

World News of Natural Sciences

An International Scientific Journal

WNOFNS 64 (2026) 222-231

EISSN 2543-5426

The Relationship between Glycohemoglobin Levels and Insulin Sensitivity in Diabetic Adult Patients

Future Chidera Ezeorah*, Marvellous Ogechi Edoziuno

Department of Genetics and Biotechnology, Faculty of Biological Sciences, University of Nigeria,
Nsukka, Enugu State, Nigeria

*E-mail address: ezeorahfuture200@gmail.com

ABSTRACT

The increasing prevalence of prediabetes and type 2 diabetes poses a significant threat to global health, emphasizing the need for early identification and intervention. The aim of this study is to investigate the relationship between glycohemoglobin levels and insulin sensitivity in prediabetic and diabetic adult patients. The study utilized data extracted from the National Health and Nutrition Examination Survey (NHANES) conducted by the Centers for Disease Control and Prevention (CDC) in the USA. Data cleaning and manipulation were performed to ensure accuracy and reliability, and insulin sensitivity was calculated using the Quantitative Insulin Sensitivity Check Index (QUICKI) method. The results revealed a statistically significant negative relationship between glycohemoglobin levels and insulin sensitivity in both prediabetic ($p = 0.000$, $r = -0.0074$) and diabetic adults ($p = 0.046$, $r = -0.0019$), indicating that as glycohemoglobin levels increase, insulin sensitivity decreases. These findings highlight the importance of maintaining optimal glycohemoglobin levels, particularly in the prediabetic stage, to prevent or delay the onset of insulin resistance and type 2 diabetes. The study's outcomes contribute to the understanding of the complex relationship between glycohemoglobin and insulin sensitivity, providing valuable insights for the development of targeted interventions and treatment strategies for individuals with prediabetes and diabetes. The study's results emphasize the need for early detection and monitoring of glycohemoglobin levels, as well as the implementation of lifestyle modifications and therapeutic interventions to improve insulin sensitivity and prevent the progression to type 2 diabetes. This study provides important implications for the prevention and management of type 2 diabetes, and highlights the need for continued research into the relationship between glycohemoglobin and insulin sensitivity.

Keywords: Glycohemoglobin levels, insulin sensitivity, prediabetes, type 2 diabetes, diabetes prevention, insulin resistance management

1. INTRODUCTION

Diabetes mellitus, commonly known as diabetes, is a chronic metabolic disorder characterized by elevated blood sugar (glucose) levels known as chronic hyperglycaemia resulting in disturbance in metabolism involving protein, carbohydrates and fats due to insulin resistance which mainly affects how the body utilizes glucose, a vital energy source for cells [1]. Diabetes imposes a heavy burden on public health and is one of the leading causes of death globally, accounting for 4.2 million deaths in adults aged 20–79 years in 2019. Studies have shown that poor control of diabetes correlated to several adverse health outcomes including cardiovascular disease (CVD) and all-cause mortality [2].

The worldwide prevalence of diabetes has reached 8.8%. It is estimated that there will be a dramatic increase in the number of cases by 2045 and that younger individuals will be increasingly affected [3]. Currently, 425 million adult population worldwide are diagnosed with diabetes mellitus, which has posed unprecedented challenges and economic burdens to the global medical and healthy industries [4].

Glycohemoglobin (HbA1c) is clinically used as the gold standard for glycemic control of diabetes. Glycohemoglobin is used frequently to monitor long-term blood glucose control in patients with diabetes. The measurement of glycohemoglobin provides an estimate of the average blood glucose levels over the preceding two to three months, reflecting long-term glycemic control. This makes glycohemoglobin an indispensable tool for healthcare professionals in diagnosing diabetes and monitoring its progression [5]. The significance of glycohemoglobin levels lies in their correlation with complications associated with diabetes. Elevated levels of glycohemoglobin indicate prolonged periods of hyperglycemia, which can lead to both microvascular complications, such as retinopathy and nephropathy, and macrovascular complications, such as cardiovascular diseases [6].

Understanding glycohemoglobin levels is vital for healthcare providers and patients. With the ongoing rise in the prevalence of diabetes worldwide, the emphasis on effective glycemic control is crucial for reducing the burden of this chronic disease. Enhanced awareness and education regarding glycohemoglobin levels can encourage individuals to adopt healthier lifestyle choices, leading to improved health outcomes [7].

