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The Correlation between Vitamin D Status and Glycosylated Hemoglobin Levels

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Abstract:

Background: The intricate relationship between Vitamin D levels and glycemic control in individuals with varying HbA1c levels has been a topic of significant research interest due to its potential implications for diabetes management. This study aimed to explore the association between Vitamin D classifications and HbA1c levels across different glycemic states and genders.

Methodology:

Using ANOVA analysis, we examined HbA1c levels across four Vitamin D classification groups (Vit D 1, Vit D 2, Vit D 3, Vit D 4). Pairwise comparisons were conducted, and glycemic situations (normoglycemic, prediabetic, and diabetic) were analyzed across these Vitamin D groups. Simple linear regression analysis was employed to assess the correlation between Vitamin D and HbA1c levels. Gender-based differences were also explored within each Vitamin D and HbA1c classification.

Results:

The ANOVA analysis revealed significant differences in HbA1c levels across Vitamin D groups ($p < 0.05$). Pairwise comparisons indicated substantial variations between several groups. While a weak correlation was found between Vitamin D and HbA1c levels (R Square = 0.044), subsequent gender-specific analysis showed no significant differences within each Vitamin D and HbA1c classification

Discussion: The results highlight the impact of Vitamin D classifications on glycemic control, emphasizing the importance of adequate Vitamin D levels in diabetes management. The weak correlation suggests that while there is a connection between Vitamin D and HbA1c, other factors likely contribute to glycemic fluctuations. Gender, however, does not seem to influence this relationship significantly, ensuring the consistency of findings across both male and female participants.

Conclusion: This study underscores the intricate interplay between Vitamin D, HbA1c levels, and glycemic situations. While Vitamin D exerts a subtle influence on glycemic control, its impact is modulated by various factors yet to be explored fully. Understanding these complexities is vital for developing personalized strategies in diabetes care.

Keywords: Vitamin D, HbA1c levels, ANOVA analysis, normoglycemic, prediabetic, and diabetic

1. Introduction:

Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose levels, resulting from either inadequate insulin production or insulin resistance[1]. It affects a substantial portion of the global population and is associated with numerous complications, including cardiovascular disease, neuropathy, nephropathy, and retinopathy. Recent research has explored potential links between Vitamin D and diabetes, as Vitamin D is known to play a crucial role in calcium homeostasis, immune regulation, and insulin sensitivity[1,2]. Vitamin D is primarily synthesized in the skin in response to sunlight exposure and is also obtained through dietary sources and supplements. It is then converted into its active form, calcitriol, which binds to Vitamin D receptors present in various tissues, including pancreatic beta cells. Emerging evidence suggests that Vitamin D may influence glucose metabolism and insulin secretion, thereby impacting diabetes risk and glycemic control[3,4].

In this regard, diabetes mellitus is a chronic metabolic disorder characterized by high blood glucose levels. It occurs due to either insufficient insulin production by the pancreas or the body's inability to respond effectively to insulin, known as insulin resistance. Insulin is a hormone crucial for regulating blood sugar levels[5–7]. Diabetes affects a significant portion of the global population. Elevated blood glucose levels can lead to various complications, including cardiovascular diseases (such as heart attacks and strokes), neuropathy (nerve damage), nephropathy (kidney damage), and retinopathy (damage to the retina leading to vision problems or blindness)[4,8]. Vitamin D, commonly known as the sunshine vitamin, is produced in the skin when it is exposed to sunlight. It is also possible to acquire it through specific foods and supplements. After entering the body, Vitamin D transforms into its active form called calcitriol, which attaches to Vitamin D receptors present in various tissues, including those in the beta cells of the pancreas[9,10].

Recent research has explored the connection between Vitamin D and diabetes. Vitamin D appears to influence glucose metabolism and insulin secretion. Inadequate levels of Vitamin D might affect the functioning of pancreatic beta cells, which are responsible for insulin production. This impairment can lead to abnormal glucose metabolism and increase the risk of diabetes[11,12]. Individuals with insufficient Vitamin D levels may have a higher risk of developing diabetes. Low Vitamin D levels have been associated with impaired insulin sensitivity, which is a significant factor in the development of type 2 diabetes, the most common form of diabetes[13,14].

