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Original Research Article

Examining the Relationship Between HbA1c Levels and the Occurrence of Diabetic Retinopathy in Patients with Type 2 Diabetes: A Cross-Sectional Observational Study in a Hospital Setting

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Abstract:

Diabetic retinopathy remains a significant cause of vision impairment among individuals with type 2 diabetes mellitus. This cross-sectional hospital-based observational study aims to investigate the correlation between HbA1c levels and the prevalence of diabetic retinopathy in a cohort of type 2 diabetes patients. The study included 40 patients, who underwent HbA1c measurements and retinal examinations. The results of the study demonstrated a clear association between elevated HbA1c levels and the presence of diabetic retinopathy. Patients with higher HbA1c values exhibited a greater likelihood of developing retinopathy, highlighting the importance of glycemic control in managing diabetic complications. Subgroup analyses were conducted to assess other potential risk factors, such as the duration of diabetes, blood pressure, and lipid profiles. The findings underscore the significance of routine HbA1c monitoring as a valuable tool in assessing the risk of diabetic retinopathy in type 2 diabetes patients. This research contributes to a better understanding of the relationship between glycemic control and retinopathy, offering insights that could guide clinical practice and improve the prevention and management of diabetic complications in this patient population. Further longitudinal studies may be warranted to confirm these findings and investigate the potential benefits of early intervention in high-risk individuals.

Materials and Methods: This study involved a total of 80 participants, comprising two distinct groups: 40 patients diagnosed with type 2 diabetes mellitus (T2DM) and concurrent retinopathy, and 40 patients with T2DM but without retinopathy. All patients are subjected to the detailed history taking, ocular examination and investigations like FBS, PPBS and HBA1C estimation.

Result: Among the 40 patients diagnosed with diabetic retinopathy, the group with proliferative diabetic retinopathy demonstrated the lowest level of glycemic control, with a mean glycated hemoglobin (HbA1c) value of 11.47 ± 2.21. Statistical analysis using a one-way analysis of variance (ANOVA) revealed a highly significant result, with a p-value of less than 0.001. This underscores a strong and statistically significant association between the severity of diabetic retinopathy and glycemic control, particularly in the context of proliferative diabetic retinopathy.

Conclusion: This study has unveiled a compelling association between glycemic control and the severity of diabetic retinopathy in a cohort of 40 diabetic retinopathy patients. Notably, among these patients, those afflicted with proliferative diabetic retinopathy exhibited the poorest glycemic control, as reflected by their markedly elevated mean glycated hemoglobin (HbA1c) level of 11.47 ± 2.21.

Keywords: Glycemiccontrol, Diabetic retinopathy, Proliferative diabetic retinopathy, HbA1c (Glycated hemoglobin).

Introduction

Diabetes mellitus poses a significant and escalating global health challenge, ranking as the ninth leading cause of mortality on a worldwide scale. Type 2 diabetes mellitus, a chronic metabolic disorder, is characterized by persistent hyperglycemia, driven by a multitude of

contributing factors. The global prevalence of diabetes across all age groups stood at 2.8% in the year 2000, but by 2030, it is estimated to have surged to 4.4%. Projections indicate a substantial increase in the total number of individuals afflicted with diabetes, with figures anticipated to climb from 171 million in 2000 to a staggering 366 million by 2030. Particularly, diabetes mellitus is expected to exhibit a twofold increase within urban populations in developing countries from 2000 to 2030. Diabetic patients are susceptible to the multi-system complications of diabetes mellitus, encompassing conditions such as retinopathy, nephropathy, neuropathy, and cardiovascular diseases. Of these complications, diabetic retinopathy ranks as one of the most prevalent ophthalmic issues associated with diabetes, and it stands as a leading cause of vision impairment among individuals of working age across the globe. According to the World Health Organization (WHO), it is estimated that diabetic retinopathy contributes to approximately 4.8% of the 37 million cases of blindness worldwide. Globally, roughly 30% of individuals with diabetes mellitus are believed to experience diabetic retinopathy. Persistent elevation of blood sugar levels, known as chronic hyperglycemia, stands as a significant risk factor in the onset of microvascular complications in diabetes mellitus. HbA1c, owing to its pronounced affinity for oxygen, can contribute to tissue oxygen deficiency, thereby playing a pivotal role in the development of both microvascular and macrovascular complications.

