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A comparative study of the impact of Vitamin B12 deficiency on spontaneous abortion in Tikrit City

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Abstract

Background: Vitamin B12 (cobalamin) is a vital water-soluble micronutrient involved in DNA synthesis, red blood cell formation, and neurological function. Its deficiency during pregnancy has been associated with adverse outcomes, including spontaneous abortion. However, the extent of this association in Iraqi women remains underexplored.

Objective: To investigate the association between serum vitamin B12 levels and spontaneous abortion, and to assess correlations with demographic, clinical, and lifestyle factors.

Methods: A comparative case-control study was conducted at [Hospital Name], involving 120 pregnant women-60 experiencing spontaneous abortion and 60 with normal pregnancies. Serum vitamin B12 concentrations were measured, and relevant variables (age, BMI, gestational age, physical activity, dietary animal intake, prior abortion history, and residence) were documented. Statistical analysis included independent sample t-tests, chi-square tests, and Pearson correlation coefficients.

Results: Women with spontaneous abortion had significantly lower mean vitamin B12 levels (168.45±39.70 pg/mL) compared to women with normal pregnancies (247.80±42.10 pg/mL; p<0.001). A significant negative correlation was observed between vitamin B12 and maternal age (r=-0.362, P=0.001) and BMI (r=-0.285, P=0.005), while a positive correlation was found with gestational age (r=0.240, P=0.011) and dietary animal intake (r=0.433, P=0.001). Women who engaged in regular physical activity (≥3 times/week) had higher vitamin B12 levels (179.25±30.60 pg/mL) compared to sedentary participants (163.20±35.95 pg/mL; P=0.041). A history of previous abortion was associated with significantly lower B12 levels (156.50±36.70 pg/mL vs. 178.20±34.40 pg/mL; P=0.014). Similarly, women residing in rural areas had lower levels (159.20±34.75 pg/mL) than those in urban areas (175.90±36.80 pg/mL; P=0.043). Although nausea/vomiting during pregnancy showed a trend toward lower B12 levels, the difference was not statistically significant (P=0.134).

Conclusion: Vitamin B12 deficiency is significantly associated with spontaneous abortion and correlates with several maternal risk factors, including age, BMI, gestational age, physical activity, previous abortion, and rural residence. These findings highlight the importance of early nutritional assessment and intervention to prevent adverse pregnancy outcomes in high-risk populations.

Keywords: Vitamin B12, Tikrit City, spontaneous, high-risk populations, underexplored

1. Introduction

A spontaneous abortion, commonly referred to as a miscarriage, is defined as the unintentional loss of a pregnancy before the 20th week of gestation. It is estimated that approximately 20% of clinically confirmed pregnancies end in miscarriage [1]. While ultrasonography remains a crucial diagnostic tool for identifying spontaneous abortion, additional investigations may be warranted if ectopic pregnancy cannot be conclusively excluded [2]. Several maternal risk factors contribute to the likelihood of miscarriage, including advanced maternal age, tobacco use, obesity, previous miscarriage history, hypertension, and diabetes [1].

Vaginal bleeding during early pregnancy is a frequent clinical finding, affecting up to 20% of pregnant women before 20 weeks' gestation. Among these, nearly half will ultimately result in pregnancy loss. Despite this, recent studies utilizing serial measurements of serum human chorionic gonadotropin (hCG) suggest that the true incidence of early pregnancy loss may be as high as 31%, including many unrecognized conceptions that are often misinterpreted as delayed or unusually heavy menstruation [2, 3].

The etiologies of spontaneous abortion are multifactorial and include chromosomal abnormalities, vascular pathologies, hormonal imbalances, uterine structural anomalies, and infections. Moreover, complications following miscarriage may involve septic abortion, cervical trauma, intrauterine hematoma, disseminated intravascular coagulation (DIC), and retained products of conception [4].

Vitamin B12, a water-soluble micronutrient, is predominantly sourced from animal-derived products such as meat, poultry, fish, eggs, and dairy. Therefore, individuals adhering to vegetarian or vegan diets are particularly susceptible to deficiency. Fortified foods, including enriched cereals and nutritional yeast, serve as alternative sources with high bioavailability [5]. Inadequate levels of vitamin B12 can lead to elevated homocysteine concentrations, which are associated with an increased risk of miscarriage [6]. Vitamin B12 plays an essential role in fatty acid and amino acid metabolism, DNA synthesis, and the remethylation of homocysteine to methionine.