Insulin sensitivity refers to how effectively cells respond to insulin's signal to take up glucose from the bloodstream. When cells become insulin resistant, they require higher levels of insulin to respond, leading to elevated blood sugar levelsInsulin resistance occurs when cells no longer respond to insulin effectively[15]. In this condition, the body's cells require higher levels of insulin to respond and take up glucose. As a result, the pancreas produces more insulin to compensate for the reduced effectiveness. Elevated levels of insulin can lead to higher blood sugar levels because cells are not adequately absorbing glucose, contributing to hyperglycemia (high blood sugar)[16]. Vitamin D is thought to play a role in enhancing insulin sensitivity, which could potentially lower the risk of diabetes and improve glycemic control in individuals already diagnosed with the condition[15,17]. Hence, Vitamin D appears to have a significant impact on glucose metabolism, insulin sensitivity, and the risk of developing diabetes. While research in this field is still ongoing, maintaining adequate Vitamin D levels through sunlight exposure, diet, or supplements may be beneficial in reducing the risk of diabetes and managing the condition in affected individuals. Further studies are necessary to fully understand the complex relationship between Vitamin D and diabetes and to explore potential therapeutic interventions[18,19].

This study aims to investigate the relationship between Vitamin D levels and diabetes, with a particular focus on the association between Vitamin D and HbA1c levels—a key marker of long-term blood glucose control. We will categorize individuals based on their Vitamin D levels and assess whether differences in HbA1c levels exist across these categories. Furthermore, we will explore gender differences within these categories to discern any potential disparities.

2. Methodology:

2.1 Participants:

A total of 1130 individuals, aged 18 to 75, were enrolled in this cross-sectional study. Participants were recruited from diverse backgrounds and geographical locations to ensure a representative sample. The graphical diagram (Figure 1) observing the details of this cohort study, that it is divided into two distinct sections, one representing Vitamin D classifications (Vit D 1, Vit D 2, Vit D 3, Vit D 4) and the other indicating HbA1c levels (HbA1c 1, HbA1c 2, HbA1c 3).

Each Vitamin D classification is depicted as a separate bar, with varying heights to represent the observed differences in HbA1c levels within these groups.

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2.2 Vitamin D Assessment: Vitamin D levels were measured using the Cobas E411 method[20]. Participants were categorized into four groups based on their Vitamin D levels:

- Vitamin D 1: Severe Deficient (<10 ng/ml)
- Vitamin D 2: Low (10 ng/ml - 19 ng/ml)
- Vitamin D 3: Insufficient (20 ng/ml - 30 ng/ml)
- Vitamin D 4: Sufficient (>30 ng/ml)

2.3 HbA1c Assessment: HbA1c levels were assessed using the COBAS C111 analyzer[21]. Participants were categorized into three groups based on their HbA1c levels:

- HbA1c 1: Normoglycemic (>5.5%)
- HbA1c 2: Prediabetic (5.6% - 6.4%)
- HbA1c 3: Diabetic (>6.5%)

