

Vitamin B12 Deficiency in the South of Jordan: A Possible Geographical Correlation

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Abstract

Objectives: Vitamin B12 deficiency has been associated with certain serious disorders such as megaloblastic anemia as well as cardiovascular, neurological, and psychological disorders. Vitamin B12 deficiency is a worldwide health concern and a severe health problem in certain developing countries. In the current study, we aimed to evaluate the situation of vitamin B12 and estimate the prevalence of vitamin B12 deficiency in southern Jordan. **Methods:** The study population included 281 participants from Aqaba city: 71.2% females and 28.8% males with a mean age of 30.01 ± 13.5 . **Results:** The results showed that the average vitamin B12 level was 277.34 ± 103.70 pg/mL. The study population showed that 69 (24.6%) participants had a vitamin B12 deficiency. The current findings showed a lower frequency of vitamin B12 deficiency in the studied population compared to the rest of Jordan, especially in the north. The females reported a significantly higher frequency of vitamin B12 deficiency (29.0%) compared to the male group (13.6%). In addition, the CBC parameters showed a significant association between the level of vitamin B12 and Hb, RBC, PCV, and platelet count with a p-value = 0.044, <0.001, 0.021, 0.025, respectively. On the other hand, the results showed a lack of association between the vitamin B12 level and MCV and age group. **Conclusion:** In conclusion, the current study supports our previous findings regarding the correlation between geographical locations and the deficiency of vitamin B12. These findings can be attributed to the lifestyle and nutrient situation in Aqaba city which relies more on seafood. Moreover, other factors such as genetic predisposition can be excluded as an association factor. Therefore, more studies are required to evaluate vitamin B12 levels in Jordan at a higher scale that will include genetic analysis as well as food habits.

Introduction

Vitamin B12 (Cobalamin; Cbl) is a water-soluble molecule characterized by its chemical complexity, large size, and cobalt ion which is centrally located in the corrin ring¹. Vitamin B12 is essentially obtained from dietary sources such as red meat, dairy products, eggs, and fish²⁻⁴. Absorption and transportation of vitamin B12 are processes that occur by hydrophobic binding protein carriers including haptocorrin (HC), intrinsic factor (IF), and transcobalamin (TCN)⁵⁻⁷. Around 80% of cobalamin is carried by inactive haptocorrin (or transcobalamin I) and 20% is transported by active TCN II in the bloodstream⁸⁻¹⁰. The deficiency of vitamin B12 is attributed to many factors including insufficient dietary supply, malabsorption, and deficient absorption cases¹¹⁻¹⁵. In addition, many risk factors are related to vitamin B12 deficiency including genetic predisposition, age, weight, gender, and ethnic variations¹⁶⁻¹⁹.

Vitamin B12 has a vital role in many processes including the synthesis of nucleic acids, regulating the metabolism of the macronutrients (proteins, fats, and carbohydrates), as well as some neurological functions²⁰⁻²⁴. Moreover, vitamin B12 plays a necessary role in myelin biosynthesis, manufacturing, and development of erythrocytes (hematopoiesis)^{11,25,26}. Therefore, vitamin B12 deficiency is associated with serious

neurological, hematological, and metabolic disorders^{21,27-30}. Vitamin B12 deficiency is most prevalent in the elderly, children, pregnant women, nursing mothers, and vegetarians³¹⁻³⁴. The most significant diagnostic characteristics and symptoms related to a deficiency of B-12 are fatigue, memory impairment, skin pallor, skin hyperpigmentation, glossitis, and severe hematological, neurological, and psychiatric disorders³⁵⁻⁴¹.

Vitamin B12 deficiency is a worldwide concern^{16,42,43}. Notably, vitamin B12 deficiency is not prevalent in wealthy countries except in the elderly, compared to developing countries where the prevalence of vitamin B12 deficiency can reach more than 50% of the population^{16,42,44-49}. For instance, the prevalence of vitamin B12 deficiency in the United States and the United Kingdom is approximately 6% in people under the age of 60 and about 20% of those over 60 years, whereas countries in Latin America have a deficiency incidence of approximately 40%⁵⁰⁻⁵⁶. In Jordan, vitamin B12 deficiency is a considerable health problem⁵⁷, where the prevalence varies according to the study population in the last decades⁵⁷⁻⁵⁹. In different studies in Jordan, vitamin B12 deficiency was estimated at different prevalence (16–50%) with the highest prevalence in the elderly above 55 years old^{16,17,59-61}.

