**A THESIS SUBMITTED TO**
**THE GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES**
**OF ÇANKIRI KARATEKİN UNIVERSITY**

# IMPLCIATING OF SERUM IRON, FERRITIN, TIBC ON PATIENTS DEVELOPED HYPOTHYROIDISM

**IN PARTIAL FULFILLMENT OF THE REQUIREMENTS**
**FOR**
**THE DEGREE OF MASTER OF SCIENCE**
**IN**
**CHEMISTRY**

**BY**

**SAZAN FERMAN AGHA KALWLS**

**ÇANKIRI**

**2022**

IMPLCIATING OF SERUM IRON, FERRITIN, TIBC ON PATIENTS DEVELOPED HYPOTHYROIDISM

By Sazan Ferman Agha KALWLS

May 2022

We certify that we have read this thesis and that in our opinion it is fully adequate, in scope and in quality, as a thesis for the degree of Master of Science

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**ABSTRACT**

# IMPLCIATING OF SERUM IRON, FERRITIN, TIBC ON PATIENTS DEVELOPED HYPOTHYROIDISM

Sazan Ferman Agha KALWLS

Master of Science in Chemistry

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May 2022

Recent research has focused on hypothyroidism, which is a prevalent medical disease caused by thyroid hormone insufficiency. If left untreated, it may cause major health problems and even death. Overt or clinical primary hypothyroidism is defined as thyroid-stimulating hormone (TSH) values above the standard range and free thyroxine concentrations below the reference range due to the wide variety of clinical presentation and overall lack of symptom specificity. TSH values that are above the reference range but free thyroxine concentrations that are within the normal range are what constitute mild or subclinical hypothyroidism. Mild or subclinical hypothyroidism is generally considered to be an early symptom of thyroid failure. The study was conducted in the Al-Kindi Teaching Hospital and in the period from February 2022 to April 2022. The clinical study included 100 patients divided two groups 50 patients primary hypothyroidism, and 50 patients with subclinical hypothyroidism. In addition to fifty volunteers from the control group. The three groups of the study were divided into two groups, 35 adults and 15 children The results indicated a significant increase in all levels of thyroid hormones, Anti- TPO, Iron, Ferritin, TIBC, Iodine, and Urea in both groups, adults and children. While FBS, creatinine showed a significant increase in the adult group, the children groups showed a significant decrease compared with control.

**2022, 34 pages**

**Keywords:** Hypothyroidism, Iron, TIBC, Ferritin, Anti-TPO, FBS, RF

## ÖZET

# IMPLCIATING OF SERUM IRON, FERRITIN, TIBC ON PATIENTS DEVELOPED HYPOTHYROIDISM

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Mayis 2022

Hipotiroidizm ile ilgili son çalışmalar, tiroid hormon eksikliğinin yaygın patolojik durumunu ifade etmektedir. Tedavi edilmezse, ciddi olumsuz sağlık etkilerine ve nihayetinde ölüme neden olabilir. Klinik sunumdaki büyük çeşitlilik ve semptom özgüllüğünün genel olmaması nedeniyle, aşikar veya klinik primer hipotiroidizm, referans aralığının üzerindeki tiroid uyarıcı hormon (TSH) konsantrasyonları ve referans aralığın altındaki serbest tiroksin konsantrasyonları olarak tanımlanmaktadır. Genellikle erken tiroid yetmezliği belirtisi olarak kabul edilen hafif veya sub-klinik hipotiroidi, TSH konsantrasyonlarının referans aralığının üzerinde ve serbest tiroksin konsantrasyonlarının normal aralıkta olması olarak tanımlanır. Çalışma Al-Kindi Eğitim Hastanesinde ve Şubat-Nisan 2022 döneminde yapılmıştır. Şubat 2022'den Nisan 2022'ye kadar. Klinik çalışma iki gruba ayrılmış 100 hastayı, 50 hasta primer hipotiroidili ve 50 sub-klinik hipotiroidili hasta olarak gruplandırılmıştır. Kontrol grubundan elli gönüllüye ek olarak. Çalışmanın üç grubu, 35 yetişkin ve 15 çocuk olmak üzere iki gruba ayrılmıştır. Sonuçlar, her iki grupta, yetişkinlerde ve çocuklarda tüm tiroid hormonları, Anti-TPO, Demir, Ferritin, TIBC, İyot ve Üre seviyelerinde önemli bir artış olduğunu göstermiştir. FBS, kreatinin yetişkin grupta anlamlı bir artış gösterdiği gözlemlenirken, çocuk gruplarında kontrole göre anlamlı bir düşüş gösterdiği görülmüştür.



**2022, 34 sayfa**

**Anahtar Kelimeler:** Hipotiroidizm, Demir, TIBC, Ferritin, Anti-TPO, FBS, RF

## PREFACE AND ACKNOWLEDGEMENTS

I would like to thank my thesis advisor, Prof. Dr. Volkan EYÜPOĞLU and Asst. Prof. Dr. Zaizafoon Nabeel NASIF, for his patience, guidance and understanding.

**Sazan Ferman Agha KALWLS**

**Çankırı-2022**

**CONTENTS**

## LIST OF SYMBOLS

| | |
|---|---|
| ± | Plus-minus |
| °C | Degrees Celsius |
| µmol | Micromole |
| % | Percent |
| µg | Microgram |
| µL | Microliter |
| dL | Deciliter |
| g | Gram |
| IU | International unit |
| L | Liter |
| mg | Milligram |
| mL | Milliliters |
| ng | Nanogram |
| nmol | Nanomoles |
| Pg | Pecogram |
| pmol | Pecomoles |

## LIST OF ABBREVIATIONS

| | |
|---|---|
| Anti-TPO | Anti-thyro peroxdase |
| FBS | Fasting blood sugar |
| ID | Iron deficiency |
| PTD | Primary hypothyroidism disease |
| SCH | Subclinical hypothyroidism |
| T3 | Triiodothyronine |
| T4 | Thyroxine |
| TBG | Thyroxine-binding globulin |
| TIBC | Total iron-binding capacity |
| TRH | Thyrotropin-releasing hormone |
| TSH | Thyroid-stimulating hormone |

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# 1. INTRODUCTION

Thyroid gland It is a butterfly-shaped endocrine gland that weighs more than one ounce and is an important regulator of the metabolic processes that are controlled by the endocrine system. In humans, it is situated in the region of the neck and is made up of two lobes that are related to one another. The term "isthmus" refers to the thin strip of tissue that connects the lowest two-thirds of each of the lobes of the thyroid gland. Below the Adam's apple on the front of the neck is where you'll find the thyroid gland. The spherical thyroid follicle is the functional unit of the thyroid gland. It is coated by follicular cells (thyrocytes), and sometimes parafollicular cells. Together, these cell types surround a lumen that contains colloid (Wang *et al*. 2020).

