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VITAMIN B12 STATUS AND ITS IMPACT ON CARDIOVASCULAR RISK FACTORS: INSIGHTS FROM A HOSPITAL BASED CROSS-SECTIONAL STUDY

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Abstract

Background: Inadequate vitamin B12 levels have been associated with adverse health outcomes, including metabolic disorders and cardiovascular risk factors. This deficiency is a concern globally, with varying prevalence rates across populations. Understanding the relationship between vitamin B12 status and atherogenic risk, particularly in the context of lipid profiles, is crucial for identifying potential cardiovascular risk factors and guiding preventive strategies. This study aimed to assess the association between vitamin B12 levels and the atherogenic index of plasma (AIP) in a diverse population, shedding light on the importance of vitamin B12 in cardiovascular health. **Materials and Methods:** A cross-sectional study was conducted at a tertiary care hospital, including 500 adults aged 18-60 years. Blood samples were collected after an overnight fast, and vitamin B12 levels were assessed via chemiluminescent immunoassay. Lipid profiles were analyzed using standardized enzymatic methods, and the Atherogenic Index of Plasma (AIP) was calculated. Statistical analysis, including ANOVA and correlation analysis, was performed using SPSS version 20. Covariates such as age and gender were considered, with p-values < 0.05 considered significant. **Result:** Among 500 participants, vitamin B12 levels categorized 291 as having normal levels, 163 with insufficiency, and 46 with deficiency. Significant differences were observed in lipid profiles and AIP among these groups (p < 0.001). Total cholesterol, triglycerides, LDL cholesterol, and AIP increased, while HDL cholesterol decreased with worsening B12 deficiency. Additionally, systolic and diastolic blood pressures were positively correlated with B12 insufficiency and deficiency. These findings underscore the potential role of vitamin B12 status in modulating cardiovascular risk factors. **Conclusion:** In this study, lower vitamin B12 levels were associated with adverse lipid profiles, higher AIP, and elevated blood pressure, highlighting the potential role of vitamin B12 in cardiovascular health. Monitoring and addressing vitamin B12 status may contribute to the prevention of cardiovascular risk factors. Further research is needed to explore the mechanisms underlying this association and its clinical implications.

INTRODUCTION

Cardiovascular diseases (CVDs) remain a leading cause of morbidity and mortality worldwide, posing a significant public health challenge. Atherogenic dyslipidemia, characterized by elevated levels of triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and reduced high-density lipoprotein cholesterol (HDL-C), plays a pivotal role in the development and progression of atherosclerosis—the underlying pathology of CVDs.[1,2] Recognizing the multifactorial nature of atherosclerosis, research has increasingly focused on identifying modifiable risk factors, including diet and nutrition, to better understand the intricate mechanisms contributing to CVD development.[2]

Atherogenic Index of Plasma (AIP) is a calculated parameter that has gained increasing attention in recent years as a valuable tool for assessing the risk of atherosclerosis and cardiovascular events. AIP is computed as the logarithmically transformed ratio of the concentration of triglycerides (TG) to high-density lipoprotein cholesterol (HDL-C), and it has been proposed as a more specific indicator of atherogenic lipid profiles than individual lipid components.[3,4]

Among the essential micronutrients, vitamin B12 has gained attention due to its role in maintaining cardiovascular health.[5] Vitamin B12, also known as cobalamin, is essential for DNA synthesis, homocysteine metabolism, and the formation of red blood cells. Its deficiency has long been associated with various health issues, including hematological disorders and neurological impairments.[6] However, emerging evidence suggests that vitamin B12 may have a broader impact, extending to lipid metabolism and atherogenesis.[6]

Several studies have explored the relationship between vitamin B12 status and lipid profiles, but the findings have been inconsistent, and the potential link between vitamin B12 and AIP, a novel marker of atherogenic risk, remains relatively unexplored. Understanding the association between vitamin B12 and AIP could provide valuable insights into the pathogenesis of atherosclerosis and inform preventive and therapeutic strategies for CVD.[7,8,9,10]

This hospital-based cross-sectional study aimed to assess the potential correlation between vitamin B12 levels and AIP in a diverse patient population. By elucidating the relationship between vitamin B12 and AIP, this research seeks to contribute to our understanding of the complex interplay of factors involved in atherosclerotic cardiovascular disease and potentially identify a novel biomarker or therapeutic target for CVD prevention and management.

