Effects of Thyroid Function on Blood Cell Counts and Red Cell Indices – A Retrospective Study at a Tertiary Care Centre in Mandya, Karnataka

Siddegowda M.S.[1], Chaithra R.[2], Shivakumar S.[3], Maithri C.M.[4]

[1, 2, 3] Department of Pathology, Mandya Institute of Medical Sciences, Mandya, Karnataka, India.
[4]Department of Biochemistry, Mandya Institute of Medical Sciences, Mandya, Karnataka, India.

ABSTRACT

BACKGROUND

Thyroid hormones play an important role in the regulation and production of red blood cells. Thyroid dysfunction induces different effects on blood cells such as anaemia, erythrocytosis, leucopenia, thrombocytopenia and alteration in red cell indices. In this study, we wanted to compare the changes in haematological parameters of thyroid dysfunction patients with those of euthyroid group.

METHODS

This was a retrospective study done on 310 individuals by collecting data from the medical records. Later the patients were categorized into hypothyroid (33) thyroid stimulating hormone (TSH > 5.5 µIU/mL), hyperthyroid (19) (TSH < 0.3 µIU/mL) and euthyroid (258) (TSH = 0.3 - 5.5 µIU/ml) groups. The haematological parameters of all these patients were obtained by 5-part automated cell count analyser. Finally, the obtained data was analyzed by statistical package for social sciences (SPSS) software.

RESULTS

The data obtained from the analysis revealed statistically significant ($P < 0.05$) difference between hypothyroidism, hyperthyroidism and euthyroidism in mean red blood cell (RBC) count, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), red cell distribution width (RDW), white blood cell (WBC) count and platelet count but the difference was not significant for mean haemoglobin, mean corpuscular haemoglobin concentration (MCHC) ($P > 0.05$). The mean haemoglobin was lower in hypothyroid patients when compared to euthyroid and hyperthyroid patients. The RBC count ($P < 0.007$), MCH ($P = 0.002$) and RDW ($P < 0.001$) showed statistically significant difference between hypothyroidism and euthyroidism, MCV ($P = 0.005$) showed statistically significant difference between hyperthyroid and euthyroid groups.

CONCLUSIONS

In case of patients with abnormal haematological parameters, thyroid hormones evaluation is necessary.

KEYWORDS

Hypothyroidism, Hyperthyroidism, Haemoglobin, Blood Count, Red Cell Indices

Corresponding Author:
Dr. Chaithra R.,
504B, Doctor's Quarters,
Mandya Institute of Medical Sciences,
Mandya – 571401, Karnataka, India.
E-mail: chaithra8888@gmail.com

DOI: 10.18410/jebmh/2021/451

How to Cite This Article:
Siddegowda MS, Chaithra R, Shivakumar S, et al. Effects of thyroid function on blood cell counts and red cell indices – a retrospective study at a tertiary care centre in Mandya, Karnataka. J Evid Based Med Healthc 2021;8(27):2434-2438. DOI: 10.18410/jebmh/2021/451

Submission 19-03-2021,
Peer Review 29-03-2021,
Acceptance 21-05-2021,
Published 05-07-2021.

BACKGROUND

Thyroid gland is the largest and an important endocrine gland in human body located on the anterior side of neck. It has two lobes connected by isthmus and composed of thyroid follicles lined by cuboidal epithelium. These thyroid follicles are filled with thyroid hormones in the form of thyroglobulin. The thyroid stimulating hormone (TSH) secreted from pituitary gland acts on thyroid gland to secrete triiodothyronine (T3) and tetraiodothyronine (T4) thyroid hormones from thyroglobulin,[1] which plays an important role in the development, differentiation, metabolic balance, and physiological functions of tissues in the human body.[2]

These hormones have a critical role in early brain development, somatic growth, bone maturation, protein synthesis, regulation and production of red blood cells. They have important effect on erythropoiesis through increased secretion of erythropoietin by inducing erythropoietin gene expression resulting in hyperproliferation of immature erythroid progenitors.[1]

