

THE RELATIONSHIP BETWEEN GLYCATED HEMOGLOBIN LEVELS AND MICROVASCULAR COMPLICATIONS IN TYPE 2 DIABETES MELLITUS: A RETROSPECTIVE COHORT STUDY

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Received : 06/05/2024
Received in revised form : 29/06/2024
Accepted : 15/07/2024

Keywords:

Type 2 diabetes mellitus, glycated hemoglobin, HbA1c, microvascular complications, diabetic retinopathy.

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DOI: 10.47009/jamp.2024.6.4.18

Source of Support: Nil.

Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (4); 82-86



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Abstract

Background: Microvascular complications are a significant concern in patients with type 2 diabetes mellitus. Glycated hemoglobin (HbA1c) is a critical marker for long-term glycemic control. This study investigates the relationship between HbA1c levels and the prevalence of microvascular complications in type 2 diabetes mellitus. **Materials and Methods:** A retrospective cohort study was conducted on 100 patients with type 2 diabetes mellitus. Patient demographics, HbA1c levels, and the presence of microvascular complications (diabetic retinopathy, nephropathy, and neuropathy) were recorded. The association between HbA1c levels and microvascular complications was analyzed using t-tests and multivariate logistic regression. **Result:** The mean age of the patients was 58 years (SD = 8), with 56% males and 44% females. The mean duration of diabetes was 10 years (SD = 4). The mean HbA1c level was 8.2% (SD = 1.5). Microvascular complications were present in 35% of patients for diabetic retinopathy, 28% for diabetic nephropathy, and 40% for diabetic neuropathy. Patients with diabetic retinopathy had a mean HbA1c of 9.1% compared to 7.7% in those without ($p = 0.002$). For diabetic nephropathy, the mean HbA1c was 8.8% versus 7.9% ($p = 0.015$), and for diabetic neuropathy, it was 8.7% versus 7.8% ($p = 0.005$). Multivariate analysis revealed that each 1% increase in HbA1c was associated with higher odds of retinopathy (OR: 1.8, $p = 0.001$), nephropathy (OR: 1.5, $p = 0.02$), and neuropathy (OR: 1.6, $p = 0.007$). **Conclusion:** Higher HbA1c levels are significantly associated with the prevalence of microvascular complications in patients with type 2 diabetes mellitus. Maintaining optimal glycemic control is crucial to reducing these risks.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and relative insulin deficiency.^[1] It is associated with a variety of long-term complications, including microvascular complications such as diabetic retinopathy, nephropathy, and neuropathy.^[2,3] These complications significantly contribute to the morbidity and mortality associated with diabetes, leading to diminished quality of life and increased healthcare costs.^[4]

Glycated hemoglobin (HbA1c) is a widely used biomarker for long-term glycemic control, reflecting average blood glucose levels over the preceding 2-3

months.^[5] Numerous studies have demonstrated that poor glycemic control, as indicated by higher HbA1c levels, is associated with an increased risk of developing microvascular complications in patients with T2DM.^[6] However, the exact relationship between HbA1c levels and the prevalence of these complications requires further elucidation, particularly in different population subsets.

This retrospective cohort study aims to investigate the relationship between HbA1c levels and the prevalence of microvascular complications in patients with T2DM. By examining a cohort of 100 patients, we seek to quantify the impact of glycemic control on the risk of developing diabetic retinopathy, nephropathy, and neuropathy. Understanding this

relationship is crucial for developing effective management strategies aimed at minimizing the risk of complications and improving the overall prognosis for patients with T2DM.

MATERIALS AND METHODS

Study Design and Period: This retrospective cohort study was conducted over a period of one year, from May 2023 to April 2024, at the Department of Biochemistry, Kakatiya Medical College, Warangal.

Study Population: The study included 100 patients diagnosed with type 2 diabetes mellitus (T2DM). Patients were selected based on the following inclusion and exclusion criteria:

Inclusion Criteria

- Diagnosed with T2DM for at least 5 years.
- Age between 40 and 75 years.
- Availability of complete medical records, including HbA1c levels and documentation of microvascular complications.