The thyroid gland secretes three hormones: the thyroid hormones triiodothyronine (T3) and thyroxine (T4) and calcitonin, a peptide hormone. This tissue of thyroid cells produces a unique collection of hormone products that perfuse throughout the body to maintain homeostatic metabolic function (Dhannoon and Al-Hadidy 2021).

The thyroid gland governs the pace of operation of every cell, tissue, and organ in the body, including muscles, bones, and skin, as well as the digestive system, brain, and heart. This is accomplished mostly by the secretion of hormones that regulate the rate and efficiency with which cells convert nutrients into energy, a chemical process known as metabolism, in order for the cells to fulfill their activities. Calcitonin is important for calcium homeostasis. The anterior pituitary gland secretes thyroid-stimulating hormone (TSH), which controls the secretion of the two thyroid hormones. The hypothalamus produces thyrotropin-releasing hormone (TRH), which regulates TSH (Hackney and Saeidi 2019).

## 1.1 Objectives of Study

1. The primary objective of this investigation is to get a precise determination of the amount of iron in the sample. TIBC, ferritin, Iodine and T3, T4, FT3, FT4, TSH, Creatinine, Urea and Anti-TPO to investigates.
2. The possible relationship between these parameters with hypothyroidism in Iraqi patients will be investigated.

# 2. LITERATURE REVIEW

## 2.1 Hypothyroidism

Hypothyroidism is characterized by abnormally low levels of the hormone thyroid, and it may have a variety of causes and presentations. Hypothyroidism that is not treated may raise the risk of morbidity and death. Autoimmune thyroid disease, also known as Hashimoto thyroiditis, is the leading cause of hypothyroidism in the United States, but a deficiency of iodine in the diet is the leading cause worldwide (Patil *et al*. 2021). The manifestation of the illness in a patient might range from asymptomatic to coma due to myxedema. Principal hypothyroidism and secondary (central) hypothyroidism are the two primary classifications of this condition, which may both be diagnosed with ease using standard blood tests in today's modern medical environment. Primary hypothyroidism occurs when the thyroid gland itself is unable to generate sufficient quantities of thyroid hormone. This kind of hypothyroidism is more common. When the thyroid gland itself is normal, but the disease is associated to the pituitary gland or hypothalamus, a condition known as the secondary form of hypothyroidism, also known as central hypothyroidism, is diagnosed (Xatzipsalti *et al*. 2021). Primary hypothyroidism is almost often brought on by an insufficient intake of iodine, which may be seen all over the globe in regions that do not get enough iodine in their diet. Autoimmune thyroid illnesses are the most common reasons for hypothyroidism in both the United States and other areas of the world that have adequate iodine. In the United States, Hashimoto thyroiditis is the most prevalent cause of lymphoma, and there is a significant correlation between the two conditions. The etiology of a disease may be impacted locally by factors such as iodine fortification and the development of new regions that are low in iodine (Taylor *et al*. 2018). Additional frequent factors that might lead to hypothyroidism, as shown in Figure 2.1.

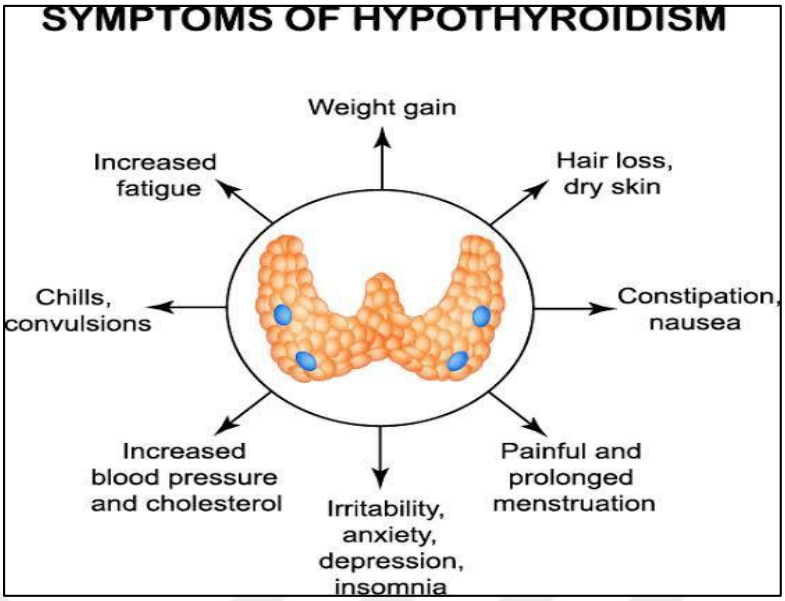


**Figure 2.1** Symptoms of an underactive thyroid (Kulkarni and Mahajan 2021)

### 2.1.1 Thyroid hormones

The anterior pituitary gland is responsible for the production of the glycoprotein hormone that is also known as thyroid-stimulating hormone, or TSH. The generation of thyroid hormone by the thyroid gland is mostly in response to this principal input. In addition to this, it promotes the proliferation of thyroid follicular cells, which ultimately results in an enlarged thyroid. The release of TSH is controlled by the hypothalamic-pituitary axis. To be more specific, neurons in the hypothalamus are responsible for the production of TRH, also known as thyroid-releasing hormone. This hormone activates thyrotrophs in the anterior pituitary to produce TSH (Pirahanchi and Jialal 2021).

In response, TSH causes the thyroid follicular cells to become stimulated, which results in the production of thyroid hormones in the form of T4 or T3. The active type of thyroid hormone is known as T3, which stands for triiodothyronine. The peripheral conversion of T4 to T3 is the source of the vast majority of T3, despite the fact that it accounts for only 20% of the hormone that is produced. Tetraiodothyronine, which is sometimes referred to as thyroxine or T4, makes up more than eighty percent of the hormone that is released. De-iodination is the process that occurs when it is put into circulation and results

in the formation of T3. T3 and T4 may then exert a negative feedback on the anterior pituitary, which results in decreased TSH secretion at high levels of T3/T4 and increased TSH secretion at low levels of T3/T4 (Eghtedari and Correa 2021).

T0, T1 and T2 are precursors of hormones and byproducts of thyroid hormone synthesis. They do not work on hormonal precursors and seem to be completely inactive. Thyroxine (T4) is also inert, but converted to triiodothyronine (T3) in the liver, kidney, brain and other organs (Gluvic *et al*. 2021).

The main thyroid hormones that are produced by the thyroid gland are as follows:

Thyroxine (also known as T4 or L-3, 5, 3, 5-tetraiodothyronine): TH may also take the form of. The follicular cells of the thyroid gland are responsible for the primary production of this hormone. Iodination and covalent bonding of the phenyl sections of tyrosine residues present in an early peptide called thyroglobulin, which is released into thyroid granules, are necessary steps in the synthesis of thyroxine. Thyroxine is produced in the thyroid gland. T4 is carried through the blood with the help of globulin. Approximately 99.95 percent of the T4 that is produced is protein bound, mostly to thyroxine-binding globulin (TBG), to transthyretin, and to serum albumin. T4 is a prohormone that acts as a storage facility for the active hormone T3. Once it has been introduced into the blood circulation system, the half-life of T4 is about one week (Qatato 2018).

