

KNOWLEDGE AND AWARENESS OF VITAMIN B12 DEFICIENCY AMONG DIABETIC PATIENTS ON METFORMIN IN SAUDI ARABIA: A CROSS-SECTIONAL STUDY.

Khalid Alghamdi¹, Ruwayda Alharbi^{*2}, Ghadeer Almasoudi³, Mohammed Alshahrani⁴, Raneem Alqattan⁵, Layal Alfaqih⁶, Zahra Alsadah⁷, Shaima Alwaladi⁸, Rahaf Almulf⁹, Khalid Alghareeb⁵, Seba Alzeair¹⁰, Khames T. Alzahrani¹¹

¹Consultant Endocrinology and Diabetes, Comprehensive Specialized Clinics of Security Forces, Jeddah, Saudi Arabia.

²Medical student, College of Medicine, Qassim University, Buraydah, Saudi Arabia.

³Medical student, College of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia.

⁴Medical student, College of Medicine, University of Bisha, Bisha, Saudi Arabia.

⁵Medical student, College of Medicine, King Faisal University, Al Ahsa, Saudi Arabia.

⁶Medical student, College of Medicine, Taif University, Taif, Saudi Arabia.

⁷Medical student, College of Medicine, Imam Abdulrahman Bin Faisal University, Al Dammam, Saudi Arabia.

⁸Medical student, College of Medicine, King Abdulaziz University, Rabigh, Saudi Arabia.

⁹Medical Intern, College of Medicine, King Khalid university, Abha City, Saudi Arabia.

¹⁰Medical student, College of Medicine, Jeddah University, Jeddah, Saudi Arabia.

¹¹BDS, PGD Endo from Stanford University, Saudi Board of Endodontic SR, King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia.

***Corresponding author:** Ruwayda Alharbi; **Email:** irowida7@gmail.com

Abstract

Background: Diabetes mellitus is a prevalent health concern globally, with Saudi Arabia also experiencing a high burden of this metabolic disorder. Metformin stands out as the recommended first-line treatment for diabetes due to its proven efficacy and safety profile. However, it is important to note that the use of metformin has been linked to an increased risk of vitamin B12 deficiency, a vital nutrient essential for optimal blood cell production, cognitive function, and cardiovascular health. **Objective:** The study aimed to evaluate the knowledge and awareness of diabetic patients regarding metformin-induced vitamin B12 deficiency and its implications on overall health. **Methods:** A cross-sectional study was conducted on diabetes patients taking the medication Metformin in Saudi Arabia. The study took place over a 6-month period from July to December 2024. Participants for the study were recruited through social media platforms. Data was gathered from the participants using structured questionnaires. **Results:** In a cross-sectional study involving 518 diabetic patients on metformin in Saudi Arabia, findings revealed significant gaps in knowledge and awareness of vitamin B12 deficiency. While 68.5% of participants recognized the risk of deficiency, a troubling 75.1% were unaware of the underlying mechanisms. Despite high awareness of vitamin B12 (87.1%), misconceptions persisted, with nearly half incorrectly believing it derives from plant sources. Only 10.4% exhibited high awareness of deficiency risk, and 62.4% had vital knowledge of its health impacts. Notably, awareness correlated significantly with demographic factors such as age, education, and occupational status, highlighting the need for targeted educational interventions. **Conclusion:** The findings of this study underscore the critical need for enhanced educational initiatives targeting diabetic patients on metformin to improve their understanding of vitamin B12 deficiency and its implications for health.

Keywords: Diabetes Mellitus, Metformin, Vitamin B12.

Introduction

Type 2 diabetes mellitus (T2DM), which accounts for around 90% of all diabetes cases, is characterized by high blood sugar levels (hyperglycemia) resulting from the body's insufficient response to insulin (insulin resistance) followed by inadequate insulin production [1]. According to the World Health Organization (WHO), Saudi Arabia has the second highest prevalence of diabetes in the Middle East region and ranks seventh globally for diabetes prevalence [2]. The American Diabetes Association (ADA) states that metformin is the preferred initial medication and the foundation for managing type 2 diabetes, due to its high efficacy in controlling macrovascular complications associated with the disease [3]. In recent years, numerous observational studies, systematic reviews, and meta-analyses have found an association between long-term metformin therapy and biochemical vitamin B12 deficiency, including both overt vitamin B12 deficiency and borderline vitamin B12 status [4]. Vitamin B12 is essential for the synthesis of DNA, normal red blood cell production (erythropoiesis), the formation of nucleoproteins and myelin, cell replication, and overall growth and development [5]. The vitamin B12 deficiency observed with long-term metformin use is believed to be caused by impaired vitamin B12 absorption, with early hypotheses suggesting this was due to metformin's effects on bile acid metabolism, small intestinal bacterial overgrowth, or intrinsic factor secretion, but the more widely accepted explanation is that metformin interferes with the calcium-dependent membrane processes responsible for the absorption of vitamin B12 bound to intrinsic factor in the terminal ileum [6].

