

Effect of Serum Ferritin Levels in Newly Diagnosed Hypothyroid Patients: A Clinical Prospective Observational Study in a Tertiary Care Hospital, Telangana, India

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Abstract

Background: Hypothyroidism is a condition caused due to decreased synthesis,metabolism or decreased action of thyroid hormone which can be due to various causes. Primary hypothyroidism is due to conditions affecting the thyroid gland itself. It accounts for approximately 99% of cases, with < 1% being due to TSH deficiency known as central or secondary hypothyroidism **Objectives:** To clinically suspect and diagnose cases of hypothyroidism.To measure serum ferritin levels in newly diagnosed hypothyroid patients.To look for a correlation between serum ferritin level and T3, T4 and TSH levels.**Methodology:** 30 patients with clinically suspected hypothyroidism were confirmed by measuring fasting serum T3, T4 and TSH levels.Complete Blood Picture, Liver Function Tests, Renal Function Tests and Urine Pregnancy Test done to rule out other causes that could alter thyroid function test.After an overnight fasting of 8 hours, 2ml of venous sample was collected in a red cap vacutainer under aseptic conditions and serum T3, T4 and TSH levels were measured using chemiluminescence immunoassay (CLIA) .In patients with confirmed hypothyroidism, serum ferritin levels were estimated.For this, 2ml of venous blood sample was collected in a red cap

vacutainer under aseptic conditions and serum ferritin levels was measured using CLIA

Results:The mean serum T3,T4 and TSH levels were 0.5203 ng/ml,3.50 ug/dl,40.02 uIU/ml respectively.The overall mean serum ferritin was 34.24 ng/ml.The mean serum ferritin among patients in whom correlation was seen was 8.2 ng/ml.The mean serum ferritin among patients in whom correlation was not seen was 45 ng/ml.A significant negative correlation of 0.01 was found between serum ferritin and TSH levels indicating that patients with lower serum ferritin had higher serum TSH levels.**Conclusion :**Patients presented with weight gain and fatigue, serum ferritin had a significant negative correlation with TSH indicating that lower ferritin levels were associated with higher TSH levels.

Keywords : Serum Ferritin,Hypothyroid Patients,Newly Diagnosed, CLIA,TSH

INTRODUCTION

Hypothyroidism is a condition caused due to decreased synthesis,metabolism or decreased action of thyroid hormone which can be due to various causes¹. Primary hypothyroidism is due to conditions affecting the thyroid gland itself. It accounts for approximately 99% of cases, with < 1% being due to TSH deficiency known as central or secondary hypothyroidism¹.Thyroid synthesis involves many steps, and it can be affected by various mechanisms at various levels. One of the steps of thyroid synthesis is iodination that leads to formation of iodotyrosines- mono-iodotyrosine (MIT) and di-iodotyrosine (DIT) which is mediated by a heme containing enzyme called thyroperoxidase (TPO)¹.

Hypothyroidism is the most common thyroid disorder in India, affecting one in ten adults. The prevalence of hypothyroidism is 11% in India, compared with U.K & U.S.A, which is only 2% and 4.6% respectively. The highest prevalence of hypothyroidism (13.1%) is noted in people of 46–54 years of age².Several studies in animals and human beings have shown thatnutritional iron deficiency may significantly lower the circulating levels of both thyroxine and triiodothyronine and may also reduce conversion of T4 to T3.

Hypothyroidism, itself, may lead to low iron levels due to poor gut absorption as a result of decreased levels of digestive acids/ enzymes or due to associated autoimmune conditions like celiac disease. It may also be due to heavy menstruation seen in some female patients. Thus, hypothyroidism and iron deficiency states are strongly interrelated where low iron stores can cause hypothyroidism probably due to decreased functioning of thyroperoxidase enzyme and conversely, hypothyroidism can also cause iron deficiency due to decreased erythropoietin and hypo proliferation of erythroid progenitors³ Being a developing nation, iron deficiency is common in general population and prevalence of hypothyroidism has also increased tremendously over the past few years. Therefore, this study was undertaken to estimate levels of serum ferritin in newly diagnosed patients of hypothyroidism.