Triiodothyronine (T3): Is often considered the active form of TH. It is 3-8 times more metabolically active than T4. Plasma T4 is forty times higher than T3 because the thyroid gland produces a bigger quantity of T4 than T3, yet despite this, T3 is more active and is only generated in small quantities. It is the most potent TH, and its effects may be seen in practically every function that occurs in the body, including temperature regulation, growth, and the pace at which the heart beats (Anita 2019).

### 2.1.2 Similarities and differences between T4 and T3.

Similarities: Both contain two iodine atoms on the tyrosine ring (inner). T4 and T3 have an effect on protein, carbohydrate and fat in metabolism, increasing oxygen consumption. Differences: T4 have two iodine on the phenyl ring (outer), whereas the T3 has only one (Morris and Galton 2019), as shown in (Figure2.2). This difference in the total number of iodine atoms is where they vary from one another.

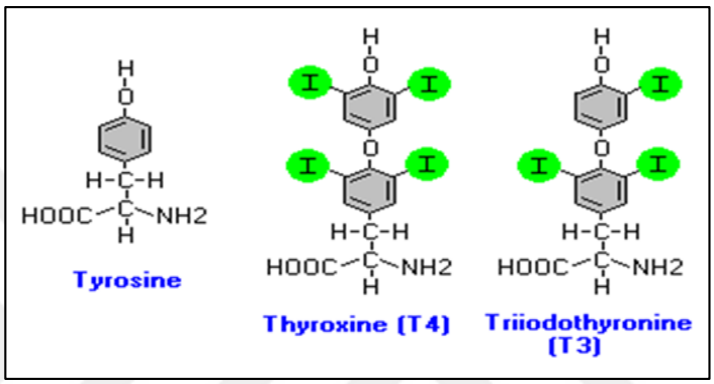


**Figure 2.2** Chemical Structure of tyrosine, thyroxine (T4) and (T3) (Morris and Galton 2019)

The second distinction is that the thyroid gland is responsible for producing just four percent of the total amount of T3, while it is solely responsible for producing all of the T4 that is generated. T3 is created in extra-thyroidal tissues to the extent of about 80 percent by the de-iodination of T4 carried out by certain intracellular enzymes. The biological activity of the hormone is determined by the free blood concentrations of thyroxine (fT3) and thyroxine (fT4), despite the fact that T4 and T3 are virtually fully bound to plasma proteins, mostly to the thyroxine-binding globulin (TBG) (Luongo *et al.* 2019).

### 2.1.3 Autoimmune with hypothyroidism

Anti-thyroid peroxidase antibodies: - is an enzyme that is necessary for the production of thyroid hormone and plays a significant part in the process. What happens is that, over

time, the immune system can cause extensive damage to thyroid peroxidase, which reduces the thyroid gland's ability to produce adequate amounts of thyroid hormone. Over a prolonged period, if the trigger isn't removed and the autoimmune response isn't suppressed, then the person with Hashimoto's will have decreased production of thyroid hormone, and as a result, thyroid hormone replacement will usually be recommended (Eric *et al*. 2018)

### 2.1.4 Anemia in hypothyroidism

Ferritin is a kind of protein that stores iron and may be found in practically every tissue in the body. Patients who suffer from thyroid illness have been shown to have abnormalities in their serum ferritin levels as well. Therefore, variations in the concentration of ferritin in the serum are indicative of thyroid function. Ferritin levels, on the other hand, might drop before iron levels do; hence, low ferritin levels suggest that action has to be taken to avoid the often symptomless slide towards anemia (Aleema Banu 2018).

Iron deficiency (ID) is a disease that affects people all over the world and requires the presence of the element iron. (ID), this condition, which shows as a reduction in the extracellular iron of the bone marrow as well as lower serum ferritin than normal, is considered as the most frequent nutritional deficit in the globe and may lead to harmful consequences on thyroid metabolism. Iron deficiency (ID) is characterized by a decreased amount of extracellular iron in the bone marrow and a blood ferritin level that is much lower than normal (Zhang *et al*. 2019).

Both the thyroid function and autoimmune response might be negatively impacted by ID. Interfering with the action of thyroxine deiodinase is one way that iodine deiodinase (ID) may control thyroid metabolism via the central nervous system. Studies have shown that this can limit the conversion of T4 to T3 as well. The low thyroid hormone levels that are associated with hypothyroidism decrease the activity of bone marrow, which is the tissue that is responsible for the production of red blood cells. Severe ID will diminish the activity of thyroid peroxidase and interfere with the manufacture of thyroid hormone.

This results in a decrease in the formation of red blood cells, which in turn causes anemia (Luo *et al*. 2021). According to the findings of certain studies, IDA is present in as many as 43 percent of patients who have symptomatic hypothyroidism. When compared to the population as a whole, this represents a difference of 29 percent. The illness is characterized mostly by persistent weariness as its primary symptom. Interfering with the natural operation of the thyroid gland may be a cause of hypothyroidism because the link between iron, red blood cells, and TSH can disrupt the thyroid gland (Kumral and Syed 2020).

The total iron-binding capacity, also known as TIBC or occasionally transferrin iron-binding capacity, is a test that is performed in a medical laboratory to determine the extent to which the blood is able to bind iron with transferrin. Transferrin has a strong propensity for combining two atoms of ferric iron ($Fe^{3+}$), which it does so by binding them together. This indicates that there is a capability for transferrin in the blood to carry roughly 1.40 to 1.49 mg of iron per gram of transferrin that is present in the circulation. This test, which determines the percentage of transport form transferrin that is saturated with iron, may be of major importance in the diagnosis of hypothyroidism (Parkes *et al*. 2018)

Iodine is a necessary trace mineral that is needed for the manufacturing of thyroid hormones by the thyroid gland. This is the sole known physiological role for iodine in the human body, and it is the only function that the iodine in question plays. Iodine may be found in tiny amounts in both the soil and the water, and it can be consumed in a number of different chemical forms. The majority of iodine compounds are converted to iodide in the digestive tract. The stomach and duodenum are the organs that do almost all of the iodide's absorption (Choudhry *et al*. 2018). The thyroid and the kidney are the primary organs responsible for the removal of iodine from the blood. Plasma iodine has a half-life of roughly 10 hours under typical conditions; however, if the thyroid is hyperactive, such as in iodine shortage or hyperthyroidism, this half-life may be reduced significantly (Olivieri *et al*. 2021). The thyroid gland is an efficient collector of iodine and has a number of protective mechanisms, both of which contribute to the preservation of normal thyroid function in spite of broad changes in the amount of iodine that is consumed on a daily basis. Iodine may cause hypothyroidism in patients who already have a preexisting

autoimmune thyroid disease, even if it is very moderate, such as Hashimoto's thyroiditis. These patients are more vulnerable to the condition (Maheshwari *et al*. 2018).

