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A Study of Some Physiological and Immunological Parameters in Patients with Type 2 Diabetes Mellitus Treated with Glucovance and Metformin

Ahmed Abbas Fadel*, Suha Abdel Khaleq Al-Jawari
Department of Biology , College of Science , University of Baghdad , Baghdad , Iraq

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Abstract

This study was designed to investigate and compare the physiological and immunological outcomes of Glucovance and Metformin therapy in patients with type 2 diabetes mellitus (T2DM). The research was carried out between March 4 and September 4, 2025, at Baghdad Hospital, Medical City, Iraq. A total of 75 male participants, aged 40–50 years and weighing 65–120 kg, were recruited and divided into three equal groups: Group 1 (n = 25) received Glucovance for five years, Group 2 (n = 25) received Metformin for five years, and Group 3 (n = 25) served as healthy controls. The evaluated parameters included fasting glucose (FGS), glycated hemoglobin (HbA1c), adiponectin (ADP), interleukin-17 (IL-17), interleukin-23 (IL-23), total antioxidant capacity (TAC), and vitamin B12. Blood samples were collected, stored at −20 °C, and analyzed using ELISA kits. The results revealed no significant differences between the two drug groups regarding HbA1c, FGS, and vitamin B12, although both showed significantly higher levels compared to the controls. ADP concentrations were markedly elevated in the Glucovance group, while IL-17 levels increased in the Metformin group. The levels of IL-23 were significantly higher in the Glucovance group compared to both the Metformin and the control groups. TAC values also differed significantly between the drug-treated groups, with both exceeding control values. These findings suggest that although Glucovance and Metformin provide comparable glycemic regulation, they differ in their immunological and oxidative stress profiles. Both treatments enhance insulin sensitivity and modulate immune responses, supporting their role in refining therapeutic strategies for T2DM management.

Keywords: Type 2 Diabetes, Glucovance, Metformin, , Hemoglobin A1c, Interleukin-17.

دراسة بعض المعايير الفسيولوجية والمناعية لدى مرضى السكري من النوع الثاني المعالجين بعقارين جلوكوفانس وميتفورمين

احمد عباس فاضل* , سهى عبد الخالق الجواري
قسم علوم الحياة, كلية العلوم , جامعة بغداد, بغداد , العراق

الخلاصة

هدفت هذه الدراسة إلى تقييم ومقارنة التأثيرات الفسيولوجية والمناعية لكلٍّ من عقاري غلوكوفانس

* Email: Son0p270@gmail.com

والميتفورمين لدى مرضى داء السكري من النمط الثاني (T2DM). أُجريت الدراسة خلال الفترة من 4 آذار إلى 4 أيلول 2025 في مستشفى بغداد، مدينة الطب، العراق. شملت العينة 75 مشاركًا من الذكور تراوحت أعمارهم بين 40–50 سنة، وأوزانهم بين 65–120 كغم. قُسم المشاركون إلى ثلاث مجموعات: المجموعة الأولى (n=25) تلقت علاج الغلوكوفانس لمدة خمس سنوات، المجموعة الثانية (n=25) تلقت الميتفورمين لمدة خمس سنوات، في حين اعتُمدت المجموعة الثالثة (n=25) كضابطة من الأصحاء. شملت المؤشرات المقاسة: سكر الصيام (FGS)، الهيموغلوبين الغليكوزيلاتي (HbA1c)، الأديبونكتين (ADP)، الإنترلوكين-17 (IL-17)، الإنترلوكين-23 (IL-23)، السعة الكلية المضادة للأكسدة (TAC)، وفيتامين B12. جُمعت عينات المصل وخُزّنت عند 0 °C – 20 ، وأُجريت القياسات باستخدام ELISA تجارية. لم تُسجَّل فروق معنوية بين الغلوكوفانس والميتفورمين فيما يتعلق بـ HbA1c وFGS، وفيتامين B12، رغم أن كلا المجموعتين أظهرت قيمًا أعلى بشكل ملحوظ مقارنة بالمجموعة الضابطة. كما ارتفع مستوى ADP بشكل معنوي في مجموعة الغلوكوفانس مقارنة بالمجموعة الضابطة. وُجد ارتفاع في IL-17 في مجموعة الميتفورمين فقط، في حين سُجّل ارتفاع معنوي في IL-23 في مجموعة الغلوكوفانس مقارنة بكل من الميتفورمين والضابطة. أما TAC فقد أظهر فروقًا معنوية بين الغلوكوفانس والميتفورمين، مع تجاوز القيم في كلا المجموعتين لمستويات المجموعة الضابطة. أظهر كلٌّ من الغلوكوفانس والميتفورمين فعالية متقاربة في ضبط المؤشرات السكرية، غير أنهما اختلفا في تأثيراتهما على مؤشرات الالتهاب والإجهاد التأكسدي. كلا العلاجين حسّنا من حساسية الإنسولين وأسهما في تعديل الاستجابات المناعية، مما يبرز أهميتهما في تحسين الاستراتيجيات العلاجية لإدارة داء السكري من النمط الثاني.

1. Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder defined by persistent hyperglycemia, which arises from defects in insulin secretion, insulin action, or a combination of both [1]. Among its several forms, type 2 diabetes mellitus (T2DM) is the most prevalent and is strongly associated with obesity, sedentary lifestyles, and unhealthy dietary practices. The condition is primarily characterized by insulin resistance accompanied by relative insulin deficiency, resulting in wide-ranging metabolic and immunological disturbances. The global incidence of T2DM continues to rise, posing a major health burden and ranking as one of the leading causes of morbidity and mortality worldwide [2]. In addition to its impact on glucose metabolism, T2DM is increasingly recognized for its association with chronic inflammation and oxidative stress, which further complicate disease progression and outcomes. Despite advances in therapeutic approaches, glycemic control remains a challenge for many patients. Metformin, considered the first-line therapy for T2DM, exerts its effects mainly by inhibiting hepatic glucose production and enhancing insulin sensitivity in peripheral tissues. Glucovance, a fixed-dose combination of Metformin and glyburide, offers a dual mechanism by simultaneously improving insulin sensitivity and stimulating insulin secretion. Given these pharmacological differences, it is important to assess whether the two treatments have distinct influences on immunological and oxidative markers[3]. This study hypothesis that treatment with two different antibiotic drugs will have distinct effects on certain physiological and immunological parameters in patients with type 2 diabetes mellitus.

2. Materials and Methods

2.1.Studied subject

A total of 75 men aged between 40 and 50 years who had type 2 diabetes were enrolled. They were visiting Baghdad Hospital in the Medical City of Baghdad, Iraq, during the period from March 4, 2025, to September 4, 2025. This study was approved by the Ethics Committee of the Department of Biology, College of Science, University of Baghdad, Baghdad, Iraq. Committee number dated CSEC/0525/0063. These men were enrolled in this study. They were divided into three groups, each group containing 25 men. These totals are as

follows. The first group is for men who have been taking Glucovance for five years. The second group includes men who have also been taking Metformin for five years. The third group consists of healthy people who are not infected. These groups are samples to study the effect of the two drugs and compare them.

2.2. Collecting blood samples

Five ml of blood was obtained from each participant by venous puncture using disposable syringes. Then place the samples in a gelatinous tube and leave them to coagulate at room temperature (approximately 20°C). Next, centrifuge them at 5000 rpm for 10 minutes. This is to collect the blood serum, which is transferred to a plate tube and then frozen at 20 °C until it is used for physiological and immunological examination. The following kits were used to measure the study parameters, which include: adiponectin (Demeditec , Germany) , fasting glucose levels (Human , Germany), Hb1Ac (Human , Germany), Interleukin-17 (Cusabio , China) , interleukin-23 (Cusabio , China) , Total antioxidant capacity (Shanghai YL Biont , China), and Vitamin B12 (Shanghai YL Biont , China).

2.3. Statistical Analysis

The Statistical Analysis System (SAS, 2018) software was employed to evaluate the effects of the different groups on the study parameters, and the least significant difference (LSD) test was applied for mean comparisons.

Result and discussion

The data presented in Table 1 indicate a highly significant difference ($p \leq 0.01$) in both HbA1c and fasting glucose (FGS) levels among the study groups. Regarding HbA1c, no significant difference ($p > 0.01$) was observed between the Glucovance and Metformin treatment groups. The mean HbA1c values were 8.27 ± 0.25% and 7.62 ± 0.36% for Glucovance and Metformin groups, respectively. However, both treatment groups showed a significant increase ($p \leq 0.01$) in HbA1c compared to the control group, which had a mean value of 4.83 ± 0.07%. Concerning FGS levels, a significant increase ($p \leq 0.01$) was observed in both Glucovance and Metformin groups compared to the control group. The mean FGS values were 145.0 ± 11.43 mg/dL and 152.84 ± 27.06 mg/dL for Glucovance and Metformin groups, respectively, while the control group had a mean value of 81.88 ± 1.50 mg/dL.

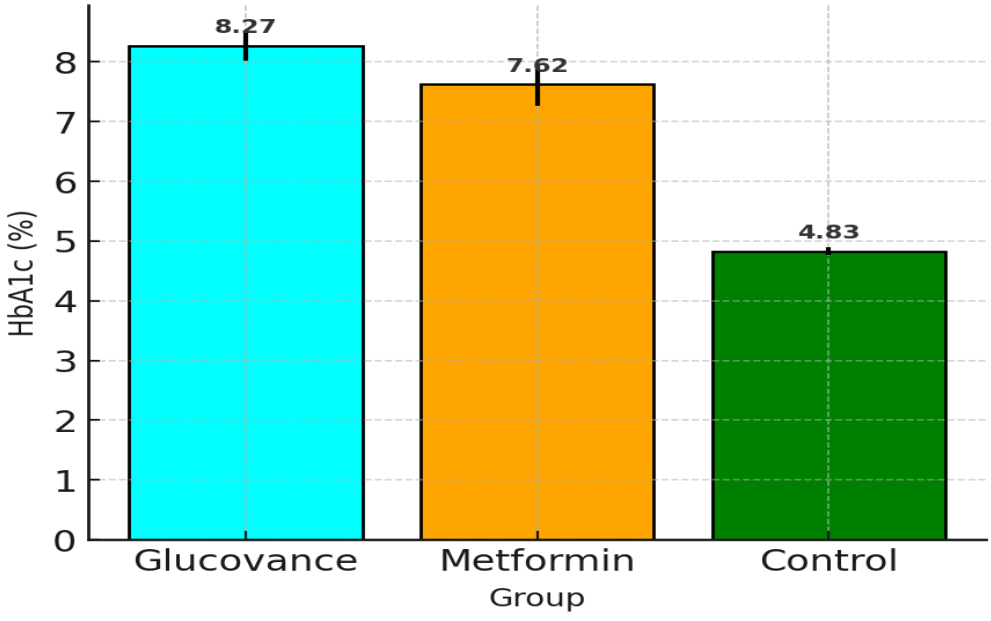

Figure 1: Comparison between the different groups in HbA1c

3.1.HbA1c levels

The relationship between HbA1c levels and Glucovance, which combines Metformin and glyburide, is significant in managing type 2 diabetes. Here are key points regarding this relationship, along with relevant references: reduction in HbA1c levels. Glucovance has been shown to effectively reduce HbA1c levels in patients with type 2 diabetes. The dual action of Metformin and glyburide helps improve glycemic control. [3-5].

