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RESEARCH ARTICLE BIOCHEMISTRY

The Effect of Metformin on Vitamin B12 in Type 2 Diabetes Patients in Wadi Etba Region, Southern Libya

Mohammad Al. Al-Tahir[1], Nawal A. Ibrahim[1], Ali M. Nouh[1], Mabrouka M. Al-Darmoun[1], Annour M. Alalem[1,*]

[1]Department of Public Health Sciences, College of Medical Technology, Fezzan University- Libya

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ABSTRACT

Metformin is the first choice for the treatment of type 2 diabetes in the world, but with the long duration of therapy, it causes a decrease in the level of vitamin B12 in diabetic patients. Vitamin B12 deficiency is associated with many clinical symptoms that significantly impact the health of diabetic patients. This study aimed to know the effect of metformin on vitamin B12 in type 2 diabetes patients in the Wadi Etba region. This study was conducted during the period from 2023/3 to 2023/6. Data was collected using the questionnaire tool, using the descriptive analytical approach. A total of 100 individuals aged 18 to 80 were surveyed (43% males, 57% females). The study found that the most common dose of metformin was 500 mg, which was taken at a rate of 61%, the longest duration of use was 2–5 years at a rate of 34%, and the dose ranged between 500 and 2000 mg. The duration and dosage of metformin were associated with the emergence of symptoms: numbness in the extremities occurred first at 73%, followed by depression at 60%, retinopathy at 58%, and digestive disorders, changes in memory, neuropathy, and heart problems at 44%, 52%, and 56%, respectively. The results show a significant link between the duration of metformin use and numbness or tingling in extremities and a connection between dosage and neuropathy or memory changes. Metformin may also cause vitamin B12 deficiency symptoms. It is recommended that type 2 diabetes patients taking metformin monitor vitamin B12 levels and consider supplements.

دراسة عن تأثير الميتفورمين على فيتامين ب 12 لدى مرضي السكري من النوع الثاني في منطقة وادي عتبة- جنوب ليبيا

محمد الطاهر[1]، نوال إبراهيم[1]، علي نوح[1]، مبروكة الدرمون[1]، النور العالم[1،*]

الكلمات المفتاحية
الميتفورمين
الاعتلال العصبي
جنوب ليبيا
مرض السكري من النوع الثاني
فيتامين ب 12
وادي عتبة

الملخص

الميتفورمين الخيار الأول في علاج مرضي السكري من النوع الثاني في العالم، لكن مع طول مدة العلاج يسبب في زيادة نقص فيتامين ب 12. حيث يرتبط نقص فيتامين ب 12 بالعديد من الأعراض السريرية التي تؤثر على الحالة الصحية لمرضى السكري.الهدف: - هدفت هذه الدراسة معرفة تأثير الميتفورمين على فيتامين B12 على مرضي السكري من النوع الثاني في منطقة وادي عتبة.. أجريت هذه الدراسة في منطقة وادي عتبة خلال الفترة الزمنية 2023/3/23 الي 2023/6/8، وقد تم استخدام المنهج الوصفي التحليلي باعتماده على أداة الاستبانة كأسلوب لجمع البيانات. حيث وزعت 100 ورقة استبيان على 100 من المرضي بالسكري النوع الثاني (43% ذكور ‘57% إناث تتراوح اعمارهم ما بين (18-80). توصلت الدراسة إلى أن الجرعة الأكثر شيوعا من الميتفورمين كانت 500 ملغم، وتم تناولها بنسبة 61%، وكانت أطول مدة استخدام 2-5 سنوات بنسبة 34%، وتراوحت الجرعة بين 500 و2000 ملغم. وتوصلت الدراسة أن استعمال الميتفورمين مرتبط بظهور مجموعة من الأعراض على مرضي السكري النوع الثاني وأبرزها تنمل في الأطراف بنسبة 73%، ويليها الاكتئاب بنسبة 58%، واعتلال بشبكية العين بنسبة 60%، واضطرابات في الجهاز الهضمي بنسبة 56%، واختلال في الذاكرة بنسبة 52%، واعتلال عصبي بنسبة 44%، ومشاكل في القلب بنسبة 39%. تُظهر النتائج وجود صلة واضحة بين مدة استخدام الميتفورمين والشعور بالخدر أو الوخز في الأطراف، وعلاقة بين الجرعة واعتلال الأعصاب أو تغيرات الذاكرة. قد يُسبب الميتفورمين أيضًا أعراض نقص فيتامين ب 12. يُنصح مرضى السكري من النوع الثاني الذين يتناولون الميتفورمين بمراقبة مستويات فيتامين ب 12 والنظر في تناول المكملات الغذائية..

