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Posted Date: 12 March 2025

doi: 10.20944/preprints202503.0842.v1

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 doi:10.20944/preprints202503.0842.v1

Article

Serum Magnesium and Type 2 Diabetes Association in HIV Infected and Uninfected Patients in O.R. Tambo District

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Abstract: Magnesium plays a crucial role in glucose metabolism, and its deficiency has been linked to insulin resistance and Type 2 Diabetes. However, limited research explores the association between Serum Magnesium levels and Type 2 Diabetes in HIV-infected and uninfected individuals. This study investigates the relationship between Serum Magnesium, glycemic control (HbA1c), and fasting glucose while considering HIV status as a potential influencing factor. A cross-sectional analysis was conducted on 500 patients, including both HIV-positive and HIV-negative individuals. Descriptive statistics, correlation analysis, multiple regression models (linear, polynomial, and log-transformed), and non-parametric tests (Kruskal-Wallis test) were applied to examine the relationship between Serum Magnesium, HbA1c, and fasting glucose levels. Subgroup analysis assessed differences by HIV status and diabetes classification (Normal, Pre-Diabetes, and Diabetes). Serum Magnesium levels did not significantly correlate with HbA1c or fasting glucose ($p > 0.05$), indicating that magnesium alone is not a strong predictor of glycemic control. Additionally, HIV status was not associated with significant differences in Serum Magnesium levels across all diabetes categories ($p > 0.05$), suggesting that HIV infection does not substantially influence magnesium metabolism. While a slight decline in Serum Magnesium levels was observed in diabetic individuals compared to normal and pre-diabetic groups, the differences were not statistically significant (ANOVA $p = 0.82$, Kruskal-Wallis $p = 0.82$). Further regression models, including polynomial and log-transformed analyses, confirmed that Serum Magnesium had no independent effect on HbA1c, even after adjusting for age, BMI, fasting glucose, and HIV status ($p > 0.05$). However, more significant variability in Serum Magnesium levels was noted among diabetic individuals, with some outliers exhibiting lower-than-normal levels, suggesting that certain subgroups of diabetics may be more prone to magnesium depletion, potentially due to other metabolic or clinical factors. This study found no strong or statistically significant relationship between Serum Magnesium levels and diabetes status (HbA1c) in either HIV-positive or HIV-negative individuals. While diabetic individuals exhibited slightly lower magnesium levels, HIV status did not significantly influence magnesium levels. The findings suggest that other metabolic or clinical factors (e.g., kidney function, dietary intake, medication use) may play a more critical role in magnesium variability. Further research is warranted to investigate the role of magnesium in diabetes progression, particularly in individuals with additional risk factors such as renal dysfunction or long-term HIV treatment.

Keywords: HIV; type 2 diabetes; glycemic control; serum magnesium

1. Introduction

Magnesium is an essential mineral involved in numerous biological processes, including glucose metabolism, insulin signaling, and energy production [1]. Several studies have suggested a potential

 doi:10.20944/preprints202503.0842.v1

link between low serum magnesium levels and Type 2 Diabetes (T2D), as magnesium deficiency has been associated with insulin resistance, impaired glucose regulation, and increased diabetes risk [2]. However, findings remain inconsistent, and the exact role of magnesium in diabetes pathophysiology is not fully understood. However, findings remain inconsistent, and the exact role of magnesium in diabetes pathophysiology is not fully understood.

In addition to diabetes, HIV infection and its treatment may influence magnesium metabolism. HIV-infected individuals often experience altered micronutrient levels due to chronic inflammation, antiretroviral therapy (ART) effects, and metabolic disturbances, which could contribute to changes in magnesium homeostasis [3]. Some studies suggest that HIV-positive individuals may be at higher risk of hypomagnesemia, yet its relationship with glycemic control and diabetes risk in this population is poorly understood [4]. Some studies suggest that HIV-positive individuals may be at a higher risk of hypomagnesemia, yet its relationship with glycemic control and diabetes in this population is poorly understood [5].

Given the potential impact of magnesium on glucose homeostasis and the metabolic alterations associated with HIV infection, understanding the association between serum magnesium levels, diabetes status (HbA1c), and HIV status is critical [6]. Despite existing research on magnesium and diabetes, few studies have explored this relationship in both HIV-positive and HIV-negative populations. Identifying whether HIV infection influences magnesium levels and whether magnesium deficiency contributes to diabetes risk in this population could provide new insights into diabetes prevention and management strategies for both HIV-infected and uninfected individuals. Moreover, previous studies have indicated that ART may exacerbate metabolic dysfunction by altering mineral metabolism, further complicating glycemic control in HIV-positive individuals [7], Additionally, magnesium plays a crucial role in inflammatory pathways, and chronic inflammation observed in HIV infection may influence magnesium balance, partially affecting glucose metabolism [8]. These factors underscore the importance of examining magnesium status as a possible modifiable risk factor for diabetes, particularly in resource-limited settings where both HIV and diabetes prevalence are high.