3.1.1.Relationship between Hb1Ac and Metformin

HbA1c is a key indicator used to assess long-term glucose control in individuals with diabetes. Metformin is a first-line medication commonly prescribed for the management of type 2 diabetes. The relationship between HbA1c and Metformin involves how Metformin helps lower HbA1c levels, thereby improving glycemic control. Metformin exerts its therapeutic effects primarily by reducing hepatic glucose production, enhancing peripheral insulin sensitivity, and improving glucose uptake in tissues. [6-8].

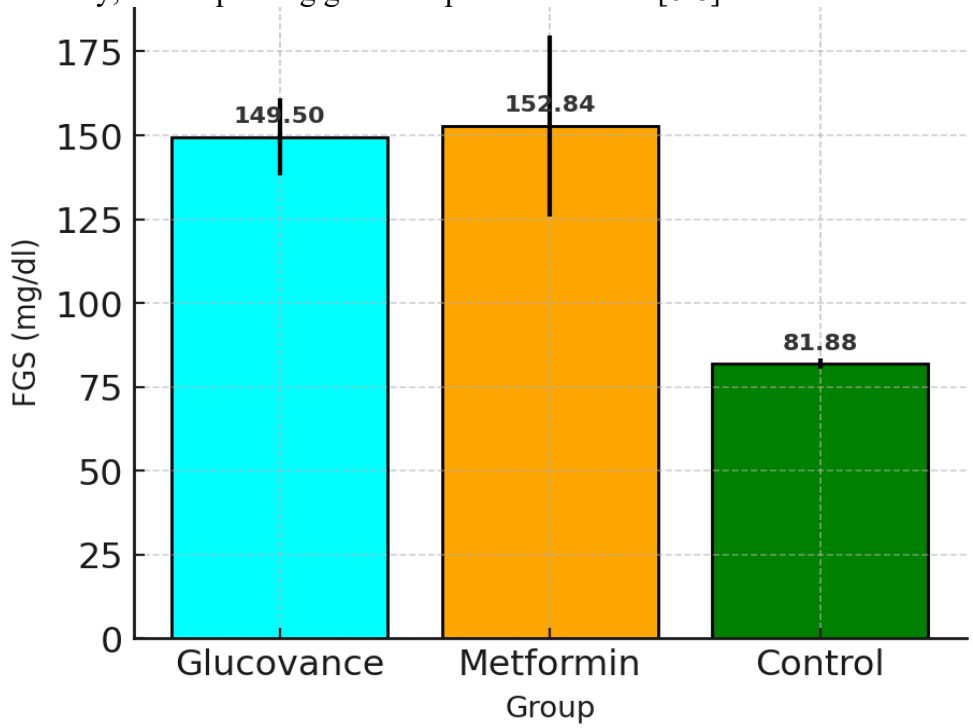

Figure 2: Comparison between the different groups in FGS

3.2.Fasting Glucose Levels (FGS)

The relationship between FGS levels and Glucovance, a combination of Metformin and glyburide, is important for managing type 2 diabetes. Here are some key points along with relevant references: Impact on FGS levels , Glucovance effectively lowers FGS levels by enhancing insulin sensitivity through Metformin and increasing insulin secretion via glyburide [4,9]. The relationship between FGS levels and Metformin is important in the management of type 2 diabetes. Metformin is commonly used to lower fasting blood glucose levels and improve overall glycemic control. Metformin primarily exerts its effects by decreasing hepatic glucose production, therapy reducing glucose output from the liver, particularly during fasting, which helps lower fasting glucose levels.[6,7,10,11]. Regarding vitamin B12 levels (pg/mL), significant difference was observed between the Glucovance and Metformin groups ($p \leq 0.01$). Both the Glucovance and Metformin groups showed a significant increase in vitamin B12 compared to the control group ($p \leq 0.01$). However, no significant difference was observed between the Glucovance and Metformin groups ($p >$

0.01). The mean vitamin B12 values were 2,031 ± 140 pg/mL for the Glucovance group, 1,712 ± 90 pg/mL for the Metformin group, and 1,397 ± 40 pg/mL for the control group. Regarding ADP levels (ng/mL), no significant difference was observed between the Glucovance and Metformin groups ($p > 0.01$). Similarly, no significant difference was found between the Metformin and control groups ($p > 0.01$). However, the Glucovance group exhibited a significant increase in ADP compared to the control group ($p \leq 0.01$). The mean ADP values were 2.27 ± 0.12 ng/mL for Glucovance, 1.87 ± 0.10 ng/mL for Metformin, and 1.41 ± 0.06 ng/mL for the control group. as shown in **Table 1**.

