International Journal of Scientific and Innovative Research 2020; 8(1) : 1-7
P-ISSN 2347-2189, E- ISSN 2347-4971

ROLE OF ANEMIA IN HYPOTHYROIDISM PATIENTS

***Anil Kumar[1], Santosh Kr. Karn[2] and RK Singh[2]**

[1]Department of Medical Laboratory Technology (Pathology) & Medical Microbiology, [2]Department of Biochemistry and Biotechnology, Sardar Bhagwan Singh University, Balawala, Dehradun ,Uttrakhand , India.

*Address for Correspondence : Dr. Anil Kumar,Department of Medical Laboratory Technology (Pathology) & Medical Microbiology, Sardar Bhagwan Singh University, Balawala, Dehradun Uttrakhand, India ; Email ID: anilpoojagupta@gmail.com

ABSTRACT

Thyroid disorders and anemia are one of the most common and biggest health problems in India. 1% of general population is affected with hypothyroidism. Anemia in association with hypothyroidism has been studied since previous 10th decades. This study will include a minimum number of 300 patients visiting the outpatient department (OPD) of Sardar Bhagwan Singh University, Balawala, Dehradun, Uttrakhand, India, from the period of May 2017 to December 2019, who are confirmed by overnight fasting based on world Health organization (WHO) criteria. Serum free tri-iodothyronine (FT3), free thyroxine (FT4) and thyroid-stimulating hormone (TSH) were determined by immunoassays including enzymes, fluorescent or light-emmitting molecules methods and complete blood count performed in Medonic three part Fully Automated hematology analyzer. The maximum value (41.2±29.3 mIU/ml) of TSH was observed between the age group of 41-50 years with low concentration (9.1±1.12 g/dl) of hemoglobin (Hb) and diminished count (3.9±1.4 10^6/mm^3) of red blood cells (RBC) with normal value (31.9±3.2 %) of hematocrit (HCT), normal value (82.3±2.0 fl) of mean corpuscular volume (MCV), normal value (31.1±1.2 pg) of mean corpuscular hemoglobin (MCH) & normal value (33.4±1.1 g/dl) of mean corpuscular hemoglobin concentration (MCHC). Anemia is a common health problem in India, which may be known as conditions and in the current study we also concluded that anemia is common finding in hypothyroidism patients.

Keywords **:** Free tri-iodothyronine (FT3); Free thyroxine (FT4); Thyroid-stimulating hormone (TSH); Hypothyroidism; Anemia

INTRODUCTION

Thyroid disorders is one of the most common and biggest medical problem in clinical practice not in India but all over the world . [1,2] The physical examination or sign and symptoms of patient suffering from thyroid disease can be difficult to elucidate for a doctor to make sure for proper treatment. [3] It is necessary to use biochemical tests for accurate diagnosis of patient suffering from thyroid dysfunction . [4] The screening and identification of primary disease of thyroid disorder is recommended by performing the thyroid stimulating hormone (TSH) level with patient blood serum, the elevated level of TSH in primary hypothyroidism and diminished level of TSH in pituitary insufficiency, may be low or low-normal in primary hypothyroidism . [5,6] The evaluating of increased level of thyroid stimulating hormone followed with normal or low level of tetra-iodthyroxine and tri-iodothyronine may help to clinicians for monitoring treatment of hypothyroidism patient. Thyroid dysfunction is due to at an early stage of evolution disorder in thyroid deficiency patient without obvious symptoms which indicate the sub clinical hypothyroidism. The prevalence rate of 3 to 8% sub clinical hypothyroidism in patient without known thyroid disorder has been observed . It is found in adult population but it is more common in women . [7-8] However, the most common and widely clinical manifestation of sub clinical hypothyroidism is minimal nonspecific or absent of signs that indicate the clear presentation of hypothyroidism leading to resulting the large degree of deterioration of the thyroid gland, disease duration of thyroid gland and

thyroid hormone deficiency in an individual as well as in hypothyroidism presence is the state of having multiple medical conditions at the same time like heart and peripheral artery diseases, depression and various biochemical disturbances. [9-10]

In sub clinical hypothyroidism there is adverse effect on cognitive performance causing memory impairment, low concentration and poor attention as found in various research studies. [9-12]

