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The Impact of Thyroid Hormones In Pregnant Women In Kerbala Province

A Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

(وَمَا أُوتِيتُمْ مِنَ الْعِلْمِ إِلَّا قَلِيلًا)

صدق الله الْعَلِيُّ الْعَظِيمُ

سورة الإسراء (الآية ٨٥)

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We certify that this thesis **(Relation between Pregnancy and Thyroid Hormones in Pregnant Females)** was placed under supervision in chemistry Department of College of Education for Pure Sciences, University of Karbala Partially fulfilling the requirements for a master's degree in Chemistry sciences for the student **(Rabab Salman Bedia Al-Khafaji)**

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Dedication

To the greatest messenger, Muhammad, may God bless him and grant him peace

To the people of the House of Prophecy, the source of knowledge, the locus of the message, and the various angels

To my dear father and my dear mother...love and respect

To my 'brothers' and sisters ... Proud and proud

To the students of knowledge... we dedicate this humble effort

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SUMMARY

This study was designed to investigate the relationship between thyroid hormones and pregnancy, as well as the prevalence and impact of thyroid dysfunction in pregnant women with risk factors for recurrent miscarriage, intrauterine growth restriction, hypertension and diabetes occurring during pregnancy. Serum of 115 pregnant women infected with risk factors distributed over different periods of pregnancy, and their ages ranged between 15-43 years, and the serum of 50 healthy pregnant women aged between 15-43 years was considered as a control group. This study was conducted in the Obstetrics and Gynecology Hospital in Karbala during the period (September) 1/9/2020 to (March) 1/3/2021. Thyroid hormones TSH, FT4, FT3 were measured using Mini Vedas.in the serum of pregnant women. The results of the study showed that there is a relationship between thyroid hormones and pregnancy, significant difference was found in TSH, FT4 and FT3 compared to the control group, Hypothyroidism led to an increase in TSH and a significant decrease in FT3 and FT4 hormones. FT4 compared to the control group by 75%, while the increase in thyroid hormones (hyperthyroidism) was a significant decrease in TSH and a significant increase in FT3 and FT4 compared to the control group by 40%. It also found a relationship between hypothyroidism and hyperthyroidism with risk factors, where the prevalence of recurrent miscarriage was 22%, hypertension 18%, diabetes mellitus 10%, and intrauterine growth restriction 25% in hypothyroidism, while the prevalence of recurrent miscarriage was in hyperthyroidism. 8%, high blood pressure 12%, diabetes 15%, intrauterine growth restriction 5%, the results of the study also showed the effect of repeated abortions on weight gain and obesity. It also found that the incidence of growth restriction factor was higher in the age group 15-24 years by 13.9%, and the rate of recurrent miscarriage 12.1% is the highest in the age group 25-34 years while hypertension

was 13%. , which is highest in the 35-43 age group. So is the relationship between intrauterine growth restriction, recurrent miscarriage, diabetes, and hypertension.

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List of abbreviations

Word or term	Abbreviation
ADHD	Attention deficit hyperactivity disorder
ANOVA	One-way analysis of variance
ATA	American thyroid association
BMI	Body mass index
DIT	Diiodothyronine
ECL	Electrochemiluminescence
FT4 Free thyroxin	Free thyroxin
GD	Gestational diabetes
HCG	Human chorionic gonadotropin
IUGR	Intrauterine growth restriction
LH	Luteinizing hormone
LT4	Levothyroxine
MIT	Mono iodylthyronine
mRNA	Messenger RNA
PCOS	Polycystic ovary syndrome
RSA	Recurrent spontaneous abortion
rT3	Reverse triiodothyronine
SD	Standard deviation
SPSS	Statistical Package for Social Sciences
T3	Triiodothyronine
T4	Tetraiodothyronine
TBG	Thyroxin binding globulin
Tg	Thyroglobulin
TH	Thyroid hormones
TPO	Thyroid peroxidase
I-	iodized salt
TRH	Thyrotropin releasing hormone
TSH	Thyroid stimulating hormone
TSHR	Thyroid stimulation hormone receptor
TSHRAbs	Antibodies to thyrotropin receptors

CHAPTER ONE

Introduction and Literature Review

1. LITERATURE REVIEW

1.1 Thyroid Gland

The thyroid gland is one of the largest endocrine glands in the body and consists of two lobes located on either side of the ventral side of the trachea, each lobe about 4 cm long and 2 cm thick connected to each other by a thin strip of connective tissue called the isthmus. The weight of the thyroid gland in adults is about 18 - 60 grams [(1)]. In the human foetus, the thyroid gland begins to appear after 3-4 weeks. The thyroid gland takes its external shape with an isthmus connecting the life lobes and the final position below the thyroid cartilage by the seventh week of embryonic development [(2)].Figure (1.1) the thyroid gland contains two types of epithelial cells, follicular cells and Para follicular cells (C cells) .The follicle lumen is a single layer of polarized cells that form the envelope of the spherical structure with an inner compartment. The cells adjacent to the scab are responsible for the formation of colloid (iodothyroglobulin) and glycolystonin (Sprenzel)[(3)]. Colloid is a protein rich component of thyroglobulin (Tg) that provides three functions which include thyroxin precursor, storage of inactive thyroid hormones (TH) and storage of iodine [(4)]. The thyroid gland receives a higher blood supply from the superior thyroid arteries [(5,6)] .

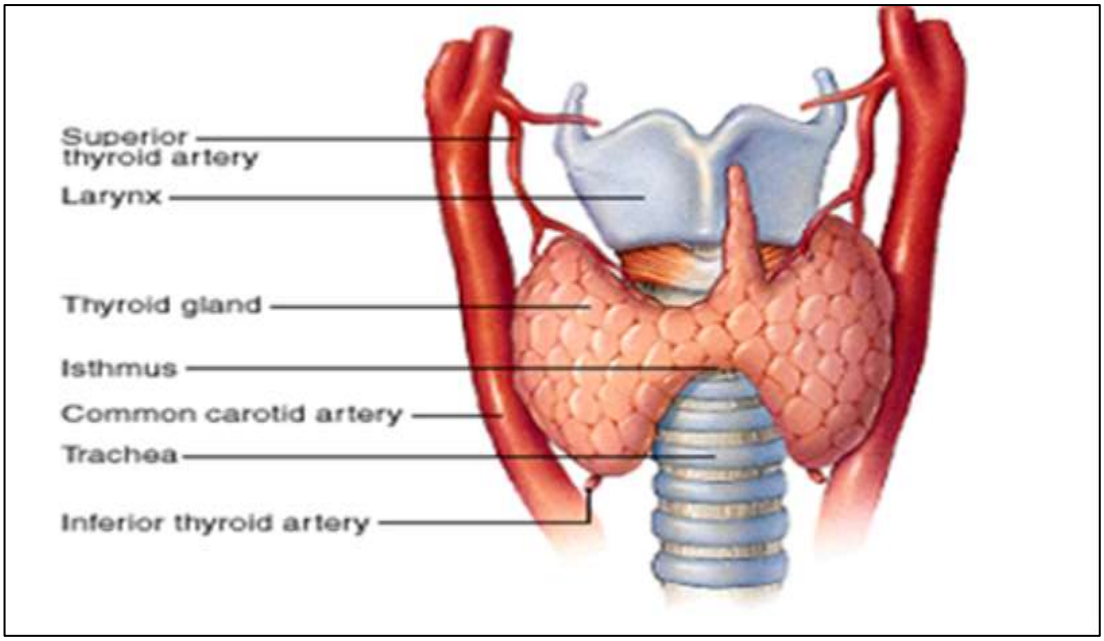

Figure 1.1 Thyroid Gland [1]

1.1. 1 Thyroid Tissue

The thyroid gland is made up of groups of cells located in the lumen called follicles. The wall of the follicle consists of a single layer of cubic follicular cells that become columnar when stimulated. These cells secrete the thyroid hormones thyroxin T4 as basic hormone and triiodothyronine T3 and thyroglobulin. Para follicular cells (C cells) that secrete calcitonin are located outside the follicles [7].

1.1. 2 Thyroid Gland Function

The function of the thyroid gland is the production of the thyroid hormones T3, T4and calcitomin which is synthesized on thyroglobulin (Tg) and participates in the regulation of metabolism, peripheral maturation, increased protein synthesis, the central nervous system, and increased oxygen consumption in all cells of the body except for the spleen, adult brain and red blood cells in the retina of the eye [8] .as shown in Figure (1.2)

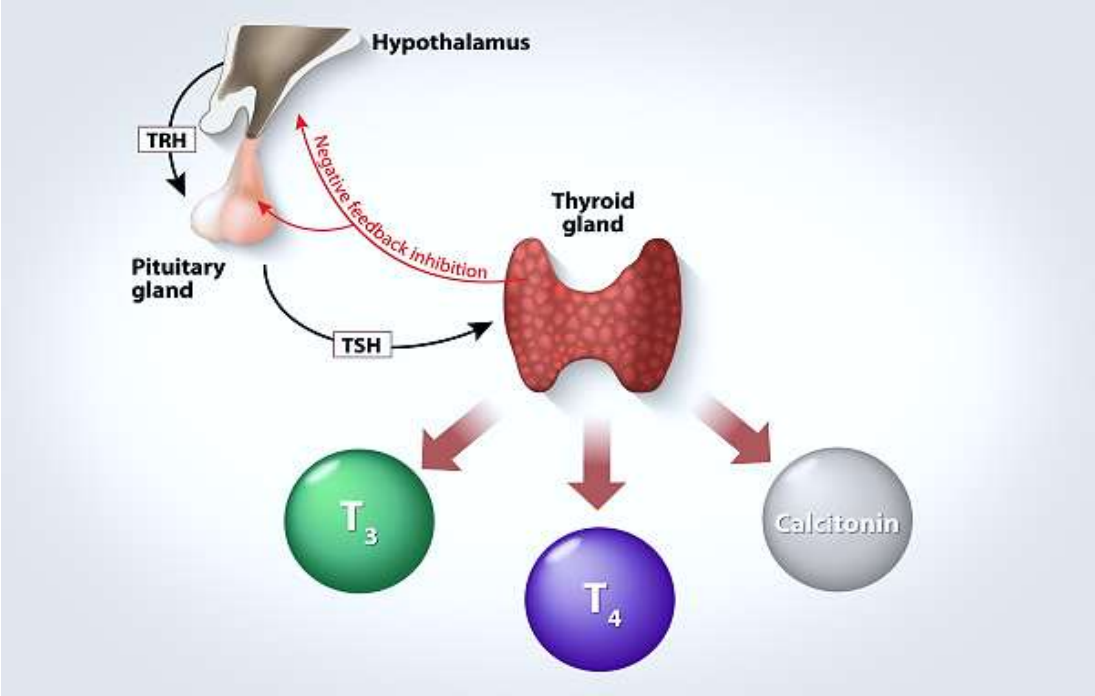

Figure 1.2 The function of the thyroid gland is to produce the hormones T3, T4 and calcitonin. [9]

1.1. 3 Physiology of Thyroid Function

Iodine absorption is the first step in the formation of thyroid hormones. Most of the iodine is rapidly absorbed from the intestines within 30 minutes and then moves to the bloodstream and binds to proteins, especially albumin. The thyroid gland efficiently extracts iodine from the blood circulation, and the remaining unbound iodine is then excreted in the urine [10]. The very low level of iodide in the plasma requires the thyroid cell to develop a highly efficient concentration force to actively transport iodine within the thyroid gland and this is called iodide trapping. After iodine is retained in the follicular cell, iodide is rapidly oxidized with the help of thyroid peroxidase and then moves to the apical membrane of the cell to generate the hormonally inactive deiodotyrosines, Mono iodylthyronine (MIT) and Diiodothyronine (DIT) through a process known as regulation.

The proteolysis of thyroglobulin will lead to the release of thyroxin T4 (tetraiodothyronine) and T3 (triiodothyronine). T4 can be considered as a pro-hormone because it is the free part of the metabolically active hormones circulating in the tissues and performing various metabolic actions [7].The thyroid gland contains a thyroid-stimulating hormone (TSHR) receptor that binds to the thyroid-stimulating hormone (TSH) and through which all steps of synthesis and secretion of thyroid hormones are stimulated .The intracellular iodide level is 500 times higher than the extracellular level [11] .as shown in Figure (1.3)

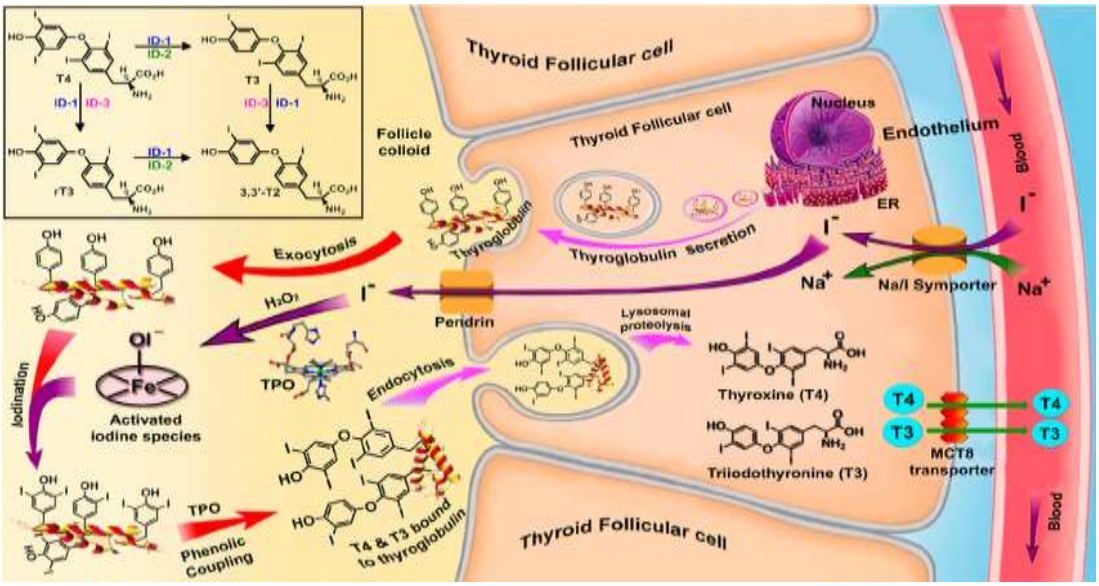

Figure 1.3 Biosynthesis of thyroid hormones from thyroglobulin by thyroid peroxidase and regioselective deiodination of thyroxin (inset). [12]

TSH binds its receptor on the tubercle cell. The TSH receptor also binds to thyroid-blocking antibodies, LH, and human chorionic gonadotropin (HCG). The latter is responsible for the physiological hyperthyroidism of early pregnancy. Physiological effects of thyroid hormone include increased mental alertness, ventilator drive, gastrointestinal motility, bone turnover, heart contractility, and heart rate [13].

It is also necessary for the optimal function of most tissues in adult life as it stimulates thermogenesis caused by cold and lack of shivering. TSH is a 31 KDa hormone containing two subunits, the alpha subunit that shares a structure similar to some other glycoprotein hormones, and the beta subunit that is unique to TSH. The thyroid axis is a classic example of an endocrine feedback loop, and T4 is the key factor in negative feedback regulation [(11)]. Binding of TSH to its receptors on the lateral surface of follicular cells leads to uptake of thyroglobulin from the follicular lumen which then undergoes protein hydrolysis within the cell cytoplasm Follicular which leads to the release of thyroid hormones into the circulation.

1.2 Thyroid Hormones

The thyroid gland forms and releases its hormones to help regulate the body's growth and metabolism. Together, T3 and T4 are known as TH thyroid hormones. The thyroid gland secretes predominantly T4, which has a plasma concentration of about 100 nmol/L .The peripheral tissues, especially the liver and kidneys, separate T4 to produce about two-thirds of the circulating T3, which appears at a lower concentration of about 2 nmol/L .Most cells are able to take up T4 and remove iodine to T3, the more biologically active, T3 that binds to the receptors and causes the effect of thyroid hormones on the organs. Alternatively, T4 can be metabolized to reverse T3, which is biologically inactive [(14)] .as shown in Figure (1.4). TH is basically two types of tyrosine bound to iodine in three or four positions on the aromatic rings. Many other iodized molecules that have little or no biological activity are produced in reverse (3, 3-5-T3) rT3.