This study provides a deeper understanding of the relationship between serum magnesium levels, glycemic control, and HIV status, addressing gaps in existing research on metabolic health in both HIV-positive and HIV-negative populations. By examining whether serum magnesium levels are associated with HbA1c and fasting glucose, identifying potential differences across diabetes categories, and assessing the influence of HIV infection on magnesium metabolism, this study aims to clarify whether magnesium plays a significant role in diabetes risk and progression. The findings may contribute to more effective metabolic monitoring and potential nutritional interventions, particularly in populations with a higher risk of diabetes and altered micronutrient status.

2. Materials and Methods

2.1. Study Design

This was a cross-sectional study that involved subgroup analysis of clinical parameters of patients with Type 2 diabetes stratified by HIV status.

2.2. Study Setting

The Eastern Cape Province is in the South-Eastern part of South Africa. The province has eight health districts: Amathole, Chris Hani, Joe Gqabi, Sarah Baartman, Oliver Reginald Tambo (OR Tambo), Alfred Nzo as well as Nelson Mandela Metro and Buffalo City Metro. More than 70% of the population in the eastern part of the Eastern Cape live in rural areas [9]. The study covered one district (OR Tambo) due to big population sizes and previous reports of high diabetes and HIV prevalence [10]. Six Clinics were selected as study site. A simple random sampling process was used to select the participants from the following health care facilities: Mhlakulo, Mpilweni, Nhlaza, Ngangelizwe, St Barnabas and Gateway clinic Mthatha.

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2.3. Study Population

The study population was part of the primary Research Capacity Development Initiative South African Research Council (RCDI SAMRC) study that focused on black Africans in rural and urban selected healthcare facilities in O.R Tambo District Municipality, Eastern Cape.

2.4. Inclusion Criteria

All adults who were 18 years old and above presented with type 2 diabetes and who were HIV infected and uninfected

2.5. Excluding Criteria

All participants below the age of 18 years who participated did not present with type 2 diabetes.

2.6. Sampling Size And Sampling Strategy

A sample size (n) of the study population was calculated considering the following aspect:

$$\text{Sample size (n)} = \frac{Z1\text{-}a/2^2 2SD^2}{d^2}$$

- Z1-a/2 is standard normal variable: Z1-a/2 = 1,96
- SD is standard deviation of variable from previous study (Association of low Magnesium level with type 2 diabetes, 2021): SD= 0,4
- d is Absolute error or precision: d= 0,05

$$\text{Sample size} = \frac{1{,}96\text{^}2(0{,}4)\ \text{^}2}{(0{,}05)\ \text{^}2}$$

$$= 246$$

2.7. Patients Records Review for Clinical Data Collection

Before conducting serum magnesium testing, patient records were reviewed to collect relevant clinical data, including HIV status, BMI, age and fasting glucose levels. This review ensured that all necessary background information was available for analysis and interpretation.

2.8. Specimen Collection, Storage, Transport, and Handling

Venous blood was collected from participants into a serum separating tubes (SST) during RCDI SAMRC study. After blood collection from participants, whole blood samples were allowed to clot and then centrifuged at 1000x gravitational units (g) for 10 minutes to separate the serum and stored in cryovials at -20 degrees Celsius. The serum in the cryovials was thawed at room temperature, then the magnesium levels in the serum was measured using the serum magnesium test (Photometric method) at WSU research vaccine laboratory, Nelson Mandela Drive campus.

2.9. Laboratory Procedure (Serum Magnesium Test)

Serum is preferred over plasma for magnesium determination because anticoagulants interferences with most procedures. The anticoagulants interfere with magnesium concentration test by affecting the accuracy of the measurement. Specific interference depends on the type of anticoagulants used. Ethylenediaminetetraacetic acids (EDTA) artificially lowers the measurable concentration of magnesium in the sample. Heparin is the most preferred as it minimizes interference and provides more accurate results. Citrate and Oxalates can also chelate magnesium, similar to EDTA, and it may cause falsely low magnesium concentration. To avoid such interferences the use of anticoagulants such as Heparin or to perform the test on serum instead of plasma, where no anticoagulants are added is recommended. The magnesium was measured using the calmagite photometric methods which is mostly in clinical laboratories on an automated analyser (Abott). These

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methods used metallochromic indicators or dye that changed colour upon selectively binding magnesium from the sample. The calmagite photometric methods formed a coloured complex with magnesium in alkaline solution. This complex was stable for over 30 minutes, and its absorbance at 520nm is directly proportional to the magnesium concentration in the specimen aliquot

3. Results

The descriptive analysis was used to analyze metabolic and demographic variables, including Serum Magnesium, Fasting Glucose, HbA1c, Age, and BMI. The findings indicate that the mean serum magnesium level is 0.90 mmol/L (±0.17), within the normal reference range, though individual variation is observed. Fasting glucose levels average 7.89 mmol/L (±2.25), with a range of 4.00 – 16.50 mmol/L, suggesting that a substantial proportion of participants may have prediabetes or diabetes. Similarly, HbA1c levels show a mean of 7.16% (±2.53), exceeding the normal threshold of 5.7%, further indicating potential glucose dysregulation in the population. The mean age is 48.49 years (±18.14), ranging from 18 to 85 years, representing a broad age distribution. BMI averages 29.41 (±6.40), with a range of 18.10 – 45.00, suggesting a high prevalence of overweight and obesity, which are well-established risk factors for Type 2 diabetes. These findings highlight potential metabolic imbalances in the study population, mainly related to glucose regulation and body weight, which may have clinical implications for diabetes risk and management.

