stimating the Prevalence of Primary Hypothyroidism in Karbala City, and Modulation of Clinical Manifestations Among Patients Receiving Levothyroxine; A Single Center Study

Zainab Hussien Ali*, Manal Khalid Abdulridha*, Qusay Baqer Alzajaji**
Department of Clinical Pharmacy, College of Pharmacy, Mustansiriyah University, Baghdad, Iraq
****Alhassan Metabolism, Endocrine and Diabetes center (HMEDC), Karbala, IRQ***

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Corresponding Author email:
pharm.mrdha@uomustansiriyha.edu
Orcid: https://orcid.org/0000-0002-5059-7963

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Abstract:

Background: Hypothyroidism has a wide range of clinical manifestations and general symptoms, including but not limited to obesity, tiredness, poor concentration, depression, widespread muscle soreness, menstruation abnormalities, and constipation. The administration of a daily dosage of levothyroxine is sufficient for the successful management of hypothyroidism, as it facilitates the restoration of serum thyroid stimulating hormone (TSH) levels to their normal range. Several factors can influence the absorption of levothyroxine in the human body, including age, weight, the presence of other medical problems, and dietary intake. The aim of this study was to assess the prevalence of primary hypothyroidism and alteration in clinical presentation associated with replacement therapy.

Methods: This was a cross-sectional, observational study conducted over at Al Hassan Metabolism, Endocrine, and Diabetes Center (HMEDC) in Karbala city. The study team created a questionnaire, and data was collected from face-to-face patient interviews, which included various sociodemographic variables, TSH and ferritin levels, drug interactions, as well as signs and symptoms exhibited both prior to and following treatment. Additionally, the patient treatment regimen and the specific doses of levothyroxine administered are also recorded.

Results: the total number of cases visited Al Hassan Metabolism, Endocrine, and Diabetes Center (HMEDC) during the study period was (10800). The prevalence of thyroid diseases was 300 (2.8%). The rate of primary hypothyroidism out of the total number of hypothyroid cases was 85.1%. (61%) of the patients had normal levels of TSH whereas (42%) of the patients were found to be undertreatment. A total of (84%) of the patients exhibited normal levels of ferritin. The patients exhibited a reduction in their signs and symptoms following the administration of therapy.

Conclusion: treatment with levothyroxine improved sluggish speech, constipation, lack of appetite, cold sensitivity, weight gain, and weariness. There is no observed correlation between the dosage of levothyroxine and the manifestation of signs and symptoms.

Keywords primary hypothyroidism, levothyroxine, TSH, Ferritin

دراسة مدى انتشار قصور الغدة الدرقية الأولي والتغيرات في العرض السريري بين عينة من المرضى العراقيين الذين يعانون من قصور الغدة الدرقية الأولي بعد إعطاء دواء الليفوثيروكسين

زينب حسين علي*، منال خالد عبد الرضا *، قصي باقر الزجاجي **

قسم الصيدلة السريرية، كلية الصيدلة، الجامعة المستنصرية، بغداد، العراق

***مركز الحسن للأيض والغدد الصماء والسكري (HMEDC)، كربلاء، العراق*

الخلاصة:

قصور الغدة الدرقية لديه مجموعة واسعة من المظاهر السريرية والأعراض العامة، بما في ذلك على سبيل المثال لا الحصر السمنة، والتعب، وضعف التركيز، والاكتئاب، وألم العضلات على نطاق واسع، واضطرابات الدورة الشهرية، والإمساك. يعد تناول جرعة يومية من ليفوثيروكسين كافيًا للإدارة الناجحة لقصور الغدة الدرقية، لأنه يسهل استعادة مستويات TSH في الدم إلى نطاقها الطبيعي. هناك عدة عوامل يمكن أن تؤثر على امتصاص ليفوثيروكسين في جسم الإنسان، بما في ذلك العمر والوزن ووجود مشاكل طبية أخرى، والمدخول الغذائي. كان الهدف من هذه الدراسة هو تقييم مدى انتشار قصور الغدة الدرقية الأولي والتغيير في العرض السريري المرتبط بالعلاج البديل.