Based on our previous findings, we proposed the geographical location as an important factor in the estimation of vitamin B12 which may be related to socioeconomic status, lifestyle, and cultural background. We reported significant differences in the frequencies of vitamin B12 deficiency in different locations in Jordan. In particular, the results showed a lower frequency of vitamin B12 deficiency in the southern parts of Jordan compared to the northern cities¹⁷. Consequently, the current study aimed to evaluate vitamin B12 levels among the Jordanian population in Aqaba city (the most southern city) and to assess the prevalence of vitamin B12 deficiency in Aqaba's Jordanian population. This study will complete the portrait of the national situation of vitamin B12 level.

Materials and Methods

Study Design

This retrospective study was performed in the most southern part of Jordan (Aqaba province). Venous blood samples were collected from different hospitals in Aqaba, with a total number of 281 samples. Written informed consent was obtained from all participants, and the data were collected where it related to location, gender, age, and general health of the participants who were living in Aqaba. Exclusion criteria included subjects who showed diseases which lead to cobalamin deficiency such as peptic ulcer, gastrointestinal problem, pregnancy, diabetes, and individuals under vitamin B12 supplementation.

Blood Sampling

Blood samples were collected from hospitals in the Aqaba governorate then serum was preserved at -70°C until use to measure the level of vitamin B12 and further study according to standard procedures using commercially available kits. Laboratory analyses were performed at hospital laboratories in Aqaba, Jordan. The level of vitamin B12 was assessed based on sandwich enzyme-linked immunosorbent assay technology, according to the manufacturer's protocol (Cyanocobalamin (Vitamin B12) ELISA Kit, Abbexa, UK).

Statistical analysis

Prevalence of Vitamin B12 deficiency was evaluated in Aqaba province where all the statistical analysis was done using SPSS software version 25. Categorical data are expressed in frequency and percentages, scale data are expressed in mean \pm SD, chi-square test of independence was used to examine the association between categorical data. Pearson's correlation was used to analyze the correlation between scale data, an independent t-test was used for B12 mean differences between both genders, *P* -values < 0.05 were considered statistically significant.

Results

Demographic characteristics of the study population

The study recruited 281 participants from Aqaba city; including 200 females (71.2 %) and 81 males (28.8 %).

The ages ranged between 0 and 80 years with a mean age of 30.01±13.5 (31.9±16.49 for males and 29.3±12.05 for females), where the age group between 0-39 years was more prominent 217(77.2%) as compared to the age group [?]40 years 64(22.8%). The mean of B12 for the study population was 277.34±103.70 pg/mL.

The cutoff value of vitamin B12 level was set at 200 pg/mL, where the individuals with vitamin B12 level less than 200 pg/mL were categorized as deficient. Based on this categorization the results showed that 212 (75.4%) of participants had a normal B12 level while 69 (24.6%) of them had a B12 deficiency. According to the gender groups, the females reported a significantly higher frequency of vitamin B12 deficiency (29.0%) compared to the male group (13.6%). In addition, the mean of Hb level for participants was 12.66±1.78 whereas the mean of RBC for participants was 4.54±0.50 as shown in table 1.

Mean differences in vitamin B12 levels between males and females.

The mean differences of serum B12 level between males and females were determined by an independent sample t-test and the results are shown in Table 2. Our study showed a statistically significant difference in the mean of serum B12 between genders (P -value = 0.002), where the mean of serum B12 in females was 265.09 ±106.35 pg/mL while it was 307.59 ±90.75 pg/mL in males.

In addition, a Chi-Square independence test was used to examine the association between B12 deficiency and gender. The findings showed that there was a statistically significant association between gender and B12 deficiency ($X^2 = 7.399$, (P -value = 0.007)) which indicates that the females had a higher proportion of B12 deficiency compared to the males as shown in table 3 and figure 1.

Association between age group and vitamin B12 level.