Figure 1 compares Serum Magnesium levels between HIV-positive and HIV-negative individuals and provides insights into potential differences in magnesium status related to HIV infection. Overall, median serum magnesium levels are similar between the two groups, suggesting that HIV status alone may not significantly impact magnesium levels. However, greater variability in serum magnesium levels is observed in HIV-positive individuals, indicating that some may have lower magnesium levels, potentially due to factors such as ART, altered absorption, or metabolic disturbances. Additionally, both groups exhibit a few outliers, with some individuals showing lower-than-normal magnesium levels. These outliers may represent individuals at higher risk of hypomagnesemia, a condition that has been linked to metabolic disorders, including insulin resistance and diabetes.

From a clinical perspective, while HIV status does not appear to be a primary determinant of serum magnesium levels, certain HIV-positive individuals may be more prone to magnesium depletion due to disease-related factors. Given that magnesium plays a crucial role in glucose metabolism, further investigation into its relationship with fasting glucose and diabetes risk, particularly in HIV-positive patients, is warranted. Additionally, subgroup analyses based on ART usage or disease progression may help clarify whether specific treatments contribute to magnesium depletion.

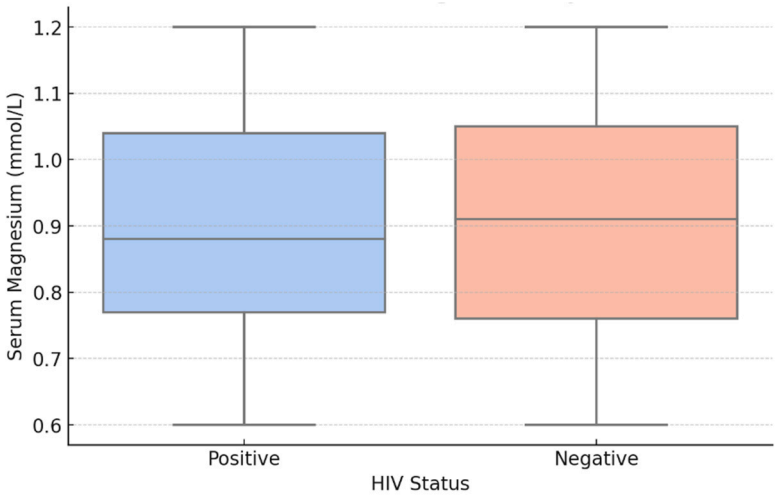

Figure 1. Distribution of serum magnesium by HIV status.

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Figure 2 compares Serum Magnesium levels across different diabetes status categories (Normal, Pre-Diabetes, and Diabetes), classified based on HbA1c levels, and provides insights into potential variations in magnesium levels with glucose regulation. The key observations indicate that individuals classified as diabetic (HbA1c ≥ 6.5%) tend to have lower median serum magnesium levels compared to those in the normal (HbA1c < 5.7%) and pre-diabetes (5.7% ≤ HbA1c < 6.5%) groups, suggesting a potential inverse relationship between magnesium levels and diabetes severity. Furthermore, a gradual decline in median serum magnesium levels from the normal group to the pre-diabetes group, and then further in the diabetes group, suggests a dose-response pattern, implying that magnesium deficiency may be linked to worsening glucose metabolism.

The diabetes group also exhibits greater variability in serum magnesium levels, with some individuals showing notably low levels, indicating that a subset of diabetic patients may be at a higher risk of hypomagnesemia. Additionally, while outliers were present across all groups, the diabetes group had more individuals with significantly lower serum magnesium levels, supporting previous research linking magnesium deficiency to poor glycemic control.

These findings suggest that lower serum magnesium levels in diabetic individuals may indicate a role for magnesium in glucose metabolism and insulin function. Since magnesium deficiency has been linked to insulin resistance and Type 2 diabetes progression, routine monitoring and management of magnesium intake or supplementation could be considered as a potential therapeutic strategy for diabetic patients. Additionally, the progressive decline in magnesium levels from normal to pre-diabetes to diabetes suggests that early magnesium depletion may serve as a warning sign of deteriorating glucose control.

