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Original Research Report

Red Blood Cell indices in patients with hypothyroidism

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Abstract

Background: Hypothyroidism is a common endocrine disorder in clinical practice. It is known to present with multiple systemic manifestations. As thyroid hormones play an important role in erythropoiesis; dysfunction usually results in hematological abnormalities.

Aim and Objective: To study the Red blood cell (RBC) indices in hypothyroidism and to differentiate the pattern of anemia in patients on thyroid supplementation.

Materials and methods: This cross-sectional observational study was done among 60 hypothyroid subjects attending to a tertiary care center at Mangalore. Thyroid Function Tests (TFT) and Red Blood Cell indices were obtained and analysed using SPSS software v20.

Results: Among 60 hypothyroid subjects, 54 (90%) were females and 6 (10%) were males. The prevalence of anemia was 60% (n=36); among whom biochemically 14 were euthyroid and 22 had overt hypothyroid status. Among these subjects; 20 had normocytic, 12 had microcytic and 4 had macrocytic anemias. The mean haemoglobin in the study population was 11.91 ± 2.26 g/dl. Statistically significant lower levels of haemoglobin, PCV and RBC count where seen among overt hypothyroids as compared to euthyroids.

Conclusion: Overt hypothyroid subjects had lower hemoglobin, PCV and RBC counts as compared to euthyroids. Early identification and treatment of hypothyroidism could prevent or revert the hematological changes; thus ensuring better quality of life.

Keywords: Hypothyroidism, Red Blood Cell indices, hemoglobin, thyroid function tests, TFT, PCV, RBC count.

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1. Introduction

Hypothyroidism is one of the most frequently encountered endocrine disorders in clinical practice. Its clinical manifestations are highly variable and involve multiple systems of the body. The prevalence of hypothyroidism in the developed world is about 4-5%[1] and is associated with haematological abnormalities in about 20-65%.[2] In a multi-centered epidemiological study conducted at eight sites in India, the prevalence of hypothyroidism was 10.95%.[3]

Thyroid hormones play an important role in the normal development, differentiation, and physiological functions of bone marrow and hematopoiesis.[4,5] Supplementation of thyroid hormones in early stages can improve the anemia in up to 25% of hypothyroid patients.[6] Various studies have identified all morphological patterns of RBCs in hypothyroidism, commonest being normocytic normochromic. Here we attempted to study the RBC indices in hypothyroidism and to differentiate the pattern in patients on thyroid supplementation.

2. Materials and methods

2.1 Methodology

This cross-sectional observational study was done among hypothyroid patients attending the in-patient or out-patient services of a tertiary care center at Mangalore. The study was study done over a period of 6 months from June 2019 after institutional ethics committee approval. Sample size was calculated as 60 with 95% power using the

following formula, n = 2($\frac{Z_\alpha+Z_\beta}{C}$)^2 +3where Z_α = relative deviate (at 95% confidence interval) i.e. 1.96; Z_β =1.6449 at 95% power; C = 0.5 ln (1+r/1-r) and; r = -0.454 [7]. After obtaining written informed consent, a total of 60 subjects fulfilling the selection criteria were included in the study. The details including the clinical history, treatment, TFT (Thyroid Function Tests) and Red Blood Cell indices were captured to a pre-formatted data sheet.

2.2 Selection criteria

The Inclusion criteria for the patients were: (1) Above 18years; (2) Newly detected hypothyroidism; (3) Diagnosed hypothyroidism on treatment; (4) Hypothyroidism on treatment- adequately or not adequately. The Exclusion criteria were: (1) Patients with history of diabetes mellitus, chronic alcohol consumption, COPD, chronic bronchitis, chemotherapy and radiotherapy; (2) Patients with acute febrile illness; (3) Patients with subclinical hypothyroidism; (4) Patients who received blood transfusion in past 3 months; (5) Patients admitted to the medical / surgical intensive care wards.

TFT was estimated by modified Electro-chemi-luminescence Immune Assay using COBAS 6000 analyser and RBC indices were measured by Beckman-Coulter LH 750 analyser. All the hypothyroid subjects in the study were further divided into 2 subgroups based on TFT values as overt hypothyroid group (low Ft4 and elevated TSH) and euthyroid group (normal Ft4 and TSH). Subjects with anemia were sub-classified into mild, moderate and severe anemia as per WHO guidelines. [8] Based on MCV values, they were classified into normocytic (normal MCV), microcytic (MCV less than 81 fl) and macrocytic (MCV more than 98 fl) anemia.

