Anaemia in Hypothyroidism

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Abstract

Background: Anaemia is very common in hypothyroid patient. The results of the type of anaemia in hypothyroid patient studied outside may not be similar on Bangladeshi population. So far, there is no such study regarding the types of anaemia in hypothyroid patients in Bangladeshi population.

Methods: This was a cross sectional study in patients with hypothyroidism who was attending in the thyroid and endocrine clinic of Bangabandhu Sheikh Mujib Medical University, Dhaka over a period of one year. All newly diagnosed cases were selected considering inclusion and exclusion criteria. A structured questionnaire was used for data collection.

Results: Fifty newly detected hypothyroid patients were studied among the study population, 52.0% was between 05 to 35 years and another 48.0% were in 36 to 65 years. 76.0% were female. Bradycardia was found in 20.0% cases. Puffiness of face, peripheral oedema and cold intolerance were found in 78.0%, 68.0% and 82.0% cases respectively. Hoarseness of voice, delayed relaxation of tendon reflexes and paraesthesia were found in about 80.0% cases. Myxoedema and vitiligo were found in 54.0% and 6% cases. FT4 level was reduced in 100.0% cases (Normal range of FT4-9.14-23.81 pmol/L). The mean of FT4 was 5.10 pmol/L. On the other hand TSH level increased in all cases (Normal range of TSH-0.47-5.0l mIU/L). The mean of TSH was 109.88 mIU/L. 50 cases were positive anti TG-Ab and also anti PO-Ab was positive in Fifty cases. Hemoglobin concentration was reduced in 70.0% cases. The mean of haemoglobin concentration was 10.67 gm/dl. In this present study, association of serum anti TG Ab and anti PO Ab of the patients with hypothyroidism and their corresponding hemoglobin concentration were found significant ($p<0.05$) but on the other hand there was no association between serum FT4 of the patients with hypothyroidism and their corresponding haemoglobin concentration ($p> 0.05$). Normocytic normochromic anaemia was found in 64.0% cases, and Microcytic hypochromic anaemia in 32% and Macrocytic anaemia in 4.0% of the cases. Iron deficiency was found in 90.0% and chronic blood loss in 44.0% of the cases.

Conclusion: Anaemia is frequently found in hypothyroid patients. So, hypothyroidism should be excluded in anaemia of non-specific origin.

Keywords: Anaemia, Hypothyroidism, Thyroid, Thyroid hormone

Introduction

Hypothyroidism is a clinical syndrome that results from deficiency of the thyroid hormones, thyroxine (T4) and tri-iodothyronine (T3). The prevalence of hypothyroidism in U.K. is about 15/1000 in females and 1/1000 in Males.[1] Whereas according to Thyroid Clinic at BSMMU, Dhaka about 10-12 percent patients were present with hypothyroidism in that Thyroid Clinic.[2] The cause of hypothyroidism may be primary thyroid disease or, much less commonly, disease of the pituitary or hypothalamus (Secondary hypothyroidism). In the developed world, more than 90% of cases of primary hypothyroidism are due to: - (i) auto-immune (Hashimoto's) thyroiditis, (ii) idiopathic atrophy, or (iii) previous treatment of hyperthyroidism with radio-iodine or surgery.[1]

Prevalence of hypothyroidism in endemic area is more common. Anaemia is very common in hypothyroidism.[3-4] In various reported series, anaemia was observed in 21- 60% of patients with hypothyroidism.[5] The degree of anaemia is seldom as marked as the degree of pallor suggests.[6] Although hypothyroidism is more common in women than in men, but anaemia is more common in hypothyroid men than in hypothyroid women.[4] There is no uniformity of opinion about the

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characteristic picture of the anaemia in hypothyroid patients, but three morphologic types are Normocytic-normochromic anaemia, Hypochromic microcytic anaemia and Macrocytic anaemia.[7]