A direct correlation exists between the extent of glycemic control and the likelihood of experiencing or advancing retinopathy. The pathogenesis of diabetic retinopathy is complex, involving multifactorial interactions, but it is widely accepted that glycemic control plays a pivotal role in its development and progression. This study delves into the intricate relationship between glycemic control, as indicated by the level of glycated hemoglobin (HbA1c), and the occurrence and severity of diabetic retinopathy. Specifically, our investigation focuses on a cohort of 40 patients diagnosed with diabetic retinopathy, categorizing them based on the severity of their retinopathy, with special attention to those with proliferative diabetic retinopathy. Proliferative diabetic retinopathy represents the advanced and vision-threatening stage of this ocular complication. Understanding the association between glycemic control and diabetic retinopathy, particularly in its most severe form, holds significant clinical relevance. Vision impairment due to diabetic retinopathy not only impacts the quality of life of affected individuals but also places a substantial burden on healthcare systems. Therefore, pinpointing the significance of glycemic control in the context of diabetic retinopathy can guide healthcare providers in implementing tailored interventions for patients at risk. This investigation aims to shed light on this critical link between glycemic control and diabetic retinopathy, ultimately contributing to a deeper comprehension of the role of glycemic management in preventing and managing this vision-threatening complication among individuals with diabetes.

Aims and Objectives

1. To assess serum HbA1c levels in individuals with type 2 diabetes mellitus, with a specific focus on those affected by diabetic retinopathy.
2. To examine the correlation between serum HbA1c levels and the severity of diabetic retinopathy.

Materials and Methods

This study involved a total of 80 participants, comprising two distinct groups: 40 patients diagnosed with type 2 diabetes mellitus (T2DM) and concurrent retinopathy, and 40 patients with T2DM but without retinopathy.

Inclusion Criteria

1. Patients admitted to a Tertiary care Teaching Govt. Hospital at North East India with Type 2 Diabetes Mellitus according to the 2020 ADA guidelines.
2. Patients or their legally acceptable representatives (LAR) who have provided informed consent for participation in the study.

Exclusion Criteria

1. Patients below the age of 30 and individuals with other types of diabetes, including Type 1 Diabetes Mellitus, MODY, LADA, and Gestational Diabetes Mellitus.
2. Patients with retinopathy caused by factors other than diabetes, such as hypertensive retinopathy, lupus retinopathy, or sickle cell retinopathy.
3. Individuals with malabsorption syndrome.
4. Patients with chronic renal failure.
5. Individuals currently taking magnesium supplements, loop diuretics, steroids, or those with a history of alcoholism.
6. Patients who have experienced an acute myocardial infarction within the past 6 months.
7. Pregnant women with hypertension, proteinuria, and preeclampsia.
8. Patients with conditions or media opacity that prevent the visualization of the posterior segment of the eye.

The research protocol involved a comprehensive evaluation encompassing the following components:

1. **Patient Selection and Information Gathering**: All participants underwent a

meticulous selection process. Detailed medical histories were collected to ascertain the duration of diabetes and any pertinent medical conditions.

2. **Ocular Examination**: A thorough ocular examination was conducted on all participants. This examination focused on the assessment of retinal health and the presence or absence of diabetic retinopathy.
3. **Laboratory Investigations:** Blood samples were collected from all participants to assess various biochemical parameters.

The following tests were performed:

1. Fasting blood sugar (FBS) analysis
2. Postprandial blood sugar (PPBS) analysis
3. Evaluation of glycated hemoglobin (HbA1c) levels

The study design ensured the comparative analysis of these parameters between the two groups (T2DM with retinopathy and T2DM without retinopathy). This approach allowed us to explore potential associations and implications of these variables in the context of diabetic retinopathy.

Ethical Permission

This study received ethical approval from the Institutional Ethics Committee(H). Prior to data collection, written informed consent, validated in the local language, was obtained from all participants. Data were collected using a pre-designed and pre-tested structured Proforma. Patient examinations were conducted following the informed consent process. The examinations involved a detailed history-taking, comprehensive ocular assessment including visual acuity determination, and fundus examination. Fundus Fluorescein Angiography (FFA) or Optical Coherence Tomography (OCT) was performed when clinically necessary. Participants were categorized into two groups: those with diabetic retinopathy and those without. Severity of diabetic retinopathy in patients was graded based on the Early Treatment Diabetic Retinopathy Study (ETDRS) classification.