The metabolic disorder associated with sub clinical hypothyroidism includes the dilution hyponatremia and anaemia . [13] Anaemia is not a disease but it is a condition which may occur before any other clinical manifestation of thyroid disease appears. Hypothyroidism has a lower volume of plasma and in lower volume of plasma anaemia is not diagnosed because it causes a false elevation in haemoglobin concentration in hypothyroid patient blood . [14] In hypothyroidism, three major types of anaemia are observed like normocytic normochromic, microcytic hypochromic and macrocytic hypochromic. [15] There is two cell lines in bone marrow involved for haematopoiesis, in hypothyroidism, there is hypoplasia seen in all myeloid cell lines by which all haematological parameter is normal while an euthyroid state is achieved . [16] The anaemia is commonly caused by inadequate dietry aspects or malabsorption of vitamin B12, folic acid, iron, etc. The normocytic normochromic anaemia appears due to thyroid dysfunction. [17]

MATERIALS AND METHODS

The current study was carried out in the Department of Medical Laboratory Technology (Pathology) in Sardar Bhagwan Singh University, Balawala, Dehradun, Uttrakhand, India. This study included a minimum number of 300 patients visiting the outpatient department (OPD) of Sardar Bhagwan Singh University, Balawala, Dehradun, Uttrakhand, India, from the period of May 2017 to December 2019, who are confirmed by overnight fasting for given the blood sample based on world Health organization (WHO) criteria.

After taking informed consent from patients, the fasting venous blood samples were collected in a plain gel vial and ethylene diamine tetraacetic acid (EDTA). Leave the plain gel vial at room temperature for five to ten minutes for proper clotting of blood and EDTA blood samples were mixed properly with rotor. Centrifuge the plain gel vial at 2500 rpm for 5-10 minutes for separation of non-hemolysed serum. Blood/serum samples were stored at refrigerator temperature (4-6^{o}C) used for the further evaluation of thyroid disorder and complete blood count (CBC) by using standard protocols with given methods.

Inclusion and Exclusion criteria

Inclusion criteria:

1. Consenting patients
2. All patients suffering from thyroid disorder with hypothyroidism.
3. Adult patients (>12yr.) with thyroid disorder.

Exclusion criteria:

1. Acute/ sub acute blood losses respiratory, gastrointestinal or genitourinary tract.
2. Patients with abnormal dietary habits like chronic Smoking, tobacco intake and alcoholism.
3. Patient taking anti thyroid drugs.
4. Medications that could cause thyroid hormone dysfunction (eg. interferon, lithium, amiodarone, corticosteroids and dopamine).
5. Patients suffering from any other metabolic complications like diabetes mellitus, cardiac diseases, renal disease, liver disease and hypertension.

The selected population has been completed their demographic characters such as age, sex, height and weight were noted. Serum free tri-iodothyronine (FT3), free thyroxine (FT4) and thyroid-stimulating hormone (TSH) were determined by immunoassays including enzymes, fluorescent or light-emmitting molecules for accurate detection of thyroid hormone disorders . [18]

EDTA blood samples were used for complete blood count by using Medonic three part Fully Automated hematology analyzer . [18-19]

The patient's blood samples first underwent to complete blood count which quantifies the red blood cells (RBC), hemoglobin (Hb), hematocrit value (HCT) and calculate the red cell indices (MCV, MCH, MCHC). The indices are calculated from the results of the hemoglobin, RBC count and

hematocrit value to define the size, shape and hemoglobin content of red blood cells. The indices are important parameters for identification of anemia.

On the basis of red cell indices (mean corpuscular volume [MCV]), patients having anemia were further classified as normocytic normochromic (MCV 80–96 fl), microcytic hypochromic (MCV <80 fl), and macrocytic (MCV >96 fl).

RESULTS

In the current study, the frequency of thyroid disorder in the form of hypothyroidism were determined in different age group of patients visit the out patients department of Sardar Bhagwan Singh University, Balawala, Uttarakhand, India from the period of May 2017 to December 2019. The total number of patients included in this study was 300. The prevalence of hypothyroidism was observed higher in the age group of patients between 41-50 years whereas prevalence of normocytic normochromic anemia was observed in all age group of hypothyroidism patients.

The results of thyroid function tests of study population was compared with normal, low and high value to determine the hypothyroidism given in **Table 1**.

The mean age group of this study population was 50±18.58 years, the mean height of the study population was 1.69±0.01 meter and the mean weight of the study population was 62.3±4.26 as shown in **Table 2**.

Anemia is defined while the hemoglobin concentration less than 12.0 gm/dl and red blood cell counts less than 3.5 millions cells cubic mm. All the study population showed the high value of TSH while compared with normal reference value and low concentration of hemoglobin and red blood cell counts as shown in **Table 3**.

