

Prevalence of Vitamin B12 Deficiency in Hypothyroid Patients

Muhammad Siddique, Muhammad Akhtar Parvez, Humaira Zafar, Awais Mustafa, Anam Shafi

ABSTRACT

Background: There is controversial data regarding prevalence of vitamin B12 deficiency in hypothyroid patients. **Objective:** The objective of the study was to determine the prevalence of vitamin B12 deficiency in hypothyroid patients. **Study design:** Cross sectional Survey. **Setting:** The study was conducted at Medicine / Endocrinology department Services Hospital Lahore. **Period:** Study was completed in six months from 26th February to 25th August 2015. **Methodology:** 225 hypothyroid patients from IPD & OPD with age range of 30-70 years of either sex willing to participate in study were included in study. Estimation of serum vitamin B12 was carried out. Cutoff value for vitamin B12 was taken <148 pmol/L. **Results:** 225 patients were included in our sampled population with mean age 47.15 ± 7.210 ranging from 40 to 66 years of age. 103 patients (45.8%) were female and rest of 122 (54.2%) were males. In our study 54 patients (24%) had Vitamin B12 Deficiency and rest of 171 (76%) showed negative results. Female gender, malnutrition, lower BMI and socioeconomic status were risk factors linked with vitamin B12 deficiency. While age was not among the risk factors. **Conclusion:** It is concluded that prevalence of vitamin B12 deficiency is high 24% in Pakistani patients with hypothyroidism. Female patients with malnutrition and lower BMI should be screened periodically to reduce the complications associated with vitamin B12 deficiency.

Keywords: Hypothyroidism, Vitamin B12 deficiency, Anemia, Pernicious Anemia, Cobalamin deficiency, Fatigue

Corresponding Author

Dr. Muhammad Akhtar Parvez

Assistant Professor, Community Medicine,
Punjab Medical College, Faisalabad

Contact: +92 324-7629005

Email: dr_akhtar@hotmail.com

Submitted for Publication: 31-07-2017

Accepted for Publication: 27-08-2017

Article Citation: Siddique M, Parvez MA, Zafar H, Mustafa A, Shafi A. Prevalence of Vitamin B12 Deficiency in Hypothyroid Patients. APMC 2017;11(3):252-256.

INTRODUCTION

The most prevalent endocrine disorder in developing countries is related to thyroid imbalance. Hypothyroidism is a common endocrine disorder with reduced production of thyroid hormones. It is a common disease with different frequency between countries. It occurs in 10% of women and 6% of men with age >65 years.^{1,2} However, the common occurrence of hypothyroidism was three times more in women than in men (12.4% versus 3.7%) in developing countries like Spain.³ Sex, geographical factors, age, ethnicity and iodine consumption are the determining factors for the occurrence of thyroid problems.^{1,2} In Pakistan prevalence of B12 deficiency in hypothyroid patients is ~ 40%.⁴ Out of total patients of hypothyroidism, about 12% with primary autoimmune type disease experience pernicious anemia.^{5,6} In hypothyroidism vitamin B12 deficiency is observed in up to 40% of patients.⁴ However few reports showed deviation as the adult patients of hypothyroidism showed no signs of microcytic and pernicious anemia.^{5,6}

Inadequate intake or improper intestinal absorption due to sluggish bowel motility, bacterial overgrowth, bowel wall oedema and the use of drugs including proton-pump inhibitors, H2 receptor antagonists or

metformin aid in the vitamin B12 deficiency in such patients.⁶⁻⁸

Patients with deficiency of vitamin B12 and hypothyroidism usually have symptoms of fatigue, weakness, poor memory retention, itching and loss of sensation.^{6,9} The clinical symptoms of vitamin B12 deficiency remain dormant for a longer period in the patients which makes the diagnosis difficult. Hematological or neuropsychiatric symptoms may serve as early indicators of deficiency but many non-specific complaints are attributed to aging but the study is seen years old.

