

Original Article

Evaluation of Vitamin B₁₂ Deficiency in Newly Diagnosed Hypothyroid Female Patients in Dhaka City

Farjana Ahmed¹, Shyamal Chandra Banik², Md. Arifuzzaman Chowdhury³, Ferdous Towhid⁴

¹Assistant Professor, Department of Physiology, Dhaka National Medical College, ²Assistant Professor, Department of Physiology, Dhaka National Medical College, ³Assistant Professor, Department of Forensic Medicine, Popular Medical College & Hospital, ⁴Lecturer, Department of Biochemistry, Dhaka National Medical College

Abstract:

Background: Vitamin B₁₂ deficiency may remain latent in the early phase of hypothyroidism. Symptoms of neuropathy may occur due to combination of deficiency of thyroxine & vitamin B₁₂ in newly diagnosed hypothyroid female patients.

Objectives: To assess the prevalence and clinical features of vitamin B₁₂ deficiency in newly diagnosed hypothyroid female patients in Dhaka.

Methods: This cross-sectional study was carried out in the Department of Physiology, Sir Salimullah Medical College (SSMC) between July' 2015 to June' 2016 on 80 newly diagnosed hypothyroid female patients with clinical features of vitamin B₁₂ deficiency. Their serum TSH, FT₄, FT₃ levels were estimated for assessment of thyroid function status by ELISA method. Vitamin B₁₂ level was also estimated to observe its level by using standard method. The statistical analysis was done by ANOVA test, paired, independent sample 't' test.

Results: In this study, a total 80 newly diagnosed hypothyroid female patients were evaluated among them 34 patients had low vitamin B₁₂ level. Generalized weakness, impaired memory, depression, numbness and decreased reflexes were more frequently noted in vitamin B₁₂ deficient patient. Additionally 16 subjects were complained of symptoms consistent with vitamin B₁₂ deficiency, but had normal range of vitamin B₁₂ level.

Conclusion: The present study revealed that there is a high (approx 42.5%) prevalence of vitamin B₁₂ deficiency in newly diagnosed hypothyroid female patients. Traditional symptoms are not a good guide to determining presence of vitamin B₁₂ deficiency. Screening for vitamin B₁₂ level should be undertaken in all newly diagnosed hypothyroid female patients.

Key words: Hypothyroidism, Thyroxine, Vitamin B₁₂.

Introduction

Hypothyroidism is a clinical condition resulting from reduced circulating levels of free thyroxine (FT₄) and triiodothyronine (FT₃).¹ However, the thyroid hormones increase the metabolic activities of almost all tissues of the body. The basal metabolic rate can increase 60 to 100 percent above normal when large amount of hormones are secreted.² The thyroid gland is not essential for life, but its absence or hypo function during fetal and neonatal life results in severe mental retardation and dwarfism.³

The prevalence of primary hypothyroidism is 10/1000 but increases to 50/1000 if patients with sub-clinical hypothyroidism (normal FT₄, raised TSH) are included and the female: male ratio is approximately 6:1.⁴

However, hypothyroidism might be reversible at early

stages; on the other hand irreversible cases might have longer duration of diseases or might present etiologies other than hypothyroidism. Long term accumulation of mucinous tissue is the possible cause of irreversibility.⁵

Most of the hypothyroid patients complain some sensory symptoms like tingling sensation, numbness, paraesthesia, burning pain and some motor symptoms like weakness, muscle fatigability, stiffness and cramp.⁶ Again, decreased tendon reflexes, decreased muscle strength, positive Phalen's test and Tinel's sign at the wrist (test for clinical diagnosis of carpal tunnel syndrome) were also found in some hypothyroid female.⁷

Some investigator revealed that, sensory and motor sign/symptoms such as tingling sensation, numbness, loss of vibration, pain, decreased muscle strength and

delayed tendon reflexes were still persisted in hypothyroid patients even after 1 year of thyroxine replacement therapy.⁸