الطريقة: كانت هذه دراسة رصدية مقطعية أجريت في مركز الحسن للأيض والغدد الصماء والسكري (HMEDC). قام فريق الدراسة بإنشاء استبيان. تم جمع البيانات من المقابلات وجها لوجه مع المرضى. تشمل البيانات التي تم جمعها من المرضى متغيرات اجتماعية ديموغرافية مختلفة، مستويات الفرتين والهرمون المحفز للغدة الدرقية في الدم ، والتفاعلات الدوائية، بالإضافة إلى العلامات والأعراض التي ظهرت قبل العلاج وبعده. بالإضافة إلى ذلك، يتم أيضًا تسجيل نظام علاج المريض والجرعات المحددة من الليفوثيروكسين التي يتم تناولها.

النتائج: بلغ إجمالي عدد الحالات التي زارت مركز الحسن للتمثيل الغذائي والغدد الصماء والسكري (HMEDC) خلال فترة الدراسة 10800 حالة. وكان معدل انتشار أمراض الغدة الدرقية 300 حالة (2.8٪). وبلغت نسبة قصور الغدة الدرقية الأولي من إجمالي عدد حالات قصور الغدة الدرقية 85.1%. (61%) من المرضى لديهم مستويات طبيعية من هرمون TSH بينما (42%) من المرضى وجد أنهم يحتاجون زيادة جرع الليفوثيروكسين. أظهر ما مجموعه (84٪) من المرضى مستويات طبيعية من الفيريتين. أظهر المرضى انخفاضًا في علاماتهم وأعراضهم بعد تناول العلاج.

االستنتاج: أدى العلاج بالليفوثيروكسين إلى تحسين الكلام البطيء والإمساك وقلة الشهية والحساسية للبرد وزيادة الوزن والإرهاق. لا توجد علاقة ملحوظة بين جرعة ليفوثيروكسين وظهور العلامات والأعراض.

الكلمات المفتاحية: قصور الغدة الدرقية الأولي,الليفوثيروكسين

Introduction

The thyroid gland is essential for maintaining homeostasis and for the growth, development, and health of the neurological, circulatory, and brain systems[1]. Triiodothyronine (T3) and thyroxine (T4) are secreted by the thyroid gland and are necessary for controlling the metabolism of all body cells[2].Hypothyroidism has a wide range of clinical manifestations and general symptoms, including but not limited to obesity, weariness, poor concentration, depression, widespread muscle soreness, menstruation abnormalities, and constipation[3,4]. Overt hypothyroidism (HT) is characterized by elevated levels of thyroid-stimulating hormone (TSH), accompanied by below-standard levels of free thyroxine (FT4). Subclinical hypothyroidism (SHT) is characterized by an elevation in TSH levels while maintaining normal levels of FT4[5].Numerous studies have documented a significant incidence of subclinical thyroid illnesses across many populations. These studies have indicated that more than 50% of individuals with subclinical thyroid disease eventually develop overt thyroid disease within a span of 20 years[6]. The estimated prevalence of hypothyroidism in the United States is said to range from (0.3%) to (3.7%), whereas in Europe, it ranges from (0.2%) to (5.3%). However, it is important to note that these figures exhibit significant variation depending on the specific definition used[7]. The administration of a daily dosage of levothyroxine (LT4) is sufficient for the successful management of hypothyroidism,

as it facilitates the restoration of serum TSH levels to their normal range[8]. The initial daily dosage of LT4 is determined by the extent of serum TSH elevation, the patient's age, and the presence of concurrent cardiac illness[9]. In order to achieve a euthyroid state, individuals diagnosed with overt hypothyroidism often necessitate a complete replacement dosage of oral LT4 at a range of (1.6-1.8) micrograms per kilogram of actual body weight each day[10]. The objective of this study was to evaluate the prevalence of primary hypothyroidism within the Iraqi population and observe any alterations in clinical manifestations before and after treatment.

