The Relationship Between Serum Vitamin B12 Level, Obesity, and Age: A Cross-sectional Study

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ABSTRACT

Background: Many studies had evaluated the association between obesity and vitamin B12 deficiency, with most having shown low vitamin B12 levels in obese and overweight people. Moreover, there is increasing evidence that susceptibility to vitamin B12 deficiency may change depending on gender and throughout life, with older males having the greatest risk. Obese patients are more prone to insulin resistance (IR); the correlation between low B12 in obese individuals and IR has been evaluated, with conflicting results. The treatment of obese individuals by bariatric surgery and other options may result in multiple nutritional deficiencies and a low baseline B12 level makes them more vulnerable to B12 deficiency.

Purpose: to investigate the relationship between vitamin B12 deficiency, body mass index and age in Jordanian adult patients.

Methods: A cross-sectional study of patients attending the Internal Medicine Outpatient clinics at Jordanian Royal Medical Services hospitals was conducted from June to December 2018. Patients living in different regions of Jordan and between the ages of 14 and 90 years were included. Height (cm), weight (kg) and body mass index (BMI) were recorded.

Result: The study enrolled 301 patients. The mean age was 52.19 years. Overall, 70.8% were in the adult group and 27.2% were in the senior adult group. The mean BMI was 29.41 (SD 5.74) and 36.9% were overweight, 25.2% were class 1 obese, 19.6% were of normal body weight, 11.3% were class 2 obese and 5.3% were class 3 obese. A significant positive correlation between BMI and age was observed (r=0.233; P<0.001). The mean B12 level was 278.82pmol/L. B12 deficiency was observed in 53.8% of patients. A significant negative correlation between BMI and serum B12 was observed (r =-0.123, P=0.032). There was no significant difference between males and females with regard to mean B12 level. A statistically insignificant negative correlation was observed between B12 level and age.

Conclusion: Lower vitamin B12 levels are associated with higher BMIs. No significant difference between males and females with regard to mean B12 level was reported. Further studies are recommended to provide more information about B12 deficiency and its association with BMI and other factors.

Keywords: *vitamin B12, Deficiency, Jordan, obesity.*

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Introduction

Vitamin B12 is naturally found in animal products, including fish, meat, poultry, eggs and dairy products. The normal level of B12 in serum is considered by most laboratories to be 200 to 900 ng per mL (1). Individuals with low dietary meat or animal product intake, vegetarians and those with malabsorptive disorders are vulnerable to vitamin B12 deficiency (2).

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Vitamin B12 deficiency is a worldwide problem (2), and is common in the Jordanian population. El-Khateeb and colleagues conducted a study of 5640 Jordanian subjects and reported that one third of Jordanian adults have vitamin B12 deficiency (3). B12 deficiency can present with a spectrum of diseases ranging from asymptomatic to serious haematological, neurological and psychiatric complications, as well as a possible risk of irreversible neurological damage (4). Another study, which was conducted on a total of 838 patients in a Jordanian hospital, showed that vitamin B12 deficiency is associated with memory impairment (5).

Obesity is a chronic and complex disease and is defined as an excess of body fat. It is associated with many medical problems, including an increased risk of metabolic syndrome, diabetes mellitus (DM), cardiovascular diseases, and mechanical disorders (6). The prevalence of obesity in Jordanian adults has increased at an alarming rate (7). Because raised BMI is a major risk factor for many diseases, studies are being conducted to look for health risks predisposed by obesity. In 2006, Kimmos and colleagues found that there are alterations in the absorption, metabolism and excretion of micronutrients in obese and overweight persons (8).
Obesity and vitamin B12 deficiency are common health problems encountered in healthcare settings. Many studies have evaluated the association between obesity and vitamin B12 deficiency, with some having shown low vitamin B12 levels in obese and overweight people (9, 10, 11). Moreover; there is increasing evidence that the susceptibility to vitamin B12 deficiency may change depending on gender and throughout life, with older males having the greatest risk and highest susceptibility (12, 13, 14). Based on the literature, we hypothesized that there is a negative correlation between BMI and low serum B12 levels and conducted a study with the purpose of investigating the relationship between vitamin B12 deficiency and BMI, age, and gender among the Jordanian adult population.

