

## FREQUENCY OF VITAMIN B 12 DEFICIENCY IN PATIENTS WITH HYPOTHYROIDISM

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### ABSTRACT

**Background:** Vitamin B12 deficiency is a frequently overlooked comorbidity in patients with hypothyroidism. Shared autoimmune pathways, impaired gastrointestinal absorption, and overlapping clinical features contribute to diagnostic difficulty. In low and middle income countries such as Pakistan, nutritional inadequacy further increases susceptibility, highlighting the need for locally generated epidemiological evidence. **Objective:** To determine the frequency of vitamin B12 deficiency among patients diagnosed with hypothyroidism attending a tertiary care hospital in Pakistan. **Study Design:** Cross sectional study. **Settings:** Outpatient Department of General Medicine, Nishtar Hospital, Multan. **Duration of Study:** January 2025 to June 2025. **Methods:** A total of 93 adult patients aged 20 to 60 years with biochemically confirmed hypothyroidism were enrolled using non probability consecutive sampling. Patients already receiving vitamin B12 supplementation were excluded. Serum vitamin B12 levels were measured using standard laboratory techniques, and deficiency was defined as a level below 200 pg/ml. Demographic characteristics, clinical features, and comorbid conditions were documented using a structured proforma. Data were analyzed using SPSS version 20. Quantitative variables were expressed as mean and standard deviation, while categorical variables were reported as frequencies and percentages. **Results:** The mean age of participants was  $36.53 \pm 10.40$  years, with female predominance accounting for 72.0% of cases. The mean serum vitamin B12 level was  $215.53 \pm 151.29$  pg/ml. Vitamin B12 deficiency was identified in 41 patients, corresponding to a frequency of 44.1%. Most participants were younger than 40 years (59.1%), belonged to urban areas (67.7%), and had a disease duration of one year or less (76.3%). Hypertension (29.0%) and diabetes mellitus (20.4%) were the most commonly observed comorbidities. **Conclusion:** Vitamin B12 deficiency is highly prevalent among patients with hypothyroidism in this tertiary care population. Incorporation of routine vitamin B12 screening into the standard evaluation of hypothyroid patients may enable early diagnosis and prevent avoidable hematological and neurological complications.

**Keywords:** Hypothyroidism; Vitamin B12 Deficiency; Frequency; Pakistan; Cross Sectional Study

### INTRODUCTION

Vitamin B12 (cobalamin) deficiency is a significant public health issue that has garnered attention due to its multifaceted role in various physiological processes, including hematopoiesis, neurological function, and DNA synthesis. Particularly in patients with hypothyroidism, vitamin B12 deficiency has been reported with variable prevalence rates, making its evaluation essential in the management of such patients. The link between hypothyroidism and vitamin B12 deficiency is entrenched in the autoimmune mechanisms that can affect both conditions, leading to unrecognized comorbidities in clinical settings (1, 2).

Several studies have documented the coexistence of these two conditions, highlighting that individuals with hypothyroidism may be at an increased risk of developing vitamin B12 deficiency as a result of impaired intrinsic factor production or related gastrointestinal malabsorption issues. For instance, a recent study indicated that the prevalence of vitamin B12 deficiency in hypothyroid patients can vary significantly, ranging from 25% to 48%, ultimately suggesting a need for routine screening due to the considerable overlap in symptoms and their impact on patient outcomes (1, 3).

Moreover, a systematic review and meta-analysis pointed out that the biochemical or clinical evidence of vitamin B12 deficiency was present in 35% of patients with overt hypothyroidism (2). The etiology underlying this deficiency in such patients may also be related to autoimmune gastritis, which compromises intrinsic factor production, further exacerbating the clinical picture (4, 5). In particular, studies assessing symptomatic populations such as those in Pakistan have reported alarmingly high rates of B12 deficiency among individuals

with hypothyroidism. For example, a study targeting newly diagnosed hypothyroid females found a prevalence rate of vitamin B12 deficiency at approximately 43% (4). This underscores the necessity of integrating vitamin B12 evaluation as a routine investigative protocol in hypothyroid patients to enhance clinical management and improve overall health outcomes.