Patients and Methods

Study design

This was a cross-sectional, observational study conducted over the course of six months at HMEDC in Karbala city From September 2022 to March 2023. 217 patients with primary hypothyroidism were enrolled in this trial; however, 106 patients dropped out due to a new diagnosis or medication noncompliance. Only 111 patients were still there by the end of the study. However, in order to accurately determine the prevalence of hypothyroidism, it is necessary to include all patients (217) who have been diagnosed with primary hypothyroidism.

Inclusion Criteria:

- People who have been diagnosed with primary hypothyroidism with or without co-morbid diseases like hypertension, diabetes, etc.
- All individuals taking part must be at least 18 years old.
- Patients have been receiving levothyroxine for a minimum of three months .

Exclusion Criteria:

- Newly diagnosed cases of primary hypothyroi dism
- patients having radioiodine ablation, surgery, and neck radiation.
- Patients with mental impairments or other psychological issues who are unable to complete the research questionnaire.

Ethical considerations

Mustansiriyah University's college of pharmacy and scientific and ethical committee reviewed and approved the research idea. Before beginning data collection, we made sure to get permission from the general health directorate at HMEDC in Karbala. Patients participated in the study after being informed of its objectives and assured of confidentiality.

Data collection

The research team designed data sheets to meet the collected data of the investigation. Patients were interviewed face-to-face to acquire the data. The questionnaire had four sections:

1.Part one included patient’s data about the sociodemographic variables of the patients (age, gender, and weight status).

2.Part two included patient’s medical history of diabetes, hypertension, immune disease, allergy, heart disease, surgical history, and drug interactions.

3. Part three included patient's signs and symptoms, such as slurred speech, constipation, loss of appetite, intolerance to cold, increased weight, and exhaustion. The collection of symptoms prior to treatment initiation involved an interview of patients regarding their pre-treatment symptomatology as well as their current symptom presentation during the period of the study.

4.The patient treatment regimen and levothyroxine doses administered.

Assessment of Serum Thyroid Stimulating Hormone

an immunoassay was used to quantify the hormone in vitro[11]. The normal range of TSH is (0.5–4.5 mIU/L) (μIU/mL)[12]

Assessment of Serum Ferritin

Trace amounts of ferritin normally present in serum were detectable by sensitive radioimmunoassay. Normal value of serum ferritin for males was (20–250 ng/ml) (20–250 mcg/L; 45–562 pmol/L) and for female was (10–150 ng/ml) (10–150 mcg/L; 22–337 pmol/L)[12].

Measurement of Body Mass Index

The body mass index (BMI) was determined by a person's weight and height. The body mass index (BMI) is a measure of obesity that is obtained by dividing a person's weight in kilograms by the square of their height in meters (kg/m2)[13].Weight / (Height) 2 = BMI

The body weight suggested for adults was based on BMI values as stated by the World Health Organization (WHO) Table (1). This was used by individuals of all genders, specifically those who were 20 years of age or older[14].

TABLE (1) obesity categorization from WHO [14]

Classification	BMI range - kg/m^2
Under weight	< 18.5
Normal weight	18.5 – 25
Overweight	>=25
Obese	>=30
Obese Class I	30 – 34.9
Obese Class II	35 – 39.9
Obese Class III	>= 40

Statistical analysis

The collected data were loaded into SPSS V26 from Excel 2016. percentages were used for categorical variables. Continuous variables were shown as means ± SD. A chi-square test was used to determine the significance of the association between related categorical data. P value less than 0.05 was considered a discrimination point of significance and was highly significant when it was below 0.01.

Results

Prevalence of Primary Hypothyroidism

Results in Figure (1) showed that the total number of cases visited the endocrine center during the study period was 10800 cases. The prevalence of thyroid diseases was 300 cases (2.8%). The rate of primary hypothyroidism out of the total number of hypothyroid cases was 85.1%, the rate of secondary hypothyroidism was 14.9%

