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العلاقة بين ارتفاع سكر الدم واستقلاب البوتاسيوم لدى مرضى السكري من النوع الثاني في العراق: دراسة حالة وضابطة

م.م.ليث عمار شياد ، م.م.وسام حسيب شاكر
جامعة واسط/كلية التربية الاساسية
أ.د. ظافر حسن غالي
كلية التربية للعلوم الصرفة
أ.م.د.علي سعد البديري
جامعة واسط/كلية التربية الاساسية

المستخلص :

داء السكري من النوع الثاني هو مرض أيضي متزايد الانتشار، ومن المتوقع أن يؤثر على نحو ٦٩٣ مليـون شخص بحلول عام ٢٠٤٥. يرتبط فرط سكر الدم باضطرابـات في أيض الشوارد، ولا سيما البوتاسيـوم .هدفت هذه الدراسة إلى استكشاف العلاقة بين مستويات البوتاسيوم في المصل وف رط سكر الدم، إضافـة إلى المضاعفات الأخرى لدى مرضى داء السكري من النوع الثاني. شملت ا لدراسة ١٠٠ مريضًا بداء السكـري من النوع الثاني (٥٠ رجلًا و٥٠ امرأة)، تراوحت أعمارهم بين ٤٠ و٧٥ عامًا. كما تم اختيار مجموعة ضابطـة مماثلة للمرضى من حيث العمر وعدد المشاركين. تم قياس كل من إجمالي البوتاسيوم في المصل ومستـوى الغلوكوز الصيامي في المصل باستخدام كوا شف جاهزة .أظهرت النتائـج انخفاضًا معنويًـا في مستويات البوتاسيوم في المصل لدى مرضى دا ء السكري مـن النوع الثاني مقارنـة بالأصحـاء (٣.٤٩٣±٠.٠٣٨مليمول/لتر) مقابل (٤.٢٦٨±٠ .٠٥ مليمول/لتـر)؛ (P = 0.0001) كما أظهرت المريضات انخفاضًا معنويًا في مستويات البوتاس يوم مقارنة بالمجموعة الضابطـة (٣.٥٠٢±٠.٠٦٥ مليمـول/لتر مقابل ٤.٢٣٦±٠.٠٦٩ مليمول/لـ تر؛(P = 0.0001)، وكذلك الحال لدى المرضى الذكور (٣.٤٨٤±٠.٠٤٣) مليمول/لتر مقابل(٤.٣٠±٠.٠٧٣ مليمول/لتر)؛ (P = 0.0001) بالإضافة إلى ذلك، وُجد ارتباط سلبي قوي بين ارتف ـاع مستويات الغلوكوز وانخفاض تركيز البوتاسيوم لدى المرضى، حيث بلغت قيمة الانحدار ٠.٨

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٨ مـــع دلالة إحصائية عاليـــة($P < 0.001$) . كشفت نتائج الدراسة عن وجود علاقة ارتباط سلبية قوية بين ارتفاع مستويات الغلوكوز وانخفاض تركيز البوتاسيوم لدى مرضى داء السكري من النوع الثاني.

الكلمات المفتاحية :بوتاسيوم المصل؛ داء السكري من النوع الثاني؛ كلوكوز المصل؛ البوتاسيوم؛ الأيـــض.

Correlation between Hyperglycemia and Potassium metabolism in Iraqi patients with Type 2 Diabetic Mellitus: A case control study

Assis.LeC. Layth Ammar Chyad, Assis.LeC. Wisam Haseeb Shakir
Wasit University /College of Basic Education
Assis.Dr.Zafir Hassan Ghali
College of Education for Pure Science
Assis.prof.Dr.Ali Saad Al-budairi
Wasit University /College of Basic Education