# 3. MATERIALS AND METHODS

## 3.1 Materials

All kits used in this study are listed, as shown in Table 3.1.

**Table 3.1** Illustrates the kits that used in the present study

| KITS | CAT.NO | MANUFACTURER |
|---|---|---|
| TSH kit | | Cobas e 411 analyzer/ Roche/Germany |
| T3 Kit | | |
| T4 Kit | | |
| FT3 Kit | | |
| FT4 Kit | | |
| TIBC Kit | | |
| Iron Kit | 518330 | |
| Ferritin Kit | | |
| Anti-TPO | | |
| Urea Kit | | |
| Creatinine Kit | | |
| Fasting Blood Sugar Kit | | |
| Iodine ELISA Kit | MBS779982 | MyBioSource / USA |

## 3.2 Methods

### 3.2.1 Study Design

This study was designed to be a case-control study conducted in the Al-Kindi Teaching Hospital and in the period from February 2022 to April 2022. Venous blood samples were collected and determine the biochemical measurements serum level of Iron, TIBC, ferritin, Iodin and thyroid function tests including T3, T4 and TSH in Iraqi patients with hypothyroidism. Figure 3.1 presents the study groups of this study.

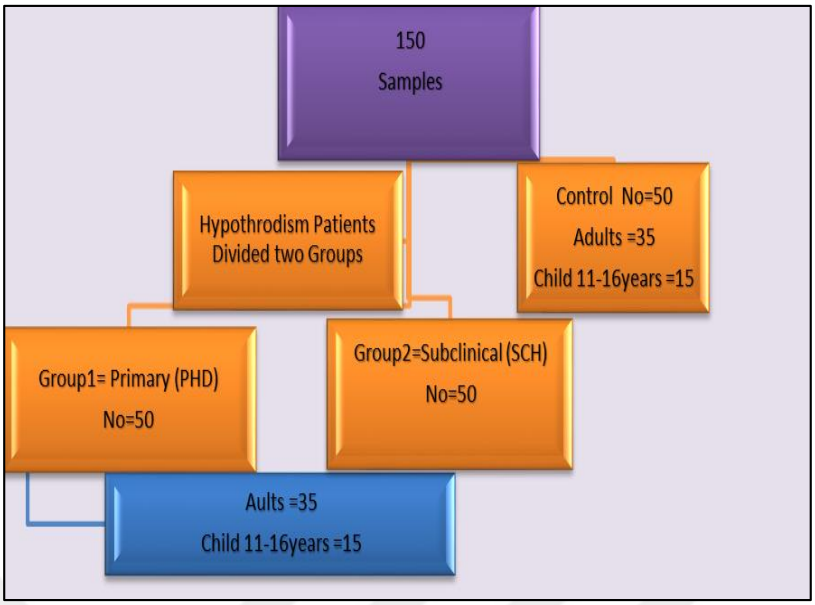


**Figure 3.1** Presents the study groups

### 3.2.2 Measurement iodin by enzyme-linked immunosorbent assay (ELISA)

Elisa assay for Iodin was performed using kit (MyBioSource / USA, Cat.No: MBS779982) according to the manufacturers protocols. This kit use competitive method to test

Expermental procedure:

1. Before beginning the test method, all of the reagents were prepared.
2. For the zero setting, simply add the chromogen solutions A and B as well as the stop solution. Do not put anything to the blank wall.
3. Standard well: put 50 L of the Standard dilution to each well, as well as 50 L of the Standard/sample dilution in the zero well. After that, added 50 L of the working solution of biotinylated antigen to each well.
4. Sample well: added 50 µL sample and then added 50 µL working solution of biotinylated antigen.
5. I then covered it with a seal plate membrane and incubated it at 37 degrees Celsius for an hour while shaking and mixing it gently.

6. Dilution of the washing concentration (25X) with distilled or deionized water for later use is the sixth step in the preparation of the washing solution.
7. For the first washing, remove the sealing film with care, drain the liquid, dry everything off, then fill each well with washing solution, let it sit for one minute, and then drain the liquid. Do this five times, and then pat the items dry.
8. After adding 50 l of avidin-HRP to both the Standard well and the sample well and covering it with a seal plate membrane, you then gave it a little shake and mixed it for an hour while the temperature was set at 37 ° C.
9. Second washing requires gently removing the plate sealer, disposing of the liquid, and drying the plate before feeding each well with wash buffer. After standing for 30 seconds, the plate should then be abandoned. Perform the procedure five times, and then dry it by clapping.
10. For the second washing, remove the sealing film with care, drain the liquid, dry everything off, then fill each well with washing solution, let it sit for one minute, and then drain the liquid. Repeat this process five times, and then pat the items dry.
11. In order to develop the color, 50 l of chromogen solution A was added to each well, followed by the addition of 50 l of chromogen solution B to each well. Gently shake it to combine everything. Incubate at 37 degrees Celsius for fifteen minutes while protecting it from the sun. This will allow the color to develop.
12. Stop: In order to halt the reaction, 50 l of Stop Solution was added to each well (the blue color changes into yellow immediately at that moment). Tap the plate on the counter lightly to verify that it is well mixed if the color in the wells is green or if the color change does not seem to be consistent.

### 3.2.3 Anti TPO

Test principle: Competition principle. 18 minutes will be allotted for the length of the test.

- In the first step of the incubation process, 20 µL of the sample is mixed with anti-TPO antibodies that have been tagged with a ruthenium complex.

- During the second round of incubation, with the addition of biotinylated TPO and streptavidin-coated microparticles, the ruthenium-labeled anti-TPO antibodies in the sample compete with the anti-TPO antibodies in the sample that are already present for the biotinylated TPO antigen. Because of the interaction between biotin and streptavidin, the whole complex is subsequently bonded to the solid phase.
- After being drawn into the measurement cell by the reaction mixture, the microparticles are then magnetically trapped on the surface of the electrode. The ProCell/ProCell M system is then used to remove any unbound compounds. The photomultiplier is used to measure the chemiluminescent emission that is induced when a voltage is applied to the electrode.
- A calibration curve that is instrument-specifically created by a two-point calibration and a master curve that is given by the reagent's barcode or e-barcode are used in order to ascertain the results of an analysis.

### 3.3 Statistical Analysis

The data analysis was carried out utilizing the software version 20.0 of the SPSS program and Excel 2016. One-way analysis of variance was used to examine and compare the differences between the groups (ANOVA). A p-value of $<0.05$ was taken into consideration to indicate significance.