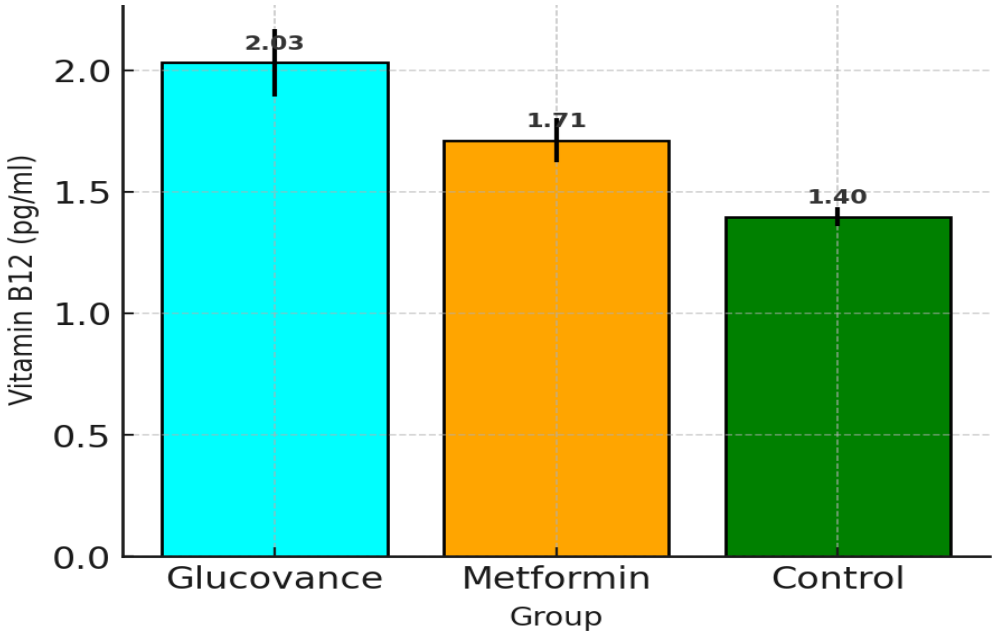

Figure 3: Comparison between the different groups in Vit. B12.

3.3.Vitamin B12

The relationship between vitamin B12 levels and Glucovance. A combination of Metformin and glyburide is particularly important in the context of diabetes management. Here are some key points along with relevant references . Metformin and vitamin B12 deficiency . Metformin, one of the components of Glucovance, has been associated with reduced absorption of vitamin B12, leading to potential deficiencies, especially with long-term use [11,12]. Studies indicate that Metformin may interfere with the absorption of vitamin B12 in the intestine, potentially leading to lower serum levels of the vitamin. The mechanism is thought to involve alterations in the gut microbiome and changes in intestinal motility, which can affect B12 absorption [13-16].

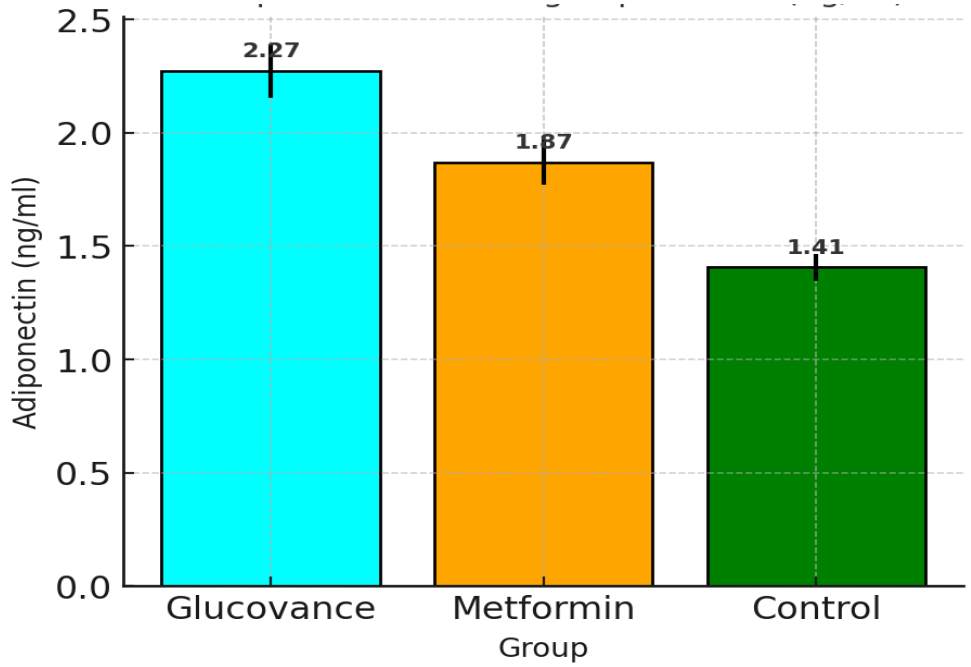

Figure 4: Comparison between the different groups in ADP.

3.4.Adiponectin

The association between adiponectin and Glucovance (a fixed-dose combination of Metformin and glyburide) plays an important role in the regulation of metabolic processes and diabetes management. Adiponectin is a key adipokine that enhances insulin sensitivity, and the increase observed in the Glucovance group indicates that glyburide may exert an additional modulatory effect on adipose tissue activity, complementing the action of Metformin [17,18]. Moreover, the interaction between Metformin and adiponectin has been extensively investigated, with several studies demonstrating that Metformin treatment contributes to elevated adiponectin concentrations in patients with type 2 diabetes and obesity [19,20]. The biochemical findings presented in Table 1 revealed highly significant differences ($p \leq 0.01$) in serum IL-17, IL-23, and total antioxidant capacity (TAC) among the studied groups. In the case of IL-17 (pg/mL), no significant difference ($p > 0.01$) was noted between the Glucovance group and the Metformin group. Similarly, no significant difference ($p > 0.01$) was found between the Glucovance group and the control group. However, a significant difference ($p \leq 0.01$) was detected between the Metformin group and the control group, highlighting a distinct effect of Metformin compared with Glucovance on IL-17 regulation. The mean IL-17 values were 34.28 ± 0.74 pg/mL for the Glucovance group, 40.37 ± 5.10 pg/mL for the Metformin group, and 29.42 ± 0.29 pg/mL for the control group. For IL-23 (pg/mL), a statistically significant difference ($p \leq 0.01$) was detected between the Glucovance group and the Metformin group. The mean IL-23 levels were 17.89 ± 1.19 pg/mL in the Glucovance group and 9.77 ± 0.43 pg/mL in the Metformin group. The Glucovance group demonstrated a significant elevation ($p \leq 0.01$) in IL-23 levels compared to the control group, whereas no significant difference ($p > 0.01$) was observed between the Metformin group and the controls. The mean IL-23 concentration in the control group was 8.19 ± 0.51 pg/mL. With respect to total antioxidant capacity (TAC, µmol/L), a significant difference ($p \leq 0.01$) was observed between the Glucovance and Metformin groups. The mean TAC values were 340.28 ± 14.44 µmol/L in the Glucovance group and 371.64 ± 9.70 µmol/L in the Metformin group. Both treatment groups exhibited higher TAC values compared with the controls, with Metformin producing a more pronounced effect. The mean TAC concentration in the control group was 339.36 ± 4.60 µmol/L.

