

Assessment of Thyroid Function during Oral thyroid Hormone Replacement Therapy in Hypothyroid Patients

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ABSTRACT:

BACKGROUND: Hypothyroidism is a major public health problem and an important area of research due to its high prevalence and being a major risk factor for cardiovascular diseases and other complications.

AIM: The aim of the study is to assess thyroid function during oral thyroid hormone replacement therapy in hypothyroid patients in a tertiary care hospital.

MATERIALS AND METHODS: The prospective observational study was conducted among 107 outpatient patients in the department of endocrinology for a period of 6 months. Patients were grouped into two groups; one group were taking Thyroxine sodium (n=86) and another group were taking Levothyroxine (n=21). Self-designed data entry form and hypothyroidism symptom scale were used for data collection. Mean scores of symptom scale were used to measure the improvement. Data analysis with ANOVA was done by using Graphpad prism.

RESULTS: Out of 107 patients, the prevalence of hypothyroidism in women (86.9%) was more exposed. Higher incidence of hypothyroidism was associated with the age group of 25-40 years (39.3%). Patients were experienced different symptoms at each four months and showed significant improvement (p value <0.05). In Thyroxine sodium group T3 (85.96 -83.54), T4 (7.15-7.00) and TSH (16.55-16.3) lab values has reduced from baseline to the end report. Whereas in Levothyroxine group (n=21), there is marked change in lab values including T3 (97.71-95.49), T4 (7.4-6.99) and TSH (23.45-30.09). Thyroxine sodium group was showed improvement with respect to their laboratory values.

CONCLUSION: The prevalence of hypothyroidism is moderately high among the population. The study highlights, the non-invasive and cost-

effective way to determine thyroid function is mainly rely on early identification of hypothyroid symptoms. So, creating awareness on the early onset of these symptoms and lab interpretation can be effective strategies to tackle the condition.

KEYWORDS: Hypothyroidism, Thyroxine Sodium, Levothyroxine, Thyroid Stimulating Hormone, Triiodothyronine.

I. INTRODUCTION:

The thyroid is a butterfly-shaped endocrine gland located in the lower front of the neck below the larynx (the voice box). The thyroid's job is to make thyroid hormones, which are secreted into the blood and then carried to every tissue in the body. The main hormone made by the thyroid is thyroxine, also called T4 because it contains four iodine atoms. Small amounts of another and more potent thyroid hormone containing three iodine atoms, triiodothyronine (T3), are also made by the thyroid gland. Thyroid hormones control the way every tissue in your body uses energy. They are essential to help each cell in your body's tissue and organs work right. If you have hypothyroidism that means you have an underactive thyroid ("hypo-" means "under" or "below normal"). In people with hypothyroidism, the thyroid does not make enough thyroid hormone to keep the body running normally. It is encountered in females more than in males. The idiopathic form of hypothyroidism occurs mainly in females older than 40 years. Hypothyroidism is usually progressive and irreversible [1]. Although hypothyroidism is associated with various co-morbidities, its relationship with increased all-cause mortality remains controversial [2]. Hypothyroidism may occur as a result of primary gland failure or insufficient thyroid gland stimulation by the hypothalamus or pituitary gland.

Pituitary gland failure can result from congenital abnormalities, auto immune destruction, iodine deficiency, surgical removal thyroid and infiltrative disease [3].

EPIDEMIOLOGY

Iodine deficiency and auto-immune disease (Hashimoto's) account for the vast majority of cases of primary hypothyroidism. A third of the world's population live in iodine deficient areas and the devastating consequences of severe iodine deficiency on fetal and child neurological development are well recognized. Furthermore, there is increasing concern of the possible effects of less severe grades of iodine deficiency during pregnancy on offspring cognitive development. Changes in diet and agricultural practices have led to the reemergence of iodine deficiency in countries previously believed to be iodine sufficient including developed countries. In Europe, 44% of school-age children still have insufficient iodine intake and countries such as the UK, Italy, and Spain now appear to be moderately iodine deficient 83%- 90%. In iodine sufficient countries, the prevalence of hypothyroidism ranges from 1-2% 1 rising to 7% in individuals aged between 85-89 years. The prevalence of overt hypothyroidism in the general population varies between 0.2% and 5.3% in Europe and 0.3% and 3.7% in the USA depending on the definition used and population studied. Longitudinal studies from large UK cohorts report an incidence rate of spontaneous hypothyroidism of 3.5 – 5.0 per 1000 and 0.6 – 1.0 per 1000 in women and men, respectively. A survey conducted in Spain reported a prevalence of treated hypothyroidism, untreated subclinical hypothyroidism, and untreated clinical hypothyroidism of 4.2% 4.6 and 0.3%, respectively. In Australia, the five-year incidence of hypothyroidism in individuals aged above 55 years was 0.5% and 4.2% respectively 34 while the