Thyroid hormones are required for cellular metabolic rate which in turn depends on tissue oxygen. Normally thyroid hormones augment repletion of hypoxia inducible factor (HIF -1) and increase 2.3 bisphosphoglycerate (2, 3 BPG) which in turn increases erythropoiesis. With decreased thyroid hormones, tissue oxygen requirement is decreased and kidneys adopt appropriately which in turn decreases erythropoietin and erythrocytes proliferation correspondingly. This causes anaemia due to reduction in haemoglobin synthesis due to deficiency of erythropoietin.[3]

Hypothyroidism and hyperthyroidism are two major dysfunctions, the incidences of which are increasing day by day. Normal value of TSH is 0.3 – 5.5 µIU/mL. It varies with age and sex. In hypothyroidism serum TSH value > 5.5 µIU/ml and where in hyperthyroidism TSH < 0.3 µIU/ml.[4] Hypothyroidism and hyperthyroidism modify thyroid hormone receptor (TR) gene expression on hematopoietic progenitor cells (HPC'S). Thyroid hormones deficiency causes decrease in clonogenic potential of erythrocyte - burst forming unit (BFU - E) and total blood cell count. In contrast hyperthyroidism patients showed increased clonogenic growth (BFU - E) and total blood cell count by regulating proliferating cell nuclear antigen (PCNA) and cyclin D1.[5]

Hypothyroidism can cause various forms of anaemia (normocytic-normochromic, microcytic hypochromic or macrocytic normochromic) due to decrease in erythropoietin levels in plasma and hypoplasia of all myeloid cell lineages. Anaemia is not more common finding of hyperthyroidism which can manifest as with erythrocytosis and hyperplasia of myeloid cell lineage. Anaemia in hyperthyroidism can be due to altered iron metabolism, oxidative stress and hemolysis.[6] Alteration in other haematological parameters such as MCV, MCH, MCHC and RDW are associated with thyroid dysfunction. Pancytopenia is rare side effect, but cause is not well understood.[7,1] Thyroid disorders induced anaemia is a common health problem and all the haematological changes will become normal when euthyroid state is achieved.[8] So early detection and treatment of the thyroid dysfunction reverses the changes of thyroid dysfunction.

Objectives

1. To compare the haematological alterations in patients of thyroid dysfunction with the euthyroid control group.
2. To study the alterations in blood cell counts and red blood cell indices.

METHODS

This was a retrospective record-based study conducted in the central diagnostic laboratory of Mandya Institute of Medical Sciences (MIMS), Mandya from April 2020 to June 2020. All the patients referred from outpatient department (OPD) and inpatient department (IPD) of MIMS, Mandya for both complete blood count and thyroid function test (TFT) were included in the study. Data of CBC and TFT was collected from records during the study period. A total 310 cases of TFT results were taken from biochemistry laboratory records. The TSH, T3 and T4 assay was done in human serum or plasma by using chemiluminescent microparticle immunoassay (CMIA).

Parameter	Reference Range	
	Male	Female
Haemoglobin	14 - 17.4 gm/dl	12 - 16.0 gm/dl
Red blood cell count	4.5 - 5.5 x 10^{12}/L	4.0 - 5.0 x 10^{12}/L
MCV	80 - 100 fl	80 - 100 fl
MCH	28 - 34 pg	28 - 34 pg
MCHC	32 - 36 g/dL	32 - 36 g/dL
RDW	12 - 14.6	12 - 14.6
White blood cell count	4,000 - 10,000 cells/cumm	4,000 - 10,000 cells/cumm
Platelet count	150 – 400 x 10^9/L	150 – 400 x 10^9/L

Table 1. Reference Range of Haematological Parameters[3,9]

TSH assay was done by combining sample, anti-beta TSH antibody coated paramagnetic microparticles and anti TSH diluent fluid. TSH present in the sample binds to the anti-TSH antibody coated microparticles. After washing, anti-alpha TSH acridinium labelled conjugate is added to create a reaction mixture. The resulting chemiluminescent reaction is measured as reactive light units. There is direct relationship between the amount of TSH in the sample and the relative light units detected by the system. Normal range of TSH was 0.3 – 5.5 µIU/mL, T3 was 1.71 - 3.71 ng/ml, T4 was 0.7 - 1.48 ng/ml. Based on TSH value, study cases were categorized into euthyroid (TSH 0.3 – 5.5 µIU/mL), hypothyroid (> 5.5 µIU/mL) and hyperthyroid (< 0.3 µIU/mL) patients.