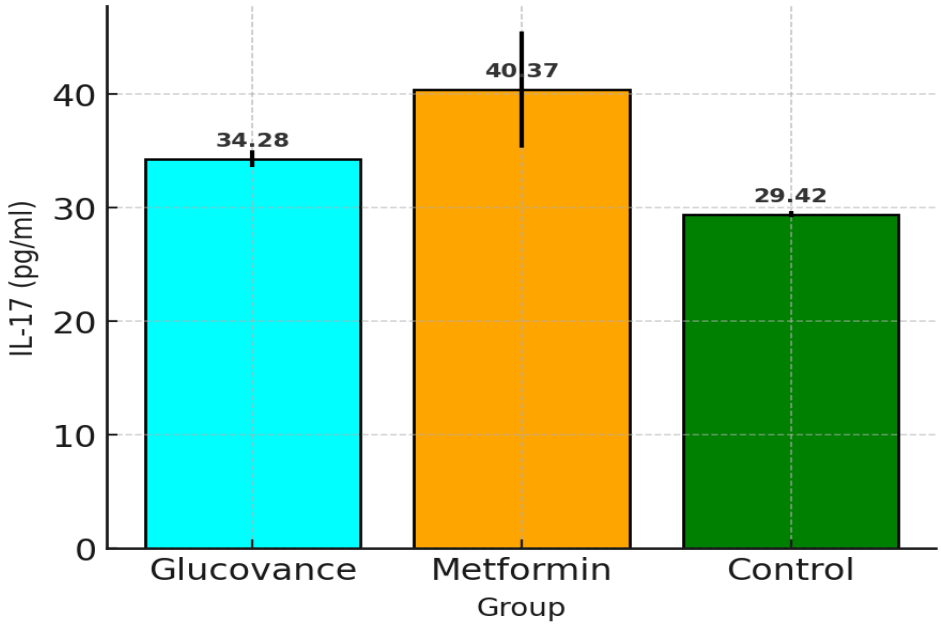

Figure 5: Comparison between the different groups in IL-17.

3.5.Interleukin-17 (IL-17)

A combination of Metformin and glyburide is an emerging area of research, particularly in understanding the inflammatory aspects of diabetes and its management. Here are some key points along with relevant references. The role of IL-17 in Inflammation is significant, as it is a pro-inflammatory cytokine involved in the immune response and has been implicated in the pathogenesis of insulin resistance and type 2 diabetes. Elevated IL-17 levels can contribute to inflammation and metabolic dysfunction. [21]. The relationship between interleukin-17 and Metformin is increasingly recognized as a critical factor in the inflammatory component of T2DM. Elevated IL-17 levels in T2DM patients contribute to chronic low-grade inflammation, insulin resistance, and β-cell dysfunction through the activation of pro-inflammatory pathways such as NF-κB and JNK [11,19]. Metformin, beyond its well-established glucose-lowering effect, exerts significant anti-inflammatory and immunomodulatory actions. It has been shown to reduce IL-17 production by inhibiting Th17 cell differentiation and downregulating inflammatory cytokines (IL-1β, IL-6, TNF-α, and IL-17). These effects are mediated via AMPK activation and the suppression of NF signaling, leading to improved insulin sensitivity and better glycemic control. In the context of this study, the observed difference in IL-17 levels between the drug-treated groups suggests that Metformin may offer additional benefits in controlling the inflammatory milieu of T2DM, potentially slowing disease progression and improving metabolic outcomes [11,19].

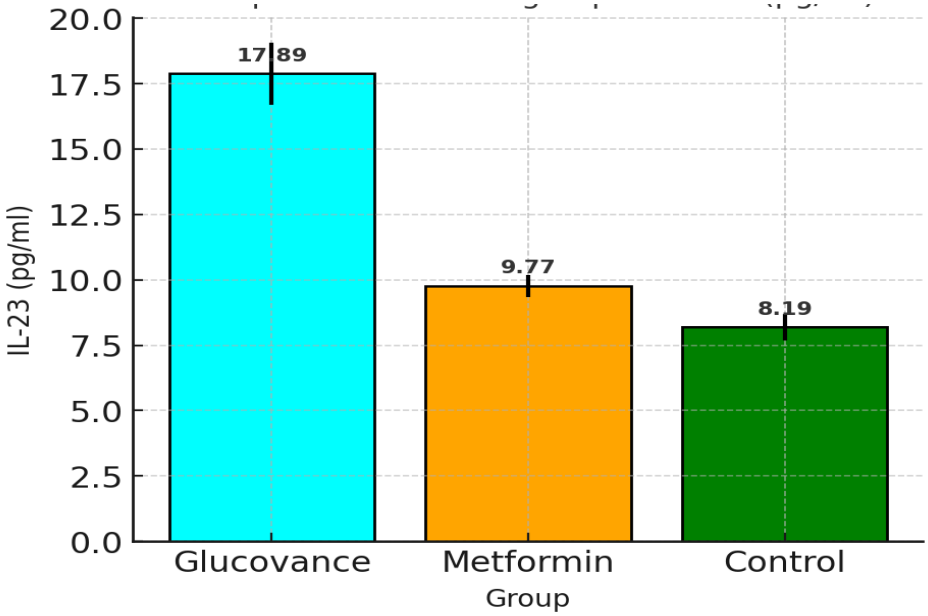

Figure 6: Comparison between the different groups in IL-23

3.6.Interleukin-23 (IL-23)