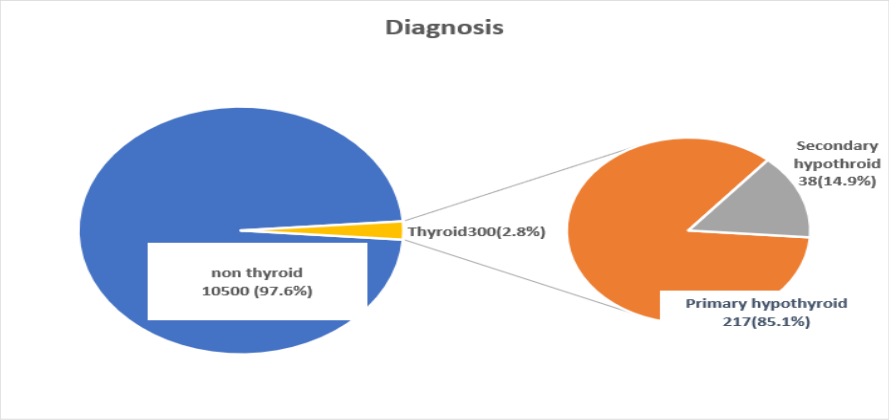

FIGURE (1) Distribution of total cases according to diagnosis

Sociodemographic Characteristics of Patients

Table (2) showed that the mean age of the studied patients was 45±11.9 years, with predominate age (49.5%) was between 40–60 years. Ninety one percent of the studied patients were female. Regarding BMI, (36%) suffered from obesity and (32.4%) were overweight. A total of (61%) of the patients had normal levels of TSH, whereas (42%) of the patients were found to be undergoing undertreatment. A total of (84%) of the patients exhibited normal levels of ferritin. (1.8%) had a history of drug interaction. 66.7% had a history of previous surgical operations, 27% had hypertension, 18.9% had diabetes mellitus, 8.1% had allergies, 1.8% had heart disease, 1.8% had a history of drug interaction, and 0.9% had immune disease.

TABLE (2) Sociodemographic characteristics of study population

Variables		**N**	**%**
Age(year)	Mean ± std	45±11.9	
	< 40 years	42	37.8
	40- 60 year	55	49.5
	> 60 years	14	12.6
Gender	Male	10	9.0
	Female	101	91.0
BMI	Normal weight	11	9.9
	Overweight	36	32.4
	Obese I	40	36.0
	Obese II	24	21.6
TSH (mIU/L)	Normal	61	55.0
	Undertreatment	42	37.8
	Overtreatment	8	7.2
Ferritin (pmol/L)	Normal	84	75.7
	Abnormal	27	24.3
Drug Interaction	Yes	2	1.8
	N0	109	98.2
Medical history	Surgical History	74	66.7
	Hypertension	30	27.0
	Diabetes	21	18.9
	Allergy	9	8.1
	Heart Disease	2	1.8
	Drug Interaction	2	1.8
	Immune Disease	1	0.9

Data presented as Number(N) and percentage (%), milli-international units per liter (mIU/L), picomoles per liter (pmol/L)

Clinical Manifestation of Study Patients

FIGURE (2) showed that prior to therapy, 68.5% of patients had slurred speech, 64.9% had constipation, 18% had decreased appetite, 73% had displayed intolerance to cold, 79.3% had gained weight, and 90.1% had fatigue.

