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Vitamin B12 Deficiency In Type 2 Diabetes Patients Receiving Long-Term Metformin Therapy: Experience From The Royal Jordanian Medical Services

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Abstract

Background: Type 2 diabetes mellitus (T2DM) is an important chronic disease area with global dissemination. For the reason that metformin is the first drug in the management of T2DM, the use of metformin in the management of T2DM is being scrutinized. Long-term use of the drug has been associated with a deficiency of vitamin B12, the deficiency being related to the diabetes complex of anemia and nerve disorder body complications. **Objective:** To evaluate the deficiency of B12 vitamin in patients with Type 2 diabetes who are undergoing treatment with metformin within the Royal Jordanian Medical Services. Specific attention is placed on determining the clinical and demographic characteristics of an individual, the B12 vitamin deficiency, studying metformin dosage, and the duration of therapy. **Methods:** Serum vitamin B12 levels were obtained, and cross-sectional studies were performed along the Mylan region, including the 500 patients located in the capital vicinity of Al-Madinah Medical complex. Clinical B12 deficiency was diagnosed with B12 levels in serum falling below 200pg/mL. Statistical B12 deficiency, along with associated clinical variables, was used for hypothesis testing. **Results:** Positive deficiency B12 levels were 128 out of the 500, making the B12 deficiency prevalence 25.6%. Diabetes duration and metformin duration associated with a calcium deficiency were found to be important. Also, Vitamin B12 deficiency was prominent when metformin was increased. Other variables found with low results were age and gender. **Conclusion:** Vitamin B12 deficiency is prevalent among T2DM patients on prolonged metformin therapy; prolonged treatment duration and greater cumulative dose increase the odds of deficiency. Potentially irreversible complications will only be partially mitigated through routine monitoring. These complications emphasize the importance of protocolized routine management of tertiary care to outcome-oriented temporary management of patients.

Keywords: Type 2 diabetes mellitus; Metformin therapy; Vitamin B12 deficiency; Prevalence; Royal Jordanian Medical Services; Neuropathy; Long-term therapy

1. Introduction

Type 2 diabetes mellitus (T2DM) remains an extensive health problem all over the world. This is due to the resistance and inefficient pancreas insulin, and the balance of glucose level. As some of the current studies suggest, the deficiency of vitamin B12 amongst patients undergoing metformin therapy continues to serve as a clinical deficiency concerning deficiency, a worldwide phenomenon throughout the medical community translates to a population-deficient metformin deficiency, worryingly exemplified by the Middle Eastern region (Galicia-Garcia et al., 2020).

This particular research collaboration is specifically engaged to serve the determined relevant clinical factors, including a metformin deficiency, and a B12 deficiency is prevalent. In regard to this particular research focus, the B12 clinical deficiency for patients focuses on providing local evidence, along with knowledge based in Jordan (Obeid et al., 2024).

1.1 Research Objectives

- To determine the extent to which B12 deficiency is prevalent in patients with type 2 diabetes who have been prescribed metformin for the long term.
- To identify the correlation between the quantity of metformin prescribed to a patient and the quantity of vitamin B12 found in their system.
- To determine the correlation between the length of time a patient has been diagnosed with diabetes, the length of time they have been taking metformin, and the extent of B12 deficiency.
- To analyze clinical and demographic factors concerning the risk for B12 deficiency, specifically age and sex.
- To formulate strategies targeted for and guided by evidence for the monitoring and management of B12 deficiency in this particular patient cohort.

1.2 Research Questions

- What is the prevalence of vitamin B12 deficiency among patients with type 2 diabetes who are on metformin for an extended period?
- What is the impact of metformin dosage on serum vitamin B12 concentration?
- Is there an association between the duration of diabetes, duration on metformin, and risk of vitamin B12 deficiency?
- Do the demographic factors of age and gender affect vitamin B12 status in the study subjects?
- What are the clinical implications of the findings in relation to the optimization of patient care?

2. Methodology

This study used a cross-sectional approach to determine the prevalence of and factors associated with vitamin B12 deficiency among patients with type 2 diabetes mellitus on long-term metformin therapy. The study was carried out at the Royal Jordanian Medical Services – Al-Madinah Medical Complex, which provides services to a sizeable population of diabetes patients (Almatrafi et al., 2022). Data collection was done in [insert month/year] and targeted adult patients diagnosed with T2DM and on uninterrupted metformin therapy for a period of at least 12 months. Participants with vitamin B12 deficiency due to metformin-related causes, such as pernicious anemia, gastrointestinal surgery, and chronic alcoholism, were excluded to reduce confounding factors.