2.3 Statistical Analysis

Statistical analysis was performed using SPSS software v20. Results were reported as mean ± standard deviation (SD) for quantitative variables and percentages for categorical variables. ANOVA test was used to evaluate the significance of differences between two groups. p-value less than0.05 was considered as a significant change.

3.Results

The study included total of 60 subjects, among whom 54 (90%) were females and 6 (10%) were males with a male: female ratio of 1:9. The mean age of the study population was 40.38±11.78 years, with most of them belonging to age group of 31-40 years (n=17 subjects). Prevalence of anemia in the study group was 60% (n=36). Among which 14 (39%) were euthyroid and 22(61%) were overt hypothyroid. The Table-1 shows Distribution of severity of Anemia in the Study Population as per WHO guidelines and values were statistically significant with p value of 0.002. Most of the euthyroid individuals had mild anemia whereas overt hypothyroid individuals had moderate anemia. Two individuals with overt hypothyroidism had severe anemia.

Table 1: Distribution of severity of Anemia in the Study Population

Anemia	Thyroid status		Total
	Euthyroid	Overt Hypothyroid	
Absent	16	8	24 (40%)
Mild	10	4	14 (23.3%)
Moderate	4	16	20 (33.3%)
Severe	0	2	2 (3.3%)
Total	30 (50%)	30 (50%)	60 (100%)

Table 2 depicts the thyroid function test and hematological parameters in the study. Mean duration of hypothyroidism was 4.32 ± 3.68 years. Mean serum TSH among euthyroid and overt hypothyroid individuals were 2.59 and 23.58 respectively. Haemoglobin, PCV and RBC count showed significant differences among the two groups. Mean haemoglobin of study population was 11.91 ± 2.26 g/dl. Overt hypothyroids had significantly lower mean haemoglobin levels (10.76 ± 1.87 g/dl) as compared to euthyroids (13.07 ± 2.03 g/dl). Similarly mean PCV and RBC count were significantly low in overt hypothyroid individuals in comparison to euthyroid individuals. Other RBC indices like MCV, MCH and MCHC did not show any statistically significant difference among the two groups. Mean WBC count among the euthyroid individuals was 9.56 x 10^3 which was higher compared to that of hypothyroid individuals in the study (7.83 x 10^3). However platelet count did not show any statistically significant difference among the two groups.

Among the individuals with anemia, based on values of MCV, they were classified into normocytic, microcytic and macrocytic anemia. 20 subjects had normocytic anemia followed by microcytic anemia in 12 subjects. Only 4 subjects had macrocytic anemia, among which 3 were from overt hypothyroid group. However the difference among both the groups were not statistically significant (p=0.672).

Table 2: Comparison of age, duration of hypothyroidism, thyroid hormone levels and hematological parameters in the study population.

Descriptive Statistics	Study population (mean±sd)	Euthyroid (mean±sd)	Overt Hypothyroid (mean±sd)	p-value (Anova Test)
Age (yrs)	40.38 ± 11.78	39.93 ± 12.38	40.83 ± 11.34	0.770
Duration of hypothyroidism (yrs)	4.32 ± 3.68	4.83 ± 3.86	3.8 ± 3.49	0.281
Sr T3 (ng/ml)	0.92 ± 0.31	1.04 ± 0.28	0.81 ± 0.29	0.003
Sr T4 (mcg/dl)	7.42 ± 2.04	8.29 ± 1.55	6.55 ± 2.13	0.001
Sr FT4 (ng/dl)	1.06 ± 0.37	1.37 ± 0.21	0.75 ± 0.21	0.000
Sr TSH (uIU/ml)	13.06 ± 30.39	2.59 ± 1.07	23.58 ± 40.6	0.006
Hemoglobin (g/dl)	11.91 ± 2.26	13.07 ± 2.03	10.76 ± 1.87	0.000
PCV (%)	34.91 ± 5.44	37.36 ± 4.43	32.45 ± 5.30	0.000
RBC Count (million/cumm)	4.16 ± 0.63	4.36 ± 0.43	3.96 ± 0.74	0.013
WBC Count (*10^3 /cumm)	8.69 ± 3.24	9.56 ± 3.41	7.83 ± 2.87	0.038
Platelet Count (*10^5/cumm)	2.68 ± 1.07	2.83 ± 1.03	2.52 ± 1.09	0.262
MCV (fl)	84.56 ± 7.11	85.59 ± 4.72	83.52 ± 8.84	0.263
MCH (pg)	27.93 ± 2.46	28.31 ± 1.75	27.54 ± 2.99	0.228
MCHC (g/dl)	33.19±0.97	33.28±1.04	33.11 ± 0.91	0.510

4. Discussion:

Thyroid hormones (THs) play vital role in physiological functions of human body. It regulates hematopoiesis in human bone marrow. [9] This study was intended to compare various RBC indices among overt hypothyroid individuals and hypothyroid individuals who were currently euthyroid. Hypothyroidism is more common among females worldwide which were evident in present study also.