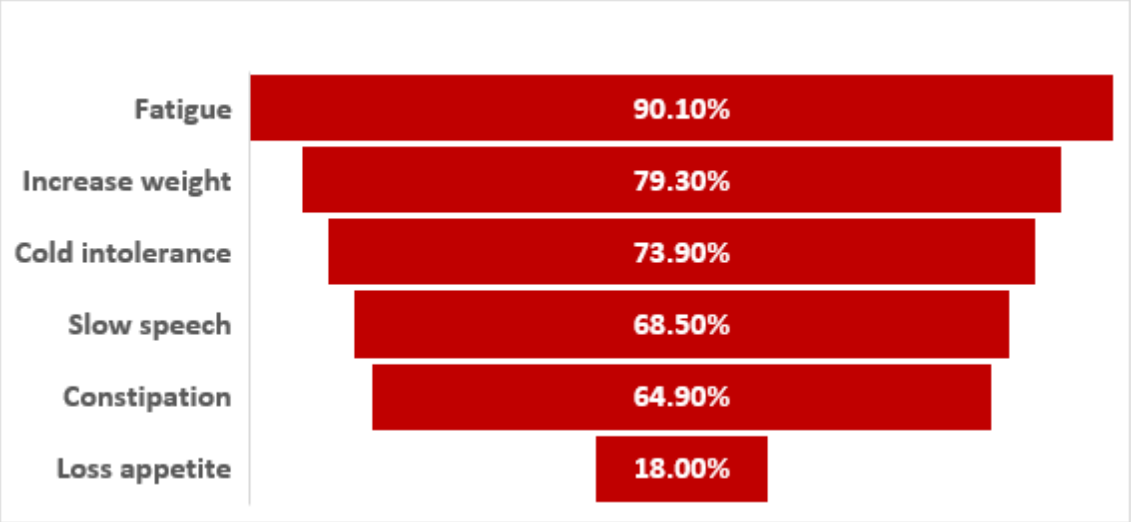

Figure (2) Percentage of signs and symptoms before treatment

Distribution of Thyroxine Dose among Study Patients

Figure (3) demonstrated that (34%) of patients-initiated therapy with 50 ug of thyroxin or less, (48%) with 75–100 ug, and (18%) with more than 100ug.

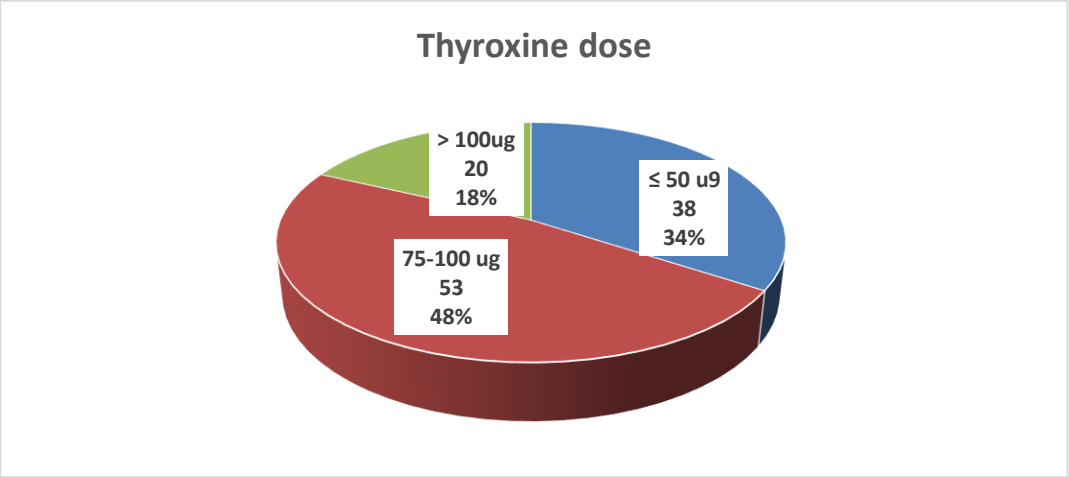

FIGURE (3) Distribution of studied cases according to thyroxine dose

Differences Percentage of Clinical Manifestation Before and After Treatment

TABLE (3) exhibited a statistically significant reduction in the proportion of patients displaying delayed speech, with the percentage decreasing from 68.5% to 53.2% following the intervention (p = 0.001). The prevalence of constipation among individuals dropped from 64.9% prior to therapy to 57.7% following therapy, with a statistically significant P value of 0.008. There was a notable decrease in the prevalence of individuals experiencing a diminished desire to eat following therapy (9%) in comparison to the period prior to treatment (18%), with a statistically significant difference indicated by a P-value of 0.002. The prevalence of cold intolerance symptoms among patients decreased

significantly from 73.8% to 63.1% after treatment (p = 0.001). A notable decrease in the number of individuals experiencing weight increase was observed after the course of therapy, with a percentage of 66.7% compared to 79.3% before to treatment (p = 0.001). Following the administration of medical intervention, there was a notable decrease in the occurrence of fatigue, with a reduction from 90.1% to 61.3%. This change was statistically significant, as indicated by a p-value of 0.001.