Blood samples were collected for the assessment of various parameters, including HbA1c levels, serum electrolytes and blood sugar levels. HbA1c levels were measured using the high-performance liquid chromatography technique. In cases of patients with asymmetric fundus findings, the eye with the more severe grade of diabetic retinopathy was considered for analysis.

Statistical Analysis

The data analysis was conducted using IBM SPSS version 23.0. Student's independent t-tests and ANOVA tests were employed to assess differences between various groups. Statistical significance was determined at a p-value of less than 0.05.

Results and Observations

During the one-year study period spanning 2020 to 2021, individuals who met the specified inclusion and exclusion criteria were included in the study, resulting in a total of 80 patients being analyzed. Of the 80 participants with type 2 diabetes, the distribution by age was as follows:

1. 5% (4) were between 30 and under 40 years.
2. 18.75% (15) fell within the age range of 40 to under 50 years.
3. 33.75% (27) were aged between 50 and under 60 years.
4. 31.25% (25) were in the 60 to under 70 years age group.
5. 11.25% (9) were 70 years of age or older.

Regarding gender distribution within the study population:

1. 56.25% (45) were male.
2. 43.75% (35) were female.

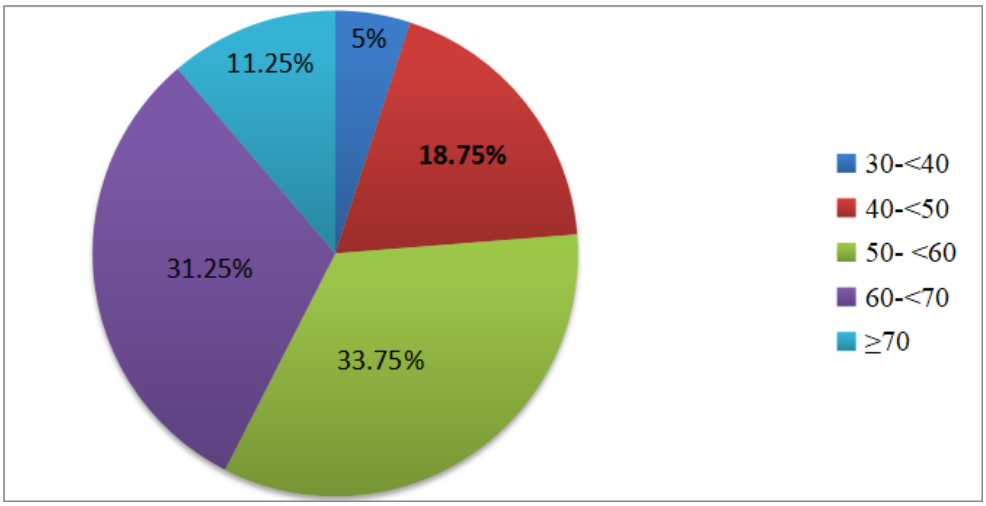

Figure 1: Diagram showing age wise distribution of the study population

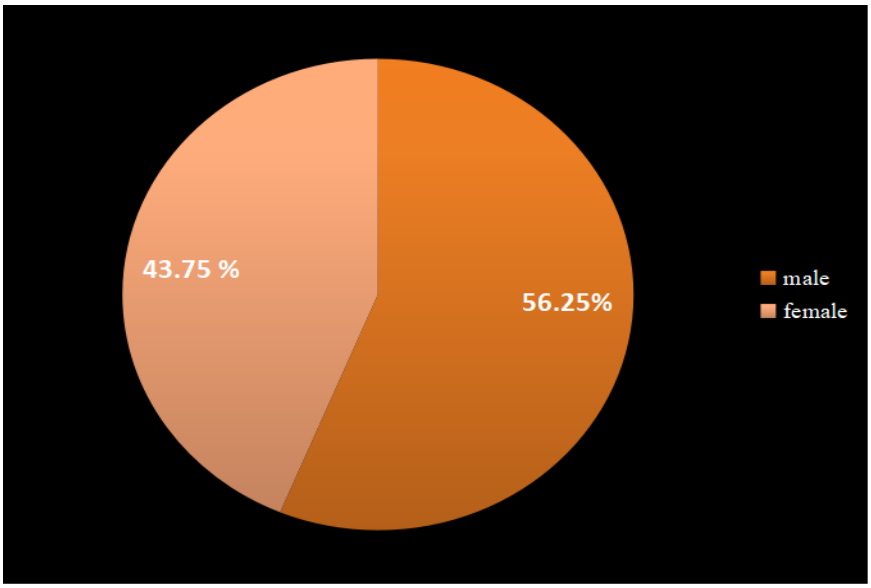

Figure 2: Diagram showing sex wise distribution of study population

Table 1:

Group	HbA1c level			P value
	≥7	<7	Mean±	
With DR(N=40)	38[48.75%]	1[1.25%]	9.42±1.28	0.02
Without DR(n= 40)	33[41.25%]	7[8.75]	8.40±1.91	

Glycated haemoglobin level in Type 2 Diabetes Mellitus with and without Diabetic Retinopathy.