The cause for anemiain hypothyroidism can be multifactorial. In the present study, we correlate hypothyroidism with anemia. Various studies done on association between hypothyroidism and anemia found that around 20-65% of hypothyroid individuals had anemia.[2,10] The pooled overall prevalence rate of anemia among hypothyroid patients from eight studies included in a meta-analysis was 33.77% with 95% CI.[11] In the present study, prevalence of anemia was 60% with most of them belonging to overt hypothyroid group. Severity of anemia had statistically significant correlation with serum TSH values.

Several studies have been done to find the association between the thyroid hormones and RBC indices. Study done by Bremner *et al*, among 1011 euthyroid individuals showed that even small changes in levels of thyroid hormones (free T4 and TSH) are associated with significant alteration in haemoglobin concentration and RBC indices.[12] However a similar study done by Schindhelm *et al*, among 701 euthyroid individuals did not show any significant correlation between thyroid hormones and RBC indices.[13] Our observations were in accordance with the study conducted by Bremner *et al* with statistically significant lower mean haemoglobin levels, PCV and RBC count in hypothyroid subjects. Other RBC indices like MCV, MCH and MCHC did not show any statistically significant difference among the two groups. Serum tri-iodothyronine (T3) hormone has been proven to be a prerequisite for normal B-cell production in the bone marrow through its regulation of pro-B-cell proliferation. [14] Hence WBC count can be low along with RBC count in hypothyroidism. This can also lead to compensatory increased production of platelets. The present study showed statistically significant changes in WBC count between the twogroups.

Among the different patterns of anemia seen among the hypothyroid individuals in present study, normocyticanemia was the commonest (55.6%), followed by microcytic anemia in 33.33% and macrocytic anemia in 11.1%. Results of studies by Anand *et al*[15], Das *et al* [16] and Patel *et al* [17] also showed that prevalence of normocytic normochromic anemia among patients with hypothyroidism were significantly higher as compared to other patterns of anemias followed by microcytic anemia. Study done by Mehmet *et al*, among 100 overt hypothyroid individuals showed that macrocytic anemia (18.6%) was more prevalent than microcytic (11.6%) and was attributed to significant vitamin B12 deficiency. [18]

Exact process of development of various patterns of anemia in hypothyroidism is not clearly understood. Suggested mechanisms include lack of stimulation of erythroid colony leading onto bone marrow repression and reduction in oxygen requirement of tissues leading onto diminution of erythroprotein level in the absence of thyroid hormones. Both these can lead to normocytic anemia which is the commonest type of anemia among the hypothyroid patients. [19, 20] Commonest cause for microcytic anemia in hypothyroidism could be malabsorption and Iron deficiency. Vitamin B_{12} and folic acid deficiency leads to Macrocytic anemiain hypothyroidism. Vitamin B_{12} deficiency is due to insufficient intake; reduced absorption due to deceleration of intestinal motility and intestinal wall edema in hypothyroidism; and deranged folate metabolism. [21]

5. Conclusion

Overt Hypothyroid individuals had higher incidence of RBC abnormalities when compared to hypothyroid individuals who were currently euthyroid. By screening all hypothyroid individuals, hematological abnormalities can be detected in early stages and initiation of appropriate treatment can reverse those abnormalities.

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Conflicts of interest: None to disclose.

References

[1]. Hollowell JG, Staehling NW, Flanders WD, Hannon WH, Gunter EW, Spencer CA *et al*. Serum TSH, T4, and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). *J Clin Endocrinol Metab* 2002; 87: 489-99.

[2]. Aybike K, Mehmet E, Sencer G, Mustafa K, Soner S, Ozgun K, *et al*. Anemia frequency and etiology in primary hypothyroidism. 2009; Available from: http://www. endocrine-abstracts.org/ea/0020/ea0020p140.htm.

[3]. Unnikrishnan AG, Kalra S, Sahay RK, Bantwal G, John M, Tewari N. Prevalence of hypothyroidism in adults: An epidemiological study in eight cities of India. *Indian J Endocrinol Metab* 2013; 17: 647-52

[4]. Yen PM. Physiological and molecular basis of thyroid hormone action. *Physiol Rev* 2001; 81(3): 1097-142.

