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General Medicine

STUDY OF ANEMIA IN HYPOTHYROIDISM

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ABSTRACT

BACKROUND: Hypothyroidism and anemia were commonly observed in the clinical practices. Hypothyroidism being one of the factor responsible for causing anemia. Hypothyroidism causes deceleration of metabolic activities in the body and almost any organ system. Hematopoietic system is one of the primary system affected in hypothyroidism resulting in anemia.

OBJECTIVE: This study was undertaken to study the prevalence, etiology, pattern and severity of anemia in hypothyroidism.

MATERIALS & METHODS: This was a case control study from the state of Uttarakhand. A total of 110 primary hypothyroid patients and 110 euthyroid controls were evaluated for anemia. Demography, clinical profile, hematological and biochemical parameters of each patient were recorded. Prevalance, pattern, etiology of anemia were studied. Severity of anemia were correlated with that of hypothyroidism.

RESULTS: Anemia was observed in 75 patients with hypothyroidism out of which 47 were overt hypothyroid and 28 were subclinical hypothyroid. In controls anemia was present in 25 patients. Cases were more symptomatic than controls. RBC morphology showed normocytic normochromic in 51 patients, microcytic hypochromic in 42 patients and macrocytic in 15 patients. Anemia was severe in cases with hypothyroidism.

CONCLUSION: Overall prevalence of anemia was 68% in cases and 22.7 % in controls. In overt hypothyroid patients prevalence of anemia was 83.9% and in subclinical hypothyroid patient it was 51.9%. Normocytic normochromic anemia was the most common type of anemia in cases as well as controls. Iron deficiency anemia was present in majority of cases. Hypothyroid patients were more symptomatic for anemia than controls. Higher TSH value were associated with more severe anemia.

KEYWORDS : Anemia, TSH, Overt hypothyroidism, Subclinical hypothyroidism

INTRODUCTION

The clinical syndrome of hypothyroidism results from a deficit of thyroid hormone, and leads to widespread metabolic deceleration[1]. The prevalence of hypothyroidism varies from 2-5% as found in various studies which increases to 15% by the age of 75 years with higher occurrence in women[2]. In areas with iodine deficiency like India, hypothyroidism is 10-20 times more incident than that of other countries of non-iodine deficient area[3]. In hypothyroid patients, the prevalence of anemia has been observed to be (20-60%)[4]. Thyroid hormone plays a role in synthesis of hemoglobin in adults as well as fetal hemoglobin maturation [5]. Thyroid hormone affects the process of hematopoiesis, also hypothyroidism slows the metabolism of oxygen resulting in anemia[6]. Hypocoagulopathies, bleeding, iron, vitamin B12 and folic acid malabsorption, lowered erythropoietin levels and hypoplasia of hematopoietic cells in the bone marrow also play a role in causing anemia in hypothyroid patients[7]. There is a metabolic deceleration in hypothyroidism, these abnormalities in metabolism related to hypothyroidism include anemia, hyperlipidemia, hypervolemic, hyponatremia, and correctable rise in creatinine [8]. Almost every organ is affected; the signs and symptoms show variable features that depend upon the age at which hypothyroidism occurred and severity of hypothyroidism [5]. The system which is chiefly affected is that concerning hematopoiesis and primarily causing anemia. Hypothyroid patients generally have moderately severe anemia [9].

A crucial role is played by the thyroid hormone in hematopoiesis, principally in erythropoiesis. Thyroid hormones have a straight stimulating outcome on the proliferation of precursors of erythrocytes, they also encourage erythropoiesis by elevating the expression of erythropoietin gene and the production of erythropoietin by the kidneys[10]. Hypothyroid patients can have normochromic normocytic anemia, microcytic hypochromic anemia, and even macrocytic anemia. Most commonly the anemia is of normocytic normochromic type while iron deficiency anemia is the subsequent most commonly occurring type of anemia seen in hypothyroid patients. The severity of anemia is related to the extent of hypothyroidism [11].