Exclusion Criteria

- Patients with type 1 diabetes mellitus or gestational diabetes.
- Incomplete medical records.
- Presence of macrovascular complications or other severe comorbidities that could confound the results.

Data Collection: Data were collected from the medical records of the patients, including demographic information (age, gender), duration of diabetes, HbA1c levels, and the presence of microvascular complications. Microvascular complications were categorized as diabetic retinopathy, nephropathy, and neuropathy based on the following criteria:

Diabetic Retinopathy: Diagnosed through fundoscopic examination by an ophthalmologist.

Diabetic Nephropathy: Determined by the presence of microalbuminuria or elevated serum creatinine levels.

Diabetic Neuropathy: Diagnosed based on clinical examination and nerve conduction studies.

HbA1c Measurement: HbA1c levels were measured using high-performance liquid chromatography (HPLC) at the Department of Biochemistry, Kakatiya Medical College. The most recent HbA1c value within the study period was used for analysis.

Statistical Analysis: Data were analyzed using SPSS software (version 26.0). Descriptive statistics were used to summarize patient demographics, HbA1c levels, and the prevalence of microvascular complications. The association between HbA1c levels and the presence of microvascular complications was assessed using independent t-tests.

Multivariate logistic regression analysis was performed to adjust for potential confounders, including age, gender, and duration of diabetes. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to quantify the risk of microvascular

complications associated with each 1% increase in HbA1c levels.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee of Kakatiya Medical College. Patient confidentiality was maintained by anonymizing personal information, and all data were stored securely. As this was a retrospective study, informed consent was waived by the ethics committee.

RESULTS

Patient Demographics: Out of the 100 patients included in the study, the mean age was 58 years (SD = 8), with 56% males and 44% females. The mean duration of diabetes was 10 years (SD = 4) (Table 1).

Glycated Hemoglobin (HbA1c) Levels

The mean HbA1c level was 8.2% (SD = 1.5). The distribution of HbA1c levels among the patients was as follows: 20% had HbA1c levels less than 7.0%, 35% had levels between 7.0% and 8.0%, and 45% had levels greater than 8.0% [Table 2].

Microvascular Complications

The prevalence of microvascular complications in the cohort was 35% for diabetic retinopathy, 28% for diabetic nephropathy, and 40% for diabetic neuropathy [Table 3].

Association Between HbA1c Levels and Microvascular Complications

A significant association was found between higher HbA1c levels and the presence of microvascular complications. Patients with diabetic retinopathy had a mean HbA1c level of 9.1% compared to 7.7% in those without retinopathy ($p = 0.002$). Similarly, patients with diabetic nephropathy had a mean HbA1c level of 8.8% compared to 7.9% in those without nephropathy ($p = 0.015$). For diabetic neuropathy, the mean HbA1c levels were 8.7% in affected patients versus 7.8% in those without neuropathy ($p = 0.005$) [Table 4].

Multivariate Logistic Regression Analysis

After adjusting for potential confounders such as age, gender, and duration of diabetes, the odds of having microvascular complications increased significantly with each 1% increase in HbA1c level. The adjusted odds ratio (OR) for diabetic retinopathy was 1.8 (95% CI: 1.3-2.5, $p = 0.001$), for diabetic nephropathy was 1.5 (95% CI: 1.1-2.1, $p = 0.02$), and for diabetic neuropathy was 1.6 (95% CI: 1.2-2.3, $p = 0.007$) [Table 5].