METHODOLOGY: This study^{3,4,5} titled “Effect of Serum Ferritin Levels in Newly Diagnosed Hypothyroid Patients: A Clinical Prospective Observational Study in a Tertiary Care Hospital, Telangana, India” was carried out during the period from January 2020 to June 2021. The study was conducted on 30 selected patients fulfilling the criteria. The study was conducted at Mallareddy institute of medical sciences, Suraram, Telangana, India. with an aim to observe the Effect of Serum Ferritin Levels in Newly Diagnosed Hypothyroid Patients.

Inclusion criteria: Patients above 18 years of age of both the genders with newly diagnosed hypothyroidism. Patients who have given informed consent

Exclusion criteria: Pregnant and lactating female, Patient with chronic liver disease and chronic renal failure., Patient having acute infections., Patient consuming drugs that reduce T3 and T4 levels- amiodarone, lithium, phenytoin, rifampicin, NSAIDs

Ethics: This study was approved by the Institutional Ethics Committee, Mallareddy institute of medical sciences, Suraram, Telangana, India. An informed written consent was taken from all the patients involved in the study after explaining regarding the study.

Study Procedure: After taking informed consent, patients with clinically suspected hypothyroidism were confirmed by measuring fasting serum T3, T4 and TSH levels. Complete Blood Picture, Liver Function Tests, Renal Function Tests and Urine Pregnancy Test (in selected patients) was done to rule out other causes that could alter thyroid function test. After an overnight fasting of 8 hours, 2ml of venous sample was collected in a red cap vacutainer under aseptic conditions and serum T3, T4 and TSH levels were measured using chemiluminescence immunoassay (CLIA) method. In patients with confirmed hypothyroidism, serum ferritin levels were estimated. For this, 2ml of venous blood sample was collected in a red cap vacutainer under aseptic conditions and serum ferritin levels were measured using chemiluminescence immunoassay (CLIA) method.

Normal values for T3- 0.87-1.78 ng/ml

Normal values for T4- 6.09-12.23 ug/dl

Normal values for TSH- 0.34-5.6 uIU/ml

Normal values for serum ferritin- 30-400 ng/ml

Statistical Analysis:

Data was collected and entered into MS Excel 2016 and analysed with SPSS version 20.0 for descriptive statistics.

Results

Total number of patients included in my study were 30 patients. Most of the patients were females with the distribution being 22 females (73%) and 8 males (27%).

Table 1- Distribution of patients by gender

Gender	Number	Percentage
Female	22	73 %
Male	8	27%

Table 2- Mean age distribution of the patients

	N	Minimum	Maximum	Mean	SD
Age in years	30	19	76	36.03	13.95

Patients in the study were between 19 years of age till 76 years of age. The number of patients between 19-29 years of age were 12 out of which 11 were female and 1 was male. The number of patients between 30-39 years of age were 9 out of which 8 were female and 1 was male. The number of patients between 40-49 years age group were 5 out of which 3 were females and 2 was male. The number of patients between 50-59 years were 2 and both the patients were females. There were no patients from 60-69 years of age. There were 2 patients between 70-79 years of age, and both were male.

The symptoms that the patients presented with in my study were weight loss, fatigue, constipation, hair loss, cold intolerance, and menstrual abnormalities in females. The most common symptoms were weight gain and fatigue that was present in a majority of the patients, 29 patients (97%).

Table 3- Number of patients with weight gain as a symptom

SYMPTOM	NUMBER	PERCENTAGE
Weight gain present	29	97%
No weight gain	1	3%

Table 4- Number of patients with fatigue as a symptom

SYMPTOM	NUMBER	PERCENTAGE
Fatigue present	29	97%
No fatigue	1	3%

The second most common symptom was hair loss that was present in 25 patients(83%).