Deficiency of thyroid hormones is responsible for the normocytic anemia, which is not due to nutritional deficiency. This normocytic anemia results due to a deficiency of thyroid hormone which causes a decreased stimulus to development of red blood cell precursors, decreased oxygen transport to tissues and also due to decreased erythropoietin level[12]. A picture of microcytic anemia can also be present due to menorrhagia which occurs secondary to imbalances in the levels of hormone and impaired absorption which is observed in hypothyroidism. Macrocytic anemia results due to impaired absorption of vitamin B12 folic acid pernicious anemia and poor nutrition. Pernicious anemia occurs 20 times more commonly in patients with hypothyroidism as compared to the general population [13]. Anemia has been commonly associated with hypothyroidism, though the prevalence of anemia in patients with hypothyroidism differs extensively in different studies. So this study is conducted to evaluate and analyse patients with hypothyroidism, to study prevalence, types and severity of anemia in the hypothyroid patient.

MATERIALS & METHODS

This case control study was carried out at a tertiary referral center of Uttarakhand over a period of one year after obtaining institutional ethical clearance. Newly diagnosed 110 overt and subclinical hypothyroid patients and 110 euthyroid controls, aged 18 years or more were included in the study after obtaining written informed consent. Inclusion criteria were laboratory confirm cases of primary hypothyroid patients [Thyroid stimulating hormone (TSH) > 5 IU/ml]. Exclusion criteria were pregnant women, patients with hemolytic anemia, secondary hypothyroid patients, patient on hematnics and antithyroid medications, post thyroidectomy hypothyroid patients. Details in clinical history, physical examination, demographic parameters, laboratory parameters of individual patients were compiled. All included subjects were subjected to a battery of lab investigations including complete hemogram, peripheral blood smear, thyroid profile test (Free T3, Free T4 and TSH) ferritin, total iron binding capacity, vitamin B12, folate, LDH tests were done to find out hypothyroidism and anemia in cases and controls. Anemia was defined as hemoglobin (Hb) levels lower than 13 g/dl in men and 12 g/dl in women. Further it was classified as Mild- Hb 10-12 g%, moderate –Hb 8-10 g%, and severe- Hb <8 g%. On the basis of red cell indices (mean corpuscular volume [MCV]) anemia was classified as normocytic normochromic (MCV 80-96 fl), microcytic hypochromic (MCV <80 fl), and macrocytic (MCV >96 fl) and were investigated to find the etiology as well as to rule out any secondary cause of anemia, if found positive were excluded from study.

Data Management & Statistical Analysis:

Statistical analysis was performed using the SPSS software 22.Descriptive statistics was used to present the data in the form of

percentages, proportions and means. Chi square test was used for testing the significance of difference between proportions and also association between two variables. Students unpaired T-test was used for comparison of continuous data. Pearson's product moment correlation coefficient was used for determining correlation between different variables. A 'p' value of < 0.05 was taken as statistically significant. Confidence Interval of 95 % was taken.

RESULTS:

All the 110 cases meeting our inclusion criteria were classified in two groups: overt hypothyroid group and subclinical hypothyroid group on the basis of thyroid profile. In the cases 51% patients had overt hypothyroidism whereas 49% patients had subclinical hypothyroidism.

Base line characteristics of cases and controls are shown in Table 1. The age range of cases and control was 18- 95 years. Female preponderance was seen in cases (67.3%) while males were more in controls.The maximum number of cases and control belonged to middle socioeconomic status.

In cases 48.2% were overweight and 15.5% were obese while in control 42.7% were overweight and 2.7% were obese. There was a significant association between hypothyroidism and obesity (p=0.001).

The clinical profile of cases and controls are shown in Table 2. Most of the subject in cases, presented with generalised weakness (33.6%), followed by tiredness (27.3%), while in controls, generalised weakness was present in (19.1%) patients and rest symptoms and signs like tiredness, generalised weakness weight gain, hair loss, constipation, pallor, delayed tendon reflex and koilonychias were significantly high in cases as compared to controls.

The pulse rate among cases and controls was 75.18 ± 13.705 beats per min and 90.14 ± 19.268 beats per min respectively. Mean Systolic BP among cases and controls was 121.91 ± 20.175 mm Hg and 120.98 ±25.034 mm Hg respectively and mean Diastolic BP among cases and controls was 74.418 ± 10.931 mm Hg and 73.545 ± 12.525 mm Hg respectively.