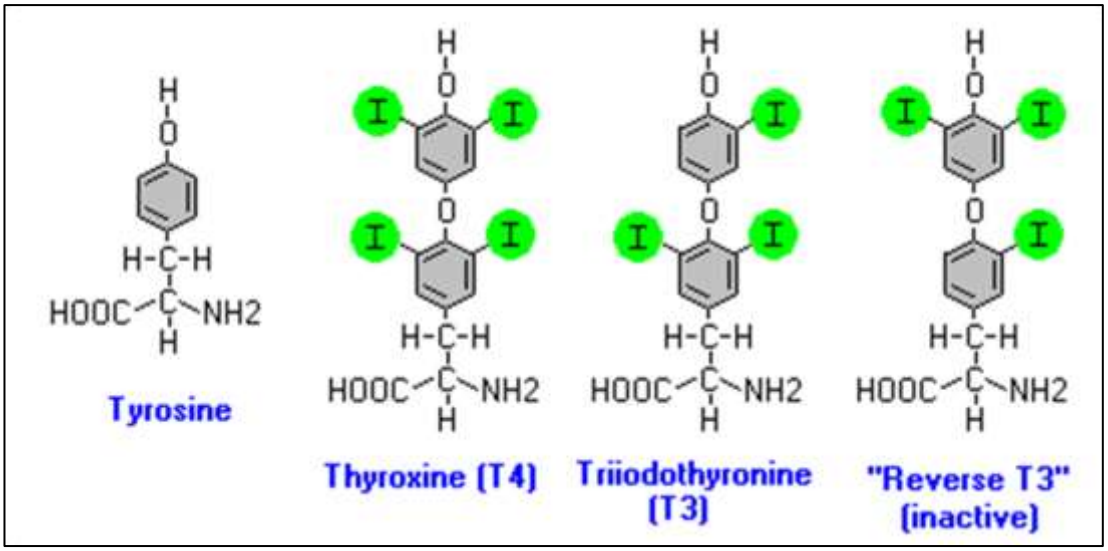

Figure 1.4 The chemical structure of the thyroid hormones T4, T3 and the inactive metabolite of T4, rT3. [1]

1.2.1 Function of Thyroid Hormone

Thyroid hormones are essential for normal growth and development and have many effects on metabolic processes. They work by entering cells and binding to specific receptors in the nucleus, where they stimulate the synthesis of different types of messenger mRNA, thus stimulating the synthesis of polypeptides including hormones and enzymes. Most general effect Pronounced on the metabolism is the stimulation of the basal metabolic rate. [15]

1.2.2 Effects of thyroid hormones (TH)

Foetal brain development and skeletal maturation depend on thyroid hormone production, and in the absence of foetal thyroid hormone cretinism results in cretinism [16]. Thyroid hormone stimulates the formation of glucose in the liver, the breakdown of glycogen, and the intestinal uptake of glucose, which leads to an increase in the level of glucose in the blood. Thyroid hormone also causes an increase in cholesterol synthesis and degradation, and increases the breakdown of fats, and this leads to a

lowering of cholesterol levels [17,18]. T3 increases oxygen consumption and heat production, which contributes to an increase in the basic metabolic rate and an increase in sensitivity to heat in the case of hyperthyroidism and an increase in sensitivity to cold in the case of hypothyroidism [19].

1.2.3 Control of the synthesis and secretion of thyroid hormones

Thyroid hormones are synthesized and stored in the follicles and depend on an adequate iodine supply. The thyroid gland acts as an iodine store and thyroid hormone levels are regulated through multiple negative feedback with control of the hypothalamic-pituitary axis and self-regulation within the thyroid gland itself. The end product of this process is the production of T4 hormone, a primary hormone that acts as a reservoir for plasma, and T3 as the active hormone [20]. (Figure 1.5)

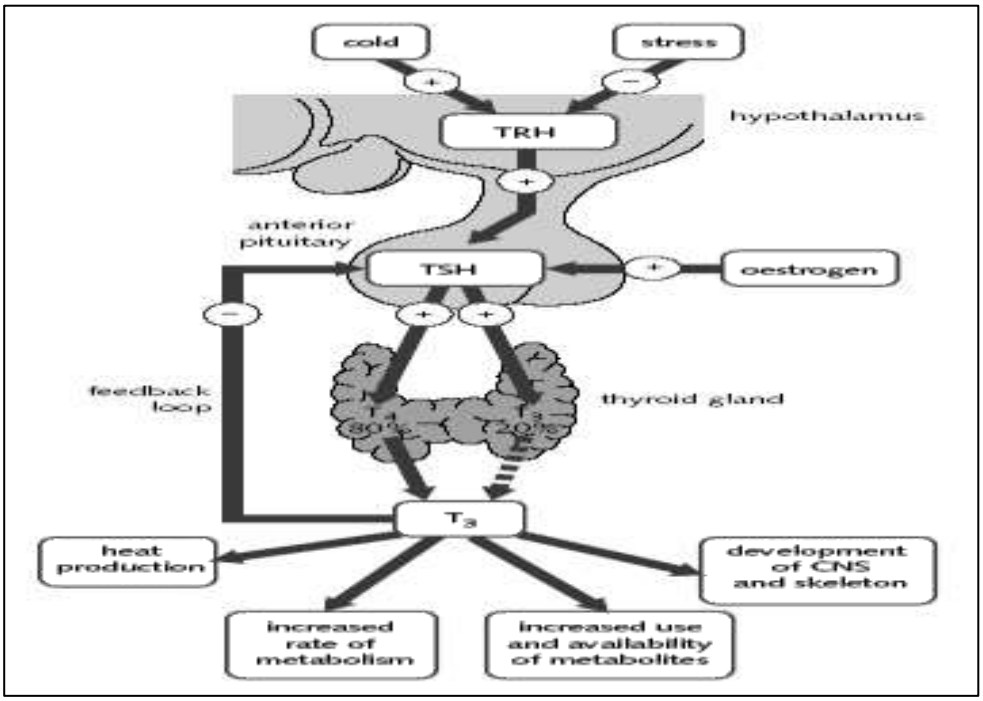

Figure 5.1 Hormonal regulation of the thyroid hormones.T3 triiodothyronine, T4 thyroxin, TRH thyrotrophin-releasing hormone, TSH thyroid-stimulating hormone [21]

1.2.4 Pathology of thyroid dysfunction

Thyroid disease mostly affects females and is common and occurs in about 5% of the population [7]. In sick or fasting individuals, T4 inhibition and the reverse transmission of rT3 to the liver, muscle, and kidneys may reduce T3 production and increase rT3 concentration [22]. The difference in thyroxin binding globulin (TBG) to thyroid hormones is more important than variation in other binding proteins. TBG variation may be caused by a mutation in the TBG gene, estrogens and androgens, and fatty acids and salicylates competitively inhibit T4 binding to TBG. Insufficient used for analysis i.e. total T4 level and not free. [11]

1.3 Pregnancy

There are three basic stages that must occur correctly for pregnancy to occur:

The first stage: Ovulation an egg is released from the ovary every month in a process called ovulation.

The second stage: Fertilization When the sperm from the man meets and penetrates the egg given by the female, this is called fertilization. At this moment, the genetic makeup of the foetus is complete, including the sex of the foetus.

The third stage: implantation. When the fertilized egg descends down the fallopian tube, it is implanted into the uterus and the embryo begins to develop [23].

1.3.1 Thyroid gland during pregnancy

During pregnancy, the mother's thyroid function is modified by three independent but interrelated factors, and these factors may be responsible for the increased thyroid demand or thyroid stress observed during pregnancy [24].

1. An increase in the concentrations of human chorionic gonadotropin (HCG) that stimulates the thyroid gland.
2. An increase in thyroxin binding globulin (TBG) related to thyroid hormone during the first 3 months of pregnancy, which leads to an increase in thyroxin binding.
3. A significant increase in urinary iodide secretion, which leads to a decrease in plasma iodine concentrations.

1.3.2 Thyroid hormones during pregnancy

In the first three months of pregnancy, the foetus depends entirely on the mother's thyroid hormones. During the second and third trimesters of pregnancy, most foetuses are able to provide some thyroid hormone, but they also continue to rely on their mothers for some hormones. Brain development problems occur when the mother is unable to meet the needs of the foetus in the first 3 months, or when neither the mother nor the foetus can provide the needs of the foetus during the remainder of the pregnancy, and other matters are the availability of iodine to the mother, as iodine is an important requirement to provide adequate production of the thyroid gland by Both the mother and the developing foetus [25].

1.3.3 Thyroid disease during pregnancy

Hypothyroidism is relatively common during pregnancy [26,27,28]. The importance of detecting thyroid abnormalities during pregnancy is that hypothyroidism may be associated with miscarriages, low birth weight, hypertension caused by pregnancy, anemia , placental abruption, premature birth, diabetes, poor vision, in addition to possible neurological defects in children [29,30,31,32]. A study by (Haddow et al), by following up on women with undiagnosed mild hypothyroidism during pregnancy for 10 years, found that 64% of women develop overt hypothyroidism [33]. Two billion people suffer from iodine deficiency, according to estimates by the world health organization.[10]

Hypothyroidism can result from:

1. defect in the thyroid gland.
2. Or secondary to insufficient secretion of TRH from the hypothalamus.
3. Insufficient secretion of TSH by the anterior pituitary gland.
4. Insufficient iodine in the diet, in which case excessive TSH secretion stimulates the abnormal growth of the thyroid gland and the development of endemic goiter. Hypothyroidism and goiter caused by iodine deficiency can be reversed by iodine supplementation.[34]

Hyperthyroidism occurs when the gland becomes overactive and produces more of its hormones. It is a condition called Graves' disease. In this disease, the body's immune system begins to attack the organs and tissues that it is supposed to protect, and this leads to an increase in the secretion of thyroid hormones. Symptoms include weight loss, a high heart rate, behavioral problems and enlarged physical growth, in addition to the

additional symptoms of a swollen neck due to an enlarged thyroid and protruding eyes. Hyperthyroidism can also occur due to hormone-producing tumors in the pituitary gland, and this reason is less common, as well as the appearance of hyperthyroidism after childbirth [35]. (Figure 1.6)

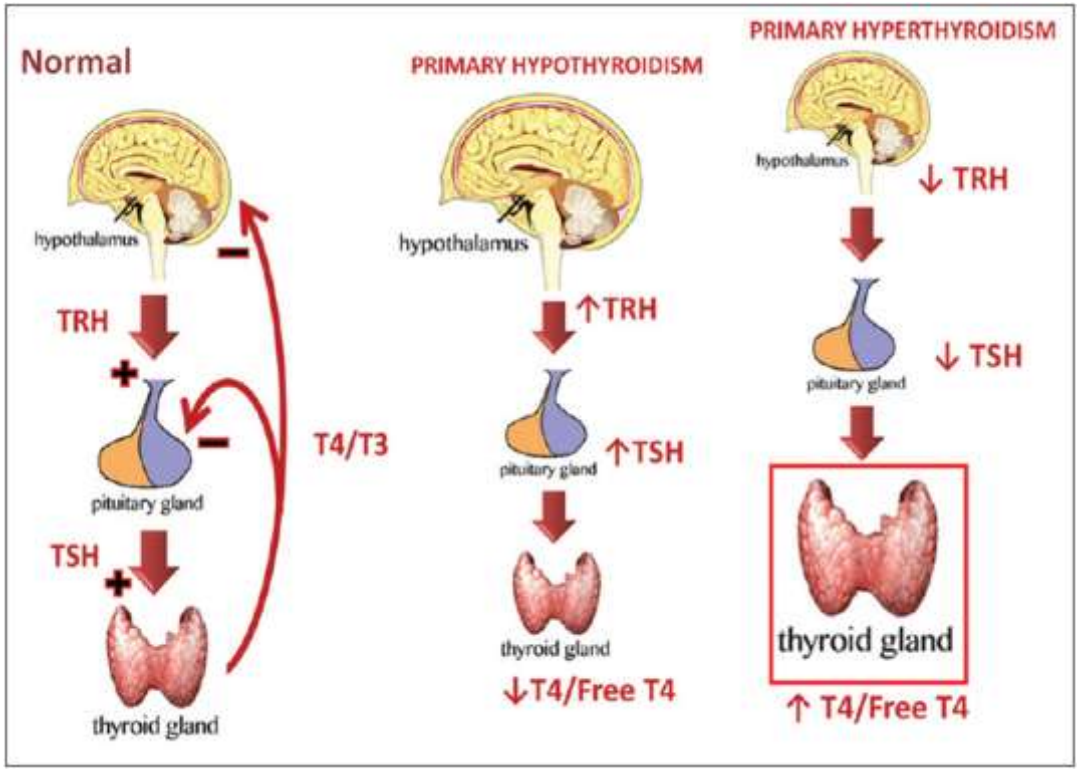

Figure 1.6 Thyroid function during hypo and hyperactivity [36]

1.3.4 Physiological changes in the thyroid gland during pregnancy

Thyroid disorders are common during pregnancy. Hyperthyroidism occurs during pregnancy in up to 0.2% of women [37]. Hypothyroidism occurs in about 3% of pregnant women [38]. Hypothyroidism due to iodine deficiency can occur at any time in life, but the most important period is during foetal development and early childhood. Overt hypothyroidism and even subclinical hypothyroidism increase the risk of obstetric complications such as miscarriage, foetal death, premature birth, growth restriction and hypertension early in pregnancy [39]. Hypothyroidism and the development

of thyroid antibodies during pregnancy are associated with maternal morbidity later in life [40]. Deficient or excessive thyroid hormone secretion affects nearly all body systems before the thyroid gland is functioning in a foetus from 12 to 14 weeks of gestation [11]. Thyroid hormones play an important role in regulating foetal organ development to meet the challenge of increasing metabolic needs during pregnancy [29]. The thyroid gland adapts through changes in the thyroid hormone economy and in the regulation of the hypothalamic-pituitary-thyroid axis [41]. Mild thyroid hormone deficiency may be masked by mild to moderate iodine deficiency during pregnancy because TSH does not necessarily increase due to stable or slightly increased T3 levels [42]. In severe iodine deficiency during pregnancy, foetal thyroid hormone production decreases as damage to the developing brain continues, and this may lead to a mental retardation called endemic cretinism. Thus, iodine deficiency disorders including endemic goitres and cretinism are the most common endocrine disorders worldwide [22]. Thyroid hormones are important for neurodevelopmental processes such as neurogenesis and cell migration [43]. Thyroid hormone deficiency in early pregnancy alters cell migration [44]. In pregnant women with iodine deficiency (hypothyroidism) even if hypothyroidism is not associated with the birth of cretin children (children with congenital iodine deficiency syndrome characterized by impaired physical and mental development due to dietary iodine deficiency during pregnancy, congenital iodine deficiency is also called hypothyroidism thyroid) [45]. Cognitive development in non-creatine offspring is affected by thyroid hormone deficiency in mothers living in areas of iodine deficiency [46]. Therefore, maintaining normal thyroid function during pregnancy is of paramount importance to the mother and children, and this can be detected. Undiagnosed hyperthyroidism in early pregnancy is more likely to occur due to stimulation of the thyroid gland by HCG [27]. Transient hyperthyroidism may be caused by

hyperemesis gravid arum. Furthermore, hydrated form moles (increased tissue masses inside the uterus) and placental carcinomas may lead to thyrotoxicosis due to very high concentrations of HCG [47]. At the beginning of pregnancy, a distinction must be made between benign transient thyrotoxicosis of pregnancy and Graves' disease, since the latter deserves ant thyroid therapy. Untreated hyperthyroidism during pregnancy can have serious consequences for the pregnant woman, pregnancy outcomes, and the foetus such as heart failure, premature birth and an increased incidence of caesarean section and placental abruption [48,49,50,51].Untreated maternal hyperthyroidism results in significant risks of death, pre-eclampsia, and congenital obstructive uropathy [49,52].

1.3.5 Laboratory changes in thyroid function during pregnancy

Normal pregnant women can have a lower TSH level than non-pregnant women [53]. Therefore, the diagnosis should be made using FT3 and FT4 measurements. In rare cases, healthy women develop transient physiological hyperactivity and have elevated serum-free T4 concentrations, making differentiation of thyroid dysfunction difficult in cases of mild to moderate iodine deficiency. Although the FT4 available to the foetus is insufficient, stable or slightly increased T3 levels may keep the TSH within the normal range and this condition may not be recognized [43]. Severe iodine deficiency can lead to overt hypothyroidism and a range of iodine deficiency disorders [54]. After conception, the concentrations of thyroxin binding globulin (TBG) and circulating total T4 increase by 6-8 weeks and remain elevated until delivery. The gradual activity of HCG results in a decrease in blood TSH during the first trimester [55]. So during pregnancy women have lower blood TSH concentrations than they did before pregnancy especially in the first trimester [56]. Most studies also report a

significant decrease in serum FT4 concentrations as pregnancy progresses. Measurements of FT4 in pregnant women who suck blood are complicated by increased TBG and decreased albumin concentration which may cause the immunoassays to be unreliable so the analytical method used to analyse FT4 should be considered [12]. Normal physiological changes in pregnancy such as blood thinning, increased thyroid-binding globulin, and increased human chorionic gonadotropin, especially in the first trimester of pregnancy, can affect the interpretation of thyroid function tests [57].