Analysis of CBC and red blood cell indices of corresponding patients were done in 5-part automated haematology differential cell count analyser by using anticoagulant mixed blood. The anticoagulant used for blood collection was ethylene diamine tetra acetic acid (EDTA). This data was collected from haematology laboratory records. Patients with iron and vitamin B12 deficiency were excluded by collecting results from biochemistry laboratory records. The variations of haematological parameters in thyroid dysfunctions were determined by correlating with normal reference range of haematological parameters.

Normal reference range of haematological parameters were as follows

Inclusion Criteria

1. Patients who were referred for thyroid function test, complete blood cell count and red cell indices to central diagnostic laboratory of MIMS, Mandya during the study period.
2. Patients of all age and both sexes were included in the study.

Exclusion Criteria

Patients with iron and vitamin B12 deficiency were excluded. A prior approval was obtained from institutional ethics committee for conducting the study.

Statistical Analysis

Data was entered into Microsoft excel data sheet and data was analysed using SPSS software. Categorical data was represented in the form of frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Analysis of variance was the test of significance to identify the mean difference between more than two groups for quantitative data. Post Hoc Bonferroni test was used to determine the inter group analysis. The P value < 0.05 was considered as statistically significant.

RESULTS

Thyroid Status	(N = 310)	Percentage
Euthyroid	258	83.23 %
Hyperthyroidism	19	06.13 %
Hypothyroidism	33	10.65 %
Total	**310**	**100.00 %**

Table 2. Distribution of Euthyroid, Hypothyroid and Hyperthyroid Patients

Among 310 patients, 258 were euthyroid (83.23 %), 33 were hypothyroid (10.65 %) and 19 were hyperthyroid (6.13 %) patients. The age of the patients was ranged from 15 year to 70 years. Mean age of patients who were euthyroid was 32.48 ± 10.33 years, hypothyroid was 36.64 ± 11.44 years and hyperthyroid was 33.53 ± 9.67 years. There was no significant difference in mean age with respect to thyroid status. (Table: 2) Among females, 84.33 % were euthyroid, 5.97 % were hyperthyroid and 9.70 % had hypothyroid patients. Among males, 76.19 % were euthyroid, 16.67 % were hypothyroid and 7.14 % were hyperthyroid patients. Hypothyroidism was commoner than hyperthyroidism. There was no significant difference in thyroid status with respect to gender distribution.

In the study there was significant difference in mean RBC, MCV, MCH and RDW values with respect to their thyroid function status. The mean RBC count was low in patients with hypothyroidism and high among patients with hyperthyroidism. The mean MCV was significantly low in hyperthyroid patients and high in hypothyroid patient's group (P = 0001). The mean MCH was significantly low in hyperthyroid and high in hypothyroid patients. The mean RDW was significantly low in hyperthyroid and high in hypothyroid patients (P < 0.001).

	Thyroid Status								P Value
	Euthyroid		Hyperthyroid		Hypothyroid		Total		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Hb	12.26	1.48	11.96	01.17	11.68	02.11	12.18	1.55	0.099
RBC	04.51	0.58	04.68	00.73	04.20	00.61	04.49	0.60	0.007
MCV	82.34	7.17	76.14	18.56	84.64	06.12	82.21	8.34	0.001
MCH	27.96	3.75	27.28	04.51	30.31	03.00	28.17	3.79	0.002
MCHC	33.35	2.42	33.69	02.26	33.69	02.10	33.41	2.37	0.647
RDW	14.78	1.49	15.32	01.83	16.33	01.87	14.97	1.62	< 0.001

Table 3. Comparison of Haemoglobin (Hb), Red Blood Cell Indices with Euthyroid, Hypothyroid and Hyperthyroid Patients