Abstract

Type 2 Diabetes Mellitus (T2DM), a growing metabolic disease that is expected to affect 693 million people by 2045. Hyperglycemia is associated with defect in ionic metabolism, particularly potassium (K+). The current study aimed to explore correlation between serum potassium levels and hyperglycemia, as well as other complication in patients with T2DM . This study included 100 T2DM patients (50 males and 50 females) , aged 40-75 years . A control groups was matched with patient in both age and numbers of participants . Total serum potassium and fasting serum glucose levels were determined using ready-made solutions for the Quantitative determination of potassium ion (IVD). The results revealed significantly lower serum potassium levels in T2DM patients compared with healthy controls (3.493±0.0389 mmol/L vs. 4.268±0.05 mmol/L; P= 0.0001). Female patients showed significantly lower serum potassium levels than controls (4.236±0.069 mmol/L vs. 3.502±0.065 mmol/L; p= 0.0001).Similarly, male patients exhibited significantly lower serum potassium levels compared with controls (3.484±0.043 mmol/L vs. 4.30±0.073 mmol/L; p=0.0001). Additionally , a strong negative correlation was observed between serum glucose levels and potassium concentration in

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patients, with a regression value of 0.88 and high statistical significance ($p<0.001$). Conclusion: our finding has explored the a strong negative correlation between elevated glucose levels and decreased in potassium concentration in T2DM patients .

Keywords: Serum potassium; Type 2 Diabetes Mellitus;Serum glucose, Pottasium, Ionic metabolism.

1. Introduction

Type 2 Diabetes Mellitus (T2DM), a rapidly growing metabolic disease, is characterised by chronic hyperglycemia due to impaired insulin secretion and action, affecting 693 million people by 2045(Cho *et al*., 2018). This illness is among the most prevalent global disease burdens (Collaborators, 2019). Various evidence lines suggest hypokalaemia as a potential risk factor for T2DM (Chatterjee *et al*., 2010). Experimental studies have demonstrated that thiazide-induced hypokalaemia can result in reduced insulin secretion. A balanced diet with adequate nutrient content can decrease the glycated hemoglobin percentage (%HbA1c) in people with T2DM by 0.3–2% (Rowe et al., 1980) . Low dietary intake or serum potassium levels, which are crucial for resting membrane potential and intracellular osmolarity, increase the risk of insulin resistance or diabetes (Association, 2018; Ekmekcioglu *et al*., 2016).

In addition to glucose dysregulation, electrolyte imbalancesparticularly alterations in potassium levels—are frequently observed in patients with T2DM. Potassium is an essential intracellular cation involved in maintaining membrane potential, nerve conduction, muscle contraction, and cellular metabolism (Yeung *et al*., 2022). Its balance is closely regulated by insulin, renal function, and acid–base status. The insulin prepared the take the K associated with glucose , any change in the level of insulin cause abnormality in the level of K(Reshma *et al*., 2020).

The patient of T2DM suffered from hypokalemia and hyperkalemia because the impact some factors such as therapy by insulin, diabetic nephropathy, and osmotic diuresis induced by hyperglycemia. These factors clinically significant due to change of level of potassium which contribute to ,

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impaired neuromuscular function ,cardiac arrhythmias (Strauss-Kruger *et al*., 2023).

Importantly, the bi-directional of metabolism correlation between levels of glucose and potassium therapeutic implications. The impairing insulin secretion from pancreatic β-cells, cause hypokalemia Thus, defect in potassium balance negative impact on the complicate the clinical management of diabetes and directly influence disease progression (Schroeder *et al*., 2020; Surendran & Sasikala, 2020). Understanding the interplay between glucose metabolism and potassium balance in T2DM is crucial for optimizing treatment strategies, preventing complications, and improving patient outcomes (Santhosh *et al*., 2021).This interaction highlights the need for regular monitoring of both blood glucose and serum electrolytes in the clinical management of type 2 diabetic patients (Kim *et al*., 2015).

Finally, aim of the current study is estimate serum potassium levels in patients with T2DM and found the correlation between serum potassium and hyperglycemia .