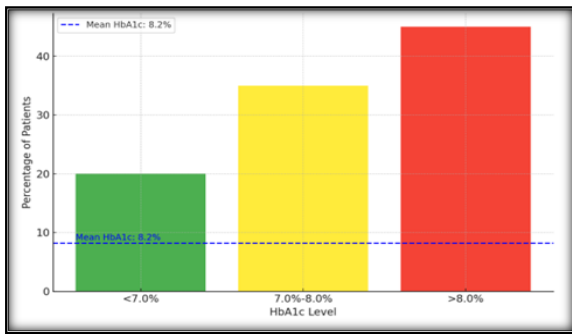


Figure 1: HbA1c Levels Distribution

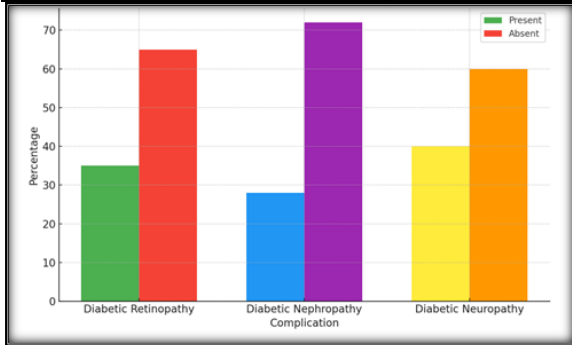


Figure 2: Prevalence of Microvascular Complications

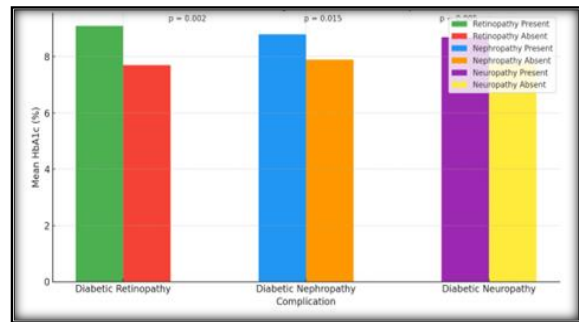


Figure 3: Mean HbA1c Levels by Microvascular Complication

Table 1: Patient Demographics.

Demographic Characteristics	Mean (SD) / Percentage
Age (years)	58 (8)
Gender	
Males	56%
Females	44%
Duration of Diabetes (years)	10 (4)

Table 2: HbA1c Levels Distribution

HbA1c Level	Number of Patients	Percentage
<7.0%	20	20%
7.0%-8.0%	35	35%
>8.0%	45	45%
Total	100	100%
Mean HbA1c (%)	8.2 (1.5)	

Table 3: Microvascular Complications Prevalence

Complication	Present (n)	Percentage	Absent (n)	Percentage
Diabetic Retinopathy	35	35%	65	65%
Diabetic Nephropathy	28	28%	72	72%
Diabetic Neuropathy	40	40%	60	60%

Table 4: Mean HbA1c Levels by Microvascular Complication

Complication	Mean HbA1c (%)	p-value
Diabetic Retinopathy		
Present	9.1	
Absent	7.7	0.002
Diabetic Nephropathy		
Present	8.8	
Absent	7.9	0.015
Diabetic Neuropathy		
Present	8.7	
Absent	7.8	0.005

Table 5: Adjusted Odds Ratios for Microvascular Complications

Complication	Adjusted Odds Ratio (95% CI)	p-value
Diabetic Retinopathy	1.8 (1.3-2.5)	0.001
Diabetic Nephropathy	1.5 (1.1-2.1)	0.02
Diabetic Neuropathy	1.6 (1.2-2.3)	0.007

DISCUSSION

This study investigates the relationship between glycosylated hemoglobin (HbA1c) levels and the prevalence of microvascular complications in patients with type 2 diabetes mellitus (T2DM). Our findings indicate a significant association between higher HbA1c levels and an increased risk of diabetic retinopathy, nephropathy, and neuropathy, underscoring the importance of stringent glycemic control in preventing these complications.

The study revealed that patients with higher HbA1c levels were more likely to develop microvascular complications. Specifically, the mean HbA1c levels were significantly higher in patients with diabetic retinopathy (9.1% vs. 7.7%, $p = 0.002$), nephropathy (8.8% vs. 7.9%, $p = 0.015$), and neuropathy (8.7% vs. 7.8%, $p = 0.005$). Multivariate logistic regression analysis confirmed that each 1% increase in HbA1c was associated with an increased risk of retinopathy (OR: 1.8, $p = 0.001$), nephropathy (OR: 1.5, $p = 0.02$), and neuropathy (OR: 1.6, $p = 0.007$).

Our results align with previous research demonstrating that poor glycemic control is a major risk factor for the development of microvascular complications in T2DM. For example, Qu et al. (2022) found that visit-to-visit HbA1c variability in adults with T2DM is associated with an increased risk of microvascular complications, emphasizing the need for consistent glycemic control. Similarly, Shao et al. (2022) highlighted the association between long-term HbA1c variability and functional limitations, suggesting that fluctuations in HbA1c levels may contribute to the development of complications over time.