Mean hemoglobin level were 9.53 g/dl in cases and 10.69 g/dl in controls respectively. On comparing it was observed that the hemoglobin level was significantly lower in cases as compared to control.

The mean MCV among cases and controls was 85.62 fl and 85.2 fl respectively with Mean corpuscular hemoglobin (MCH) among cases and controls was 27.9 pg and 27.8 pg respectively.

On analyzing RBC morphology it was found that normocytic normochromic anemia was most common in cases (46.4%), microcytic hypochromic (38.2%),macrocytic anemia (13.6%) and dimorphic anemia (1.8%) patients respectively. In the subgroup analysis it was found that normocytic normochromic anemia was common in overt hypothyroid patients and microcytic anemia in subclinical hypothyroid patients. On the basis of etiology it was found that iron deficiency anemia was more in cases.Among controls, out of 110 subjects 54.5% of them had normocytic normochromic RBC morphology, 30.9% had microcytic hypochromic morphology and 10.9% patient had macrocytic RBC morphology.

The serum TSH level (mIU/ml) in the cases and controls was 27.169 ± 50.762 and 2.020 ±1.67 respectively. On comparing it was found that the serum TSH level was significantly higher in cases as compared to controls.

Applying Pearson's correlation analysis between TSH and Hb level, there was a negative correlation between these two factors in cases. Pearson's correlation coefficient was -0.14 which was statistically not significant *(P* = 0.142).

In controls, after applying Pearson's correlation analysis between TSH and Hb level, positive correlation was found between these two factors and Pearson's correlation coefficient was 0.071 which is statistically non-significant.

Table 1. Baseline characteristics of cases (n = 110) and controls (n = 110)

Characteristics	Number of cases (%)	Number of controls (%)
Age Group (years)		
18-30	4 (3.6)	12 (10.9)
31-45	27 (24.5)	23 (20.9)
46-60	51 (46.4)	36(32.5)
61-75	21 (19.1)	32 (29.1)
76-95	7 (6.4)	7 (6.4)
Mean age (years)	51.96 ± 14.80	51.29 ± 15.07
Gender		
Males	36 (32.7)	56 (50.9)
Females	74 (67.3)	54 (41.82)
Socioeconomic status		
High	4 (3.6)	0
Middle	81 (73.6)	80 (72.7)
Low	25 (22.7)	30 (27.3)
Co-morbidites		
Type 2 DM	39 (35.5)	34 (30.9)
Hypertension	26 (23.6)	25 (22.7)
Dietary Habits		
Mixed Diet	45 (40.9)	43 (39.1)
Vegetarian	65 (59.1)	67(60.9)
BMI (kg/m2)		
Underweight	0 (0)	4 (3.6)
Normal	40 (36.4)	56 (50.9)
Overweight	53 (48.2)	47 (42.7)
Obese	17 (15.5)	3 (2.7)
Smoker	14 (12.7)	12 (10.9)
Alcoholic	13 (11.8)	13 (11.8)

Table 2. Clinical profile and laboratory parameters of cases (n = 110) and controls (n = 110)

Symptoms	Number of cases (%)	Number of controls (%)
Tiredness	30 (27.3%)	0 (0%)
Generalised weakness	37 (33.6%)	21 (19.1%)
Weight gain	8 (7.3%)	0 (0%)
Hair loss	18 (16.4%)	0 (0%)
Constipation	19 (17.3%)	0 (0%)
Menorrhagia	2 (1.8%)	0 (0%)
Signs		
Pedal edema	1 (0.9%)	0 (0%)
Pallor	74 (67.3%)	18 (16.3%)
Icterus	0 (0%)	1(0.9%)
Delayed tendon reflex relaxation	12 (10.9%)	0 (0%)
Koilonychia	15 (13.6%)	0 (0%)
Pulse rate (per min)	75.18 ± 13.70	90.14 ± 19.26
Systolic BP(mmHg)	121.91 ± 20.175	120.98 ± 0.752
Diastolic BP(mmHg)	74.41 ± 10.	73.15 ± 12.52
Laboratory parameters		
Haemoglobin (g/dL)	9.53 ± 2.45	10.69 ± 1.90
RBC (million/mme3)	3.71 ± 1.03	3.78 ± 0.752
Platelet Count (thousand/mm3)	204.83 ± 113.53	223 ± 141.61
MCV (fl)	85.6 ± 13.1	85.22 ± 11.50
MCH (pg)	27.95 ± 5.17	27.82 ± 4.55
MCHC (g/dl)	32.45 ± 1.61	32.52 ± 1.65
RDW(%)	17.67 ± 4.3	18.74 ± 4.5
PCV (%)	31.40 ± 7.3	30.92 ± 5.8
Serum TSH (mIu/ml)		
TSH	27.1629 ± 50.762	2.020 ± 1.167