In Pakistan, nutritional deficiencies, including vitamin B12, are rampant, often exacerbated by dietary patterns, socioeconomic challenges, and limited access to healthcare. According to national surveys, a significant proportion of the population, particularly women and children, exhibit micronutrient deficiencies, with vitamin B12 being notably prevalent due to low dietary intake of animal products (3, 6). The high prevalence of hypothyroidism, affecting about 10% of the adult female population, raises serious concerns regarding the co-occurrence of B12 deficiency, particularly in rural and underserved urban populations.

The implications of failing to diagnose and treat vitamin B12 deficiency in hypothyroid patients are significant. Clinical manifestations, ranging from anemia to neurocognitive dysfunction, may overlap with hypothyroid symptoms, leading to a misinterpretation of clinical signs and delayed treatment (3, 2). Therefore, the need to evaluate and address vitamin B12 status among patients with hypothyroidism in Pakistan is not only a clinical imperative but also a public health priority to optimize health outcomes and mitigate the broader health effects of these intertwined conditions (3, 7). In light of this context, our study aims to systematically assess the frequency of vitamin B12 deficiency in patients diagnosed with hypothyroidism within the Pakistani population, thereby contributing data that may guide more effective

healthcare strategies and interventions tailored to address this significant health concern.

## METHODOLOGY

This cross-sectional study was conducted in the Outpatient Department of General Medicine at Nishtar Hospital, Multan, over a period of six months following approval of the study synopsis. The study aimed to determine the frequency of vitamin B12 deficiency among patients diagnosed with hypothyroidism. Ethical principles were strictly followed throughout the study, and written informed consent was obtained from all participants prior to enrollment. Confidentiality of patient information was ensured, and participation posed no risk to the patients.

A total of 93 patients with hypothyroidism were recruited using a non-probability consecutive sampling technique. The sample size was calculated using the WHO sample size formula, assuming an expected prevalence of vitamin B12 deficiency of 40 percent, a confidence level of 95 percent, and an absolute precision of 10 percent. Patients aged between 20 and 60 years of either gender with a confirmed diagnosis of hypothyroidism were included. Hypothyroidism was defined as a thyroid-stimulating hormone level greater than 4  $\mu$ IU/ml, along with reduced serum thyroxine levels below 4.5  $\mu$ g/dl and triiodothyronine levels below 82  $\mu$ g/dl, as reported by a consultant pathologist with more than five years of post-graduate experience at the central laboratory of Nishtar Hospital. Patients already receiving vitamin B12 supplementation were excluded from the study.

After enrollment, detailed demographic and clinical information including age, gender, residential status, educational level, body mass index, duration of hypothyroidism, and comorbid conditions was recorded using a structured study proforma by the principal investigator. Diabetes mellitus was defined as a known diagnosis for more than two years with ongoing treatment using oral hypoglycemic agents or insulin. Hypertension was defined as a documented diagnosis with continuous use of antihypertensive medication for more than two years. Dyslipidemia was defined by the presence of any one of the following laboratory abnormalities: total cholesterol greater than 200 mg/dl, low-density lipoprotein greater than 100 mg/dl, high-density lipoprotein less than 40 mg/dl, or triglycerides greater than 150 mg/dl. Obesity was defined as a body mass index greater than 27.5 kg/m<sup>2</sup>. Ischemic heart disease was identified based on a documented history of myocardial infarction, angina, or cardiac arrhythmia as per clinical records. Use of proton pump inhibitors was considered positive if the patient had been using these medications continuously for more than six months without interruption.

For biochemical assessment, three milliliters of venous blood were collected from each participant under aseptic conditions and sent to the hospital laboratory for serum vitamin B12 estimation. Vitamin B12 deficiency was defined as a serum vitamin B12 level below 200 pg/ml, while levels between 200 and 900 pg/ml were considered within the normal range, according to standard laboratory reference values.