1.4 Thyroid disorders and risk factors in Pregnancy

There are a number of risk factors that contribute to the development of thyroid disease, as well as thyroid disease causing the emergence of many risk factors during pregnancy that lead to negative pregnancy outcomes:

1.4.1 Recurrent miscarriage

miscarriage is the incomplete growth and loss of the foetus (meaning the termination of pregnancy by the exit or removal of the foetus from the uterus) and there are many reasons for recurrent miscarriage, such as genetic or health reasons, and other reasons It delves into the lifestyle of the mother, and 30% of the abortion rate has been identified, while the rest is unknown and which cannot be diagnosed by laboratory tests [58] .Recurrent miscarriage is the occurrence of miscarriage before the 20th week (the fifth month of pregnancy) three or more consecutive times. [59]

Reasons for recurrent miscarriage:

- Genetic causes: it constitutes 3-5% of the causes of recurrent miscarriage and is a chromosomal abnormality in one or both spouses [60].
- An anatomical defect in the uterus: it constitutes 10-15% of the causes of recurrent miscarriage, and its causes include a congenital defect such as the uterine septum. It constitutes 70% of the causes of the anatomical defect and is diagnosed by vaginal ultrasound. The problem lies in the uterine septum, which changes the anatomical shape of the uterus. Plus it contains fewer capillaries, which are not enough to nourish the pregnancy. Treatment is often carried out surgically through hysteroscopy. Intrauterine adhesions may result from severe infections of the uterus, relaxation of the cervix, and miscarriage during the second part of pregnancy. Cervical ligation can benefit a few cases [61] .
- Hormonal causes: It constitutes 10-15% of the causes of recurrent miscarriage and is represented by a lack of progesterone secretion. Only in these cases can the well-known stabilization treatments be resorted to such as pills, suppositories, progesterone needles or the hormone human chorionic gonadotropin, and cases of diabetes out of control through medications. Whether drug therapy oral insulin or insulin needles, and a deficiency to control the disease Diabetes increases the chances of miscarriage and congenital malformations of the foetus and PCOS accompanied by an increase in the hormone LH, which has a role in infertility problems and recurrent miscarriages and ovulatory disorders that result in malformed, immature, or incompatible eggs with the endometrium. [62]

- Bacterial or viral infections: Any severe infection, whether bacterial or viral, can lead to miscarriage either through Toxoplasmosis or German measles. [63]
- Causes related to the immune system: It makes up 3-4% of cases, and since half of the foetus comes from the man, it must be the mother's body it reacts in such a way that it accepts this foreign part without attacking or rejecting the foetus, and this plays a role of the immune system in the woman's body, which stops this interaction with the so-called blocking of antibodies, and the presence of any defect in this system leads to considering the foetus as a foreign body that must be attacked to be the result Recurrent miscarriage [64].

1.4.2 Gestational hypertension

Hypertension is the most common medical problem during pregnancy, complicating 2-3% of pregnancies.[65]

Hypertension during pregnancy is pressure exceeding 140/90 mm Hg before conception or before 20 weeks of pregnancy. Pre-eclampsia occurs in 20-25% of women with a history of hypertension and transient hypertension during pregnancy is closely related [66]. The subsequent development of post-pregnancy hypertension [67]. maternal diastolic blood pressure greater than 110 mmHg is closely associated with an increased risk of placental abruption and foetal growth restriction [68]. Furthermore, hypertension before or during early pregnancy is associated with an increased risk of gestational diabetes Premature birth and stillbirth [69].

Blood pressure is the force of blood pressure on the walls of the arteries as it flows through them. Arteries are the blood vessels that carry oxygenated blood from the heart to the body's tissues.

Normal blood pressure is when the readings are less than (120/80 mm Hg) and high blood pressure occurs when the readings are (140/90 mm Hg). [70] Figure (1.7)

When blood flows through the arteries, it pushes against the inner arterial walls and the more pressure the blood exerts on the arterial walls, the higher the pressure.

The size of the small arteries also affects blood pressure. When the walls of the muscular arteries relax or widen, the pressure of blood flowing through them is lower than when the arteries narrow or constrict.

Blood pressure is at its peak when the heart is beating to push blood into the arteries, when the heart relaxes to fill with blood again. The pressure is at its lowest. The blood pressure when the heart is beating has been called the systolic pressure and when the heart is at rest, it is called the diastolic blood pressure. Hypertension can lead to thickening and hardening of the arterial walls, as happens when the arterial walls thicken, narrowing the blood vessels from the inside. Cholesterol and fat are more likely to build up on damaged artery walls, making them narrower, and blood clots can become lodged in narrowed arteries, blocking blood flow [71].

Because of atherosclerosis, the narrowed arteries do not deliver enough blood to other organs and tissues. Reducing or preventing blood flow to the heart leads to a heart attack, and if one of the arteries leading to the brain is blocked, a stroke may result. Hypertension makes the heart work harder to pump blood to the body. The extra work can cause the heart muscle to thicken and stretch. When the heart becomes too enlarged to pump enough blood, it can lead to heart failure [72].

The dangers of hypertension during pregnancy

- Decreased blood flow to the placenta: If the placenta does not get enough blood, the foetus may get less oxygen and nutrients, which leads to problems in the mental development of the foetus.
- Placental abruption: In this case, the placenta separates from the inner wall of the uterus before birth.
- Reducing the growth of the foetus inside the womb: Hypertension may lead to a slowdown or decrease in the growth of the child [71].
- Injury to other organs: Hypertension leads to injury of the brain, heart, lungs, kidneys, liver and other major organs.
- Premature birth: Sometimes premature birth is necessary to prevent life-threatening complications [72].

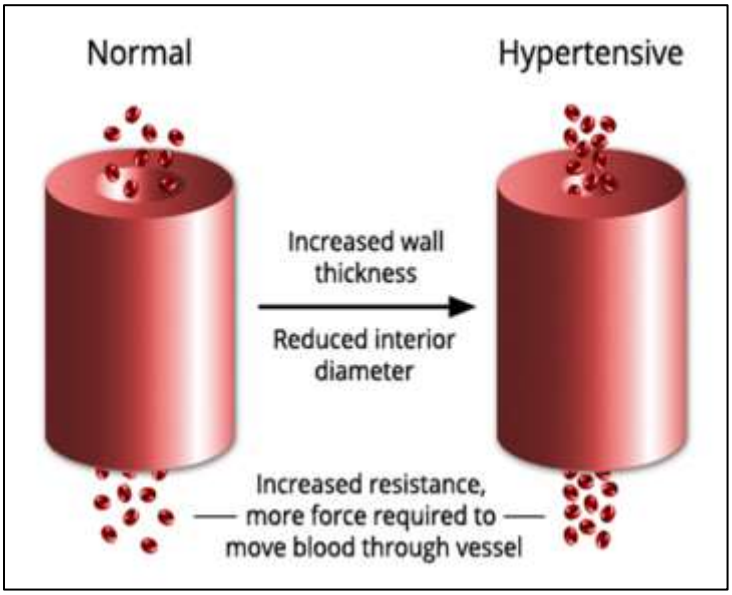

Figure 1.7 The difference between a hypertensive artery and a normal artery [73].

1.4.3 Intrauterine growth retardation (IUGR)

The birth of a foetus weighing less than 10% of its birth weight. IUGR is classified into two types symmetrical and asymmetric. Children

with symmetric developmental delays have relatively proportional bodies but appear to be smaller than other children. While those with asymmetric developmental delays do not have a life-size head, their bodies are much smaller than they should be, and appear on ultrasound as their heads appear much larger than their bodies [(74)].

Causes of intrauterine growth retardation:

- Parental factors: chronic diseases such as diabetes, stress, heart and respiratory diseases, infections and the immune system.
- Foetal factors: These are health conditions that the foetus may suffer from and that increase the risks of delayed growth, such as chromosomal abnormalities and congenital anomalies.
- Intrauterine factors that lead to intrauterine growth retardation: reduced blood flow to the uterus and placenta, and inflammation of the tissues surrounding the foetus.

Complications of intrauterine growth retardation:

They may suffer from inability to learn, low blood sugar, oxygen level and feeding problems, while babies with severe developmental delays lead to death in utero or during birth [(75)].

1.4.4 Diabetes

Diabetes mellitus is a common chronic disease caused by an increased level of sugar in the blood. It occurs when the body cannot produce enough insulin (a hormone produced by beta cells). In the pancreas or when the normal amount of insulin is ineffective or because it is not effective by cells different body, where insulin acts as a key to enter glucose into the cells of the body, resulting in High blood sugar instead of entering

the cells of the body (lack of enough insulin) [76]. It is excreted in the urine when the amount of sugar in the blood exceeds (181 mg) and energy is lost.

Diabetes is divided into the following types:

- Type 1 diabetes: it is insulin-dependent diabetes, and it usually affects young children and young people under 21 years of age. This type is characterized by the inability of the pancreas to secrete insulin .
- Type 2 diabetes: type 2 diabetes is the most common type and accounts for 10% of diabetes patients. this type is called non-insulin-dependent diabetes is the most common type in adults over 41 years of age or older those who are overweight [77].

Gestational diabetes is a type of diabetes that occurs during pregnancy, usually in the fifth or sixth month of pregnancy (between 24 to 28 weeks of pregnancy as a result of the resistance of the hormones secreted by the placenta to insulin, and therefore the body cannot burn sugars in the blood as it should, so the level of sugar in the blood rises Blood cannot be used by cells as energy. Usually 3-10% of pregnant women suffer from it during pregnancy, thus it is considered one of the most common health problems in pregnant women. In most cases, gestational diabetes disappears after the baby is born, but the likelihood that it will return with another pregnancy in the future is great, and studies have shown that its recurrence increases the likelihood that it will develop into type 2 diabetes later [78].

Risk factors for gestational diabetes

- Overweight and obesity before pregnancy.
- Rapid weight gain during the first three months of pregnancy.
- Mother's age.
- Endocrine disorder.

Complications of gestational diabetes on the mother:

Abortion, Caesarean section, high pressure, urinary tract infection as a result of high sugar in the urine [79] .

1.5 Aims of the Study

This study is designed to provide information on the following items:

1. Knowing the relationship between thyroid hormones and pregnancy.
2. The prevalence of thyroid disease in pregnant women.
3. The relation between thyroid disease and recurrent miscarriage, diabetes, hypertension and intrauterine growth restriction in pregnant women.

CHAPTER Two

Materials and Methods

2.1 Design of study

This study is conducted between September 1/9/2020 to march 1/3/2021.The participants in this cross-sectional study were pregnant women who were chosen from among the women attending the obstetrics and Gynecology hospital and the outpatient clinics in Karbala-Iraq. Obstetricians are required are instructed to refer pregnant women whit risk factors who have routine prenatal visits to assess thyroid status by performing medical tests for thyroid hormones. This study included 165 pregnant women distributed over different periods of pregnancy. Pregnant women underwent a physical examination and a brief questionnaire, including the woman's age, duration of pregnancy, weight, height, family history of thyroid disease, Addition to academic achievement and financial condition. All information from pregnant women was stored in computerized systems in the SPSS program.The clinical chart of the study has been presented in table (2.1).

Table 2.1 The questionnaire of the study

Patient profile			
Name :		Age :	
Weight :		Length :	
Economic situation :		Education stage:	
Gestational age :		Family history:	
Rick factors : recurrent abortion	hypertension	Diabetes	IUGR
TSH (µIU/ml)			
FreeT4(ng/dl)			
FreeT3 (ng/ml)			

2.2 Study Groups

This was verified in two study groups:

1. Control group (healthy): The control group consists of 50 apparently healthy pregnant women, their ages range from (15-43) years.
2. Patients group: 115 pregnant women with thyroid disease and recurrent miscarriage (30), hypertension (30), diabetes (25) and intrauterine growth restriction (30).Their ages range from (15-43) years .

All women provided verbal informed consent and the research protocol was approved by Karbala University.

2.3 Collect Blood Samples

Blood samples are taken from pregnant women in obstetrics and gynecology hospital and outpatient clinics for the purpose of medical tests for thyroid hormones (free T3, freeT4, TSH). Five ml of blood was taken using a 5 ml medical syringe and the blood was placed in gelatine tubes (gell tube) free of anti-clotting material, as it contains a gelatinous substance that helps to increase the separation of serum formed after the centrifugation process. The samples were left for 15 minutes at room temperature, after which they were inside a centrifuged at a speed of 2500 (round / minute) for 10 minutes to obtain the serum that was stored at (-20) ° C, unless it was used immediately.

2.4 Exclusion Criteria

Women with chronic diseases such as chronic hypertension, chronic diabetes and heart disease as well as women with thyroid disease and the use of medications known to affect thyroid function, such as amiodarone, lithium, steroids and non-steroidal anti-inflammatory drugs .

2.5 Chemicals

The chemicals used in this study with their companies which are showed with suppliers are shown in table (2.2).

Table 2.2 chemicals and their suppliers

Chemicals	Company and Origin
TSH Kit	France
FT4 Kit	France
FT3 Kit	France

2.6 Equipment and Instrument

Equipment's and instrument which are used in the present study found in table (2.3).

Table (2.3): The equipment's and instrument used in this study

Instruments	Manufacturers
Mini VIDAS	Biomerieux - France
Refrigerator	Kiriazi- Egypt
Centrifuge	Hettich- Germany
gelatin tubes(Jell tube)	Germany

Figure 2.1 Mini vidas device from Bio Merieux Company from franc.

2.7 Body Mass Index (BM)

They were classified into three groups, those with a body mass index (BMI) of 25 kg/m2 classified as normal weight and those with a BMI (>25–30 kg/m2) classified as overweight. while those whose weight exceeds (30 kg/m2) are obese.

2.8 Thyroid Activity Tests

2.8.1 Measurement of serum thyroxin FT4 levels

The levels of thyroxin (FT4) in the blood serum were measured using the Mini VIDAS device manufactured by the French company Biomerieax with the ready-made test kit (Kit),following the instructions attached to the FT4 test kit.

Principle of Reaction

The principle of the interaction works in measuring the concentration of FT4 hormone based on the immunoassay for binding to the enzyme, while revealing the final radiation formed an enzyme immunoassay. The steps for

measuring the FT4 hormone are automatically done by the Mini VIDAS device, and the reaction medium is periodically moved to and from the SPRs and the solutions in the strip several times and include the sample into the hole containing the Anti-T4 antibodies labelled with conjugated Alkaline phosphates and the mixture (Conjugate / Sample) moves periodically to and from the SPRs. Methyl periodically to and from SPRs, and the enzyme then breaks down the matrix into a radioactive product, which is a 4-methyl umbelliferone whose radiation amount is measured at a wavelength of (450) nanometres. The radiation indicates the relative concentration of the antigen present in the sample. At the end of the calibration process, the results are calculated automatically by the Mini VIDAS device, using the standard curve stored in the device's memory, after which the results are printed by the device.

Procedure

1. I placed the MLE card of the test kit in its place on the device. The Mini VIDAS for the device to automatically recognize the test, as without it the device cannot show the result and then print it.
2. A single (FT4) SPR, STR strip was used for each sample of serum and control solution Standard S1 and placed in the designated place in the device.
3. A (200µL) serum sample was withdrawn and placed in its own hole on the (FT4) STR tape as well as for the control and standard solution.
4. I followed the steps for the device in the practical manual for the device, for the device to start the calibration automatically, and the process takes (40) minutes.

5. After the calibration is done and the results are printed, the STRs as well as the SPRs are extracted and placed in a special container, because they are used only once.

2.8.2 Measuring Serum Levels of The Thyroid Hormone Tri-Iodine (FT3)

FT3 levels were measured in the blood serum using the Mini VIDAS device, following the steps in the instruction manual attached to the FT3 test kit imported from Biomerienx, as the same steps used to measure the FT4 concentration were followed.

2.8.3 Measurement of TSH Levels in Blood Serum

TSH levels were measured in the blood serum using the French-origin Test Kit using Mini VIDAS, following the instructions attached to the TSH test kit.

Principle of Reaction

The principle of measuring TSH levels is based on the immunological competition for binding to the enzyme with the investigation of the final radiation formed .An Enzyme immunoassay competition method with final detection (ELFA). The steps for measuring TSH levels are done automatically by the Mini VIDAS device, and the medium of reaction periodically moves to and from the SPRs and solutions in the tape several times, and the sample is transferred to the hole that contains Anti-TSH antibodies labelled with alkaline phosphatase. The binding agent, as the mixture (Conjugate / Sample) moves periodically to and from SPRs, thus binding the antigen to the antibodies on the SPRs, as well as to the linker forming a sandwich and during the final steps of the titration the base

material moves Umbelliferl phosphate 4-Methyl periodically to and from SPRs. The enzyme then works by breaking down the matrix into a radioactive product, which is 4-methyl umbelliferone whose amount of radiation is measured over a wavelength of 450 nanometres. The radiation indicates the relative concentration of the antigen present in the sample And, at the end of the calibration process, the results are calculated automatically by the Mini VIDAS device, using the standard curve stored in the device's memory, after which the results are printed by the device.