prevalence of overt and subclinical hypothyroidism is estimated at 0.5% and 5.0% respectively. The longest follow-up study is from the UK Wickham cohort where the mean annual incidence of spontaneous hypothyroidism during a 20year follow-up period was 35 cases per 10,000 surviving women and 6 per 10,000 surviving men 27. Higher TSH levels and antibody positive were associated with increased risk of developing hypothyroidism with a positive interactive effect.

The prevalence of hypothyroidism in India is 11%, compared with only 2% in the UK and 4.6% in the reported a significantly higher prevalence of hypothyroidism (11.73%) than those (Mumbai, Chennai and Goa) in the coastal areas (9.45%), P=0.01.

North India recorded the maximum cases of hypothyroidism, the analysis is based on inhouse data collected from over 33 lakh adults pan India from 2014 – 2016 and revealed about 32% of Indian population suffering from various kinds thyroid disorder. The prevalence of hypothyroidism was the highest in the age-group of 46-54 years (13.11%) and the lowest in that of 18-35 years (7.53%). Hypothyroidism in adults is very high in this era and it is more common in women than men [4].

SYMPTOMS OF HYPOTHYROIDISM

The clinical manifestations of hypothyroidism range from life threatening—in the case of myxedema coma—to no signs or symptoms. The symptoms for the diagnosis of hypothyroidism are nonspecific, especially in the elderly patients who present with fewer and less classic signs and symptoms than younger individuals. An increase in the severity of symptoms might predict hypothyroidism. The major signs and symptoms of hypothyroidism include the following [5];

System	Presentations	Signs and Implications
General metabolism	Weight gain, cold intolerance, fatigue	Increase in body-mass index, low metabolic rate, myxoedema, hypothermia

Cardiovascular	Fatigue on exertion, shortness of breath	Dyslipidaemia, bradycardia, hypertension, endothelial dysfunction or increased intima-media thickness, diastolic dysfunction, pericardial effusion, hyperhomocysteinemia, electrocardiogram changes
Neurosensory	Hoarseness of voice, decreased taste, vision, or hearing	Neuropathy, cochlear dysfunction, decreased olfactory and gustatory sensitivity
Neurological and psychiatric	Impaired memory, paraesthesia, mood impairment	Impaired cognitive function, delayed relaxation of tendon reflexes, depression, dementia, ataxia, Carpal tunnel syndrome and other nerve entrapment syndromes, myxoedema coma

System	Presentations	Signs and implications
Gastrointestinal	Constipation	Reduced oesophageal motility, non-alcoholic fatty liver disease, ascites (very rare)
Endocrinological	Infertility and subfertility, menstrual disturbance, galactorrhoea	Goiter, glucose metabolism dysregulation, infertility, sexual dysfunction, increased prolactin, pituitary hyperplasia
Musculoskeletal	Muscle weakness, muscle cramps, arthralgia	Creatine phosphokinase elevation, Hoffman's syndrome, osteoporotic fracture (most probably caused by overtreatment)

Haemostasis and haematological	Bleeding, fatigue	Mild anaemia, acquired von Willebrand disease, decreased protein C and S, increased red cell distribution width, increased mean platelet volume
Skin and hair	Dry skin, hair loss	Coarse skin, loss of lateral eyebrows, yellow palms of the hand, alopecia areata
Electrolytes and Kidney dysfunction	Deterioration of Kidney function	Decreased estimated glomerular filtration rate, hyponatraemia

MANAGEMENT

Healthcare providers treat hypothyroidism with synthetic thyroxine, a medication that is identical to the hormone T4. The exact dose will depend on the patient's age and weight, the severity of the hypothyroidism, the presence of other health problems, and whether the person is taking other drugs that might interfere with how well the body uses thyroid hormone. Health care providers test TSH levels about 6 to 8 weeks after a patient begins taking thyroid hormone and make any necessary adjustments to the dose. Each time the dose is adjusted, the blood is tested again. Once a stable dose is reached, blood tests are normally repeated in 6 months and then once a year. Hypothyroidism can almost always be completely controlled with synthetic thyroxine, if the recommended dose is taken every day as instructed [6].

II. OBJECTIVES:

- To evaluate socio-demographics of the study group.
- Measuring the changes in hypothyroidism symptoms by using a hypothyroidism symptom scale.
- To identify the effectiveness of thyroid hormone replacement therapy by comparing baseline and follow-up data.