2. Materials and Methods:

2.1 Design of Study

This study included (100) T2DM patients (50 males and 50 females) and control groups were match to both sex and number of participants. The study recruited participants from Al-Aziziyah General Hospital in Wasit Governorate.All participants were obtained oral consent coordinating the standardized questionnaires, included age, gender, medications, and medical or family history of diabetes.The study obtain on the ethic approval from Wasit university at 2025/3/5 with number 22256.

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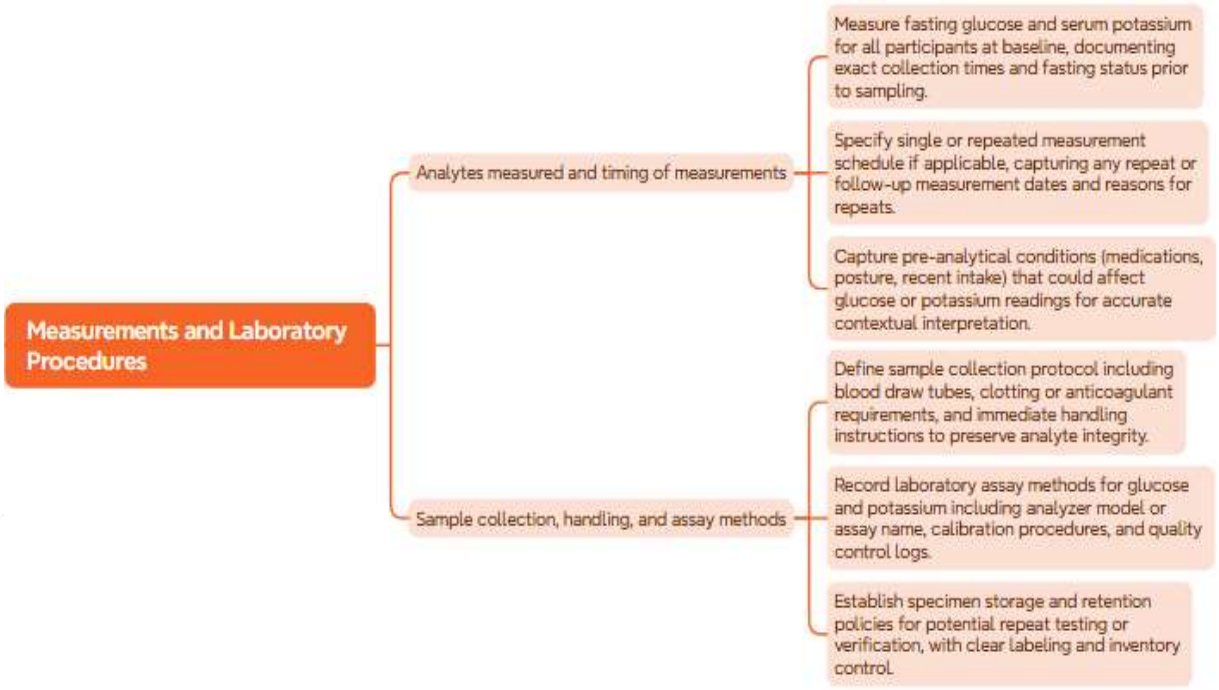

Figure 1 : flow work of study design

Inclusion criteria.

The patients suffered T2DM and treated by insulin along two time were included in the current study.

Exclusion criteria.

the patients suffering the renal failure and other disease were excluded from the study.

2.2 Estimation of biochemistry markers (K, and Fasting Blood Glucose).

Both total serum potassium and fasting glucose were determined using ready-made solutions. Furthermore, the serial numbers of kits used in the study (K, 55898 and Glucose, 22369 from biosystem company).

2.3 Statistical Analysis

The JASP (IL, USA) statistical packages were used for data analysis. Furthermore ,T- test was used to identify the difference between participants and Line regression applied to find the value of correlation between the parameters. The S = Significant difference ($P < 0.05$), HS = Highly Significant difference ($P<0.01$), and NS = Non Significant difference were the categories used to compare the significance (P-value) in any test.