Procedure

1. The MLE card of the test kit has been placed in its place on the scanner. The Mini VIDAS for the device to automatically recognize the test, as without it the device cannot show the result and then print it.
2. Use one strip of (TSH) SPR, STR for each sample of serum, control, and standard S1 solution, and put it in the designated place in the machine.
3. (200µL) was drawn from the serum sample and placed in its hole on the (TSH) STR tape as well as for Standard, Control.
4. The steps for the device and in the Manual were followed, for the device to start the calibration automatically, which takes a period of (40) minutes .
5. After the calibration was done and the results printed, the STRs as well as the SPRs were extracted from the device and placed in a special container, because they are used for one time only.

2.9 Statistical Analysis

Statistical analysis was performed by the SPSS 2020 statistical Package for social science . All values were expressed as Mean ± Standard Deviation of the mean (M±SD).Statistical analysis were performed using students chi-square to estimate the difference between the groups pregnant and control groups, taking ($P<0.05$) as the lowest limit of significance. P value <0.05 was regarded as statistically significant.

CHAPTER THREE

The Results

3.1 Levels of biochemical parameters for pregnant women with a thyroid disorder and a control group

In this research the relations of thyroid disorders and hormonal parameters of 115 pregnant women suffering from thyroid disorders (Hyperthyroidism and hypothyroidism) with risk factors Hypertension, recurrent miscarriage, diabetes and intrauterine growth restriction and 50 pregnant women as a control group.

3.1.1 Thyroid hormone tests:

Hormones:

The results of the thyroid stimulating hormone test TSH and FT4 in the blood of pregnant women with thyroid disorder showed a significant difference (P <0.001) when compared with the control group. It was also found that there was a significant difference in the FT3 triiodothyronine hormone, to a significant difference (P =<0.001) when compared with the control group. As shown in Table (3.1). The correlation coefficient was negative (r = 0.911) between TSH level with FreeT4 levels in patients, as shown in Figure (3.1)A.

In addition, the correlation coefficient is negative (r = 0.950) between TSH level with FreeT3 levels in patients as shown in Figure (3.1)B. And the presence of a positive correlation coefficient (r = 0.892) between the level of freeT3 and the levels of FreeT4 in pregnant women with thyroid disorder as shown in Figure (3.1)C .

Body mass Index (BMI):

The body mass index levels of the pregnant women patients showed a significant increase (P = 0.01) compared to the control group, as shown in Table (3.1).

Table 3.1 Mean levels and standard deviation of thyroid hormones and parameter for both pregnant women and the control group.

patients			Control		
Parameter	Mean $\pm SD$	Range	Mean $\pm$ SD	Range	P value
Age	29.62± 7.177	15-43	25.14 ± 5.29	15-39	NS
BMI(kg/m^2)	35.6 ± 6.39	23.05-52.19	29.903 ± 5.71	19.61-47.8	0.01
Gestational age	2.85 ± 0.751	1-3	2.22 ± 0.64	1-3	NS
TSH (µIU/ml)	3.513 ± 2.427*	0.38-4.31	1.992 ± 1.112	0.38-4.31	≤ 0.001
Free T4(ng/dl)	1.112 ±1.1267*	0.70-1.48	1.060 ± 0.26	0.70-1.48	≤ 0.001
FreeT3(ng/ml)	2.379 ± 1.572*	1.71-3.71	2.496 ± 0.396	1.71-3.71	≤ 0.001

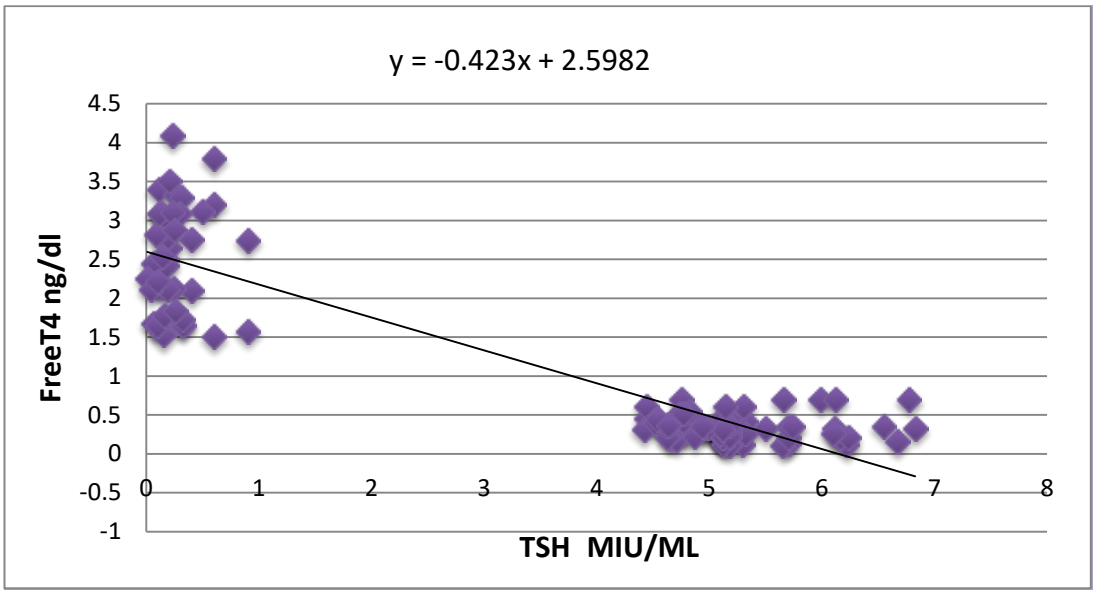

Figure (3.1)A: Necative correlation of TSH concentration and FreeT4 concentration in pregnant women with thyroid disorders (r=0.911)(p.v=0.000).

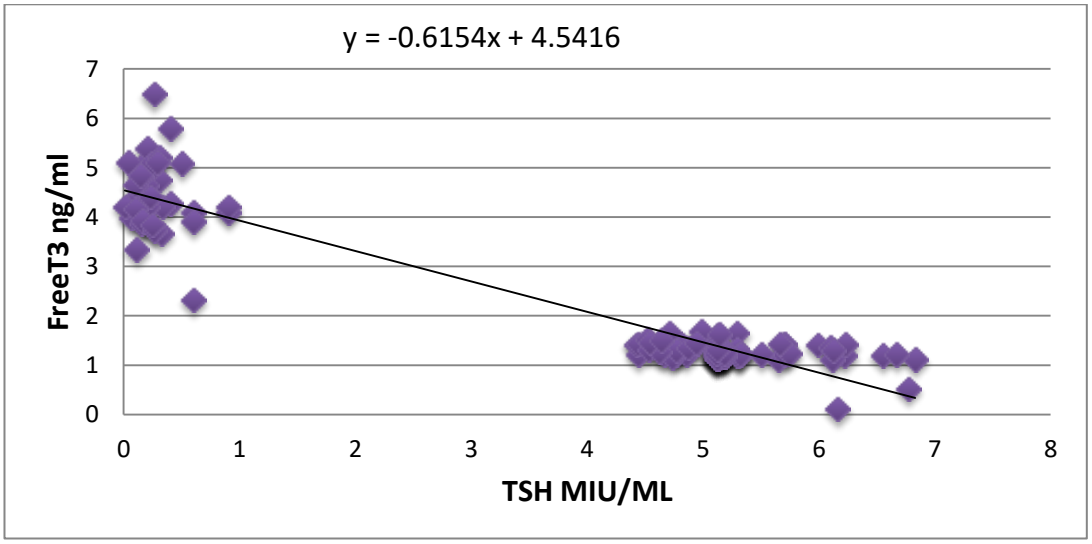

Figure (3.1)B:Necative correlation of TSH concentration and FreeT3 concentration in pregnant women with thyroid disorders (r=0.950)

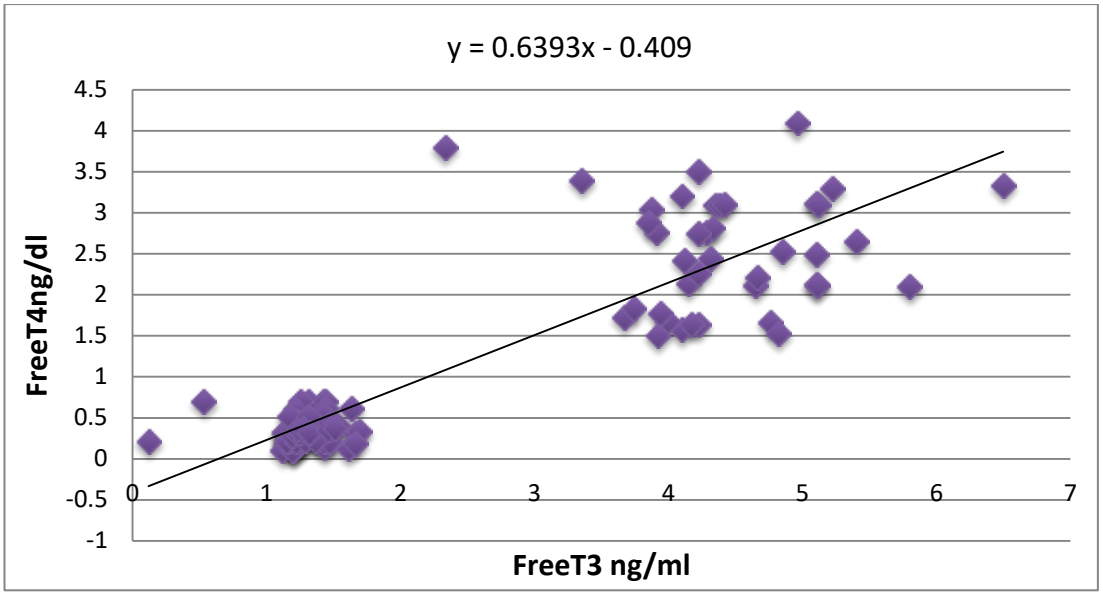

Figure (3.1) C: Positeve correlation of FreeT3 concentration and FreeT4 concentration in pregnant women with thyroid disorder (r=0.892)

3.2 personal family of thyroid disease

It was found through the results of the research that there were significant differences for pregnant women with thyroid diseases with a personal family history (for thyroid diseases), which were positive by 2.25 % and negative by 74.8% compared with the control group. As in Table (3.2).

Table 3.2: Levels of personal family history of thyroid disease for pregnant women with thyroid disorder and the control group

Family History	Patient	Control	Total	P.V
Yes	29 25%	3 6%	32 19%	0.00
No	86 75%	47 94%	133 81%	0.00
Total%	115 100%	50 100%	165 100%	0.01

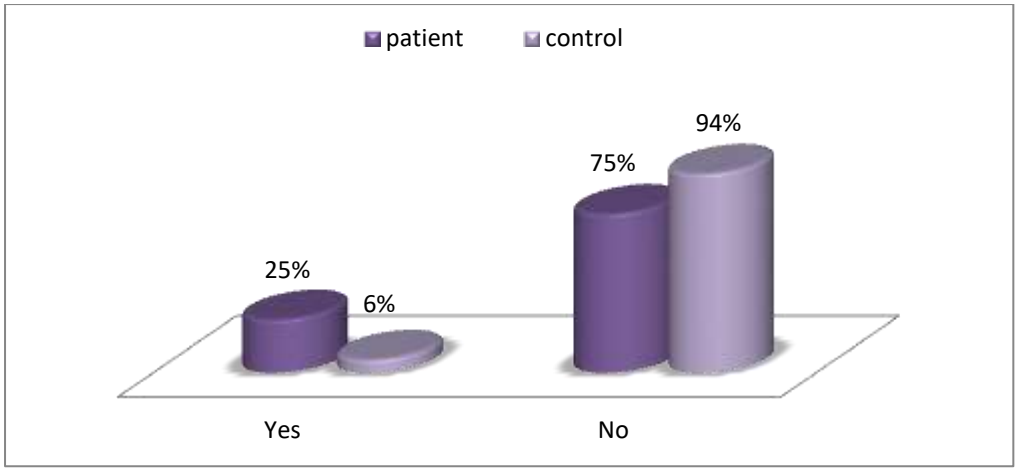

Figure (3.2): Percentage distribution of pregnant women with a personal family history of thyroid disease.

3.3 Relation of thyroid hormones parameters of pregnant women with risk factors and thyroid disorders

Women patients have been divided into hypothyroidism and hyperthyroidism.

A. Hormones in hypothyroidism

The results of the freeT4, freet3, and TSH test in the blood of pregnant women with hypothyroidism showed a significant difference P = < 0.001 compared to the control group. As shown in Table (3.3.A)

Table (3.3.A): Mean levels and standard deviation of thyroid hormones in pregnant women with hypothyroidism

Parameter	Hypothyroidism	Control	P value
TSH (µIU/ml)	5.246 ± 0.557*	1.992±1.112	<0.001
FreeT4(ng/dl)	0.352 ± 0.151*	1.060±0.206	0.001
FreeT3 (ng/ml)	1.284 ± 0.2143*	2.496±0.396	<0.001

No.of hypothyroidism=75

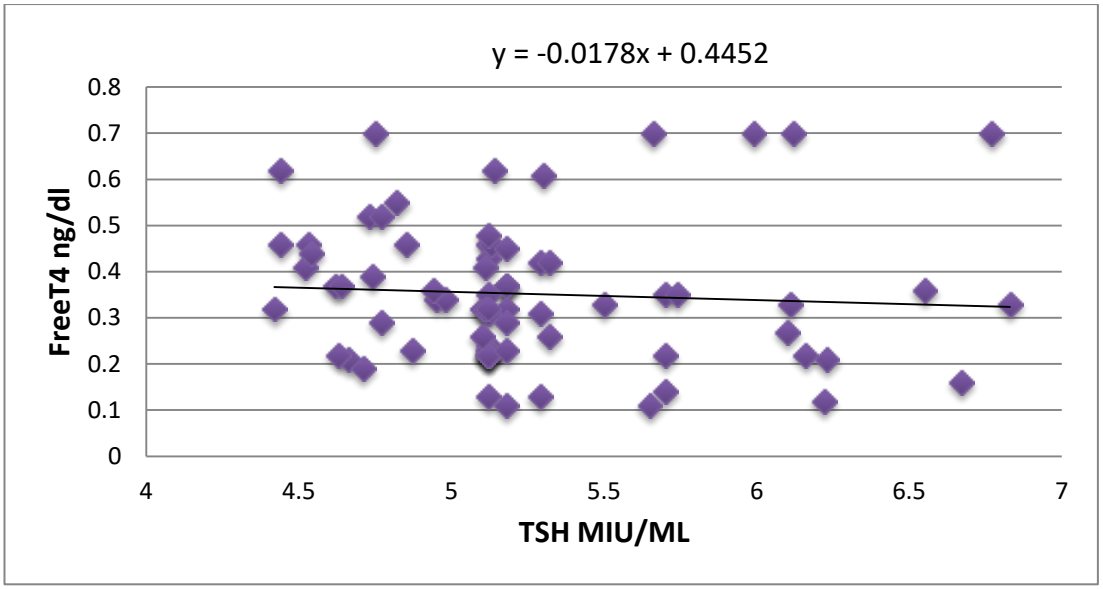

Figure (3.3.A) A: Negative correlation of TSH concentration and FreeT4 concentration in pregnant women with hypothyroidism(r=0.065).

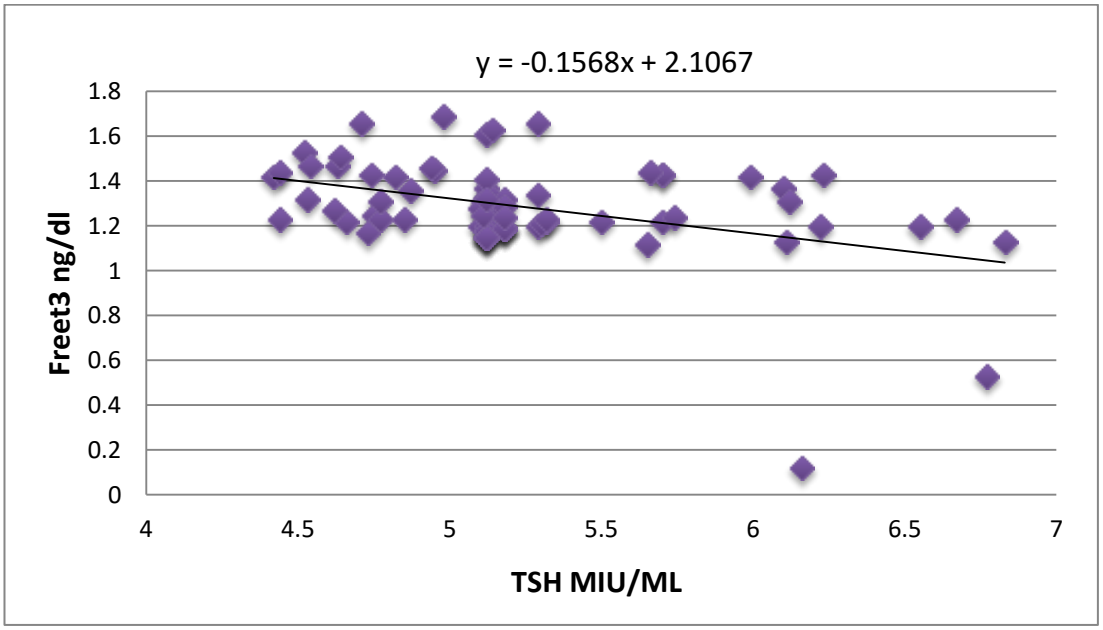

Figure (3.3.A) B: Negative correlation of TSH concentration and FreeT3 concentration in pregnant women with hypothyroidism(r=0.407).