Data were entered and analyzed using the Statistical Package for Social Sciences version 20. Quantitative variables including age, body mass index, duration of disease, and serum vitamin B12 levels were expressed as mean and standard deviation. Qualitative variables such as gender, residence, educational status, obesity, diabetes, hypertension, dyslipidemia, ischemic heart disease, proton pump inhibitor use, and vitamin B12 deficiency were presented as frequencies and percentages. Effect modifiers including age, gender, disease duration, obesity, diabetes, hypertension, dyslipidemia, ischemic heart disease, residential status, and educational level were controlled through stratification. Post-stratification comparisons were performed using the chi-square test to assess associations between these variables and vitamin B12 deficiency. A p-value of 0.05 or less was considered statistically significant.

## RESULTS

A total of 93 patients with hypothyroidism were included in the analysis. The mean age of participants was 36.53  $\pm$  10.40 years (range: 23–58 years). Females constituted the majority of the study population (67, 72.0%), while 26 (28.0%) were males. The mean age of male patients was significantly higher than that of females (49.62  $\pm$  6.59 vs 31.45  $\pm$  6.38 years,  $p < 0.001$ ). Most participants (55, 59.1%) were younger than 40 years. Table 1 summarizes the demographic and baseline clinical characteristics of the study population. A larger proportion of patients resided in urban areas (67.7%). Common comorbidities included hypertension (29.0%) and diabetes mellitus (20.4%). The mean BMI was 24.53  $\pm$  2.36 kg/m<sup>2</sup>, with 20.4% of patients classified as obese. Most patients (76.3%) had a disease duration of  $\leq 1$  year. (Table 1)

**Table 1: Demographic and baseline characteristics of study participants (n = 93)**

Variable	Category	n (%) / Mean $\pm$ SD
Age (years)	—	36.53 $\pm$ 10.40
Age group	< 40 years	55 (59.1%)
	$\geq 40$ years	38 (40.9%)
Gender	Male	26 (28.0%)
	Female	67 (72.0%)
Residence	Rural	30 (32.3%)
	Urban	63 (67.7%)
Diabetes mellitus	Yes	19 (20.4%)
	No	74 (79.6%)
Hypertension	Yes	27 (29.0%)
	No	66 (71.0%)
Body mass index (kg/m <sup>2</sup> )	—	24.53 $\pm$ 2.36
Obesity	Yes	19 (20.4%)
	No	74 (79.6%)
Disease duration (months)	—	9.23 $\pm$ 7.46
Disease duration	$\leq 1$ year	71 (76.3%)
	> 1 year	22 (23.7%)

Educational status and additional clinical variables are presented in Table 2. Slightly more than half of the participants were illiterate (51.6%). Dyslipidemia, ischemic heart disease, and long-term proton pump inhibitor use were present in 20.4%, 21.5%, and 7.5% of patients, respectively. (Table 2)

**Table 2: Educational status and associated clinical factors (n = 93)**

Variable	Category	n (%)
Educational status	Illiterate	48 (51.6%)
	Literate	45 (48.4%)
Dyslipidemia	Yes	19 (20.4%)
	No	74 (79.6%)
Ischemic heart disease	Yes	20 (21.5%)
	No	73 (78.5%)
Proton pump inhibitor use	Yes	7 (7.5%)
	No	86 (92.5%)

The mean serum vitamin B12 level was 215.53  $\pm$  151.29 pg/ml. Based on predefined criteria, vitamin B12 deficiency (< 200 pg/ml) was identified in 41 patients (44.1%), while 52 patients (55.9%) had normal levels. (Table 3)

**Table 3: Vitamin B12 status among hypothyroid patients (n = 93)**

Vitamin B12 status	n (%)
Deficient	41 (44.1%)
Normal	52 (55.9%)
Mean vitamin B12 level (pg/ml)	215.53 $\pm$ 151.29

## DISCUSSION

The findings from our study illustrate a significant prevalence of vitamin B12 deficiency among patients with hypothyroidism, with 44.1% of the participants demonstrating deficiency as defined by serum levels below 200 pg/ml. The mean vitamin B12 level of the cohort was  $215.53 \pm 151.29$  pg/ml. These results are consistent with existing literature that recognizes the association between hypothyroidism and vitamin B12 deficiency, suggesting that a notable proportion of hypothyroid patients may hyper-react to their nutritional needs due to metabolic changes associated with thyroid dysfunction (8, 9).