MATERIALS AND METHODS

Study Design and Participants

This hospital-based cross-sectional study was conducted in the Department of Biochemistry at a tertiary care hospital over a one-year period between July 2022 and June 2023. The research involved 500 adult individuals aged between 18 and 60 years who were assessed for potential vitamin B12 deficiency. These assessments included concurrent laboratory evaluations of their lipid profiles, conducted during clinical examinations in the General Medicine Outpatient Department (OPD). Exclusion criteria comprised individuals with a history of known cardiovascular disease (CVD), liver disease, renal disease, or any other chronic illnesses that could potentially influence lipid metabolism. Additionally, pregnant or lactating women and individuals taking vitamin B12 supplements were excluded from the study.

Sample Size Calculation

The sample size calculation was based on the expected effect size and statistical power required to detect a significant association between vitamin B12 levels and the Atherogenic Index of Plasma (AIP). A sample size of 500 participants was determined to achieve a power of 0.80 at a significance level of 0.05. This calculation considered an estimated effect size of 0.2, as reported in a previous study by Adaikalakoteswari et al., conducted in a similar population.[11]

Data Collection

Demographic information, including age, gender, and medical history, was collected through structured interviews and a review of medical records. Trained healthcare professionals measured participants' weight, height, BMI (Body Mass Index), and blood pressure using standardized procedures. Venous blood samples were collected from participants using aseptic techniques after an overnight fast of at least 12 hours. These blood samples were collected in ethylenediaminetetraacetic acid (EDTA) tubes for plasma separation and stored at 4°C until further analysis.

Laboratory Analysis

Measurement of Vitamin B12 Levels: Plasma vitamin B12 levels were quantified using a chemiluminescent immunoassay (CLIA) method. The assay's detection range was 50-2000 pg/mL, and the coefficient of variation (CV) was 4.5%.

Categorization of Vitamin B12 Levels: Vitamin B12 levels in individuals were categorized into three groups based on cutoff levels according to WHO recommendations:[12]

- Normal Vitamin B12 Levels: Participants with vitamin B12 levels of 221 picograms per milliliter (pg/mL) or above were considered to have normal levels, indicating sufficiency to meet nutritional requirements.
- Vitamin B12 Insufficiency: Participants with vitamin B12 levels below 221 pg/mL but above 148 pg/mL were categorized as having insufficiency, signifying a marginal deficiency that may require monitoring or dietary adjustments.
- Vitamin B12 Deficiency: Participants with vitamin B12 levels consistently below 148 pg/mL were classified as deficient in this essential nutrient.

Lipid Profile Analysis

Fasting lipid profiles, including total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C), were determined using standardized enzymatic method.

Calculation of Atherogenic Index of Plasma (AIP)

AIP was calculated as log10 (TG/HDL-C), where TG and HDL-C levels were expressed in mg/dL.

Statistical Analysis

Statistical analysis was conducted using SPSS version 20.0. Descriptive statistics, such as means and standard deviations (SD) for continuous variables, and frequencies for categorical variables, were calculated. The normality of data distribution was assessed using the Shapiro-Wilk normality test. ANOVA (Analysis of Variance) was used to compare continuous data among the three distinct vitamin B12 categories, with a focus on evaluating the influence of vitamin B12 status as the primary independent variable on these continuous variables.

The correlation between vitamin B12 levels and lipid profiles, as well as AIP, was evaluated using Pearson correlation analysis. Statistical significance was defined as p-values less than 0.05.

Ethical Considerations

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki and received ethical approval from the Institutional Review Board (IRB) of the Hospital. Informed consent was obtained from all participants prior to their inclusion in the study.

RESULTS

Among the 500 individuals included in this study, 291 (58.2%) exhibited normal vitamin B12 levels, while 163 (32.6%) fell into the category of insufficiency, indicating a marginal deficiency. Notably, 46 (9.2%) participants were classified as deficient in vitamin B12, with consistently low levels of this essential nutrient [Table 1].

Among the 500 study participants, those with normal vitamin B12 levels (n=291) had an average age of 40.2 years (±6.3), while individuals with vitamin B12 insufficiency (n=163) were slightly older, averaging 45.8 years (±7.1). Those categorized as having vitamin B12 deficiency (n=46) were the oldest, with an average age of 51.5 years (±8.4). Gender distribution was balanced, with a slight male predominance across all groups (51.0% males, 49.0% females). Additionally, participants with normal vitamin B12 levels had an average BMI of 26.4 kg/m² (±3.1), those with insufficiency had a higher mean BMI of 29.0 kg/m² (±3.5), and those with deficiency had the highest mean BMI of 30.8 kg/m² (±4.2). These findings highlight age-related differences and BMI variations across vitamin B12 categories within the study population [Table 2].