Table 3: Distribution of patients based on RBC morphology in cases & controls

		Group		Total
		Cases	Controls	
RBC morphology	Microcytic hypochromic	42 (38.2%)	34 (30.9%)	76 (34.5%)
	Macrocytic	15 (13.6%)	12 (10.9%)	27 (12.3%)

	Normocytic Normochromic	51 (46.4%)	60 (54.5%)	111 (50.5%)
	Dimorphic	2 (1.8%)	4 (3.6%)	6 (2.7%)
	Total	110 (100%)	110 (100%)	220 (100%)

Table 4: Prevalence of anemia in patient with hypothyroidism

		Types of Hypothyroidism		Total
		Overt Hypothyroidism	Subclinical Hypothyroidism	
Anemia	Yes	47 (83.9%)	28 (51.9%)	75(68.1%)
	No	9 (16%)	26 (48.1%)	35(31.8%)
	Total	56 (100%)	54 (100%)	110 (100%)

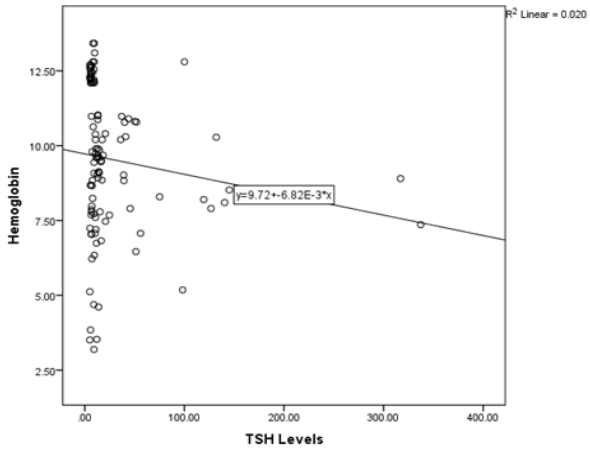
Table 5: Etiology of anemia in overt and subclinical hypothyroidism.

Etiology	Overt hypothyroidism (n=56)	Subclinical hypothyroidism (n=54)	Total (n=110)	P Value
Iron deficiency	27 (50%)	12 (21.4%)	39	0.002
Vitamin B-12 deficiency	6 (10.7%)	5 (9.3%)	11	0.52
Anemia of chronic disorder	21 (39.9%)	11 (20.4%)	35	0.01

Table 6 : Association between hypothyroidism and anemia

		Group		Total	P Value
		Cases	Controls		
Anemia	Yes	75 (68.1%)	25(22.7%)	100(45.4%)	0.001
	No	35(25.5%)	85(77.2%)	120(54.5%)	0.001

Correlation between Hemoglobin & TSH



DISCUSSION:

Various factors are responsible for etiology of anemia which include age factor nutritional and stress factors along with long standing diseases [12] Anemia is a severe public health problem in india which may precipitate by conditions such as hypothyroidism. To carry out the treatment of the patient with anemia correctly it is necessary to determine the etiological cause.

In our study anemia was present in 75 patients out of 110 cases (68.1%) with normocytic normochromic anemia as the most common type of anemia among hypothyroid patients. On analyzing the age and sex wise distribution in our study it was found that maximum patients affected were the female under the age group 46-60 yrs. This was similar to observations by Kulkarni VK et al [14] and Das C et al [15]. On the basis of results of various studies which revealed higher female preponderance among cases. There were many factors which can influence this gender based prevalence of hypothyroidism and anemia which may be due to under nutrition as well as menstrual blood loss.