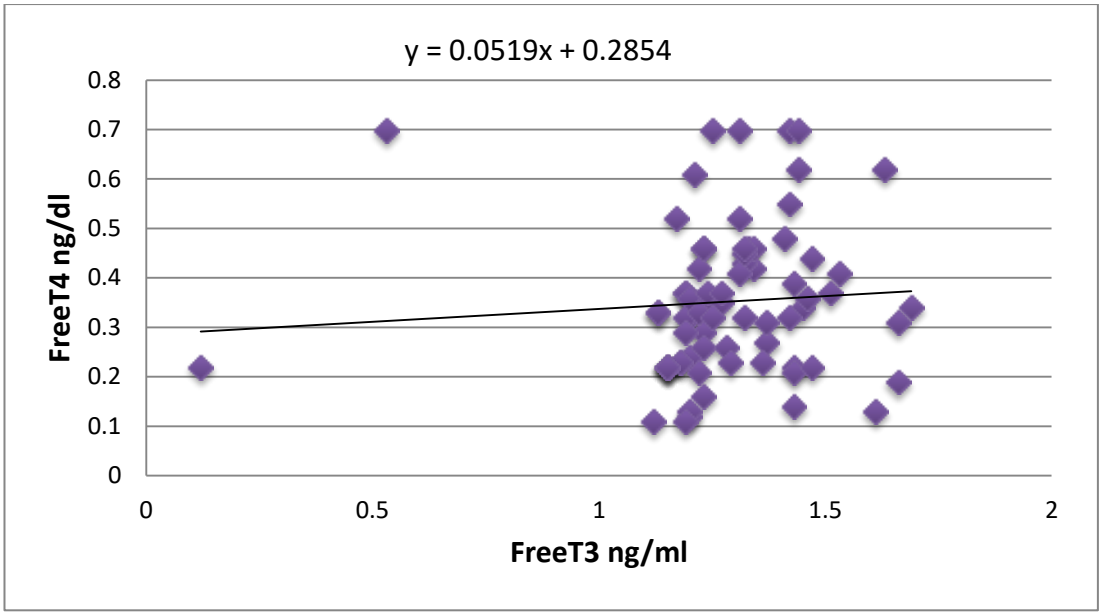

Figure (3.3.A) C: Negative correlation of FreeT3 (ng/ml) concentration and FreeT4 (ng/dl) concentration in pregnant women with hypothyroidism (r=0.074).

3.3.B Hormones in hyperthyroidism

The results of the thyroid hormone test FT3 and FT4 in the blood of pregnant women with thyroid disorder showed a significant difference ($P < 0.001$) when compared with the control group.

It was also found that there was a significant difference in TSH, to a significant difference $P = (0.004)$ when compared with the control group. As shown in Table (3.3.B).

Table (3.3.B) : Mean levels and standard deviation of thyroid hormones in pregnant women with hyperthyroidism.

Parameter	Hyperthyroidism	Control	P value
TSH (µIU/ml)	0.265 ± 0.209*	1.992±1.112	0.004
FreeT4(ng/dl)	2.537 ± 0.688*	1.061±0.206	< 0.001
FreeT3 (ng/ml)	4.432 ± 0.711*	2.496±0.396	< 0.001

No. of hyperthyroidism= 40

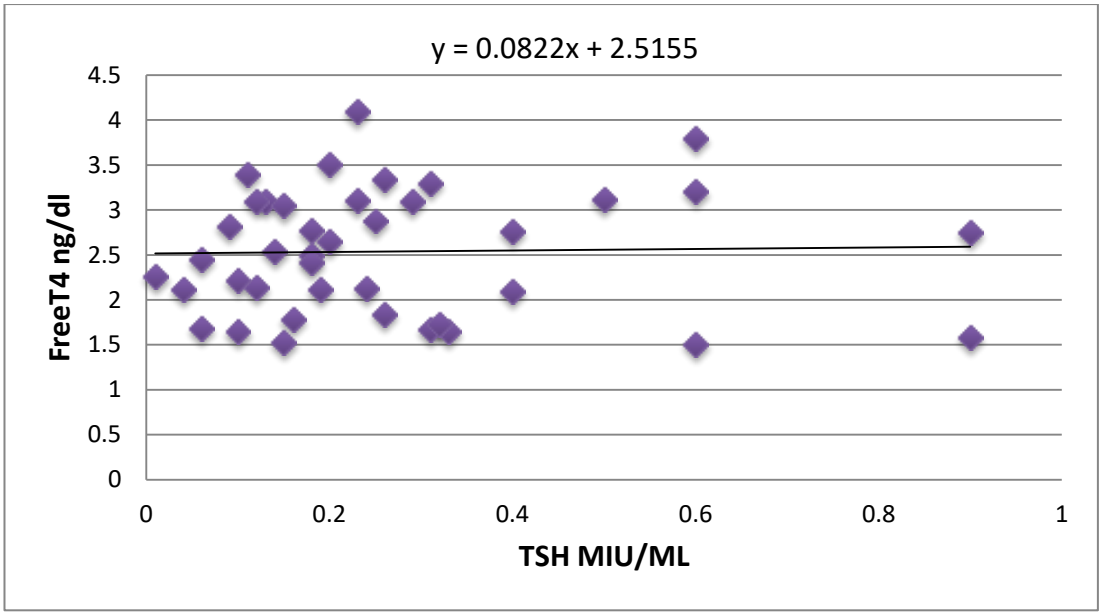

Figure (3.3.B) A: Positive correlation of TSH concentration and FreeT4 concentration in pregnant women with hyperthyroidism (r=0.024) .

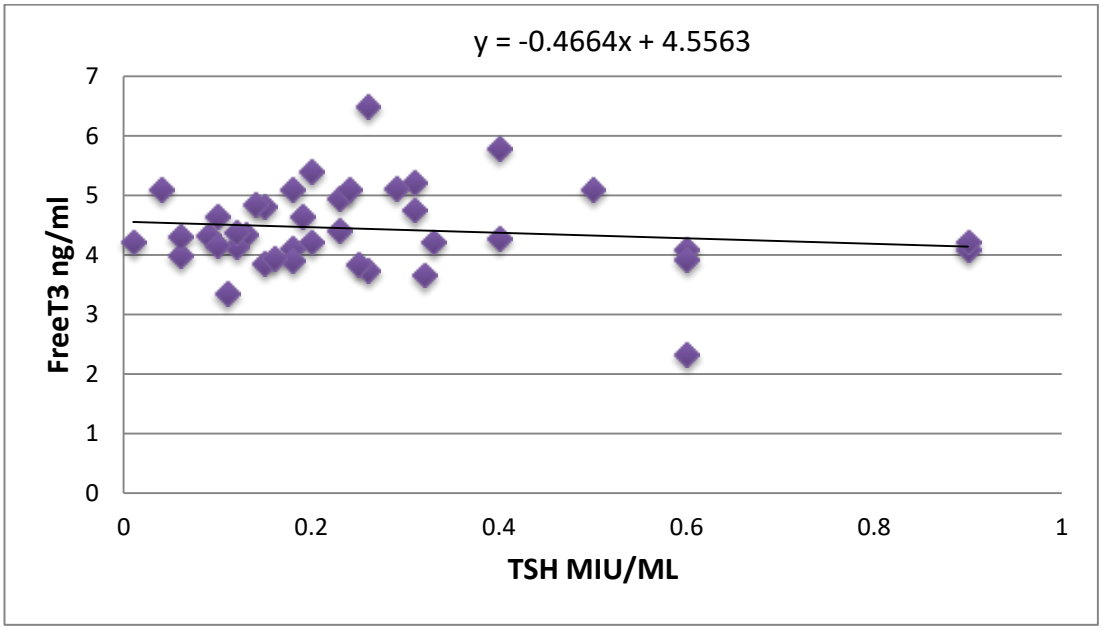

Figure (3.3.B) B: Negative correlation of TSH concentration and FreeT3 concentration in pregnant women with hyperthyroidism (r=0.137) .

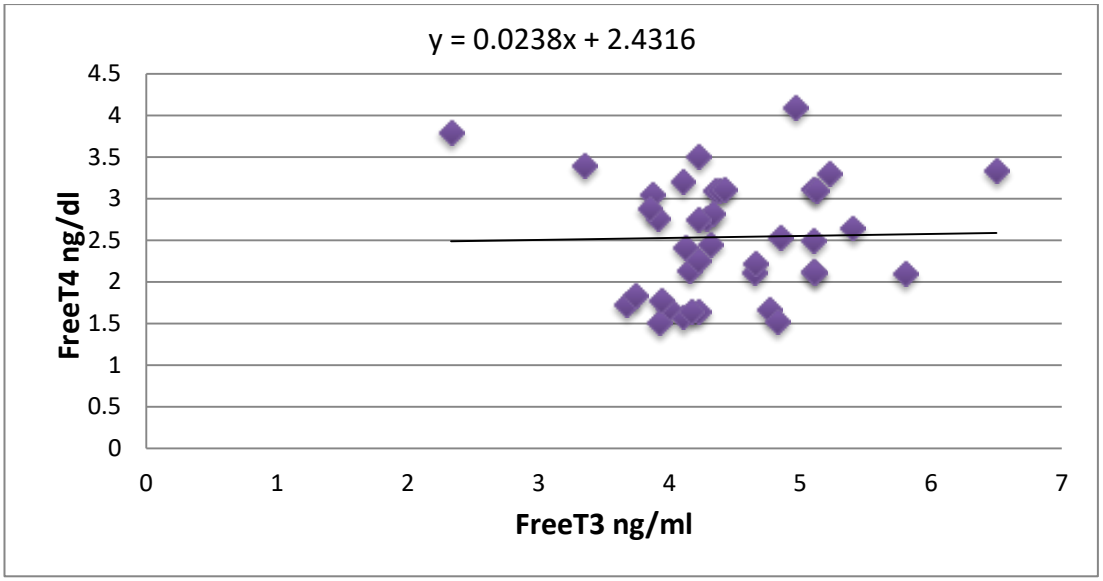

Figure (3.3.B) C: Positive correlation of FreeT3 concentration and FreeT4 concentration in pregnant women with hyperthyroidism (r=0.024).

3.4 Relation of thyroid hormones parameters of pregnant women with thyroid disorder and recurrent miscarriage

Pregnant women with risk factors were divided into recurrent miscarriage, gestational hypertension, diabetes, and intrauterine growth restriction, and each factor group was compared with the control group as described below.

The results of the thyroid hormone test FT3 and FT4 in the blood of pregnant women with thyroid disorder showed a significant difference ($P < 0.001$) when compared with the control group.

It was also found that there was a significant difference in TSH, to a significant difference $P = (<0.001)$ when compared with the control group. As shown in Table (3.4).

Table (3.4): Levels of hormonal factors in pregnant women with recurrent miscarriage and thyroid disease with a control group

Parameter	recurrent miscarriage	Control	P value
TSH (µIU/ml)	4.314 ± 2.519*	1.992±1.112	<0.001
FreeT4(ng/dl)	0.981 ± 1.200*	1.061±0.206	<0.001
FreeT3 (ng/ml)	2.017 ± 1.542*	2.496±0.396	<0.001

No. of Recurrent abortion =30

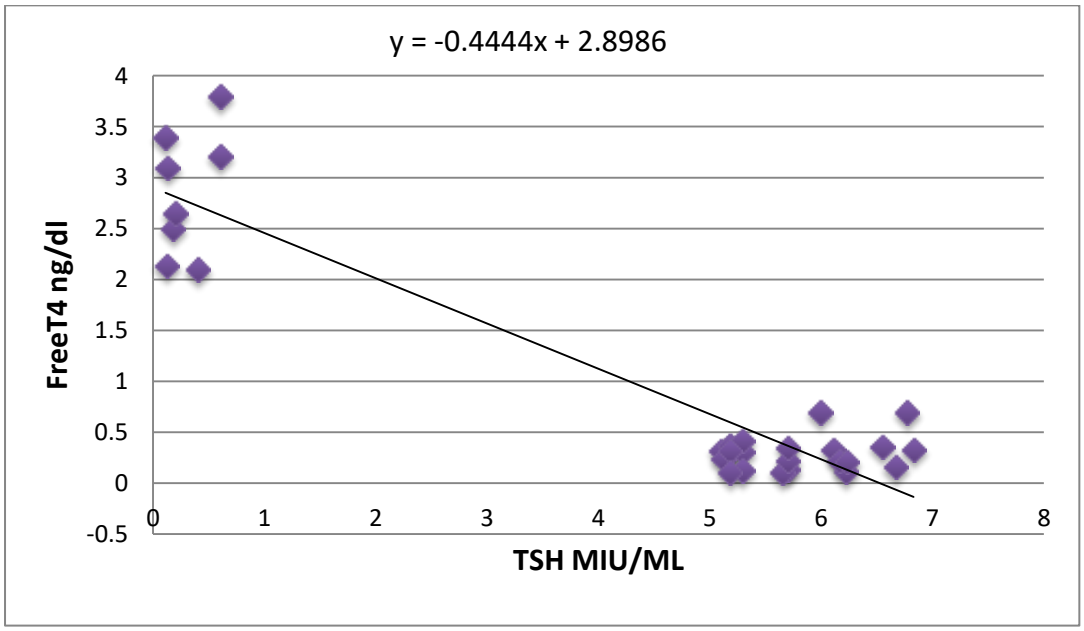

Figure (3.4) A: Negative correlation of TSH concentration and free T4 concentration in pregnant women with thyroid disease and recurrent miscarriage (r = 0.933).

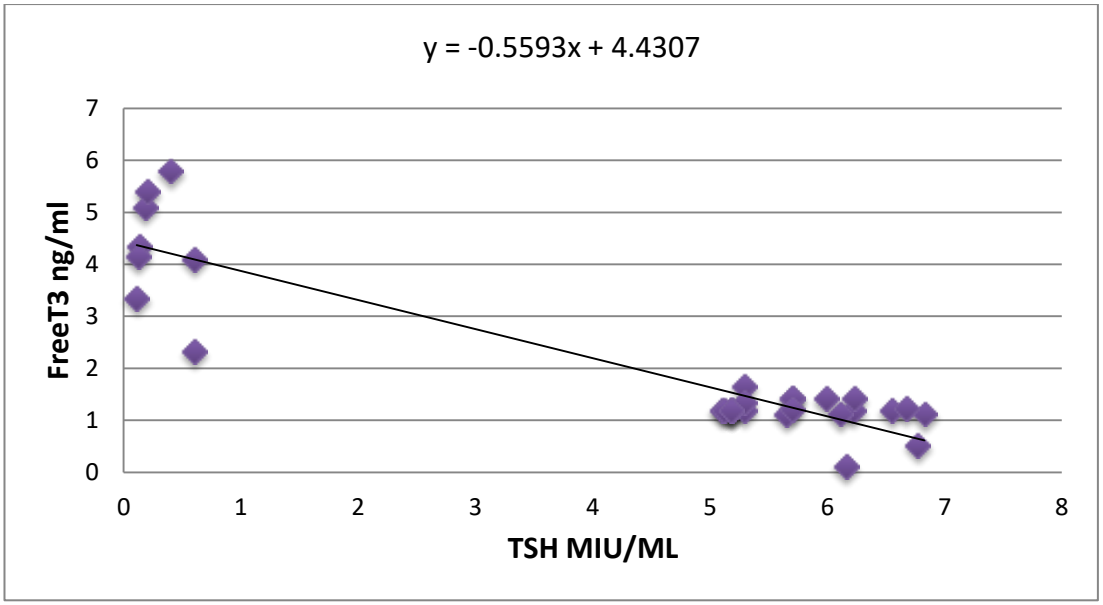

Figure (3.4) B: Negative correlation of TSH concentration and FreeT3 concentration in pregnant women with thyroid disease and current miscarriage (r = 0.913) .