# 4. RESULTS AND DISCUSSION

## 4.1 Age

According to the findings, there is a direct connection between patients' ages and their likelihood of having primary or subclinical hypothyroidism. Patients were found in people aged 30 years. The highest incidence was in the age group (50-60) years for patients with primary hypothyroidism and subclinical (19%) and (13%), respectively, while the two age groups (20-30) and (30-40) years recorded the same infection rate for patients with primary hypothyroidism (8%), as for patients with hypothyroidism Subclinical, the percentage of patients in the age group (50-60) years was higher than the age group (30-40) years, and between that in the age group (40-50) years, respectively (13%) (11%) (7%). While the age group (10-20) years for children, the incidence of subclinical hypothyroidism was higher than primary hypothyroidism (9.12) (8.12) as shown in Figure 4.1, 4.2.

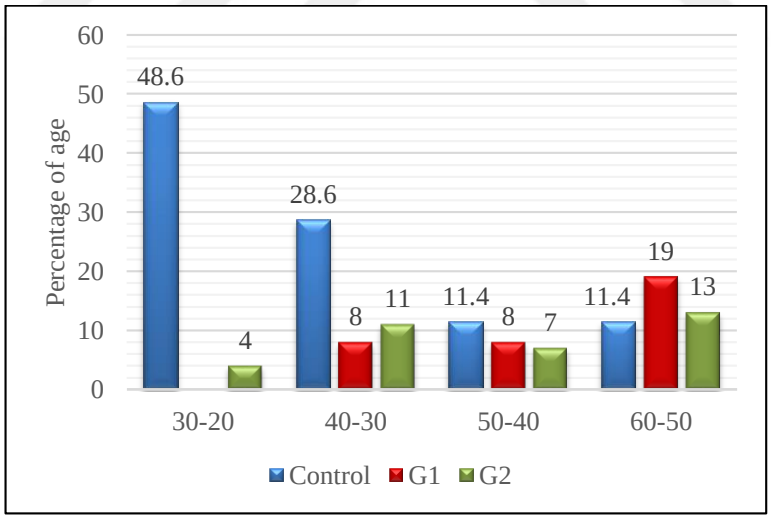


**Figure 4.1** Distribution of age-stages in study groups of adults

*G1= Primary hypothyroidism disease (PTD), G2= Subclinical hypothyroidism (SCH)

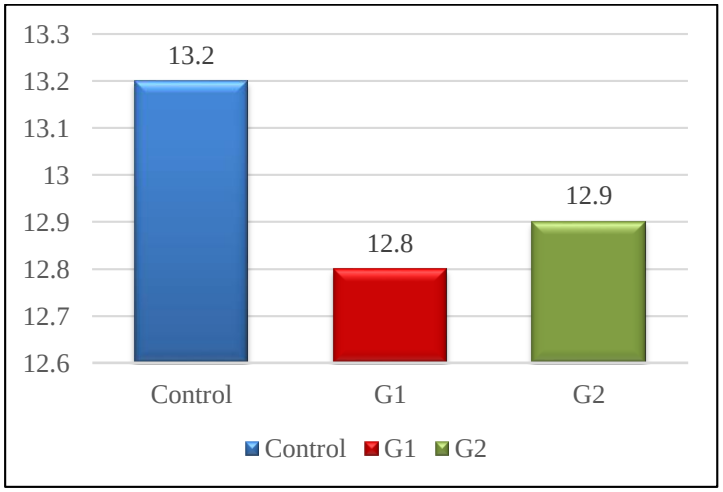


**Figure 4.2** Distribution of mean age in study groups of children

Thyroid dysfunctions are among the most prevalent disorders that coexist in children. They have been documented in anywhere from 28 percent to 40 percent of patients, and the frequency of occurrence increases with age, reaching up to 54 percent in certain cases (Loane *et al*. 2013, Casto, *et al*. 2021). The prevalence of primary hypothyroidism is increasing with age, with a peak incidence between the ages of 30 and 50 years (Zaman *et al*. 2021). Overt hypothyroidism was reported to have a frequency of 0.3 percent among individuals in the United States (12 years of age and older), whereas subclinical hypothyroidism had a prevalence of 4.3 percent according to the NHANESIII (National Health and Nutrition Examination Survey) research (Das *et al*. 2021) this is agreement with our study.

## 4.2 Gender

The results obtained show that there is a clear relationship to the gender of patients with thyroid disorders. Where the results showed that the percentage of female is higher than male with infection in childhood and adults for the G1 and G2, illustrated in Figure 4.3, 4.4.

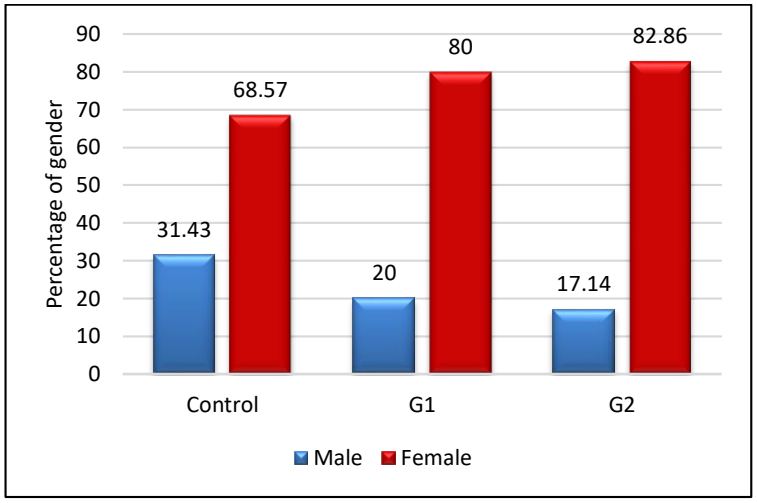


**Figure 4.3** Graphic shows gender for adults in the three study groups

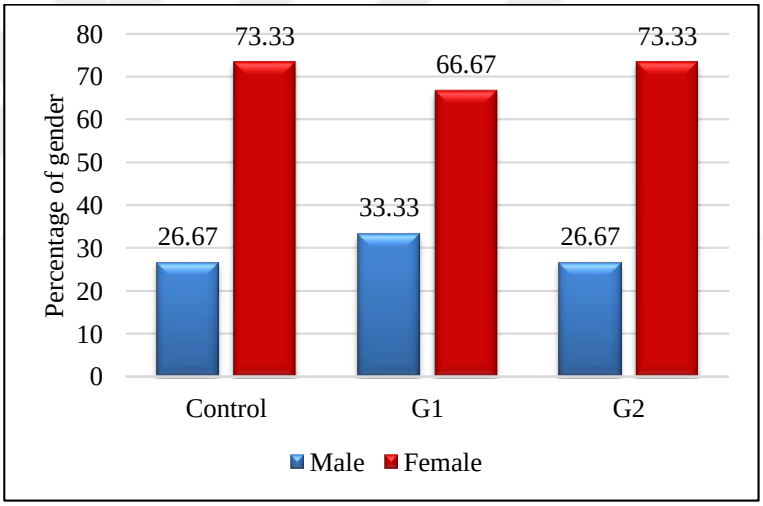


**Figure 4.4** Graphic shows gender for children in the three study groups

Primary hypothyroidism is up to eight to nine times more prevalent in females than it is in males, and the frequency rises with increasing age (Florindez *et al.* 2021). An estimated 4 percent of women in the United States between the ages of 18 and 24 have hypothyroidism, while 21 percent of women over the age of 74 have the condition. These numbers for males are 3 percent and 16 percent, respectively (Pizzato, *et al*. 2022).