HbA1c level <7 found maximum in diabetic patient without diabetic retinopathy and HbA1c ≥ 7 found maximum in diabetic retinopathy patients. Mean±SD HbA1c Level found 9.42±1.28 and 8.40±1.91 in diabetic retinopathy and without diabetic retinopathy in type 2 diabetic patients respectively.

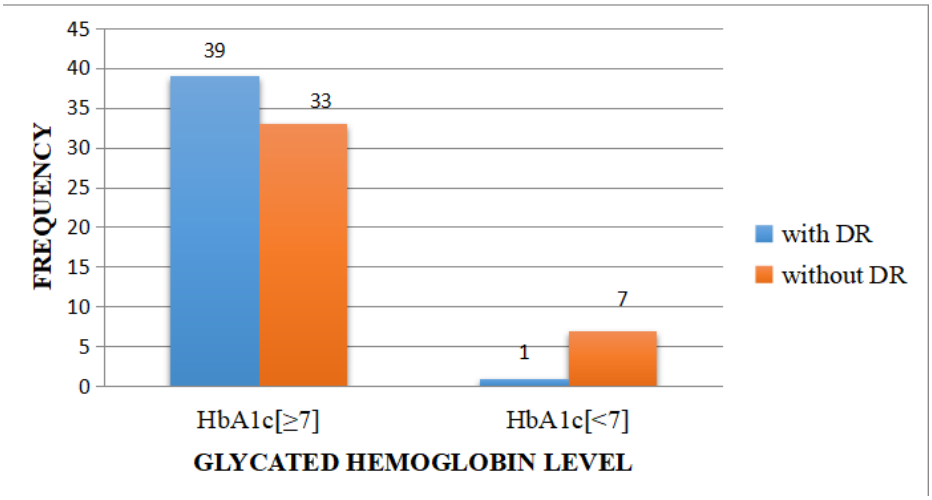

Figure 3: Glycated haemoglobin level

Bar Diagram showing HBA1C Level in Type 2 diabetes mellitus with and without Diabetic Retinopathy.

Table 2:

Group	FBS	PPBS
With DR	227±42.40	292.05±48.69
Without DR	178.73±46.89	244.03±55.05
P value	<0.001	<0.001
	t = 4.830	t = 4.133

The mean ± standard deviation (SD) values of fasting blood sugar (FBS) and postprandial blood sugar (PPBS) levels were compared between diabetes patients with and without retinopathy.In the study involving 80 type 2 diabetes patients, the mean fasting blood sugar (FBS) level was

227±42.40 mg/dl in those with diabetic retinopathy and 178.73±46.89 mg/dl in those without diabetic retinopathy. The application of an independent t-test revealed a statistically significant difference between these groups (p-value <0.001). Similarly, the mean postprandial blood sugar (PPBS) levels were 292.05±48.69 mg/dl in the diabetic retinopathy group and 244.03±55.05 mg/dl in the group without diabetic retinopathy. Notably, higher FBS and PPBS values were observed in the diabetic retinopathy group, underlining a significant association between elevated blood sugar levels and the presence of diabetic retinopathy.