Although macrocytosis might occur with frequency in patients with thyroid disorders, there is controversial information on the metabolic relationship between thyroid stimulating hormone and B12 in the general population. People suffering from hypothyroidism are advised thyroid hormone replacement. However, even with the replacement therapy, some patients do not fully recover from the symptoms due to the deficiency of vitamin B12. Therefore, why this study was designed to find out the vitamin B12 deficiency in hypothyroid patients.

METHODOLOGY

Setting: Department of Medicine / Endocrinology department Services Hospital, Lahore.

Period: Six months from 26th February to 25th August 2015

Study design: Cross sectional study.

Sample size: Sample size of 225 was calculated using 40% prevalence rate, 7% margin of error, using 95% confidence interval.

Sampling technique: Non-probability convenient sampling.

Inclusion criteria

- All hypothyroid patients from IPD & OPD with age range of 30-70 years of either sex willing to participate in study and meeting criteria set by operational definition were included in this study.

Exclusion criteria

- Not giving consent to participate in study.
- Patient with congenital or familial thyroid disorders
- Patient with depression or obesity.
- Patients having other co-morbid conditions like cerebrovascular and neurological diseases, pregnancy chronic renal impairment, ischemic heart disease, and diabetes mellitus, (these conditions were properly investigated by history, examination & on laboratory investigation record).
- Already diagnosed cases of hypothyroidism on thyroxine.

Data Collection Procedure

225 patients of medical /Endocrinology department of Services Hospital Lahore were part of the study in accordance with the inclusion and exclusion criteria. Informed consent was taken from every patient. The history of each patient was recorded by physical examination and questionnaire. All the relevant investigations were estimated. Estimation of serum vitamin B12 was carried out by means of Immulite 1000 analyser and vitamin B12 level was labelled as per operational definition.

About 5.0 ml blood sample was taken from patients, centrifuged and serum was stored at -20°C until use. Hemolyzed samples were rejected.

Data Analysis

Data was analyzed by SPSS version 20. Mean \pm SD was calculated for age and biochemical parameters including serum vitamin B12. Frequency and percentage was calculated for given vitamin B12 deficiency for qualitative analysis. Data was arranged for age, gender, BMI, nutritional status, socioeconomic status to deal with effect modifiers. Post stratification chi -square test was used. A p value \leq 0.05 was considered significant.

RESULTS

225 patients were included in our sampled population with mean age 47.15 ± 7.210 ranged from 40 to 66 years of age. (Table 1)

161 patients (71.6%) were below 50 years of age and remaining 64 (28.4%) were 50 years or above in age. (Table 2)

Table 1: Age distribution of sampled population

	N	Minimum	Maximum	Mean	Std. Deviation
Age (years)	225	40	66	47.15	7.210

Table 2: Frequency distribution of sampled population by Age groups

Age Group	Frequency	Percent
Below 50 Years	161	71.6
50 Years & above	64	28.4
Total	225	100.0

103 patients (45.8%) were female and rest of 122 (54.2%) were males. (Table 3)

54 patients (24%) had Vitamin B12 Deficiency and rest of 171 (76%) showed negative results. (Table 4)

Table 3: Frequency distribution of sampled population by gender

Gender	Frequency	Percent
Male	103	45.8
Female	122	54.2
Total	225	100.0

Table 4: Frequency distribution of sampled population by Vitamin B12 Deficiency

	Frequency	Percent
No	171	76.0
Yes	54	24.0
Total	225	100.0

Body mass index of 15 patients (6.7%) was below 24.9 kg/m^2 however only 210 patients (93.3%) had body mass index above 24.9 kg/m^2 (Table 5).

In our study population 72 patients (32.0%) were having monthly income below 10000, 69 patients (30.7%) had monthly income between 10000 to 15000 and remaining 84 (37.3%) had more than 50000 per month. (Table 6)

Table 5: Frequency distribution of sampled population by body mass index < 24.9 Kg/m²

BMI <24.9 kg/m ²	Frequency	Percent
No	210	93.3
Yes	15	6.7
Total	225	100.0

Table 6: Frequency distribution of sampled population by socioeconomic status

	Frequency	Percent
<10000 /month	72	32.0
10000- 50000 /month	69	30.7
More than 50000/month	84	37.3
Total	225	100.0

73 patients (32.4%) of sampled population were presented with malnutrition. (Table 7)

When we cross tabulated gender with vitamin B12 deficiency, among 54 patients with vitamin B12 deficiency 40 patients were female and remaining 14 patients were male. When Pearson chi square test was applied, results were statistically significant with p-value 0.001 (Table 8).