The maximum value (41.2±29.3 mIU/ml) of TSH was observed between the age group of 41-50 years with low concentration (9.1±1.12 g/dl) of hemoglobin (Hb) and diminished count (3.9±1.4 $10^6/mm^3$) of red blood cells (RBC) with normal value (31.9±3.2 %) of hematocrit (HCT), normal value (82.3±2.0 fl) of mean corpuscular volume (MCV), normal value (31.1±1.2 pg) of mean corpuscular hemoglobin (MCH) & normal value (33.4±1.1 g/dl) of mean corpuscular hemoglobin concentration (MCHC).

The minimum value (15.4±7.1mIU/ml) of TSH was observed between the age group of 18-30 years with low concentration (10.2±1.11 g/dl) of hemoglobin (Hb) and decreased count (4.4±1.1 $10^6/mm^3$) of red blood cells (RBC) with normal value (33.8±3.2 %) of hematocrit (HCT), normal value (83.8±3.8 fl) of mean corpuscular volume MCV, normal value (30.1±3.2 pg) of mean corpuscular hemoglobin (MCH) & normal value (33.1±1.2 g/dl) mean corpuscular hemoglobin concentration (MCHC).

Table 1: Refence ranges for interpretation of thyroid function test.

Condition	TSH (mIU/L)	FT4 (ng/dl)	FT3 (pg/ml)
Normal	0.4-4.0	0.8-1.9	1.5-4.1
Low	< 0.4	< 0.8	< 1.5
High	> 4.0	> 1.9	> 4.1

Table 2: Distribution of demographic characters such as age, height and weight in hypothyroidism patients (n=300) results are expressed in (Mean ± SD).

Age- groups	No. of Patients	Age (Years)	Height (mt)	Weight (Kg)
18-30	59	24.4±4.11	1.71±0.01	54.6±5.12
31-40	130	35.1±3.32	1.70±0.03	62.4±3.14
41-50	60	45.5±2.25	1.69±0.02	63.2±4.11
51-60	37	55.7±2.12	1.69±0.01	66.3±2.21
61-70	10	66.2±3.14	1.66±0.03	66.1±5.15
71-80	04	73.1±1.21	1.70±0.05	61.6±2.24
Total	300	50±18.58	1.69±0.01	62.3±4.26

Table: 3 Laboratory values of Complete Blood Count in hyperthyroidism patient (n=300) results are expressed in (Mean ± SD) of all age group patients.

Age groups (Years)	TSH (mIU/ml)	FT3 (pg/ml)	FT4 (ng/dl)	Hb (g/dl)	RBC (10^6/mm^3)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/dl)
18-30	15.4±7.1	1.19±0.71	0.79±0.13	10.2±1.11	4.4±1.1	33·8±3.2	83.8±3.8	30.1±3.2	33.1±1.2
31-40	17.3±5.4	1.06±0.92	0.69±0.15	9.9±1.06	4.2±1.3	32.3±2.3	84.1±4.8	32.1±1.2	31.2±2.2
41-50	41.2±29.3	1.14±0.83	0.59±0.12	9.1±1.12	3.9±1.4	31.9±3.2	82.3±2.0	31.1±1.2	33.4±1.1

51-60	33.1±11.3	1.13±0.61	0.73±0.13	10.1±0.76	4.2±1.5	32.1±2.4	84.6±4.8	29.1±2.2	30.1±1.7
61-70	22.3±2.2	1.14±0.81	0.79±0.11	10.1±1.14	4.5±1.6	32.7±2.2	83.3±3.3	29.1±4.2	32.4±1.6
71-80	23.1±3.3	1.18±0.52	0.69±0.18	10.1±1.23	4.7±1.3	33.2±2.2	83.1±5.8	31.1±1.1	31.2±1.6
Total	25.4±9·89	1.14±0.04	0.71±0.77	10.0±0.50	4.3±0.27	32.6±0.72	83.5±0.81	30.4±1.21	31.9±1.27