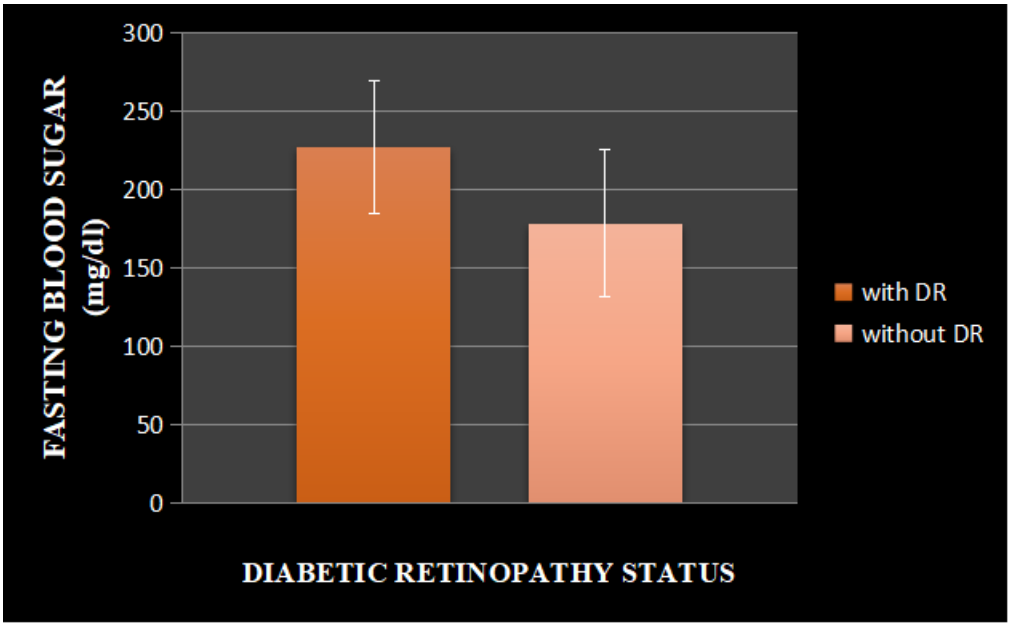

Figure 4: Diabetic Retinopathy status

The mean ± standard deviation (SD) values of fasting blood sugar (FBS) levels were compared between diabetes patients with and without retinopathy.

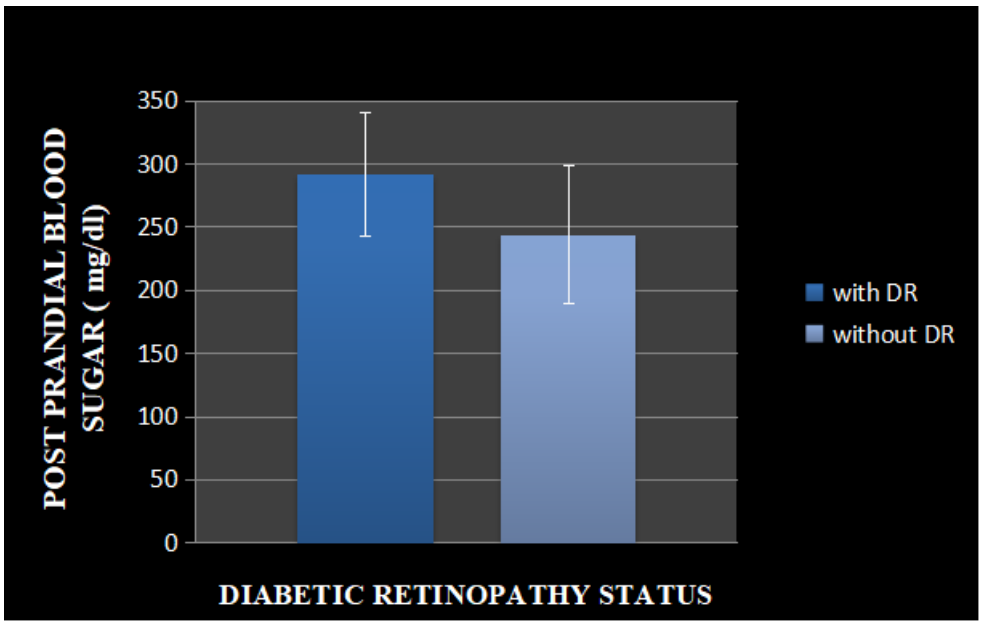

Figure 5: Diabetic Retinopathy status

The mean ± standard deviation (SD) values of postprandial blood sugar (PPBS) levels were compared between diabetes patients with and without retinopathy.

Table 3:

Group	Duration of Diabetes [Mean±SD]	P value
With DR	10.46±2.90	<0.001
Without DR	5.20±2.90	

The mean ± standard deviation (SD) duration of diabetes was compared between diabetic patients with and without diabetic retinopathy. Within the diabetic patient population, the mean duration of diabetes differed notably between those with diabetic retinopathy and those without, with mean durations of 10.46 ± 2.90 years and 5.20 ± 2.72 years, respectively.

Employing an independent t-test, a statistically significant difference was observed (p-value = 0.001), highlighting the clinical significance of this disparity.