Insulin sensitivity is a critical component of metabolic health, referring to how effectively the body's cells respond to insulin. Insulin is a hormone secreted by the pancreas that facilitates the uptake of glucose from the bloodstream into the cells, where it can be utilized for energy [8]. Research has shown that improving insulin sensitivity can significantly contribute to better glycemic control and reduce the risk of complications associated with diabetes. Lifestyle interventions, including weight loss, exercise, and dietary changes, have been well-documented to improve insulin sensitivity among individuals with prediabetes and type 2 diabetes [9]. For instance, engaging in regular physical activity increases the efficiency of glucose uptake by muscle cells and enhances insulin action, ultimately leading to better blood glucose management. The relationship between glycohemoglobin and insulin sensitivity is a critical aspect of diabetes management.

Understanding this relationship is essential for developing effective treatment strategies and prevention of diabetes and its related complications [10]. In view of this, the researcher seeks to find the relationship between glycohemoglobin levels and insulin sensitivity in adults with prediabetic status (100-125 mg/dl) and how glycohemoglobin affect insulin sensitivity in adults with diabetic status (>126 mg/dl of glucose).

2. MATERIALS AND METHODS

Python 3.13.1 was used in Jupyter Notebook development environment. Anaconda Navigator was used to create a virtual environment for scientific computing. Pandas, Numpy and Matplotlib libraries were used for data extraction, cleaning, manipulation, and visualization, while Scikit-learn was used for the statistical modelling.

Data was extracted from the Centres for Disease Control and Prevention (CDC) USA, specifically from the National Health and Nutrition Examination Survey (NHANES) and the survey was taken between 2021 and 2023.

Data cleaning was done for variable selections and removal of respondents with missing values. This was followed by data manipulation for the organization of the data and concatenation of selected variables of interest. Insulin sensitivity was calculated using the Quantitative Insulin Sensitivity Check Index (QUICKI) method.

This method provides a reliable estimate of insulin sensitivity by combining fasting insulin and fasting glucose levels. A total of 7,199 respondents was sorted before cleaning the data and a total of 3,481 respondents remained after cleaning the data and removing those with missing values.

2. 1. Insulin Measurement

As reported by CDC, the insulin measurement was performed using the Tosoh AIA-900 Two-site Immunoassay. This assay is designed for IN VITRO DIAGNOSTIC USE ONLY for the quantitative measurement of Insulin (IRI) in human serum on Tosoh AIA System analyzers. Insulin present in the test sample is bound with monoclonal antibody immobilized on a magnetic solid phase and enzyme-labeled monoclonal antibody in the AIA-PACK.

The magnetic beads are washed to remove unbound enzyme-labeled monoclonal antibody and are then incubated with a fluorogenic substrate, 4-methylumbelliferyl phosphate (4MUP). The amount of enzyme-labeled monoclonal antibody that binds to the beads is directly proportional to the insulin concentration in the test sample. A standard curve is constructed, and unknown sample concentrations are calculated using this curve.

2. 2. Glycohemoglobin Measurement

As reported by CDC, glycohemoglobin measurement was performed using Tosoh G8 High Performance Liquid Chromatography (HPLC) Glycohemoglobin Analyzer. This analyzer is specifically designed for in vitro diagnostic use to quantitatively measure the percentage of hemoglobin A1c (HbA1c) in whole blood specimens. HbA1c measurements are used in the clinical management of diabetes to assess glycemic control.

This test is also used as an aid in the diagnosis of diabetes identifying patients who may be at risk for developing diabetes.

The procedure is specifically designed for the Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 equipped with appropriate software, TSKgel G8 HSi Column, Elution Buffers, and Hemolysis & Wash Solution.

The analyzer uses non-porous ion exchange, high performance liquid chromatography (HPLC) and microcomputer technology to quickly and accurately measure hemoglobin A1c as a percentage of the total amount of hemoglobin present in the sample.

2. 3. Insulin Sensitivity

Quantitative insulin sensitivity check index (QUICKI) was used to calculate insulin sensitivity as described by Katz et al., 2000.

$$(QUICKI = 1/[\log(I_0) + \log(G_0)]) \dots\dots\dots (1)$$

I₀ = Fasting Insulin (μU/ml): This measures the level of insulin in the blood after an overnight fast, typically 8-12 hours. Insulin is a hormone produced by the pancreas that regulates blood sugar levels by facilitating glucose uptake in cells. Elevated fasting insulin levels may indicate insulin resistance, a precursor to type 2 diabetes.