Methods

A cross-sectional study was conducted of Jordanian adult patients attending Internal Medicine outpatient clinics at Royal Medical Services hospitals during the period from June to December 2018. Patients living in different regions of Jordan and between the ages of 14 and 90 years were included. Patients were excluded if they are vegetarian, using vitamin supplements, if treated by metformin, or corticosteroids, are pregnant, or are known to have DM or malabsorption diseases. The socioeconomic status and it's relation to vitamin B12 level was not analyzed, as most patients refused to give information regarding their income.
All included patients signed a consent form after the aim of the study was explained to them. Height (cm) and weight (kg) were recorded and body mass index (BMI) was calculated using the following formula: kg/height (m^2). Blood samples were taken to determine vitamin B12 levels. According to the WHO classification of obesity, patients were classified as mild thin (BMI of 17–18.5), normal (BMI of 18.5–25), overweight (BMI of 25–30), obese class 1 (BMI of 30–35), obese class 2 (BMI of 35–40), and obese class 3 (BMI of >40) (21). The subjects were classified into three age groups: children and adolescents (<19 years), adults (19–64 years) and senior adults (65 years and above). Three descriptive cut-off points of vitamin B12 were used: normal (>250pmol/L), low (150–249pmol/L), and acute deficiency (<149pmol/L) (15).
Data were analyzed using SPSS 16.0 (SPSS Inc., Chicago, IL, USA). Bivariate correlation tests with Pearson's correlation coefficient were used to assess the association between vitamin B12s level and BMI, with probability values of $p<0.05$ being considered significant. The study was approved by the ethics committee of the Royal Medical Services.

Results

The study enrolled 301 patients from different regions of Jordan. The majority, 197 (65.4%), were female, and 104 (34.6%) were male. Patients' ages ranged from 14 to 88 years, with a mean age of 52.19 years. Overall, 213 (70.8%) patients were among the adult age group (19–64 years), 82 (27.2%) patients were in the senior adult age group (>65 years) and 6 (2%) were younger than 19 years. Table II

The mean BMI was 29.41 (SD 5.74). Overall, 111(36.9%) patients were overweight, 76 (25.2%) patients were class 1 obese, 59 (19.6%) were of normal body weight, 34 (11.3%) were class 2 obese, 16 (5.3%) were class 3 obese and 5 (1.7%) patients were mild thin. Female patients fell within the overweight and obesity categories more often than male patients, with a mean BMI of 28.24 and 30.03 for males and females, respectively. In addition, in the adult age group, there were 48 females versus 28 males who were overweight, and 71 females versus 23 males who were obese (class 1, 2 and 3). In the senior adult group, 18 males versus 16 females were overweight, and 11 males versus 21 females were obese (class 1, 2 and 3) (table III). The correlation between BMI and age showed a significant positive correlation (r =0.233; P<0.001), reflecting an increase in BMI with increasing age (Table I).

Table I: Correlations between age, B12 levels and BMI

		Age	**B12 level**	**BMI group**
Age	Pearson Correlation	1	-0.051-	.233**0
	Sig. (2-tailed)		.3820	.0000
	N	301	301	301
Vitamin B12 level	Pearson Correlation	-0.051-	1	-0.123*
	Sig. (2-tailed)	0.382		.0320
	N	301	301	301
BMI group	Pearson Correlation	0.233**	-0.123*	1
	Sig. (2-tailed)	.00000	0.032	
	N	301	301	301

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Table II: Mean B12 level, BMI and age

	Age	BMI	B12 level
Mean	52.19	29.4137	278.8256
Std. Deviation	17.785	5.74594	169.05770
Minimum	14	16.10	.000
Maximum	88	51.36	1402.00