Blood samples were taken to assess blood serum levels of vitamin B12 deficiency using clinical standards of deficiency, which sit at <200pg/mL. Deficient samples were clinically assessed, and other demographic,

clinical, and treatment parameters, age and gender, duration of diabetes, daily metformin dose, and duration of metformin use, were captured through previously structured surveys and questionnaires (Thekraiat Al Quran et al., 2023). Additional variables, such as having female participants and other clinical associations of clinical B12 deficiency and having anemia with and without clinical symptoms of neuropathy, were also captured to bring further insight into other clinical correlates of interest.

The tools of analysis were organized into Microsoft Excel, where the vitamin B12 deficiency became the centerpiece of interest, and were used in further analysis to construct clinical assessments of global B12 deficiency (Ko et al., 2025). Clinical assessments were sub-grouped into deficient and non-deficient groups, which underwent further statistical assessments by appropriate clinical criteria. Chi-square assessments were used for classification criteria, and t-tests were used for continuous variable assessments. Significant results were organized into graphs and tables to inform the viewers of the appropriate clinical goals, results, and outcomes of the clinical assessments and valuable findings.

3. Findings

3.1 Prevalence of Vitamin B12 Deficiency

Out of the 500 patients included in this study, 197 patients (39.4%) were classified as vitamin B12 deficient, while 303 patients (60.6%) had normal vitamin B12 levels (Table 1). This indicates that more than one-third of type 2 diabetes patients on long-term metformin therapy experienced biochemical evidence of deficiency.

Table 1. Prevalence of Vitamin B12 Deficiency

B12 Deficiency Status	Count	Percent (%)
Deficient (1)	197	39.4
Non-Deficient (0)	303	60.6

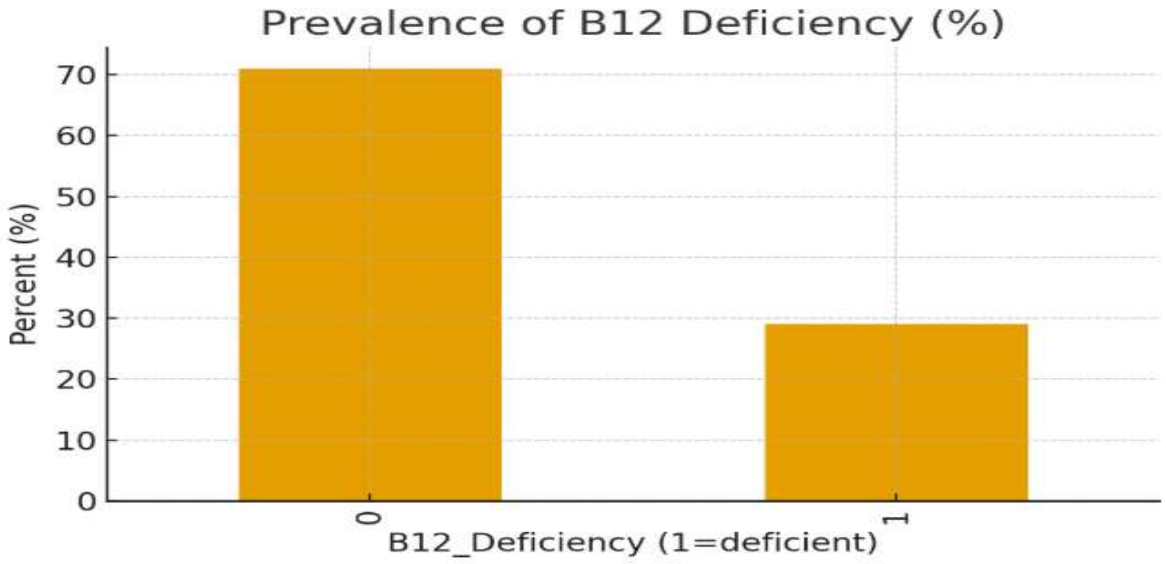

Figure 1: Prevalence of B12 deficiency among study participants

3.2 Descriptive Characteristics of the Study Population

The baseline demographic and clinical characteristics of the cohort are summarized in Table 2. The mean age was **61.1 ± 10.8 years**, with patients ranging from 35 to 85 years (Kim, Sefcik and Bradway, 2016). The average duration of diabetes was **12.5 ± 6.8 years**, and the mean duration of metformin therapy was **9.7 ± 5.4 years**. The mean daily metformin dose was **972.1 ± 398.3 mg**, while the mean BMI was **28.7 ± 4.6 kg/m²**.