The relative incidence of the three types differ considerably in three large series reported since 1960.[5] The reasons for the differences are not clear but they may have been related to factors not directly concerned with the thyroid disease as well as to it's degree and duration.[1] When hypochromic microcytic anaemia is found in association with myxoedema, it almost always is attributable to iron deficiency.[4,8-10] Serum iron values are subnormal and the anaemia responds to iron therapy, even if thyroid hormone is not administered; it is not relieved by hormone therapy if iron is withheld.[4] Thyroid hormone stimulate erythropoiesis and tissue oxygen utilization is reduced in hypothyroidism. However, plasma volume is also increased and part of the anaemia in hypothyroidism is dilutional and or due to defective iron utilization.[11] Often, iron deficiency in myxoedema produces normocytic anaemia.[5]

Therefore, an important step is to estimate the serum iron concentration, regardless of the morphologic picture. Iron deficiency occurs in association with myxoedema in part because menorrhagia is a common manifestation of the illness, in part because the achlorhydria found in myxoedema subjects may lead to impaired absorption of food iron, and in part because thyroid hormone itself may be essential for normal iron absorption.[4,9,12,13] Distinctly, macrocytic anaemia usually results from complicating deficiency of vitamin B-12 or folate.[14] The increased incidence of pernicious anaemia in thyroid disease possibly is the result of an autoimmune mechanism. If the patients with iron, folate or vitamin B-12 deficiency are excluded, a significant population of hypothtyroid patients with anaemia remains. This type of anaemia constitute the so-called uncomplicated anaemia of hypothyroidism and is a manifestation of the hormone deficiency itself.[3,9,14] The anaemia usually is mild, the VPRC (volume of packed red blood cells) rarely falling below 0.35 L/L.[5,9]. The degree of anaemia is related to both the severity and the duration of the hypothyroidism.[1] The VPRC continues to fall for as long as 6 months after thyroidectomy in previously euthyroid subjects, even though the basal metabolic rate remains at a stable or even reduced level.

The MCV may be increased in hypothyroid patient, even in the absence of anaemia. Anisocytosis, poikilocytosis or other red cell morphologic abnormalities are not impressive, but acanthocytes are apparent in about 20% of patients.[4] Usually the leukocyte and platelet counts are within the normal range, but sometime both may be slightly reduced The bone marrow may be mildly to moderately hypoplastic with marrow fragments containing an increased proportion of fat and cell trails being less cellular than normal. The hypoplasia affects both red cell and white cell precursors and thus the myeloid: erythyroid ratio is normal.[6] From the kinetic point of view, the anaemia of myxoedema seems to be explained entirely by reduced red cell production. Erythrocyte survival is normal or even slightly prolonged in man but plasma iron transport and erythrocyte iron turnover rates are reduced, indicating subnormal red cell production.[5,9,15] Finally erythropoietin secretion is apparently reduced in hypothyroid patients and 2,3 DPG levels are not increased as occurs in most anaemias and hypoxic states.[16] Thyroid hormones, however, may have direct effects on erythropoiesis as well and may act by modulating the effects of adrenergic agonists on erythropoietic stem cells in the presence of erythropoietin.[5] The response of anaemia in hypothyroidism to thyroid hormone is sluggish. Characteristically, no distinct reticulocytosis occurs and the VPRC returns to a normal value only gradually occurs about 6 months period (range 3 to 12 months).[3,8-9] The MCV tends to reach stable levels after about 4 months or more. Iron, Vitamin B-12 or folic acid should be administered to those patients with hypothyroidism who also have proven deficiencies of these substances.[6]

Anaemia is very common in hypothyroid patients. Hypothyroidism is very common in Bangladesh. Bangladesh is a hyperendemic area where iron deficiency anaemia is quite common.[17] The results of the types of anaemia in hypothyroid patient studied outside may not be similar in our population. So far, there is no such study regarding the types of anaemia in hypothyroid patients in our population. So, the study was aimed to find out types of anemia with hypothyroid and its possible aetiological factors.

Materials and Methods

A cross sectional study was done in the Department of Haematology and Thyroid and Endocrine Clinic, BSMMU, Dhaka from June 2001 to May 2002. Fifty cases were selected by inclusion criteria who had been attended in the "Thyroid and Endocrine Clinic" at BSMMU. Treated case, study population having pregnancy, lactation and other diseases which may affect the anaemia were excluded from the study. The following laboratory investigations were conducted.