Introduction

Diabetes is a leading cause of death and illness worldwide [1, 2], with Type 2 diabetes (T2DM) representing 90–95% of cases. Key risk factors for T2DM include genetics, family history, age, obesity, a sedentary lifestyle, poor dietary habits, and lack of physical activity [3]. Metformin is one of the most commonly prescribed oral antidiabetic medications due to its proven effectiveness, low risk of side effects, and compatibility with other antidiabetic drugs. It is estimated that over 150 million diabetics use Metformin regularly around the globe [4]. One notable benefit of this medication

*Corresponding author
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is its potential for weight loss, making it a valuable option for obese individuals with Type 2 diabetes [5].

Metformin is an effective medication for controlling blood glucose levels and improving the body's response to insulin, making it the preferred treatment for the majority of patients with type 2 diabetes. However, research indicates that patients taking metformin may develop vitamin B12 deficiency [6, 7]. Over the past 20 years, evidence has increasingly shown that diabetic patients treated with metformin are at higher risk for vitamin B12 deficiency [8, 9]. Several studies have linked vitamin B12 deficiency to malabsorption of the vitamin among these patients [10]. It is important to consider the potential complications of vitamin B12 deficiency for diabetic patients when developing their treatment plans [1, 11].

Vitamin B12 is primarily obtained from animal-based foods, including red meat, poultry, shellfish, milk, eggs, and other dairy products, as well as from foods that are fortified with vitamin B12 [12]. While vitamin B12 is generally not present in plant foods, fortified breakfast cereals serve as a readily available source with high bioavailability [13]. Vitamin B12, along with zinc, copper, and magnesium, plays a crucial role in supporting the health of individuals with type 2 diabetes [14, 15].

Deficiency in vitamin B12 can lead to a range of symptoms, including hematological issues (such as megaloblastic anemia and macrocytic anemia), neurological symptoms (like demyelination and paresthesia), gastrointestinal problems (including anorexia and glossitis), as well as psychological symptoms. Patients with vitamin B12 deficiency may experience depression, bipolar disorder, and panic disorder. Additionally, adults may exhibit symptoms such as psychosis, phobia, and dementia, often accompanied by emotional or psychotic disturbances [16].

This study aims to investigate the effect of metformin on vitamin B12 levels in patients with type 2 diabetes in the Wadi Etba region of southern Libya.

Materials and methods

Study Methodology: A descriptive analytical approach was employed in this study. This method focuses on accurately describing a phenomenon or reality [17]. **Study Tools**: A questionnaire consisting of 14 questions was developed and distributed to diabetic patients who are undergoing metformin treatment. **Study Sample**: The target sample comprised 100 diabetic patients, selected randomly from various areas of Wadi Atba. The participants were visiting Al-Abidin Laboratory and Tsawa Rural Hospital Laboratory. The questionnaire was distributed during the period from March 2023, to June 2023.

Statistical analysis

The data were emptied and the results were analyzed using the SPSS statistical program. Data are expressed as frequencies (%) based on their distribution. Means are presented as ±SD. The Chi-square test for independence was employed for analysis. All p-values were two-tailed, with statistical significance defined as $p < 0.05$.

Results

Characteristics and features of the study population

Distribution of sample members by gender

The results showed that the majority of patients enrolled in the study were females(57%), while the remaining (43%) were males, as shown in Figure 1.

