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High Burden of Vitamin B12 Deficiency among Adults and Elderly

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ABSTRACT

Background: Deficiency of vitamin-B12 is widespread. Adults and the elderly are particularly susceptible to vitamin-B12 deficiency. This study investigated the burden of vitamin-B12 deficiency and insufficiency among adults and the elderly attending a tertiary care hospital in Nepal.

Methods: This is a retrospective chart review conducted at Dhulikhel hospital. We reviewed records of 1615 patients investigating Vitamin-B12 level (pmol/L) at the clinical biochemistry laboratory from laboratory management database MIDAS between June 2020 and December 2021. Vitamin-B12 level was measured using enzyme immunoassay in Abbott Architect i1000SR analyzer. The categorical variables are presented as frequency and percentage; and numerical variables as means and standard deviations, or median and Interquartile range. Pearson Chi-square test was used to determine association between categorical variables. Mann Whitney test and Kruskal Wallis H test were used to compare Vitamin-B12 level by categories.

Results: There were 1454 participants of which 33.5% of the patients were deficient, 27.9% were borderline deficient, while 38.7% had adequate vitamin B12 levels. Young adults(170.4 pmol/L) had a lower median vitamin B12 level than middle-aged adults (183.7pmol/L) and the elderly population (247.9pmol/L) ($P<0.001$). Compared to females (186.7 pmol/L), males(171.9 pmol/L) had lower vitamin B12 level ($P<0.05$).

Conclusions: The study revealed that a significant proportion of young adults, middle aged adults and elderly population visiting a tertiary care hospital of Nepal are having vitamin B12 deficiency and borderline deficiency of public health concern.

Keywords: Adults; deficiency; elderly, vitamin B12.

INTRODUCTION

The magnitude of Vitamin B12 deficiency is high worldwide.[1] Vitamin B12 deficiency is associated with hematological and neurological disturbances.[2] Age related differences in Vitamin B12 deficiency has been observed.[3,4]

Vitamin B12 deficiency affects adults to elderly.[2] High prevalence of Vitamin B12 deficiency has been reported among adults from North and Latin America, Africa, Europe and Asia.[2] Likewise, Vitamin B12 deficiency among elderly varies across countries with prevalence as 4.4%, 27% and 46% in USA, Latin America and India.[5] In addition, 15% of adults and more that 20% of older adults are afflicted by marginal deficiency.[6] Identification of vitamin B12 deficiency and subclinical deficiency will allow early intervention so as to prevent the deficiency related complications.[7]

There is limited evidence on current prevalence of vitamin B12 among adults and elderly in Nepal. Hence, the aim of this study was to determine the prevalence of Vitamin B12 deficiency among adults and elderly.

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METHODS

We conducted a retrospective chart review, based on laboratory records at Dhulikhel Hospital, a tertiary care hospital in Nepal. We extracted 1615 records of patients, who were investigated for serum vitamin B12 at the Department of Clinical Biochemistry between June 2020 and December 2021, from Laboratory software, Modular Interactive Data Acquisition System (MIDAS) version 3.2. Patient confidentiality was maintained, and the requirement of consent was waived due to the secondary nature of the data. We obtained approval from Dhulikhel hospital and ethical clearance from the Institutional Review Committee of Kathmandu University School of Medical Sciences (Reference number. 259/2021, December 2021).

A total of 1615 data was extracted, of which 161 were excluded. Those aged under 18, incomplete laboratory record and with missing, clerical error and duplicate values of Vitamin B12 were excluded from the study. The total of 1454 patients data included age (years), gender (male/female), and the value of serum total Vitamin B12 (pmol/L) measured in Abbott Architect i1000 SR analyzer.