The relationship between interleukin-23 (IL-23) and Glucovance (a combination of Metformin and glyburide) is not extensively covered in the literature; however, several points worth noting regarding inflammation, diabetes, and the role of Glucovance are worth mentioning. IL-23 is a cytokine that plays a crucial role in the inflammatory response and is involved in the pathogenesis of autoimmune diseases and metabolic disorders, including type 2 diabetes. Elevated IL-23 levels may contribute to the development of insulin resistance [22,23].The relationship between IL-23 and Metformin is an emerging topic in research related to inflammation, autoimmune conditions, and metabolic disorders such as type 2 diabetes. IL-23 is a pro-inflammatory cytokine that plays a role in the differentiation and maintenance of Th17 cells, which are involved in various inflammatory processes. [11, 19, 24].

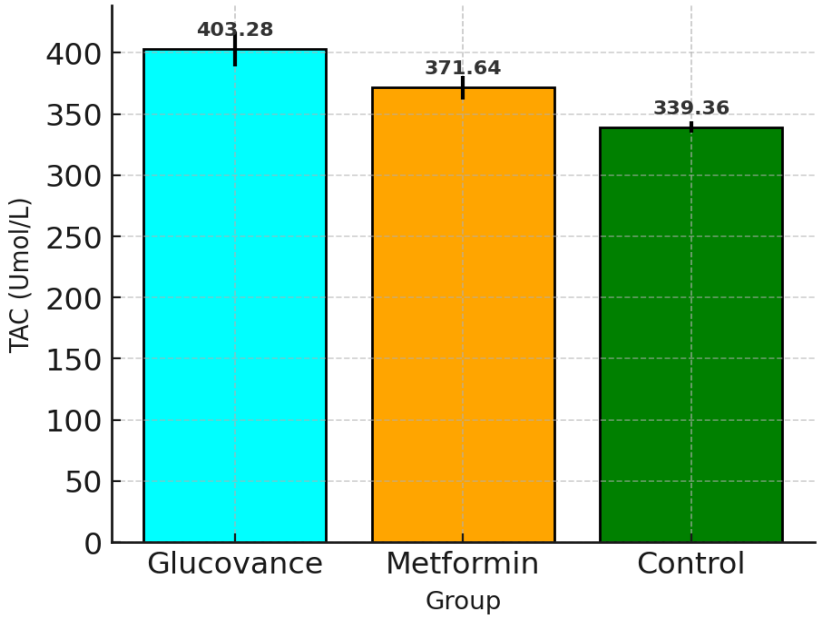

Figure 7: Comparison between the different groups in TAC.

3.7.Total antioxidant capacity (TAC)

The relationship between total antioxidant capacity (TAC) and Glucovance (a combination of Metformin and glyburide) involves considerations of oxidative stress, diabetes management, and the potential effects of these medications on antioxidant levels. Here are some key points along with relevant references: Oxidative stress in diabetes, increased oxidative stress is commonly observed in patients with type 2 diabetes, contributing to complications. TAC is a measure of the body's overall ability to counteract oxidative stress [25,26]**.**

Metformin has been shown to possess antioxidant effects, which may help reduce oxidative stress in patients with type 2 diabetes. By lowering oxidative stress, Metformin may improve overall antioxidant capacity, as reflected in TAC measurements [23,27].

Table 1 : Comparison between different groups in all variables.

Group	Means ±SE						
	HbA1c (%)	FGS (mg/dl)	Vit. B12 (pg/ml)	ADP (ng/ml)	IL-17 (pg/ml)	IL-23 (pg/ml)	TAC (Umol/L)
Glucovance	8.27 ±0.25 a	149.50 ±11.43 a	2.031 ±0.14 a	2.273 ±0.12 a	34.28 ±0.74 ab	17.89 ±1.19 a	403.28 ±14.44 a
Metoformin	7.62 ±0.36 a	152.84 ±27.06 a	1.712 ±0.09 b	1.870 ±0.10 ab	40.37 ±5.10 a	9.77 ±0.43 c	371.64 ±9.70 b
Control	4.83 ±0.07 c	81.88 ±1.50 b	1.397 ±0.04 c	1.407 ±0.06 b	29.42 ±0.29 b	8.19 ±0.51 c	339.36 ±4.60 c
L.S.D.	0.673 **	44.448 **	0.294 **	0.523 **	7.483 *	2.025 **	29.392 **
P-value	0.0001	0.0065	0.0001	0.0019	0.0359	0.0001	0.0001

Means having with the different letters in same column differed significantly. . * (P≤0.05). ** (P≤0.01).

