ORIGINAL ARTICLE

Vitamin B_{12} Deficiency and Hyperhomocysteinemia and their Inter-relationship in General Population of Coimbatore District of India

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Abstract:
Background: Vitamin B_{12} deficiency is one of the leading vitamin deficiencies in India leading to anemia and other disorders. An important adverse effect of B_{12} deficiency is elevation of homocysteine levels which may lead to cardiovascular and cerebrovascular incidents. *Objectives:* This study aimed to identify the prevalence of B_{12} deficiency and prevalence of hyperhomocysteinemia in people living in Coimbatore region of Tamil Nadu, India. Also, we studied the relationship between decreased B_{12} and elevated homocysteine levels. *Material and Methods:* Four hundred eighty five apparently normal persons were recruited for this study. They were assessed for Vit B_{12} levels and Homocysteine levels and r value calculated using Pearson's correlation. *Results:* Wefound that 12% of study participants suffered from B_{12} deficiency and 23% had hyperhomocysteinemia. Pearson's correlation revealed r value of -0.05 which showed a mild correlation between decreasing B_{12} levels versus elevation of homocysteine. *Conclusion:* This study revealed B_{12} deficiency and hyperhomocysteinemia are common in people living around Coimbatore region of Tamilnadu and Low B_{12} levels may be a leading cause of hyperhomocystenemia in this population.

Keywords: Vitamin B_{12}, Homocysteine, Cardiovascular disease, cerebrovascular disease.

Introduction:

Vitamin B_{12} is an important human micronutrient.[1] It is a cobalt-containing compound, also called Cobalamin and belongs to a group of "complete" corrinoids. In humans, cobalamins are important coenzymes: methylcobalamin, which serves as the co-factor for methionine synthase (figure 1) and adenosyl-cobalamin, which is the cofactor for methyl malonylCoA mutase. Vitamin B_{12} also helps in odd chain fatty acid catabolism. Methyl malonyl-CoA mutase transforms methyl malonyl-CoA into succinyl-CoA and the adenosyltransferase incorporates the organometallic group of Coenzyme B_{12} (figure 2). [2]It also provides protection against chronic diseases, and neural tube defects, and also augments the benefits of folic acid.[3]Methionine formation is essential for providing methyl groups for methionine processes.[4]Meat, milk, egg, and fish are the sources of vitamin B_{12} in animal foods while the plant sources are dried purple laver (nori), a type of seaweed and is considered the most suitable source of vitamin B_{12} for vegetarians.[5,6] To absorb vitamin B_{12}, the formation of a primary complex between the vitamin and intrinsic factor should take place which then binds to particular receptors in the ileum of the small intestine which facilitates the transport of vitamin B_{12}.[7]Bioavailability of Vitamin B_{12} from meats of fish, goat, and chicken is 42%, 56-89% and 61-

Figure 1: Methionine synthase needed for conversion of Homocysteine to Methionine

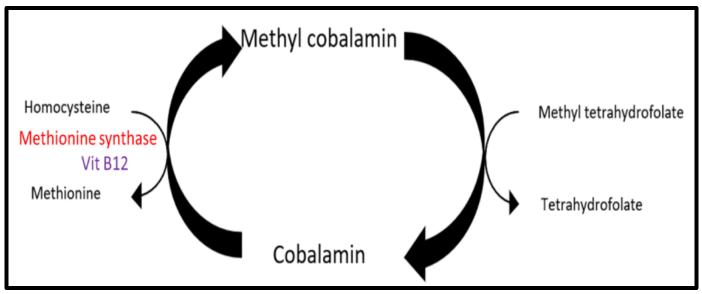
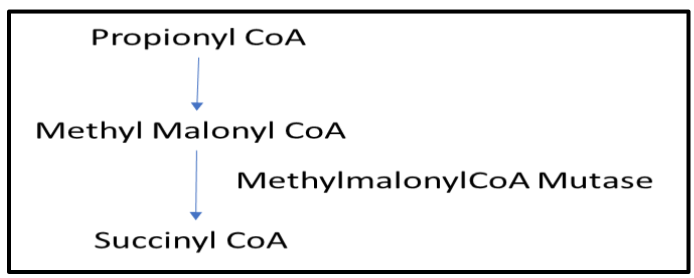