We categorized Vitamin B12 status into normal, borderline-deficient and deficient according to WHO criteria which is universally accepted. Patients were classified as deficient if Vitamin B12 was less than 148 pmol/L, borderline deficient if vitamin B12 was between 148 pmol/L to 221 pmol/L and normal if vitamin B12 was more than 221pmol/L.[8] We adopted the classification of the age groups as young (18-39years), middle aged (40-59years), and elderly (≥60years).[9]

We imported data from Microsoft Excel into R-programming software (R-version:4.0.3) for cleaning, coding and statistical analysis. Numerical variables were tested for normality using the Shapiro-Wilk test. Normally distributed numerical variables were expressed as mean and standard deviation (SD),and non normally distributed variables as median and interquartile range(IQR). Pearson Chi-square test was used to determine association between categorized vitamin B12 status with age and gender. The vitamin B12 was compared between male and female using Mann-Whitney U test and between young, adult and old age participants using Kruskal Wallis H test. A p value of <0.05 was considered statistically significant.

RESULTS

As can be seen in table 1 there were 1454 participants, aged between 18 to 97 years with the mean age 43.6±16.9 years. Most were young adults (44.5%) followed by middle aged (37.4%) and elderly(18.1%). There were more females (66%) than males(34%) in the study. The mean concentration of total vitamin B12 was 276.3pmol/L (SD 283.0). Median concentration observed was 180.8pmol/L (IQR 163. 2) which is in borderline deficient range as per the WHO reference interval (148 pmol/L to 221 pmol/L).

Table 1. Characteristics of the study participants in mean(SD), median (IQR) and proportions.

Characteristics	n(%) (n=1454)	Young aged (18-39 years)	Middle aged (40-59 years)	Old aged (≥60 years)
Age in years, Mean±SD [min-max]	43.6±16.9 [18.0-97.0]	28.15± 5.82 [18.0-39.0]	49.06±5.68 [40.0-59.0]	70.26±7.77 [60.0-97.0]
Female	**959 (66%)**	442 (46.1%)	361 (37.6%)	156 (16.3%)
Male	**495 (34%)**	205 (41.4%)	183 (37%)	107 (21.6%)
Vitamin-B12 (pmol/L) Median	180.8	170.4	183.7	247.9

Figure 1 illustrates the distribution of vitamin B12 deficiency.

Vitamin B12 deficiency was detected in 33.5% of the participants, borderline deficiency in 27.8% and normal levels in 38.7% of the participants using WHO defined reference interval.

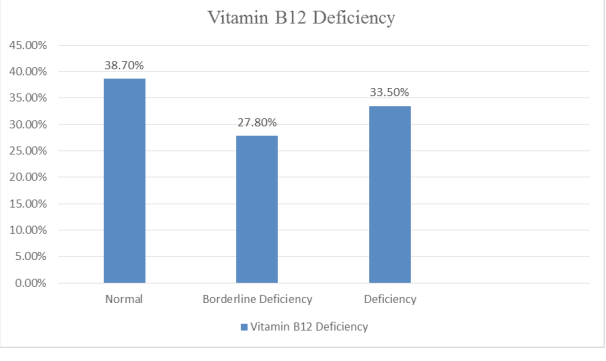

Figure 1. Prevalence of vitamin B12 deficiency and borderline deficiency.

Table 2 illustrates the distribution of vitamin B12 levels in male and females.

As B12 values in male and female was not normally distributed median values were calculated. The median levels of vitamin B12 were significantly different between the sexes, with males having lower level of 171.9 pmol/L compared to females having 186.7 pmol/L (P=0.046). There was not significant difference between different categories of vitamin B12 deficiency and gender (p value = 0.08).

Table 2. Vitamin B12 deficiency by gender.

Vitamin B12 level	Gender		P-value
	Female, n=959	Male, n=495	
Normal	377 (39.3%)	185 (37.4%)	0.086*
Borderline	279 (29.1%)	126 (25.4%)	
Deficiency	303 (31.6%)	184(37.2%)	
Vitamin B12, Median (pmol/L)	186.7	171.9	<0.046#

*Pearson chi-square #Man Whitney U test

Table 3 presents the prevalence of vitamin B12 by age groups of the participants.

Pearson chi square revealed statistical significance between age group and prevalence of vitamin B12 deficiency (P<0.001).Compared to middle aged adults and elderly individuals, young adults showed significantly higher levels of vitamin B12 deficiency (38.6%) and borderline deficiency (33.3%). The Kruskal Wallis H test revealed significance between the age group and their median serum vitamin B12 levels(p<0.01).