A study investigating the relationship between metformin use, vitamin B12 deficiency, and peripheral neuropathy in Saudi individuals with type 2 diabetes mellitus discovered that the prevalence of vitamin B12 deficiency was 7.8%. Notably, metformin users exhibited a higher B12 deficiency rate at 9.4% compared to 2.2% in non-metformin users [7]. In Riyadh, it was observed that routine testing of patients' serum vitamin B12 levels is not a common practice. Moreover, a significant number of physicians are unfamiliar with the current American Diabetes Association (ADA) guidelines on vitamin B12 supplementation and screening [8]. Another research study in the Qassim region highlighted that many type 2 diabetic patients using metformin were unaware of vitamin B12 deficiency and its potential effects on the body [9].

Despite the importance of managing diabetes mellitus and the widespread use of metformin as the first-line treatment, as well as the established association between long-term metformin use and vitamin B12 deficiency, there is a significant gap in the literature regarding the awareness and knowledge of diabetes patients about the risk of metformin-induced vitamin B12 deficiency.

Objectives: The purpose of this study is to assess diabetes patients on metformin's knowledge and awareness of vitamin B12 deficiency caused by the medication.

Methodology:

Study Design and Setting:

This cross-sectional study was carried out in Saudi Arabia from July to December 2024 using an online questionnaire survey distributed through social media platforms. The research involved participants with type 2 diabetes who were taking metformin.

Sample size:

The sample size was calculated to ensure that the number of respondents adequately represents the entire population. Using the Raosoft sample size calculator, with an indicator percentage of 50%, a margin of

error of 5%, and a 95% confidence interval (CI), the required sample size was determined to be 384.

Inclusion and Exclusion Criteria:

Patients diagnosed with DM from the Saudi population who were 18 years and above on oral metformin were included in the study and patients who are below 18 years, or not on metformin were excluded from the study.

Method for data collection, instrument, and score system:

An electronic questionnaire was used to gather data. The questionnaire was used from a related studies conducted in Saudi Arabia [9–11]. The final version of the questionnaire consisted of 20 questions classified into 3 sections. Section one contained characteristics a sociodemographic data questions such as age, gender, residential area and duration of metformin use in years. The second section includes questions to test the participants' awareness of metformin-induced B12 deficiency. The third section includes questions that assess the participants' knowledge about vitamin B12 deficiency.

Scoring system:

Part I: Awareness

Using a 6-item questionnaire with "Yes" (1 point) and "No" (0 points) alternatives, awareness was measured. The range of the overall Awareness score was 0–6. Bloom's cut-off point was used to evaluate the overall level of awareness. This cut-off point indicated that a score of 80–100% (5–6 points) indicated good awareness, a score of 60–79% (3–4 points) indicated moderate awareness, and a score of less than 60% (2–0 points) indicated weak preventative actions.

Part II: Knowledge

Knowledge was examined using a 7-item questionnaire with "Yes" (1 point) and "No" (0 point) options. The total knowledge score ranged from 0 to 7. The general level of knowledge was measured using Bloom's cut-off point. Based on this cut-off point, a score of 80–100% (5–7 points) was considered high knowledge, 60–79% (4 points) intermediate knowledge, and less than 60% (3–0 points) as weak preventative measures.

Pilot test:

The questionnaire was distributed to 20 individuals who were asked to complete it. This was conducted to evaluate the simplicity of the questionnaire and the feasibility of the study. The data obtained from this pilot study were excluded from the final analysis.

Analyses and entry method:

Data was entered on the computer utilizing the "Microsoft Office Excel Computer program" (2016) version for windows. Data was then sent to the Statistical Package of Social Science Software (SPSS) program, using version 20 (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.)

Results:

Table (1) displays various demographic parameters of the participants with a total number of (518). This has a mean age of 42 years and a standard deviation of 14.1 years, so it is a fairly age diverse distribution. According to the cultural context of this study, notable majority of the participants (72.2%) are female and 90.2% are Saudi nationals. The residential distribution is somewhat evenly spread across regions, Central and Western together comprising over 62% of the sample. The sample presents a strong slant toward higher educational background; more than half (52.9%) have bachelor's degree, perhaps as a reflection of a socioeconomic status of the sample. Physically, 46.9% of people are unemployed, a portion known to have occupational status barriers that may coalesce with health ones—namely with diabetes management. More than half of the patients in this demographic are relatively new to having diabetes—spanning less than five years—and they have been using Metformin for the same length of time.

Table (1): Sociodemographic characteristics of participants (n=518).