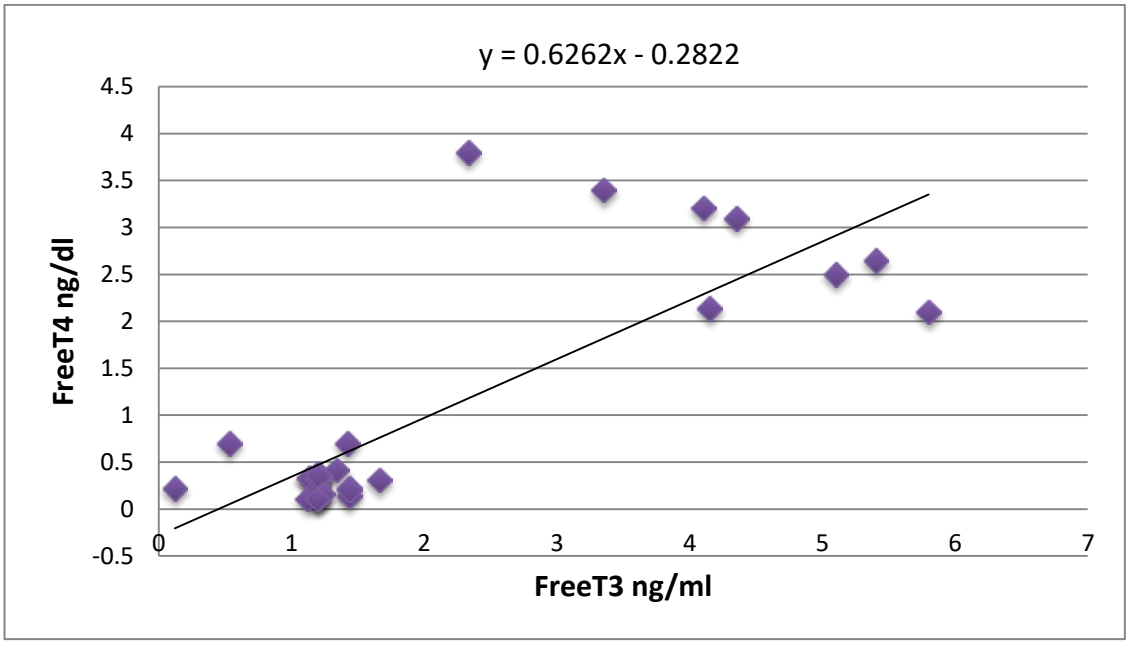

Figure (3.4) C: Positive correlation of free T3 concentration and free T4 concentration in pregnant women with thyroid disease and recurrent miscarriage (r = 0.804).

3.5 Relation of thyroid hormonal parameters of pregnant women with thyroid disorders and hypertension

The results of the thyroid hormone test FT3 and FT4 in the blood of pregnant women with thyroid disorder showed a significant difference ($P < 0.001$) when compared with the control group. It was also found that there was a significant difference in TSH, to a significant difference P = (<0.001) when compared with the control group. As shown in Table (3.5).

Table (3.5) : Levels of hormonal factors in pregnant women with hypertension and thyroid disease with a control group

Parameter	Hypertension	Control	P value
TSH (µIU/ml)	3.312 ± 2.775*	1.992±1.112	<0.001
FreeT4(ng/dl)	1.166 ± 1.153*	1.061±0.206	<0.001
FreeT3 (ng/ml)	2.544 ± 1.662*	2.496±0.396	<0.001

No. of hypertension =30

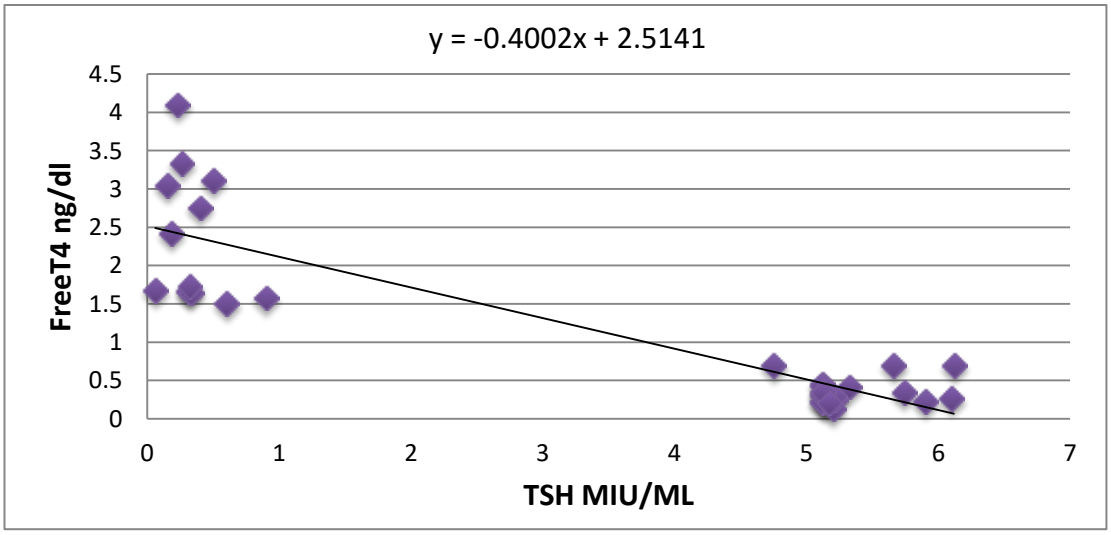

Figure (3.5) A: Negative correlation of TSH concentration and FreeT4 concentration in pregnant women with thyroid disease with hypertension (r = 0.875) .

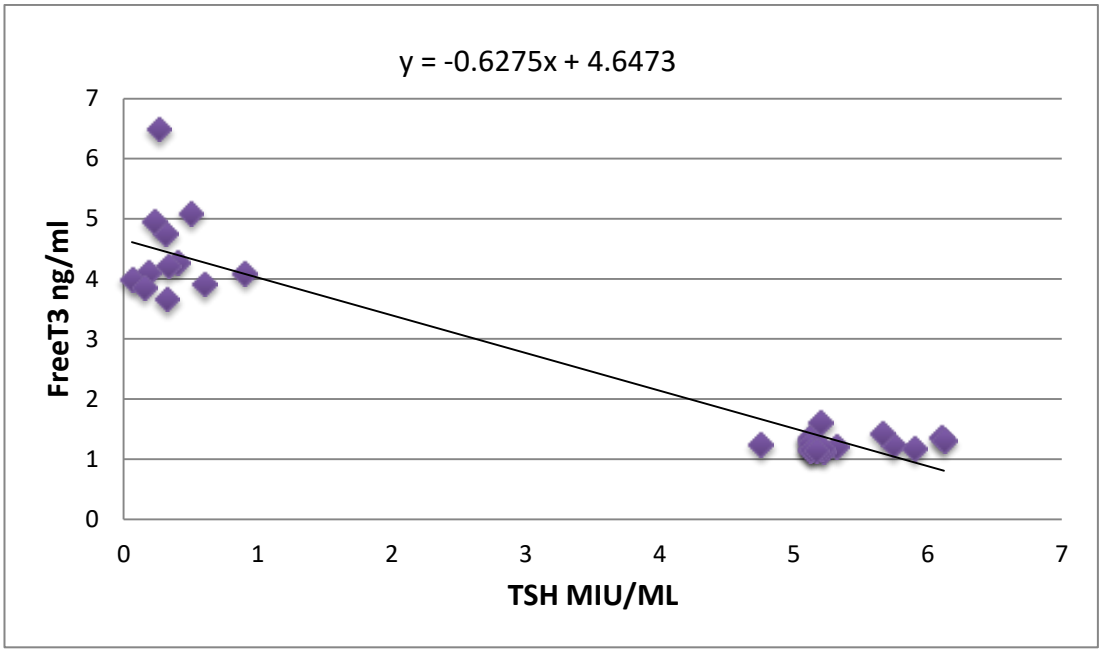

Figure (3.5) B: Negative correlation of TSH concentration and FreeT3 concentration in pregnant women with thyroid disease with hypertension (r = 0.947).

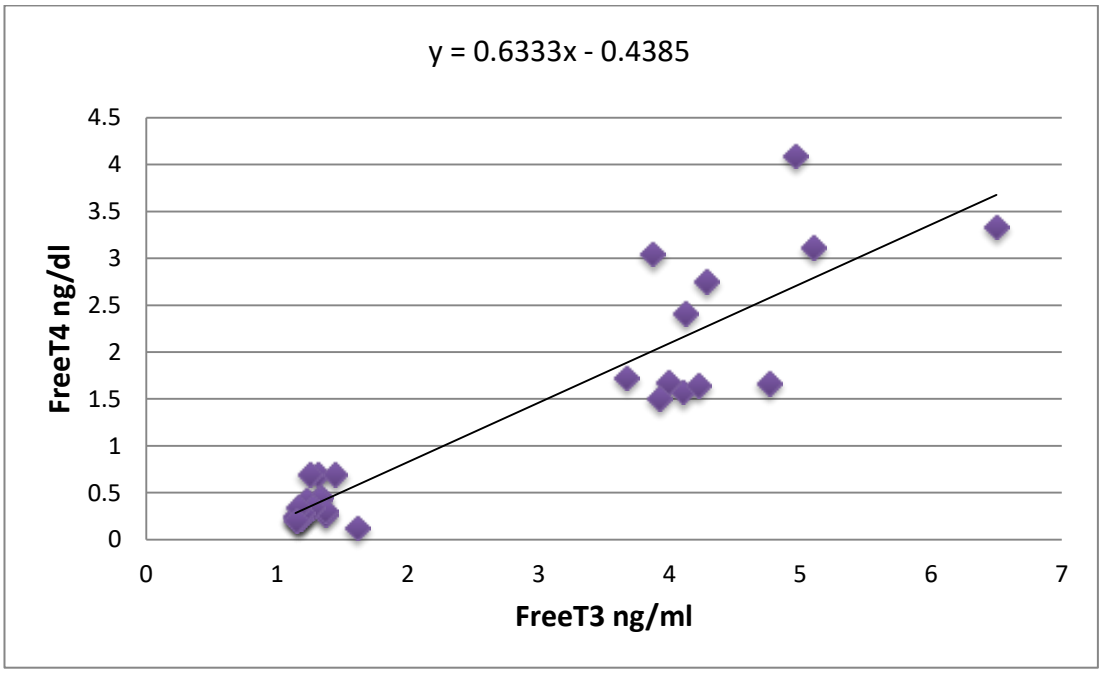

Figure (3.5) C: Positive correlation of free T3 concentration and free T4 concentration in pregnant women with thyroid disease with hypertension (r = 0.917) .

3.6 Relation of thyroid hormonal parameters of pregnant women with thyroid disorders and diabetes

The results of the thyroid hormone test FT3 and FT4 in the blood of pregnant women with thyroid disorder showed a significant difference ($P < 0.001$) when compared with the control group. It was also found that there was a significant difference in TSH, to a significant difference P = (<0.001) when compared with the control group. As shown in Table (3.6).

Table (3.6): Levels of hormonal factors in pregnant women with diabetes and thyroid disease with a control group

Parameter	Diabetes	Control	P value
TSH (µIU/ml)	2.078 ± 2.361*	1.992±1.112	<0.001
FreeT4(ng/dl)	1.598 ± 1.118*	1.061±0.206	<0.001
FreeT3 (ng/ml)	3.168 ± 1.607*	2.496±0.396	<0.001

No. of diabetes=25

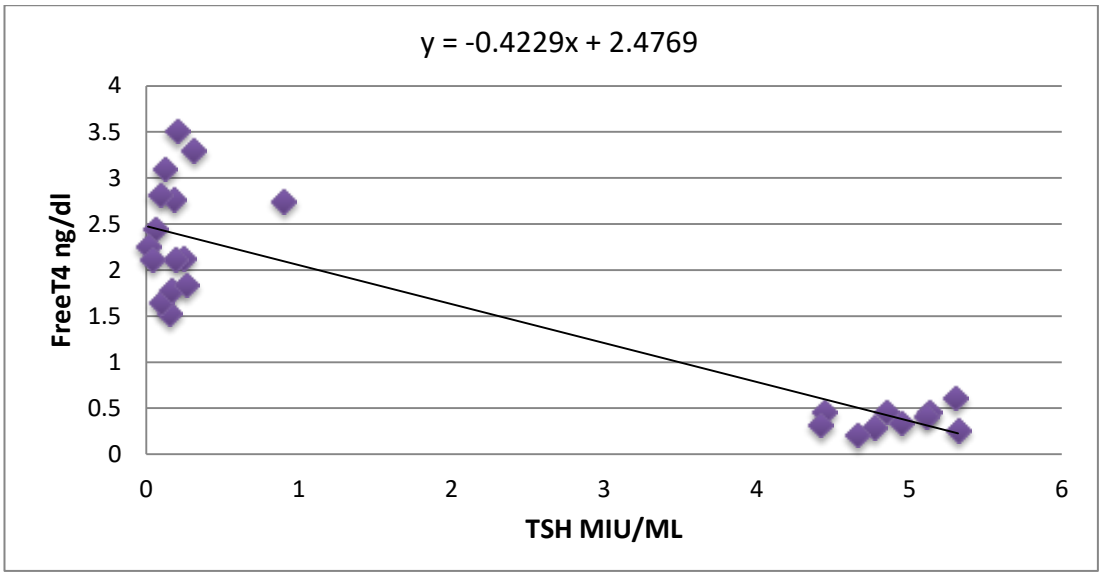

Figure (3.6) A: Negative correlation of TSH concentration and FreeT4 concentration in pregnant women with thyroid disease with diabetes mellitus (r = 0.892) .

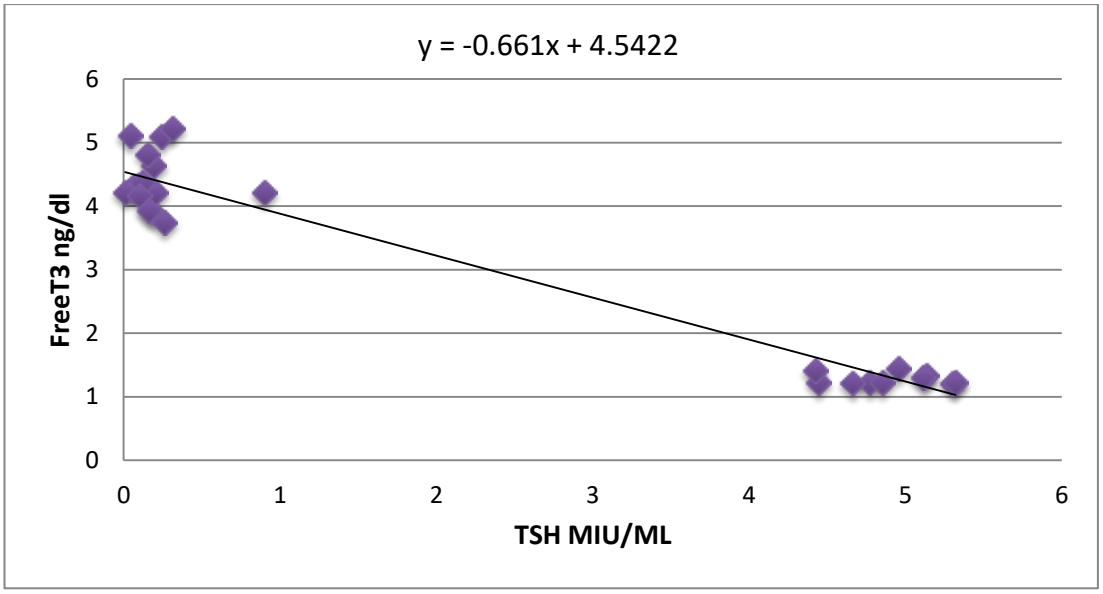

Figure (3.6) B: Negative correlation of TSH and FreeT3 concentrations in hypothyroid pregnant women with diabetes mellitus (r = 0.971).

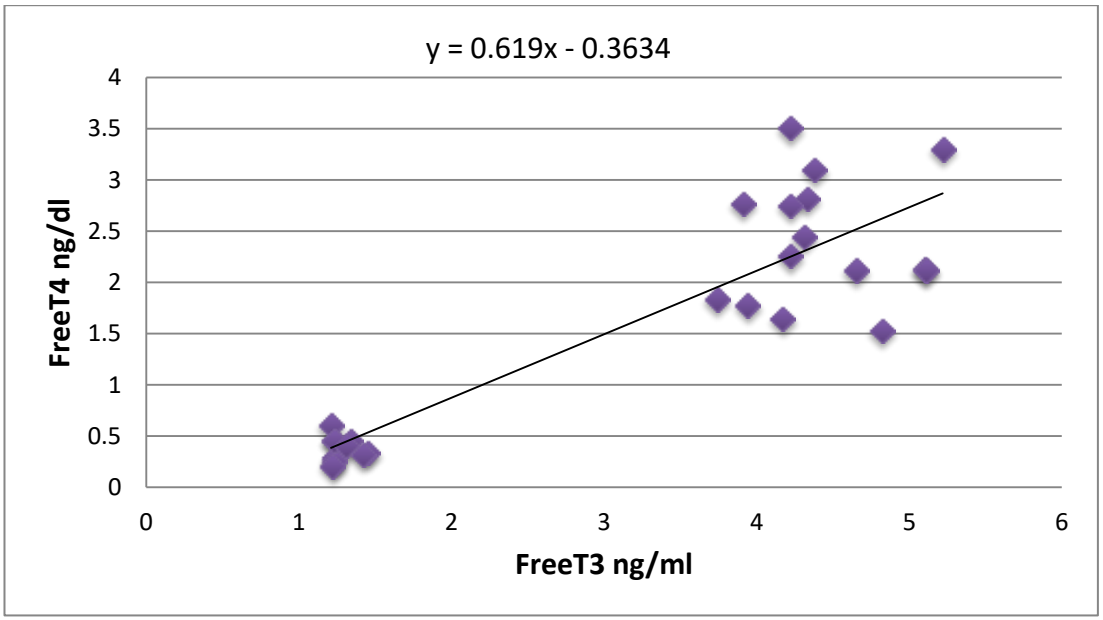

Figure (3.6) C: Positive correlation of FreeT3 and FreeT4 concentrations in pregnant women with thyroid disease with diabetes mellitus (r = 0.889).