2. PLAN OF THE STUDY

PHASE I

- Preparation of protocol
- Identification of need of work
- Literature review on hypothyroidism
- Obtaining consent from ethical committee and from hospital authorities

PHASE II

- Designing the proforma (Data collection form and symptom scale)
- Selection and sample size determination
- Collection of patient details (patient case history, diagnosis, lab reports, medication order sheets)

PHASE III

- Data entry to Microsoft Excel and Graph Pad Prism (Statistical graphing software)
- Data analysis (Two-Way ANOVA)

PHASE IV

- Data interpretation
- Conclusion and documentation
- Report writing

III. RESULTS & DISCUSSION

Table 1: Gender wise distribution of patients with hypothyroidism

Gender	Total no of population (n=107)	Percentage (%)

Female	93	86.9
Male	14	13.1

Total of 107 patients with hypothyroidism were collected from the hospital for a period of six months, out of which 93(86.9%) were females and 14(13.1%) were males (Table 1). Female patients were more exposed

to hypothyroidism than male patients because of, the thyroid disorders are often triggered by autoimmune responses, which happen when the body's immune system starts to attack its own cells.

Table 2: Age wise distribution of patients with hypothyroidism

Age in years	Total no of population (n=107)	Percentage (%)
25 and < 25	14	13.1
25-40	42	39.3
40-55	30	28.0
Above 55	21	19.6

The demographic report of the present study showed higher incidence of hypothyroid patient with the age group of 25-40 years 42 (39.3%) followed by 40-55 years 30 (28.0%) and above 55 years 21

(19.6%) and below 25 years 14 (13.1%). This incidence rate of hypothyroidism may be due to the changes in the life style modification and the hormonal changes.

Table 3: Distribution of symptoms in hypothyroid patient for a period of four months

Symptoms	First Month	Second Month	Third Month	Fourth Month
Weight gain	53	48	52	26
Constipation	40	51	28	48
Dry skin	53	0	0	0
Muscle stiffness	41	45	32	27
Memory loss	34	27	29	22

Earlyawakening	0	0	24	28
Totalno.of Symptoms	221	171	165	151

The distribution of total number of symptoms in hypothyroid patients for a period of first month was 221 followed by 171 in second month and 165 in third months and 155 in fourth months respectively. It was found that, first month weight gain (53) and dry skin (53) was noted higher followed by higher

incidence of constipation (51) in second month, weight gain (52) in the third month and again higher incidence of constipation (48) in fourth month (Table 3). The present study identified that the patients were exposed to different symptoms at each four months.

Table 4: Treatment pattern in hypothyroid patients

Drugs Name	Total no of population (n=107)	Percentage (%)
Thyroxinesodium	86	80.4
Levothyroxine	21	19.6

Table 4 indicates the overall treatment pattern among hypothyroid patients and it explained as, about 86 (80.4%) patients were taking thyroxine sodium and 21 (19.6%) patients were

taking levothyroxine. The present study showed that most of the patients were taking thyroxinesodium when compared to levothyroxine.

Table 5: Averaged dose of oral thyroid hormone replacement therapy in patients with hypothyroidism

Month	Averaged dose of Thyroxinesodium (n=86)	Averaged dose of Levothyroxine (n=21)
First Month	103.77	117.85
Second Month	102.18	123.8
Third Month	101.57	118.45
Fourth Month	99.68	125.59

The averaged dose of Thyroxinesodium was found to be declined from first month (103.77) to fourth month (99.68) whereas in Levothyroxine group the dose

has escalated from first month (117.85) to fourth month (125.59) with an exception in third month (118.45).

Table6: Distribution of symptoms in patient taking Thyroxinesodium

Symptoms	Thyroxinesodium(n=86)				Average
	Firstmonth	Secondmonth	Thirdmonth	Fourthmonth	
Weightgain	43	40	45	22	37.5
Constipation	34	46	24	40	36
Dryskin	39	0	0	0	9.75
Musclestiffness	39	40	27	23	32.25
Memoryloss	29	22	24	22	24.25
Earlyawakening	0	0	19	22	10.25

Table7: Distribution of symptoms in patient taking Levothyroxine

Symptoms	Levothyroxine(n=21)				Average
	Firstmonth	Secondmonth	Thirdmonth	Fourthmonth	
Weightgain	10	8	7	4	7.25
Constipation	6	5	4	8	5.75
Dryskin	14	0	0	0	3.5
Musclestiffness	14	5	5	4	7

Memory loss	5	5	5	5	5
Early awakening	0	0	5	6	2.75

Discussion of Table 6 & 7:

- Table 6 and 7 explained the pattern of symptom distribution among Thyroxine sodium (n=86) and Levothyroxine (n=21) groups.
- It was shown that there is a significant reduction in symptoms in Thyroxine sodium group except

constipation and in Levothyroxine group (n=21) all the patients were improved symptomatically. Both the groups showed a progress in their symptoms and this symptomatic progress was found to be statistically significant (P value > 0.001).