Parameter		No.	Percent (%)
Age (Mean:42.0, STD:14.1)	26 or less	98	18.9
	27 to 38	103	19.9
	39 to 44	103	19.9
	45 to 52	106	20.5
	53 or more	108	20.8
Gender	Female	374	72.2
	Male	144	27.8
Nationality	Saudi	462	89.2
	Non-Saudi	56	10.8
Residential region	Northern region	37	7.1
	Southern region	70	13.5
	Central region	165	31.9
	Eastern region	87	16.8
	Western region	159	30.7
Educational level	Primary school	11	2.1
	Middle school	27	5.2
	High school	94	18.1
	Diploma	57	11.0
	Bachelor's degree	278	53.7
	Master's degree	28	5.4
	PHD	7	1.4
	Uneducated	16	3.1
Occupational status	Student	43	8.3
	Employee	151	29.2
	Unemployed	243	46.9
	Retired	81	15.6
Marital status	Single	108	20.8
	Married	353	68.1
	Divorced	27	5.2

	Widowed	30	5.8
<i>Duration of DM in years</i>	Less than 5 years	280	54.1
	5-10 years	100	19.3
	More than 10 years	138	26.6
<i>Duration of Metformin use</i>	Less than 5 years	324	62.5
	5-10 years	91	17.6
	More than 10 years	103	19.9

As shown in figure 1, The importance of regular monitoring is noted by 155 of whom (approximately 30% of the sample) advocate for annual assessments. On the other end of the scale, a considerable proportion — some 12.5% — suggests that testing should only be done if symptoms of deficiency are present, indicating a possible lack of awareness concerning a high risk of B12 deficiency from long term metformin use. But alarmingly, an overwhelming majority, or 266 out of 516 or about 51.3%; are unsure as to how often testing should take place.

Figure (1): Illustrates frequency of b12 level testing among participants.

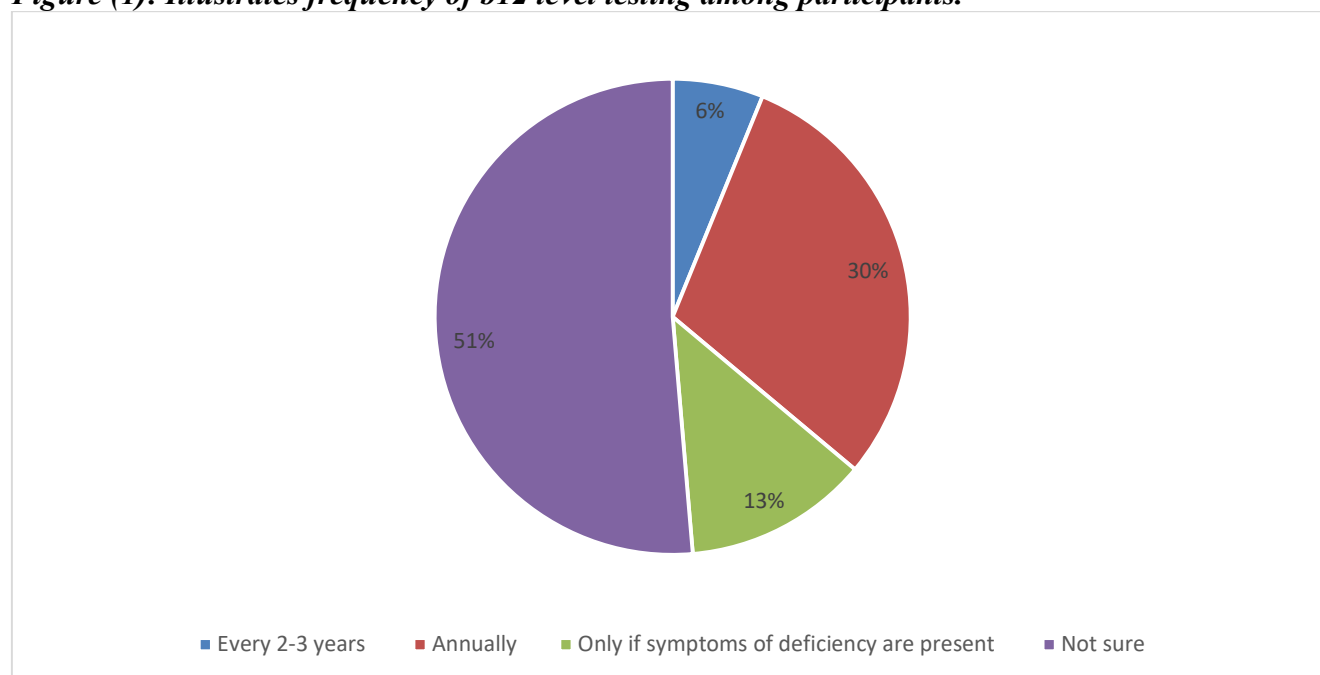


Table 2 shows a sample of 518 diabetics on metformin for whom the data presented would provide significant insights into how many know they are deficient in vitamin B12. A whopping 68.5% of respondents were aware of the possibility of metformin inducing vitamin B12 deficiency and most respondents listed their own doctors as their primary source of information. Nevertheless, while the former was aware, a concerning 75.1% of participants were unaware of the underlying mechanism by which metformin can cause this deficiency. Similarly, the absence of understanding is also found in the answers for the question how often is Vitamin B12 level checked a number of who (51.4%) indicated unsure. Despite the fact there is a high prevalence of awareness regarding the deficiency, only 63.9 per cent of patients were taking supplements to ensure they ingested adequate vitamin B12.