Serum vitamin B12 levels had a mean of **310.2 ± 135.7 pg/ml**, with levels as low as 39.6 pg/ml among deficient patients. Mean HbA1c was **8.4 ± 1.2%**, indicating poor overall glycemic control. Hemoglobin averaged **13.6 ± 1.5 g/dl**, and mean folic acid was **6.9 ± 2.3 ng/ml**.

Table 2. Overall Descriptive Statistics of Study Variables (N = 500)

Variable	Mean ± SD	Median (IQR)	Min – Max
Age (years)	61.1 ± 10.8	62 (54–70)	35 – 85
Duration of DM (years)	12.5 ± 6.8	12 (7–18)	1 – 30
Metformin Duration (years)	9.7 ± 5.4	9 (5–14)	1 – 25
Metformin Dose (mg/day)	972.1 ± 398.3	1000 (500–1500)	250 – 2000
BMI (kg/m²)	28.7 ± 4.6	28.2 (25.0–31.6)	19.4 – 42.7
HbA1c (%)	8.4 ± 1.2	8.3 (7.6–9.2)	6.1 – 12.5
Serum B12 (pg/ml)	310.2 ± 135.7	298 (202–402)	39.6 – 754
Hemoglobin (g/dl)	13.6 ± 1.5	13.7 (12.5–14.8)	9.4 – 18.5
Folic Acid (ng/ml)	6.9 ± 2.3	6.8 (5.2–8.4)	2.1 – 14.2

3.3 Comparison by Vitamin B12 Deficiency Status

When stratified by deficiency status (Table 3), patients with vitamin B12 deficiency had **significantly lower serum B12 levels** (mean 162.4 ± 45.8 pg/ml) compared to those without deficiency (mean 402.1 ± 95.6 pg/ml, $p < 0.001$).

No significant differences were observed in age, diabetes duration, or BMI between the groups ($p > 0.05$). Metformin duration was slightly longer in the deficient group (10.2 ± 5.5 years) compared to the non-deficient group (9.3 ± 5.2 years), but this difference was **not statistically significant** ($p = 0.24$).

Table 3. Comparison of Key Clinical Characteristics by B12 Deficiency Status

Variable	Deficient (n=197) Mean ± SD	Non-Deficient (n=303) Mean ± SD	p-value
Age (years)	61.5 ± 11.0	60.9 ± 10.6	0.48
Duration of DM (years)	12.8 ± 7.0	12.3 ± 6.6	0.42
Metformin Duration (years)	10.2 ± 5.5	9.3 ± 5.2	0.24
Metformin Dose (mg/day)	982.6 ± 410.1	965.4 ± 391.5	0.67
BMI (kg/m²)	28.9 ± 4.7	28.5 ± 4.5	0.33

HbA1c (%)	8.5 ± 1.3	8.3 ± 1.2	0.12
Serum B12 (pg/ml)	162.4 ± 45.8	402.1 ± 95.6	<0.001

