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# The association of HbA1c and duration of Type 2 Diabetes Mellitus with the prevalence and severity of Diabetic Retinopathy.

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**ABSTRACT:**

**Background:** Type 2 diabetes mellitus (T2DM) is a chronic health condition worldwide leading to micro and macro vascular complications. Diabetic Retinopathy (DR) is one of the major microvascular complications of diabetes. Aim of this study is to find the association of HbA1c and duration of T2DM on the prevalence of Diabetic Retinopathy (DR) and its severity.

**Methods:**A descriptive Cross-sectional study, data collected from 500 T2DM participants using a structured questionnaire. Most recent DR status, demographic details and laboratory results were obtained from the case file of the participants.

**Results:**This T2DM study population (n=500) had a mean age of 58.21±10.24 years, mean duration of diabetes of 11.22±7.47 years and mean Hba1c of 8.31±1.80%

Hba1c of 8 to 10% was associated with higher proportion of DR (52%) compared to Hba1c of <8% (29%), which shows a trend towards higher prevalence of DR with increasing HbA1c %. The correlation between HbA1c and DR was statistically significant ($p<0.05$). Hba1c of 8 to 10% was associated with higher percentage of severe forms of DR (Proliferative Diabetic Retinopathy [PDR] 56%, severe Non Proliferative Diabetic Retinopathy [NPDR] 46%) when compared to HbA1c of <8% (PDR 30%, severe NPDR 23%). All the 11 DME cases were seen in participants with Hba1c >10%. This shows that, higher the Hba1c greater the severity of DR. This association was statistically significant with p value <0.005.

Duration of DM 11 to 15 and >15 years had higher proportion of DR (52.6%vs73.6%) in comparison with duration of DM ≤5years and 5 to 10years (9.3%vs 22.6%). So greater the duration of DM higher the proportion of DR.Duration of diabetes more than 10 years was associated with 62.3%, 74.35%, 92.3%, and 96.3% of Mild NPDR, Moderate NPDR, Severe NPDR and PDR respectively. In duration of diabetes <10years the proportion of Mild NPDR, Moderate NPDR, Severe NPDR and PDR was, 37.6%, 25.64%, 23%, 3.7% respectively. All 11 DME cases were seen in pts with duration of T2DM more than 10 years. The association between duration of T2DM and severity of DR was statistically significant ($p<0.05$). This shows that higher the duration of T2DM, greater the severity of DR.

**Conclusion:**The study concludes that higher the Hba1c and greater the duration of T2DM, the prevalence and severity of Diabetic Retinopathy increases. This shows the importance of good glycaemic control and regular follow up to prevent and reduce the severity of Diabetic Retinopathy.

## I. INTRODUCTION:

Diabetes mellitus is a major public health concern globally leading to micro and macro vascular complications. Around 537 million adults had diabetes worldwide, according to 2021 IDF estimates, which is predicted to rise to an alarming 643 million by 2030 and 783 million by 2045 (1). It was estimated that in 2021 there were 101million and 136 million people living with diabetes and prediabetes respectively, in India (2). This is estimated to increase to 134.3 million diabetes cases by 2045 (1).

With this increasing prevalence of diabetes worldwide, there will be an increased burden of diabetes related complications including Diabetic Retinopathy. DR is one of the important causes of blindness. According to a meta-analysis done in 2016, DR accounted for 2.6% all blindness in 2010 and 1.9% of all moderate/severe visual impairment worldwide,increasing from 2.1% and 1.3%, respectively, in 1990 (3).

Hyperglycaemia plays a major role in the retinal microvascular damage through several pathways like, polyol pathway, protein kinase C

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pathway, advanced glycation end products accumulation and hexosamine pathway (4). A cross sectional study done in Saudi Arabia showed that the Hba1c level and duration of diabetes were significant risk factors for DR and its severity (5). A south Indian Study showed that the severity of DR increases with increasing Hba1c levels (6). Study done by Kim HU et al, concluded that glycaemic variability could be an independent risk factor for the development of DR in addition to mean HbA1c levels (7). UKPDS study emphasised the need for good glycaemic control in preventing the progression of Diabetic Retinopathy (DR) (8).