The UK Prospective Diabetes Study (UKPDS) demonstrated that intensive glucose control significantly reduces the risk of microvascular complications. Zoungas et al.^[10] (2012) extended these findings, showing that specific glycemic thresholds are associated with vascular complications and mortality in T2DM patients. Our study adds to this body of evidence by providing contemporary data from a cohort of patients in Warangal, India.

Further supporting our findings, Carral et al.^[11] (2021) reported that the presence of microvascular complications is associated with poor metabolic control in patients with type 1 diabetes mellitus, highlighting the broader implications of glycemic management across different types of diabetes. Sartore et al.^[12] (2023) conducted a meta-analysis updating the relationship between long-term HbA1c variability and vascular complications, confirming that consistent and stable HbA1c levels are crucial in mitigating risks.

Kim et al.^[13] (2021) emphasized that achieving target HbA1c levels promptly after diagnosis is associated with durable glycemic control and a lower risk of complications, underscoring the importance of early and aggressive intervention in diabetes management. In another study, Kim et al.^[14] (2012) discussed the

role of HbA1c in screening for diabetes mellitus, further supporting the utility of HbA1c as a critical marker for diabetes management and complication prevention.

Clinical Implications

The strong association between HbA1c levels and microvascular complications underscores the need for effective diabetes management strategies aimed at achieving optimal glycemic control. Clinicians should prioritize regular monitoring of HbA1c levels and implement personalized treatment plans to maintain HbA1c within target ranges. Patient education on the importance of glycemic control, adherence to medication, lifestyle modifications, and regular screening for complications are critical components of comprehensive diabetes care.

Limitations

This study has several limitations. First, the retrospective design may be subject to selection bias and does not allow for the establishment of causality. Second, the study was conducted at a single center, which may limit the generalizability of the findings to other populations. Third, potential confounders such as socioeconomic status, diet, physical activity, and medication adherence were not accounted for in the analysis. Future studies should consider these factors and employ prospective designs to validate our findings.

CONCLUSION

This study highlights a significant relationship between higher HbA1c levels and the prevalence of microvascular complications in patients with T2DM. Maintaining optimal glycemic control is crucial in reducing the risk of these complications. These findings reinforce the importance of regular HbA1c monitoring and comprehensive diabetes management to improve patient outcomes.

REFERENCES

1. Boye KS, Thieu VT, Lage MJ, Miller H, Paczkowski R. The Association Between Sustained HbA1c Control and Long-Term Complications Among Individuals with Type 2 Diabetes: A Retrospective Study. *Adv Ther.* 2022 May;39(5):2208-2221. doi: 10.1007/s12325-022-02106-4. Epub 2022 Mar 22. PMID: 35316502; PMCID: PMC9056490.
2. Suh J, Choi Y, Oh JS, Song K, Choi HS, Kwon A, et al. Association between early glycemic management and diabetes complications in type 1 diabetes mellitus: A retrospective cohort study. *Prim Care Diabetes.* 2023 Feb;17(1):60-67. doi: 10.1016/j.pcd.2022.12.006. Epub 2023 Jan 4. PMID: 36609067.
3. Jude EB, Nixon M, O'Leary C, Myland M, Gooch N, Shaunik A, et al. Evaluating Glycemic Control in Patients with Type 2 Diabetes Suboptimally Controlled on Basal Insulin: UK ATTAIN Real-World Study. *Diabetes Ther.* 2019 Oct;10(5):1847-1858. doi: 10.1007/s13300-019-0667-6. Epub 2019 Jul 18. PMID: 31321748; PMCID: PMC6778546.
4. Tan JK, Lim GH, Mohamed Salim NN, Chia SY, Thumboo J, Bee YM. Associations Between Mean HbA1c, HbA1c Variability, and Both Mortality and Macrovascular Complications in Patients with Diabetes Mellitus: A Registry-Based Cohort Study. *Clin Epidemiol.* 2023 Jan 25;15:137-