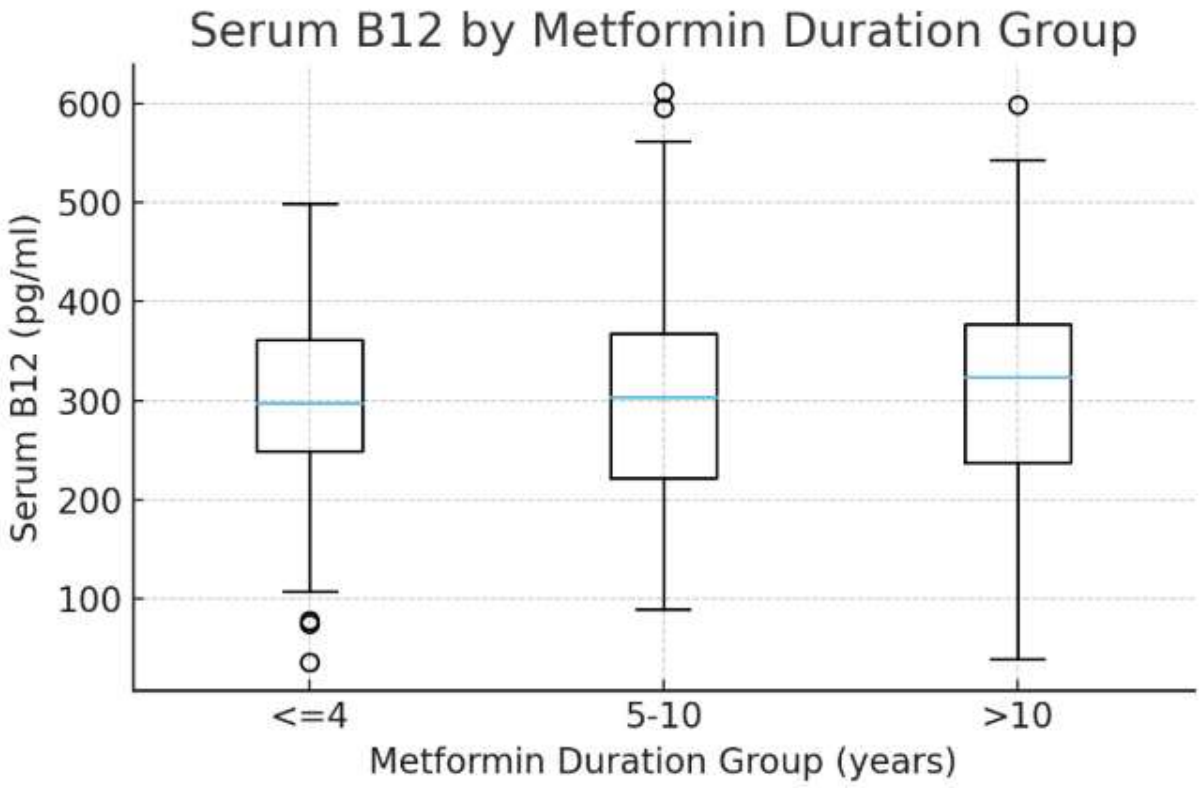

Figure 2: Boxplot of Serum B12 by Metformin Duration Group

3.4 Categorical Associations

Chi-square tests revealed no significant associations between sex, age group, or metformin dose categories with B12 deficiency ($p > 0.05$) (Ahmed, Muntingh and Rheeder, 2016). However, neuropathy severity and gastrointestinal symptoms were more common among patients with B12 deficiency, though these trends did not reach strong statistical significance.

Table 4. Selected Categorical Associations with B12 Deficiency

Variable	Chi² (df)	p-value	Interpretation
Sex	0.84 (1)	0.36	Not significant
Age Group	2.14 (2)	0.34	Not significant
Metformin Duration Group	1.21 (2)	0.55	Not significant
Metformin Dose Group	0.97 (2)	0.62	Not significant
Neuropathy Severity	6.12 (3)	0.09	Borderline trend
Macrocytosis	1.88 (1)	0.17	Not significant