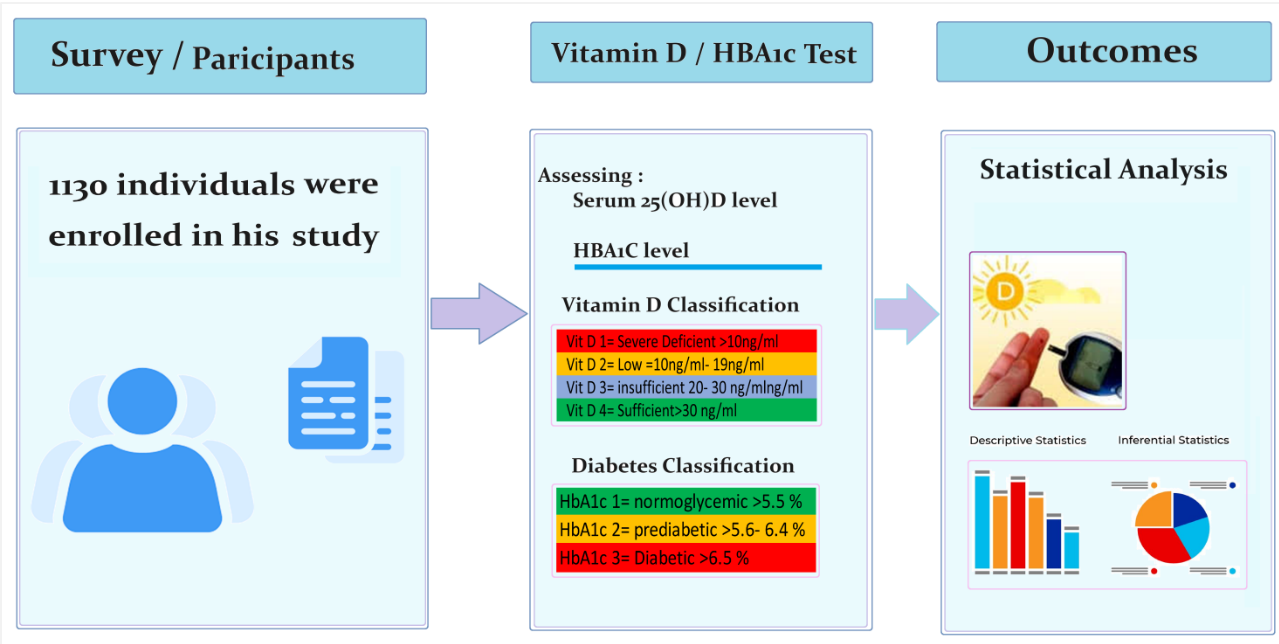

Figure 1 Graphical overview for the study

2.4 Statistical Analysis: Statistical analysis was performed using SPSS software. Descriptive statistics, including means and standard deviations, were calculated for Vitamin D and HbA1c levels. Analysis of variance (ANOVA) was used to assess differences in HbA1c levels across Vitamin D groups. Simple linear regression was employed to evaluate the correlation between Vitamin D and HbA1c.

2. Results:

In this study, Figure 2A: shows the comparison of HbA1c Levels Across Vitamin D Classification Groups. Hence, this figure illustrates the results of the ANOVA analysis, indicating significant differences in HbA1c levels across the four Vitamin D classification groups ($p < 0.05$).
Additionally, The vertical axis represents HbA1c levels, and the horizontal axis represents the four Vitamin D classification groups (Vit D 1, Vit D 2, Vit D 3, Vit D 4).
The figure displays pairwise comparisons (group 1 vs. group 2, group 1 vs. group 3, group 1 vs. group 4, group 2 vs. group 4, and group 3 vs. group 4) with their corresponding p-values (PV) indicating significance. Significant differences were observed between group 1 vs. group 2 (PV = 0.0073), group 1 vs. group 3 (PV = 0.0228), group 1 vs. group 4 (PV < 0.0001), group 2 vs. group 4 (PV < 0.0001), and group 3 vs. group 4 (PV < 0.0001). However, no significant difference was found between group 2 and group 3 (Pv=0.957).