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3. Results and Discussion

The results revealed that the concentrations of total serum potassium declined significantly in patients with T2DM compared with healthy control, 3.493±0.0389 mmol/L, vs. 4.268±0.05 mmol/L. (P= 0.0001), as shown in the Figure-2 , Table-1.

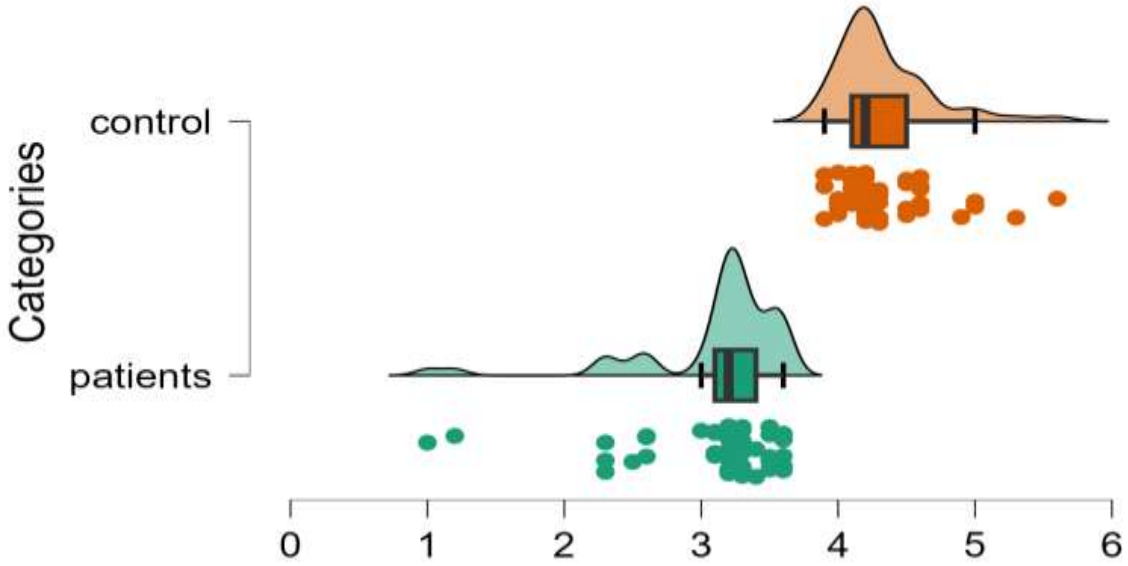

Figure2,Raincloud Plots explain the comparison between concentration of patient and healthy control with difference high significant P ≤ 0.0001**

The current study suggest that Type 2 Diabetes Mellitus (T2DM), reduced 24-hour urine potassium excretion is associated with poor outcomes, including greater all-cause mortality . T2DMresearch indicated that individuals with random blood sugar levels over 300 mg/dl had higher potassium levels, demonstrating the link between potassium and glucose (Reshma et al., 2020; Yeung et al., 2022). Research comparing white and black persons found decreased urine potassium levels, suggesting ethnicity may affect potassium metabolism and diabetes (Strauss-Kruger et al., 2023). Chronic diabetics require monitoring as their potassium levels decline to prevent serious health concerns (Surendran & Sasikala, 2020). A Dutch T2DM study indicated that insufficient potassium consumption substantially increases all-cause death (Yeung et al., 2022). A meta-analysis (Neuen et al., 2022) suggests that sodium-glucose cotransporter 2 inhibitors may lower the

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risk of hyperkalaemia in people with T2DM who have a high risk of heart disease or chronic kidney disease. Potassium abnormalities are common in patients with T2DM, and they can cause serious clinical problems (Schroeder et al., 2020). Black persons reported lower urine potassium levels than White adults, suggesting ethnicity may affect potassium metabolism and diabetes (Strauss-Kruger et al., 2023). The research emphasizes the importance of adequate potassium levels in T2DM patients, as well as measures to improve health.