The current study reported a lack of association between the B12 deficiency and age groups (< 40, [?] 40 years) according to the chi-square test ($X^2 = 2.428$, (P -value = 0.119)) as illustrated in table 4. An independent sample t-test was also used to test the mean differences of B12 concerning age groups and the results showed no statistically meaningful differences between them ($P = 0.661$) as shown in table 5.

Association between CBC parameters and serum vitamin B12

The association between vitamin B12 and CBC parameters was analyzed using Pearson's correlation where our results revealed that there was a statistically significant correlation between Hb level and vitamin B12 level as shown in table 6. In addition, a statistically significant correlation was observed between RBC and vitamin B12 level ($r = 0.311, P < 0.001$). Pearson product-moment showed there was a statistically significant positive correlation between serum B12 and PCV ($R = 0.192, P = 0.021$), B12 serum and PLT ($R = 0.193, P = 0.025$) while no statistically significant correlation was found with MCV ($R = -0.080, P = 0.354$) as illustrated in table 6.

The relationship between geographical location and vitamin B12 levels.

The results of this study support the previous findings for the four regions in Jordan; Irbid, Karak, Tafila, and Ma'an, where the percentages of B12 deficiency in these regions were 41%, 35%, 27% and 26% respectively⁵⁷. The current study evaluated B12 deficiency in Aqaba, which was found to be 24.6%. Figures 2 and 3 illustrate a comparison between the frequencies of vitamin B12 deficiencies in five regions that cover Jordan from north to south.

Discussion

In the Middle East, different countries have reported a high prevalence of vitamin B12 deficiency that is resulted in pernicious anemia [94]. Similarly, the deficiency of vitamin B12 in Jordan is a health concern that needs to be considered seriously. Previous studies showed differences in the prevalence of vitamin B12 deficiency in Jordan. For instance, in a study that included two different populations, the researchers reported 50.8% of vitamin B12 deficiency among the Arab population and 46.9% among Circassians⁶². Other studies reported 10%⁵⁸, 24%⁵⁷, 27%⁶³, 30%¹⁶ and 44.6%⁶⁴ of vitamin B12 deficiency. The variation in the prevalence can be attributed to the differences between the study populations and age groups^{16,57-61}.

In a recent study, it was shown that vitamin B12 deficiency varies in different provinces of Jordan; Irbid, Karak, Tafilah, and Ma'an⁵⁷. In this retrospective study, we evaluated vitamin B12 levels in a Jordanian population in Aqaba city and correlated it with gender, age, and CBC parameters. The current study reported a 24.6 % vitamin B12 deficiency in the Aqaba province population. These findings support our previous report detailing the trend of vitamin B12 deficiency according to the geographical location in Jordan. Additionally, the results reported a significant difference between the means of vitamin B12 levels in males and females, 307.59 \pm 90.75, 265.09 \pm 106.35, respectively ($p = 0.002$). In particular, females showed a higher frequency of vitamin B12 deficiency (29%) compared to the male group (14%). Inconsistently with a previous study, the researchers showed that males had a higher frequency of vitamin B12 deficiency than females in Arab and Caucasian populations⁶². However, there is some evidence that females have a higher frequency of vitamin B12 deficiency than males⁶⁵. On the contrary, another study revealed a higher percentage of vitamin B12 deficiency in males (15.2%) compared to females (11.5%)⁶⁶. Nevertheless, different findings have reported a lack of relationship between gender and vitamin B12 level⁶⁰. Therefore, other risk factors have to be considered in addition to gender, such as genetic predisposition, and physiological differences, and pregnancy frequency.

The current findings did not report a difference in the vitamin B12 deficiency between age groups, < 40 years and > 40 years ($P = 0.119$), which is consistent with the results of a previous study⁶². On the other hand, most studies showed a significant association between vitamin B12 deficiency and age^{54,63,67,68}. In another previous survey that evaluated vitamin B12 deficiency in Jordan for participants whose ages ranged between 19 and 90, the study concluded that mean serum vitamin B12 levels rise with age, however, individuals aged < 40 years had the lowest vitamin B12 levels among all ages, which is consistent with our findings¹⁶. Nevertheless, the deficiency of vitamin B12 may commonly affect the elderly. Therefore, the lack of association between the age group and vitamin B12 deficiency can be attributed to the size of the study population from each group.