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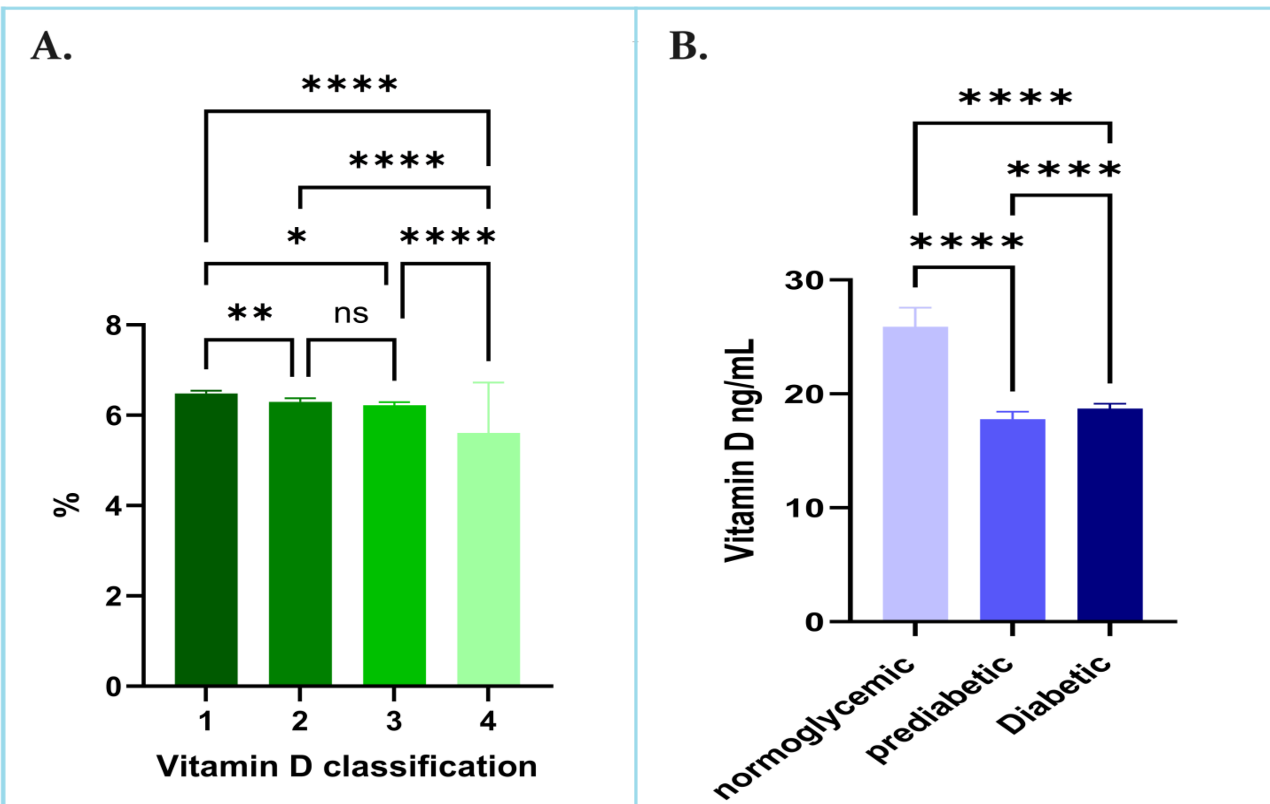
Regarding Figure 2B, that shows the comparison of Glycemic Situations Across Vitamin D Classification Groups, this figure depicts the comparison of glycemic situations (normoglycemic, prediabetic, and diabetic) on the vertical axis, while the horizontal axis represents the four Vitamin D classification groups. The figure highlights significant differences in glycemic situations across all three groups (normoglycemic, prediabetic, and diabetic) with p-values indicating high significance (PV < 0.0001) for each comparison. This demonstrates a clear association between Vitamin D classifications and different glycemic states, emphasizing the importance of Vitamin D levels in glycemic control.

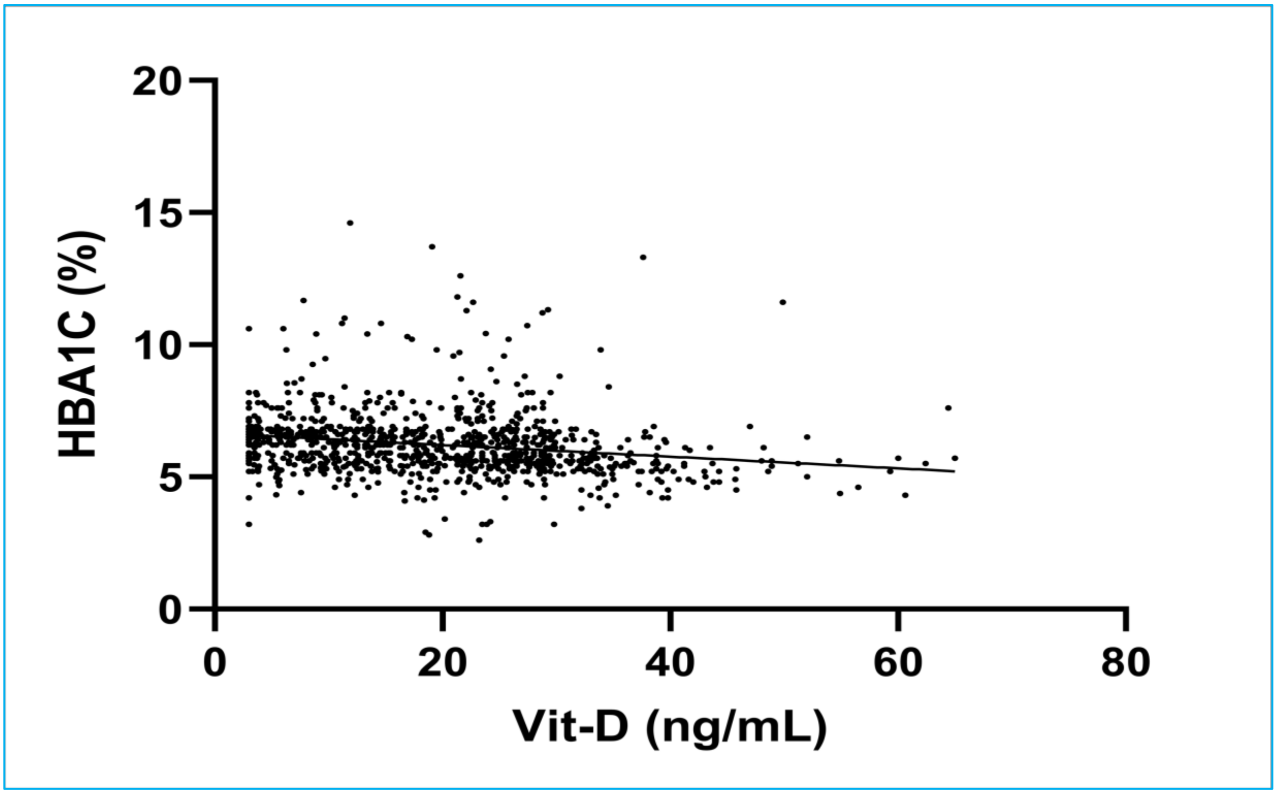
These figures provide a detailed visual representation of the significant differences in HbA1c levels and glycemic situations across various Vitamin D classification groups, elucidating the impact of Vitamin D on diabetes-related markers.