Deficiency may arise from insufficient dietary intake or malabsorption conditions. During pregnancy, low serum vitamin B12 concentrations (typically defined as < 148 pmol/L) have been linked to a higher risk of spontaneous abortion, representing a significant global public health concern [7, 8].

Although public awareness remains limited, vitamin B12 deficiency affects individuals across all age groups, with a higher prevalence noted among pregnant women, young children, and the elderly [9, 10]. Maternal B12 deficiency has been associated not only with adverse pregnancy outcomes but also with detrimental effects on fetal development and postnatal growth. These include long-term neuro-developmental deficits in the offspring, many of which may be irreversible [11-13].

2. Methods

2.1 Sample size and sampling technique

The sample size was calculated based on previous literature and statistical power considerations, targeting 60 women per group to detect a clinically significant difference in vitamin B12 levels with 95% confidence and 80% power. A non-probability consecutive sampling technique was used.

2.2 Data Collection Procedure

Data were collected through a structured, interviewer-administered questionnaire. This tool was divided into sections covering demographic details, medical and obstetric history, gestational age, dietary habits, and socioeconomic status. Body mass index (BMI) was calculated based on the measured weight and height of each participant.

2.3 Blood sample collection and Vitamin B12 measurement

A venous blood sample of approximately 4 milliliters was collected from each participant using sterile techniques. The samples were immediately transported to the hospital laboratory for analysis. Serum was separated and stored at -20 °C until testing. Vitamin B12 levels were measured using automated chemiluminescence immunoassay or electro-chemiluminescence techniques, depending on the equipment available. The reference range for serum vitamin B12 was considered to be 190 to 950 pg/mL, and levels below 190 pg/mL were classified as deficient.

2.4 Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS), version 25. Descriptive statistics were used to summarize participant characteristics. Continuous variables such as age, BMI, and vitamin B12 levels were presented as means and standard deviations, and differences between the case and control groups were analyzed using the Student's t-test. Categorical variables, including dietary patterns and socioeconomic status, were analyzed using the chi-square test. A p-value less than 0.05 was considered statistically significant. Correlation analyses were also conducted to assess the relationship between vitamin B12 levels and factors such as age, gestational age, and history of prior abortion. Binary logistic regression analysis was used to identify independent predictors of spontaneous abortion.

3. Results

3.1 Comparison of demographic and clinical characteristics between women with spontaneous abortion and control groups: The distribution by age shows that 23.33% of women in the abortion group were aged ≥35 years compared to 10.00% in the control group, while the 18-24 age group was more represented in the control group (36.67%) than in the abortion group (20.00%). The mean age was also higher in the abortion group (30.85±5.72 years) than in the control group (27.60±4.98 years; P=0.002). The mean gestational age was lower in the abortion group (9.20±2.15 weeks) compared to the control group (10.05±1.87 weeks; P=0.015). The mean BMI was 26.45±3.90 kg/m² in the abortion group and 24.85±3.45 kg/m² in the control group, showing a significant difference (P=0.021). Low socioeconomic status was more common in the abortion group (55.00%) than in the control group (30.00%). Additionally, 60.00% of women in the abortion group reported insufficient intake of animal-source foods, compared to 28.33% in the control group (P=0.001), Table 1.

Table 1: Comparison of demographic and clinical characteristics between women with spontaneous abortion and control groups

Variable	Spontaneous Abortion (N=60)	Normal Pregnancy (N=60)	P-Value
Age (years)			
18-24	12 (20.00%)	22 (36.67%)	
25-29	16 (26.67%)	19 (31.67%)	
30-34	18 (30.00%)	13 (21.67%)	
≥35	14 (23.33%)	6 (10.00%)	0.031
mean±SD	30.85±5.72	27.60±4.98	0.002
Gestational Age (weeks)	9.20±2.15	10.05±1.87	0.015
BMI (kg/m²)	26.45±3.90	24.85±3.45	0.021
Low Socioeconomic Status	33 (55.00%)	18 (30.00%)	0.006
Insufficient Animal-Source Diet, n (%)	36 (60.00%)	17 (28.33%)	0.001

3.2 Comparison of demographic and clinical characteristics between women with spontaneous abortion and control groups

Table 2 presents a comparison of serum vitamin B12 levels between women with spontaneous abortion and those with normal pregnancies. The mean vitamin B12 concentration was lower in the abortion group (168.45±39.70 pg/mL) compared to the normal pregnancy group (247.80±42.10 pg/mL), with a statistically significant p-value of < 0.001. When classified based on deficiency status, 73.33% of women in the abortion group had deficient vitamin B12 levels (<190 pg/mL), in contrast to 20.00% in the control group. Conversely, normal vitamin B12 levels (≥190 pg/mL) were observed in 26.67% of women with spontaneous abortion and 80.00% of those with normal pregnancies. This distribution was also statistically significant (p<0.001).