Herein, the level of vitamin B12 showed a significant association with the level of Hb ($P = 0.044$). On the contrary, Qutob et al have shown that there was no correlation between B12 status and Hb ($p=0.545$)⁶³. Additionally, we observed a statistically significant positive correlation between RBCs count and vitamin B12 level ($r= 0.354$, $p=0.001$). Metabolically, vitamin B12 is an essential cofactor that results in normal blood cell maturation. Macrocytosis is a cause of ineffective erythropoiesis due to vitamin B12 or folate deficiency⁶⁹⁻⁷². Therefore, our results support the role of vitamin B12 in the erythropoietic process. Moreover, PCV and platelet count showed a significant association with the vitamin B12 level in the studied population. On the other hand, our findings did not show any significant association between the level of vitamin B12 and the MCV. On the contrary, many studies confirmed the inverse relation between B12 level and MCV^{63,73,74}. An elevated MCV refers to the average red blood cell volume that may arise with or without reduced hemoglobin levels⁶⁵. Overall, Pernicious anemia leads to B12 deficiency and results in producing abnormal and unhealthy RBCs, which means fewer functional erythrocytes⁷⁵⁻⁷⁷.

The current study also aimed to complete the portrait of the prevalence of B12 deficiency in Jordan. In a previous study, we evaluated the prevalence of vitamin B12 deficiency in several regions, starting from the northern part of Jordan, Irbid (41%), Karak (35%), Tafilah (27%) and Ma'an (26%) where we moved in a southerly direction⁵⁷. Here, we reached the most southern part of Jordan, Aqaba which reported 24.6% vitamin B12 deficiency. This study confirms the association between the geographical location and the frequency of vitamin B12 deficiency in Jordan⁵⁷. Fora and Mohammed reported similar observations in the north of Jordan (48%), where their study emphasized high B12 deficiency in northern regions⁶¹. Moreover, southern regions had reported lower B12 deficiency than central regions (Amman), and Hakooz et al (2006) reported lower rates of B12 in Amman (48.5%)⁶². However, the current results showed a similar mean level of vitamin B12 in Aqaba's population compared to the Irbid's population and lower level of vitamin B12 compared to the other parts of Jordan (Middle-South). Overall, the current study showed that the deficiency of vitamin B12 in Aqaba is lower than in other parts of Jordan.

Conclusions

To our knowledge, this is the first study to determine the prevalence of B12 deficiency in Aqaba province. Vitamin B12 levels were strongly and significantly correlated with gender and Hb, RBCs, PCV and Platelet count with non-significant relation to age and MCV. Additionally, the study confirmed that Aqaba, like other southern regions in Jordan, is characterized by a lower frequency of vitamin B12 deficiency compared to the other regions in Jordan. Further studies are needed in other regions of Jordan such as the eastern regions (Mafraq and Azraq) to complete the national portrait of the vitamin B12 level in Jordan.

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Conflict of Interest:

All authors declare the lack of conflict of interest in this work.