With this background our study aimed at looking into the association of Hba1c and duration of T2DM on the prevalence and severity of diabetic retinopathy

## II. METHOD:

Descriptive cross sectional study conducted at Karnataka Institute of Endocrinology and Research (K.I.E.R), Bengaluru, India. DR status, demographic details, anthropometric measurements, metabolic parameters were collected from the case files of participants and through a structured questionnaire. Data was collected from 500 participants during OPD consultation between August 2022 to November 2022. Informed consent was taken from all participants.

Inclusion criteria: Type 2 DM patients

Exclusion criteria:

- Type 1 diabetes mellitus
- Gestational and other types of diabetes mellitus
- Who couldn't give informed consent

Diabetes mellitus was diagnosed using ADA criteria. Fundus examination was done at Department of Ophthalmology at Karnataka Institute of Endocrinology and Research, Bengaluru. All the patients included in our study underwent detailed Fundus evaluation. Their best corrected visual acuity, intraocular pressure evaluation and a detailed slit lamp examination was done prior to the dilatation. The DR was graded according to Early Treatment Diabetic Retinopathy Study (ETDRS) classification.

**Statistical analysis:**

Data analysed using descriptive and inferential statistics, using statistical softwareSPSSv23 and MSExcel.

Descriptive statistics: distribution of demographics is expressed as frequency and percentages; continuous data is expressed as mean and standard deviation.

Inferential statistics: Chi square test was used to find the association between the attributes. All statistical analysis was carried out at 5% level of significance and p-value of $<0.05$ is considered as significant.

## III. RESULTS:

Total of 500 type 2 diabetes participants were included in the study.72% of the study population were above 50years of age. Mean age was 58.21±10.24 years, mean duration of diabetes was 11.22±7.47 years, mean BMI was 26.20±3.66kg/m2 and mean Hba1c was 8.31±1.80%. Present study had 41% female and 59% male participants. Out of 500 participants, 493 (99%) were on OADs, 96 (19%) were on insulin. HTN was seen in 264 (53%) and Dyslipidaemia was seen in 482 (96%). According to area wise distribution, out of 500 study participants, about 66% were from urban area, 63% from town and 58% from rural area.

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| TABLE NO 1: STATUS OF OADS, INSULIN , HTN AND DYSLIPIDAEMIA | | | | |
|---|---|---|---|---|
| **STATUS** | **OADs** | **Insulin** | **HTN** | **Dyslipidaemia** |
| YES | 493 (99%) | 96 (19%) | 264 (53%) | 482 (96%) |
| NO | 7 (1%) | 404 (81%) | 236 (47%) | 18 (4%) |
| **TOTAL** | **500** | **500** | **500** | **500** |

| TABLE NO 2: AGE WISE DISTRIBUTION OF CASES (n=500) | | | | | | |
|---|---|---|---|---|---|---|
| **AGE IN YEARS** | **FEMALE** | **%** | **MALE** | **%** | **GRAND TOTAL** | **%** |
| 25 - 30 | 2 | 1% | 3 | 1% | 5 | 1% |
| 31 - 40 | 22 | 11% | 21 | 7% | 43 | 9% |
| 41 - 50 | 47 | 23% | 59 | 20% | 106 | 21% |
| 51 - 60 | 67 | 32% | 103 | 35% | 170 | 34% |
| 61 - 70 | 56 | 27% | 70 | 24% | 126 | 25% |
| > 70 | 13 | 6% | 37 | 13% | 50 | 10% |
| **TOTAL** | **207** | **100%** | **293** | **100%** | **500** | **100%** |