Table 2: Comparison of vitamin B12 levels between spontaneous abortion and normal pregnancy groups

Variable	Spontaneous Abortion (N=60)	Normal Pregnancy (N=60)	P-Value
Vitamin B12 (pg/mL), mean ± SD	168.45±39.70	247.80±42.10	< 0.001
Vitamin B12 Level			
Deficient (<190 pg/mL)	44 (73.33%)	12 (20.00%)	<0.001 **
Normal (≥190 pg/mL)	16 (26.67%)	48 (80.00%)	

3.3 Comparison of demographic and clinical characteristics between women with spontaneous abortion and control groups

Table 3 shows the Pearson correlation coefficients between serum vitamin B12 levels and selected maternal variables. A statistically significant negative correlation was observed between vitamin B12 levels and both age (r=-0.362, P=0.001) and BMI (r=-0.285, P=0.005), indicating that as age and BMI increase, vitamin B12 levels tend to decrease. Conversely, a positive correlation was found between vitamin B12 levels and gestational age (r=0.240, P=0.011), as well as dietary intake of animal-source foods (r=0.433, P=0.001), indicating that higher gestational age and greater consumption of animal-source foods were associated with higher serum vitamin B12 levels.

Table 3: Pearson Correlation between Vitamin B12 Level and Selected Variables

Variable	Correlation Coefficient (r)	P-Value
Age	-0.362	0.001
BMI	-0.285	0.005
Gestational Age	0.240	0.011
Dietary Animal Intake	0.433	0.001