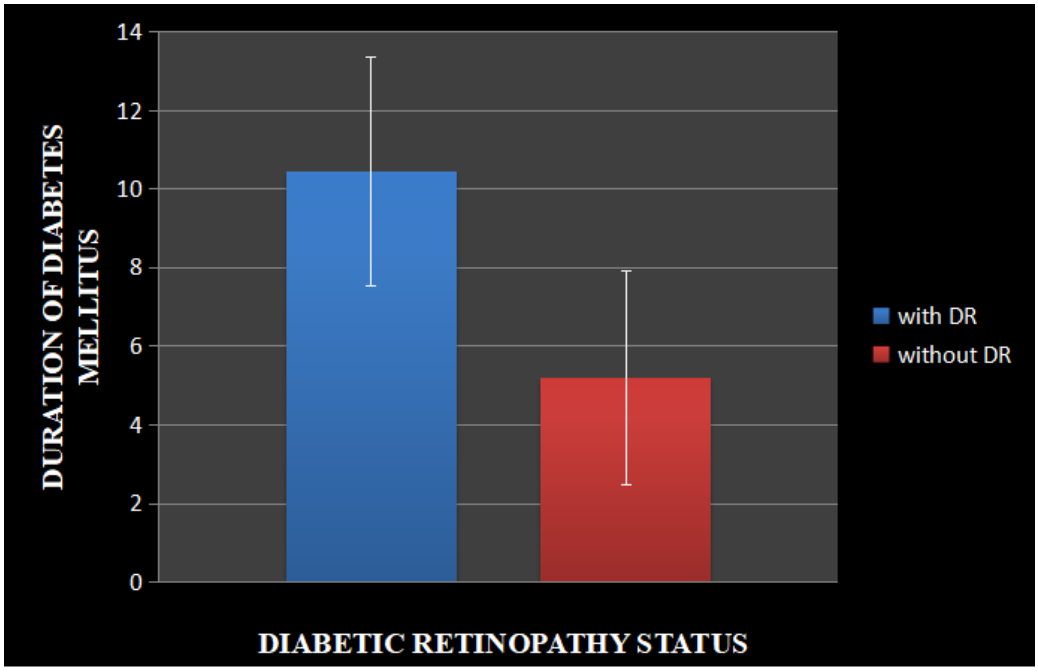

Figure 6: Diabetic Retinopathy status

The mean ± standard deviation (SD) duration of diabetes was compared between diabetic patients with and without diabetic retinopathy.

Table 4:

Stages	No. Of cases(n=40)	Percentages(%)
Mild NPDR	12	30
Moderate NPDR	14	35
Severe NPDR	7	17.5
Very Severe NPDR	4	10
PDR	3	7.5

Diabetic retinopathy manifests in various stages.

Discussion

Demography of the present study

In the current study, the distribution of age groups among type 2 diabetes patients was as follows:

Age distribution

The highest proportion, 33.75% (27 individuals), was in the age group of 50 to under 60 years. The second-highest proportion, 31.25% (25 individuals), fell within the 60 to under 70 years age group. A study conducted by Singh C et al. reported the following age group distribution among 330 subjects:

The majority, 69.09% (228 subjects), were in the age group of 51 to 65 years.16.36% (54 subjects) were aged between 36 and 50 years.13.33% (44 subjects) were in the age group of 66 to 80 years.0.91% (3 subjects) were between 21 and 35 years.0.3% (1 subject) was above 80 years. Similarly, Bagzai DS et al. observed the following age group distribution in their study: The majority of the patients, 54.87%, were in the age group of 41 to 60 years.25.63% were in the age group of 61 to 80 years. Consistent findings were reported by Uppara V et al., who noted that 29% of their study's 100 diabetic patients were in a similar age group.

Sex distribution

In the current study comprising 80 diabetic patients, 56.25% were males, and 43.75% were females, resulting in a male-to-female ratio of 1.28:1. This indicates a male predominance in the sample. These findings align closely with those of Singh C et al., who reported that among 330 diabetic patients, 57.88% were males, and 42.12% were females. Similarly, Bagzai DS et al. found in their study of 472 patients that 55.29% were males,

and 44.71% were females. The present study's results were consistent with the observations of Reddy et al., who reported that among 210 type 2 diabetes patients, 58.5% were men, and 41.5% were women. Rana HM et al. documented similar sex distribution in their study, with 50.8% males and 49.1% females among 167 diabetes patients.