Table III: Number of subjects in each BMI category correlated to age and sex

		Obesity category and number of subjects					
Age group and Sex		Class 1 obese	Class 2 obese	Class 3 obese	Mild thin	Normal BMI	Over weight
Children & adolescent (<19yrs)	***Males***	0	0	0	0	1	0
	Females	0	0	0	1	3	1
Adult (19–64yrs)	***Males***	18	5	0	1	12	28
	Females	37	21	13	2	28	48
Senior adult (>65yrs)	***Males***	10	1	0	1	9	18
	Females	11	7	3	0	6	16

The mean level of serum B12 was 278.82 pmol/L (SD:169.05) among all subjects (Table I). B12 deficiency was observed in more than half of patients; in total, 130 (43.2%) patients had low B12 levels (150–249pmol/L), 32 (10.6%) patients had acute deficiency (<149pmol/L) and 138 (45.8%) had normal B12 levels (>250pmol/L) (Figure 1). Among all of the age groups, the mean levels of vitamin B12 were: 281.7 pmol/L, 265.7 pmol/L, and 354.8 pmol/L in the adult group, senior adult group, and children and adolescents group, respectively (Figure 2). There were significantly lower B12 levels among obese and overweight individuals compared to normal weight subjects (Figure 3). A significant and negative correlation between BMI and serum B12 was observed (r =-0.123, P=0.032) (Table I), and higher BMI remained an independent predictor of lower serum B12 upon correlation analysis. On the other hand, there was no significant difference observed between males and females in mean B12 level (Table IV), as there was a statistically insignificant negative correlation between B12 level and age (r=-0.051; P>0.05) (Table 1). The mean B12 levels for male and female patients of the different BMI groups are shown in Table IV.

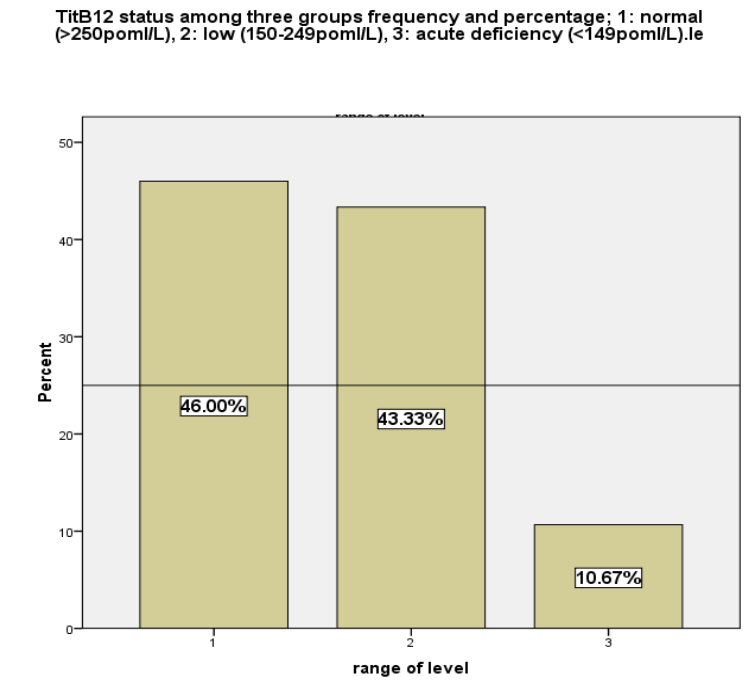

Figure 1: The percentage of each descriptive cut-off point of B12 status: 1 - normal (>250pmol/L), 2 - low (150-249pmol/L), 3 – acute deficiency (<149pmol/L).