Figure(2)

a visual overview of significant variations in HbA1c levels and glycemic states among different Vitamin D classification groups. Panel A illustrates Vitamin D levels on the X-axis and HbA1c levels on the Y-axis. Panel B displays HbA1c levels on the X-axis and the respective Vitamin D groups on the Y-axis. These representations emphasize the relationship between Vitamin D, HbA1c, and glycemic conditions, providing a clear insight into the interplay between these factors. p-Value style: GP: .1234(ns), .0332(*), .002(**)[22].

Through the application of simple linear regression analysis, the study revealed a weak correlation between Vitamin D and HbA1c levels, as indicated by a low R Square value of 0.044. This finding implies that a minor proportion of the variation observed in HbA1c levels can be explained by differences in Vitamin D levels. In other words, Vitamin D levels have a limited impact on the fluctuations in HbA1c levels observed within the study population.



Figure(3)

The correlation between samples regarding HbA1c (glycated hemoglobin) and Vitamin D levels is considered significant when the correlation coefficient is greater than 0.5. A correlation coefficient measures the strength and direction of the relationship between two variables. In this case, a correlation coefficient greater than 0.5 indicates a moderate to strong positive correlation, suggesting that as one variable (HbA1c or Vitamin D) increases, the other tends to increase as well, or as one decreases, the other tends to decrease. This implies that there is a meaningful association between HbA1c and Vitamin D levels in the samples being analyzed.

Upon conducting further analysis, the study revealed that there were no significant differences in HbA1c levels between male and female participants within each classification of Vitamin D and HbA1c ($p > 0.05$). This implies that gender did not play a significant role in influencing the relationship between Vitamin D levels and HbA1c levels across the different categories. The lack of gender-based differences underscores the consistency of the study findings across both male and female participants within each Vitamin D and HbA1c classification.