Table (2): Parameters related to awareness of vitamin B12 deficiency among diabetic patients on metformin (n=518).

Parameter		No.	Percent (%)
<i>Have you ever heard of metformin-induced vitamin B12 deficiency and its potential impact on diabetic patients` health?</i>	No	163	31.5
	Yes	355	68.5
<i>If yes, tell us how you found out about this information: (n=355)</i>	Internet	106	29.9
	Pharmacist	15	4.2
	Doctor	156	43.9
	Educational Campaign	14	3.9
	Other	64	18.0
<i>Do you know why metformin can cause vitamin B12 deficiency?</i>	No	389	75.1
	Yes	129	24.9
<i>How frequently should vitamin B12 levels be checked in patient who are on metformin?</i>	Every 2-3 years	32	6.2
	Annually	155	29.9
	Only if symptoms of deficiency are present	65	12.5
	Not sure	266	51.4
<i>Have you ever been tested by your doctor for vitamin B12 levels while taking metformin?</i>	No	170	32.8
	Yes	348	67.2
<i>If yes, what was your vitamin B12 level? (n=348)</i>	Normal	181	52.0
	High	15	4.3
	Low	152	43.7
<i>Are you currently taking any supplement to ensure adequate vitamin B12 intake?</i>	No	187	36.1
	Yes	331	63.9

As shown in figure (2), This results presentation provides the dietary sources of vitamin B12 for a total sample size of 518 respondents. It is important to note that vegetables and fruits were the most mentioned sources, with 47.7% (247 people) identifying their role, indicating possibly a great degree of awareness of vegetable and fruit-based nutrients. However, seafood, another important source of vitamin B 12, was known to 26.2% (136) of the population, a moderately well-informed part of the population in regards to marine foods. In addition (26.0%, 135 individuals) were able to recognize animal products.

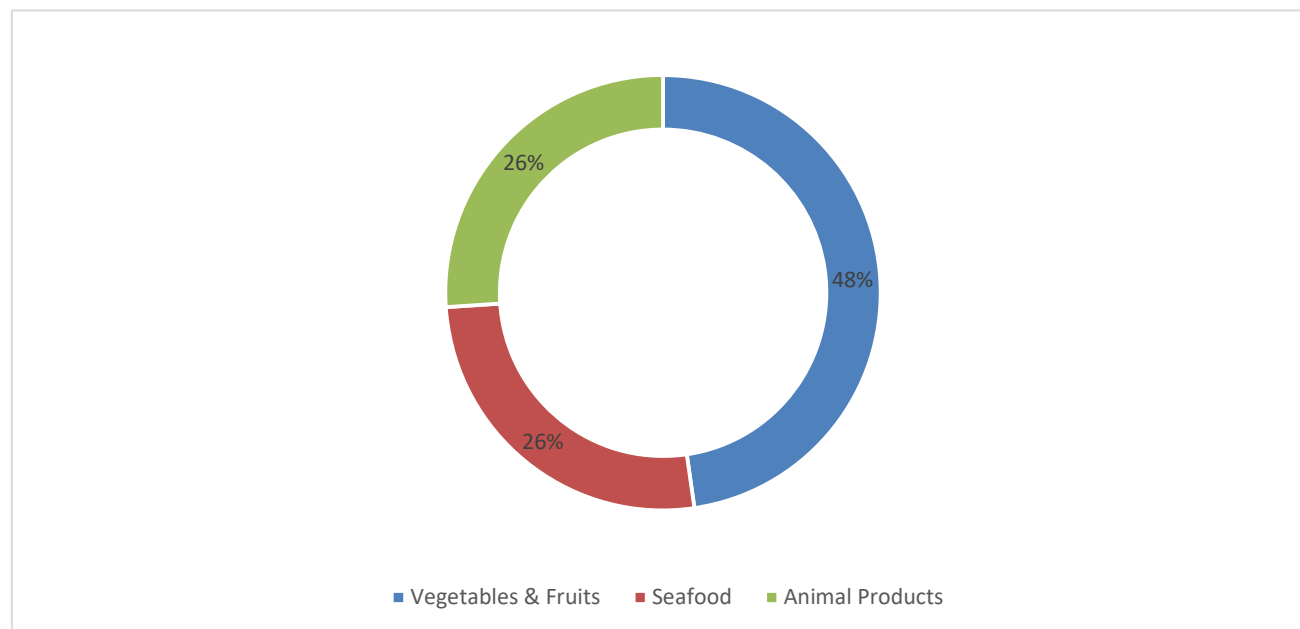
Figure (2): Illustrates foods that contain vitamin B12 among participants.

