0.005], (p<0.05). The risk was 5-times more in abnormal than normal but not significant. According to HbA1C, β-regression value = 0.218, [AOR:1.34; 95%CI: (1.02–1.75); p=0.035], (p<0.05), 34% risk increase as shown in Table-2.

Table – 2 List of predictor variables in the multivariate logistic regression equation, β-Values, its significance, odds ratios and 95% Confidence Interval

<table>
<thead>
<tr>
<th>Variables in the Multivariate Logistic Regression Equation</th>
<th>β Value</th>
<th>OR</th>
<th>Significance</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (X_1)</td>
<td>0.458</td>
<td>0.97</td>
<td>&gt;0.05, NS</td>
<td>0.92</td>
</tr>
<tr>
<td>Smoking habit (X_2)</td>
<td>0.002</td>
<td>15.39</td>
<td>&lt;0.01, HS</td>
<td>2.66</td>
</tr>
<tr>
<td>History of HTN (X_3)</td>
<td>0.013</td>
<td>1.10</td>
<td>&lt;0.05, S</td>
<td>1.02</td>
</tr>
<tr>
<td>Medication (X_4)</td>
<td>0.009</td>
<td>5.72</td>
<td>&lt;0.01, HS</td>
<td>1.93</td>
</tr>
<tr>
<td>Duration of DM (X_5)</td>
<td>0.085</td>
<td>1.18</td>
<td>&lt;0.01, HS</td>
<td>1.07</td>
</tr>
<tr>
<td>Total Cholesterol (X_{11})</td>
<td>0.001</td>
<td>5.86</td>
<td>&lt;0.05, NS</td>
<td>0.90</td>
</tr>
<tr>
<td>HbA1C (X_{12})</td>
<td>0.218</td>
<td>1.34</td>
<td>&lt;0.05, S</td>
<td>1.02</td>
</tr>
<tr>
<td>FBS (X_{13})</td>
<td>0.002</td>
<td>1.01</td>
<td>&lt;0.05, S</td>
<td>1.00</td>
</tr>
<tr>
<td>Constant</td>
<td>1.486</td>
<td>0.72</td>
<td>&lt;0.05, S</td>
<td>1.00</td>
</tr>
</tbody>
</table>

In bivariate analysis, the association between groups (with and without DR) and duration of DM was showed a highly statistically significant with p-value<0.01 as shown in Figure-1.

Figure: 1 Relationship between with and without diabetes and classifications of duration of diabetes mellitus

The other variables like medication, duration of hypertension, smoking habit, HbA1C, and FBS were also showed statistically significant with and without DR with p<0.05. HbA1C in the progression of DR. Next, to find the probability of the development of DR in a DM patient. Here, we have taken clinical data of a DM patient with DR and in high and substitute in the equations (1) and (2), the variables were as follows: smoking habit (X_0) = yes = 1; history of hypertension (X_1) = yes = 1; medication (X_2) = yes = 1; duration of diabetes mellitus (X_3) = 20 years; hba1c (X_{12}) = 7.2%;
fasting blood sugar \((X_{13}) = 190\) mg/dL. Substitute in equation – 1, Hence, the binary logistic regression equation (1) became,

\[
Y = \beta_0 + \beta_1X_1 + \beta_2X_2 + \beta_3X_3 + \ldots \ldots + \beta_{13}X_{13} \quad \text{(1)}
\]

According to final multivariate logistic regression analysis, the above equation was rewritten as follows, ie., modified (1) equation was,

\[
Y = \beta_0 + \beta_6X_6 + \beta_7X_7 + \beta_8X_8 + \beta_9X_9 + \beta_{12}X_{12} + \beta_{13}X_{13} \\
Y = 1.486 + (0.002) (1) + (0.013) (1) + (0.009) (1) + (0.085) (20) + (0.218) (7.2) + (0.002) (190) \\
Y = 4.160
\]

Therefore, \(e^Y = 64.072\) and Substitute, the value of \(e^Y = 64.072\) in the equation (2), We have got following,

\[
P \quad \text{(2)}
\]

\[
P = 0.984 \sim 98\%
\]

Hence, the probability of developing DR was \(P = 0.984\) (Odds Ratio). So, the probability of developing DR in a known T2DM patient was estimated as 98%.

**Discussion:**

This is the study in Kerala related to find the influencing factors and probability to the progression of DR in diabetic patients. DR is one of the public health problems in Worldwide. [3] DM patients have not controlled their blood glucose level over a period of time then, they will have to effect by retinopathy. If not screened in time and not properly controlled the risk factors then, it will affect the retina and it will cause to vision loss. In bi-variave analysis, duration of DM, medication, total cholesterol, HbA1C, fasting blood sugar were showed a significant with development of DR. But body mass index wasn’t showed any significance with the progression of DR.

In the final statistical model in the BLR analysis the variables HbA1C, FBS, smoking habit, intake of tablet/insulin, duration of DM and history of hypertension were only showed a significant with the development of DR. In our present study, the newly diagnosed with Type 2 DM patients, 26% had DR. After the multivariate analysis the related factors, smoking was a prominent risk factor in the development of DR, ie, smoking habit was very highly significantly associated with DR \((AOR = 15.39, p=0.002)\). Similar type of result was mentioned by Kumari et al. [11] In some other studies that the history of smoking was found as a factor of DR development. [12, 13] Medication i.e., insulin use \((AOR = 5.72, 95\%CI:(1.93–16.91))\); \(p<0.05\). Similar results were found by Kumari et al. [11, 14] History of hypertension was a risk factor in the progression of DR. Similar type results were determined by Hong et al., Pradeepa et al. [15, 16] But, in our study also the history of hypertension was showed a significant association in the progression of DR.

Duration of diabetes mellitus 10 years or longer was showed a significant factor in the development of DR in diabetes. Similar type result was found by Roberts et. al., Kawasaki et. al. [17, 18] HbA1C was a risk factor and association with the development/progression of DR. The same type of results was found by Song et al. [19] In this study, we have got total cholesterol was a prominent risk factor with 5-fold with DR and it was an influencing with the development/progression of DR but not showed any significant with DR in the multivariate analysis.

In a study by Abougalamou and Abougalamou. [20] have obtained fasting blood sugar was a risk factor in the progression of retinopathy. Brambilla et al. has also arrived similar result in the study. [21] There was a positive correlation between DR and age with 60 years and above but, not showed any significant with DR development. But in a study by Stratton et al. has determined the older age was associated with the progression of DR. [22]

**Conclusion:** From this study revealed that the influencing variables were HbA1C, smoking habit, intake of tablet/insulin, duration of DM (longer years), history of hypertension and fasting blood sugar in a known T2DM patient. The chance/probability of developing retinopathy was very high among diabetes patients those who have had longer duration of diabetes mellitus. Hence, we have to recommend to the diabetic/retinopathy patients to get health education and eye care from their family physician/endocrinologist/authorized diabetic/retina Centre public health professionals. Moreover, the diabetic patients have to go for a periodic eye screening once in six months to prevent from the development of DR, or to avoid, or to retain in the same severity stage or to rescue themselves from loss of eye sight.

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**Authors’ contributions:** AP, SV: Conception and Study design; AP: Acquisition of Data; AP, SV: Data processing, Analysis and Interpretation of Data; Both the authors – AP and SV were drafting the article, revising it for intellectual content; Both authors were checked and approved of the final version of the manuscript.

Here, AP – Amitha Prasad; SV – Senthilvel Vasudevan

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**References:**