Comparative Analysis of Glycated Hemoglobin Levels in Type 2 Diabetes Patients With and Without Diabetic Retinopathy: In our current study, we observed a notably higher level of glycated hemoglobin in the diabetic retinopathy group when compared to diabetic patients without diabetic retinopathy. The statistical analysis yielded a p-value of 0.002, indicating a statistically significant difference.

Table 5:

Study	With DR	Without DR	P value
Singh c et. al.[90]	9.50	8.49	<0.05
Khalid m et. al.[91]	9.32	7.29	,0.001
Parasar v et al.[110]	8.53	7.50	<0.01
Haddad NS et al.[147]	9.3	7.4	0.001
Present study	9.42	8.40	0.002

Comparative Analysis of Fasting and Postprandial Blood Sugar Levels in Type 2 Diabetes Patients With and Without Diabetic Retinopathy

In our study of 80 diabetic patients, we observed that mean fasting blood sugar (FBS) levels were significantly higher in the diabetic retinopathy group, with a mean of 227±42.40 mg/dl, compared to 178.73±46.89 mg/dl in diabetics without diabetic retinopathy. This difference was statistically significant with a p-value of less than 0.001. Similarly, the mean postprandial blood sugar (PPBS) levels were significantly elevated in the diabetic retinopathy group, with a mean of 292.05±48.69 mg/dl, as opposed to 244.03±55.05 mg/dl in the group without retinopathy. Our findings were consistent with those of Parasar V et al., who reported higher FBS and PPBS levels in subjects with diabetic retinopathy, and these differences were statistically significant ($p<0.05$).In agreement with our study, Jihan Abdallah et al. also found a significant increase in FBS ($p=0.003$) and PPBS ($p=0.017$) in diabetic retinopathy patients compared to those without retinopathy. Hegde SS et al. reported similar results with higher fasting and postprandial sugar levels in diabetic retinopathy patients when compared to those without retinopathy, showing the significance of these differences.

Similarly, Kauser MM et al. observed significant differences in serum FBS between diabetic patients with and without retinopathy ($p<0.001$). In our present study, we observed that among 40 diabetic retinopathy patients, the least glycemic control was evident in those with proliferative diabetic retinopathy (11.47±2.21). Employing a one-way ANOVA, a highly statistically significant p-value of <0.001 was obtained, underscoring the importance of this finding.

Relationship Between Glycated Hemoglobin Levels and the Severity of Diabetic Retinopathy

This observation aligns with the results of Bagzai DS et al., who also documented a statistically significant association ($p < 0.001$) between the severity of retinopathy and HbA1c values. Consistent findings were reported by Sewak S et al., who noted that glycated hemoglobin exhibited a clear increasing trend with the worsening of diabetic retinopathy, and the analysis revealed high statistical significance ($p < 0.01$). Similarly, the results of our study were in agreement with the observations made by Lokesh S et al., who found that more severe forms of diabetic retinopathy were more common among patients with higher HbA1c levels compared to those with lower HbA1c levels. Similarly, Prasad JR et al. also observed a trend where the value of glycated hemoglobin (HbA1c) increased with the severity of diabetic retinopathy, indicating poorer metabolic control. This increase in HbA1c was significantly associated with the severity of retinopathy, which aligns with the findings of the present study.

Limitation of the study

The study's sample size was limited, and it was conducted at a single center, potentially affecting the generalizability of the findings to a broader population**.** The study did not account for variations in dietary patterns among subject groups, which could have influenced the results.

Conclusion

In this study involving type 2 diabetes patients, a higher prevalence of the disease was observed among the male population, particularly within the 50 to under 60-year age group. Additionally, it was noted that the severity of diabetic retinopathy increased in patients with higher HbA1c levels, making HbA1c a robust predictor of diabetic retinopathy's severity. These findings underscore

the importance of incorporating HbA1c testing as a routine screening measure for all individuals with type 2 diabetes mellitus. This screening can facilitate the early diagnosis of diabetic retinopathy severity, enabling timely intervention and treatment initiation to prevent the progression of this condition.