TABLE (3) differences between rate of signs and symptoms before and after treatment

		After			P value
	Before	Yes	N0(%)	Total	
Slow Speech	Yes	59	17	**76 (68.5)**	0.001**
	No	0	35	**35 (31.5)**	
	Total	**59 (53.2)**	**52(46.8)**	**111**	
Constipation	Yes	64	8	**72 (64.9)**	0.008**
	No	0	39	**39(35.1)**	
	Total	**64(57.7)**	**47(42.3)**	**111**	
Loss Appetite	Yes	10	10	**20(18)**	0.002**
	No	0	91	**91(82)**	
	Total	**10(9)**	**101(91)**	**111**	
Cold Intolerance	Yes	70	12	**82(73.8)**	0.001**
	No	0	29	**29(26.2)**	
	Total	**70 (63.1)**	**41(36.9)**	**111**	
Increase weight	Yes	74	14	**81(79.3)**	0.001**
	No	0	23	**23(20.7)**	
	Total	**74 (66.7)**	**37(33.3)**	**111**	
Fatigue	Yes	67	33	100**(90.1)**	0.001**
	No	1	10	11**(9.9)**	
	Total	68 **(61.3)**	43**(38.7)**	111	

Data presented as Number(N) and percentage (%) McNemar test comparing categorical variables P-value ≥0.05, NS, non-significant*(P<0.05), significant, **(P <0.01), highly significant

Change in Clinical Manifestation According to Thyroxine Dose After Treatment

Chi square test in Table (4) showed that there was no significant association between signs and symptoms and the dose of treatment at the end point of treatment. point (p value >0.05) in all conditions.

TABLE (4) Change in sign and symptoms according to Levothyroxine dose after treatment

Signs and symptoms		**Levothyroxine Dose**						
		=< 50 ug		**75-100 ug**		**> 100ug**		**P value**
		N	**%**	**N**	**%**	**N**	**%**	
slow speech A	Yes	17	44.7	28	52.8	14	70.0	0.186 NS
	N0	21	55.3	25	47.2	6	30.0	
Constipation A	Yes	21	55.3	30	56.6	13	65.0	0.758 NS
	N0	17	44.7	23	43.4	7	35.0	

Loss Appetite A	Yes	2	5.3	5	9.4	3	15.0	0.464 NS
	N0	36	94.7	48	90.6	17	85.0	
Cold Intolerance A	Yes	22	57.9	31	58.5	17	85.0	0.080 NS
	N0	16	42.1	22	41.5	3	15.0	
Increase weight A	Yes	22	57.9	35	66.0	17	85.0	0.114 NS
	N0	16	42.1	18	34.0	3	15.0	
Fatigue A	Yes	23	60.5	34	64.2	11	55.0	0.769 NS
	N0	15	39.5	19	35.8	9	45.0	

Data presented as Number(N) and percentage (%) Chi square test comparing categorical variables The degree of significance was ascertained by the use of the student t-test, P-value ≥0.05, NS, non-significant.

Levels of TSH and S. Ferritin According to the Dose of Levothyroxine After Treatment

Table (5) showed no significant association between levothyroxine dose and levels of TSH and serum ferritin (P values = 0.761) and (P values = 0.158) respectively).

TABLE (5) Levels of TSH and S. Ferritin according to the dose of Levothyroxine after treatment

Levothyroxine Dose (ug)	TSH mIU/L		P value	Serum ferritin pmol/L		P value
	High	Normal		Low	Normal	
	No. (%)	No. (%)		No. (%)	No. (%)	
=< 50	11 (28.9)	27 (71.1)	0.761 NS	11 (28.9)	27 (71.1)	0.158 NS
75-100	19 (35.8)	34 (64.2)		26 (49.1)	27 (50.9)	
> 100	6 (30.0)	14 (70.0)		8 (40.0)	12 (60.0)	

Data presented as Number (No.) and percentage (%), The degree of significance was ascertained by the use of the student t-test, P-value ≥0.05 NS, non-significant, milli-international units per liter (mIU/L), picomoles per liter (pmol/L)

Table (6) showed that no significant correlation between TSH and S. Ferritin levels (R value= -0.021 and P value =0.824)

TABLE (6) correlation Between TSH level with Ferritin

Variables		Ferritin pmol/L
TSH mIU/L	R	-0.021-
	P Value	0.824

Correlation Coefficient (r), The degree of significance (p value) was ascertained by the use of the student t-test, milli-international units per liter (mIU/L), picomoles per liter (pmol/L)

Discussion

Suboptimal thyroid hormone therapy, under-replacement and over-replacement, is common amongst patients with hypothyroidism. hypothyroidism, one of the most frequent but least recognized

chronic health disorders worldwide, has a significant negative impact on health.