(I) Diagnosis of hypothyroidism: (a) Thyroid hormone assay: FT 4 & TSH level were assessed by the Microparticle Enzyme Immunoassay (MEIA) (b) Detection of anti thyroid antibodies:

Anti TG Ab, anti PO Ab. By an Enzyme linked immunosorbent assay (ELISA).

(II) Diagnosis of anaemia: (a) Estimation of hemoglobin concentration by Cyanmethaemoglobin method, (b) Measurement of ESR by Westergren method, (c) Peripheral blood film by Leishman stain and examined under microscope (d) TC, DC and platelet count through peripheral blood film, (e) Red cell indices with Haematocrit was determined by automated blood cell counter. In selected cases the tests were carried out by i) Serum iron, TIBC by Auto analyser, ii) Serum ferritin by Microparticle Enzyme Immunoassay (MEIA) and iii) Lipid profile (serum cholesterol, HDL, LDL, Serum triglyceride) by autoanalyser.

Data were analysed by using SPSS programme and expressed as frequency, percentage, mean SD and SEM unless mentioned otherwise. Comparison between groups were done by analysis of variance (ANOVA). Chi-Square test, student's t-test as applicable. Level of significance was expressed as *p* values. *p* value <0.05 was considered as the level of significance.

Results

In this study, the numbers of patients were 50. Among them, 18.0% of the cases were the age group of 5 to 15 years, 16.0% in 16-25 years, 18.0% in 26 to 35 years, 30.0% of the study populations were the age group of 36-45 years and again 10.0% in 46-55 years and 8.0% study populations were the age group of 56 to 65 years. The mean age group was 32.61 years. Age group was done on the basis of ten years interval among the selected 50 cases in this study. Distribution of the patients according to their sex where male was in 24.0% and female was in 76.0% cases (table I).

Table I: Distribution of the patients by dermatological findings (n=50)

Dermatological findings	Number	Percentage
Dry coarse skin		
Present	37	74%
Absent	13	26%
Myxoedema		
Present	27	54%
Absent	23	46%
Vitiligo		
Present	03	06%
Absent	47	94%
Hair loss		
Present	18	36%
Absent	32	64%
Cold peripheral extremities		
Present	40	80%
Absent	10	20%

In dermatological findings of this study population, there had 74.0% dry coarse skin, 54.0% myxoedema, 03% vitiligo, 36.0% hair loss, and 80.0 % cold peripheral extremities (table II).

Table II: Distribution of the patients by hormonal assay for hypothyroidism (n = 50)

Hormone level	Number	Percentage	
A. FT4			
7.13-913 pmol/L	11	22.0%	Normal range FT4 → 9.14-23.81 pmolIL.
4.02-7.12 pmol/L	22	44.0%	Normal range TSH. → 0.47 - 5.01 MIU/L
1.05-4.01 pmol/L	17	34.0%	Mean = 5.10 pmol/L SD = ± 2.11 pmolIL
B.TSH			Mean = 109.88 MIU/L SD = ± 59.62 MIU/L
5.01-75 MIU/L	17	34.0%	
76-150 MIU/L	19	38.0%	
151-230 MIU/L	14	28.0%	

Findings of hormonal assay for hypothyroidism in these number of patients shown that Serum FT4 level was reduced in 100.0% cases (Normal range FT4 → 9.14-23.81 pmollL). FT4 was 7.13 - 9.13 pmol/L in 22.0%, 4.02 - 7.12 pmol/L in 44.0% and 1.05-4.01 pmol/L in 34%. Serum TSH level was increased in 100.0% (Normal range TSH. → 0.47 - 5.01 MIU/L) study population. TSH was 5.01-75 MIU/L in 34.0%, 76-150 MIU/L in 38.0%, 151-230 MIU/L 28.0%. (Table III).

Table-III: Distribution of the patients by antithyroid antibody level for hypothyroidism (n=50).