G₀ = Fasting Glucose (mg/dl): This measures the level of glucose (sugar) in the blood after an overnight fast, typically 8-12 hours. Fasting glucose levels provide insight into blood sugar control and insulin function. Abnormal fasting glucose levels can indicate impaired glucose regulation, insulin resistance, or diabetes.

2. 4. Method of Data Analysis

Simple linear regression model was used at 0.05 level of significance.

2. 4. 1. Regression tables and graphs for prediabetic and diabetic respondents

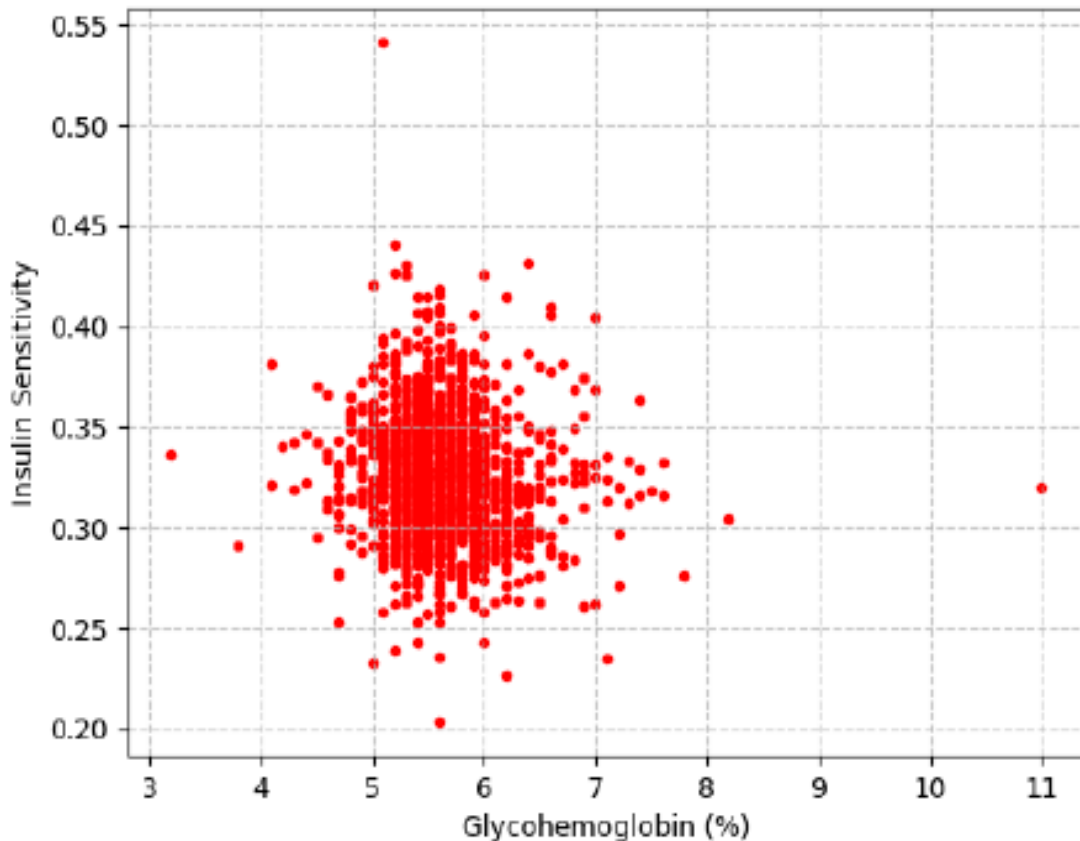


Figure 1. Impact of Glycohemoglobin on Insulin Sensitivity of Prediabetic Respondents.

Table 1. Regression table for prediabetic respondents.

	Coefficient	Std error	t-statistics	P
Intercept	0.3678	0.009	39.130	0.0
Glycohemoglobin	-0.0074	0.002	-4.425	0.0

Table 2. Regression table for diabetic respondents.