Table 3 shows that a sample size of 518 participants had awareness and knowledge of diabetic patients taking metformin in vitamin B12 deficiency data presented in it. What's more noteworthy, a very large share, 87.1 percent, have heard of vitamin B12, a level of awareness merits praise. While only 85.1 percent of Americans understand it's important to overall health, there is a knowledge gap about how the vitamin may help prevent complications with deficiency. We find that nearly half of respondents (47.7%) indicate vitamin B12 comes from vegetables and fruits, even though plant-based foods do not contain this important nutrient indicating potential misperceptions about dietary knowledge. Additionally, a large percentage of respondents said they had experienced symptoms including numbness or tingling (67.8%), lack of concentration (69.1%), dizziness (57.5%).

Table (3): participants' knowledge of vitamin B12 deficiency among diabetic patients on metformin (n=518).

<i>Parameter</i>		<i>No.</i>	<i>Percent (%)</i>
<i>Have you ever heard about Vitamin B12?</i>	No	67	12.9
	Yes	451	87.1
<i>Do you know the importance of vitamin B12 intake to the body?</i>	No	77	14.9
	Yes	441	85.1
<i>Do you know what kind of foods contain vitamin B12?</i>	Vegetables & Fruits	247	47.7
	Seafood	136	26.3
	Animal Products	135	26.1
<i>Do you follow a vegetarian diet?</i>	No	435	84.0
	Yes	83	16.0
<i>Have you ever felt numbness or tingling in your</i>	No	167	32.2

<i>extremities?</i>	Yes	351	67.8
<i>Do you suffer from lack of concentration and forgetfulness?</i>	No	160	30.9
	Yes	358	69.1
<i>Do you feel dizzy and lightheaded?</i>	No	220	42.5
	Yes	298	57.5

Table 4 shows a worrying trend in data showing diabetic patients prescribed metformin are significantly less aware of their risk of becoming deficient in vitamin B12. Only 10.4 percent of participants showed a high level of awareness, 41.3 percent moderate awareness, and 48.3 percent low awareness of a potential vitamin B12 deficiency were found.

Table (4): Shows awareness of vitamin B12 deficiency among diabetic patients on metformin score results.

	Frequency	Percent
High level of awareness	54	10.4
Moderate awareness level	214	41.3
Low awareness level	250	48.3
Total	518	100.0

Table 5 provides some insights from the data presented in Table 5 regarding how diabetic patients on metformin know about vitamin B12 deficiency. It is worth noting that a very high 62.4 percent of the people that got surveyed have a vital information regarding the consequences and health risks involved in vitamin B12 deficiency. On the contrary, the data indicate that 19.5 % of these consumers have very low knowledge levels and can benefit from targeted educational education to improve their knowledge about the condition. The moderate knowledge comprises 18.1% while the remaining 18.1% is the rest.

Table (5): Shows knowledge of vitamin B12 deficiency among diabetic patients on metformin score results.

	Frequency	Percent
High level of knowledge	323	62.4
Moderate knowledge	94	18.1
Low knowledge level	101	19.5
Total	518	100.0

Table (6) shows that awareness of vitamin B12 deficiency among diabetic patients on metformin has statistically significant relation to age (P value=0.008), nationality (P value=0.048), residential region (P value=0.0001), educational level (P value=0.0001), occupational status (P value=0.0001), marital status (P value=0.0001), duration of DM (P value=0.001), and duration of metformin (P value=0.0001). It also shows statistically insignificant relation to gender.

Table (6): Relation between awareness of vitamin B12 deficiency among diabetic patients on metformin and sociodemographic characteristics.

Parameters		Awareness level		Total (N=518)	P value*
		High moderate awareness	or Low awareness level		
Gender	Female	184	190	374	0.062
		68.7%	76.0%	72.2%	
	Male	84	60	144	
		31.3%	24.0%	27.8%	
Age	26 or less	51	47	98	0.008
		19.0%	18.8%	18.9%	
	27 to 38	47	56	103	
		17.5%	22.4%	19.9%	
	39 to 44	41	62	103	
		15.3%	24.8%	19.9%	
	45 to 52	65	41	106	
		24.3%	16.4%	20.5%	
Nationality	Saudi	246	216	462	0.048
		91.8%	86.4%	89.2%	
	Non-Saudi	22	34	56	
		8.2%	13.6%	10.8%	
Residential region	Northern region	17	20	37	0.0001
		6.3%	8.0%	7.1%	
	Southern region	23	47	70	
		8.6%	18.8%	13.5%	
	Central region	105	60	165	
		39.2%	24.0%	31.9%	
	Eastern region	25	62	87	
		9.3%	24.8%	16.8%	
Educational level	Western region	98	61	159	0.0001
		36.6%	24.4%	30.7%	
	Primary school	5	6	11	
		1.9%	2.4%	2.1%	
	Middle school	26	1	27	
		9.7%	0.4%	5.2%	
	High school	40	54	94	
		14.9%	21.6%	18.1%	
	Diploma	25	32	57	
		9.3%	12.8%	11.0%	
	Bachelor's degree	143	135	278	
		53.4%	54.0%	53.7%	