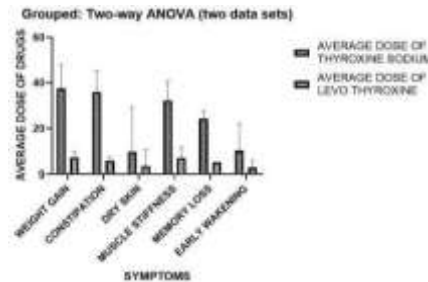


Table 8: Interpretation of laboratory investigation of thyroid hormones in patient taking Thyroxine sodium

Variables	Thyroxine sodium (n=86)			
	First Month	Second Month	Third Month	Fourth Month
T3	85.96	87.38	84.45	83.54
T4	7.15	6.93	6.96	7
TSH	16.55	19.64	19.32	16.3

Table9: Interpretation of laboratory investigation of thyroid hormones in patient taking Levothyroxine

Variables	Levothyroxine(n=21)			
	FirstMonth	SecondMonth	ThirdMonth	FourthMonth
T3	97.71	101.83	93.91	95.49
T4	7.4	7.35	7.76	6.99
TSH	30.09	23.45	22.25	19.98

Discussion of Table 8 & 9:

- Table 8 and 9 showed the laboratory interpretation details among both groups of Thyroxine sodium (n=86) and Levothyroxine (n=21).
- In Thyroxine sodium group T3 (85.96-83.54), T4 (7.15-7.00) and TSH (16.55-16.3) lab values has reduced from baseline to the

end report.

- Whereas in Levothyroxine group (n=21), there is marked change in lab values including T3 (97.71-95.49), T4 (7.4-6.99) and TSH (23.45-19.98) both the treatment groups were showed an improvement with respect to their laboratory values.

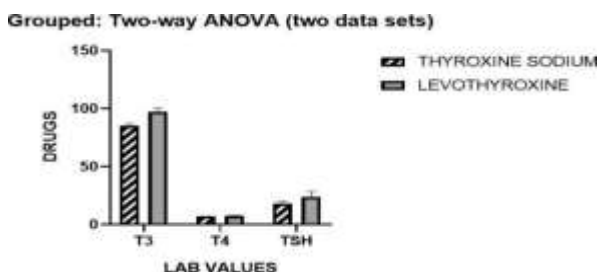


Table 10: Severity level of hypothyroid symptoms among patients.

Symptoms	Minimal	Mild	Moderate	Severe
Weight gain	18	63	31	0
Constipation	15	45	28	0
Dry skin	40	12	0	0
Muscle stiffness	11	82	25	0

Memory loss	09	19	13	0
Early awakening	0	38	22	0

Table 10 showed that the severity of hypothyroid symptoms was found, most of the patients were experiencing mild symptoms followed by moderate and minimal symptoms.

IV. CONCLUSION

- The study conducted that the prevalence of hypothyroidism is moderately high among the population.
- A population of female gender and adult age group were more affected.
- The current or a thyroid hormonal replacement therapy with Thyroxine sodium and Levothyroxine has showed symptomatic improvement in study subjects; even though treatment with Levothyroxine group have imparted a significant progress in both lab and symptom factor.
- So, creating awareness on the early onset of these symptoms and also lab interpretation can be effective strategies to tackle the condition.

V. LIMITATION

- The duration of the study was 6 months and sample size was small.
- Since it is a single centered study, the result may vary with result obtained from multi-centered.
- During the study period, the safety of the medicine was not monitored. As the study not focused on medication adherence measurement, the underline cause of certain fluctuations in the laboratory interpretation and symptoms distribution during every four months cannot be identified.

VI. FUTURE OF THE STUDY

- Identifying factors affecting thyroid functional status and evaluating medication adherence among the study population.
- Further research can be focused

on novel cardiovascular risk factors are other pathways could shed light on the exact mechanisms, which would be crucial to support treatment decisions and monitor strategies in patients with asymptomatic hypothyroidism.

- More research is needed to identify which adverse health events occur after long-term thyroid dysfunction.

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