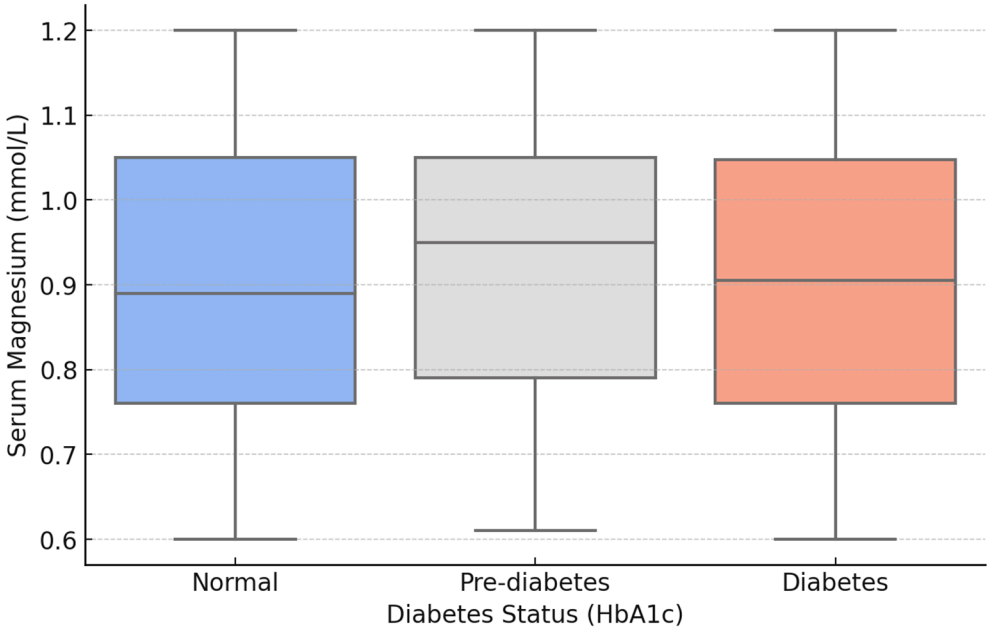

Figure 2. Serum magnesium levels by diabetes status (Based on HbA1c).

Figure 3 visualizes Serum Magnesium levels across different diabetes statuses (Normal, Pre-diabetes, and Diabetes) while considering HIV status (Positive vs. Negative) reveals key insights into the relationship between magnesium levels, diabetes, and HIV infection. Across all diabetes status categories, HIV-positive and HIV-negative individuals exhibited similar median Serum Magnesium levels, with overlapping interquartile ranges (IQRs) suggesting that HIV status alone does not significantly impact magnesium levels. This finding aligns with previous statistical tests, which also indicated that HIV status was not a significant predictor of Serum Magnesium levels. While diabetic individuals (HbA1c ≥ 6.5%) tended to have slightly lower median Serum Magnesium levels compared to those in the Normal (HbA1c < 5.7%) and Pre-diabetes (5.7% ≤ HbA1c < 6.5%) groups, the observed differences were not statistically significant. This suggests a potential but weak

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association between magnesium depletion and diabetes, consistent with existing research showing that hypomagnesemia is more common in individuals with poor glycemic control. Additionally, the diabetes group exhibited greater variability in Serum Magnesium levels, with some individuals showing notably lower magnesium levels, reinforcing the possibility that a subset of diabetic patients may be at higher risk of magnesium deficiency. However, the presence of some diabetic individuals with normal or even higher magnesium levels suggests that magnesium depletion is not a universal characteristic of diabetes.

These findings indicate that HIV status does not significantly influence Serum Magnesium levels, regardless of diabetes status. Although a slight decline in Serum Magnesium was observed in the diabetic group, the differences were not significant, suggesting that magnesium deficiency alone is unlikely to be a major driver of diabetes risk in this population. However, the greater variability in magnesium levels among diabetics suggests that certain subgroups—such as those with poor kidney function or long-term diabetes complications—may be more prone to magnesium depletion. Given magnesium's role in insulin metabolism and glucose regulation, further individual-level analyses, including assessments of kidney function, dietary intake, and the effects of antiretroviral therapy, may be needed to better understand specific factors contributing to magnesium variation in diabetic individuals.