While a population study in Denmark found that the lifetime risk of overt hypothyroidism was 4.1 percent in women and 1.3 percent in men, a survey conducted in the United Kingdom found that approximately 7.5 percent of women and 2.8 percent of men have elevated serum levels of TSH (Tunbridge *et al*. 1977). In addition, this same survey found that approximately 2.8 percent of men have this condition (Strikić Đula *et al*. 2022).

Primary hypothyroidism is up to eight to nine times more prevalent in females than it is in males, and the frequency rises with increasing age (Florindez et al. 2021). An estimated 4 percent of women in the United States between the ages of 18 and 24 have hypothyroidism, while 21 percent of women over the age of 74 have the condition. These numbers for males are 3 percent and 16 percent, respectively.

Thyroid dysfunctions are one of the most prevalent disorders that coexist in children who have Down syndrome. They have been recorded in anywhere from 28 percent to 40 percent of the patients, and the frequency of occurrence increases with age to reach up to 54 percent (Casto *et al*. 2021).

### 4.3 Thyroid Hormones

Descriptive measurements data of study groups for adults and child are shown in Table 4.1, 4.2. The mean±SD serum level of TSH was 6.83 ±0.32 highly significantly in G2 when comparing with G1 and control, while the mean ±SD level of T3, and F.T3 2.08± 0.09, and 5.15± 0.12 respectively in G2 the results showed significant change when comparing with G1, and anon-significant with control group, and the mean ±SD level of T4, and F.T4 was 156.30± 0.62, and 14.44± 0.55 respectively in G2.

The results showed significant difference when comparing with G1. Significant changes in the serum anti-TPO were observed in G2 40.23±0.77, which was significantly higher than G1 and controls, with p = 0.0001 for all parameters. While the results in child showed a non-significant differences were found in TSH values between G1 and G2 whereas differences were found between both groups and control (p=0.0001).

Also significantly lower were found in T.T3, T.T4, F.T3, and F.T4 concentrations between G1 and G2, while high significantly in control group ($p = 0.0001$), Anti- TPO was evaluated during the study and significant difference was found between patients and control group (p=0.0001).

**Table 4.1** Descriptive measurements data of the adults groups

| PARAMETER | PATIENTS GROUPS | | CONTROL | P-VALUE |
|---|---|---|---|---|
| | Mean ±SD G1, N=35 | Mean ±SD G2, No=35 | Mean ±SD N=35 | |
| TSH(UIU/mL) | 5.19± 0.11 | 6.83 ±0.32 | 2± 0.14 | 0.0001 |
| T.T3(nmol/L) | 0.42±0.01 | 2.08± 0.09 | 2.06± 0.08 | 0.0001 |
| T.T4(nmol/L) | 52.80± 1.22 | 156.30± 0.62 | 80.92± 1.36 | 0.0001 |
| F.T3(pmol/L) | 2.10± 0.13 | 5.15± 0.12 | 5.30± 0.11 | 0.0001 |
| F.T4(Pg/mL) | 3.83± 0.24 | 14.44± 0.55 | 14.03± 0.54 | 0.0001 |
| Anti -TPO(IU/mL) | 35.75±1.50 | 40.23±0.77 | 19.63±1.99 | 0.0001 |
| *G1= Primary Hypothyroidism Disease(PTD), G2= Subclinical hypothyroidism (SCH) | | | | |

**Table 4.2** Descriptive measurements data of the child groups

| PARAMETER | PATIENTS GROUPS | | CONTROL | P-VALUE |
|---|---|---|---|---|
| | Mean ±SD G1, N=15 | Mean ±SD G2, No=15 | Mean ±SD N=15 | |
| TSH(UIU/mL) | 4.97± 0.13 | 4.36 ±0.17 | 2.04± 0.22 | 0.0001 |
| T.T3(nmol/L) | 0.41±0.02 | 2.99± 0.24 | 2.13± 0.12 | 0.0001 |
| T.T4(nmol/L) | 50.00± 1.46 | 154.71± 0.91 | 82.90± 1.66 | 0.0001 |
| F.T3(pmol/L) | 2.38± 0.19 | 5.00± 0.13 | 5.05± 0.17 | 0.0001 |
| F.T4(Pg/mL) | 4.91± 0.30 | 13.37± 0.37 | 13.09± 0.59 | 0.0001 |
| Anti- TPO (IU/mL) | 25.27±2.22 | 38.53±1.14 | 19.05±2.46 | 0.0001 |

In the group of people who did not take any medication for their thyroid condition, the research carried out by (Bromicka *et al*. 2017) revealed a substantial link between TSH levels and anti-TPO titers. It was consequently determined that even within blood samples

in which antibody levels were below the threshold value, an increase in their titers is related with the rise in TSH. This was the conclusion that was reached as a result.

The unique finding that other researchers have demonstrated comparable benefits, but only in people with increased levels of anti-TPO in the circulation is the most interesting aspect of this study. In addition, they discovered that a positive anti-TPO was connected not only with hypothyroidism but also with hyperthyroidism. This data may be corroborated by the findings of study conducted by Whickham, in which increased blood TSH and TPO antibody levels, either alone or together, were presented as a risk factor for hypothyroidism (Vanderpump 2011).

In addition, referencing prummel, the unintentional revelation of increased anti-TPO blood titers should compel us to examine thyroid function. Evaluation of anti-TPO antibodies may be conducted as a first laboratory test in the presence of other autoimmune illnesses in relatives of patients with ATD, high-risk pregnant women, subjects on specialized pharmacological treatment, and women considering pregnancy with certain risk factors for autoimmune disorders (Szybiński *et al*. 2010).

Anti-TPO was thought to be a sensitive sign for autoimmune thyroid illness until quite recently. According to the findings of a research that was carried out in Norway, there is a correlation between the Anti-TPO level and unusually low or high concentrations of TSH (Fadhil *et al*. 2019).

According to the findings of a research conducted by Jayashankar, around 80 percent of clinical cases and 50 percent of subclinical cases are positive for Anti-TPO (Jayashankar *et al*. 2015).