Distribution of sample members by age

The results showed that 63% of sample members were between the ages of 31-60 years, 35% were between the ages of 61-80 years, and minority of 2% were between the ages of 18-30 years, as shown in Figure 2.

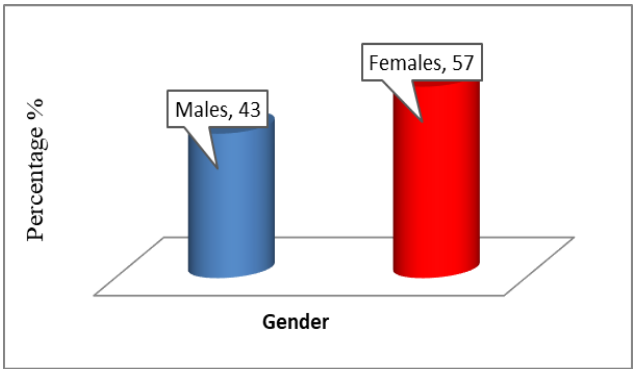

Fig. 1: Distribution of study population according to gender.

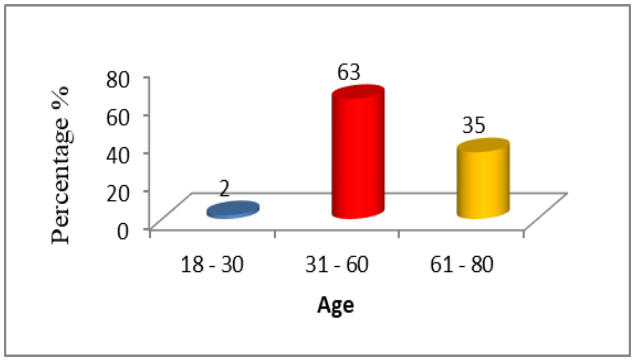

Fig. 2: Distribution of study population according to age

Duration of use of metformin

The results show that the majority of patients use the drug from 2 to 5 years, and their percentage is 34%, while the lowest percentage was 18% for those who use it for one year, as shown in Figure 3.

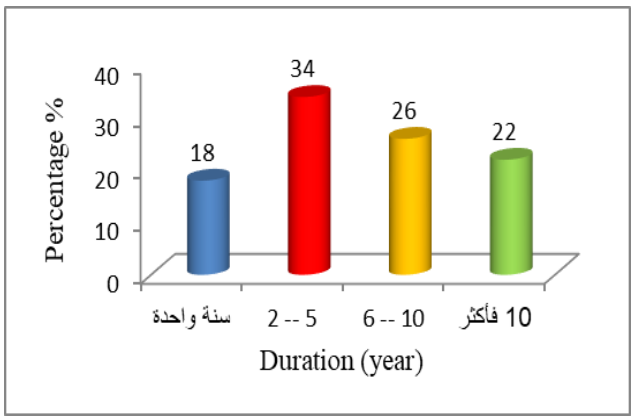

Fig. 3: Distribution of patients according to the duration of use

Metformin dose taken

The results showed that 61% of the sample individuals were taking a 500 mg dose, 23% were taking 850 mg dose, 16% were taking 1000 mg dose, and none of the individuals were taking 2000 mg of metformin, as shown in Figure 4.

Analysis of the responses of the study population regarding the accompanying symptoms

Depending on the value of the relative weight, it can be said that the most common symptom is “numbness or tingling in the extremities (feet and hands)” with a relative weight of 73%, while the least common is “suffering from heart disease” with a relative weight of 39%, (Table 1).