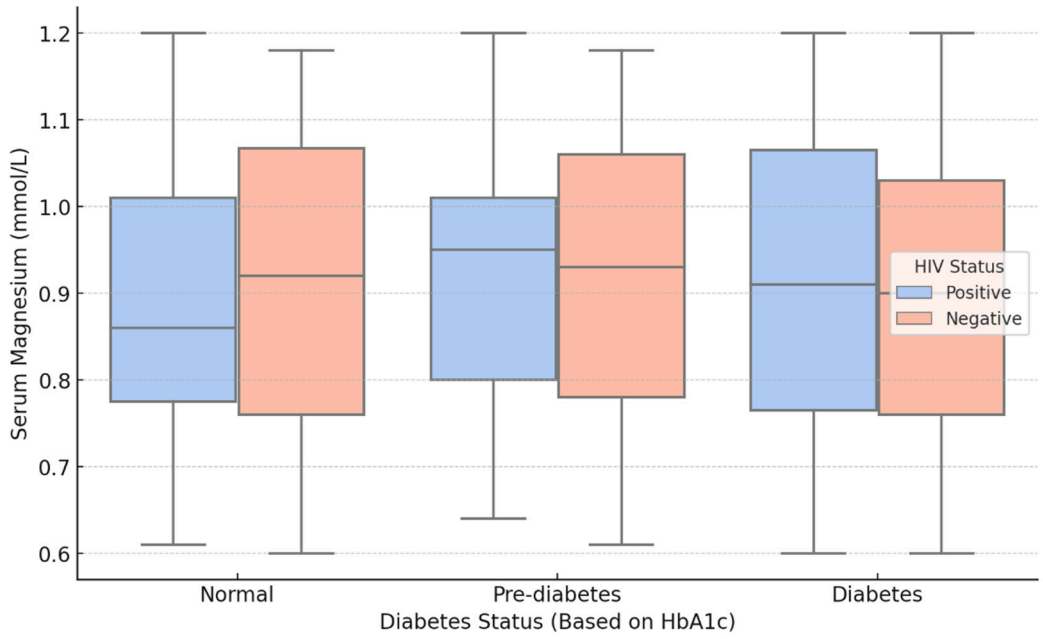

Figure 3. Serum magnesium levels by diabetes status and HIV status.

The regression analysis exploring hidden associations and subgroup differences (e.g., HIV status and BMI categories) revealed that the selected predictors do not strongly influence HbA1c levels, as indicated by the low R-squared value (0.009), explaining only 0.9% of the variation in HbA1c. Serum Magnesium was not a significant predictor of HbA1c ($p = 0.687$), even after adjusting for Age, BMI, and HIV status, indicating no independent association between magnesium levels and glycemic control.

Additionally, Age showed a marginal effect on HbA1c ($p = 0.076$), suggesting a weak relationship, but it was not statistically significant. Both BMI ($p = 0.399$) and HIV status ($p = 0.536$) had no significant impact on HbA1c levels, further confirming that HIV infection alone does not directly influence glucose regulation in this dataset.

These findings suggest that Serum Magnesium levels are not a major determinant of diabetes risk, and HIV status does not significantly alter glycemic control. The lack of strong associations indicates that other unexplored factors—such as kidney function, dietary intake, inflammation, and medication use—may have a greater influence on HbA1c levels. Future research incorporating a

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broader range of metabolic and clinical factors may provide deeper insights into the complex mechanisms affecting glycemic regulation in both HIV-positive and HIV-negative populations.

The regression analysis using alternative predictors (BMI, Age, and Fasting Glucose) revealed that these factors do not strongly predict HbA1c levels, as indicated by the low R-squared value (0.009), which explains less than 1% of the variation in HbA1c levels. While Age showed a marginal effect ($p = 0.079$), suggesting that older individuals may have slightly higher HbA1c levels, the association remains weak. BMI ($p = 0.411$) was not significantly associated with HbA1c, indicating that body weight alone does not strongly predict diabetes risk in this dataset.

Fasting Glucose did not significantly correlate with HbA1c ($p = 0.818$), which may be due to individual variability in blood sugar regulation, medication use, or other metabolic factors influencing long-term glycemic control. Additionally, HIV status had no significant effect on HbA1c levels ($p = 0.540$), reinforcing that HIV-positive individuals do not exhibit significantly different glycemic control compared to HIV-negative individuals. These findings suggest that other metabolic or clinical factors, such as kidney function, inflammation, or medication effects, may play a more substantial role in influencing HbA1c levels and diabetes risk.

A series of statistical analyses, including polynomial regression, log-transformed regression, and non-parametric tests, were conducted to explore potential relationships between Serum Magnesium levels and glycemic control (HbA1c). Across all models, Serum Magnesium did not emerge as a significant predictor of HbA1c levels, reinforcing the finding that magnesium levels alone are not a major determinant of diabetes risk in this population.

In the polynomial regression analysis, introducing a non-linear (quadratic) term for Serum Magnesium did not improve predictive power, as evidenced by the low R-squared value (0.009), indicating that the model explained less than 1% of the variation in HbA1c levels. Additionally, neither Serum Magnesium ($p = 0.993$) nor its squared term ($p = 0.979$) showed a significant association with HbA1c, suggesting no strong curvilinear relationship. Other variables, such as Age ($p = 0.076$) showed only a marginal effect, while BMI ($p = 0.400$) and HIV status ($p = 0.536$) were not significant predictors of HbA1c.

Similarly, the log-transformed regression analysis confirmed that transforming Serum Magnesium did not enhance its predictive power (R-squared = 0.009, $p = 0.694$), further supporting the weak association between magnesium levels and glycemic control. Once again, Age displayed a slight but non-significant effect ($p = 0.076$), while BMI ($p = 0.399$) and HIV status ($p = 0.536$) remained non-significant.