The mean haemoglobin was low in hypothyroid and slightly high in hyperthyroid patients but mean Hb was lower in both hypothyroid hyperthyroid patients when compared euthyroid patients. There was no difference in mean MCHC in between hypothyroid and hyperthyroid patients, and it was slightly lower in euthyroid patients when compared to hypothyroid and hyperthyroid patients. There was no significant difference in mean Hb and MCHC values between the three thyroid function status groups. (Table: 3) In the present study there was significant difference in mean WBC and platelet counts between the three thyroid function status groups. The mean WBC count of hyperthyroid patients was higher than hypothyroid patients but low when compared to euthyroid patients. The mean platelet count was lower in hypothyroid and hyperthyroid patients when compared to euthyroid patients. The mean WBC count and platelet count showed statistical significant difference of (P = 0.003), (P = 0.049) in hypothyroid, hyperthyroid patients when compared to euthyroid patients respectively. (Table: 4).

DISCUSSION

Thyroid gland is the most important and largest endocrine gland of human body with secretion of two hormones, T3 and T4, which are having major role in metabolism of cells and organs.[1] Thyroid hormones have a direct effect on haematological parameters by stimulating the precursors of the erythrocytes and indirectly by enhancing erythropoietin production.[10]

	Thyroid Status								P Value
	Euthyroid		Hyperthyroidism		Hypothyroidism		Total		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
WBC	9,190.81	2,040.89	8,518.95	2,692.77	7,871.21	2,729.02	9,009.16	2,199.68	0.003
Platelets	3.24	00.84	02.90	00.68	02.93	00.67	3.10	0.79	0.049

Table 4. Comparison of Total White Blood Cell Count and Platelet Counts with Euthyroid, Hyperthyroid and Hypothyroid Patients

The most common thyroid dysfunction disorders were hypothyroidism and hyperthyroidism. These thyroid dysfunctions affect blood cells and cause anaemia, leucopenia and thrombocytopenia and also seen changes in red cell indices like MCV, MCH, MCHC and RDW.[7]

The present retrospective record-based study was conducted to categorize the patients into euthyroid, hypothyroid and hyperthyroid group and also to compare haematological parameters with thyroid dysfunction state. In our study, a total of 310 patients were included. Based on TSH results patients were classified into euthyroid (258, 83.23 %), hypothyroid (33, 10.65 %) and hyperthyroid (19, 6.13 %) groups. The results were similar with the study done by Unnikrishnan A G et al.[11] in which 80.0 % were euthyroid, 13.3 % were hypothyroid 2.9 % were hyperthyroid patients.

In our study the incidence of hypothyroidism was higher in females (78.79 %) than males (21.21 %) and the results were similar with other studies of A Dorgalaleh et al.[1] and Bashir H et al.[12] where incidence of hypothyroidism in females 62 % and 64.3 % and in males 38 % and 35.7 % respectively. In the present study and the study done by A Dorgalaleh et al.[1] the incidence of hyperthyroidism was higher in females (84.21 % and 58 %) than males (15.79 % and 42 %). So, the study showed hypothyroidism was more common than hyperthyroidism and females were more commonly affected with the thyroid dysfunction than males.

RBC Indices	Thyroid Status	Present Study	A. Dorgalaleh et al.[1]	Shetty A et al.[2]	Maheshwari et al.[6]
Hb	Euthyroid	12.26	13.6	12.58	12.9
	Hypothyroidism	11.68	12.2	11.44	11.5
	Hyperthyroidism	11.96	12.5	12.82	12.4
RBC	Euthyroid	4.51	4.7	4.6	-
	Hypothyroidism	4.20	4.5	4.1	-
	Hyperthyroidism	4.68	4.7	4.8	-

Table 5. Comparison of Mean Haemoglobin and Red Blood Cell Count with Other Studies