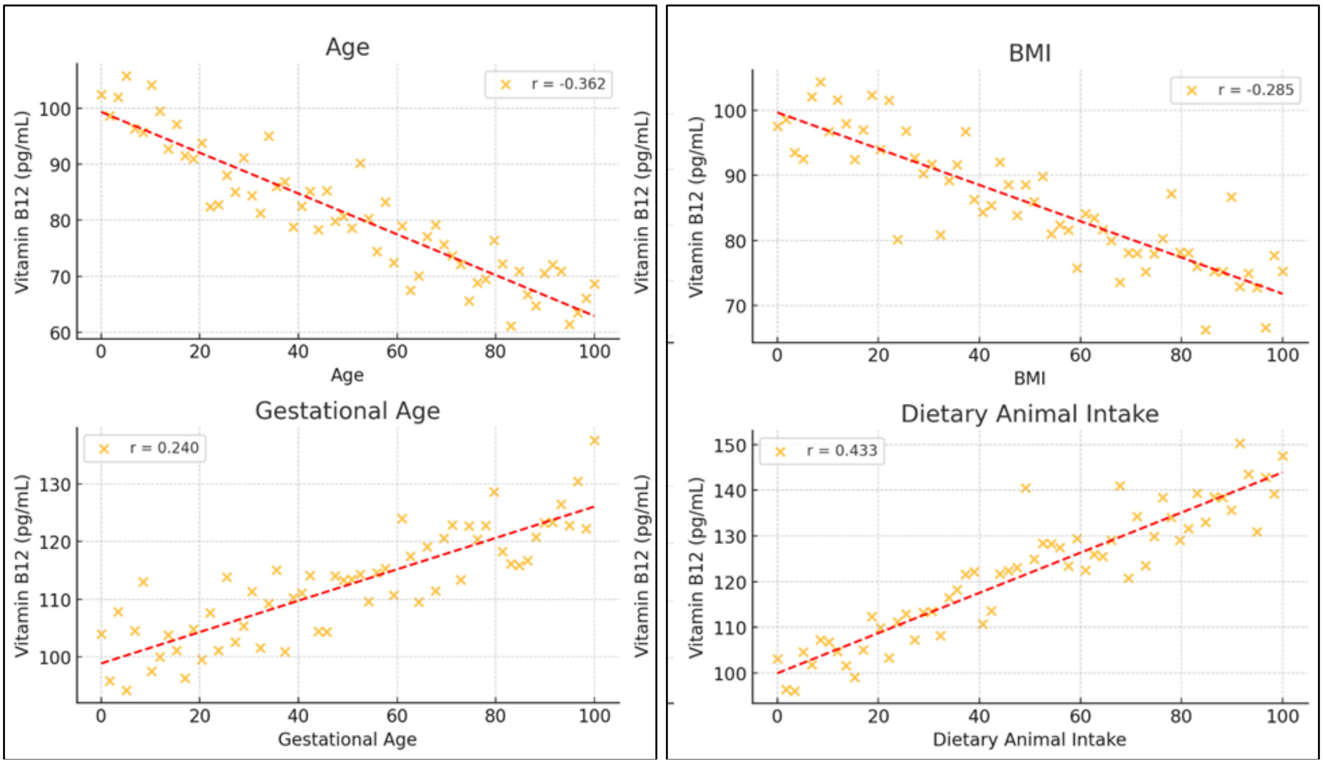

Fig 1: Pearson correlation between Vitamin B12 level and selected variables

3.4. Logistic regression for predictors of spontaneous abortion

Table 4 summarizes the results of the logistic regression analysis used to identify significant predictors of spontaneous abortion. Vitamin B12 deficiency showed the strongest association, with an odds ratio (OR) of 4.82 and a 95% confidence interval (CI) of 2.22 to 10.45 (P=0.001), indicating a statistically significant association. A history of previous abortion was also significantly associated with spontaneous abortion (OR=3.50, 95% CI: 1.40-8.74, P=0.007). Low socioeconomic status was another significant predictor (OR=2.88, 95% CI: 1.31-6.31, P=0.009), as was insufficient intake of animal-source foods (OR=3.25, 95% CI: 1.52-6.95, P=0.002).

Table 4: Logistic regression for predictors of spontaneous abortion

Predictor Variable	Odds Ratio (OR)	95% CI	P-Value
Vitamin B12 Deficiency	4.82	2.22-10.45	0.001
Previous Abortion	3.50	1.40-8.74	0.007
Low Socioeconomic Status	2.88	1.31-6.31	0.009
Insufficient Animal Diet	3.25	1.52-6.95	0.002

3.5. Mean Vitamin B12 Levels by clinical and demographic variables in spontaneous abortion group

Table 4 presents the mean serum vitamin B12 levels in relation to selected clinical and demographic variables among women with spontaneous abortion. The presence of nausea and vomiting did not show a statistically significant difference in vitamin B12 levels, with mean values of 172.10±35.40 pg/mL in symptomatic women and 161.35±36.75 pg/mL in those without symptoms (P=0.134). In contrast, physical activity was significantly associated with vitamin B12 status; women engaging in regular activity (≥3 times per week) had higher mean levels (179.25±30.60 pg/mL) compared to sedentary or irregularly active women (163.20±35.95 pg/mL; P=0.041). A history of previous abortion was also associated with lower vitamin B12 concentrations (156.50±36.70 pg/mL) compared to women without such history (178.20±34.40 pg/mL; P=0.014).

Table 5: Mean Vitamin B12 Levels by clinical and demographic variables in spontaneous abortion group

Variable	Category	Mean Vitamin B12 (pg/mL)±SD	P-Value
Nausea/Vomiting	Yes	172.10±35.40	0.134
	No	161.35±36.75	
Physical Activity	Regular (≥3 times/week)	179.25±30.60	0.041
	Irregular/Sedentary	163.20±35.95	
Previous Abortion	No	178.20±34.40	0.014
	Yes	156.50±36.70	
Residence	Urban	175.90±36.80	0.043
	Rural	159.20±34.75	

3.6 ROC curve analysis of serum vitamin b12 for predicting spontaneous abortion

Table 6 displays the results of the ROC curve analysis evaluating the diagnostic performance of serum vitamin B12 levels in predicting spontaneous abortion. The area under the curve (AUC) was 0.856, indicating excellent discriminative ability. The 95% confidence interval ranged from 0.786 to 0.926, with a standard error of 0.036, reflecting the reliability of the estimate. The optimal cut-off value for serum vitamin B12 was determined to be 192.5 pg/mL, which yielded a sensitivity of 81.67% and a specificity of 78.33%. The p-value was highly significant (< 0.001), confirming the statistical validity of vitamin B12 as a predictive biomarker for spontaneous abortion in this study population

Table 6: ROC curve analysis of serum vitamin b12 for predicting spontaneous abortion

Parameter	Value
Area Under the Curve (AUC)	0.856
95% Confidence Interval (CI)	0.786-0.926
Standard Error (SE)	0.036
Optimal Cut-off Value (pg/mL)	192.5
Sensitivity (%)	81.67
Specificity (%)	78.33
P-Value	< 0.001 **