Notably, participants with normal vitamin B12 levels (n=291) exhibited lower levels of total cholesterol (192.5 mg/dL ± 25.3), triglycerides (143.6 mg/dL ± 37.4), LDL cholesterol (118.4 mg/dL ± 20.2), and SBP (125.8 mmHg ± 11.5) compared to those with vitamin B12 insufficiency (n=163) and deficiency (n=46). Conversely, individuals with vitamin B12 insufficiency and deficiency displayed elevated levels of total cholesterol, triglycerides, LDL cholesterol, and SBP, with statistically significant differences (p<0.001 for total cholesterol, triglycerides, and SBP; p=0.001 for LDL cholesterol). Additionally, HDL cholesterol levels were highest in the normal B12 group (51.3 mg/dL ± 7.4) compared to the insufficiency and deficiency groups (p=0.003). The atherogenic index was also notably increased in the deficiency group (0.05 ± 0.16) compared to the other groups (p<0.001). Furthermore, diastolic blood pressure (DBP) showed a significant increase in individuals with B12 insufficiency and deficiency, with the highest levels observed in the deficiency group (88.1 mmHg ± 7.6, p<0.001). These findings underscore the substantial impact of vitamin B12 status on lipid profile parameters and blood pressure, indicating potential cardiovascular implications associated with vitamin B12 deficiency and insufficiency [Table 3].

Lower vitamin B12 levels are positively correlated with higher total cholesterol (r=0.245, p<0.001) and triglycerides (r=0.318, p<0.001), indicating a potential link between vitamin B12 deficiency or insufficiency and adverse lipid profiles. Additionally, there is a positive but weaker correlation with LDL cholesterol (r=0.163, p=0.012) and a negative correlation with HDL cholesterol (r=-0.197, p=0.004), suggesting potential implications for both "bad" and "good" cholesterol levels. The atherogenic index, a marker of cardiovascular risk, is positively correlated with lower vitamin B12 levels (r=-0.283, p<0.001), highlighting the importance of adequate vitamin B12 status in cardiovascular health. Although both systolic blood pressure (SBP) and diastolic blood pressure (DBP) show positive correlations with vitamin B12 levels, the association with DBP did not reach statistical significance (r=0.104, p=0.071) [Table 4].

Table 1: Vitamin B12 Categories and Distribution

Vitamin B12 Category	**Frequency**	**%**
Normal Levels	291	58.2
Insufficiency	163	32.6
Deficiency	46	9.2

Table 2: Demographic Characteristics of Study Participants

Characteristic	**Normal B12 Levels (n=291)**	**B12 Insufficiency (n=163)**	**B12 Deficiency (n=46)**	**Total (n=500)**
Mean Age (years)	40.2 ± 6.3	45.8 ± 7.1	51.5 ± 8.4	43.7 ± 7.2
Gender				
Male	150 (51.5)	81 (49.7)	24 (52.1)	255 (51.0)
Female	141 (48.5)	82 (50.3)	22 (47.9)	245 (49.0)
Mean BMI (kg/m²)	26.4 ± 3.1	29.0 ± 3.5	30.8 ± 4.2	27.8 ± 3.6

Table 3: Comparison of Lipid Profile Parameters, SBP, and DBP among Vitamin B12 Categories (ANOVA)

Lipid Profile Parameter	**Normal B12 Levels (n=291)**	**B12 Insufficiency (n=163)**	**B12 Deficiency (n=46)**	**p-value**
Total Cholesterol*	192.5 ± 25.3	204.7 ± 28.9	218.2 ± 30.1	<0.001
Triglycerides*	143.6 ± 37.4	156.2 ± 45.6	173.4 ± 55.8	<0.001
LDL Cholesterol*	118.4 ± 20.2	125.6 ± 22.5	138.1 ± 24.7	0.001

HDL Cholesterol*	51.3 ± 7.4	47.9 ± 6.8	44.2 ± 7.2	0.003
Atherogenic Index	0.05 ± 0.11	0.25 ± 0.14	0.58 ± 0.16	<0.001
SBP (mmHg)	125.8 ± 11.5	132.1 ± 13.2	138.5 ± 14.9	0.001
DBP (mmHg)	78.3 ± 6.8	82.6 ± 7.2	88.1 ± 7.6	<0.001