Table 1: **Comparsion between concentration of potassium in the serum of patient and healthy control according sex.**

Gender	Group	Potassium concentration (mmol/L, Mean ± SE)	P-value
Female	Control	4.236 ± 0.069	
	Patients	3.502 ± 0.065	**0.0001**
Male	Control	4.300 ± 0.073	
	Patients	3.484 ± 0.043	**0.0001**
P-value		**0.0001**	

Mean (SE) values of serum potassium (mmol/L)P ≤ 0.0001****

According to gender, the mean serum potassium concentration between the female and male patient groups was similar. There aren't any big differences in potassium levels between men and women with T2DM, even though some studies show that serum potassium levels rise in diabetic patients with insulin resistance (Kim et al., 2015; Santhosh et al., 2021). Other studies show that potassium levels don't differ much between diabetics and healthy controls (Jiskani et al., 2018). Additionally, a survey of diabetes patients found that only a tiny percentage adhered to the recommended potassium guidelines, indicating a general lack of dietary adherence (Baqar et al., 2020). The study suggests that the lack of significant differences in potassium concentration between males and females with T2DM may be due to a complex interplay of factors .

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Conversely, Željka et al.,(2022) found that males had significantly higher potassium concentrations than females, indicating gender-specific differences in electrolyte levels among diabetic patients (Dragila et al., 2022). Additionally, Valdivielso et al., (2024) found that hyperkalaemia prevalence and risk factors vary by gender in chronic kidney disease patients, with smoking being a significant risk factor in men. Therefore, studies show significant differences in potassium concentration between males and females with T2DM but also suggest more nuanced gender-specific variations, highlighting the complexity of electrolyte regulation in diabetic populations (Valdivielso et al., 2024 .(

According to gender, the mean of serum potassium level values among females in the patient's group was lower than the control group (4.236±0.069 mmol/L) versus (3.502±0.065 mmol/L) with a significant difference P= 0.0001. Furthermore , the mean serum potassium level values among male patients were lower than the control group (3.484±0.043 mmol/L) versus (4.30±0.073 mmol/L) in patients and control groups respectively with a significant difference. p = 0.0001. As shown in table 2. The decrease in potassium consumption among women with diabetes is associated with an increased risk of all-cause mortality in patients with T2DM in the Netherlands, highlighting its importance for longevity (Yeung et al., 2022). A Korean study found a link between reduced potassium intake and an increased risk of metabolic syndrome (MetS) and insulin resistance in women, highlighting the importance of potassium in metabolic health (Lee et al., 2013). Low levels of potassium in the blood may prevent glucose and potassium from entering the muscles, which limits insulin secretion and leads to diabetes, according to 2017 Indian research. Tarun et al. (2017) state that managing diabetes and reducing health risks necessitates that women maintain appropriate potassium levels through dietary interventions (Saxena et al., 2017.(

Research indicates that males with T2DM who suffer from hyperkalemia, potentially due to renal impairment, insulin insufficiency, or hypertonicity, exhibit significantly elevated blood potassium levels (21-23). Samantha et al. (2023) found that those with poorly managed T2DM who also have

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insulin resistance tend to have blood potassium values that are greater than those who do not have insulin resistance. Hyperkalaemia is more common in diabetes patients, and their blood potassium levels are far greater than in healthy controls, according to the research 2023). Sitholayet al. (2017), the research emphasizes the importance of monitoring potassium levels in the blood in men with T2DM to prevent issues such as electrolyte imbalances (Sitholay et al., 2017.(

There was a significant difference in concentrations of total serum glucose when compared to type 2 diabetes mellitus and controls (Mean 171.240±5.087 mg/dL, vs. 104.383±1.741 mg/dL. (p= 0.0001). As shown in the Figure-3 and Table-2 .