Of the hypothyroid patient cases in our study majority of cases belonged to middle class (73.6%) which is different from study done by Kulkarni VK et al.[14] in which there was the predominance of the poor class. This difference might be due to less access of poor population to private hospital.

Most of the subject in cases, presented with generalised weakness (33.6%), followed by tiredness (27.3%), pallor was found in (67.3%) patients, among controls, generalised weakness was present in (19.1%) patients other symptoms like weight gain, hair loss, constipation, pallor, and koilonychias were significantly high in cases as compared to controls.

The pulse rate among cases and controls was 75.18 ± 13.705 beats per min and 90.14 ± 19.268 beats per min respectively. On comparing it was found that the pulse was significantly lower in cases as compared to controls. Mean Systolic BP among cases and controls was 121.91 ± 20.175 mm Hg and 120.98 ±25.034 mm Hg respectively. Mean Diastolic BP among cases and controls was 74.418 ± 10.931 mm Hg and 73.545 ± 12.525 mm Hg respectively. Similar findings were observed in study done by by Kulkarni VK et al.[14]

The Hb levels in hypothyroid patients was lower (9.53 g %) compared to controls (10.6 g %) in our study. The hypothyroid patients are at risk of having lower Hb as compared to general population similar to study by Kulkarni VK et al [14]

In our study the MCV in cases and controls was 85.62 fl and 85.2 fl respectively and was comparable. Findings was similar to the findings of Mehmet E et al [16.]

The study of RBC morphology in our study revealed that the 46.4% of cases and 54.5% of controls were havings normocytic normochromic RBC. Microcytic hypochromic RBC were greater in hypothyroid patients (38.2%) than in the control (30.9%). On subgroup analysis normocytic normochromic anemia was more common in overt hypothyroid group while microcytic hypochromic anemia was commonly present in subclinical hypothyroid patient. So the study of RBC morphology revealed greater abnormalities in hypothyroid population. This finding were similar to findings in the study by Anand R et

Of the study population iron deficiency anemia was present in 50% patient of overt hypothyroidism and in 21.4% in subclinical hypothyroidism. Iron deficiency anemia was significantly high in overt hypothyroid patients.

In this study, prevalence of anemia among cases was found to be 68.1%, out of which in overt hypothyroidism 83.9% patients were anemic while in subclinical hypothyroidism 51.9% patients were anemic and prevalence of anemia was significantly higher in overt hypothyroidism. Our observations were in accordance with study done by Anand R et al.[17] which reported higher prevalence of anemia in overt hypothyroidism (69%) than subclinical hypothyroid patients (56%).

In our study anemia was significantly associated with hypothyroidism with p value of 0.001. On analysis of subgroup it was found that severity of anemia was more in overt hypothyroid as compared to subclinical hypothyroid patients (p=0.002). Significant association was seen between hemoglobin level and type of hypothyroidism.

The mean serum TSH levels in our study were 27.19 mIU/ml in cases and 2.020 mIU/ml in controls. The serum TSH level were significantly higher in hypothyroid patients compared to controls.These findings were similar to study done by Kulkarni VK et al [14] and Mehmet E et al [16].

In our study there was negative correlation between TSH levels and Hb levels in cases. Similar observations was seen in study done by Kulkarni VK et al [14].

CONCLUSION-

Prevalence of anemia in hypothyroid patients was 68.1% which was higher than control 22.7%. RBC morphology in hypothyroid patient was normocytic normochromic- 46.4% (most common), microcytic hypochromic- 38.2% (second most common) and macrocytic anemia- 13.6%. The most common etiology of anemia in hypothyroid cases was iron deficiency. Symptoms of anemia was more in hypothyroid patient than controls. High level of TSH was associated with higher prevalence of moderate to severe anemia. Both hypothyroidism and anemia were commonly observed in the clinical practices. Hypothyroidism being one of the factor responsible for causing anemia.

Screening for anemia in all hypothyroid patients and vice versa, will be the best practice which will eventually help in correcting the underlying hypothyroidism and thus indirectly anemia.

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