This finding is in keeping with the findings of the research that was carried out in Iraq by (Fadhil *et al*. 2019), who discovered that the hypothyroid group had a significantly higher level of Anti-TPO.

## 4.4 Iodine

In this study, Iodine concentration in adults and children was higher in the cases with G2 (12.72 ±0.45, 11.31 ±0.47 ) and G1 (10.51± 0.71, 10.51± 1.25 ) as compared to controls (8.84± 0.40, 7.93± 0.60 ) (P = 0.006, 0.001) respectively, as seen in Table 4.3, this was consistent with the findings of the research carried out by (Kotwal et al. 2015) Another research that was carried out by (Zhao et al. 2014). According to their findings, a high consumption of iodine was likely to lead to the emergence of thyroid illnesses, via a long-term mechanism, and individual iodine detection was advised for the imbalance of the iodine nutritional status among normal persons.

**Table 4.3** Comparison of iodine concentration among studied groups

| PARAMETER | PATIENTS GROUPS ADULTS | | CONTROL | P-VALUE |
|---|---|---|---|---|
| | Mean ±SD G1, N=35 | Mean ±SD G2, N=35 | Mean ±SD N=35 | |
| Iodine (ng/mL) | 10.51± 0.71 | 12.72 ±0.45 | 8.84± 0.40 | 0.006 |
| | Patients Groups Child N=15 | | | |
| | 10.51± 1.25 | 11.31 ±0.47 | 7.93± 0.60 | 0.001 |

Iodine insufficiency has been shown to be the root cause of thyroid dysfunction in each and every one of the aforementioned investigations in which iodine status was evaluated. According to a review written by (Inoue et al. 2018), the underlying processes of iodine-induced hypothyroidism are unknown; nonetheless, it is possible to attribute it to a failure to completely escape from the acute Wolff-Chaikoff effect (Eftychia *et al*. 2017).

People who have a history of thyroid disease or thyroid autoimmunity and fetuses are both examples of vulnerable groups that may not be able to escape the effects of this phenomenon. There has been very little research conducted on the topic of how or whether infants and young children may adapt to an excess of iodine, and as a result, the mechanisms are not well understood. In spite of the fact that there is evidence suggesting that an excess of iodine and a shortage in iodine may have comparable effects on thyroid

hormones (Inoue *et al.* 2018), the outcomes of these research were conflicting (Charlton *et al.* 2011).

It is possible that an overabundance of iodine was the source of thyroid malfunction and, as a result, the lower developmental score in our group; nevertheless, it is impossible to rule out the possibility of additional causative variables. In a number of studies, researchers have shown that infants born to mothers who did not produce enough thyroid hormone during pregnancy had problems with their cognitive and motor development (Panth *et al.* 2019). Congenital hypothyroidism has been linked to motor deficits in adulthood in children who have had the condition from childhood (Lamônica *et al*. 2020).

### 4.5 Iron, Ferritin and TIBC

Table 4.4 Demonstrates the comparison of Iron, ferritin and TIBC between hypothyroidism and control group in adults and children. There was a significant reduced in serum iron, and ferritin while a significant increase in TIBC in hypothyroidism compared to control group, (P≤0.01).

**Table 4.4** Comparison of iron, ferritin and TIBC between the studied groups

| **PARAMETER** | **PATIENTS GROUPS ADULTS** | | **CONTROL** | **P-VALUE** |
|---|---|---|---|---|
| | Mean ±SD G1, N=35 | Mean ±SD G2, N=35 | Mean ±SD N=35 | |
| Iron (µg/dL) | 15.63± 0.06 | 19.35 ±0.84 | 127.89± 6.42 | 0.0001 |
| Ferritine (ng/mL) | 9.80±0.59 | 10.65± 0.51 | 94.53± 3.43 | 0.0001 |
| TIBC (mg/dL) | 324.46± 11.73 | 328.47± 10.49 | 286.39± 11.96 | 0.019 |
| | Patients Groups Child, N=15 | | | |
| Iron (µg/dL) | 35.93± 1.95 | 38.73 ±1.54 | 81.93± 1.65 | 0.0001 |
| Ferritine (ng/mL) | 13.42±1.01 | 9.66± 0.90 | 62.17± 12.22 | 0.0001 |
| TIBC (mg/dL) | 246.67± 19.06 | 299.87± 16.51 | 223.73± 15.25 | 0.009 |

## 4.6 Fasting Blood Sugar

The calculated mean ± SD values for FBS control, patients with primary hypothyroidism patients with subclinical hypothyroidism are summarized in Table 4.5. The results here showed that revealed significant differences in adult patients with hypothyroidism (G1 and G2), and control (P=0.0001), While there are no statistically significant differences in children patients with hypothyroidism, and control (p=0.086).

**Table 4.5** Serum levels of FBS in study groups

| PARAMETER | PATIENTS GROUPS ADULTS | | CONTROL | P-VALUE |
|---|---|---|---|---|
| | Mean ± SD G1, N=35 | Mean ± SD G2, N=35 | Mean ±SD N=35 | |
| FBS (nmol/L) | 5.26± 0.42 | 5.66 ±0.20 | 4.24± 0.14 | 0.002 |
| | Patients Groups Child, N=15 | | | |
| | 5.60± 0.66 | 5.53 ±0.29 | 4.33± 0.27 | 0.086 |

The most prevalent types of endocrine diseases are those that affect the thyroid gland and the metabolism of carbohydrates. These conditions include diabetes mellitus (DM) and prediabetes (Duntas *et al*. 2011).

Diabetes mellitus has a prevalence that rises with age, with a rate of roughly 0.2 percent in persons under the age of 20 years old, 11.3 percent in those over the age of 20 years, and more than 26.9 percent in people over the age of 65 (Zheng *et al*. 2018).

According to the findings of (Han *et al.* 2015), persons with T2DM who also have subclinical hypothyroidism are at an increased risk for developing diabetic neuropathy.

In the current research, there was a considerable disparity in terms of the ages of the participants between the two groups. In this respect, the studies conducted by (Yang *et al.* 2010, Chen *et al.* 2007) show that the age of diabetic patients in the subclinical hypothyroidism group and the euthyroid (the thyroid gland is working properly) group are not significantly different from one another. Patients with diabetes who had

subclinical hypothyroidism had an age that was much older than that of euthyroid patients, according to the findings of a research that was conducted by Yasuda and colleagues (Yasuda *et al.* 2011). Our findings were in accordance with these findings. It's possible that the differences in the sample sizes used in these two research are to blame for the dissimilar findings they produced. According to the findings of epidemiological research that investigated the incidence of subclinical hypothyroidism in patients with type 2 diabetes, the age of patients with diabetes does not play a significant role in the progression of subclinical hypothyroidism (Zhu *et al*. 2019). According to the findings of the current study as well as those of earlier research, it would seem that there is a correlation between the progression of diabetic patients age and the onset of subclinical hypothyroidism.