3.7 Relation of thyroid hormonal parameters of pregnant women with thyroid disorder and intrauterine growth restriction (IUGR)

The results of the thyroid hormone test TSH and FT4 in the blood of pregnant women with thyroid disorder showed a significant difference ($P < 0.001$) when compared with the control group; there is no significant difference in the hormone FT3. As shown in Table (3.7).

Table (3.7): Levels of hormonal factors in pregnant women with intrauterine growth restriction (IUGR) and thyroid disease with a control group

Parameter	IUGR	Control	P value
TSH (µIU/ml)	0.202 ± 0.079*	1.992±1.112	0.024
FreeT4(ng/dl)	2.770 ± 0.385*	1.061±0.206	0.009
FreeT3 (ng/ml)	4.580 ± 0.482*	2.496±0.396	NS

No. of Intrauterine growth restriction (IUGR) =30

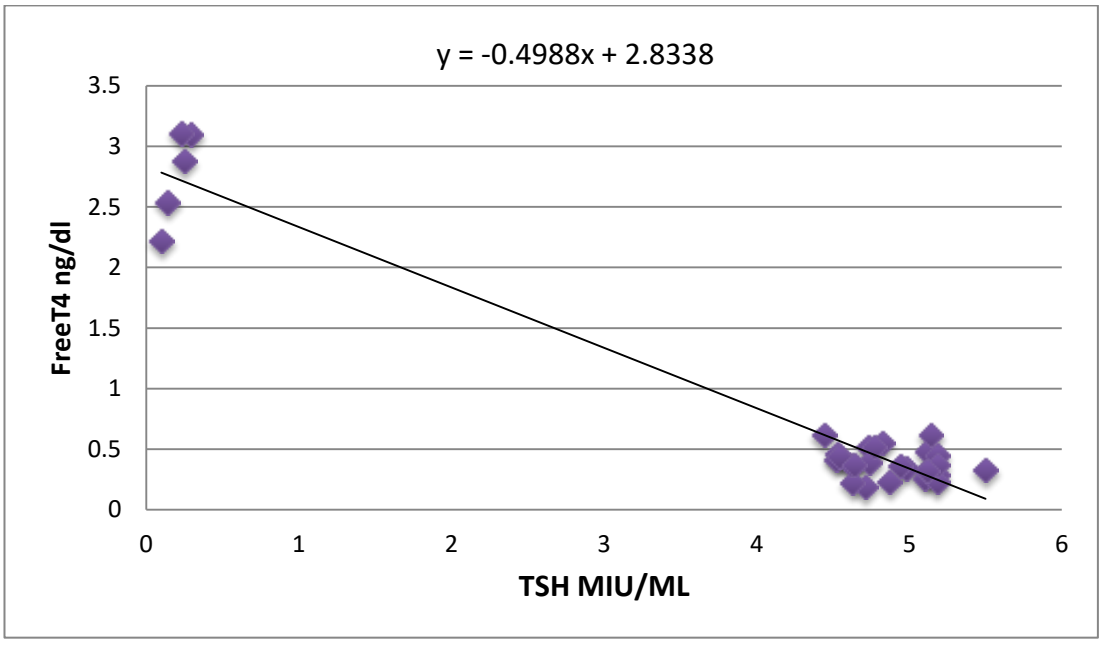

Figure (3.7) A: Negative correlation of TSH concentration and FreeT4 concentration in pregnant women with thyroid disease with IUGR (r = 0.972).

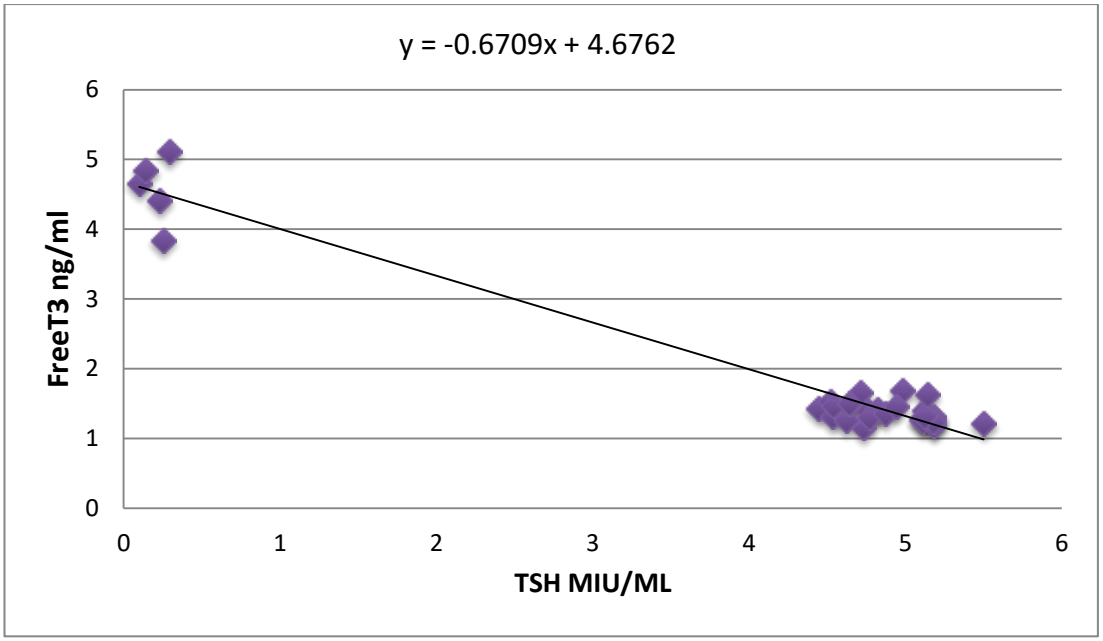

Figure (3.7) B: Negative correlation of TSH concentration and FreeT3 concentration in pregnant women with thyroid disease with IUGR (r = 0.979).

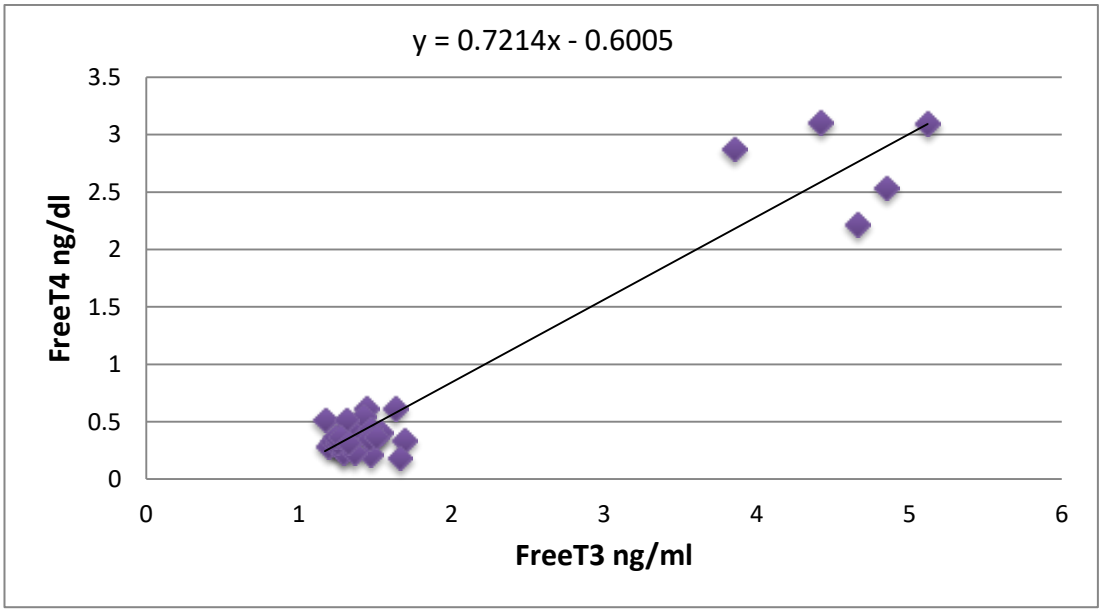

Figure (3.7) C: Positive correlation of FT3 concentration and FreeT4 concentration in pregnant women with thyroid disease with IUGR (r = 0.963).

3.8 Levels of thyroid hormones for pregnant women with recurrent abortion.

Pregnant women with risk factors were divided into recurrent miscarriage, gestational hypertension, diabetes, and intrauterine growth restriction, and each factor group was compared with the control group as described below.

3.8.A Hormonal test pregnant women with recurrent miscarriage in hypothyroidism

The results of the TSH test in the blood of pregnant women with recurrent miscarriage showed a significant difference P = 0.046 when compared to the control group, as Table (3.8.A) shows that the mean and standard deviation of TSH (5.776 + 0.587) is higher than the mean and standard deviation of the control group. It was also found through the results of FT4 and FT3 hormone test for pregnant women with recurrent miscarriage that there were significant differences for FT3, P = (0.049) and (FT4, P = 0.022) compared to the control group. As shown in Table (3.8.A).

Table (3.8.A): Levels of thyroid hormone in pregnant women with recurrent miscarriages in hypothyroidism compared to the control group

Parameter	recurrent miscarriage	Control	P value
TSH (µIU/ml)	5.776 ± 0.587*	1.992±1.112	0.046
FreeT4(ng/dl)	0.297 ± 0.162*	1.061±0.206	0.022
FreeT3 (ng/ml)	1.179 ± 0.313*	2.496±0.396	0.049

No. of Recurrent abortion =22

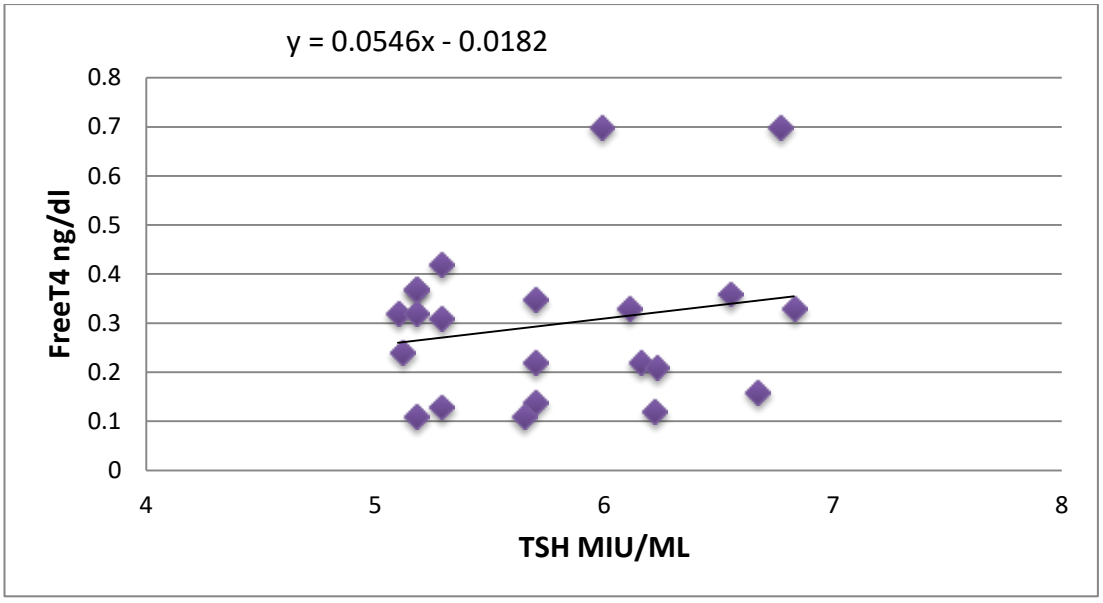

Figure (3.8.A) A: Positive correlation of TSH concentration and free T4 concentration in hypothyroid pregnant women with recurrent miscarriage (r=0.197).

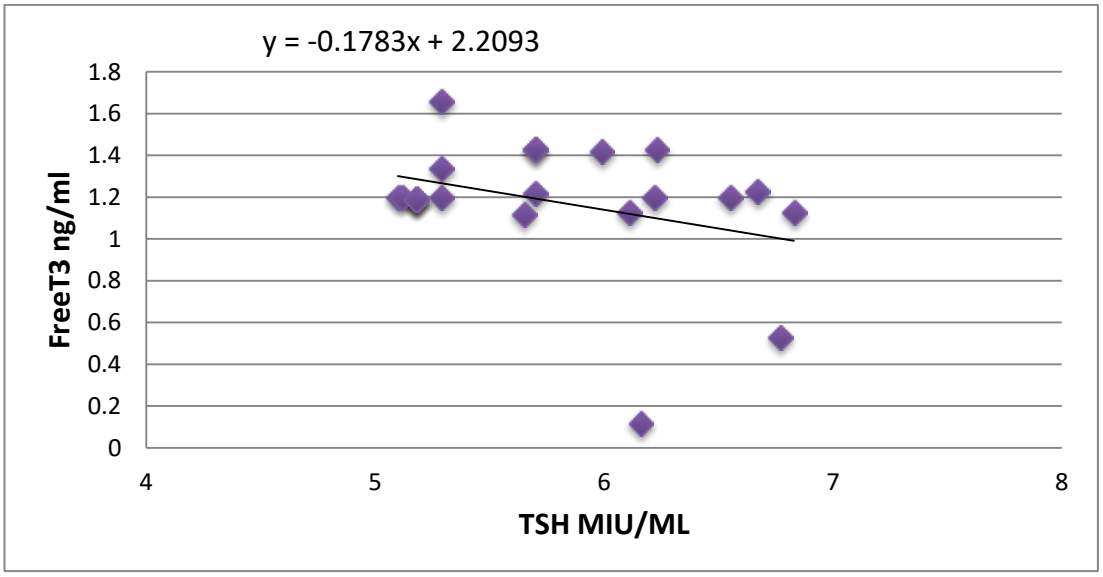

Figure (3.8.A) B: Negative correlation of TSH concentration and FreeT3 concentration in hypothyroidism pregnant women with recurrent miscarriage (r = 0.334).

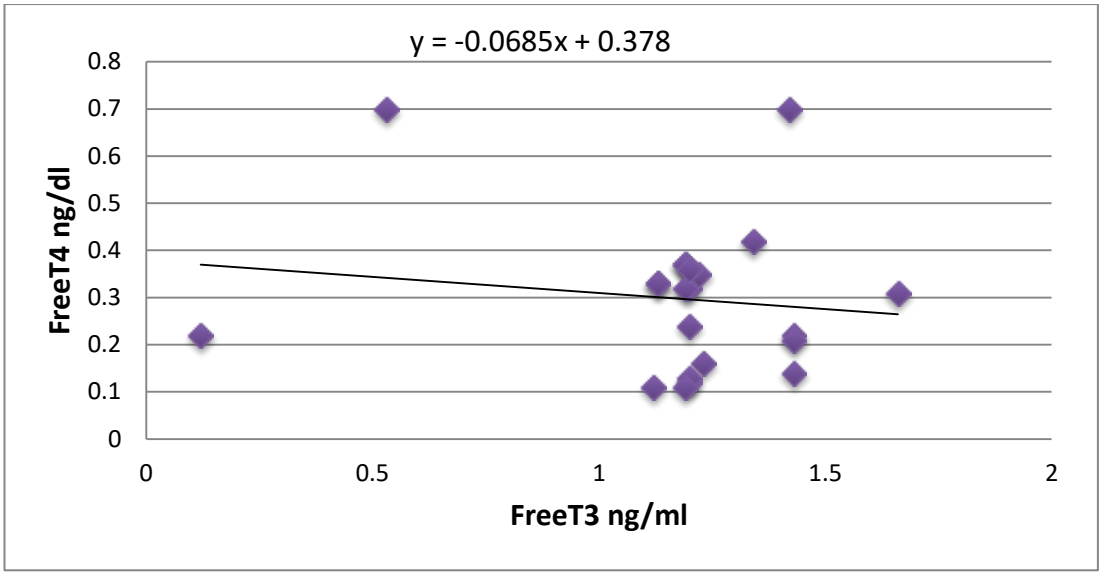

Figure (3.8.A) C: Negative correlation of free T3 concentration and free T4 concentration in hypothyroidism pregnant women with recurrent miscarriage (r = 0.132).