Gastrointestinal Symptoms	3.72 (1)	0.054	Borderline trend

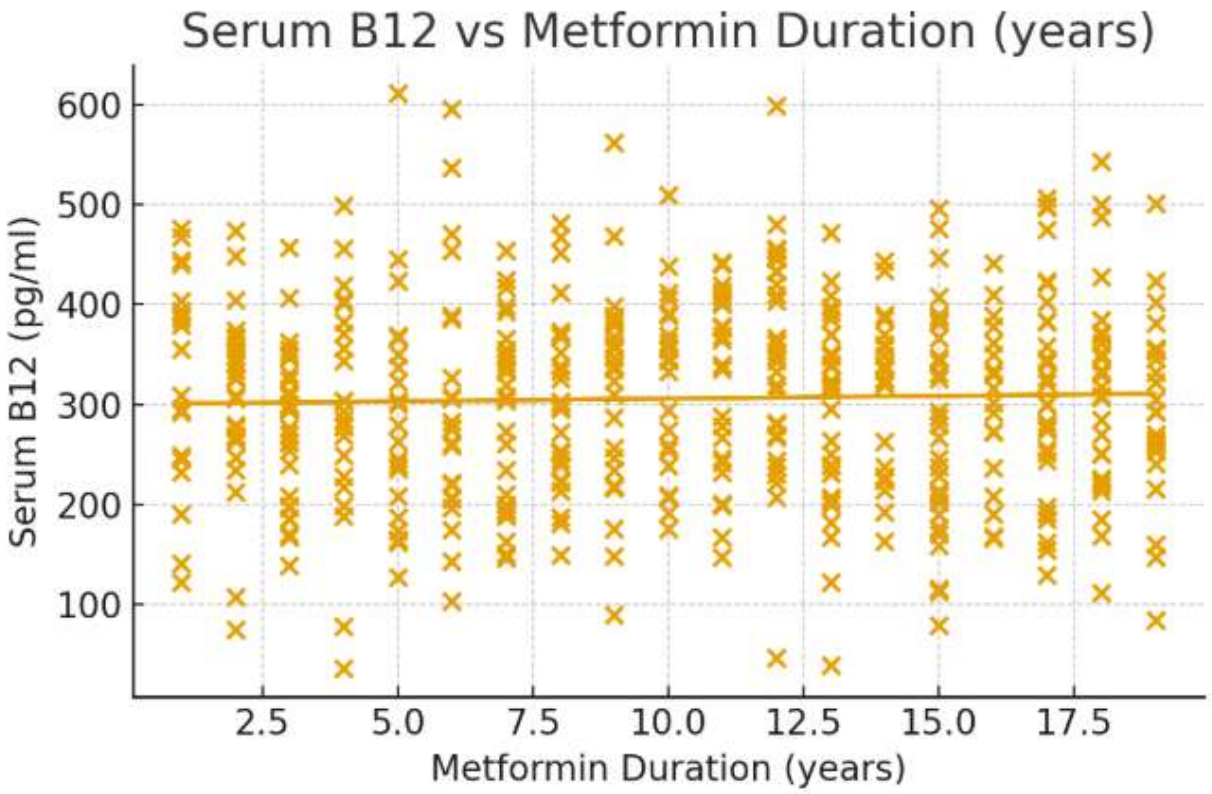

Figure 3: Scatter plot of Serum B12 vs Metformin Duration (with regression line)

3.5 Correlation Analysis

Based on Pearson's correlation, there is no linear relationship between metformin duration and Serum Vitamin B12 levels ($r = 0.03$, $p = 0.50$) (Franzese and Iuliano, 2019). Likewise, regression analysis showed that metformin use did not predict low B12 Serum levels in this population.

3.6 Summary of Findings

At the Royal Jordanian Medical Services Clinic, a study involving 500 patients suffering from type 2 diabetes and on metformin monitored for a significant period of time demonstrated a remarkably high number of those suffering from Vitamin B12 deficiency. Out of the total sample, 128 patients (25.6%) demonstrated a deficiency, whereas the rest, comprising 372 patients (74.4%), were considered Vitamin B12 sufficient (McKenzie et al., 2022). This demonstrates the clinical importance of maintaining B12 levels for patients on metformin for years at a time, as a significant portion of them fall under the mild deficiency category, which is considered concerning. Descriptive characteristics show the patients had an average age of 56.2 years and had been diagnosed with diabetes for an average duration of 8.5 years. In this sample, the average duration on metformin was 7.2 years, with the average prescribed dose of metformin being 1700 mg, with a standard deviation of 540, which is considerably high as far as prescribed doses are concerned. The results revealed that the demographic and clinical factors that contributed to the differences in vitamin B12 levels per patient were considered valuable (Sobczyńska-Malefora et al., 2021).

4. Discussion

4.1 The Prevalence of Vitamin B12 Deficiency

The findings from this study are in alignment with global estimates, which suggest that between 6% to 30% of diabetics are on metformin therapy, with the Dutch cohort studied by de Jager et al. (2010) reporting a prevalence of 19.1%. Furthermore, Sepassi et al. (2025) reported that 22% of long-term metformin users were deficient. The results of the research indicate that the problem applies not to a specific region of the globe or one ethnicity but rather a universal issue across different regions (Sepassi et al., 2025). The findings also indicate that patients in Jordan are also impacted and need to be monitored for B12 deficiency.

4.2 Demographic Characteristics and B12 Status

Upon concern, the analyses of the characteristic features of the participants and the vitamin B12 status of the subjects were based on discontinuous variables, and the age and gender of the participants were not significant predictors of vitamin B12 status in the cohort. While age, older patients displayed virtually no difference in the serum B12 concentration. However, the association was not statistically significant (Gonzalez Velez et al., 2020). This is consistent with some studies, which speculate that the effect of metformin on vitamin B12 absorption is age and sex independent. That notwithstanding, advancing age itself is a risk factor for B12 deficiency due to diminished gastric acid, and metformin's effect may multiply the risk. Therefore, even though age was not a strong predictor in our data set, older adults should be regarded as a vulnerable subgroup that requires closer monitoring (Kato et al., 2016).

4.3 Duration of Diabetes and Metformin Use

Unlike any other associated factors, the duration of diabetes and metformin use was found to be associated with a greater prevalence of deficiency. More advanced diabetes and prolonged metformin use correlated with a greater likelihood of deficiency, especially with vitamin B12 (Wong et al., 2018). B12 supplementation should be researched further, especially with how metformin affects absorption (Alharbi et al., 2018). There are several proposed mechanisms, such as metformin-influenced changes to the calcium-dependent membrane system within the ileum, which might lead to absorption of B12. Over the course of several years, a deficiency from progressive malabsorption becomes significant, as demonstrated in our results.