## 4.7 Renal Function

For patients with hypothyroidism The calculated mean ± SD values for renal function (Urea and creatinine) for control and patients with primary and subclinical hypothyroidism are summarized in Table 4.6 The results showed that revealed significant with the level of urea in the blood differences in adult and children patients of three study groups (control, G1 and G2) respectively (p=0.003) and (P=0.0001), also, creatinine level in adult patients was significantly higher (P= 0.0001).While there is no statistically creatinine level differences in in children patients with hypothyroidism, and control (p=0.065).

**Table 4.6** Serum levels of urea and creatinine in study groups

| PARAMETER | PATIENTS GROUPS ADULTS | | CONTROL | P-VALUE |
|---|---|---|---|---|
| | Mean ± SD G1, N=35 | Mean ± SD G2, N=35 | Mean ±SD N=35 | |
| Urea (mmol/L) | 4.55± 0.23 | 5.62 ±0.22 | 5.17± 0.20 | 0.003 |
| creatinine (µmol/L) | 64.11± 1.53 | 52.54 ±2.64 | 38.64± 0.53 | 0.0001 |
| | Patients Groups Child, N=15 | | | |
| Urea (mmol/L) | 4.27± 0.16 | 5.89 ±0.20 | 4.99± 0.32 | 0.0001 |
| creatinine (µmol/L) | 46.93± 3.61 | 45.07 ±3.45 | 37.57± 0.58 | 0.065 |

The lack of thyroid hormones (TH) causes problems in renal function because it lowers cardiac output, which results in a widespread hypodynamic condition throughout the circulatory system (Perticone and Perticone 2021).

In hypothyroidism, there is typically just a little decrease in renal function. In a condition of hypothyroidism, it was found that the alterations in routine clinical biochemical markers of renal function are not well described. This was a finding that was made. Even though there is no mention of variations in serum urea or creatinine levels in any of the classic reference books (Akagunduz and Akcakaya 2021, Den Bakker *et al*. 2018), This runs counter to the findings of our investigation. There are a few isolated instances that link increased blood creatinine levels to the simple form of hypothyroidism (Kizilgul *et al*. 2022).

Primary hypothyroidism is linked to a temporary rise in blood creatinine levels, which may occur in both adults and children (Kreisman and Hennessey 1999), and children (Mooraki *et al*. 2003, Karanikas *et al*. 2004). This rise may be seen in more than half (55%) of persons who have been diagnosed with hypothyroidism (Akagunduz and Akcakaya 2021).

This is agreement with our study. According to research done by (Vandana *et al.* 2012), people with overt and subclinical hypothyroidism had significantly higher amounts of urea and creatinine in their blood when compared to euthyroid controls. Primary hypothyroidism in humans has been linked in some past research to a temporary increase in blood creatinine levels, which can be reversed (Kizilgul *et al*. 2022).

## 4.8 Correlations

The Pearson correlation analysis was used to investigate the link between all of the factors that were considered for this study in relation to the chemical measurements that were taken. Tables 4.7 and 4.8 include an accumulation of the findings obtained as a whole.

**Table 4.7** Correlations between variables in hypothyroidism patients (r-value)

| VARIABLES | TSH | TT3 | TT4 | FT3 | FT4 |
|---|---|---|---|---|---|
| TSH | 1 | -0.378** | -0.469** | -0.450** | -0.515** |
| TT3 | -0.378** | 1 | 0.911** | 0.862** | 0.794** |
| TT4 | -0.469** | 0.911** | 1 | 0.901** | 0.897** |
| FT3 | -0.450** | 0.862** | 0.901** | 1 | 0.830** |
| FT4 | 0.515** | 0.794** | 0.897** | 0.830** | 1 |
| Anti TPO | 0.107* | 0.042 | -0.014 | 0.086 | 0.030 |
| Iron | -0.350** | 0.622** | 0.454** | 0.500** | 0.374** |
| Ferritine | -0.214* | 0.100 | 0.095 | 0.203 | 0.047 |
| TIBC | 0.035* | -0.178 | -0.319** | -0.219 | -.0243* |
| Iodine | 0.309** | 0.329** | 0.419** | 0.328** | 0.422** |
| *: Correlation is significant at the 0.05 level, **: Correlation is significant at the 0.01 level | | | | | |

**Table 4.8** Analyses of the correlations between factors in individuals with hypothyroidism (r-value)

| VARIABLES | ANTI TPO | IRON | FERRITINE | TIBC | IODINE |
|---|---|---|---|---|---|
| TSH | 0.107* | -0.350** | -0.214 | 0.035* | 0.309** |
| TT3 | 0.042 | 0.622** | 0.100 | -0.178 | 0.329** |
| TT4 | -0.014 | 0.454** | 0.095 | -0.319** | 0.419** |
| FT3 | .086 | 0.500** | 0.203 | -0.219 | 0.328** |
| FT4 | 0.030 | 0.374** | 0.047 | -0.243* | 0.422** |
| Anti TPO | 1 | 0.003 | -0.075 | 0.177 | 0.032 |
| Iron | .003 | 1 | 0.112* | 0.110 | 0.175 |
| Ferritine | -0.075 | 0.112* | 1 | -0.101 | 0.006 |
| TIBC | 0.177 | 0.110 | -0.101 | 1 | -0.191 |
| Iodine | 0.032 | 0.175 | 0.006 | -0.191 | 1 |
| *: Correlation is significant at the 0.05 level, **: Correlation is significant at the 0.01 level | | | | | |

The analysis revealed the presence of a positive correlation between the levels of TSH with Anti-TPO, TIBC and Iodine in patients with hypothyroidism negative correlation were observed between the level of TSH with TT3, TT4, FT3, FT4 and Iron as shown in Table 4.7.

The analysis also revealed a positive correlation between the level of TT3 with TT4, FT3, FT4, iron and iodine in addition, the statistical data analysis showed a positive correlation between the level of TT4 and the level of TT3, FT3, FT4, iron and iodine.

Finaly positive correlation between the level of FT4 with TSH, TT3, TT4, FT3, iron and iodine.

# 5. CONCLUSIONS AND RECOMMENDATION

## 5.1 Conclusions

1. The results of the current work indicated that the average values of thyroid hormones are directly related to primary and subclinical hypothyroidism in children and adults.
2. As well as the element iodine, iron, ferritin and the total iron binding capacity has a direct relationship
3. Fasting blood sugar test with kidney function showed a close association with the disease
4. 4-There is a correlation between iodine and all thyroid hormones
5. Finally, as well as iron with ferritin and thyroid hormones

## 5.2 Recommendation

1. Study the relationship between the level of Selenium and Zinc with hypothyroidism in adults and children.
2. Further studies are needed to clarify the relationship between the level of the protein Thyroglobulin with hypothyroidism in adults and children.
3. Identification of pituitary thyrotropin signature genes 1 and regulatory elements

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