Figure 2: Degradation of odd chain carbon fatty acids



66% respectively in a healthy human. Vitamin B_{12} from eggs is poorly absorbed (< 9%) as compared to other animal-derivedfoods. It is generally assumed that adults with healthy gastrointestinal function can absorb around 50% of dietary vitamin B_{12}.[6] Prevalence of micronutrient deficiencies including vitamin B_{12} ranged from 19 to 88 % across 5 different cities in India.[8]Prevalence of subclinical Vitamin B_{12} deficiency in India is large among vegetarians.[9]Vegans are subset of people who even avoid milk and milk products. Vegans, found to have higher deficiency rates as compared to vegetarians who took milk. 62% among pregnant woman, 25-86% among children, 21-41%of adolescents and 11-90% of elderly were found to be vitamin B_{12} deficient.[10]Inadequate intake, poor bioavailability, or malabsorption can lead to a deficiency of vitamin B_{12}. Defects of Vitamin B_{12} transport in the blood, deranged cellular uptake and metabolism, may lead to clinical deficiency of this vitamin.[11] Vitamin B_{12} deficiency leads to the failure to synthesize dUTP (deoxyUridine Tri phosphate), which impairs the maturation of red blood cells and results in macrocyticanemia. So, deficiency of vitamin B_{12} can cause megaloblasticanemia which results due to ineffective erythropoiesis in the bone marrow.[12]Autoimmune defects of intrinsic factor may lead to pernicious anemia. Cobalamin deficiency can also cause a range of nervous disorders, including neuropathic symptoms, optic atrophy and dementia. In case of Sub acute combined degeneration, the symptoms manifest as dysfunction of the lateral and posterior columns of the spinal cord, leading to reduced vibratory sensation, lack of co-ordination (ataxia), and weakness.[13]Deficiency of vitamin B_{12} impairs the conversion of homocysteine to methionine, which leads to the accumulation of homocysteine and causes various conditions such as chronic kidney disease, cerebrovascular and cardiovascular problems.[14]

To diagnose B_{12} deficiency, there are certain biomarkers in the blood. These include decreased levels of circulating total B_{12} as well as abnormally increased levels of homocysteine. These biomarkers help to assess the B_{12} status of an individual and guide appropriate treatment.[15,16] We aimed to estimate the B_{12} and homocysteine levels of general population of Coimbatore district of India so that this study can throw light on prevalence of B_{12}deficiency and hyperhomocysteinemia in our population. We also aimed to identify any relationship between B_{12} deficiency and hyperhomocysteinemia in the selected population.

Material and Methods:

This was a Cross-sectional study conducted on people who attended our medical college hospital OPD, Coimbatore for a period of three months. People with a history of Cerebrovascular disease, heart attack, coronary artery disease, high homocysteine, critically ill patients, pregnancy and lactation were excluded from the study. A group of 485 individuals who matched the inclusion and exclusion criteria were enrolled.

Sample size calculation was done using the below formula

$$\text{Sample size} = \frac{\dfrac{z^2 \times p\,(1-p)}{e^2}}{1 + \left(\dfrac{z^2 \times p\,(1-p)}{e^2 N}\right)}$$

Clearance from the ethical committee was obtained and after obtaining informed consent from the participants, they were identified by name and date of birth. After providing instructions to the patients, he/she was made to sit and venipuncture was performed. Puncture sites were identified and sterilised using alcohol. After applying a tourniquet, a needle was inserted and blood was collected, after that tourniquet was removed and needle withdrawn. Hemostasiswas secured by pressure using a gauze pad. Blood wastranferred into the sterile red tube labelled with the patient name and Id. Blood was centrifuged within 30 minutes and serum stored in -20 degree Celsius till evaluation. Vitamin B_{12} levels was assessed by CLIA-chemiluminescence immunoassay. Reference Range for vitamin B_{12} is 206-678 pg/ml. Serum homocysteine levels measured using Spectrophotometry and its normal range was taken as < 20 umol/L. Prevalence of low Vitamin B B_{12} and high levels of homocysteinewas calculated using MS Excel and is given as percentage. Pearson's correlation between B_{12} levels and homocysteine levels were given as r value.

Results:

The general characteristics of all participants are given in Table 1. More number of males participated in the study than females. Out of 700 study subjects only 485 were taken up for the study. Others were eliminated due to very high levels of B_{12} (most of them were B_{12} supplements). As we can see from Table 1, least number of participants were from age group of 18-25 and maximum number is in age group 26-35. The overall and age and sex related Vitamin B_{12}deficiency prevalence is given in Table 2. The prevalence of B12 deficiency (<206ng/mL) among study participants is around 12 %. We observed maximum number of B_{12} deficiency in ages 36-45 of female population and 26-35 years of male population. Females less than 25 years were 18 in number and only one among them had Vitamin B_{12} deficiency. Similar picture obtained in males also.

Table 1. General characteristics of participants

	Number of Participant				
Age in Years	All Ages	18-25	26-35-	36-45	46-55
Total	485	34	162	179	110
Males	270	16	75	111	68
Females	215	18	87	68	42

The overall and age and sex related Vitamin B_{12}deficiency prevalence is given in Table 2. The prevalence of B12 deficiency (<206ng/mL) among study participants is around 12 %. We observed maximum number of B_{12} deficiency in ages 36-45 of female population and 26-35 years of male population. Females less than 25 years were 18 in number and only one among them had Vitamin B_{12} deficiency. Similar picture obtained in males also.