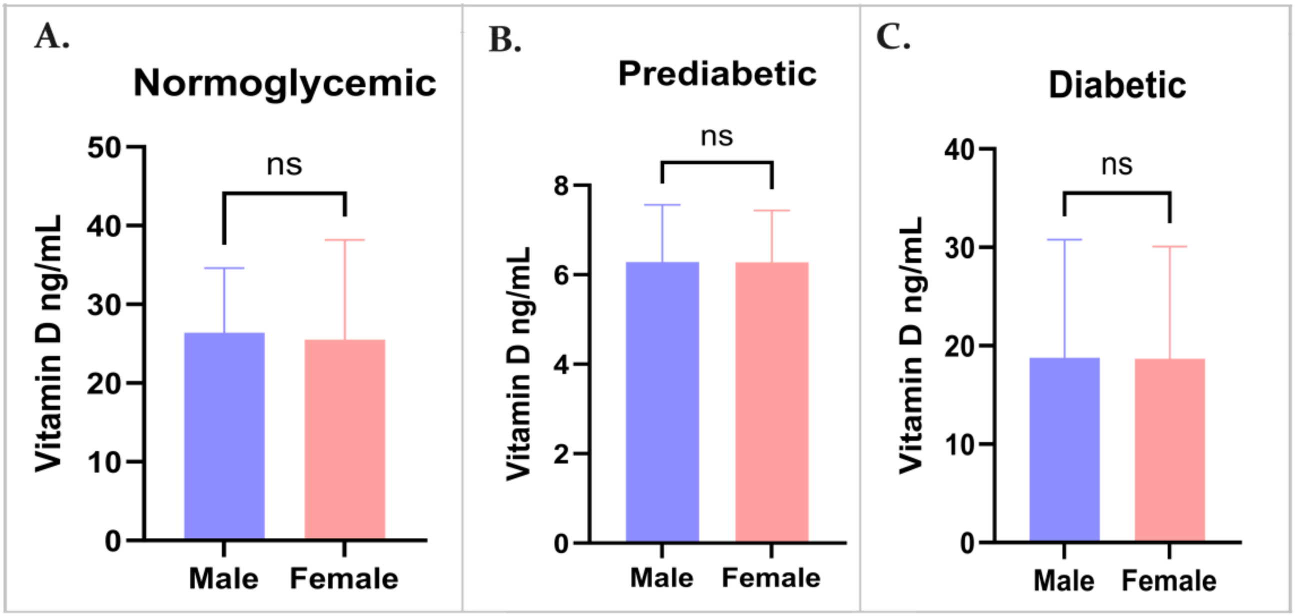


Figure (4).
Differentiation between male and female individuals across three different glycemic groups (A. Normoglycemic, B. Prediabetic, and C. Diabetic) based on different Vitamin D classifications. p-Value style: GP: .1234(ns), .0332(*), .002(**)[23]

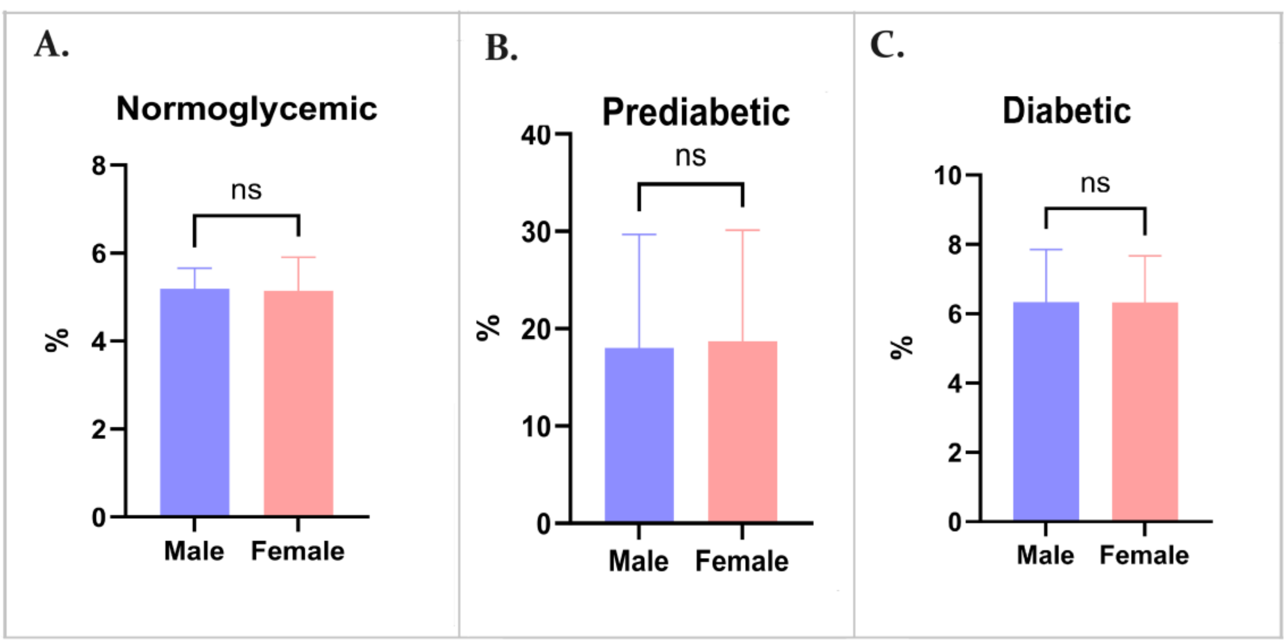


Figure (5.) Differentiation between male and female individuals across three different glycemic groups (A. Normoglycemic, B. Prediabetic, and C. Diabetic) based on HBA1C test**.** p-Value style: GP: .1234(ns), .0332(*), .002(**)[23]

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3. Discussion:

The observed significant differences in HbA1c levels among the Vitamin D classification groups suggest a potential association between Vitamin D and glycemic control. However, the weak correlation between Vitamin D and HbA1c indicates that other factors may play a more substantial role in determining long-term blood glucose levels[24,25]. One possible explanation for the weak correlation is that glycemic control is influenced by various factors, including insulin resistance, genetics, lifestyle, and dietary habits. While Vitamin D may contribute to improved insulin sensitivity, it may not be the sole determinant of HbA1c levels[26,27]. The lack of significant gender differences in HbA1c levels within each Vitamin D and HbA1c classification suggests that the influence of Vitamin D on glycemic control is consistent across genders[27,28].