149. doi: 10.2147/CLEP.S391749. PMID: 36721457; PMCID: PMC9884453.
5. Alqahtani RM, Alsulami EF. The Association Between Glycated Hemoglobin (HbA1c) Level and Vitamin D Level in Diabetes Mellitus Patients: A Cross-Sectional Study. *Cureus*. 2023 Oct 17;15(10):e47166. doi: 10.7759/cureus.47166. PMID: 38022364; PMCID: PMC10652031.
 6. Sugimoto T, Sakurai T, Uchida K, Kuroda Y, Tokuda H, Omura T, et al. Impact of Type 2 Diabetes and Glycated Hemoglobin Levels Within the Recommended Target Range on Mortality in Older Adults With Cognitive Impairment Receiving Care at a Memory Clinic: NCGG-STORIES. *Diabetes Care*. 2024 May 1;47(5):864-872. doi: 10.2337/dc23-2324. PMID: 38470970.
 7. Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients. *Biomark Insights*. 2016 Jul 3;11:95-104. doi: 10.4137/BML.S38440. PMID: 27398023; PMCID: PMC4933534.
 8. Qu F, Shi Q, Wang Y, Shen Y, Zhou K, Pearson ER, et al. Visit-to-visit glycated hemoglobin A1c variability in adults with type 2 diabetes: a systematic review and meta-analysis. *Chin Med J (Engl)*. 2022 Oct 5;135(19):2294-2300. doi: 10.1097/CM9.0000000000002073. PMID: 35952315; PMCID: PMC9771337.
 9. Shao D, Wang SS, Sun JW, Wang HP, Sun Q. Association Between Long-Term HbA1c Variability and Functional Limitation in Individuals Aged Over 50 Years: A Retrospective Cohort Study. *Front Endocrinol (Lausanne)*. 2022 Apr 29;13:847348. doi: 10.3389/fendo.2022.847348. PMID: 35574024; PMCID: PMC9099190.
 10. Zoungas S, Chalmers J, Ninomiya T, Li Q, Cooper ME, Colagiuri S, et al. ADVANCE Collaborative Group. Association of HbA1c levels with vascular complications and death in patients with type 2 diabetes: evidence of glycaemic thresholds. *Diabetologia*. 2012 Mar;55(3):636-43. doi: 10.1007/s00125-011-2404-1. Epub 2011 Dec 21. PMID: 22186981.
 11. Carral F, Tomé M, Fernández JJ, Piñero A, Expósito C, Jiménez AI, et al. The presence of microvascular complications is associated with a poor evolution of metabolic control in patients with type 1 diabetes mellitus. *Endocrinol Diabetes Nutr (Engl Ed)*. 2021 Jun-Jul;68(6):389-397. doi: 10.1016/j.endien.2021.10.001. Epub 2021 Oct 8. PMID: 34742472.
 12. Sartore G, Ragazzi E, Caprino R, Lapolla A. Long-term HbA1c variability and macro-/micro-vascular complications in type 2 diabetes mellitus: a meta-analysis update. *Acta Diabetol*. 2023 Jun;60(6):721-738. doi: 10.1007/s00592-023-02037-8. Epub 2023 Jan 30. PMID: 36715767; PMCID: PMC10148792.
 13. Kim KJ, Choi J, Bae JH, Kim KJ, Yoo HJ, Seo JA, et al. Time to Reach Target Glycosylated Hemoglobin Is Associated with Long-Term Durable Glycemic Control and Risk of Diabetic Complications in Patients with Newly Diagnosed Type 2 Diabetes Mellitus: A 6-Year Observational Study. *Diabetes Metab J*. 2021 May;45(3):368-378. doi: 10.4093/dmj.2020.0046. Epub 2020 Oct 20. PMID: 33081424; PMCID: PMC8164945.
 14. Kim JH, Kim GW, Lee MY, Shin JY, Shin YG, Koh SB, et al. Role of HbA1c in the Screening of Diabetes Mellitus in a Korean Rural Community. *Diabetes Metab J*. 2012 Feb;36(1):37-42. doi: 10.4093/dmj.2012.36.1.37. Epub 2012 Feb 17. PMID: 22363920; PMCID: PMC3283825.