Table 5- Number of patients with hair loss as a symptom

SYMPTOM	NUMBER	PERCENTAGE
Hair fall present	25	83%
No hair fall	5	17%

The next most common symptom was constipation that was present in 19 patients(63%).

Table 6- Number of patients with constipation as a symptom

SYMPTOM	NUMBER	PERCENTAGE
Constipation present	19	63%
No constipation	11	37%

Among female patients, menstrual abnormalities were present in 15 patients(68%) and in these 15 patients, menorrhagia was present in 11 patients (73%)and amenorrhea in 4 patients (27%).

Table 7– Number of patients with menstrual abnormalities

SYMPTOMS	NUMBER	PERCENTAGE
Menstrual abnormalities present	15	68%
No menstrual abnormalities	7	32%

Table 8- Type of menstrual abnormality

TYPE OF MENSTRUAL ABNORMALITY	NUMBER	PERCENTAGE
Menorrhagia	11	73%
Amenorrhea	4	27%

The least common symptom was cold intolerance that was present in only 7 patients (23%).

Table 9- Number of patients with cold intolerance as a symptom

SYMPTOM	NUMBER	PERCENTAGE
Cold intolerance present	7	23%
No cold intolerance	23	77%

On clinical examination, pallor was seen in 16 patients (54%)

Table 10 – Number of patients with pallor

PALLOR	NUMBER	PERCENTAGE
Present	16	54%
No pallor	14	46%

Table 11- Mean level of thyroid hormones, TSH and serum ferritin among the study participants

	N	Minimum	Maximum	Mean	SD
T3	30	0.11	0.80	0.5203	0.22
T4	30	0.90	5.90	3.50	1.49
TSH	30	6.59	150.00	31.68	40.02
Serum ferritin	30	3.2	310.6	34.24	57.51

Table 12- Comparison of the mean difference between the two groups of thyroid hormone, TSH and serum ferritin

	Not found		Found		t-test (p-value)
	Mean	SD	Mean	SD	
T3	0.57	0.22	0.48	0.23	0.293
T4	3.88	1.59	3.17	1.38	0.197
TSH	37.04	52.23	26.99	26.14	0.502
Serum Ferritin	45.0	24.3	8.2	2.9	0.001**

Table 13- Pearson correlation between the thyroid hormone, TSH with the serum ferritin

		T3	T4	TSH
Serum Ferritin	r	.016	-.267	.570**
	Sig.	.932	.154	.001

** . Correlation is significant at the 0.01 level (2-tailed).

In present study, on assessment of strength of association between the serumferritin with the thyroid hormone and TSH, we found a significant positive strength of association between the variables ($p < 0.05$).

Table 14: Distribution of the correlation between the serumferritin and thyroid hormones

		Frequency	Percent
Correlation	Found	16	53.3
	Not found	14	46.7
	Total	30	100.0

Discussion :

Thyroid disorders are the second most common endocrine disorder following diabetes mellitus.¹⁴ Thyroid hormones are required to maintain harmonium between many organ systems. There exists a strong connection between the thyroid status and iron status of the body. A total of 30 patients were included in my study who fulfilled the inclusion criteria from the outpatient and inpatient departments at Malla Reddy Hospital, Suraram. In my study, the mean age of presentation was 36.03 years with majority of patients belonging to 19-39 years age group. This was consistent with findings of other studies. In a study done by Kiran Dahiya et.al. conducted at B.D.S. PGIMS, Rohtak, Haryana, India, with fifty newly diagnosed patients of hypothyroidism and fifty apparently healthy age and sex matched euthyroid controls, the mean age was 39.5 years.^{6,7,8,15} In a study done by Ashuma Sachdeva et.al. at Department of Biochemistry, Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences, Rohtak, a total of 50 newly diagnosed patients with hypothyroidism were included in the study and the mean age was 34.89 years.¹¹ In a study done by Rohit Anand et.al. at Department of Medicine, King George Medical University (KGMU), Lucknow for a period of 1 year, from August 2016 to July 2017, the mean age group was 38.8 years. There was a female