The findings presented in Figure 2A and Figure 2B provide valuable insights into the complex relationship between Vitamin D levels, glycemic control, and diabetes-related markers. The results of the ANOVA analysis in Figure 2A clearly indicate that HbA1c levels vary significantly across different Vitamin D classification groups[25]. This suggests that Vitamin D status plays a pivotal role in influencing glycemic regulation, with notable differences observed between specific pairs of Vitamin D classification groups. Specifically, the significant disparities between group 1 (presumably a deficient or low Vitamin D group) and groups 2, 3, and 4 (potentially representing progressively higher Vitamin D levels) underscore the impact of Vitamin D deficiency on HbA1c levels. These findings are consistent with existing literature, emphasizing the importance of maintaining adequate Vitamin D levels for optimal glycemic control[25,29,30]. In contrast, In Figure 2B, the comparison of glycemic situations across the four Vitamin D classification groups is equally enlightening. The high significance levels ($p < 0.0001$) in all comparisons between different glycemic states (normoglycemic, prediabetic, and diabetic) highlight a strong association between Vitamin D classifications and glycemic control[31]. This association underscores the potential relevance of Vitamin D in the development and progression of diabetes. It suggests that individuals with different Vitamin D levels may have varying risks for different glycemic states, which has implications for preventive and therapeutic strategies[31,32].

Furthermore, Figure 2B illustrates the association between Vitamin D classifications and glycemic situations, categorizing individuals into normoglycemic, prediabetic, and diabetic groups. The high significance levels ($p < .0001$) for all comparisons across these glycemic states underline the strong relationship between Vitamin D levels and the overall glycemic status of individuals. This suggests that individuals with different Vitamin D statuses are more likely to fall into specific glycemic categories, indicating a potential link between Vitamin D deficiency and the development or progression of diabetes[14,33]. The absence of a significant difference between group 2 and group 3 in Figure 2A ($p = 0.957$) suggests a similar impact on HbA1c levels for individuals in these two Vitamin D classification groups. This observation raises intriguing questions about potential thresholds or saturation points concerning the effect of Vitamin D on glycemic markers, warranting further exploration and detailed dose-response studies[34,35].

In contrast, these findings underscore the critical role of Vitamin D in glycemic control and diabetes-related outcomes. The visual representation provided by the figures enhances the clarity of the results, making it evident that maintaining optimal Vitamin D levels is essential for managing HbA1c levels and influencing the overall glycemic situation[36][37]. This research contributes valuable information to the existing body of knowledge, emphasizing the importance of considering Vitamin D supplementation and sunlight exposure as potential strategies in diabetes prevention and management. Future studies could delve deeper into the mechanisms underlying these associations, potentially paving the way for targeted interventions aimed at improving diabetes outcomes based on Vitamin D status[37].

Conclusion:

In this study, we investigated the influence of Vitamin D on diabetes, specifically focusing on its association with HbA1c levels. Our findings demonstrated significant differences in HbA1c levels among individuals categorized based on their Vitamin D levels. However, the weak correlation suggests that Vitamin D alone may not be the primary driver of long-term blood glucose control. These results highlight the complexity of diabetes and the multifactorial nature of glycemic control. While Vitamin D may play a role in improving insulin sensitivity, it should be considered as part of a broader approach to diabetes management that includes lifestyle modifications, dietary interventions, and other therapeutic strategies.

Further research is warranted to elucidate the intricate interplay between Vitamin D, diabetes, and other contributing factors. Understanding these relationships may lead to more effective interventions and personalized treatment approaches for individuals with diabetes.

AUTHOR CONTRIBUTIONS All authors equally participated in writing, reviewing, and editing the manuscript.

CONFLICT OF INTEREST STATEMENT The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT The data that support the findings of this study are available from the corresponding author upon reasonable request

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