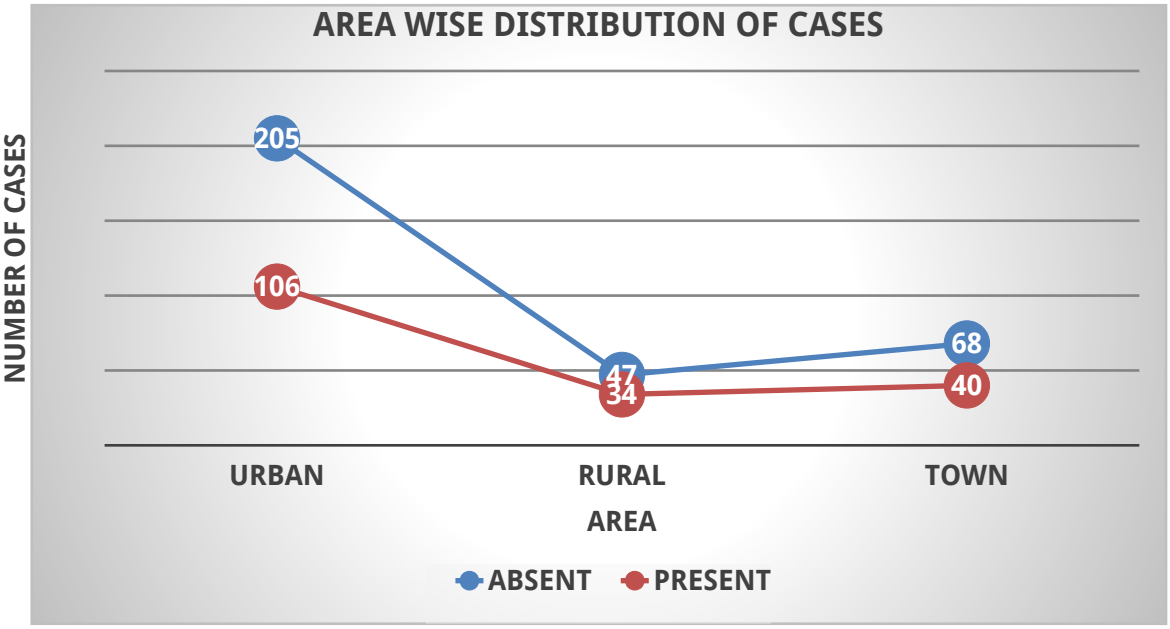


Figure 1:

Total of 180 (36%) out of n=500 had DR. Out of which 101 (20%), 39 (8%), 13 (3%), 27 (5%) had, Mild Non Proliferative Diabetic Retinopathy (NPDR), Moderate NPDR, Severe NPDR and Proliferative Diabetic Retinopathy (PDR) respectively. Out of these 180 participants with DR only 11participants had DME (6% of 180 DR cases).

Among female and male study participants DR was seen in 28.5% and 41.3% of the respective gender group, with an 12.8% difference.Though this study had predominantly urban population (62.2%), Rural population (16.2%), had relatively higher proportion of DR cases (42%) compared to Town (37%) and urban (34%) areas.

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| TABLE NO 3: DIABETIC RETINOPATHY PRESENT STATUS | | | | |
|---|---|---|---|---|
| GENDER | NUMBER OF CASES | DIABETIC RETINOPATHY | | DIABETIC RETINOPATHY PRESENT PERCENTAGE |
| | | ABSENT | PRESENT | |
| MALE | 293 | 172 | 121 | 41.3% |
| FEMALE | 207 | 148 | 59 | 28.5% |
| TOTAL | 500 | 320 | 180 | 36.0% |

| TABLE NO 4: INCIDENCE OF DIABETIC RETINOPATHY BASED ON SEVERITY (n=500) | | |
|---|---|---|
| DIABETIC RETINOPATHY SEVERITY | NO.OF PATIENTS* | PERCENTAGES |
| MILD NDPR | 101 | 20% |
| MODERATE NPDR | 39 | 8% |
| SEVERE NPDR | 13 | 3% |
| PDR | 27 | 5% |
| DME | 11 | 2% |