Table 7: Frequency distribution of sampled population by malnutrition

Malnutrition	Frequency	Percent
No	152	67.6
Yes	73	32.4
Total	225	100.0

Table 8: Sex and vitamin B12 deficiency

			Vitamin B12 Deficiency		Total
			No	Yes	
Sex	Female	Count	82	40	122
		% within Sex	67.2%	32.8%	100.0%
	Male	Count	89	14	103
		% within Sex	86.4%	13.6%	100.0%
Total		Count	171	54	225
		% within Sex	76.0%	24.0%	100.0%

Pearson chi square test = .001 (significant)

On cross tabulating body mass index <24.9kg/m² and Vitamin B12 Deficiency, results were significant (p=0.001). All of the 15 patients had BMI below 24.9kg/m² found with Vitamin B12 Deficiency whereas in patients with BMI above 24.9kg/m², 39 had Vitamin B12 Deficiency (Table 9).

When we cross tabulated socioeconomic status with vitamin B12 deficiency, it showed statistically significant results (p=0.016). As we move from high socioeconomic status to poor, frequency of patients with vitamin B12 Deficiency decreased. (Table 10) Cross tabulation between age group and Vitamin B12 Deficiency showed up with statistically non-significant results (p=0.245). Among 64 patients with age above 50 years, only 12 were having Vitamin B12 Deficiency however out of 119 patients with age below 50 years, 42 patients were showed up with Vitamin B12 Deficiency. (Table 11)

Table 9: Cross tabulation between body mass index < 24.9kg/m² & vitamin B12 deficiency

			Vitamin B12 Deficiency		Total
			No	Yes	
Body mass index < 24.9kg/m ²	Yes	Count	0	15	15
		% within Body mass index < 24.9kg/m ²	0.0%	100.0%	100.0%
	No	Count	171	39	210
		% within Body mass index < 24.9kg/m ²	81.4%	18.6%	100.0%

Pearson chi square test = 0.001 (significant)

Table 10: Cross tabulation between socioeconomic status & vitamin B12 deficiency

			Vitamin B12 Deficiency	
			No	Yes
Socioeconomic Status	More than 50000/month	Count	55	29
		%	65.5%	34.5%
	10000- 50000 /month	Count	56	13
		%	81.2%	18.8%
< 10000 /month	Count	60	12	
	%	83.3%	16.7%	
Total		Count	171	54
		%	76.0%	24.0%

Pearson chi square test = .016(significant)

Table 11: Age groups & vitamin B12 deficiency

			Vitamin B12 Deficiency		Total
			No	Yes	
Age groups	50 Years & above	Count	52	12	64
		%	81.3%	18.8%	100.0%
	Below 50 Years	Count	119	42	161
		%	73.9%	26.1%	100.0%
Total		Count	171	54	225
		%	76.0%	24.0%	100.0%

Pearson chi square test = .245 (non-significant)

When we cross tabulated malnutrition with Vitamin B12 Deficiency, among 73 patients with malnutrition 32 were having vitamin B12 deficiency. Results were statistically significant with p value 0.01. (Table 12)

Table 12: Cross tabulation between malnutrition & vitamin B12 deficiency

			Vitamin B12 Deficiency		Total
			No	Yes	
Malnutrition	Yes	Count	41	32	73
		% within Malnutrition	56.2%	43.8%	100.0%
	No	Count	130	22	152
		% within Malnutrition	85.5%	14.5%	100.0%
Total		Count	171	54	225
		% within Malnutrition	76.0%	24.0%	100.0%

Pearson chi square test, p value = 0.001 (significant)

DISCUSSION

Hypothyroidism is a common endocrine disorder with reduced production of thyroid hormones. It is a common disease with varying frequency between countries. It occurs in 10% of women and 6% of men with age > 65 years.^{1,2} Sex, geographical factors, age, ethnicity and iodine consumption are the determining factors for the occurrence of thyroid problems.