	Master's degree	18	10	28	
		6.7%	4.0%	5.4%	
	PHD	7	0	7	
		2.6%	0.0%	1.4%	
	Uneducated	4	12	16	
		1.5%	4.8%	3.1%	
Occupational status	Student	14	29	43	0.0001
		5.2%	11.6%	8.3%	
	Employee	62	89	151	
		23.1%	35.6%	29.2%	
	Unemployed	135	108	243	
		50.4%	43.2%	46.9%	
Marital status	Single	57	24	81	0.0001
		21.3%	9.6%	15.6%	
	Married	40	68	108	
		14.9%	27.2%	20.8%	
	Divorced	205	148	353	
		76.5%	59.2%	68.1%	
Duration of DM in years	Widowed	14	13	27	0.001
		5.2%	5.2%	5.2%	
	Less than 5 years	9	21	30	
		3.4%	8.4%	5.8%	
	5-10 years	124	156	280	
		46.3%	62.4%	54.1%	
Duration of Metformin use	More than 10 years	56	44	100	0.0001
		20.9%	17.6%	19.3%	
	Less than 5 years	88	50	138	
		32.8%	20.0%	26.6%	
	5-10 years	140	184	324	
		52.2%	73.6%	62.5%	
	More than 10 years	62	29	91	
		23.1%	11.6%	17.6%	
	Less than 5 years	66	37	103	
		24.6%	14.8%	19.9%	
	5-10 years				

***P value was considered significant if ≤ 0.05 .**

Table (7) shows that knowledge of vitamin B12 deficiency among diabetic patients on metformin has statistically significant relation to age (P value=0.0001), nationality (P value=0.039), residential region (P value=0.050), occupational status (P value=0.0001), marital status (P value=0.002). It also shows statistically insignificant relation to gender, duration of DM and duration of metformin.

Table (7): knowledge of vitamin B12 deficiency among diabetic patients on metformin in association with sociodemographic characteristics.

Parameters		Knowledge level		Total (N=518)	P value*
		High level of knowledge	Moderate or low knowledge		
Gender	Female	236	138	374	0.572
		73.1%	70.8%	72.2%	
	Male	87	57	144	
		26.9%	29.2%	27.8%	
Age	26 or less	70	28	98	0.0001
		21.7%	14.4%	18.9%	
	27 to 38	75	28	103	
		23.2%	14.4%	19.9%	
	39 to 44	49	54	103	
		15.2%	27.7%	19.9%	
	45 to 52	73	33	106	
		22.6%	16.9%	20.5%	
Nationality	Saudi	56	52	108	0.039
		17.3%	26.7%	20.8%	
	Non-Saudi	42	14	56	
		13.0%	7.2%	10.8%	
Residential region	Northern region	26	11	37	0.050
		8.0%	5.6%	7.1%	
	Southern region	38	32	70	
		11.8%	16.4%	13.5%	
	Central region	98	67	165	
		30.3%	34.4%	31.9%	
	Eastern region	65	22	87	
		20.1%	11.3%	16.8%	
Educational level	Western region	96	63	159	N/A
		29.7%	32.3%	30.7%	
	Primary school	11	0	11	
		3.4%	0.0%	2.1%	
	Middle school	12	15	27	
		3.7%	7.7%	5.2%	
	High school	56	38	94	
		17.3%	19.5%	18.1%	
	Diploma	24	33	57	
		7.4%	16.9%	11.0%	
	Bachelor's degree	186	92	278	
		57.6%	47.2%	53.7%	

	Master's degree	11	17	28	0.0001
		3.4%	8.7%	5.4%	
	PHD	7	0	7	
		2.2%	0.0%	1.4%	
	Uneducated	16	0	16	
		5.0%	0.0%	3.1%	
Occupational status	Student	30	13	43	0.0001
		9.3%	6.7%	8.3%	
	Employee	96	55	151	
		29.7%	28.2%	29.2%	
	Unemployed	164	79	243	
		50.8%	40.5%	46.9%	
Marital status	Retired	33	48	81	0.002
		10.2%	24.6%	15.6%	
	Single	78	30	108	
		24.1%	15.4%	20.8%	
	Married	201	152	353	
		62.2%	77.9%	68.1%	
Duration of DM in years	Divorced	19	8	27	0.775
		5.9%	4.1%	5.2%	
	Widowed	25	5	30	
		7.7%	2.6%	5.8%	
	Less than 5 years	174	106	280	
		53.9%	54.4%	54.1%	
Duration of Metformin use	5-10 years	60	40	100	0.864
		18.6%	20.5%	19.3%	
	More than 10 years	89	49	138	
		27.6%	25.1%	26.6%	
	Less than 5 years	203	121	324	
		62.8%	62.1%	62.5%	
	5-10 years	58	33	91	0.864
		18.0%	16.9%	17.6%	
	More than 10 years	62	41	103	
		19.2%	21.0%	19.9%	

***P value was considered significant if ≤ 0.05 .**

Discussion:

The present study was designed to assess the diabetic patients on metformin in Saudi Arabia and their knowledge and awareness about vitamin B12 deficiency. Especially now in light of the rising rate of diabetes and metformin's use as a first line treatment, this investigation is especially relevant. Finally, findings of this study demonstrate that participants were not aware of or understood this deficiency of vitamin B12, which corresponds with past research highlighting that this is a common theme in other populations. Results show that most participants acknowledged vitamin B12 deficiency as a possibility if metformin is used, but most don't know how or why this could happen.