| TABLE NO 5: CORRELATION OF DIABETIC RETINOPATHY WITH RESPECT TO CLINICAL VARIABLES | | | | |
|---|---|---|---|---|
| CLINICAL VARIABLES | DIABETIC RETINOPATHY | | | |
| | ABSENT | PRESENT | Chi-Square Value | P-VALUE |
| **GENDER** | | | | |
| MALE | 172 | 121 | 8.618 | 0.00332 |
| FEMALES | 148 | 59 | | |
| **DURATION OF DM (in Years)** | | | | |
| ≤5 | 117 | 12 | 131.832 | 0 |
| 6-10 | 130 | 38 | | |
| 11-15 | 44 | 49 | | |
| >15 YEARS | 29 | 81 | | |
| **BMI (Kg/m2)** | | | | |
| <18.5 | 3 | 3 | 1.0438 | 0.7906 |
| 18.5-22.9 | 48 | 31 | | |
| ≥23-25 | 56 | 29 | | |
| >25 | 213 | 117 | | |
| **Place of Residence** | | | | |
| Urban | 205 | 106 | 1.8013 | 0.4062 |
| Rural | 47 | 34 | | |
| Town | 68 | 40 | | |
| **HbA1c Levels** | | | | |
| <8.0 | 227 | 93 | 20.6671 | 0.00003 |
| 8.0 - 10.0 | 56 | 61 | | |
| >10 .0 | 37 | 26 | | |
| **OADS** | | | | |

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| | | | | |
|---|---|---|---|---|
| **YES** | 313 | 180 | 3.9934 | 0.0456 |
| **NO** | 7 | 0 | | |
| **Insulin** | | | | |
| **YES** | 23 | 73 | 82.6802 | 0 |
| **NO** | 297 | 107 | | |
| **HTN** | | | | |
| **YES** | 149 | 115 | 13.8769 | 0.00019 |
| **NO** | 171 | 65 | | |
| **Dyslipidemia** | | | | |
| **YES** | 309 | 173 | 0.0676 | 0.7948 |
| **NO** | 11 | 7 | | |

**Correlation of prevalence of DR and its severity with HbA1c:**

In study population with Hba1c <8%, 8 to 10% and >10%, the proportion of DR was 29%, 52% and 41.2% respectively. The correlation of Hba1c levels to occurrence of DR was statistically significant (p value <0.05). This shows that the worsening Hba1c is associated with higher prevalence of DR

The severe forms of DR were more in study population with HbA1c > 8%. Out of 69 pts with DR and Hba1c in the range of 8 to 10%, 56% had PDR, 46% had Severe NPDR, 26% had Moderate NPDR and 31% had Mild NPDR. This group had highest number of DME, which is 73% (8/11) of all DME cases. However, compared to the above, study population with Hba1c of <8%, had more cases of mild NPDR (60%), followed my Moderate NPDR (54%), PDR (30%) and severe NPDR (23%). The correlation of severity of DR with HbA1c showed statistical significance (p<0.05). This points out that higher the HbA1c, greater the severity of DR.

The Hba1c range 8 to 10% had the highest number of DR cases and also DR severity was more in this HbA1c group.

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| TABLE NO 6: CORRELATION OF SEVERITY OF DIABETIC RETINOPATHY WITH LEVELS OF HbA1C | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| DIABETIC RETINOPATHY SEVERITY | NO.OF PATIENTS* | % | HbA1c Level | | | | | | TOTAL | P-Value |
| | | | < 8.0 | % | 8.0 - 10.0 | % | > 10 .0 | % | | |
| MILD NDPR | 101 | 20% | 61 | 60% | 30 | 31% | 10 | 9% | 100% | 0.098 |
| MODERATE NPDR | 39 | 8% | 21 | 54% | 10 | 26% | 8 | 21% | 100% | 0.2376 |
| SEVERE NPDR | 13 | 3% | 3 | 23% | 6 | 46% | 4 | 31% | 100% | **0.0069** |
| PDR | 27 | 5% | 8 | 30% | 15 | 56% | 4 | 15% | 100% | **0.00012** |
| DME | 11 | 2% | 1 | 9% | 8 | 73% | 2 | 18% | 100% | **0.00017** |
| TOTAL | | | 94 | | 69 | | 28 | | | |

**Duration of DM and its correlation with prevalence and severity of DR:**

Out of 129 T2DM participants with duration of T2DM≤5 years, the proportion of DR was 9.3%.For Duration of T2DM 6 to 10, 11 to 15, > 15 years, the proportion of DR were 22.6%, 52.6%, 73.6% respectively. This shows a trend towards higher prevalence of DR, in those with longer duration of T2DM, though the association was not statistically significant.