[5]. Kawa MP, Grymula K, Paczkowska E, Baśkiewicz-Masiuk M, Dabkowska E, Koziolek M, *et al*. Clinical relevance of thyroid dysfunction in human haematopoiesis: biochemical and molecular studies. *Eur J Endocrinol* 2010; 162(2): 295-305.

[6]. Cinemre H, Bilir C, Gokosmanoglu F, Bahcebasi T. Hematologic effects of levothyroxine in iron-deficient subclinical hypothyroid patients: A randomized, double-blind, controlled study. *J Clin Endocrinol Metab* 2009; 94: 151-6.

[7]. Mahajan AS, Lal R, Dhanwal DK, Jain AK, Chowdhury V. Evaluation of autonomic functions in subclinical hypothyroid and hypothyroid patients. *Indian J Endocr Metab* 2013; 17: 460-4.

[8]. WHO. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and Mineral Nutrition Information System. Geneva, World Health Organisation (WHO), 2011 (WHO/NMH/NHD/MNM/11.1); Available from: http://www.who.int/vmnis/indicators/haemoglobin.

[9]. Golde DW, Bersch N, Chopra IJ, Cline MJ. Thyroid hormones stimulate erythropoiesis in vitro. *The British Journal of Haematology* 1977; 37(2): 173–7.

[10]. Kazemi-Jahromi M, Shahriari-Ahmadi A, Samedanifard S-H, Doostmohamadian S, Abdolahpoor E, Allameh SF. The Association between Hypothyroidism and Anemia: a Clinical Study. *International Journal of Hematology-Oncology and Stem Cell Research* 2010; 4(3): 6-9.

[11]. Saeed AA, Alfaify NM, Alhilali AI, Al-wadaI NW, Shubaili MH, Alasiri SJ *et al*. Prevalence of Anemia in Hypothyroidism: Systematic Review and Meta-Analysis. *EC Microbiology* 2019; 15(6): 514-22**.**

[12]. Bremner AP, Feddema P, Joske DJ, Leedman PJ, O'Leary PC, Olynyk JK, *et al*. Significant association between thyroid hormones and erythrocyte indices in euthyroid subjects. *Clin Endocrinol* 2012; 76: 304-11.

[13]. Schindhelm RK, Ten BE, Heima NE, van Schoor NM, Simsek S. Thyroid hormones and erythrocyte indices in a cohort of euthyroid older subjects. *Eur J Intern Med* 2013; 24: 241-4.

[14]. Foster MP, Rodriguez EM, Dorshkind K. Proliferation of bone marrow pro-B cells is dependent on stimulation by the pituitary/thyroid axis. *Journal of Immunology* 1999; 163(11): 5883–90.

[15]. Anand R, Mishra AK, Mahdi AA, Verma SP, Gupta KK. A study of prevalence and pattern of anemia in primary hypothyroidism. *Int J Med Sci Public Health* 2018; 7(2): 153-9.

[16]. Das C, Sahana PK, Sengupta N, Giri D, Roy M, Mukhopadhyay P. Etiology of anemia in primary hypothyroid subjects in a tertiary care center in Eastern India. *Indian J Endocr Metab* 2012; 16(2): 361-3.

[17]. Patel RP and Jain A. Study of anemia in primary hypothyroidism. *Thyroid Research and Practice* 2017; 14(1): 22-4.

[18]. Mehmet E, Aybike K, Sencer G, Mustafa K. Characteristics of anemia in subclinical and overt hypothyroid patients. *Endocrine Journal* 2012; 59(3): 213-20.

[19]. Kuhr T, Hala K, Dietrich H, Herold M, Wick G. Genetically determined target organ susceptibility in the pathogenesis of spontaneous autoimmune thyroiditis: aberrant expression of MHC-class II antigens and the possible role of virus. *J Autoimmune* 1994; 7: 13-25.

[20]. Christ-Crain M, Meier C, Huber P, Zulewski H, Staub JJ, Muller B. Effect of restoration of euthyroidism on peripheral blood cellsand erythropoietin in women with subclinical hypothyroidism. *Hormones (Athens)* 2003; 2: 237-42.

[21]. Jabbar A, Yawar A, Wasim S, Islam N, Haque NU, Zuberi L *et al*. Vitamin B_{12} deficiency common in primary hypothyroidism. *J PakMed Assoc* 2008; 58(5): 258-61.