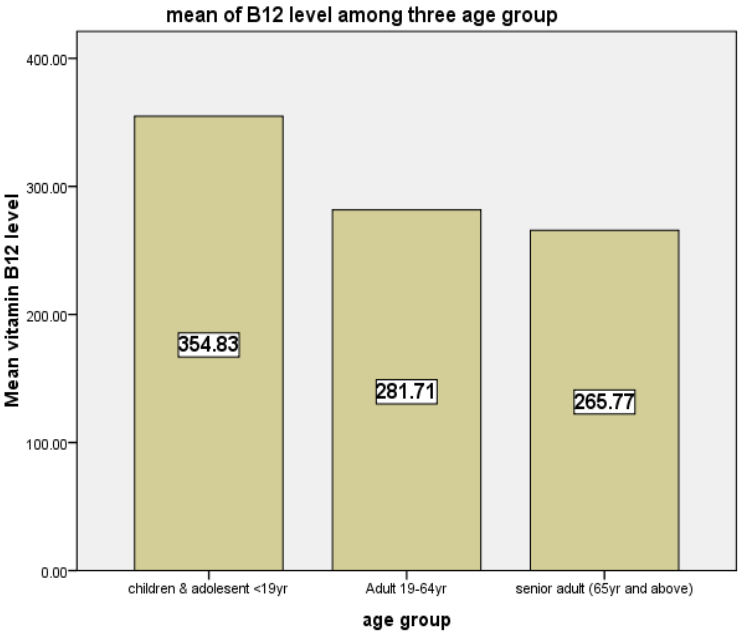

Figure 2: The mean B12 levels of the three age groups

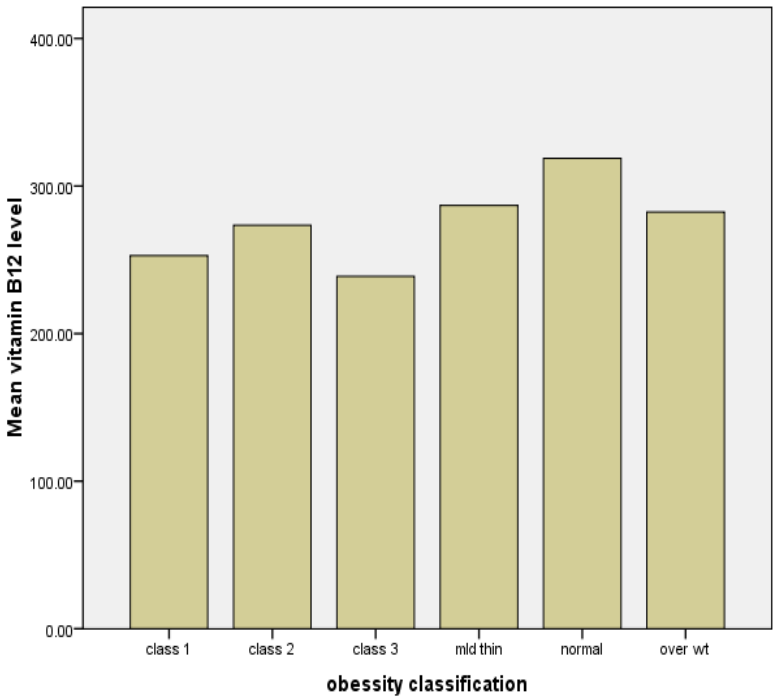

Figure 3: The mean B12 levels among different BMI categories

Table IV: the mean of B12 level for different BMI groups among male and female subjects

			BMI category					
			Obese Class 1	***Obese Class 2***	***Obese Class 3***	***Mild thin***	***normal***	***overweight***
Mean B12	***Sex***	***Males***	231.70	281.50	-	196.50	329.90	285.36
		Females	265.21	271.70	238.84	347.00	312.20	280.32

Discussion

The association of B12 deficiency and obesity has been evaluated in several studies worldwide, as well as among the Jordanian population. A study carried out on Turkish women found that B12 level was negatively correlated with BMI (15). In 2018, a cross-sectional study enrolled 2403 healthy Indian school adolescents and found that B12 deficiency is associated with high BMI; more than half (51.2%) of obese adolescents were vitamin B12-deficient (11). Abu-Samak and colleagues enrolled 120 Jordanian young adults in a study in 2008 which showed lower levels of B12 in overweight but not obese youths (10). These results may explain some of the findings of our study, which demonstrated that low levels of serum vitamin B12 were more prevalent among both obese and

overweight adults, than in those who have a normal body weight, with the lowest mean B12 level observed in obese class 3 individuals.