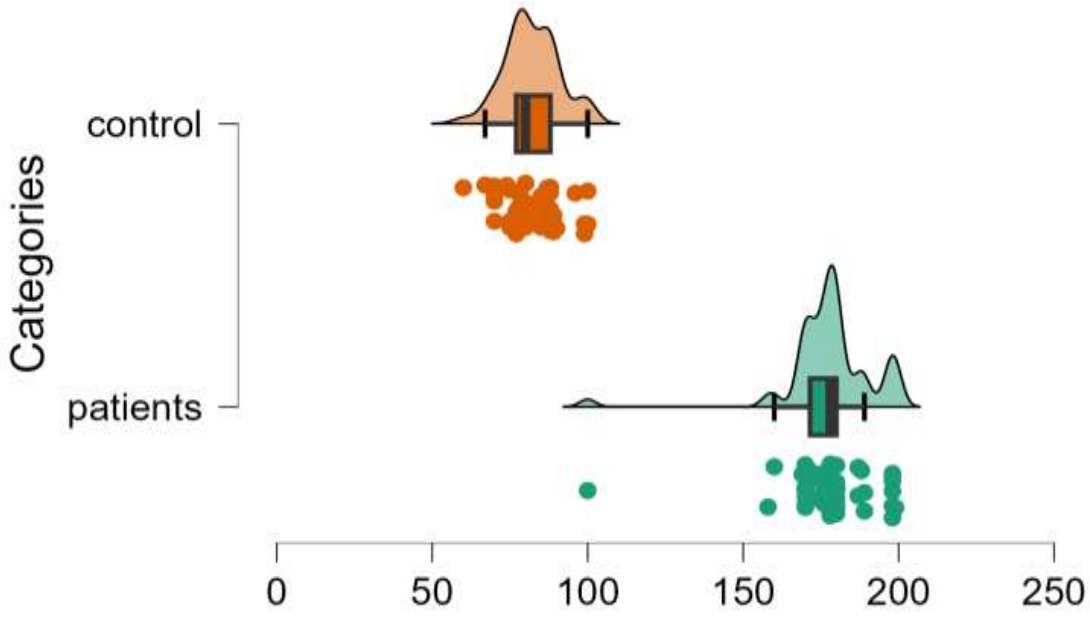

Figure3, Raincloud Plots explain the comparison between concentration of glucose in the serum patient and healthy control with difference high significant P ≤ 0.0001 **

The current study agreed with Putra *et al*. (2023), who suggest that several characteristics, including gender, age, treatment type, and length of diabetes, may contribute to unmanageable high blood glucose levels in individuals with T2DM (Maha Putra *et al.*, 2023). Elevated blood glucose levels in T2DM individuals are associated with stress and obesity, which may heighten insulin resistance (Wardani *et al.*, 2018). Injury to organs such as the pancreas, liver, and adipose tissues may cause impairment of insulin

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signalling, a frequent symptom of T2DM (Abdulwahid, 2016). Researchers have shown that those with T2DM who have microvascular problems are more likely to have high glycemia levels (Sulastri & Harjati, 2022). Qinghua *et al*. (2019) cite research that suggests increased FBG levels as a possible pathophysiological feature of sick organs or tissues, which might result in prediabetes or T2DM (Zhang et al., 2019).

Table2: Serum glucose levels among females and males with T2DM compared to controls

Gender	Group	Glucose level (mg/dL, Mean ± SE)	P-value
Female	**Control**	**104.66 ± 2.407**	
	Patients	**173.52 ± 7.369**	**0.0001**
Male	**Control**	**104.1 ± 2.55**	
	Patients	**168.96 ± 7.076**	**0.0001**
P-value		**0.0001**	

Mean ±(SE) values of serum glucose level(mg/dL)P ≤ 0.0001****

The mean serum glucose levels were significantly higher in patients compared to controls for both genders. Among females, the control group had a mean glucose level of 104.67 ± 2.41 mg/dL, while female patients exhibited a significantly elevated level of 173.52 ± 7.37 mg/dL (p = 0.0001). Similarly, in males, the control group showed a mean glucose level of 104.10 ± 2.55 mg/dl, whereas male patients had a significantly higher level of 168.96 ± 7.08 mg/dl (p = 0.0001).