In our study, 54 patients (24%) were found to have Vitamin B12 Deficiency. This result is lower than reported by previous studies. In a previous study, reported prevalence of B12 deficiency in hypothyroid patients was about 40%.⁴ the reason for difference may be changing dietary habits and consecutive sampling from a tertiary care hospital.

103 patients (45.8%) were female and rest of 122 (54.2%) were males. When we cross tabulated gender with vitamin B12 deficiency, among 54 patients with vitamin B12 deficiency 40 patients were female and remaining 14 patients were male. When we applied Pearson chi square test, results were statistically significant with p-value 0.001. It implies that there is difference in frequency of vitamin B12 deficiency among male and female patients with hypothyroidism. Female population was more prone to develop vitamin B12 deficiency. 225 patients were included in sampled population with mean age 47.15 ± 7.210 ranged from 40 to 66 years of age. 161 patients (71.6%) were below 50 years of age and remaining 64 (28.4%) were 50 years or above in age. It implies that hypothyroidism is a disease of young and productive span of life. Cross tabulation between age group and Vitamin B12 Deficiency showed up with statistically non-

significant results ($p=0.245$). Among 64 patients with age above 50 years, only 12 were having Vitamin B12 Deficiency however out of 119 patients with age below 50 years, 42 patients were showed up with Vitamin B12 Deficiency. It implies that age does not predict development of vitamin B12 deficiency in hypothyroid patients.

When we cross tabulated socioeconomic status with vitamin B12 deficiency, it showed statistically significant results ($p=0.016$). As we move from high socioeconomic status to poor, frequency of patients with vitamin B12 Deficiency decreased. It indicates that patients with higher socioeconomic status are also at risk to develop vitamin B12 deficiency.

Body mass index of 15 patients (6.7%) was below 24.9 kg/m^2 however 210 patients (93.3%) had body mass index above 24.9 kg/m^2 . It implies that obesity is much more common among patients with hypothyroidism. On cross tabulating body mass index < 24.9 kg/m^2 and vitamin B12 deficiency, results were significant ($p=0.001$). All of the 15 patients had BMI below 24.9 Kg/m^2 found with vitamin B12 deficiency whereas in patients with BMI above 24.9 kg/m^2 , 39 had Vitamin B12 Deficiency. All non-obese were at risk of having vitamin B12 deficiency.

Cross tabulation between age group and Vitamin B12 Deficiency showed up with statistically non-significant results ($p=0.245$). Among 64 patients with age above 50 years, only 12 were having Vitamin B12 Deficiency however out of 119 patients with age below 50 years, 42 patients were showed up with vitamin B12 deficiency. As results were non-significant, it may be concluded that age is not associated with development of vitamin B12 deficiency at current sample size

CONCLUSION

It is concluded that Pakistani patients with hypothyroidism have a higher prevalence (24%) of vitamin B12 deficiency. Female gender, malnutrition, lower BMI and socioeconomic status are risk factors associated with vitamin B12 deficiency. At the current sample size age was not associated as factor affecting vitamin B12 deficiency.

Limitations of study include smaller sample size along with non-representative sample from a tertiary care hospital. Further studies should be encouraged in this regard.

REFERENCES

1. Vanderpump MP, Turnbridge WM. Epidemiology and prevention of clinical and subclinical hypothyroidism. *Thyroid*. 2002;12:839–47.