The maintenance of an optimal status of vitamin B12 is not only dependent on adequate dietary intake, but more critically on effective absorption, which diminishes with age (16). The results of our study showed an insignificant negative correlation of B12 level and age, as well as a significant positive correlation between BMI and age i.e. BMI increases with age. Figure 2 shows that the mean B12 level was higher in the adult age group than in the senior adult group. Loikas et al. and Sánchez et al. showed a high prevalence of B12 deficiency among older adults (12, 14). These findings become interesting when correlated with the fact that aging is associated with increased risks to different diseases, and the presence of vitamin B12 deficiency may complicate the health condition further, or be complicated and unmasked by the treatments of such diseases; e.g. DM diagnoses increase with increasing age, and metformin, which is commonly used for DM management, can cause B12 malabsorption (17) which may deteriorate the neurological complications associated with DM, such as diabetic neuropathy.

Obesity is well-known to induce insulin resistance (IR) and increase the risk of DM. Dursun et al. conducted a study of 110 children aged 10–16 years and found that vitamin B12 levels were significantly lower in obese children with IR (18). Accordingly, in addition to screening for IR and other co-morbidities in obese patients, vitamin B12 levels might also need to be investigated, especially before starting metformin therapy for obesity-induced IR. Furthermore, the presence of low levels of vitamin B12 among obese and overweight patients warrants investigation of the effects of B12 on insulin sensitivity. As a result of insufficiency in the synthesis of methionine by inducing the leakage of cellular folate, B12 deficiency increases stress in the endoplasmic reticulum by causing a deficiency of the oxidation of free fatty acids; because B12 is a cofactor in the conversion of methylmalonic acid to succinylcholine, methylmalonic acid accumulates in B12 deficiency, and can cause lipogenesis and insulin resistance (18).

Generally, treatment approaches for obesity include lifestyle modifications, medical treatments with drugs suppressing appetite or decreasing intestinal absorption, and surgical interventions such as bariatric surgery. Obesity treatment can lead to multiple nutritional deficiencies, especially with bariatric surgery (19). The presence of low B12 levels in obese patients may make them more vulnerable to B12 deficiency following bariatric surgery and other treatment options, leading to unfavorable results. Therefore, we suggest evaluation of obese patients for B12 deficiency, especially those intending to lose weight by any of the different approaches, and to offer B12 supplements for those with low or deficient levels before introducing obesity management, even if asymptomatic.

Although our study and others had shown lower levels of B12 with increasing BMI, some studies had shown the opposite or found no correlation between B12 levels and BMI. El-Qudah and colleagues conducted a study of 84 Jordanian healthy adults and found that the concentration of B12 appears to increase as BMI increases (1). Another study, which enrolled 100 patients to investigate the relationship between obesity and serum Vitamin B12, folic acid and vitamin D concentrations in obese adults, did not find any significant correlation between B12 levels and obesity (20).

These contradicting results might be related to the number of subjects included, as small samples might not reflect the association properly, necessitating larger studies to be conducted. Moreover, methylmalonic acid and homocysteine levels, which are more sensitive to B12 deficiency, were not evaluated in our study; and given the number of subjects we evaluated, we recommend additional studies involving larger cohorts to assess the relation between BMI and B12, along with other serum parameters, and to assess the possible role of B12 deficiency in inducing IR observed in obese patients.

Conclusion

Lower vitamin B12 levels were associated with overweight and obesity, with the lowest mean B12 level observed in obesity class 3. No significant difference between males and females was found for mean B12 level, and a statistically insignificant negative correlation between B12 level and age was observed. The evaluation of obese and older patients for B12 deficiency, especially those intending to lose weight, needs to be considered. Further studies are recommended to provide more information about B12 deficiency and its association with BMI and other factors.

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