Our finding agreed with Wuni *et al*. (2022) study, which revealed that T2DM patients have an average blood sugar level of 326 mg/dL, with a higher percentage of females having uncontrolled HbA1c levels (Lestari *et al.*, 2022). Arslan *et al.* (2022), found that males had higher serum glucose levels and higher insulin resistance levels compared to females (Sajjad *et al.*, 2022). Additionally, Dinda *et al*., (2021), study found that female patients had better glycemic control, and HbA1c levels above 7% decreased the

estimated glomerular filtration rate in both genders. According to the study, there are gender-specific variations in the levels of serum glucose and glycaemic control among individuals with T2D (Ratri *et al.*, 2021).

Serum glucose levels differ greatly between type 2 diabetic women and healthy people. Wuni Sri Lestari et al. observed that uncontrolled T2DM patients had 326 mg/dL blood sugar on average in 2022 (Lestari *et al.*, 2022). Moreover, Salah *et al*. (2022) found that overweight or obese women with T2DM had far higher fasting blood glucose levels than normal-weight individuals (Hussein et al., 2022). Also, Fadhel *et al*., (2018) that in women with T2DM, blood triglycerides and total cholesterol were higher, which may indicate metabolic issues (Fadhel *et al*., 2018). Since Israt *et al*. (2021) found a drop in serum zinc levels in female T2DM patients, monitoring them is crucial for improved health. According to study, T2DM women have different metabolic profiles and serum glucose levels than healthy women (Israt *et al*., 2021).

Studies have shown that males with T2DMhave significantly higher serum glucose levels compared to healthy controls. A Bangladesh study found that male T2DM patients had a significantly lower mean fasting serum glucose level than healthy controls (Mumu et al., 2022). Similarly, Research in Indonesia indicates that patients with uncontrolled HbA1c levels have an average blood sugar level of 326 mg/dL, indicating poor blood sugar control in T2DM patients (Lestari *et al*., 2022).

Several studies demonstrated that males had higher serum levels of glucose than females (Avnon Ziv *et al*., 2023). Additionally, significantly in males patients with T2DM have lower serum levels of testosterone compared to non-diabetic males(Obi *et al*., 2016). Furthermore, consistently men have higher fasting levels of glucose than women in all ages (Elizabeth, Barrett-Connor. (1980).there was that study underscores the significance of considering sex ,age, and factors of hormones associated increased the serum of glucose in males (Barrett-Connor, 1980).

Figure -4 shown , there is a strong negative correlation between levels of serum potassium and glucose in the patient T2DM ($r = -0.80$, $p < 0.0001$).

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The result revealed that levels of glucose increase, compared to decrease serum potassium levels.