DISCUSSION

Hypothyroidism is not only problem in Indian population but it is also common problem in world population, affecting with 1% of general population and about 5% of individuals over age 60 years. [20] Anemia in association with hypothyroidism has been studied since 1881. [21] In hypothyroidism, the disorder of all organ systems can be affected with the sign of abnormal physiology primary hematopoietic systems one among these affected systems, which initiated the diminished formation of red blood cells with decreased amount of conjugated proteins that refer a condition anemia. [22] Anemia is a condition that is not a disease but it is a severe public health problem in population of India and it may be precipitated by conditions such as hypothyroidism. It is very important for physician to carry out the treatment of the patient with anemia correctly, it is necessary to determine the etiological causes of anemia. [20-22] Anemia may occur even before any other manifestation of thyroid disorder appears at the same time or late the course of hypothyroidism. There are so many common causing factors of anemia in hypothyroidism like obesity, life style with dietary aspects, physical inactivity, etc. . [23] The population suffering with hypothyroidism for long time also includes the complications of different diseases like, hashimotos disease, graves's disease, goiter, thyroid nodules disease, etc. increasing the huge medical and economical burden on patients. [22-23]

In current study, there was significant increased level of thyroid stimulating hormone (TSH) with deficient level of free tri-iodothyronine (FT3) or normal level of free tetra-iodthyroxine (FT4) followed with diminished concentration of hemoglobin (Hb) and also decreased count of red blood cells (RBC).

In the current study the maximum value (41.2±29.3 mIU/ml) of TSH was observed between the age group of 41-50 years with low concentration (9.1±1.12 g/dl) of hemoglobin (Hb) and diminished count (3.9±1.4 10^6/mm^3) of red blood cells (RBC) with normal value (31.9±3.2 %) of hematocrit (HCT), normal value (82.3±2.0 fl) of mean corpuscular volume (MCV), normal value (31.1±1.2 pg) of mean corpuscular hemoglobin (MCH) & normal value (33.4±1.1 g/dl) of mean corpuscular hemoglobin concentration (MCHC). Our observation were in accordance with the study conducted by Tapper et al. [3] and Kulkarni and Jadhav [10] which reported the prevalence of anaemia in hypothyroidism patients. The similar pattern observed by us, the normocytic and normochromic anemia was the most common in hypothyroidism patient.

The comparable finding was observed with high level of TSH followed with normal level of FT3 and diminished level of FT4 by Anand et al. [6] ; Das et al. [23] ; Erdogan et al. [24] and Bremner et al. [26]

In this study, we also reported that the most common type of anemia was normocytic normochromic type. The study elaborated the role of anemia in thyroid disorder with detailed evaluation of increased level of thyroid stimulating hormone (TSH) in patients with decreased count and concentration of hemoglobin and red blood cells with normol value of red cell indices (like MCV, MCH, MCHC) and hematocrit value (HCT). Thus, we found an increased anemic frequency in hypothyroidism patients.

Further suggestive tests were performed for the anemic patients to differentiate the type of annemia with normocytic normochromic anemia which were investigated by Coombs test and bone marrow examination. Stool for occult blood, upper GI scopy, and Iron studies were done in patients with a microcytic hypochromic anemia. Patients with macrocytic anemia were examined by performing the Vitamin B12 and folic acid levels of patient blood samples which help to treat hypothyroidism in anemic patients and whether its treatment can optimize the results of treatment of iron, folate or Vitamin B12 deficiencies which can have wider implications.

CONCLUSION

In the current study, we concluded that anemia is common finding in hypothyroid disorder. Anemia is a common health problem in India, which may be known as conditions. It also arises in the association of different diseases. The one of the most common associated diseases where the anemic condition is found in highly reflection in hypothyroidism patients in all over world. The normocytic and normochromic anemia is the most common type of anemia found in hypothyroidism patients. Presence of anemia in hypothyroidism is also significantly high so it will be difficult to find euthyroidism or correct types of anemia with iron or other aspects of deficiency. In this way, the effects of all these is due to endocrine disorders which evaluate the impact of subclinical hypothyroidism. The thyroid function tests (TFT) are used for evaluation for the hypothyroidism.

ACKNOWLEDGEMENT

Authors are thankful to Dr. G.D. Singh, Managing Secretary, Sardar Bhagwan Singh University, Dehradun, Uttrakhand, India for providing laboratory facility and resources for this research work.

Financial Support: The study does not have any financial support.

Conflict of interest: The authors of the article have no conflict of interest.