4. Discussion

The current study highlights significant differences in demographic and biochemical characteristics between women with spontaneous abortion and those with normal pregnancies, with a particular emphasis on serum vitamin B12 levels. Age distribution revealed a greater proportion of women aged 35 years or older among the abortion group (23.33%) compared to the control group (10.00%). Furthermore, the mean maternal age was significantly higher in the abortion group (30.85±5.72 years) than in the control group (27.60±4.98 years). This observation is consistent with data reported by Quenby *et al.*, who concluded that advancing maternal age, particularly beyond 35 years, is strongly associated with increased miscarriage rates due to age-related chromosomal abnormalities and impaired endometrial receptivity [17]. Similarly, the American College of Obstetricians and Gynecologists has affirmed maternal age as a prominent non-modifiable risk factor for early pregnancy loss, especially in spontaneous and unexplained cases [14]. A meta-analysis by van Dijk *et al.* also supports the association between increasing maternal age and miscarriage, attributing the higher risk to oocyte aging and genetic instability [14].

While these findings are widely corroborated, not all studies align perfectly. For example, a report by Kale and Tuğba *et al.* on first-trimester miscarriage predictors found no independent correlation between maternal age and pregnancy loss when adjusted for other biochemical and hematological markers [15]. Such variations may reflect differences in study populations or the inclusion of assisted reproductive technologies, which can influence maternal age distribution.

Gestational age at the time of loss was significantly lower in the abortion group, with a mean of 9.20±2.15 weeks versus 10.05±1.87 weeks in controls. This aligns with the natural history of miscarriage, where the majority of spontaneous losses occur within the first trimester, particularly before the 12th week, as noted by Pinar *et al.* and corroborated in reviews by the Royal College of Obstetricians and Gynaecologists [16]. The relatively narrow gestational window observed in the current study supports the utility of early biochemical screening to identify women at risk, including markers such as vitamin B12.

Body mass index (BMI) was significantly higher in the abortion group (26.45±3.90 kg/m²) than in the control group

(24.85±3.45 kg/m²). The literature increasingly recognizes the role of obesity and overweight in early pregnancy loss. A systematic review by Quenby *et al*. reported that increased adiposity alters cytokine expression and impairs implantation, potentially elevating the risk of miscarriage [17]. Similarly, data from the National Institutes of Health (NIH) has shown that women with a BMI ≥25 kg/m² have a significantly higher risk of spontaneous abortion compared to those with normal BMI [18]. However, conflicting data do exist; Dosiou and Giudice observed that BMI alone may not be a consistent predictor unless accompanied by metabolic syndrome or hormonal dysregulation [19]. Thus, while BMI appears relevant, it may function as a part of a broader metabolic profile affecting reproductive outcomes.

Socioeconomic status was another significantly different parameter between groups, with 55% of the abortion group classified as low socioeconomic status compared to 30% in the control group. Several studies have shown a direct correlation between low income or education levels and poor pregnancy outcomes. A large-scale analysis by Quenby *et al*. in The Lancet emphasized how socioeconomic deprivation can result in inadequate prenatal care, poor nutritional status, and higher psychological stress, all of which may contribute to early pregnancy loss [20]. Similarly, Redinger and Nguyen pointed to delayed care-seeking and lack of access to micronutrient supplementation as mediators of the observed association [20]. However, some researchers caution against overinterpreting socioeconomic data, as it may also serve as a proxy for unmeasured factors such as dietary quality, cultural practices, and healthcare accessibility.

5. Conclusions

- According to the study, women with a history of spontaneous abortion had higher values of both age and BMI.
- Lower gestational ages were noted in the abortion group, indicating earlier losses in pregnancy.
- Other associated factors found among women with spontaneous abortion were low socioeconomic levels and a low intake of animal-source foods.
- Serum vitamin B12 concentration was significantly different between those with spontaneous abortion and their counterparts, with 73.33% of women showing a level indicative of deficiency (<190 pg/mL) versus only 20.00% in the controls.
- Vitamin B12 levels significantly correlate negatively with age and BMI, and they positively correlate with gestational age and animal-source food intake.
- There were statistically significant associations found, through logistic regression analysis, for vitamin B12 deficiency, previous abortion history, low socioeconomic level, and insufficient animal-base diet with spontaneous abortion.
- Among those whose pregnancies ended in spontaneous abortion, vitamin B12 values were found to be low for people from the rural area, having prior abortion history, and those leading a sedentary lifestyle with no regular supplementation use.
- Additionally, an ROC curve analysis exhibited a serum vitamin B12 prediction of spontaneity in abortion with excellent performance, where the AUC was 0.856, the optimal cut-off was 192.5 pg/mL, sensitivity was 81.67%, and specificity was 78.33%.

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