Table 2. Prevalence of vitamin B12 deficiency

	Number of People	Mean B_{12} Levels	Deficiency %
Total	58	170.37	11.9
Total Males	34	165.4	12.5
Males ages			
18-25	2	106.6	12.5
26-35	11	164.8	14.6
36-45	12	173.1	10.8
46-55	9	166.5	13.2
Total Females	24	171.26	11.1
Females ages			
18-25	1	184	5.55
26-35	10	174.4	11.4
36-45	10	163.12	14.7
46-55	13	169.47	31

According to Table 2, it can be observed that, in females the prevalence of vitamin B_{12} deficiency increase with age. With 12 participants, the age group of males between 36-45 showed the highest incidence of vitamin B_{12} deficiency. Among the female participants, the age group of 46-55 years has the highest number (13) of individuals with vitamin B_{12} deficiency. The overall and age and sex related hyperhomocysteniemia prevalence is given in table 3. The prevalence of hyperhomocysteniemia (>20µmol/L) among study participants is around 23%. We observed maximum number of hyperhomocysteniemia in ages 18-25 of female population and 26-35 years of male population.

Table 3. Prevalence of hyperhomocysteinemia

	No. of People	Mean Homoc-ysteine	Hyper Homocystei-nemia %
Total	110	26.3	22.6
Total Males	72	27.75	26.6
Males ages			
18-25	3	42.6	18.75
26-35	23	26.12	30.6
36-45	26	27.7	23.4
46-55	20	27.37	29.4
Total Females	38	24.02	17.6
Females ages			
18-25	4	24.81	22.2
26-35	18	23.13	20.6
36-45	8	24.3	11.7
46-55	8	21.29	19

The analysis of homocysteine levels in a sample of 485 participants revealed that 23% of them have elevated homocysteine levels (>20 µmol/L), while 11% of the participants showed a deficiency in vitamin B_{12} (Table 3). The age group of males between 36-45 showed the highest prevalence of hyperhomocysteinemia with 26 participants. Among the female participants, the age group of 26-35 years has the highest number (18) of individuals with Hyperhomocysteniemia according to the bar diagram (Table 3). On doing the pearson's test for the correlation between Vitamin B_{12} and Homocysteine, it was found that r value is -0.059 and it indicates a weak negative correlation between the two variables. (negative correlation-as one variable increases, the other decreases). In this case, it suggests that as Vitamin B_{12} levels increase, Homocysteine levels tend to decrease.

Discussion:

Understanding the relationship between vitamin B_{12} and homocysteine is important for identifying and preventing potential health issues associated with their deficiency or imbalance. Many studies found a relationship between B_{12} deficiency and hyperhomocysteinemia.[17-22]The presented data highlights the prevalence of vitamin B_{12} deficiency and hyperhomocysteinemia among study participants, as well as the relationship between these two variables. The study included 700 subjects, with 485 participants considered for the analysis due to the exclusion of individuals with very high levels of vitamin B_{12}, most of whom were taking supplements. The prevalence of vitamin B_{12} deficiency and hyperhomocysteinemia, with around 12% of participants showing a deficiency in vitamin B_{12}, and 23% having elevated levels of homocysteine. Interestingly, the prevalence of vitamin B_{12} deficiency was higher among male participants (6%) than female participants (4%). However, the prevalence of hyperhomocysteinemia was higher among female participants (14%) than male participants (9%). For vitamin B_{12} deficiency, it was observed that the highest incidence is seen in the age In addition to the prevalence of vitamin B_{12} deficiency and hyperhomocysteinemia, the data also highlights the relationship between these two variables. A Pearson correlation test revealed a small negative correlation between vitamin B_{12} and homocysteine levels. This indicates that as vitamin B_{12} levels increase, homocysteine levels tend to decrease. Overall, these findings suggest that there are differences in the incidence of vitamin B_{12} deficiency and hyperhomocysteinemia across different age and sex groups. The fact that the highest incidence of vitamin B_{12} deficiency is seen in older age groups may be due to a decreased ability to absorb vitamin B_{12} from food The small negative correlation observed between vitamin B_{12} and homocysteine levels highlights the potential importance of vitamin B_{12} in regulating homocysteine levels. This is supported by previous researches that have demonstrated the role of vitamin B_{12} in the conversion of homocysteine to methionine, a process that is essential for the proper functioning of the body. However, it is important to note that the presented data is limited by several factors. The study was conducted on a relatively small sample size of 485 participants, and the exclusion of individuals with very high levels of vitamin B_{12} may have biased the results. Additionally, the study was conducted in a specific population and may not be generalizable to other populations. Finally, the study was cross-sectional in nature, and therefore causality cannot be inferred.

Conclusion:

The deficiency of Vitamin B_{12} and its resulting condition of homocysteinemia are not uncommon ailments, and they may affect individuals of any gender or age, as evidenced by the data presented. Therefore, it is crucial to include these factors in a comprehensive health screening program to mitigate the risk of cardiovascular issues, neuropathies, anemia, and Cerebrovascular disease. The presented data highlights the prevalence of vitamin B_{12} deficiency and hyperhomocysteinemia, as well as the relationship between these two variables. The findings suggest that there are differences in the incidence of these conditions across different age and sex groups, and that vitamin B_{12} may play a role in regulating homocysteine levels. However, further research is needed to confirm these findings and explore potential underlying mechanisms. Additionally, it is important for individuals to consult with their healthcare provider before taking any vitamin supplements, as excessive intake of certain vitamins may have adverse effects on health.

Sources of supports: Nil

Conflicts of Interest: Nil

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