Table 3. Vitamin B12 deficiency by age.

Vitamin B12 Level	Age			p-value
	Young Adults n=647	Middle Aged Adults n=544	Old, n=263	
Normal	195 (30.1%)	223 (41.0%)	144 (54.8%)	<0.001*
Borderline	216 (33.4%)	137 (25.2%)	52 (19.8%)	
Deficiency	236 (36.5%)	184 (33.8%)	67 (25.5%)	
Vitamin B12, Median (pmol/L)	170.4	183.7	247.9	<0.001#

*Pearson Chi square # Kruskal Wallis H test

DISCUSSION

In this study we assessed the prevalence of vitamin B12 deficiency and insufficiency among adults and elderly visiting tertiary care hospital of Nepal using WHO defined reference range.

We observed that overall prevalence of Vitamin B12 deficiency in our study was 33.5% and borderline deficiency of 27.8%. The prevalence of Vitamin B12 deficiency was significantly higher among young than middle aged and lowest in old age. In addition, we report a higher prevalence of vitamin-B12 deficiency and insufficiency in men and women respectively in all age groups.

Vitamin B12 deficiency leads to hematological, neuropsychiatric and gastric neoplastic manifestations.[2] Serum total vitamin B12 remains the first line test to confirm the status of Vitamin B12 in the body.[10] A study from South Indian urban parts reports overall deficiency (35%) and borderline deficiency(36%) of vitamin B12.[4] The vegetarian diet may play part in such deficiency in India and Nepal. This concurs with the findings of Paudel et al. from Nepal, which reported high vitamin B12 deficiency (56%) among vegetarians.[11] Accordingly, in India significant proportion of vitamin deficiency was found in vegetarian population.[12] Additionally, Nepalese meals are high in carbohydrates and low in meat and dairy, which exposes the population to micronutrient deficiencies, including vitamin B12.[13] Foods of animal origin such as meat, fish, or dairy provide the majority of vitamin B12 synthesized by microbes.[10] Deficit of vitamin B12 is more likely to occur in people who follow a strict vegetarian diet.[14] Vitamin B12 deficiency is multifactorial resulting from various causes such as gastric(H pylori infection, gastric surgeries) nutritional(inadequate intake, vegetarian diet) and drug(proton pump inhibitors, metformin) etc.[10] Malla et al. found that 50.95% of patient under metformin therapy were deficient in total Vitamin B12 in Nepal.[15] Inadequate intake(vegetarian diet) and food cobalamin malabsorption(atrophic gastritis, pernicious anemia) are major cause among the elderly.[16] Low levels of vitamin B12 was found among a 55% of healthy vegetarian population of elderly in Nepal.[11] There is a need of further studies to identify the risk factors associated with vitamin B12 deficiency in adults and elderly Nepalese population.

An important percentage of adults and the elderly (19.8%) have borderline deficiencies defined as 148-221 pmol/L in our study. Notably high prevalence of marginal deficiencies has been found in United States

and various countries from South America, Africa and Asia.[2] Vitamin B12 deficiency progress through a stage characterized by cellular deficiency in absence of sign and symptoms called as subclinical vitamin B12 deficiency.[9] Marginal deficiency has been described at the total B12 concentration between 148- 221pmol/L.[2] Hence vitamin B12 ranges between 148-221 pmol/L has to properly investigated to identify risk factors and instigate appropriate management.

Variations in prevalence of vitamin B12 deficiency within age groups have been observed.[1] Among the findings of our study, we also found that a higher proportion young(36.5%) and middle-aged(33.8%) adults were deficient in vitamin B12 as compared to the elderly (25.5%). The results are consistent with those from the urban part of South India, which also reports higher vitamin B12 deficiency in the 21-40 (44%) and 41-60 age groups (40%) when compared with the >60 group (30%).[4] Among Costa Rican adults between the ages of 20-30, vitamin B12 deficiency and insufficiency was found to be 11.6% and 24.4% respectively, while adults aged 30-40 had vitamin B12 deficiency of 11% and vitamin B12 insufficiency of 36%.[17]