Antithyriod antibody	Number	Percentage	
A. Anti TO Ab			
100-150 u/ml	10	20.0%	Normal range → <100u/ml
151-200 u/ml	26	52.0%	Moderate positive →151-200 u/ml
> 201 u/ml	14	28.0%	Weak positive →15-50 Au/rnl
Mean = 179.4 u/ml			Strong positive →>101 Au/rnl
SD = ± 75.61 u/ml			
B. AntiPoAb			
15-50 Au/rnl	12	24.0%	
51-100 Au/ml	29	67.0%	Normal range → <15Au/rnl
>101 Au/rnl	09	09.0%	Weak positive →100-150u/rnl
Mean = 61.63 Au/ml			Moderate positive → 51-100
SD = ± 32.28 Au /ml			

Antithyroid antibody level for hypothyroidism of these patients revealed that serum anti TO Ab was positive in 50 (100%) cases. Weak positive in 20%, moderate positive in 52% and strong positive in 28% cases. Anti PO Ab weak positive was in 24%, moderate positive in 67% and strong positive in 09% cases. (table IV).

Table IV: Distribution of the patients by hemoglobin concentration level. Class interval of Hb concentration was done on basis of 2 gm / dl variation.

Hemoglobin concentration level	Number	Percentage
5.5 – 7.4 gm/dl	02	4.0%
7.5 – 9.4 gm/dl	06	12.0%
9.5 – 11.4 gm/dl	27	54.0%
11.5 – 13.5 gm/dl	15	30.0%
Total	**50**	**100.0%**

In this present study it was shown that haemoglobin concentration 5.5-7.4 gm/dl in 4.0%, 7.5-9.4 gm/dl. in 12%, 9.5-11.4 gm/dl in 54.0% and 11.5-13.5 gm / dl in 30% cases.

According to peripheral blood film findings of the patients (N=50), the types of anaemia were normocytic normochromic anaemia was in 64.0%, microcytic hypochromic anaemia in 32.0% and macrocytic anaemia in 4.0% cases.

In this study, ninety six percent study populations were clinically anaemic, 68.0% patients had peripheral oedema and 94.0% of the patients had weakness. Sixty-four (64.0%) percent patients had no dyspnoea, 82.0% Patients experienced with cold intolerance. Puffyness of face and periorbital swelling were found in 78.0% and 20.0% cases respectively. Seventy six percent patient had weight gain. Eighty percent patient complained of somnolence. Bagginess of eyelid was found in 52.0% cases. Poor memory in 76.0%, hoarseness of voice in 82.0%, impaired hearing in 46.0%, delayed relaxation of tendon reflexes in 84.0%, carpal tunnel syndrome in 34.0%, paresthesia in 76.0% and depression in 68.0% were disclosed by this present study in this study. Poor appetite was in 50.0% population, constipation in 60.0% cases. Ninety eight percent had no ascites, anorexia in 52.0% & felt fullness of stomach is 76.0% cases in this study.

Discussion

Hypothyroidism is a clinical syndrome that results from deficiency of the thyroid hormones, thyroxine (T_4) and tri-iodothyronine (T_3). One of the commonest cause of primary hypothyroidism are due to auto -immune (Hashimoto's) thyroiditis in which antibodies to thyroglobulin or thyroid peroxidase are typically strongly positive.[5] Hashimoto's thyroiditis typically affects middle aged and elderly women; it is 15 times more common in women than men.[5] This study is similar to the present study in BSMMU (Thyroid Clinic) where majority of the cases were in the age group of 36 to 45 years and all of the 50 patients were anti TG Ab and anti PO Ab positive. A study on "The haematology of hypothyroidism" in between September 1970 to January 1971 at North wick Park Hospital in London was done by Horton et al where the mean age of women was 58 years and men was 65 years.[4] Seventy six percentage study population were female and rest of the cases were male.

Hypothyroidism is more common in women than in man which was revealed by Horton L et al on study of hypothyroidism in England.[4] In another study on" Spectrum of thyroid disorders" in between, January 1994 to June 1995 at IPGMR in Dhaka, where they had studied 188 hypothyroid patients; among them 149 cases were female and 39 cases were male. This study is consistent with the present.

In the present study, general physical examination was done. Most important findings were recorded. Sixty eight percent of the patient were mildly anaemic, 28.0% of the patients were moderate to severely anaemic and 4.0% were clinically non anaemic. Anaemia is very common in hypothyroidism which was observed in various reported series.[3,4] The degree of anaemia is seldom as marked as the degree of pallor suggests.[6] Patient with myxoedema in hypothyroidism may manifest pallor without anaemia.[18] According to peripheral blood film examination, the different morphological types of anaemia were found in 50 cases. Among them, normocytic normochromic anaemia was in 64.0% cases, microcytic hypochromic in 32.0% cases and only 4.0% cases were macrocytic anaemia.