Our results further highlight the variability in the prevalence of vitamin B12 deficiency among metformin users when compared with other literature. One example, a study carried out by Raizada and colleagues, demonstrated a vitamin B12 deficiency in 5.8 percent of diabetic subjects on metformin, less than the 9.4 percent calculated in our study [12]. Differences in study populations, sample sizes and methodologies may account for this discrepancy. As seen, Khan et al. noted that metformin dosage alone does not immediately induce vitamin B12 deficiency and the extent of development relies on duration of metformin therapy [13]. This notion is corroborated by our findings, which showed a statistically significant relationship of metformin use duration to vitamin B12 deficiency awareness.

In addition, the awareness levels regarding B12 deficiency were patently alarmingly low among our participants and only 10.4% showed high awareness. These findings are similar to previous work by Alshammari et al., who found that many healthcare providers in Saudi Arabia do not receive sufficient information about the need for vitamin B12 deficiency screening in metformin users [14]. Lack of awareness among patients and healthcare providers emphasizes the imperative of educational interventions to increase knowledge about vitamin B12 deficiency and their implications on health. That's especially important since vitamin B12 is needed for many bodily functions, including creating red blood cells and maintaining neurological health.

Furthermore, the study showed that most participants (75.1%) did not know how metformin works to cause vitamin B12 deficiency. This finding is in line with the conclusions presented by Ko et al. who suggested the significance of understanding the pathophysiological mechanisms leading to vitamin B12 deficiency in diabetic patients on metformin [16]. A critical gap exists in patient education with regard to the absorption issues involving vitamin B12, most notably the interference of metformin with calcium dependent membrane processes. Additionally, almost half of our participants believed that they could get vitamin B12 from plant sources, which demonstrates the requirement for targeted nutritional education.

With respect to dietary supplementation, our study indicated that 63.9% of participants reported the use of a vitamin B12 supplement, though this risk of deficiency is well known. Given that Kumar et al found that vitamin B12 insufficiency was associated with longer duration of metformin use and could cause nerve damage [17]. Our results indicate that the low supplementation rates among our participants may represent a target for future intervention aimed at reducing the risk of deficiency and its complications through regular supplementation.

Demographic analysis showed strong association with awareness of vitamin B12 deficiency with several factors such as age, educational level and occupational status. As can be demonstrated by previous studies [18], a relation between health literacy and awareness is often found to be positive with a higher education level. It's also possible the prevalence of women in our study may also be reflecting broader social trends with respect to health seeking behaviors and access to health information. Interestingly though, gender did not significantly affect awareness levels suggesting that gender shouldn't matter in the application of educational interventions.

While all the insights gained from this study are important, limitations have to be noted. However, using self reported data may result in bias from the fact that participants may overestimate the amount of vitamin B12 deficiency which they know about. Further, the utilization of social media to recruit participants may decrease generalizability of the results because those who are more active on social media may be dissimilar to the wider diabetic population. Future studies may wish to expand the recruitment strategy so as to have a more representative sample.

Conclusion:

The findings of this study highlight the urgency for increased efforts on the part of the educational community to educate diabetic patients on metformin regarding their vitamin B12 deficiency, and the corresponding health implications. Knowledge and awareness gaps observed are critical to add nutritional education to diabetes management programs. With a growing epidemic of diabetes comes a growing importance of addressing vitamin B12 deficiency in this population, given the importance of properly addressing their diabetes and their vitamin B12 deficiency in order to optimize health outcomes and prevent complications associated with both conditions.

Acknowledgement:

We acknowledge all of the volunteers who provided samples for this research.

Ethical approval:

After fully explaining the study and emphasizing that participation is optional, each participant gave their informed consent. The information gathered was safely stored and utilized exclusively for study.

Funding:

This study was not supported by any outside sources.

Conflict of interests:

The authors declare no conflict of interest.

Informed consent:

Written informed consent was acquired from each individual study participant.

Data and materials availability:

All data associated with this study are present in the paper.

References:

1. AlHarbi M, Othman A, Nahari AA, Al-Jedai AH, Cuadras D, Almalky F, et al. Burden of Illness of Type 2 Diabetes Mellitus in the Kingdom of Saudi Arabia: A Five-Year Longitudinal Study. *Adv Ther* [Internet]. 2024;41(3):1120–50. Available from: <https://doi.org/10.1007/s12325-023-02772-y>
2. Abdulaziz Al Dawish M, Alwin Robert A, Braham R, Abdallah Al Hayek A, Al Saeed A, Ahmed Ahmed R, et al. Diabetes Mellitus in Saudi Arabia: A Review of the Recent Literature. *Curr Diabetes Rev*. 2016;12(4):359–68.