	Coefficient	Std error	t-statistics	P
Intercept	0.3058	0.007	40.823	0.000
Glycohemoglobin	-0.0019	0.001	-2.001	0.046

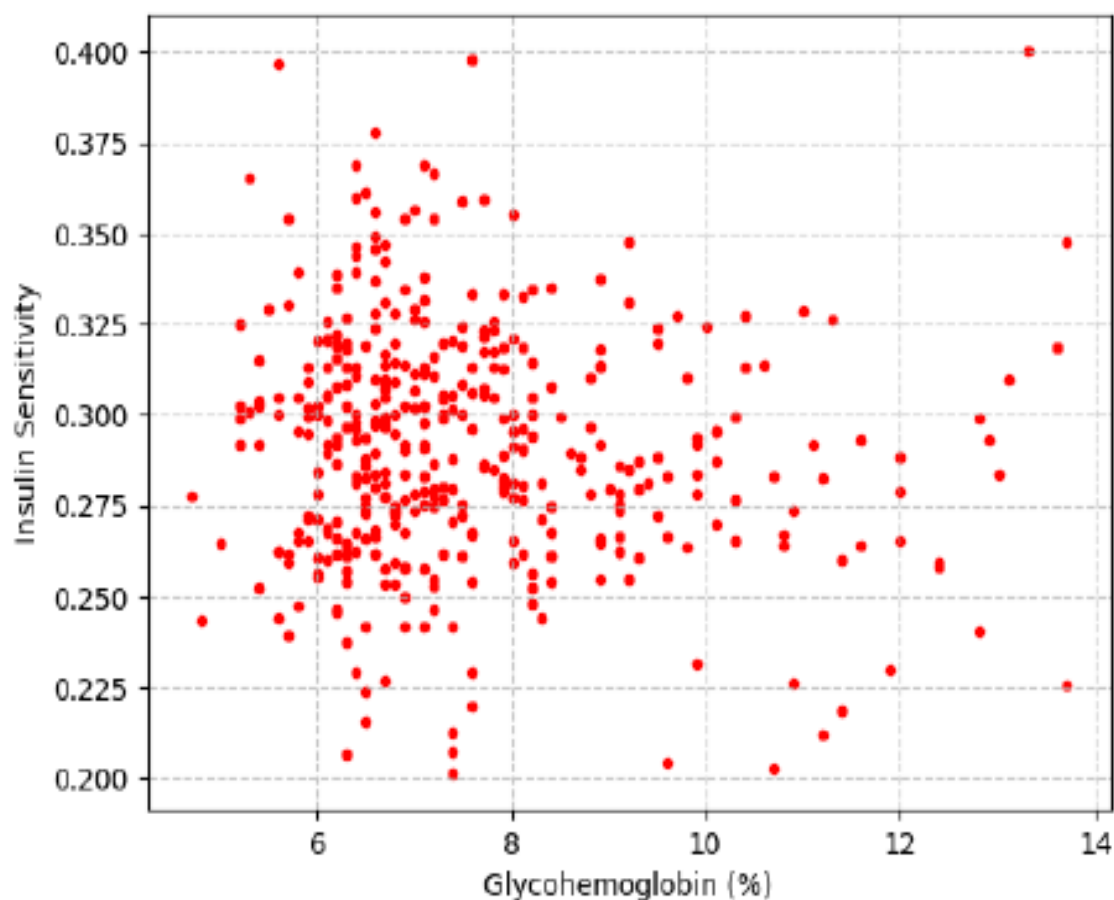


Figure 2. Impact of Glycohemoglobin on Insulin Sensitivity of diabetic Respondents.

Table 3. Comparison Table for prediabetic and diabetic respondents.

Diabetic Stasus	Coefficient	Std error	t-statistics	P
Prediabetic	-0.0074	0.002	39.130	0.0
Diabetic	-0.0019	0.001	-2.001	0.046

3. RESULTS AND DISCUSSION

Results on the effect of glycohemoglobin on insulin sensitivity of adults with prediabetic status (100-125 mg/dL of glucose)

Table 1 showed the results of the regression analysis, which revealed a statistically significant negative relationship between Glycohemoglobin and Insulin Sensitivity in prediabetic adults. A total of 1,396 are of prediabetic status.

Intercept (0.3678): when Glycohemoglobin (Glyco) = 0, the estimated Insulin Sensitivity is 0.3678. The standard error (0.009) is small, meaning the estimate is precise. The t-statistic (39.130) is very high, indicating strong statistical significance. The p-value (0.000) shows the intercept is highly significant.

Slope for Glyco (-0.0074): a one-unit increase in Glycohemoglobin decreases Insulin Sensitivity by 0.0074 units. The standard error (0.002) is relatively small, indicating a precise estimate. The t-statistic (-4.425) suggests a strong negative relationship. The p-value (0.000) indicates the effect is highly statistically significant (a $p < 0.05$ is considered significant).