To assess group differences in Serum Magnesium levels across diabetes categories (Normal, Pre-Diabetes, and Diabetes), a Kruskal-Wallis test (a non-parametric alternative to ANOVA) was conducted. The results (test statistic = 0.404, p-value = 0.817) indicated no statistically significant differences in Serum Magnesium levels between these groups, confirming that magnesium levels do not vary meaningfully across diabetes categories.

Across all statistical approaches—including linear regression, polynomial regression, log-transformed regression, and non-parametric tests—Serum Magnesium was not identified as a significant determinant of HbA1c levels or diabetes status. These findings suggest that other metabolic, dietary, or clinical factors, such as kidney function, inflammation, medication use, or nutritional intake, may play a more substantial role in diabetes risk and progression than Serum Magnesium alone. Future research should incorporate a broader range of metabolic markers and longitudinal data to further explore potential confounders and refine our understanding of the role of magnesium in glycemic regulation.

The correlation matrix in Figure 4 revealed weak associations between Serum Magnesium, Fasting Glucose, and HbA1c, indicating that while some trends may exist, the direct linear relationship between these variables is not strong. To further assess whether Serum Magnesium is an independent predictor of HbA1c levels (as a marker of Type 2 Diabetes), a regression analysis was conducted, adjusting for HIV status, age, and BMI. The regression analysis confirmed that Serum Magnesium is not a significant predictor of HbA1c (%), as indicated by a small coefficient (0.2675)

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and a high p-value (0.687), suggesting no statistically significant association. Additionally, Age and BMI showed weak effects, with Age having a marginal association (p = 0.076), while BMI was not significant (p = 0.399). Furthermore, HIV status did not significantly affect HbA1c levels, as the coefficient for HIV-Positive individuals (0.1406) had a high p-value (0.536), indicating no clear impact.

Overall, these findings suggest that Serum Magnesium levels do not independently predict glycemic control (HbA1c), and HIV status does not significantly alter this relationship. Other metabolic and lifestyle factors may play a more substantial role in diabetes risk and progression, warranting further investigation into potential confounders such as kidney function, inflammation, dietary intake, and medication use.

The heatmap visually represents the relationships between Serum Magnesium, Fasting Glucose, and HbA1c (%), with correlation coefficients indicating weak associations among these variables. Serum Magnesium and Fasting Glucose exhibited a very weak correlation (r = 0.05), suggesting that magnesium levels have little to no direct linear relationship with fasting glucose and are unlikely to significantly influence short-term blood sugar regulation. Similarly, Serum Magnesium and HbA1c showed an even weaker correlation (r = 0.01), indicating that magnesium levels do not have a substantial predictive value for long-term glucose control, as individuals with higher or lower magnesium levels did not consistently exhibit differences in HbA1c levels. The correlation between Fasting Glucose and HbA1c was also weak (r = 0.01), which may reflect individual variations in glucose regulation, medication effects, or the presence of other metabolic conditions affecting glycemic control. These findings suggest that Serum Magnesium levels alone are not a strong determinant of diabetes markers (HbA1c and fasting glucose) in this population. Instead, additional confounding factors such as dietary intake, kidney function, medication use, and HIV-related metabolic changes may play a more significant role in influencing blood sugar regulation. Further studies incorporating a broader range of metabolic and clinical factors are needed to clarify the complex relationship between magnesium status and glycemic control.

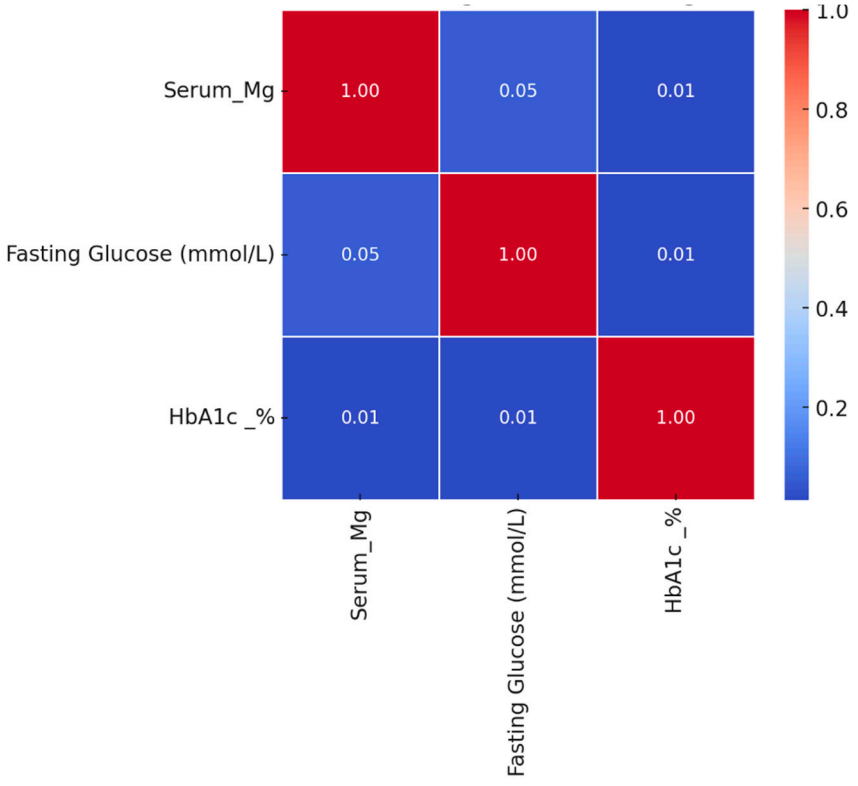

Figure 4. Correlation matrix of serum magnesium, fasting glucose and HbA1c.