Prevalence and Baseline Demographics and Characteristics of Participants

In the current study, Primary hypothyroidism was reported to be prevalent in (85.1%) out of the 10800 patients who visited the Al Hassan Endocrine and Diabetes Centre during the study period. The gender distribution of the patients under study revealed that 91% of them were female. Furthermore, the prevalence of the condition exhibited an upward trend with advancing middle age, reaching its highest point between the ages of 40 and 60. Numerous investigations yielded comparable findings[15–18].One recent national study by Mousa *et al* in 2023 encompassed a total of 120 samples, hypothyroidism presented in (68.75%) of patients [15].

Another recent screening study in India of (312) thyroid dysfunction patients found that (70.83%) had hypothyroidism and only (29.17%) had hyperthyroidism, and both disorders were higher in women (87.49%) compared to men (12.49%)[16], a higher prevalence of hypothyroidism among women aged (30–45)[17] .Also in agreement with current findings, study in Makkah reported that (91%) of hypothyroidism were women while only (9%) were men among a total of (177) people , (35.6%) were 45 years old or older[18]. The occurrence of hypothyroidism is influenced by genetic, intrinsic (such as sex), and environmental variables[19]. In present study, (61%) of patients had normal TSH levels, while (42%) had high levels. Normal ferritin levels were found in (84% of patients). The findings of a study conducted in Iraq revealed a notable disparity in the concentrations of ferritin and TSH[20]. Hypothyroid patients may present with one or more hypothyroid symptoms, and abnormal thyroid test results[19]. The blood TSH concentration is influenced by various non-thyroid hormone factors, including pregnancy, age, sex, exercise, individual thyroid hormone set points, the timing of levothyroxine administration, steroids, and medications. Furthermore, it is worth noting that TSH levels may also experience variations across different seasons and within a 24-hour period[21] .The dose of levothyroxine administered to patients varied based on their specific illness status[22]. This study found that (34%) started thyroxin at (50 ug) or less and (48%) at (75–100 ug). Thyroxin exceeding (100 ug) was only given to (18%) of patients. Age, serum TSH elevation, and past cardiac illness alter the recommended beginning daily LT4 dose. Overt hypothyroidism requires (1.6–1.8 mcg/kg) of BW per day of oral LT4 to achieve an euthyroid state[23]. The assessment of the optimal LT4 dosage is a significant challenge for individuals with obesity[24].Weight-based first dosing in obese people may produce an overdose when weight is assessed. The LT4 dose for obese hypothyroid individuals is better determined by lean body mass[25].

Changes in Clinical Manifestation After Replacement Therapy

The present study found that hypothyroidism treatment improved sluggish speech, constipation, lack of appetite, cold sensitivity, weight gain, and weariness. This improvement was better than the patients' on pre-treatment status significantly, (P = 0.001). Previous study stated that many people who test negative for hypothyroidism still present with classic hypothyroidism-like symptoms despite achieving euthyroidism may be due to the tissue-level inadequacy of thyroxine or may be totally unrelated to thyroid dysfunction. An alternative explanation for the persistent symptoms should be considered, apart from the possibility of hypothyroidism[26]. The symptoms of hypothyroidism are often vague and hard to tell apart from those of other diseases or just being generally

unhealthy[27]. A certain level of correlation can be observed between the increase in TSH levels and the manifestation of symptoms resembling hypothyroidism. However, it is worth noting that many symptoms occur with similar frequency in both individuals with hypothyroidism and those with normal thyroid function. The Colorado Thyroid Disease Prevalence Study found that patients with overt or subclinical hypothyroidism were more likely to have three or more of these symptoms than euthyroid subjects[28]. The findings of population-based cohort research conducted in Denmark indicate that the existence of symptoms resembling hypothyroidism alone is not a reliable indicator of the presence of overt hypothyroidism[29].