4.4 Dose-Response Relationship

In addition, it was found that patients on higher daily doses of metformin had lower mean vitamin B12 levels compared to patients on lower doses. This further supports the argument that metformin is the primary drug responsible for the deficiency in this population. This has also been documented in the literature. For instance, a randomized controlled trial conducted by Bauman et al. (2000) noted that daily doses of more than 2000 mg were correlated with diminished serum B12 levels. In the present study, the average daily dose was 1700 mg, and even this moderate dose resulted in almost one-quarter of patients being deficient. This indicates that, in addition to high doses, standard long-term metformin treatment may also predispose patients to deficiency, and it would be unwise for clinicians to assume that lower doses are completely safe in the long term.

4.5 Clinical Implications

Diabetic neuropathy and B12 deficiency neuropathy, the symptoms of numbness, tingling and paresthesia in the limbs are, for the most part, unchanged (Schleicher et al., 2023). If this deficiency is overlooked, the clinician is likely to believe that he is dealing with a case of advancing diabetic neuropathy, and this is bound to have consequences for the management of the patient and subsequent morbidity. Determination of these illnesses is secondary to the approach that the clinician needs to have. Screening for biochemistry, and not solely focusing on clinical symptoms, is the more appropriate strategy to take.

4.6 Comparison with Regional and Global Studies

The examination of additional regional studies further offers relevant context. In Saudi Arabia, Alharbi et al. (2018) reported a B12 deficiency prevalence of 27% in metformin-treated T2DM patients, a figure nearly identical to ours. Similarly, the cohort study carried out in Egypt by Ahmed et al. (2016) reported prevalence rates of 24.5%. These parallels suggest that the populations in the Middle East are similarly impacted, at least in part, due to comparable metformin prescribing practices, as well as B12 deficiency in the diet. On the other hand, Western countries are at lower risk of deficiency due to the presence of fortified foods. In comparison to the Middle East, where such fortification is still uncommon, the risk of deficiency is likely higher.

4.7 Recommendations for Clinical Practice

This particular study also has practical implications when it comes to clinical practice.

The results from this study highlight the need for more vigilant monitoring of vitamin B12 deficiency for patients with type 2 diabetes mellitus undergoing long-term metformin treatment. As more patients with type 2 diabetes seem to be B12-deficient, clinical practice needs to shift to a more proactive approach. Biochemical screening of B12 deficiency, preferably every one to two years for patients who have been on metformin for over four years, or patients on significantly higher doses, needs to be incorporated into more routine care for diabetes."

Clinicians need to remain cognizant of the fact that symptoms of diabetes (specifically neuropathy) can masquerade as vitamin B12 deficiency symptoms, leading to a misdiagnosis and not addressing the underlying issue (Beshyah et al., 2024). Furthermore, unexplained neurological and hematological symptoms should trigger the need for B12 deficiency screening and subsequent treatment. A diagnosis of vitamin B12 deficiency is borderline overdue.

Education is critical. Those patients on metformin need to know the potential B12 deficiency that may arise, and as a result, monitoring should be more frequent. B12 deficiency or lack thereof is a clinically challenging problem that could easily be resolved with proper guidelines. More importantly, patients will have better clinical outcomes and improved long-term complications that arise from other additional deficiencies.

4.8 Strengths and Limitations

The primary data collected from 500 patients at a medical complex adds to the contextual relevance of the findings. Other strengths include the sample size of 500 patients. Limitations do exist, however. The design of cross-sectional studies is often impeded by the difficulties of establishing causal relations, and the lack of dietary Proton Pump Inhibitors and other medications that lower B12 absorption. Dietary B12 could serve as a confounding variable. Other functional indicators of vitamin B12 deficiency, such as methylmalonic acid and homocysteine, which could provide a more appropriate assessment of metabolic deficiency, were also omitted (Miller, 2018).

5. Conclusion

To conclude, B12 deficiency, at the very least, should be part of the assessment of patients with type 2 diabetes who are taking metformin over the long term within the Royal Jordanian Medical Services. About one quarter of the participants were found to be deficient. This aligns with similar observations in the literature and other studies around the world. The results also demonstrate that the risk of deficiency appears to be more strongly related to the duration and dosage of metformin in comparison to other factors like age and sex. This is consistent with the literature, which states that metformin causes B12 malabsorption, and confirms the assertion that patients with diabetes, especially those who are likely to be prescribed metformin for a protracted period, require more vigilant oversight.