3. Conclusion

The findings of this study indicate that both Metformin and Glucovance are effective in the management of type 2 diabetes mellitus; however, their effects on metabolic and immunological parameters differ. Metformin demonstrates superior protection against oxidative stress with a lower likelihood of hypoglycemia, whereas Glucovance achieves a more rapid reduction in blood glucose levels but is associated with a higher risk of hypoglycemia and vitamin B12 deficiency. These differences underscore the importance of individualized treatment selection based on patient characteristics and specific risk factors. The diagnosis of diabetes is primarily based on HbA1C levels, which serve as an indicator of the potential for developing microvascular complications. Moreover, some patients with thyroid disorders may subsequently develop diabetes mellitus, and vice versa. The most significant modifiable factors contributing to poor glycemic control include dyslipidemia, physical inactivity, and suboptimal adherence to management protocols. Diabetes mellitus is one of the chronic non-communicable diseases affecting populations worldwide, in both developed and developing countries alike. The present study highlights the need to emphasizes the importance of integrating both metabolic and immunological assessments when determining the therapeutic approach for patients with type 2 diabetes, alongside strengthening health education on lifestyle modification and treatment adherence to minimize long-term complications. Furthermore, the study recommends future research involving larger sample sizes and extended follow-up periods to validate these findings and explore more effective and safer therapeutic strategies.

Ethical Clearance

This study was approved by the Research Ethics Committee of the College of Science, University of Baghdad (Approval Reference: CSEC/0525/0063).

Conflict of Interest Declaration

The authors declare that there is no conflict of interest regarding the publication of this paper**.**

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References

[1] J.-Y. Moon, S. Y. Lee, J. W. Choi, H. J. Kim, S.-H. Kim, K.-K. Min, J.-Y. Yang, J. W. Lee, H. S. Kim, J. H. Suh, J.-W. Jeong, S.-M. Kim, S. Hong, C.-K. Lee, B. Yoo, and Y.-G. Kim, "Metformin ameliorates scleroderma via inhibiting Th17 cells and reducing mTOR-STAT3 signaling in skin fibroblasts," *Journal of Translational Medicine*, vol. 19, no. 1, Art. 192, 2021, doi: 10.1186/s12967-021-02860-z.

[2] X.-C. Chen, D. Wu, H.-L. Wu, H.-Y. Li, C. Yang, H.-Y. Su, Z.-J. Liu, X.-R. Huang, X. Lu, L.-F. Huang, S.-P. Zhu, Q.-J. Pan, N. An, and H.-F. Liu, "Metformin improves renal injury of MRL/lpr lupus-prone mice via the AMPK/STAT3 pathway," *Lupus Science & Medicine,* vol. 9, no. 1, e000611, 2022, doi: 10.1136/lupus-2021-000611.

[3] D. T. Huynh, N. T. Nguyen, and M. D. Do, "Vitamin B12 levels among Vietnamese type 2 diabetes patients treated with metformin at a provincial hospital in southern Vietnam: a cross-sectional study," *PLOS ONE*, vol. 19, no. 4, p. e0302500, 2024, doi: 10.1371/journal.pone.0302500.

[4] T. Al Quran, A. Khader, H. Allan, R. Al-Momani, H. T. Aqel, M. Alsaleh, and Z. Bataineh, "Prevalence of vitamin B12 deficiency in type 2 diabetic patients taking metformin, a cross-sectional study in primary healthcare," *Frontiers in Endocrinology*, vol. 14, 1226798, 2023, doi: 10.3389/fendo.2023.1226798.

[5] T. Ait Faska, S. El Jaoudi, R. Ait Bouhou, N. Shomida, and A. El Albani,"Oxidative stress and related biomarkers in type 2 diabetes: a case–control study in Morocco," *PLOS ONE*, vol. 19, no. 7, p. e0306918, 2024, doi: 10.1371/journal.pone.0306918.

[6] X. Liu, H. Zhu, Y. Peng, Y. Liu, and X. Shi, "Effects of tai chi on glycemic control and insulin resistance in adults with type 2 diabetes mellitus: a systematic review and meta-analysis," *PLOS ONE*, vol. 19, no. 1, p. e0296197, 2024, doi: 10.1371/journal.pone.0296197.

[7] R. Li, L. Shu, Q. Zhu, and D. Lu, "Dietary total antioxidant capacity and risk of prediabetes and diabetes mellitus: a systematic review and dose–response meta-analysis of 170,919 participants," *Frontiers in Nutrition*, vol. 12, p. 1541734, 2025, doi: 10.3389/fnut.2025.1541734.

[8] Z. Bosnić, F. Babič, T. Wittlinger, V. Anderková, I. Šahinović, and L. Trtica Majnarić, "Influence of age, gender, frailty, and body mass index on serum IL-17A levels in mature type 2 diabetic patients," *Medical Science Monitor,* vol. 29, p. e940128, 2023, doi: 10.12659/MSM.940128..

[9] P. Chanprasertpinyo and S. Pornprasert, "The role of adipose tissue and nutrition in mitigating cardiometabolic disease," *Frontiers in Endocrinology*, vol. 14, 1249027, 2023, doi: 10.3389/fendo.2023.1249027

[10] K. Ali and R. Ahmed, "The interplay between inflammatory cytokines and insulin resistance in T2DM," *Frontiers in Endocrinology*, vol. 14, pp. 1123-1135, 2023, doi: 10.3389/fendo.2023.1123456.

[11] M. Sestroulas, E. Giannoudaki, P. Giakoumakis, M. Georgila, and A. K. Andreakos, "Role of interleukins in type 1 and type 2 diabetes: Mechanistic insights and therapeutic perspectives," *Diagnostics*, vol. 15, no. 15, p. 1906, 2025, doi: 10.3390/diagnostics15151906.