The current investigation found no significant association between signs and symptoms and the dose of treatment at the end point of treatment, there was no variation in symptoms among patients who took different doses. The athyreotic patients need a daily dose of levothyroxine ranging from (1.6 to 1.8) mcg/kg of their real body weight (BW) in order to attain normal levels of TSH. The computation of lean body mass (LBM) has the potential to provide a more precise estimation of the appropriate dosage of levothyroxine in individuals who are obese[23]. The assessment of signs and symptoms, in conjunction with the varied doses supplied to specific patients, may have significant implications. In the present investigation, the process of titration was conducted to determine the optimal dose. Subsequently, each patient was administered a consistent and suitable dose throughout the study.

The present study revealed a lack of statistically significant correlation between the dosage of thyroxin and the levels of TSH (P values = 0.761). In previous study, it was shown that a consistent TSH level during levothyroxine medication exhibited an inverse correlation with the dosage of levothyroxine administered. The finding may imply that individuals who required lower doses of levothyroxine experienced less fluctuation in TSH levels due to the presence of residual thyroid function, which acted as a protective mechanism[30].

Additionally, the findings of this study indicate that there is no significant link between the dosage of thyroxin and serum ferritin (p value 0.158). In contrast, a previous study indicated that low serum ferritin levels are associated with hypothyroidism. The measurement of blood ferritin levels can provide valuable insights into the etiopathogenesis, diagnosis, and monitoring of individuals with hypothyroidism[31]. A comparative analysis revealed a significant difference in the mean serum ferritin concentration between euthyroid participants (67.75 ± 57.47 ng/ml) and hypothyroid subjects (43.80 ± 75.44 ng/ml), with the former exhibiting a higher mean value[32]. Similar finding where reduction in serum ferritin levels among patients diagnosed with hypothyroidism when compared to individuals without the condition [31], and that hypothyroidism patients had lower iron and ferritin levels and a higher total iron binding capacity than healthy people[33].

When considering the half-life of levothyroxine, which is roughly 1 week, it is recommended to evaluate the thyroid status by serum TSH levels. If desired, free thyroxine levels can also be assessed after (6) weeks of medication, since this is the point at which the pharmacokinetic steady state is achieved. In case that TSH does not align with the intended target, it is possible to modify the dosage of levothyroxine either upwards or downwards[22]. When a patient's dosage is stable, they only need to be evaluated clinically and have their biochemistry monitored every six months to a year[8]. In the current investigation, since individuals had to be on medicine for three months, dose titration was done before the current study starting point. Thus, each

patient received the prescribed dose at the study's onset.

The current investigation found inverse correlation between TSH and serum ferritin. The subclinical hypothyroid patients had lower mean hemoglobin, serum ferritin, and red blood cell indices than euthyroid patients[34]. Since both serum ferritin and thyroid hormone status were low in hypothyroid patients, patients may benefit from serum ferritin measurements for thyroid hormone evaluation[35].

Limitation of study

The current study has some drawbacks. Patients were first gathered from one Iraqi center. The extent to which they reflect a fair sample of Iraqi patients' needs additional examination. Thus, this study may be limited in generalizability. Second, researcher-reported answers may be prone to recall and societal want bias. Third, Serum ferritin measurement was complicated because many patients were using iron supplements.

Conclusion

High prevalence of primary hypothyroidism in Karbala city attending single center with a positive family history of thyroid disorder. Hypothyroidism treatment improved sluggish speech, constipation, lack of appetite, cold sensitivity, weight gain, and weariness. This improvement was better than the patients' on pre-treatment status significantly, with no association between signs and symptoms and the dose of levothyroxine.

Recommendations

1- In future studies, large sample and multicenter studies should be included in other regions of Iraq to show whether the results here can be confirmed in other patients.

2- Further clinical studies of potential impact of serum ferritin on response to levothyroxine are required to create evidence-based recommendations for patients with uncontrol outcomes.

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