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4. Discussion

This study investigated the association between Serum magnesium levels, Type 2 Diabetes (HbA1c and fasting glucose), and HIV status in a cohort of both HIV-positive and HIV-negative individuals. The serum magnesium levels did not significantly correlate with glycemic control (HbA1c) or fasting glucose levels, suggesting that magnesium alone may not be a strong determinant of diabetes status in this population. Previous studies have reported mixed findings regarding the role of magnesium in diabetes, with some indicating a potential protective effect against insulin resistance, while others have found no significant relationship **[11,12]**. The relationship between serum magnesium levels, type 2 diabetes (T2D), and HIV status is a complex interplay that has garnered attention in recent research. Magnesium is an essential mineral that plays a critical role in various physiological processes, including glucose metabolism and insulin signaling. Low serum magnesium levels have been consistently associated with increased insulin resistance and poor glycemic control in individuals with T2D, as evidenced by studies showing a negative correlation between serum magnesium and both HbA1c and fasting glucose levels **[13]**. Also, a study by Eker and Ataoğlu found that hypomagnesemia was significantly associated with higher HbA1c and fasting blood glucose levels, indicating that magnesium deficiency may exacerbate glycemic dysregulation in T2D patients **[14].** Therefore, further research is necessary to establish whether magnesium plays a role in the progression of diabetes, particularly in populations with high HIV prevalence.

HIV-positive individuals did not exhibit significant differences in serum magnesium levels compared to HIV-negative individuals, regardless of their diabetes status. While some diabetic individuals showed slightly lower magnesium levels, the differences were not statistically significant, and substantial variability was observed across all diabetes categories. This suggests that magnesium depletion may not be a universal characteristic of diabetes but could affect specific subgroups, such as those with underlying kidney dysfunction, malabsorption, or long-term metabolic complications **[15,16].** Additionally, ART has been implicated in mineral metabolism alterations, which could influence magnesium status in HIV-positive individuals **[17,18].** Future studies should explore the potential mechanisms linking HIV, ART and magnesium homeostasis in diabetic risk.

When examining the impact of HIV status on serum magnesium levels, evidence appears to indicate that HIV-positive individuals do not exhibit significant differences in magnesium levels compared to their HIV-negative counterparts, regardless of their diabetes status **[19].** A review by Piuri et al. emphasized that magnesium deficiency is prevalent in various metabolic conditions, including obesity and T2D, but did not specifically highlight significant differences in magnesium levels between HIV-positive and HIV-negative individuals **[20]**. This suggests that while both populations may experience magnesium deficiency, the HIV status itself may not be a determining factor in serum magnesium levels.

These findings align with some previous studies that report inconsistent associations between magnesium levels and diabetes, highlighting that other metabolic and lifestyle factors (e.g., dietary magnesium intake, kidney function, and inflammation) may play a greater role in glucose homeostasis **[21,22].** Several epidemiological studies have explored the relationship between serum magnesium levels and diabetes risk, with varying results depending on study population, measurement methods, and confounding factors [23,24]. Some studies have reported that low magnesium levels correlate with higher HbA1c and fasting glucose, suggesting a potential role for magnesium in insulin sensitivity and glucose **regulation [25,26].** Given magnesium's influence on glucose transport, insulin receptor function, and beta-cell activity, deficiency has been proposed as a risk factor for worsening glycemic control **[27,28].** However, other research, including the present study, has found no significant association between Serum Magnesium and diabetes markers after adjusting for confounding factors, indicating that magnesium's impact on glucose metabolism may be highly context-dependent **[29,30]**. Underlying conditions such as renal function, inflammation, and dietary intake may play a more significant role in magnesium status and its effects on diabetes **[31].**

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Additionally, prior research has suggested that HIV-positive individuals may experience altered magnesium metabolism, potentially due to ART, chronic inflammation, or metabolic **changes [32].** However, the findings of this study did not show significant differences in Serum Magnesium levels between HIV-positive and HIV-negative individuals, reinforcing the idea that HIV infection alone is not a significant determinant of magnesium status. These results suggest that while magnesium plays an essential role in metabolic health, its direct association with glycemic control and diabetes risk remains uncertain. It warrants further research to explore potential interactions with other metabolic factors, such as kidney function, dietary intake, and long-term ART effects.