*** mg/dL**

Table 4: Correlation between Vitamin B12 Levels, Blood Pressure, and Lipid Profile Parameters

Lipid Profile Parameter	Pearson Correlation Coefficient (r)	p-value
Total Cholesterol	0.245	<0.001
Triglycerides	0.318	<0.001
LDL Cholesterol	0.163	0.012
HDL Cholesterol	-0.197	0.004
Atherogenic Index	0.283	<0.001
SBP (mmHg)	0.135	0.028
DBP (mmHg)	0.104	0.071

DISCUSSION

The current study aimed to investigate the association between vitamin B12 levels and the atherogenic index of plasma (AIP), as well as various lipid profile parameters and blood pressure, in a cohort of 500 adults. Our findings demonstrate significant correlations between vitamin B12 status and these cardiovascular risk factors, shedding light on the potential implications of vitamin B12 deficiency and insufficiency in the context of cardiovascular health.

In our study notably, 46 (9.2%) participants were classified as deficient in vitamin B12, with consistently low levels of this essential nutrient, which was similar to study by Dali-Youcef et al., (4%), El-Khateeb et al., (6%), but in contrast to study by Singla et al., where 47% of participants were deficient in vitamin B12.[13,14,15] In our study those categorized as having vitamin B12 deficiency (n=46) were the oldest, with an average age of 51.5 years (±8.4), which was similar to study by Yildirim et al., which showed that with the increase in age, more participants were deficient in vitamin B12 (64% in elderly).[16]

In our study those with deficiency had the highest mean BMI of 30.8 kg/m² (±4.2), which similar to studies by Sukumar et al., Thomas-Valdés et al., Wiebe et al., Lee et al., and Sun et al., where positive correlation between lower vitamin B12 levels was observed.[17-21]

One of the key observations in this study is the positive correlation between lower vitamin B12 levels and adverse lipid profiles. Specifically, individuals with vitamin B12 insufficiency and deficiency exhibited higher levels of total cholesterol, triglycerides, and LDL cholesterol. These findings align with previous studies by Boachie et al., Sadeghian et al., Wasilewska et al., Delisle et al., Iqbal et al., and Dierkes et al., highlighting the role of vitamin B12 in lipid metabolism.[22-27] Vitamin B12 is essential for the conversion of homocysteine to methionine, and deficiency can lead to elevated homocysteine levels, which have been associated with unfavorable lipid profiles and increased cardiovascular risk. The positive correlation between vitamin B12 and HDL cholesterol levels, observed in our study, also has important implications, as higher HDL cholesterol is generally considered cardioprotective.

The atherogenic index, which reflects the balance between pro-atherogenic (triglycerides) and anti-atherogenic (HDL cholesterol) factors, showed a significant positive correlation with lower vitamin B12 levels, which was also noted in the study by Mendonça et al., Pawlak et al., Chakraverty et al., Mahalle et al., Rafnsson et al., Ng et al., and Kwok et al.[28-34] This suggests that vitamin B12 deficiency or insufficiency may contribute to an unfavorable atherogenic profile, increasing the risk of atherosclerosis and cardiovascular events.

Furthermore, our study revealed a positive correlation between lower vitamin B12 levels and higher blood pressure, as evidenced by elevated systolic blood pressure (SBP). While the association with diastolic blood pressure (DBP) did not reach statistical significance, the trend is noteworthy. Hypertension is a well-established risk factor for cardiovascular diseases, and our findings suggest that vitamin B12 status may play a role in blood pressure regulation.

The observed correlations do not imply causation, and the mechanisms underlying these associations warrant further investigation. Potential mechanisms may include the influence of vitamin B12 on homocysteine metabolism, oxidative stress, and endothelial function, all of which can impact cardiovascular health.

CONCLUSION

In conclusion, our study highlights the significance of vitamin B12 in modulating lipid profiles, the atherogenic index, and blood pressure, all of which are critical determinants of cardiovascular health. Maintaining adequate vitamin B12 levels may be important in reducing cardiovascular risk, and future interventional studies are needed to explore the potential benefits of vitamin B12 supplementation in individuals with deficiency or insufficiency. Additionally, our findings emphasize the importance of regular monitoring of vitamin B12 status in clinical practice, especially in individuals at risk of cardiovascular diseases.

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