In a follow-up study, some researchers demonstrated that these symptoms to be common among our hypothyroid patients & to evaluate vitamin B₁₂ levels in patients with primary hypothyroidism.⁹

Methods

This cross-sectional study was carried out in the Department of Physiology, Sir Salimullah Medical College (SSMC) between July' 2015 to June' 2016. In this study, 80 newly diagnosed hypothyroid female patients with symptom of peripheral neuropathy, age ranged from 20-45 years was selected. All the study subjects were selected from out patients department of SSMC and BSMMU. They were belonged to middle socioeconomic status. Subjects with hypertension, diabetic Mellitus, heart disease, kidney disease, hyperthyroidism, past history of neuropathy or neuromuscular diseases, use of drugs known to cause neuropathy or myopathy, malignancy or other serious diseases, pregnancy or lactation, history of gastric or ileal resection were excluded from the study. Their serum TSH, FT₄, FT₃ levels were estimated for assessment of thyroid function status by ELISA method. Vitamin B₁₂ level was also estimated to observe its level by using standard method. The ethical permission was taken from the authority.

Results

In this study, 80 newly diagnosed hypothyroid female were evaluated, age ranges from 20-45 years, among them 34(42.5%) had vitamin B₁₂ deficiency (Figure: 01). Symptoms of numbness, paraesthesia were seen more commonly in B₁₂ deficiency patients compared to B₁₂ sufficient patients. The frequency of the commonly recognized symptom associated with vitamin B₁₂ deficiency among our hypothyroid patients is noted in table-I.

Figure-I:



Table-I: Frequency of symptoms in hypothyroid patients with low & normal B₁₂ level

Symptom	Total No.	vitaminB ₁₂ <200pg/ml	vitaminB ₁₂ >200pg/ml
Weakness	61/80	35 (43.75%)	26 (32.5%)
Numbness	22/80	14 (17.5%)	8 (10%)
Loss of vibration	11/80	8 (10%)	3 (3.7%)
Muscle weakness	33/80	21 (26.25%)	12 (15%)
Delayed tendon reflex	21/80	15 (18.75%)	6 (7.5%)
Decreased sensitivity	16/80	11 (13.75%)	5 (6.25%)

Discussion

Vitamin B₁₂ is known as cobalamin, was first isolated in 1948 & soon after found to be effective in treatment of pernicious anemia.¹⁰ Prevalence of vitamin B₁₂ has been reported up to 15-25% in certain population groups particularly in elderly.¹¹ We have studied prevalence of vitamin B₁₂ in hypothyroid patients & found 34 out of 80 patients (42.5%) have low B₁₂ level.

Vitamin B₁₂ deficiency may occur as a result of autoimmune pernicious anemia, malabsorption, malnutrition or use of drugs including proton pump inhibitors, H₂ receptor antagonists or metformin.¹² Metformin may cause malabsorption secondary to its effects on ileal mucosa or membrane receptors.¹³ Proton pump inhibitors & H₂ receptor antagonists causes gastric hypochlorhydria and malabsorption of vitamin B₁₂. Untreated helicobacter pylori infection is occasionally associated with B₁₂ deficiency.¹⁴ In our study we found no association between use of drugs and B₁₂ deficiency but we found frequent occurrence of B₁₂ deficiency in hypothyroid patients, it was not possible to determine the underlying etiology of this association.

Clinical signs of vitamin B₁₂ deficiency may take long to manifest & often affected patients as asymptomatic for several years. Occasionally, hematological or neuropsychiatric manifestations may presents as a early marker of deficiency but non specific complaints are attributed to aging.¹⁵ The neuropsychiatric features include fatigue, weakness, numbness, loss of vibration, delayed tendon reflex, loss of memory, demensia and depression.¹⁶ Hypothyroid & vitamin B₁₂ deficient patients often have common symptoms of weakness, lethargy, memory impairment, numbness and tingling.¹⁷ We have noticed that several patients, despite being on adequate thyroxine replacement, had persistence of symptoms and subsequently we found to be B₁₂ deficient.