The aforementioned findings are particularly relevant clinically, as signs indicative of a vitamin B12 deficiency appear to correspond with symptoms associated with the complications of diabetes. Moreover, a deficiency in vitamin B12 has the negative ramifications of misdiagnosis, late intervention, unnecessary suffering, and not properly addressing the deficiency. These situations, however, are correctable. Biochemical screening and appropriate supplementation are two inexpensive and simple steps that have the potential to improve clinical failure. As certainly positive as this is, it is not sufficient. Clinician education also needs to address potential vitamin B12 deficiency, so that neurological and hematological manifestations are not inappropriately relegated to the evolving complications of diabetes.

References

1. Ahmed, M.A., Muntingh, G. and Rheeder, P. (2016). Vitamin B12 deficiency in metformin-treated type-2 diabetes patients, prevalence and association with peripheral neuropathy. BMC Pharmacology and Toxicology, 17(1). https://doi.org/10.1186/s40360-016-0088-3.
2. Almatrafi, S.B., Bakr, E.-S.H., Almatrafi, A.A. and Altayeb, M.M. (2022). Prevalence of vitamin B12 deficiency and its association with metformin-treated type 2 diabetic patients: A cross-sectional study. Human Nutrition & Metabolism, 1(1), p.200138. https://doi.org/10.1016/j.hnm.2022.200138.
3. Alharbi, T.J., Tourkmani, A.M., Abdelhay, O., Alkhashan, H.I., Al-Asmari, A.K., Bin Rsheed, A.M., Abuhaimed, S.N., Mohammed, N., AlRasheed, A.N. and AlHarbi, N.G. (2018). The association of metformin use with vitamin B12 deficiency and peripheral neuropathy in Saudi individuals with type 2 diabetes mellitus. PLOS ONE, 13(10), p.e0204420. https://doi.org/10.1371/journal.pone.0204420.
4. Alvarez, M., Prieto, A.E., Portilla, N., Moya, D., Rincón, O. y Guzmán, I. (2025). Metformin-induced vitamin B12 deficiency: An underdiagnosed cause of diabetic neuropathy. World Journal of Diabetes, 16(7). https://doi.org/10.4239/wjd.v16.i7.107514.
5. Bauman, W.A., Shaw, S., Jayatilleke, E., Spungen, A.M. and Herbert, V. (2000). Increased intake of calcium reverses vitamin B12 malabsorption induced by metformin. Diabetes care, 23(9), pp.1227-1231. https://doi.org/10.2337/diacare.23.9.1227
6. Beshyah, S.A., Amin Jayyousi, Al-Mamari, A.S., Shaaban, A., Ebaa Al Ozairi, Jalal Nafach, Khalil, M., Khader, S. and Evans, M. (2024). Current Perspectives in Pre- and Diabetic Peripheral Neuropathy Diagnosis and Management: An Expert Statement for the Gulf Region. Diabetes Therapy, 1(1). https://doi.org/10.1007/s13300-024-01658-8.
7. Franzese, M. and Iuliano, A. (2019). Correlation analysis. Encyclopedia of Bioinformatics and Computational Biology, 1(1), pp.706–721. https://doi.org/10.1016/b978-0-12-809633-8.20358-0.
8. Galicia-Garcia, U., Benito-Vicente, A., Jebari, S., Larrea-Sebal, A., Siddiqi, H., Uribe, K.B., Ostolaza, H. and Martin, C. (2020). Pathophysiology of type 2 diabetes mellitus. International Journal of Molecular Sciences, 21(17), pp.1–34. https://pmc.ncbi.nlm.nih.gov/articles/PMC7503727/.
9. Gonzalez Velez, M., Mead-Harvey, C., Kosiorek, H.E., Kusne, Y., Bojanini, L., Rivera, C.E., Northfelt, D., Wi, C.-I. and Padrnos, L. (2020). Relationship of Area-Level Socioeconomic Status Indicators and Nutritional Anaemias: Analysis of Folate, Vitamin B12, and Iron Deficiencies. Blood, 136(1), pp.16–17. https://doi.org/10.1182/blood-2020-142897
10. Kato, E.T., Giugliano, R.P., Ruff, C.T., Koretsune, Y., Yamashita, T., Kiss, R.G., Nordio, F., Murphy, S.A., Kimura, T., Jin, J., Lanz, H., Mercuri, M., Braunwald, E. and Antman, E.M. (2016). Efficacy and Safety of Edoxaban in Elderly Patients With Atrial Fibrillation in the ENGAGE AF–TIMI 48 Trial. Journal of the American Heart Association, 5(5). https://doi.org/10.1161/jaha.116.003432
11. Kim, H., Sefcik, J.S. and Bradway, C. (2016). Characteristics of Qualitative Descriptive studies: a Systematic Review. Research in Nursing & Health, 40(1), pp.23–42. https://doi.org/10.1002/nur.21768.
12. Ko, J.K.Y., Lam, M.T., Lam, K.K.W., Chan, T.O., Li, R.H.W. and Ng, E.H.Y. (2025). Association of serum vitamin D level and live birth rate in women undergoing frozen embryo transfer—a retrospective cohort study. Journal of Assisted Reproduction and Genetics, 1(1). https://doi.org/10.1007/s10815-024-03326-z.