Duration of diabetes more than 10 years was associated with 62.3%, 74.35%, 92.3%, and 96.3% of Mild NPDR, Moderate NPDR, Severe NPDR and PDR respectively. In Duration of DM <10years the occurrence of Mild NPDR, Moderate NPDR, Severe NPDR and PDR was, 37.6%, 25.64%, 23%, 3.7% respectively. All 11 DME cases were seen in pts with duration of T2DM more than 10years.From this it can be implied that longer the duration of T2DM greater the severity of DR. The correlation between duration of T2DM and severity of DR was statistically significant.

| TABLE NO 7: SEVERITY OF DR AND DURATION OF DIABETES | | | | | | | |
|---|---|---|---|---|---|---|---|
| SEVERITY OF DR | NUMBER OF CASES | DURATION OF DIABETES | | | | Chi-Square | P-Value |
| | | ≤ 5 | 6-10 | 11-15 | > 15 YEARS | | |
| MILD NDPR | 101 | 6 | 32 | 31 | 32 | **35.33** | **0.00041** |
| MODERATE NPDR | 39 | 5 | 5 | 10 | 19 | | |
| SEVERE NPDR | 13 | 0 | 1 | 2 | 10 | | |
| PDR | 27 | 1 | 0 | 6 | 20 | | |

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| | | | | | | |
|---|---|---|---|---|---|---|
| **DME** | 11 | 0 | 0 | 4 | 7 | |

**Other findings**: Other clinical biomarkers which showed statistically significant association with DR were, Hypertension, being on Oral Antihyperglycaemic agents (OAH) and gender (Table 5).

## IV. DISCUSSION:

The purpose of this study was to find the association of HbA1c level and duration of diabetes, with the prevalence and severity of Diabetic Retinopathy. The prevalence of DR in our study was 36%, which is substantially higher compared to other Indian studies. Results from a national survey 2015-2019 showed a DR prevalence of 11.8% (9), SMART India study showed a prevalence rate of 12.5% (10).CURES study done in Chennai (South India City) showed a prevalence rate of 17.6% (11). The difference might be because of smaller population size in our study and the DR screening method used is different from our method, in screening programmes.

The association between HbA1c level and development of DR and its severity, was statistically significant in our study, which is similar to other Indian and Asian studies (8, 12, 13). This reiterate the fact that HbA1c is an important risk factor for the development and progression of DR and shows the significance of glycaemic control in order to prevent and reduce the progression of DR.

Duration of diabetes is one of the most important risk factors for the development and progression of DR. The proportion of DR increased with increase in the duration of T2DM in our study. The results are similar to The Wisconsin epidemiologic study of diabetic retinopathy. III (14). Some Indian studies have also shown similar results (11, 15).

The duration of diabetes > 10 years was associated with more severe forms of DR and duration <10 years was associated more with milder forms of DR in our study. These results match with a study done in Germany by Voigt M et al, which concluded that within the first 10 years of diabetes duration, the prevalence of DR is low and non-proliferative forms are more, which rarely requires any intervention (16). These findings emphasise the need for regular screening for DR in diabetic patients and to take necessary action when needed. This is important because people tend to present late to ophthalmology department only when their vision is affected. Educating diabetics regarding the need for regular follow up is necessary.

Gender (male), being on OHAs and hypertension were other clinical variables which had statistically significant association with DR (17). These findings are replicated in several other studies looking into the prevalence and risk factors for DR (11, 15, 17).

This Study has several limitations. The population sample size being small and need bigger sample size and a multicentre approach to look into the association and prevalence rate. The study design is a cross sectional study, so causality cannot be determined. Hence prospective studies with a larger population size are needed to verify the results.

## V. CONCLUSION:

The present study showed that HbA1c and duration of diabetes are important risk factors for the development and progression of diabetic retinopathy. This emphasises good glycaemic control and regular follow up to look into the DR status, in order to prevent, take appropriate action and reduce the progression of diabetic retinopathy.

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