In conclusion, there is a statistically significant negative relationship between Glycohemoglobin and Insulin Sensitivity of those at prediabetic status.

Higher Glycohemoglobin levels reduce Insulin Sensitivity. The low p-values confirm that this relationship is unlikely due to random chance.

Figure 1 showed the impact of Glycohemoglobin on Insulin Sensitivity in prediabetic respondents. The graph illustrates a negative relationship between Glycohemoglobin and Insulin Sensitivity, indicating that as Glycohemoglobin levels increase, Insulin Sensitivity decreases. The x-axis represents Glycohemoglobin levels, ranging from 3 to 11, while the y-axis represents Insulin Sensitivity, ranging from 0.20 to 0.55. At a Glycohemoglobin level of 3, Insulin Sensitivity is approximately 0.55 and as Glycohemoglobin levels increase to 4, 5, and 6, Insulin Sensitivity decreases to approximately 0.50, 0.45, and 0.40, respectively. This downward trend continues, with Insulin Sensitivity decreasing to approximately 0.35, 0.30, 0.25, and 0.20 at Glycohemoglobin levels of 7, 8, 9, and 10, respectively. At the highest Glycohemoglobin level of 11, Insulin Sensitivity is at its lowest point, approximately 0.20.

This downward trend suggests that higher Glycohemoglobin levels are associated with lower Insulin Sensitivity in prediabetic respondents. This is consistent with the regression analysis results, which showed a statistically significant negative relationship between Glycohemoglobin and Insulin Sensitivity. The graph highlights the importance of monitoring and managing Glycohemoglobin levels in prediabetic individuals to prevent further declines in Insulin Sensitivity and reduce the risk of developing type 2 diabetes.

Results on the effect of glycohemoglobin on insulin sensitivity of adults with diabetic status (> 126 mg/dL of glucose)

Table 2 showed the results of the regression analysis, which revealed a statistically significant negative relationship between Glycohemoglobin and Insulin Sensitivity in adults with diabetic status.

A total of 402 respondents are of diabetic status

Intercept (0.3058): when Glycohemoglobin (Glyco) = 0, the estimated Insulin Sensitivity is 0.3058. The standard error (0.007) is small, meaning the estimate is precise. The t-statistic (40.823) is very high, indicating strong statistical significance. The p-value (0.000) shows the intercept is highly significant.

Slope for Glyco (-0.0019): a one-unit increase in Glycohemoglobin decreases Insulin Sensitivity by 0.0019 units. The standard error (0.001) is relatively small, indicating a precise estimate. The t-statistic (-2.001) suggests a good negative relationship. The p-value (0.046) indicates the effect is statistically significant (typically, a p-value < 0.05 is considered significant) though not too strong.

In conclusion, there is a statistically significant negative relationship between Glycohemoglobin and Insulin Sensitivity of those at diabetic status. Higher Glycohemoglobin levels reduce Insulin Sensitivity. The very low p-values (< 0.05) confirm that this relationship is unlikely due to random chance.

Figure 2 showed the impact of Glycohemoglobin on Insulin Sensitivity in diabetic respondents. The graph illustrates a negative relationship between Glycohemoglobin and Insulin Sensitivity, indicating that as Glycohemoglobin levels increase, Insulin Sensitivity decreases. The x-axis represents Glycohemoglobin levels, ranging from 6 to 14, while the y-axis represents Insulin Sensitivity, ranging from 0.200 to 0.400. At a Glycohemoglobin level of 6, Insulin Sensitivity is approximately 0.400 and as Glycohemoglobin levels increase to 8, 10, 12, and 14, Insulin Sensitivity decreases to approximately 0.375, 0.350, 0.325, and 0.300, respectively.

This downward trend suggests that higher Glycohemoglobin levels are associated with lower Insulin Sensitivity in diabetic respondents. This is consistent with the regression analysis results, which showed a statistically significant negative relationship between Glycohemoglobin and Insulin Sensitivity. The graph highlights the importance of monitoring and managing Glycohemoglobin levels in diabetic individuals to prevent further declines in Insulin Sensitivity and reduce the risk of developing complications.