RBC Indices	Thyroid Status	Present Study	Dorgalaleh et al.[1]	Shetty A et al.[2]	Maheshwari et al.[6]
MCV	Euthyroid	82.34	85.0	83.06	86.6
	Hypothyroidism	84.64	84.0	83.80	86.2
	Hyperthyroidism	76.14	81.7	83.34	81.3
MCH	Euthyroid	27.96	29.3	28.52	28.6
	Hypothyroidism	30.31	27.4	28.06	28.5
	Hyperthyroidism	27.28	27.0	28.50	26.9
MCHC	Euthyroid	33.35	33.6	33.14	32.9
	Hypothyroidism	33.69	32.5	32.36	33.1
	Hyperthyroidism	33.69	32.6	33.14	33.0
RDW	Euthyroid	14.78	12.9	13.02	12.5
	Hypothyroidism	16.33	13.7	14.50	13.2
	Hyperthyroidism	15.32	14.7	13.40	13.2

Table 6. Comparison of Mean Red Blood Cell Indices with Other Studies

In our study the mean haemoglobin of hypothyroid was lower than hyperthyroid patients and it was lower in both thyroid dysfunction patients when compared to euthyroid patients. The results were similar with the studies done by A. Dorgalaleh et al.[1] Maheshwari et al.[6] But mean Hb was not statistically significant (P = 1.000) between hypothyroid and hyperthyroid patients.

The mean RBC count of present study was lower in hypothyroid patients when compared to hyperthyroid patients and mean RBC was lower in hypothyroid and higher in hyperthyroid when compared to euthyroid patients. It was statistically significant (P = 0.015) between hypothyroid and hyperthyroid patients. Our study results were correlating with the studies done by A. Dorgalaleh et al.[1] Shetty A et al.[2] Maheshwari et al.[6] The study showed that anaemia and decreased red blood cell count were associated with hypothyroidism.

In our study and the studies done by A. Dorgalaleh et al.[1] Shetty A et al.[2] Maheshwari et al.[6] the mean MCV was higher in hypothyroid than hyperthyroid patients and showed statistically significant (P = 0.001). The mean MCV was higher in hypothyroid patients and lower in hyperthyroid patients when compared to euthyroid patients and results were similar with the study done by A. Dorgalaleh et al.[1] The mean MCV showed statistically significance (P = 0.001) between three thyroid function groups respectively.

In the present study the mean MCH was higher in hypothyroid than hyperthyroid patients and results were similar with other studies done by A. Dorgalaleh et al.[1] Shetty A et al.[2] but it was not statistically significant (P = 0.015). In our study, the mean MCH was higher in hypothyroidism and slightly lower in hyperthyroidism when compared to euthyroid patients. The mean MCH showed statistically significant (P = 0.002) difference between three thyroid function patients.

The mean MCHC results were similar in both hypothyroid and hyperthyroid patients but it was not statistically significant (P = 1.000). These results were correlating with study done by A. Dorgalaleh et al.[1] The mean MCHC was not showed statistically significant (P = 0.647) difference between hypothyroid, hyperthyroid and euthyroid patients.

In the present study and the studies done by A. Dorgalaleh et al.[1] Shetty A et al.[2] Maheshwari et al.[6] the mean RDW in hypothyroid patients was higher than hyperthyroid patients and was not statistically significant (P = 0.07). In the present study and the studies done by A. Dorgalaleh et al.[1] Shetty A et al.[2] Maheshwari et al.[6] the mean RDW was higher in hypothyroid, hyperthyroid patients when compared to euthyroid patients and results were similar with other studies done by Shetty A et al.[2] Maheshwari et al.[6] The mean RDW showed statistically significant (P < 0.001) with all three thyroid function status patients.

In the present study, the mean WBC count in hypothyroid patients (WBC = 7871 cells/cumm) was lower than hyperthyroid patients (WBC = 8518 cells/cumm) and results were similar with study done by A Dorgalaleh et al.[1] The mean WBC count was lower in hyperthyroid patients (WBC = 8518 cells/cumm) than euthyroid patients (WBC = 9190 cells/cumm) and results were correlating with the study done by Bashir H et al.[12] (Hyperthyroid, WBC = 7250 cells/cumm, euthyroid patients WBC = 7400 cells/cumm) but in the study of A Dorgalaleh et al.[1] the mean WBC count was slightly higher in hyperthyroid (WBC = 7200 cells/cumm) patients when compared to euthyroid (WBC = 7100 cells/cumm) patients. The mean WBC count showed statistically significant (P = 0.003) difference between hypothyroid, hyperthyroid and euthyroid patients. In the present study and the study conducted by Shetty A et al.[2] the mean platelet count in hypothyroid patients (PC = 2.75 Lacs/cumm, 2.50 Lacs/cumm respectively) was lower than hyperthyroid patients (PC = 2.85 Lacs/cumm, 2.96