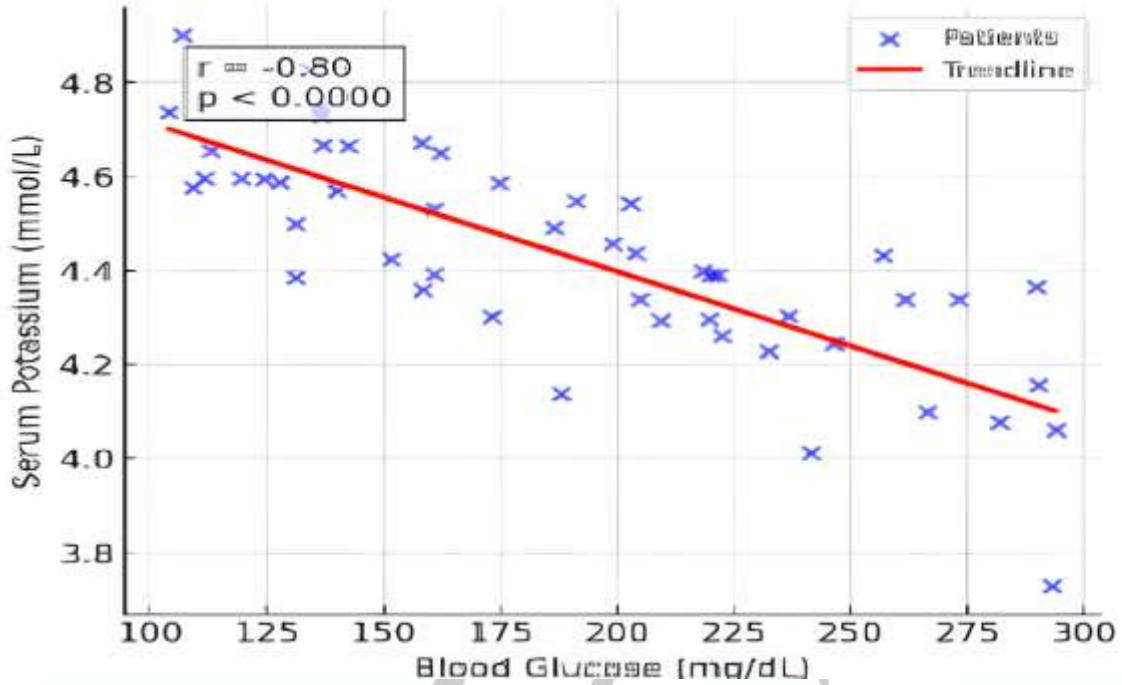

Figure4: Correlation between levels of both potassium and serum glucose in patients with type2 DM. r= -0.80, p= 0.0001.

The present study revealed that decrease in potassium and increasing glucose can be attributed to the osmotic effects of hyperglycemia. Additionally, high levels of glucose stimulated the release of insulin, which promotes the shift of potassium from the extracellular to intracellular space, further lowering serum potassium levels.

Our finding observed a significant reduce in levels of potassium with patients compared to increase to level of glucose. This phenomenon can be explored by physiological effects of hyperglycemia on homeostasis of potassium. Hyperglycemia induces osmotic diuresis, as outcome in elevated urination process which cause loss of potassium and other electrolytes, which contributes to a net depletion of total potassium reduction sometimes normal or elevated serum levels initially (Kitabchi *et al*., 2009). Moreover, insulin, whether endogenously administered therapeutically, promotes the

uptake of potassium into cells via the sodium-potassium ATPase, further lowering level of potassium (Musso *et al*., 2012).

These mechanisms explored the inverse correlation between serum of both glucose and potassium. Clinically, this fact is importance in the monitoring potassium with hyperglycemic patients, as rapid correction of hyperglycemia without potassium replacement may precipitate dangerous hypokalemia, with potential cardiac and neuromuscular complications (Friedrich *et al.*, 2018).

4.Conclusions

This present study revealed that patients with T2DM have significantly lower level of potassium compared to healthy controls. Furthermore, it indicated a strong association between T2DM and hypokalemia. Our study recommended expand future work to investigate the mechanisms driving potassium imbalance in T2DM and assess whether potassium correction strategies could enhance glycemic control and reduce disease complications.

Source of funding: No source of funding.

Ethical clearance: This study was approval by the ethics committee of the College of basic Education, Wasit University (Approval No 22/ 8554, data march 16/ 2025). All collected data were used solely for research purpose ,and strict measures were taken to ensure participant confidentiality and privacy. Written informed consent was obtained from all participant and the confidentiality of medical records was preserved in full compliance with ethical standards.

Conflict of interest: The authors affirm that they have no competing interests.

Use of Artificial Intelligence(AI): The authors have not used the AI.

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