The dietary intake of Vitamin B12 was not assessed in our study. However, one study from Nepal conducted in the similar setting as ours, reports high intake of mixed food(lentil fruits, vegetables, fatty food, noodle tea, coffee), fast food(fast food, sweet and soda), refine grain- meat-alcohol food pattern among young adult.[18] Hence the higher proportion of deficiency of vitamin B12 could be attributed to such dietary indulgence among young adults compared to older adults in our population. Food pattern rich in animal protein such as meat and fish is positively associated with serum vitamin B12.[19] Additional investigations are needed to determine the dietary and other risk factor for vitamin B12 deficiency among various age group.

In contrast with our findings, an increasing trend of vitamin B12 deficiency with age has been observed in the United States of at least 3% , 4% , and 6% of those aged 20–39, 40–59 years, and > 60 years old.[6] The prevalence among elderly varies from 5-40% based on the cut-off value selected.[16] National survey from various countries indicated the prevalence of vitamin-B12 deficiency as 2.7 % in United States, 12.0% in New Zealand and 31.0% in United Kingdom at cut-off of <150 pmol/L among elderly.[1] Accordingly, in our study when the deficiency cutoff of <148 pmol/L is applied, the proportion of elderly deficient in vitamin B12 was 26.5%. Utilizing <150pmol/L as a single cutoff value significantly underestimates the true prevalence of vitamin B12 deficiency.[20] Vitamin-B12 levels far above 150 pmol/L appear to be associated with neurological symptoms.[20] Furthermore, cellular cobalamin deficiency at serum vitamin B_{12} levels >148pmol/L as indicated by elevated serum methylmalonic acid (MMA) has been observed.[6] The elderly suffer from a variety of clinical symptoms that are not easily distinguishable from those of normal aging.[21] New research has linked vitamin B12 deficiency to cognitive deficit and dementia[22]. Consequently, for greater sensitivity when screening for vitamin-B12 deficiency, a cut-off value close to 221pmol/l is recommended.[20] When the cut-off of 221pmol/L was used, a further increase in the prevalence of vitamin-B12 insufficiency by 20.5% was observed in our study. Hence assessment of vitamin B12 deficiency should incorporate wide reference range in order to identify marginal deficiencies.

Our study found out vitamin-B12 deficiency of 37.2% and 31.6% and insufficiency of 25.4% and 29.1% in male and female respectively. The median Vitamin B12 levels was significantly different for male (171.9 pmol/L) and female (186.7 pmol/L) respectively. In an Indian study, 44 % of men and 29 % of women had low levels of serum vitamin B12.[4] Whereas 8% of men and 13% of women in Bangladesh were found to be vitamin B12 deficient.[23]. Similar to our study a significantly lower vitamin B12 level was observed among male than in female (537.0±222.0 vs. 664.1±309.8 ng/mL) in a study from Korea.[24] Women are more likely to have vitamin B12 than men because of physiological conditions such as pregnancy and lactation.[25] On the contrary, in a large cohort study from Isarel found higher susceptibility among men than women suggesting the role of genetics.[26] Future studies should aim at identifying the cause of Vitamin B12 deficiency according to gender.

Finally a number of important limitations have to be considered. The major limitation of our study is the retrospective nature of data which incorporates serum total vitamin B12 as a sole marker for assessment of vitamin B12 deficiency. The dietary history, use of supplement and clinical characteristics and were not determined in our study. The diagnostic value of Vitamin B12 as a lone marker is limited by the fact that a low level of serum vitamin B12 is not necessarily indicative of deficiency and deficiency can be present despite the normal or high level of vitamin B12.The functional deficiency of Vitamin B12 was not assessed using more sensitive markers such as MMA, holotranscobalamin and homocysteine.

CONCLUSIONS

The present study has shown a significant proportion of vitamin B12 deficiency and borderline deficiency of public health concern among young, middle aged adults and elderly visiting a tertiary care hospital in Nepal. Future studies directed at identifying age and gender specific risk factors and identification of concurrent functional B12 deficiency using additional sensitive bio-markers such as MMA, homocysteine and holotranscobalamin are advised.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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