Although this study did not establish a strong association between Serum Magnesium levels and glycemic control (HbA1c and fasting glucose), previous research suggests that magnesium supplementation may still benefit individuals with confirmed magnesium deficiency and impaired glucose tolerance **[33].** Routine screening of Serum Magnesium levels in diabetic individuals, especially those with kidney disease, gastrointestinal malabsorption, or long-term metabolic disorders, could help identify at-risk patients who may benefit from targeted interventions.

Since HIV status was not a significant predictor of Serum Magnesium levels, routine metabolic monitoring in HIV-positive individuals should continue to focus on other key markers such as lipid profiles, kidney function, and inflammatory status, which may have a more direct impact on long-term health. Additionally, further investigation into the long-term effects of ART on mineral metabolism is warranted to determine whether specific antiretroviral therapies contribute to potential micronutrient imbalances, including magnesium deficiency.

To better understand the complex relationship between magnesium levels, diabetes, and metabolic health, future research should incorporate additional confounding factors such as dietary magnesium intake, kidney function tests, and inflammatory markers. Moreover, longitudinal studies tracking magnesium status over time are needed to determine whether magnesium depletion is a precursor to diabetes onset or a secondary consequence of metabolic dysregulation. Expanding research in this area could help clarify the role of magnesium in diabetes prevention and management, particularly in individuals with multiple risk factors.

5. Limitations

This study has several limitations that should be considered when interpreting the findings. First, the cross-sectional design only captures associations at a single point in time, making it impossible to establish causality between Serum Magnesium levels and diabetes risk. A longitudinal study would be necessary to determine whether low magnesium levels contribute to diabetes onset or if diabetes itself leads to magnesium depletion. Second, dietary magnesium intake from food and supplements was not measured, which may have influenced Serum Magnesium levels and overall glucose metabolism. Since dietary habits play a crucial role in magnesium status, future studies should incorporate dietary assessments to provide a more comprehensive understanding of the relationship between magnesium and glycemic control. Third, several potential confounding factors, such as kidney function, medication use, and inflammation, were not included in the analysis. These factors could significantly impact both Serum Magnesium levels and diabetes risk, as kidney dysfunction can alter magnesium excretion, medications (e.g., diuretics, antiretroviral therapy) can affect magnesium balance, and chronic inflammation may influence both magnesium metabolism and insulin sensitivity. Future research incorporating these additional variables could help refine the findings and provide a clearer picture of the role of magnesium in diabetes and metabolic health.

6. Conclusions

This study found no strong or statistically significant association between Serum Magnesium levels and glycemic control (HbA1c and fasting glucose) in either HIV-positive or HIV-negative individuals. Although diabetic individuals exhibited slightly lower magnesium levels, the differences were not statistically significant, suggesting that magnesium depletion is not a universal

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characteristic of diabetes. Additionally, HIV status did not influence magnesium levels, indicating that HIV infection alone does not significantly impact magnesium metabolism in this population. Future research should focus on longitudinal studies to determine whether magnesium deficiency plays a causal role in diabetes development and incorporate dietary magnesium intake, kidney function tests, and inflammatory markers to explore potential confounding factors. Additionally, investigating targeted magnesium supplementation strategies for individuals with documented magnesium deficiency and poor glycemic control may help identify subgroups that could benefit from magnesium-related interventions. The findings contribute to the ongoing discussion on magnesium's role in metabolic health and diabetes management, reinforcing the need for a multifactorial approach in diabetes prevention and treatment that considers a combination of micronutrient status, metabolic markers, and lifestyle factors.

Author Contributions: Conceptualization, M.M and T.A.; methodology, M.M.; formal analysis, M.M and L.M.F.; investigation, M.M..; resources, T.A.; data curation, L.M.F.; writing—original draft preparation, M.M. and L.M.F.; writing—review and editing, T.A.; visualization, M.M. and L.M.F.; supervision, T.A.; project administration, M.M.; funding acquisition, T.A. All authors have read and agreed to the published version of the manuscript.

Funding: This research was fully funded by the National Research Foundation (NRF) (PMDS22062828655) and the South African Medical Research Council under the Research Capacity Development Initiative (MRC-RFA-CC 01-2014). The funders had no role in study design, data collection and analysis, decision to publish, or manuscript preparation.

Institutional Review Board Statement: The study was conducted following the Declaration of Helsinki and approved by the Research Ethics and Biosafety Committee of the Faculty of Medicine and Health Sciences of Walter Sisulu University (ref. no. 068/2024) and Eastern Cape Department of Health (ref. No. EC_202410_010).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Data can be requested from the corresponding author.

Acknowledgments: I sincerely thank my supervisor, Professor T**.** Apalata, for his invaluable guidance and support throughout my research. I also appreciate Professor EV Blanco-Blanco for his mentorship and insightful contributions. Special Thanks to Dr. Pulido for expert advice and constructive feedback. Lastly, I acknowledge the support and resources provided by Walter Sisulu University, the financial support from the NRF, and the broader support of the RCDI-SAMRC parent project, which facilitated this work.

Conflicts of Interest: The authors declare no conflicts of interest.

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