preponderance in the gender distribution in my study with females being 22 patients (73%) and males being 8 patients (27%). This is in concordance with majority of studies done on hypothyroidism. In a study done by Maldonado-Araque C et.al at Department of Endocrinology and Nutrition, Spain, on 3846 patients, the number of female patients were 2079 (54%) and the number of male patients were 1767 (45%)⁹ In a study done by Rohit Anand et. al. at Department of Medicine, King George Medical University (KGMU), Lucknow for a period of 1 year, from August 2016 to July 2017, the number of female patients were 290 (75.7) and the number of male patients were 93 (24.3%). In a study done by Ashish Shukla et.al. at Department of Biochemistry, Subharti Medical College in association with Endocrine and Metabolic OPD of Chatrapati Shivaji Subharti Hospital, Meerut, India from March 2016 to August 2016, the number of female patients were 76 (76%) and the number of male patients were 24 (24%).⁹ In a study done by Kiran Dahiya et.al. at B.D.S. PGIMS, Rohtak, Haryana, India, the number of female patients were 30 (60%) and the number of male patients were 20 (40%).¹⁰ There was a female preponderance in the gender distribution in my study with females being 22 patients (73%) and males being 8 patients (27%). This is in concordance with majority of studies done on hypothyroidism. In a study done by Maldonado-Araque C et.al at Department of Endocrinology and Nutrition, Spain, on 3846 patients, the number of female patients were 2079 (54%) and the number of male patients were 1767 (45%)¹¹ In a study done by Rohit Anand et. al. at Department of Medicine, King George Medical University (KGMU), Lucknow for a period of 1 year, from August 2016 to July 2017, the number of female patients were 290 (75.7) and the number of male patients were 93 (24.3%).⁷ In a study done by Ashish Shukla et.al. at Department of Biochemistry, Subharti Medical College in association with Endocrine and Metabolic OPD of Chatrapati Shivaji Subharti Hospital, Meerut, India from March 2016 to August 2016, the number of female patients were 76 (76%) and the number of male patients

were 24 (24%).¹²In a study done by Kiran Dahiya et.al. at B.D.S. PGIMS, Rohtak, Haryana, India, the number of female patients were 30 (60%) and the number of male patients were 20 (40%).¹⁵In a study done by Ashuma^{13,14} Sachdev et.al. at Department of Biochemistry, Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences, Rohtak, the number of female patients were 29 (58%) and the number of male patients were 21 (42%).¹⁶In a study done by Banday TH et.al. at Department of Medicine, Adichunchingiri Institute of Medical Sciences and Research, Karnataka, India, the number of female patients were 46 (65%) and the number of male patients were 24 (34%). The higher prevalence of thyroid disorders in women suggests that estrogen might be involved in the pathophysiology of thyroid dysfunction. Estrogen has an anti-thyroid action by inhibiting the peripheral conversion of T4 to T3. Estrogen also competes with T3 and T4 for binding sites on the receptors. Thus, in reproductive age group, female propensity is seen in hypothyroid patients¹⁵.

The most common symptoms that patients presented with in my study were weight gain and fatigue in 29 patients (97%) followed by hair loss in 25 patients (83%), constipation in 19 patients (63%) and the least common symptom was cold intolerance in 7 patients (23%).