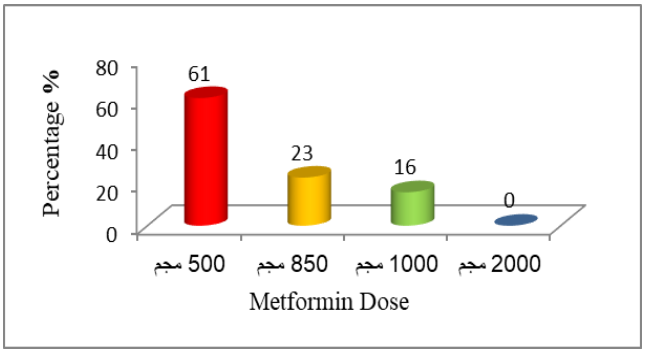

Fig. 4: Distribution of patients according to the dose of metformin

The first null hypothesis states that metformin does not significantly relate to its symptoms. The chi-square test shows probability values greater than 5%, so we cannot say there is a significant relationship between the drug and symptoms at a 5% significance level. However, when we lower the significance level to 10%, we find a significant relationship between metformin use and the symptom of numbness and tingling in the extremities (Table 2).

The second null hypothesis states that there is no statistically significant relationship between the dose of metformin and the accompanying symptoms. According to the results of the chi-square test, there was not enough evidence to reject this hypothesis, as the probability values of the chi-square test statistic were greater than 5%. Therefore, we cannot confirm the existence of a statistically significant relationship between the dose of the drug and the occurrence of symptoms at a significance level of 5%. When the significance level is reduced to 10%, we observe a statistically significant relationship between the drug dose and the symptoms of "neuropathy" and "memory changes" (Table 3).

Study hypothesis testing

Table 1: The arithmetic mean, standard deviation, relative weight and ranking of the search tool phrases

No	Expression Statements	Mean	STD	Relative Weight %	Rank
1	Have you ever taken vitamin B12	1.810	±0.918	60.3	3
2	Do you regularly check your vitamin B12 levels	1.400	± 0.667	46.7	7
3	Do you have problems with your retina	1.740	±0.906	58	4
4	Do you have problems with neuropathy	1.320	±0.680	56.7	8
5	Do you have problems with nausea, vomiting or diarrhea	1.700	±0.798	56.7	5
6	Do you have heart disease	1.17	±0.533	39	9
7	Do you have numbness or tingling in your extremities (feet and hands)	2.190	±0.873	73	1
8	Do you have Depression or mood swings	1.810	±0.837	60.3	2
9	Do you suffer from memory changes	1.570	± 0.756	52.3	6

Table 2: Relationship between drug use and symptoms

No	Expression Statements	Chi-square tes	P= value
1	Have you ever taken vitamin B12	9.81	0.133
2	Do you regularly check your vitamin B12 levels	7.64	0.266
3	Do you have problems with your retina	1.84	0.934
4	Do you have problems with neuropathy	5.15	0.525
5	Do you have problems with nausea, vomiting or diarrhea	4.80	0.569
6	Do you have heart disease	6.11	0.569
7	Do you have numbness or tingling in your extremities (feet and hands)	12.42	0.053
8	Do you have Depression or mood swings	7.47	0.279
9	Do you suffer from memory changes	2.66	0.850

Table 3: Relationship between the drug dose and symptoms

No	Expression Statements	Chi-square test	P= value
1	Have you ever taken vitamin B12	5.16	0.271
2	Do you regularly check your vitamin B12 levels	0.680	0.954
3	Do you have problems with your retina	4.61	0.330
4	Do you have problems with neuropathy	8.59	0.07
5	Do you have problems with nausea, vomiting or diarrhea	3.19	0.525
6	Do you have heart disease	1.40	0.843
7	Do you have numbness or tingling in your extremities (feet and hands)	6.85	0.156
8	Do you have Depression or mood swings	4.69	0.320
9	Do you suffer from memory changes	8.09	0.08

Discussion

This study assessed vitamin B12 deficiency in relation to metformin dosage and treatment duration among type 2 diabetes patients. Our findings align with a study that noted a higher prevalence of diabetes in females, likely due to their greater susceptibility [18]. Additionally, their study found a negative correlation between age and vitamin B12 levels, often attributed to increased B12 supplementation among the elderly [19]. The study found that metformin use varied from one to over ten years, with the most common duration being 2-5 years (34%), as illustrated in Figure 3.