3. Al Saeed RR, Baraja MA. Vitamin B12 deficiency in patients with type 2 diabetes mellitus using metformin and the associated factors in Saudi Arabia. *Saudi Med J*. 2021;42(2):161–5.
4. Infante M, Leoni M, Caprio M, Fabbri A. Long-term metformin therapy and vitamin B12 deficiency: an association to bear in mind. *World J Diabetes*. 2021;12(7):916–31.
5. Butola LK, Kute PK, Anjankar A, Dhok A, Gusain N, Vagga A. Vitamin B12 - Do You Know Everything? *J Evol Med Dent Sci*. 2020;9(42):3139–46.
6. Aroda VR, Edelstein SL, Goldberg RB, Knowler WC, Marcovina SM, Orchard TJ, et al. Long-term metformin use and vitamin B12 deficiency in the diabetes prevention program outcomes study. *J Clin Endocrinol Metab*. 2016;101(4):1754–61.
7. Alharbi TJ, Tourkmani AM, Abdelhay O, Alkhashan HI, Al-Asmari AK, Rsheed AMB, et al. The association of metformin use with vitamin B12 deficiency and peripheral neuropathy in Saudi individuals with type 2 diabetes mellitus. *PLoS One*. 2018;13(10):1–15.
8. Alshammari, Amal N.; Iqbal, Rafay; Baksh IP. Vitamin B12 deficiency and the knowledge and practice of physicians regarding screening for vitamin B12 deficiency among type 2 diabetic patients on metformin in selected hospitals in Riyadh, Saudi Arabia. *J Fam Med Prim Care*. 2019;8(4):2306–11.
9. Shehzad K, Alomairi AA, Aldakheel YS, Aljabali AA. Awareness of Vitamin B12 Deficiency and Its Effects on the Body among Diabetic Type II Patients Taking Metformin in Al Qassim Region, Saudi Arabia. Khalid Shehzad, Abdulrahman A Alomairi, Yasser S Aldakheel, IOSR J Dent Med Sci. 2018;17(9):68–71.
10. Alqurashi RM, Aladwani A, Alosaimi TH, Yousef DB, Alkhalidi MH, Amer MG. Awareness of the Effect of Vitamin B12 Deficiency on the Nervous System Among the General Population in Taif, Saudi Arabia. *Cureus*. 2023;15(11).
11. Almufarej S, Alharshan R, Alismail A, Boradha M, Almasoud F, Alkhalifah F. Awareness of the Importance and Deficiency of Vitamin B12 among Saudi Population. Available online www.ijpras.com Int J Pharm Res Allied Sci [Internet]. 2019;8(4):187–91. Available from: www.ijpras.com
12. Raizada, N., Jyotsna, V., Sreenivas, V., & Tandon, N. (2017). Serum vitamin b12 levels in type 2 diabetes patients on metformin compared to those never on metformin: a cross-sectional study. *Indian Journal of Endocrinology and Metabolism*, 21(3), 424. https://doi.org/10.4103/ijem.ijem_529_16
13. Khan, A., Shafiq, I., & Shah, M. (2017). Prevalence of vitamin b12 deficiency in patients with type ii diabetes mellitus on metformin: a study from khyber pakhtunkhwa. *Cureus*. <https://doi.org/10.7759/cureus.1577>
14. Alshammari, A., Iqbal, R., & Baksh, I. (2019). Vitamin b12 deficiency and the knowledge and practice of physicians regarding screening for vitamin b12 deficiency among type 2 diabetic patients on metformin in selected hospitals in riyadh, saudi arabia. *Journal of Family Medicine and Primary Care*, 8(7), 2306. https://doi.org/10.4103/jfmpc.jfmpc_416_19
15. Akabwai, G., Kibirige, D., Mugenyi, L., Kaddu, M., Opio, C., Lalitha, R., ... & Sajatovic, M. (2015). Vitamin b12 deficiency among adult diabetic patients in uganda: relation to glycaemic control and haemoglobin concentration. *Journal of Diabetes & Metabolic Disorders*, 15(1). <https://doi.org/10.1186/s40200-016-0250-x>
16. Ko, S., Ko, S., Ahn, Y., Song, K., Han, K., Park, Y., ... & Kim, H. (2014). Association of vitamin b12 deficiency and metformin use in patients with type 2 diabetes. *Journal of Korean Medical Science*, 29(7), 965. <https://doi.org/10.3346/jkms.2014.29.7.965>

17. Kumar, S. (2023). Prevalence of vitamin b12 deficiency and its associated neuropathy in patients taking long term metformin therapy in type 2 diabetes mellitus. *Journal of Applied Pharmaceutical Research*, 11(5), 39-43. <https://doi.org/10.18231/j.joapr.2023.11.5.39.43>
18. Alharbi, T., Tourkmani, A., Abdelhay, O., Al-Khashan, H., Alasmari, A., Rashed, A., ... & AlHarbi, N. (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), e0204420. <https://doi.org/10.1371/journal.pone.0204420>