Our study showed vitamin B₁₂ deficiency to be common in the hypothyroid female patients. Screening for B₁₂ deficiency should be undertaken early in the diagnosis of hypothyroidism and periodically thereafter. Patients should be followed and evaluated for suggestive symptoms.

Conclusion

From the result of the study, it can be concluded that, peripheral neuropathy along with deficiency of vitamin B₁₂ was observed in newly diagnosed hypothyroid female before starting their treatment.

Acknowledgement

Authors of this study acknowledge the huge support from Neurology departments of BSMMU for conducting nerve conduction study. The authors are also thankful to the study subjects for their active and enthusiastic participation.

References

1. Keele CA, Neil E, Joels N. Samson Wright's Applied Physiology, 13th ed. New York: Oxford University Press; 1982. 542-545.
2. Hall JE. Textbook of Medical Physiology, 12th ed. Elsevier India Private limited; 2016. 550-552.
3. KE Barman, SM Boitano, S Brooks. Review of Medical Physiology, 24th ed. New York: McGraw-Hill Company; 2010. 587-588.
4. Edwards CRW, Toft AD, Walker BR. 'Endocrine Disease' in Haslett C, Chilvers ER, Hunter JAA, Boon NA. Davidson's principle & practice of Medicine. 22nd ed. Churchill Livingstone. India; 2014. 568-571.
5. Kecei H, Degirmenci. Hormone replacement therapy in hypothyroidism and nerve conduction study. *Neurophysiol Clin* 2006; 35(2): 79-83.
6. Garg R, Bansal N, Singh N, Maria AK, Arora KS. Nerve conduction studies in newly diagnosed cases of Hypothyroidism. *Sch. Acad. J. Biosci.* 2015; 3(5): 479-488.
7. Mahadule AA, Jadhao PS, Phatak MS. Motor conduction parameters in recently diagnosed and untreated hypothyroidism. *Annals of Neurosciences* 2015; 22(1): 6-10.
8. Duyff RF, Bosch JVD, Laman DM, Loon BJPV, Linssen WHJP. Neuromuscular findings of thyroid dysdysfunction: prospective clinical electrodiagnostic study. *J Neurol Neurosurg Psychiatry* 2000; 68: 750-755.
9. Jabbar A, Yawar A, Wasim S, Islam N, Haque N, Zuberi L, et al. Vitamin B₁₂ deficiency common in J. Dhaka National Med. Coll. Hos. 2020; 26 (02): 20-22
10. Dharmarajan TS, Norkus EP. Approaches to vitamin B₁₂ deficiency, early treatment may prevent devastating complication. *Postgraduate Medicine* 2001; 99: 99-106.
11. Wynn M, Wynn A. The danger of Vitamin B₁₂ deficiency in the elderly. *Nutrihealth* 1998; 12: 215-226.
12. Green R, Kinsella LJ. Current concepts in diagnosis of cobalamin deficiency. *Neurology* 1995; 45: 435-440.
13. Banman WA, Shaw S, Jayatilake E. Increased intake of calcium reverses vitamin B₁₂ malabsorption induced by metformin. *Diab Care* 2000; 23: 1227-1231.
14. Kaptan K, Beyan C, Ural U, Cetin T. Helicobacter Pylori is it a novel causative agent in vitamin B₁₂ deficiency. *Arch Intern Med* 2000; 160: 1349-53.
15. Serin E, Gumurula Y, Ozar B, Kayaseluk F, Yimaz U. Impact of helicobacter pylori on the development of vitamin B₁₂ deficiency in the absence of gastric atrophy. *Helicobacter* 2002; 7: 337-41.
16. Yaqoob J, Jafri W, Abid S. Helicobacter pylori infection and micronutrient deficiency. *World J Gastroenterol* 2003; 9: 2137-2139.
17. Lindenbaum J, Heaton B, Savage D. Neuropsychiatric disorders caused by cobalamin deficiency in the absence of anemia or macrocytosis. *N Eng J Med* 1988; 318: 1720-1722.