The most frequently prescribed dose among diabetic patients was 500 mg (61%), as shown in Figure 4. Additionally, previous study demonstrated a statistically significant vitamin B12 deficiency in diabetic patients taking metformin, highlighting an inverse relationship between the duration and dose of metformin use and vitamin B12 levels [20].

Our study found statistical evidence linking the duration of metformin use to paresthesia and extremity numbness (P = 0.053, see Table 2). It also indicated associations between metformin dosage, neuropathy, and memory changes, with P-values of 0.07 and 0.08, respectively (Table 3). Additionally, research by recently study demonstrated a correlation between the duration of diabetes, metformin usage, dosage, and vitamin B12 deficiency, with a P-value of 0.05. This suggests a relationship between metformin usage, its dosage, and vitamin deficiency symptoms [21].

Conclusion and Recommendations

The study confirms a link between metformin use and the onset of symptoms such as extremity numbness, depression, retinopathy, digestive issues, memory changes, and neuropathy related to vitamin B12 deficiency. It suggests that, alongside maintaining normal blood sugar levels, type 2 diabetic patients on metformin should have their vitamin B12 levels monitored and may need to take supplements.

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References

[1] E. Sayedali, A. Yalin, and S. Yalin, "Association between metformin and vitamin B12 deficiency in patients with type 2 diabetes," *World journal of diabetes*, vol. 14, no. 5, p. 585, 2023. https://doi.org/10.4239/wjd.v14.i5.585.

[2] A. Mosbah, A. Yhmed, A. Elwafa, and M. Alzwayi, "Prevalence of Type 2 Diabetes and Prediction of Renal Failure Phases in Males Attending Brack AlShatti Hospital," *Wadi Alshatti University Journal of Pure and Applied Sciences*, pp. 18-23, 2025. https://doi.org/10.63318/waujpas. v3i1.04

[3] S. Almatrafi, E. Bakr, A. Almatrafi, and M. Altayeb, "Prevalence of vitamin B12 deficiency and its association with metformin-treated type 2 diabetic patients: A cross sectional study," *Human Nutrition & Metabolism*, vol. 27, p. 200138, 2022. https://doi.org/10.1016/j.hnm.2022. 200138.

[4] A. Konopka, *et al.*, "Hyperglucagonemia Mitigates the Effect of Metformin on Glucose Production in Prediabetes," *Cell Reports*, vol. 15, no. 7, pp. 1394-1400, 2016. http://dx.doi.org/10.1016/j.celrep.2016.04.024

[5] J. R. Petrie, "Metformin beyond type 2 diabetes: Emerging and potential new indications," *Diabetes, Obesity and Metabolism*, vol. 26, pp. 31-41, 2024. https://doi.org /10.1111/dom.15756

[6] J. Kim, C. Ahn, S. Fang, H. Lee, and J. Park, "Association between metformin dose and vitamin B12 deficiency in patients with type 2 diabetes," *Medicine*, vol. 98, no. 46, p. e17918, 2019. https://doi.org/ 10.1097/MD. 0000000000017918

[7] K. Shahjahan, *et al.*, "Vitamin B12 deficiency in patients taking metformin: pathogenesis and recommendations," *Cureus*, vol. 16, no. 9, 2024. https://doi.org/10.7759/cureus. 68550

[8] A. Al-Hamdi, M. Al-Gahhafi, S. Al-Roshdi, S. Jaju, A. Al-Mamari, and A. M. Al Mahrezi, "Vitamin B12 deficiency in diabetic patients on metformin therapy: a cross-sectional study from Oman," *Sultan Qaboos University Medical Journal*, vol. 20, no. 1, p. e90, 2020. https://doi.org/ 10.18295/squmj.2020.20.01.013.

[9] T. J. Alharbi *et al.*, "The association of metformin use with vitamin B12 deficiency and peripheral neuropathy in Saudi individuals with type 2 diabetes mellitus," *PloS one*, vol. 13, no. 10, p. e0204420, 2018, doi: https://doi.org/10.1371/journal.pone.0204420.