REFERENCES

1. Banday TH., Bhat SB., Bhat SB., Bashir S., Naveed S. Incipient iron deficiency in primary hypothyroidism. Thyroid Res Pract. 2018; 15:138-141.
2. Khorasani F., Nematollah R., Ahmad G., Mohammad R., Mohajeri T., Mostafa Q. Subclinical Hypothyroidism on Auditory Divided Attention. JMR. 2019; 13(1):39-48.
3. Tapper MA., Francis CA., Dilworth LL., McGrowder DA. Evaluating thyroid function in the clinical laboratory. Thyroid Res Pract. 2017; 14:118-121.
4. Verghese A., Sudeep K., Malathi M. Concordance between free T4 and T4 in thyroid function tests. Int J Clin Biomed Res. 2016; 2:9-13.
5. Clark PM., Holder RL., Haque SM., Hobbs FD., Roberts LM., Franklyn JA. The relationship between serum TSH and free T4 in older people. J Clin Pathol. 2012; 65:463-465.
6. 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):153-159.
7. Nancy CA., Jhon PG., Rodgers GM. Wintrobe's Cinical hematology. 13th ed. Vol. 1. 2014. p. 810-815.
8. Carvalho GA., Perez CL., Ward LS. The clinical use of thyroid function tests. Arq Bras Endocrinol Metabol. 2013; 57:193-204.
9. Kazerouni F., Amirrasouli H. Performance characteristics of three automated immunoassays for thyroid hormones. Caspian J Intern Med. 2012; 3:400-404.
10. Kulkarni VK., Jadhav DU. A study of anemia in primary hypothyroidism. Int J Adv Med. 2017; 4:383-389.
11. Gamit MJ., Talwelkar HS. Survey of different types of anemia. Int J Med Sci Public Health. 2017; 6:493-496.

12. Rabet-Bensalah K., Aubert CE., Coslovsky M., Collet TH., Baumgartner C., Den Elzen WP., et al. Thyroid dysfunction and anaemia in a large population-based study. Clin Endocrinol (Oxf). 2016; 84:627-631.
13. Schindhelm RK., Boekel E., Heima NE., Schoor NM., Simsek S. Thyroid hormones and erythrocyte indices in a cohort of euthyroid older subjects. Eur J Intern Med. 2013; 24:241-244.
14. Erdogan M., Kösenli A., Ganidagli S., Kulaksizoglu M. Characteristics of anemia in subclinical and overt hypothyroid patients. Endocr J. 2012; 59:213-220.
15. Kahapola., Arachchige KM., Hadlow N., Wardrop R., Lim EM., Walsh JP. Age-specific TSH reference ranges have minimal impact on the diagnosis of thyroid dysfunction. Clin Endocrinol (Oxf). 2012; 77:773-779.
16. Kazemi., Jahromi M., Shahriari AA., Samedanifard SH., Doostmohamadian S., Abdolahpoor E., Allameh SF. The Association Between Hypothyroidism and Anemia: a Clinical Study. IJHOSCR. 2010; 4:6-9.
17. Wang YP., Lin HP., Chen HM., Kuo YS., Lang MJ., Sun A., et al. Hemoglobin, iron, and vitamin B12 deficiencies and high blood homocysteine levels in patients with anti-thyroid autoantibodies. J Formos Med Assoc. 2014; 113:155-160.
18. Joshi S. Laboratory evaluation of thyroid function. JAPI. 2011; 49:14-20.
19. Ladenson PW., Singer PA., Ain KB., Bagchi N., Bigos ST., Levy EG., et al. American thyroid association guidelines for detection of thyroid dysfunction. Arch Intern Med. 2000; 160:1573-1575.
20. Papadakis MA., McPhee SJ., Rabow MW. Current medical diagnosis & treatment 2013. New York: McGraw Hill Medical, 2013.
21. Tunbridge WM., Caldwell G. The epidemiology of thyroid diseases. In: Braverman LE., Utiger RD., editors. Werner and Ingbar's The Thyroid. 6th ed. Philadelphia: J. B. Lippincott; 1991. 578-88.
22. Melmed S., Polonsky KS., Larsen PR., Kronenberg H. Williams Textbook of Endocrinology: Expert Consult. London: Elsevier Health Sciences, 2011.
23. Das KC., Mukherjee M., Sarkar TK., Dash RJ., Rastogi GK. Erythropoiesis and erythropoietin in hypo-and hyperthyroidism. J Clin Endocrinol Metab. 1975; 40:211-20.
24. Erdogan M., Kösenli A., Ganidagli S., Kulaksizoglu M. Characteristics of anemia in subclinical and overt hypothyroid patients. Endocr J. 2012; 59:213-220.
25. 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 (Oxf). 2012; 76:304-11.