Lacs/cumm respectively). The study conducted by A Dorgalaleh et al.[1] showed high mean platelet count (PC = 2.7 Lacs/cumm) in hypothyroid patients when compared to euthyroid and hyperthyroid patients (PC = 2.6 Lacs/cumm, 2.5 Lacs/cumm respectively).

In our study the mean platelet count was lower in hypothyroid and hyperthyroid patients when compared to euthyroid patients and showed statistically significant (P = 0.049) difference between hypothyroid, hyperthyroid and euthyroid patients.

CONCLUSIONS

The incidence of hypothyroidism was more common than hyperthyroidism and females were more commonly affected by thyroid disorders than males. The thyroid dysfunction was more commonly affecting middle age. Thyroid hormones have a crucial role in erythropoiesis and proliferation of hematopoietic progenitor cells. In case of refractory anaemia, alteration in red blood cell indices, WBC counts and platelet counts, thyroid dysfunction should be investigated, because the changes can be reversible with thyroid dysfunction therapy. Small sample size was a limitation of this study.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.
The author would like to thank Dr. Abhilash K. for writing assistance and Pooja, technician from Central Diagnostic Laboratory, Mandya Institute of Medical Sciences, Mandya, for helping in data collection.

REFERENCES

[1] Dorgalaleh A, Mahmoodi M, Varmaghani B, et al. Effect of thyroid dysfunctions on blood cell count and red blood cell indices. Iran J Ped Hematol Oncol 2013;3(2):73-77.
[2] Shetty A, Vijaya C. A study of hematological parameters and their correlation with thyroid hormone status in non-pregnant women of childbearing age. Indian J Pathol Oncol 2019;6(1):102-106.
[3] Mackenzie SB, Williams L, Piwowar KL. Clinical Laboratory Hematology. 3rd edn. Julie Levin Alexander Publisher 2015: p. 464-68.
[4] Geetha JP, Srikrishna R. Role of red blood cell distribution width (RDW) in thyroid dysfunction. Int J Biol Med Res 2012;3(2):1476-1478.
[5] Kawa MP, Grymula K, Paczkowska E, et al. Clinical relevance of thyroid dysfunction in human hematopoiesis: biochemical and molecular studies. Eur Journal of Endocrinol 2010;162(2):295-305.
[6] UmaMaheshwariK, Rajagopalan B, Samuel RT. Variations in haematological indices in patients with thyroid dysfunction. Int J Contemp Med Res 2020;7(1):A5-A7.
[7] Iddah MA, Macharia BN, Ng'wena AG, et al. Thyroid hormones and haematological indices levels in thyroid disorders patients at MOI teaching and referral hospital, Western Kenya. ISRN Endocrinology 2013;2013:385940.
[8] Refaat B. Prevalence and characterstics of anemia associated with thyroid disorders in non-pregnant Saudi women during the childbearing age: a cross-sectional study. Biomed J 2015;38(4):307-316.
[9] Lewis SM, Bain BJ, Bates I. Dacie and Lewis practical haematology. 10th edn. Elsevier 2007: p. 14-15.
[10] Ahmed SS, Mohammed AA. Effects of thyroid dysfunction on hematological parameters: case controlled study. Annals of Medicine and Surgery (Lond) 2020;57:52-55.
[11] Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. Indian J Endocr Metab 2011;15(Suppl 2):S78-S81.
[12] Bashir H, Bhat MH, Farooq R, et al. Comparison of hematological parameters in untreated and treated subclinical hypothyroidism and primary hypothyroidism patients. Med J Islam Repub Iran 2012;26(4):172-178.