Different studies were done on hypothyroidism in different countries in the world. In 1960, Sheffield in England revealed that 4% people were normocytic-normochromic, 14.0% were hypochromic microcytic and 13.0% people were macrocytic anaemia.[5] This study is inconsistent with present study. University of Virginia studied and observed that 26.0%, 3.0% and 14.0% cases were normocytic normochromic, hypochromic microcytic and macrocytic anaemia respectively.

Above study is also not similar to this present. Hypothyroidism is very common in Bangladesh.[6]

Erythropoiesis is reduced in hypothyroidism.[4] Bangladesh is an hyperendemic area for hypothyroidism where iron deficiency anaemia is quite common.[17] The results of the types of anaemia in hypothyroid patient studied out side may not be similar group. The Bangladeshi population which explored in this present study in Thyroid Clinic, BSMMU.

Same percentage study population were found in reduced FT_4 level and had 7.13-9.13 Pmol/L in 22% cases, 4.02-7.12 pmol/L in 44% and 1.05--4.01 pmol/L in 34% cases. The mean FT_4 level was 5.10 pmol/L in both sexes. On the other hand 100 % patients had increased TSH level. TSH level were 5.01-75 mIU/L in 34% cases, 76-150 mIU/L in 38% and more than 151 mIU/L in 28% cases. The mean TSH level was 109.88 mIU/L.

In this study, hundred percent patients were positive anti TG Ab About 52.0% were moderate positive, weak positive in 20.0% and strong positive in 28.0% cases. The mean anti TG Ab was 179.6 u/ml. 100.0% study population was positive anti PO Ab. Among them, about 67% cases were moderate positive and weak positive in 24.0% and strong positive in 9.0% cases.

Haemoglobin concentration was 9.5-11.4 g1dl in 54.0% study population, 11.5-13.5 gm/dl in 30.0%, 7.5-9.4 gm/dl in 12.0% and 5.5-7.4 gm/dl in 4.0% cases. The mean haemoglobin concentration was 10.67 gm/dl.

Means reported in 1948 that about half the cases of hypthyroidism, the haemoglobin concentration was 11.2 gm/dl. This present study is consistent with Means's report.[1] Mean haemoglobin concentration was 12.9 gm/dl which was disclosed by Harton L et al

In this study, investigation of red cell indices was done in 20 cases among 50 cases. MCV, MCH, MCHC were normal in 85.0%, 50.0% and 75.0% cases, increased in 10.0%, 25.0% and 20.0% cases in both sexes respectively.

Serum iron, total iron binding capacity (TIBC) and ferritin level were examined in 20 cases among 50 cases in this study. Serum iron, total iron binding capacity and ferritin level were found normal in 87.5% case of male and 50.0% cases of female, 80.0% and 85.0% cases in both sexes respectively. Serum iron level was increased in 6.25% male cases and 25.0% female cases. Total Iron Binding capacity and Ferittin level were increased in 06.25% and 25.0% cases.

The mean of serum iron was 108.5 mg/dl in male and 90.75 mg/dl in female. The mean of total iron binding capacity and ferittin level were 291 mg/dl and 72.7 mg/dl respectively. Predisposing factors explored in this study. Iron deficiency in 90.0%, iodine deficiency in 92.0% cases, chronic blood loss in 44.0% and malabsorption syndrome in 54.0% cases were observed.

In present study, statistically proved that there was association between anti TG Ab and anti PO Ab of the patients with hypothyroidism and their corresponding haemoglobin concentration respectively ($p < 0.05$). Statistically also proved that there was no association between FT4 of the patients and their corresponding haemoglobin concentration ($p > 0.05$).

Conclusion

This was a hospital based study only. This study does not accurately represent the exact picture of anaemia in hypothyroidism in this country. According to thyroid clinic, BSMMU, Dhaka among the attending patients, the incidence of hypothyroidism was 10-12% which has not exactly reflected the with due hypothyroidism in our country. So, with a large sample size a multicentre study was suggested.

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