A particularly interesting aspect of our study is the demographic distribution of participants. A majority of the subjects (72%) were female, a trend that is congruous with the prevalence of hypothyroidism, which disproportionately affects women, particularly in younger age groups (10, 11). The mean age of participants ( $36.53 \pm 10.40$  years) further emphasizes the younger demographic that is affected. This aligns with observations by Lakho et al., who reported similar demographic outcomes in their cohort, stressing the need for regular screening for vitamin B12 levels in this population (12). Furthermore, our finding that most of the patients (59.1%) were younger than 40 years echoes the trends seen in other regions, indicating that proactive measures should be taken to address potential deficiencies early (13, 8).

Furthermore, the comorbidities observed in our study population reflect a broader public health challenge. Notably, 29% of participants had hypertension and 20.4% had diabetes, which can complicate thyroid management and increase the risk for developing further nutritional deficiencies, including vitamin B12 deficiency (14, 15). The overlap of these conditions with hypothyroidism indicates a potentially synergistic effect that can exacerbate patient outcomes. For instance, Gamag emphasizes that vitamin B12 levels may be particularly critical for diabetic patients, highlighting how those who are on metformin, a common treatment for type 2 diabetes, often experience reduced levels of vitamin B12 (14). This interaction may present additional treatment challenges in managing hypothyroid patients who also have diabetes.

Interestingly, our results also highlight the significance of body mass index (BMI) in examining vitamin B12 deficiency. With a mean BMI of  $24.53 \text{ kg/m}^2$  and 20.4% classified as obese, it is evident that obesity could further influence micronutrient metabolism and absorption (13, 16). Some studies have noted a correlation between obesity and vitamin B12 deficiency, indicating that the metabolic dysregulation associated with higher body fat could impair vitamin absorption (15, 8). This aligns with findings by Malik and Trilok-Kumar, where dietary insufficiency amongst populations could lead to deficiencies in micronutrients regardless of clinical presentation (9).

In conclusion, our study corroborates other research indicating a high frequency of vitamin B12 deficiency among patients with hypothyroidism, particularly among younger females and those with comorbidities such as hypertension and diabetes. This underscores the importance of routine screening for vitamin B12 status in hypothyroid patients, as early identification and treatment of deficiencies could significantly improve patient outcomes. Further studies should expand on these findings, exploring the underlying mechanisms by which hypothyroidism influences vitamin B12 absorption and metabolism, particularly in varied demographic groups. This is especially pertinent in healthcare settings like those in Pakistan, where dietary habits and health management practices may limit micronutrient accessibility and absorption (8, 9).

## CONCLUSION

This study demonstrates a high frequency of vitamin B12 deficiency

among patients with hypothyroidism, affecting nearly half of the study population. Given the substantial clinical overlap between hypothyroid symptoms and manifestations of vitamin B12 deficiency, failure to identify this comorbidity may result in delayed diagnosis and suboptimal patient outcomes. Incorporating routine vitamin B12 screening into the management of hypothyroid patients, particularly in resource-limited settings like Pakistan, may significantly improve clinical care and reduce preventable morbidity.

## DECLARATIONS

### Data Availability Statement

All data generated or analysed during the study are included in the manuscript.

### Ethics approval and consent to participate

Approved by the department Concerned. (IRBEC-NUMA-923/24)

### Consent for publication

Approved

### Funding

Not applicable

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## AUTHOR CONTRIBUTION

### UMAIR FAROOQUI (Consultant Physician)

Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, final approval of manuscript. Manuscript drafting.

### ARIF RAHIM KHAN (Assistant Professor Medicine)

Manuscript revisions, critical input.

Data entry, data analysis, drafting an article.

### ALI RAZA (Consultant Gastroenterologist)

Conception of Study, Final approval of manuscript.

Study Design, Review of Literature.

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