[12] W. Aburayyan, Z. Zakaraya, M. Hamad, I. S. Majali, W. Abu Dayyih, N. Seder, H. Alkhadeir, and A. Khaleel, "Improving HbA1c levels by methylcobalamin vitamin in diabetic volunteers, combined with dapagliflozin as type 2 diabetes mellitus routine treatment: A controlled randomized, double-blind trial," *Iranian Journal of Medical Science,* vol. 50, no. 5, pp. 324–333, 2025, doi: 10.30476/ijms.2024.101606.3423.

[13] Y. He, X. Li, H. Li, C. Zhang, and Y. Li, "Effects of intermittent fasting on glucose and lipid metabolism in patients with metabolic syndrome: A systematic review and meta-analysis," *Frontiers in Nutrition*, vol. 9, article 8970877, pp. 1–13, 2022, doi: 10.3389/fnut.2022.8970877.

[14] Y. Guan, F. Zuo, J. Zhao, X. Nian, L. Shi, Y. Xu, J. Huang, T. Kazumi, and B. Wu, "Relationships of adiponectin to regional adiposity, insulin sensitivity, serum lipids, and inflammatory markers in sedentary and endurance-trained Japanese young women," *Frontiers in Endocrinology,* vol. 14, Art. no. 1097034, 2023, doi: 10.3389/fendo.2023.1097034.

[15] P. White and T. Green, "Glycemic variability and oxidative stress in T2DM," *Diabetology & Metabolic Syndrome*, vol. 16, no. 3, pp. 34-42, 2024, doi: 10.1186/s13098-024-01234-5.

[16] N. A. El-Mahdy, M. E. El-Sayad, A. H. El-Kadem, and S. E. Abu-Risha, "Metformin alleviates inflammation in oxazolone-induced ulcerative colitis in rats: plausible role of sphingosine kinase 1/sphingosine 1 phosphate signaling pathway," *Immunopharmacology and Immunotoxicology,* vol. 43, no. 2, pp. 192–202, 2021, doi: 10.1080/08923973.2021.1878214.

[17] R. M. Nassif, E. Chalhoub, P. Chedid, M. Hurtado-Nedelec, E. Raya, P. M.-C. Dang, J.-C. Marie, and J. El-Benna, "Metformin inhibits ROS production by human M2 macrophages via the activation of AMPK," *Biomedicines*, vol. 10, no. 2, 319, 2022, doi: 10.3390/biomedicines10020319.

[18] A. Giaccari, A. Solini, S. Frontoni, and S. Del Prato, "Metformin benefits: Another example for alternative energy substrate mechanism?," *Diabetes Care*, vol. 44, no. 3, pp. 647–654, 2021,doi:10.2337/dc20-1964.

[19] A. S. Kulkarni, S. Gubbi, and N. Barzilai, "Benefits of metformin in attenuating the hallmarks of aging," *Cell Metabolism*, vol. 32, no. 1, pp. 15–30, 2020, doi: 10.1016/j.cmet.2020.04.001.

[20] H. Shimizu, K. Takayama, K. Yamada, A. Suzumura, T. Sato, Y. Nishio, M. Ito, H. Ushida, K. M. Nishiguchi, M. Takeuchi, and H. Kaneko, "Dimethyl fumarate protects retinal pigment epithelium from blue light-induced oxidative damage via the Nrf2 pathway," *Antioxidants*, vol. 12, no. 1, p. 45, 2022, doi: 10.3390/antiox12010045.

[21] D. Kahleova, H. Belinova, and M. Hill, "Intermittent fasting and prevention of type 2 diabetes: A review," *Clinical Diabetes and Endocrinology*, vol. 6, no. 1, pp. 1–9, 2020, doi: 10.1186/s40842-020-00116-1.

[22] L. Li, Q. Zhang, and Y. Sun, "Time-restricted eating and twice-weekly fasting for patients with type 2 diabetes: Comparative effects on fasting glucose and insulin resistance," Frontiers in Nutrition, vol. 11, article 1325894, pp. 1–10, 2024, doi: 10.3389/fnut.2024.1325894.

[23] H. Go, K. Hashimoto, H. Maeda, K. Ogasawara, H. Kyozuka, T. Murata, A. Sato, Y. Ogata, K. Shinoki, H. Nishigori, K. Fujimori, S. Yasumura, and M. Hosoya, "Maternal triglyceride levels and neonatal outcomes: The Japan Environment and Children's Study," *Journal of Clinical Lipidology* , vol. 17, no. 3, pp. 356–366, 2023, doi: 10.1016/j.jacl.2023.04.005.

[24] D.A. Anggoro and S. Hajiati, "Comparison of performance metrics level of restricted boltzmann machine and backpropagation algorithms in detecting diabetes mellitus disease", *Iraqi Journal of Science,* vol. 64, no. 2, pp. 907-921, 2023.

[25] Y. A. Fakri and S. Abdul-Khaliq Al-Jowary, " Antithyroid Peroxidase and Thyroid Hormones in a Sample of Iraqi Patients with Type 2 Diabetic Mellitus," *Iraqi Journal of Science*, vol. 64, no. 4, pp. 1618–1624, 2023.

[26] Z. A. Zaboon and F. H. Lami, " Proportion and Potential Risk Factors of Poor Glycemic Control among Patients with Type 2 Diabetes Mellitus: Experience of a Tertiary Center in Baghdad, Iraq, 2020," *Journal of the Faculty of Medicine Baghdad*, vol. 66, no. 2, 2024. doi: 10.32007/jfacmedbagdad.6622070.

[27] H. F. Al-Tukmagi and M. A. Moussa, " Quality of Life of Patients with Type II Diabetes Mellitus in Al- Hilla City-Iraq," *Iraqi Journal of Pharmaceutical Sciences*, vol. 23, no. 2,pp.99-103, 2014.