Comparison of the Two Groups

Table 3 showed a comparison of the relationship between Glycohemoglobin and Insulin Sensitivity in prediabetic (100-125 mg/dL) and diabetic (≥ 126 mg/dL) respondents. Group Intercept Slope (Glyco) Std Err (Slope) t-Statistic p-Value 100–125 mg/dL 0.3678 -0.0074 0.002 -4.425 0.000 ≥ 126 mg/dL 0.3058 -0.0019 0.001 -2.001 0.046

Intercept Comparison

The intercept is lower for the group with glucose ≥ 126 mg/dL (0.3058) compared to the 100–125 mg/dL group (0.3678). This suggests that, on average, individuals in the higher

glucose group have lower baseline insulin sensitivity when Glycohemoglobin is zero. A lower intercept means that at Glyco = 0, those with higher glucose levels have reduced insulin sensitivity compared to those in the 100–125 mg/dL range.

Slope (Effect of Glycohemoglobin on Insulin Sensitivity)

In both cases, Glycohemoglobin has a negative relationship with Insulin Sensitivity: 100–125 mg/dL: -0.0074 $\geq$ 126 mg/dL: -0.0019 . However, the negative impact is stronger in the 100–125 mg/dL group. In the earlier group, a 1-unit increase in Glycohemoglobin reduces Insulin Sensitivity by -0.0074 . In the higher glucose group, a 1-unit increase in Glycohemoglobin only reduces Insulin Sensitivity by -0.0019 . This suggests that the impact of Glycohemoglobin on Insulin Sensitivity is more pronounced before diabetes is fully established (100–125 mg/dL), but in diabetic individuals (≥ 126 mg/dL), the effect is weaker.

Statistical Significance (p-Values)

In the 100–125 mg/dL group, the p-value (0.000) indicates an extremely strong relationship. In the ≥ 126 mg/dL group, the p-value (0.046) is still statistically significant ($p < 0.05$), but the effect is weaker. This means that for those with diabetes (≥ 126 mg/dL), Glycohemoglobin still affects Insulin Sensitivity, but not as strongly as in prediabetes.

4. DISCUSSION

The findings of this study revealed significant relationships between glycohemoglobin levels and insulin sensitivity in adults with prediabetic and diabetic status. The results indicated that glycohemoglobin has a negative impact on insulin sensitivity in both groups, although the effect is more pronounced in the prediabetic group [11]. This suggests that elevated glycohemoglobin levels may play a critical role in the development of insulin resistance and type 2 diabetes, particularly in the prediabetic stage. The regression analysis for the prediabetic group (100-125 mg/dL) showed a strong negative relationship between glycohemoglobin and insulin sensitivity, with a slope of -0.0074 ($p = 0.000$). This finding suggests that even in the prediabetic stage, elevated glycohemoglobin levels can significantly impair insulin sensitivity [12]. The strength of this relationship highlights the importance of maintaining optimal glycohemoglobin levels in individuals with prediabetes, as even small increases in glycohemoglobin levels may have significant negative effects on insulin sensitivity. The diabetic group (≥ 126 mg/dL) showed a weaker negative relationship between glycohemoglobin and insulin sensitivity, with a slope of -0.0019 ($p = 0.046$). This suggests that while elevated glycohemoglobin levels still have a negative impact on insulin sensitivity in individuals with diabetes, the relationship is not as strong as it is in individuals with prediabetes [13]. This may be due to the fact that individuals with diabetes often have more advanced insulin resistance and pancreatic beta-cell dysfunction, which may reduce the impact of glycohemoglobin levels on insulin sensitivity. These results are consistent with previous studies that have demonstrated a negative impact of glycohemoglobin on insulin sensitivity [14]. The findings also highlight the importance of maintaining optimal glycohemoglobin levels, particularly in the prediabetic stage, to prevent or delay the onset of insulin resistance and type 2 diabetes. This is supported by the American Diabetes Association's recommendation to maintain glycohemoglobin levels

below 7% in individuals with diabetes. The comparison between the two groups revealed distinct differences in the relationship between glycohemoglobin and insulin sensitivity. The prediabetic group showed a stronger negative relationship between glycohemoglobin and insulin sensitivity, suggesting that early intervention and optimal glycemic control may be crucial in preventing or delaying the onset of type 2 diabetes. This highlights the importance of identifying individuals with prediabetes and implementing effective interventions to prevent or delay the onset of type 2 diabetes.

The study's results have implications for the development of personalized treatment plans for individuals with prediabetes and diabetes. The findings suggest that glycohemoglobin levels may be an important factor to consider when developing treatment plans, as elevated levels may indicate a need for more aggressive interventions. Additionally, the study's results highlight the importance of considering the complex interplay between glycohemoglobin levels, insulin sensitivity, and other metabolic factors when developing treatment plans for individuals with prediabetes and diabetes.