The most common symptom that is weight gain is attributable to the retention of water rather than increased intake of food since most of the patients with hypothyroidism have decreased appetite¹. The reduction in cutaneous circulation is responsible for the coolness and pallor of the skin and the sensitivity to cold¹. Peristaltic activity is decreased and, together with the decreased food intake, is responsible for the frequent complaint of constipation¹. On clinical examination, pallor was seen in 16 patients (53%) out of a total of 30 patients. These 16 patients with pallor also showed low levels of serum ferritin (less than 30ng/ml) indicating iron deficiency state. Few studies have indicated that the functioning of thyroperoxidase enzyme is altered even in state of iron deficiency i.e. negative iron balance and does not necessarily need state of iron deficiency anemia. In the study done by Banday TH et.al. at Department of

Medicine, Adichunchingiri Institute of Medical Sciences and Research, Karnataka, India, a total of 70 patients with primary hypothyroidism, that included both newly diagnosed and previously diagnosed hypothyroid patients, were included in the study. The prevalence of iron deficiency in primary hypothyroidism was 34.2% among which 28.57% were females and 5.7% were males. Out of a total of 70 hypothyroid patients, patients who manifested with anemia were 20%, whereas prevalence of iron deficiency was 34.2%, showing that frequency of iron deficiency(with or without anemia) is higher than iron deficiency anemia. This study concluded that frequency of iron deficiency state is higher than iron deficiency anemia and the presence of iron deficiency state may also alter the thyroid status. In the present study the mean value of T3 was 0.52 ng/ml, the mean value of T4 was 3.50 ug/dl and the mean value of TSH was 31.68 uIU/ml. The overall mean value of ferritin was 34.24 ng/ml. In 14 patients in whom no correlation was found the mean ferritin level was 45 ng/ml. In patients in whom correlation was found the mean ferritin level was 8.2 ng/ml. Out of the three parameters of thyroid function test i.e. T3, T4 and TSH, significant correlation was found between TSH and ferritin levels indicating that lower ferritin levels were associated with higher TSH values. This finding is in concordance with few studies as mentioned below. In a study done by Amera Kamal Mohammed et.al., at Department of Clinical Laboratory Sciences., College of Pharmacy, University of Kirkuk, 52001, Kirkuk, Iraq for a period of five months from September 2017 to January 2018, a significant negative correlation was observed between TSH and ferritin. Additionally, they also concluded that hypothyroidism is related to the lack of serum ferritin, which means that the thyroid functions are influenced by the level of serum ferritin.¹⁸ Similar finding was also seen in a study done by Akhter S et.al., at Department of Biochemistry, Bangabandhu, Sheikh Mujib Medical University, Dhaka for a period of one year from June 2006 to June 2007, a total of 72 patients were included. In this study, a positive correlation was seen between serum ferritin with T4 and TSH but no correlation with serum ferritin and T3. There

was a statistically significant correlation between serum ferritin and TSH but there was no statistically significant correlation between serum ferritin and T4 indicating that lower serum ferritin levels were associated with higher TSH levels¹⁷.

In the present study, serum ferritin levels were used to indicate the iron status. Indicators of iron status span an array of measures and can be confounded by factors ranging from inflammation to analytic challenges. Moreover, given that iron status is a continuum from iron deficiency anemia to iron overload, different indexes may be more useful than others depending on the interest.¹³

Classically, iron deficiency is defined when examination of bone marrow aspirate under microscopy with the use of an iron stain (Perl's stain) reveals an absence of hemosiderin. This standard reflects an absence of iron available to the bone marrow for erythropoiesis, thereby resulting in anemia. Diagnosis of iron deficiency through sampling of bone marrow to identify the absence of body iron stores is impractical in most cases. Although many indexes are available, determination of status by using serum ferritin concentrations is the most commonly deployed strategy used in clinical and public health settings.¹³

Conclusion :

From the results it can be concluded that patients presented with in my study was weight gain and fatigue. Serum ferritin had a significant negative correlation with TSH indicating that lower ferritin levels were associated with higher TSH levels. This implies that low ferritin levels and low iron levels could be a contributing factor to the development of hypothyroidism. Further studies may conclude that in patients with hypothyroidism and anemia, treatment with levothyroxine and iron supplements may help in achieving euthyroid state faster than treatment with levothyroxine alone

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