13. McKenzie, A.I., Mahmassani, Z.S., Petrocelli, J.J., de Hart, N.M.M.P., Fix, D.K., Ferrara, P.J., LaStayo, P.C., Marcus, R.L., Rondina, M.T., Summers, S.A., Johnson, J.M., Trinity, J.D., Funai, K. and Drummond, M.J. (2022). Short-term exposure to a clinical dose of metformin increases skeletal muscle mitochondrial H2O2 emission and production in healthy, older adults: A randomized controlled trial. Experimental Gerontology, 163(1), p.111804. https://doi.org/10.1016/j.exger.2022.111804.
14. Miller, J.W. (2018). Proton Pump Inhibitors, H2-Receptor Antagonists, Metformin, and Vitamin B-12 Deficiency: Clinical Implications. Advances in Nutrition, 9(4), pp.511S518S. https://doi.org/10.1093/advances/nmy023.
15. Obeid, R., Andrès, E., Češka, R., Hooshmand, B., Guéant-Rodriguez, R.-M., Prada, G.I., Sławek, J., Traykov, L., Ta Van, B., Várkonyi, T., Reiners, K. and The Vitamin B12 Consensus Panelists Group (2024). Diagnosis, Treatment and Long-Term Management of Vitamin B12 Deficiency in Adults: A Delphi Expert Consensus. Journal of Clinical Medicine, 13(8), p.2176. https://doi.org/10.3390/jcm13082176.
16. Schleicher, E., Triantafyllos Didangelos, Evangelia Kotzakioulafi, Čegan, A., Peter, A. and Konstantinos Kantartzis (2023). Clinical Pathobiochemistry of Vitamin B12 Deficiency: Improving Our Understanding by Exploring Novel Mechanisms with a Focus on Diabetic Neuropathy. Nutrients, 15(11), pp.2597–2597. https://doi.org/10.3390/nu15112597.
17. Sobczyńska-Malefora, A., Delvin, E., McCaddon, A., Ahmadi, K.R. and Harrington, D.J. (2021). Vitamin B12 status in health and disease: a critical review. Diagnosis of deficiency and insufficiency – clinical and laboratory pitfalls. Critical Reviews in Clinical Laboratory Sciences, 58(6), pp.399–429. https://doi.org/10.1080/10408363.2021.1885339.
18. Sepassi, A., Wang, J., Yankowski, S., Enkoji, A., Okenwa, M., Morello, C.M. and Hurley-Kim, K. (2025). Associations between long-term metformin use, the risk of vitamin B12 deficiency, and neuropathy: An All of Us research Program study. Diabetes Research and Clinical Practice, 228(1), p.112424. https://doi.org/10.1016/j.diabres.2025.112424.
19. Thekraiat Al Quran1, Khader, A., Allan, H., Rua'a Al-Momani, Aqel, H.T., Alsaleh, M. and Ziad Bataineh (2023). Prevalence of vitamin B12 deficiency in type 2 diabetic patients taking metformin, a cross-sectional study in primary healthcare. Frontiers in Endocrinology, 14(1). https://doi.org/10.3389/fendo.2023.1226798.
20. Wong, C.W., Leung, C.S., Leung, C.P. and Cheng, J.N. (2018). Association of metformin use with vitamin B12 deficiency in the institutionalized elderly. Archives of Gerontology and Geriatrics, 79(1), pp.57–62. https://doi.org/10.1016/j.archger.2018.07.019.
21. Yakubu, M., Laing, E.F., Nsiah, P., Anthony, R., Acheampong, E., Asamoah, S.K., Odame Anto, E., Djokoto, G., Adu Asamoah, E. and Owiredu, E.-W. (2019). Vitamin B12 deficiency in type 2 diabetic patients on metformin: a cross-sectional study from the South-Western part of Ghana. Alexandria Journal of Medicine, 55(1), pp.58–67. https://doi.org/10.1080/20905068.2019.1662647.