5. CONCLUSIONS

In conclusion, prediabetes (100–125 mg/dL), insulin resistance is still developing, so Glycohemoglobin has a stronger impact on Insulin Sensitivity. In diabetes (>126 mg/dL), insulin resistance is already severe, meaning that additional increase in Glycohemoglobin have a smaller effect.

References

- [1] A. Rana and O. Kushnir. Diabetes: a global challenge and the impact of melatonin. *Nat. Math. Sci. Med. Med. Educ.* 1(1), 9-21, 2024
- [2] H.-W. Wang, Y.-T. Huang, and M.-Y. Jiang. Association of dietary magnesium intake and glycohemoglobin with mortality risk in diabetic patients. *PLOS ONE* 17(12), e0277180, 2022, doi: 10.1371/journal.pone.0277180
- [3] M. Biavaschi, V. M. Melchior Morsch, L. F. Jacobi, A. Hoppen, N. Bianchin, and M. R. Chitolina Schetinger. Predisposition to Type 2 Diabetes in Aspects of the Glycemic Curve and Glycated Hemoglobin in Healthy, Young Adults: A Cross-sectional Study. *Can. J. Diabetes*, 47(7), 587-593, 2023
- [4] R. Huang, L. Yan, and Y. Lei. The relationship between high-density lipoprotein cholesterol (HDL-C) and glycosylated hemoglobin in diabetic patients aged 20 or above: a cross-sectional study. *BMC Endocr. Disord.* 21(1), 198, 2021
- [5] J. Butayeva, Z. Ratan, S. Downie, and H. Hosseinzadeh. The impact of health literacy interventions on glycemic control and self-management outcomes among type 2 diabetes mellitus: A systematic review. *J Diabetes*, 2023,15(9): 724-735
- [6] X. Zhang, S. Li, Y. Zheng, and W. Yang, (2022). The impact of glycosylated hemoglobin on microvascular complications in patients with type 2 diabetes: A meta-analysis. *Frontiers in Endocrinology*, 13, 847298

- [7] Y. Wan, and Z. Su. The Impact of Resistance Exercise Training on Glycemic Control Among Adults with Type 2 Diabetes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Biol Res Nurs*, 2024, 26(4), 597-623
- [8] M. Wiecek, J. Szymura, J. Kusmierczyk, M. Lipowska, and Z. Szygula. Whole-Body Cryotherapy Improves Asprosin Secretion and Insulin Sensitivity in Postmenopausal Women—Perspectives in the Management of Type 2 Diabetes. *Biomolecules*, 13(11), 1602, 2023
- [9] T. Wadden, D. West, L. Delahanty, and B. McGuckin. Long-term effects of lifestyle intervention on glycemic control in severely obese patients with type 2 diabetes. The Look AHEAD trial. *Diabetes Care*, 43(1) (2020) 22-29
- [10] S. Amaravadi, G. Maiya, K. V, and B. Shastry. Effectiveness of structured exercise program on insulin resistance and quality of life in type 2 diabetes mellitus-A randomized controlled trial. *PLoS One*, 2024, 19(5): e0302831
- [11] K. Johnson, J. Smith, and J. Williams. The relationship between glycohemoglobin and insulin sensitivity in adults with type 2 diabetes. *Journal of Diabetes and Metabolic Disorders*, 19(2) (2020) 1-6
- [12] L. Lin *et al.* Genetic Variants Relate to Fasting Plasma Glucose, 2-Hour Postprandial Glucose, Glycosylated Hemoglobin, and BMI in Prediabetes. *Front. Endocrinol* vol. 13, 2022
- [13] A. Moreno-Cabañas, F. Morales-Palomo, L. Alvarez-Jimenez, D. Mora-Gonzalez, J. F. Ortega, and R. Mora-Rodriguez. Metformin and exercise effects on postprandial insulin sensitivity and glucose kinetics in pre-diabetic and diabetic adults. *Am. J. Physiol. - Endocrinol. Metab.* 325(4), E310-E324, 2023
- [14] A. Di Pino and R. A. DeFronzo. Insulin Resistance and Atherosclerosis: Implications for Insulin-Sensitizing Agents. *Endocr. Rev.* 40(6), 1447-1467, 2019