References

1. Zheng Y, Ley SH, Hu FB. Global epidemiology of type 2 diabetes mellitus and its complications. Nature Reviews Endocrinology. 2018 Feb;14(2):88-98.
2. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, Ostolaza H, Martín C. Pathophysiology of type 2 diabetes mellitus. International Journal of Molecular Sciences. 2020 Jan; 21(17):6275.
3. Wild S, et al. Global prevalence of Diabetes. Diabetes Care. 2004; 27:1047-53.
4. Joseph TD, et al. Pharmacotherapy: A Pathophysiologic Approach. Endocrinology Disorders. 7th ed. New York, NY: McGraw Hill Medical; 2008. p. 1206.
5. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 2020;43(Suppl.1):S14–S31.
6. Whiting DR, Guariguata L, Weil C, Shaw J. IDF Diabetes Atlas: Global Estimates of the Prevalence of Diabetes for 2011 and 2030. Diabetes Research and Clinical Practice. 2011 Dec 1;94(3):311-21.
7. Resnikoff S, Pascolini D, Etya'Ale D, Kocur I, Pararajasegaram R, Pokharel GP, Mariotti SP. Global Data on Visual Impairment in the Year 2002. Bulletin of the World Health Organization. 2004; 82: 844-51.
8. Zheng Y, He M, Congdon N. The Worldwide Epidemic of Diabetic Retinopathy. Indian Journal of Ophthalmology. 2012 Sep; 60(5):428-431.
9. Bhavsar AR, Emerson GG, Emerson MV. Epidemiology of Diabetic Retinopathy. In: Browning D, editor. Diabetic Retinopathy: Evidence-based Management. New York: Springer; 2010. p. 53–75.
10. Farmer A. Monitoring Diabetes. In: Holt RIG, Cockram CS, Flyvbjerg Goldstein BJ, eds. Textbook of Diabetes. 5th ed. Wiley Blackwell; 2017:374-384.
11. Kareem I, Jaweed SA, Bardapurkar JS, Patil VP. Study of Magnesium, Glycosylated Hemoglobin, and Lipid Profile in Diabetic Retinopathy. Indian Journal of Clinical Biochemistry. 2004 Jul;19(2):124-127.
12. Kotoula MG, Koukoulis GN, Zintzaras E, Karabatsas CH, Chatzoulis DZ. Metabolic Control of Diabetes Is Associated with an Improved Response of Diabetic Retinopathy to Panretinal Photocoagulation. Diabetes Care. 2005 Oct 1;28(10):2454-2457.
13. Maltezos E, Papazoglou D, Exiara T, Kambouromiti G, Antonoglou C. Serum Magnesium Levels in Non-Diabetic Offspring of Patients with Type 2 Diabetes Mellitus. Diabetes, Nutrition & Metabolism. 2004 Feb 1;17(1):12-16.
14. R, Ryder KW. Frequency of Hypomagnesemia. JAMA. 1990; 263:3063-3064.
15. Nadler JC, Rude RK. Disorders of Magnesium Metabolism. Endocrinology and Metabolism Clinics of North America. 1995;24:623-641.
16. McNair P, Christiansen MS, Christiansen C, Madsbad S, Transbiol I. Renal Hypomagnesemia in Human Diabetes Mellitus: Its Relation to Glucose Homeostasis. European Journal of Clinical Investigation. 1982;12: 81-85.
17. Mathers CD, Loncar D. Projections of Global Mortality and Burden of Disease from 2002 to 2030. PLoS Medicine. 2006 Nov 28;3(11):e442.
18. Roglic G, Varghese C, Thamarangsi T. Diabetes in South-East Asia: Burden, Gaps, Challenges, and Ways Forward. WHO South-East Asia Journal of Public Health.
19. Kruszynska YT, Olefsky JM. Cellular and Molecular Mechanisms of Non-Insulin-Dependent Diabetes Mellitus. Journal of Investigative Medicine: The Official Publication of the American Federation for Clinical Research. 1996 Oct 1;44(8):413-428.
20. Valdez R. Epidemiology. Nutrition Reviews. 2000; 58:S4–S6.
21. Laakso M. How Good a Marker Is Insulin Level for Insulin Resistance?. American Journal of Epidemiology. 1993 May 1;137(9):959-965.
22. Shepherd PR, Kahn BB. Glucose Transporters and Insulin Action—Implications for Insulin Resistance and Diabetes Mellitus. New England Journal of Medicine. 1999 Jul 22;341(4):248-257.
23. Goodyear LJ, Giorgino F, Sherman LA, Carey J, Smith RJ, Dohm GL. Insulin Receptor Phosphorylation, Insulin Receptor Substrate-1 Phosphorylation, and Phosphatidylinositol 3-Kinase Activity Are Decreased in Intact Skeletal Muscle Strips from Obese Subjects. The Journal of Clinical Investigation. 1995 May 1;95(5):2195-2204.