2. Das C, Sahana PK, Sengupta N, Giri D, Roy M, Mukhopadhyay P. Etiology HYPERLINK " Eastern India. Indian J Endocrinol Metab. 2012;16(2):361-3.
3. Mariscal. Prevalence and clinical characteristics of subclinical hypothyroidism in an opportunistic sample in the population of Castile-León (Spain). <http://www.ncbi.nlm.nih.gov/pubmed/25524153> Sanit 2014 Dec 15.
4. Jabbar A, Yawar A, Waseem S, Islam N, UI Haque N, Zuberi L, Khan A, Akhter J. Vitamin B12 deficiency common in primary hypothyroidism. J Pak Med Assoc 2008;58(5):258-61.
5. Dhamarajan TS, Norkus EP. Vitamin B12 deficiency in the elderly population based research. In Herbert V et al. Royal Society Med Press London 1999:27-34.
6. Snow CF. Laboratory diagnosis of vitamin B12 deficiency. Arch Inter Medicine 1999;159:1289-98.
7. Dharmarajan TS, Norkus EP. Approaches to vitamin B12 deficiency, early treatment may prevent devastating complications. Postgrad Med 2001;110(1):99-106.
8. Marcuard SP, Aibernaz L, Khazanie PG. Omeprazole therapy causes malabsorption of cyanocobalamin (vitamin B12). Ann Int Med 1994;120:211-5.
9. Green R, Kinsella LJ. Current concepts in diagnosis of cobalamin deficiency. Neurol 1995;45:435-40
10. Garber JR, Cobin RH, Gharib H, Hennessey JV, Klein I, Mechanick JI, Pessah-Pollack R, Singer PA, Woeber KA. American Association of Clinical Endocrinologists and the American Thyroid Association Taskforce on Hypothyroidism in Adults. "Clinical Practice Guidelines for Hypothyroidism in Adults". Thyroid 2012;22(12):1200–35.
11. Brabant G, Beck-Peccoz P, Jarzab B, Laurberg P, Orgiazzi J, Szabolcs I, Weetman AP, Wiersinga WM. Is there a need to redefine the upper normal limit of TSH? Eur J Endocrinol 2006;154(5):633-7.
12. Verkerk PH, Buitendijk SE, Verloove-Vanhorick SP. Congenital hypothyroidism screening and the cutoff for thyrotropin measurement: recommendations from The Netherlands. Am J Public Health 1993;83(6): 868-71.
13. Bailey RL, Carmel R, Green R, Pfeiffer CM, Cogswell ME, Osterloh JD et al. Monitoring of vitamin B-12 nutritional status in the United States by using plasma methylmalonic acid and serum vitamin B-12. Am J Clin Nutr 2011;94:2552-561.
14. Tunbridge WM, Evered DC, Hall R. The spectrum of thyroid disease in a community: the Whickham survey. Clin Endocrinol (Oxf) 1977;7:481-7.
15. Vanderpump MP, Tunbridge WM. The epidemiology of thyroid diseases. In: The thyroid: A fundamental and clinical text, 8th, Braverman LE, Utiger RD (Eds), Lippincott Williams and Wilkins, Philadelphia 2000. p. 467-72.
16. Aoki Y, Belin RM, Clickner R. Serum TSH and total T4 in the United States population and their association with participant characteristics: National Health and Nutrition Examination Survey (NHANES 1999-2002). Thyroid 2007;17:1211-15.
17. Walsh JP, Bremner AP, Feddema P. Thyrotropin and thyroid antibodies as predictors of hypothyroidism: a 13-year, longitudinal study of a community-based cohort using current immunoassay techniques. J Clin Endocrinol Metab 2010;95:1095-9.
18. Surks MI, Hollowell JG. Age-specific distribution of serum thyrotropin and antithyroid antibodies in the US population: implications for the prevalence of subclinical hypothyroidism. J Clin Endocrinol Metab 2007;92:4575-9.
19. Beck-Peccoz P, Amr S, Menezes-Ferreira MM. Decreased receptor binding of biologically inactive thyrotropin in central hypothyroidism. Effect of treatment with thyrotropin-releasing hormone. N Engl J Med 1985;312:1085-9.

AUTHORSHIP AND CONTRIBUTION DECLARATION

AUTHORS	Contribution to The Paper	Signatures
Dr. Muhammad Siddique Medical Officer Services Hospital Lahore	Main Author, Data Collection	
Dr. Muhammad Akhtar Parvez Assistant Professor, Community Medicine Faisalabad Medical University, Faisalabad	Proof Reading & Supervision	
Dr. Humaira Zafar Women Medical Officer Services Hospital Lahore	Discussion Writing	
Dr. Awais Mustafa Medical Officer Services Hospital Lahore	Results & Tabulation	
Dr. Anam Shafi House Officer Services Hospital Lahore	Final Layout	