[10] K. Gupta, A. Jain, and A. Rohatgi, "An observational study of vitamin b12 levels and peripheral neuropathy profile in patients of diabetes mellitus on metformin therapy," *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, vol. 12, no. 1, pp. 51-58, 2018. https://doi.org/ 10.1016/j.dsx.2017.08.014.

[11] O. Albai, B. Timar, D. L. Paun, A. Sima, D. Roman, and R. Timar, "Metformin treatment: a potential cause of megaloblastic anemia in patients with type 2 diabetes mellitus," *Diabetes, Metabolic Syndrome and Obesity*, pp. 3873-3878, 2020. https://doi.org/10.2147/DMSO.S270393.

[12] R. Obeid, S. Heil, M. Verhoeven, E. Heuvel, L. De Groot, and S. Eussen, "Vitamin B12 intake from animal foods, biomarkers, and health aspects," *Frontiers in nutrition*, vol. 6, p. 93, 2019. https://doi.org/ 10.3389/fnut.2019.00093.

[13] M. Garg *et al.*, "Vitamins in cereals: a critical review of content, health effects, processing losses, bioaccessibility, fortification, and biofortification strategies for their improvement," *Frontiers in nutrition*, vol. 8, p. 586815, 2021. https://doi.org/10.3389/fnut.2021.586815.

[14] A. Almajdoub, M. Alzwayi, and N. Alaasswad, "Estimated blood levels of zinc and copper among type-2 diabetic patients and their relationship to insulin resistance," *Wadi Alshatti University Journal of Pure and Applied Sciences*, vol. 1, no. 1, pp. 9-15, 2023. https://www.waujpas. com/index.php/journal/article/view/4

[15] A. Abubaker. and I. Eshnaf, "The Association between Serum Magnesium Level and Microalbuminuria in Diabetic Patients Attending Sebha Diabetic and Endocrine Centre, Sebha-Libya," *Wadi Alshatti University Journal of Pure and Applied Sciences*, pp. 135-141. 2025 https://doi.org/ 10.63318/waujpasv3i1_20.

[16] A. Tufan, R. Bilici, G. Usta, and A. Erdoğan, "Mood disorder with mixed, psychotic features due to vitamin b12 deficiency in an adolescent: case report," *Child and Adolescent Psychiatry and Mental Health*, vol. 6, pp. 1-5, 2012. https://doi.org/10.1186/1753-2000-6-25.

[17] S. Loeb, S. Dynarski, D. McFarland, P. Morris, S. Reardon, and S. Reber, "Descriptive Analysis in Education: A Guide for Researchers. NCEE 2017-4023," *National Center for Education Evaluation and Regional Assistance*, 2017. http://ies.ed.gov/ncee/.

[18] G. Sulaiman, N. Ferrara, A. Elbahi, and S. Elbaruni, "Vitamin B12 Deficiency in Type 2 Diabetes Patients Using Metformin," *AlQalam Journal of Medical and Applied Sciences*, pp. 160-165, 2023. https://uta.edu.ly/journal/ index.php/Alqalam/article/view/232.

[19] J. Watson, M. Lee, and M. Garcia-Casal, "Consequences of inadequate intakes of vitamin a, vitamin B 12, vitamin D, calcium, iron, and folate in older persons," *Current geriatrics reports*, vol. 7, pp. 103-113, 2018. https://doi.org/ 10.1007/s13670-018-0241-5.

[20] M. Elhabiby, A. Tabash, A. Yousof, and A. Mohealdeen, "Correlation Between Metformin and Vitamin B12 level among type II Diabetics in Southern Gaza," *Al-Aqsa University Journal (Natural Sciences Series)*, vol. 21, pp. 24-43, 2017. https://www.alaqsa.edu.ps/site_resources/ aqsa_magazine/files/1173.

[21] D. T. Huynh, N. T. Nguyen, and M. D. Do, "Vitamin B12 deficiency in diabetic patients treated with metformin: A cross-sectional study," *Plos one*, vol. 19, no. 4, p. e0302500, 2024. https://doi.org/10.1371/journal.pone.0302500.