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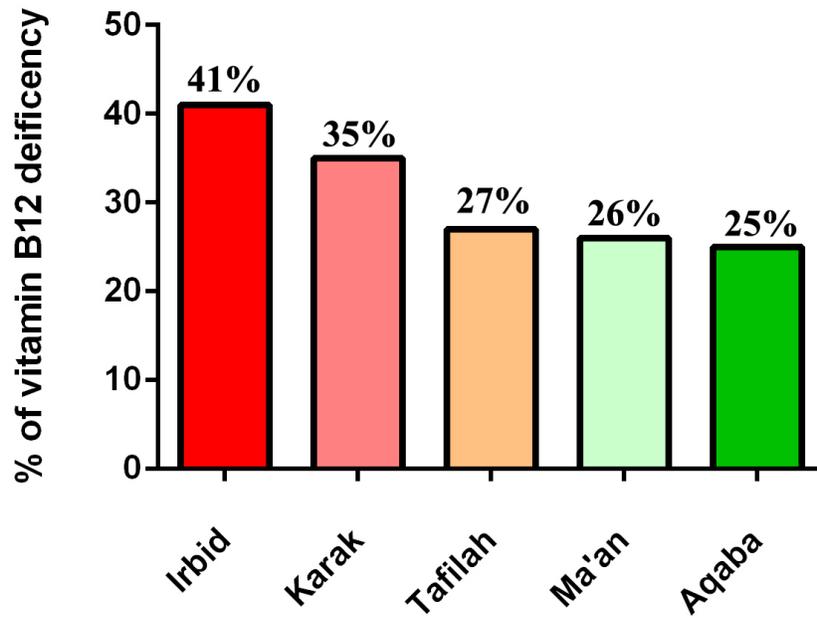
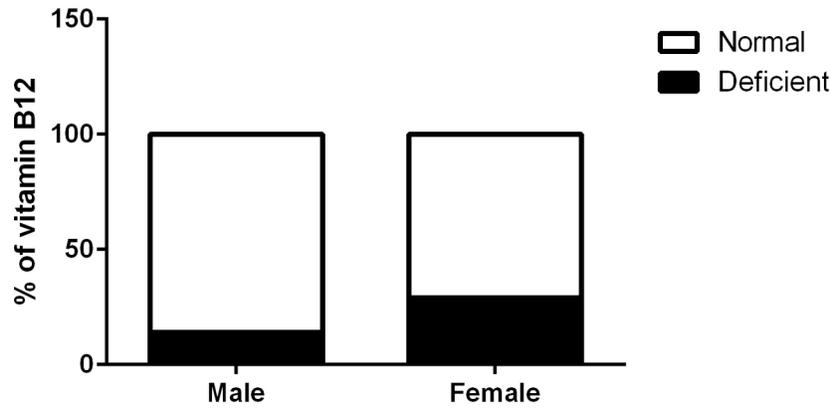
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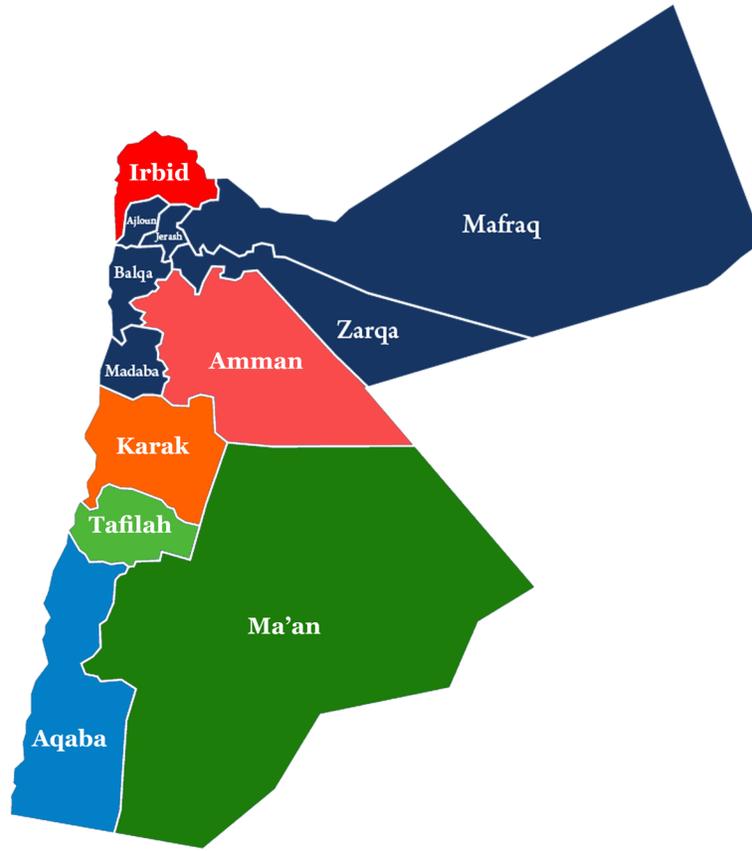
Figures legends:

Figure 1. Frequency of vitamin B12 deficiency in females and males in Aqaba.

Figure 2. The frequency of vitamin B12 deficiency in different regions in Jordan (Irbid is representing the most northern part of Jordan while Aqaba is the most southern part of Jordan).

Figure 3. Heat map of Jordan according to the frequency of vitamin B12 deficiency. (Irbid, Karak, Tafilah, Ma'an, and Aqaba)





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Tables.pdf available at <https://authorea.com/users/372436/articles/490472-vitamin-b12-deficiency-in-the-south-of-jordan-a-possible-geographical-correlation>