3.8.B Hormonal test pregnant women with recurrent miscarriage in hyperthyroidism

The results of the FT3 and FT4 test in the blood of pregnant women with recurrent miscarriage showed a significant difference P = < 0.001 when compared to the control group, as the table (3.8.B) .It was also found through the results of the TSH test for pregnant women with recurrent miscarriages that there were statistically significant differences for TSH P = (0.015) compared to the control group. As shown in Table (3.8.B).

Table (3.8.B): Levels of thyroid hormone in pregnant women with recurrent miscarriage in hyperthyroidism compared to the control group

Parameter	recurrent abortion	Control	P value
TSH (µIU/ml)	0.292 ± 0.210*	1.992±1.112	0.015
FreeT4(ng/dl)	2.862 ± 0.612*	1.061±0.206	<0.001
FreeT3 (ng/ml)	4.322 ± 1.130*	2.496±0.396	<0.001

No. of Recurrent abortion =8

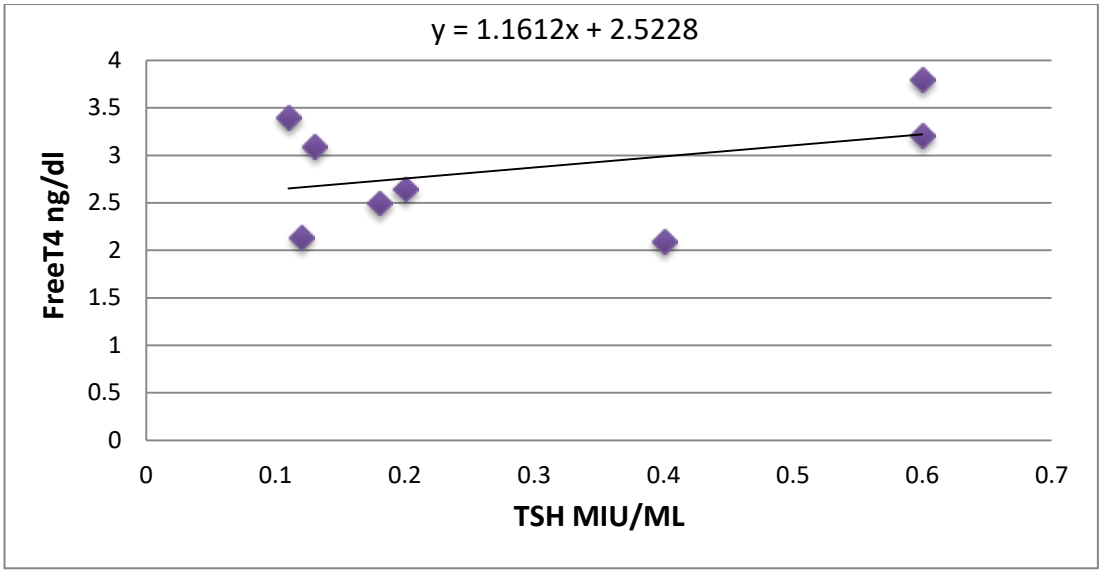

Figure (3.8.B) A: Positive correlation of TSH concentration and free T4 concentration in hyperthyroid pregnant women with recurrent miscarriage (r = 0.399).

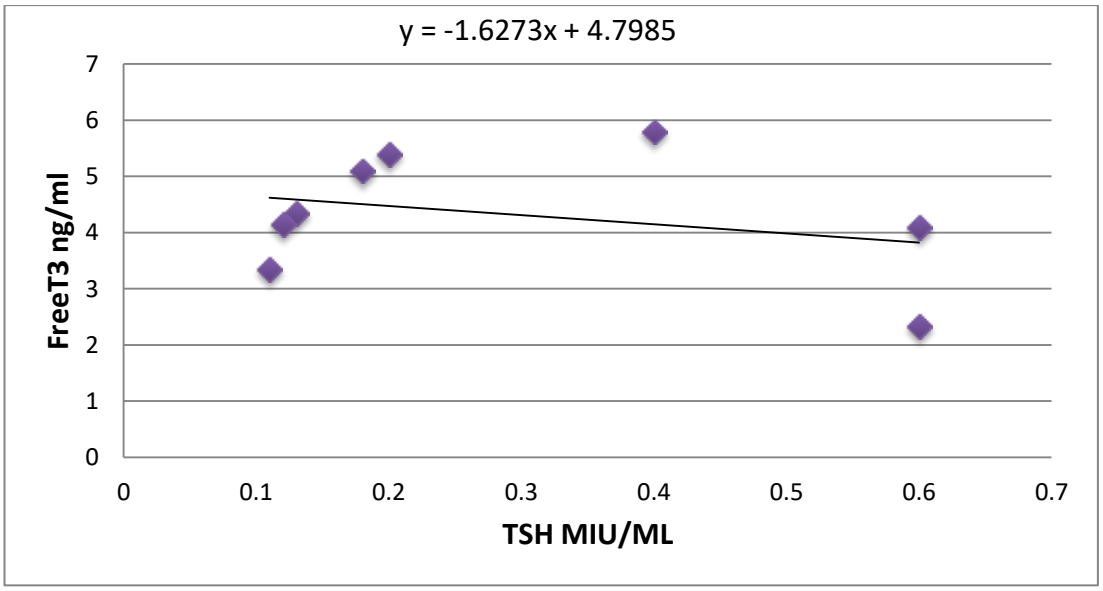

Figure (3.8.B) B: Negative correlation of TSH concentration and FreeT3 concentration in hyperthyroid pregnant women with recurrent miscarriage (r = 0.303).

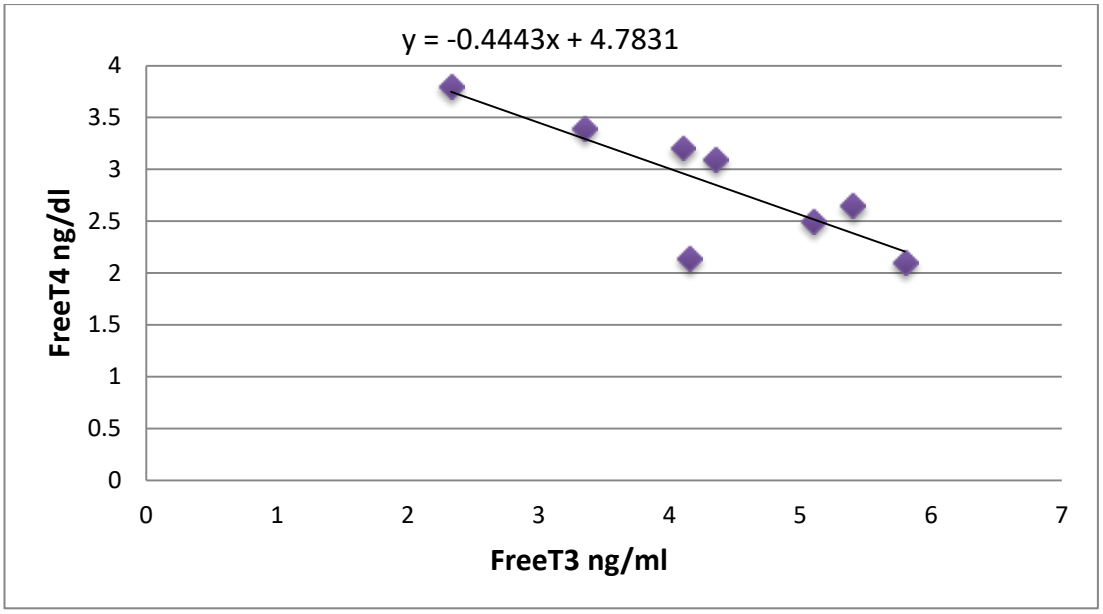

Figure (3.8.B) C: Negative correlation of free T3 concentration and free T4 concentration in hyperthyroid pregnant women with recurrent miscarriage (r = 0.820).

3.9 Levels of thyroid hormones for pregnant women with hypertension

3.9.A Hormonal test pregnant women with hypertension in hypothyroidism

The results of the thyroid hormones test in the serum of hypertensive women showed statisticall significant differences ($P < 0.05$) when compared with the control group, where the results indicated a significant increase in TSH hormone, ($P = 0.003$) and in FT3 hormone ($P= 0.001$) And there was a significant difference in FreeT4 hormone ($p = 0.099$) compared to the control group as shown in Table (3.9.A).

Table (3.9.A):Levels of thyroid hormone in pregnant women with hypertension in hypothyroidism compared to the control group

Parameter	Hypertension	Control	P value
TSH (µIU/ml)	5.285 ± 0.369*	1.992±1.112	0.003
FreeT4(ng/dl)	0.354 ± 0.182*	1.061±0.206	0.099
FreeT3 (ng/ml)	1.268 ± 0.125*	2.496±0.396	0.001

No. of hypertension =18

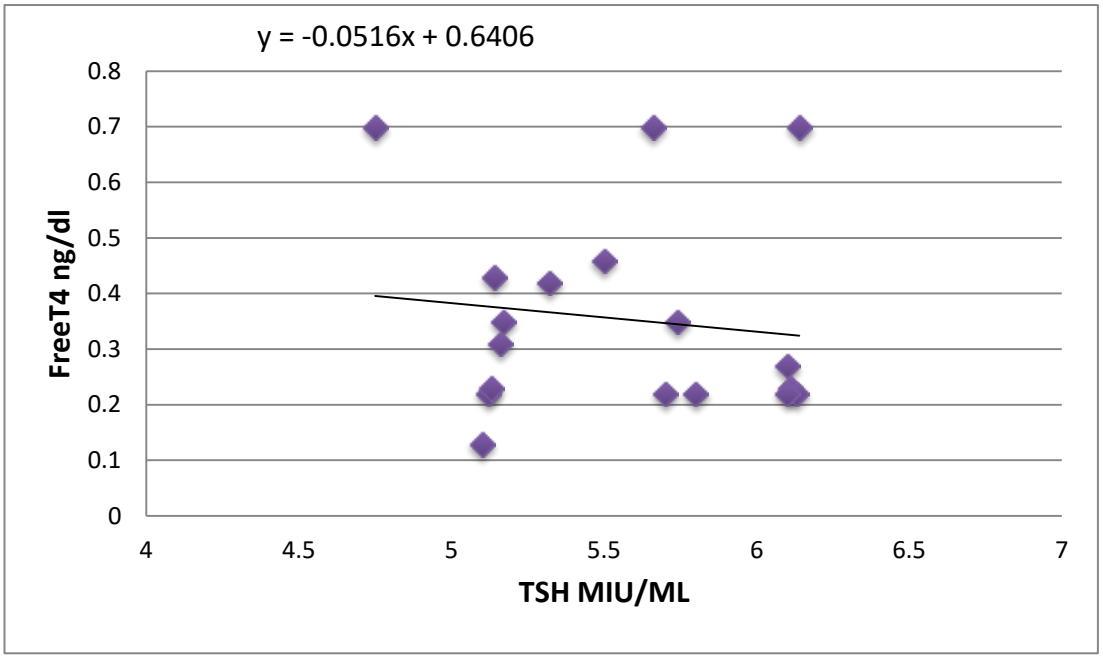

Figure (3.9.A) A: Negative correlation of TSH concentration and FreeT4 concentration in hypothyroid pregnant women with hypertension (r = 0.128).

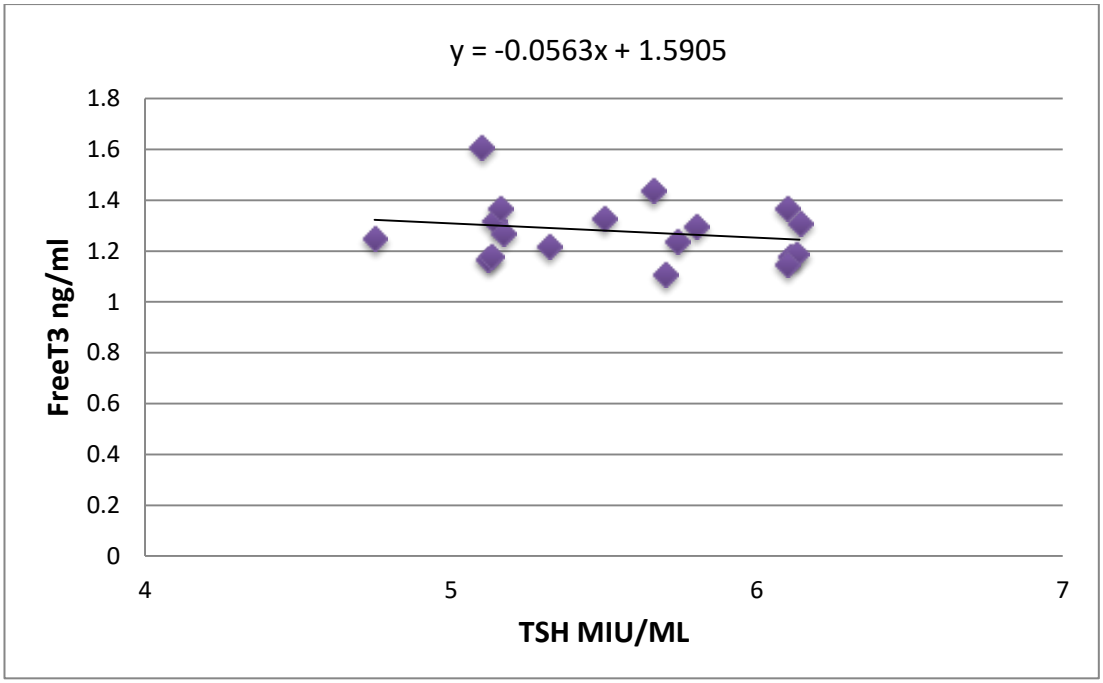

Figure (3.9.A) B: Negative correlation of TSH concentration and FreeT3 concentration in hypothyroid pregnant women with hypertension (r = 0.21).

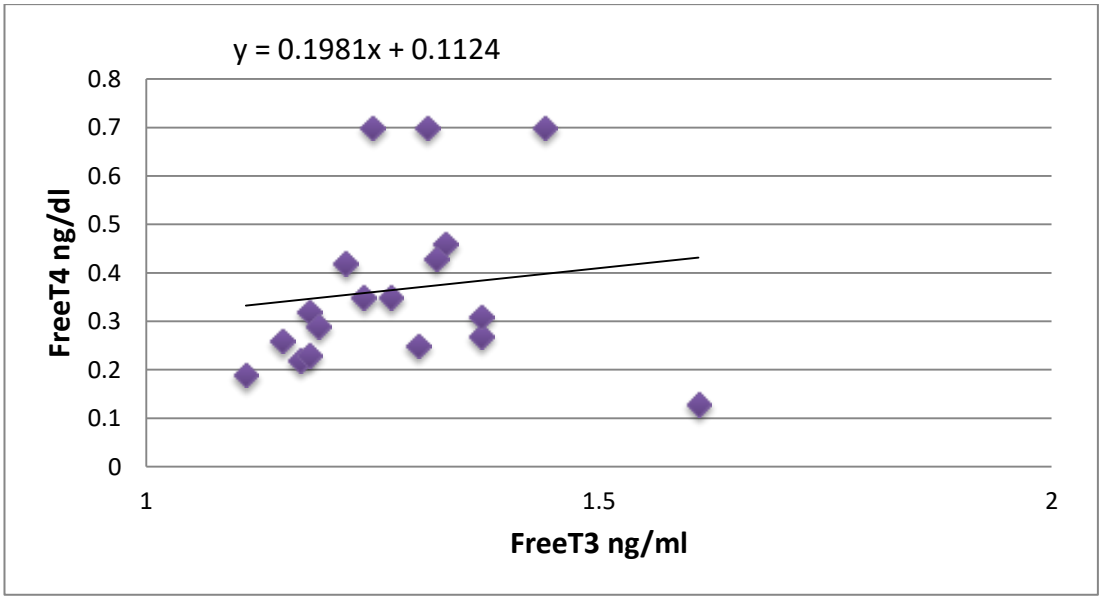

Figure (3.9.A) C: Positive correlation of free T3 concentration and free T4 concentration in hypothyroid pregnant women with hypertension (r = 0.136) .

3.9.B Hormonal test pregnant women with hypertension in hyperthyroidism

The results of the thyroid hormones test in the serum of women with high blood pressure showed statistically significant differences (P < 0.05) when compared with the control group, where the results indicated a significant increase in TSH (P = <0.001) and FT3 (P = 0.112) and there was a significant difference in FreeT4 hormone (p =< 0.001) compared to the control group as shown in Table (3.9.B).

Table (3.9.B): Levels of thyroid hormone in pregnant women with hypertension in hyperthyroidism compared to the control group

Parameter	hypertension	Control	P value
TSH (µIU/ml)	0.353 ± 0.227*	1.992±1.112	<0.001
FreeT4(ng/dl)	2.384 ± 0.872*	1.061±0.206	< 0.001
FreeT3 (ng/ml)	4.457 ± 0.782*	2.496±0.396	0.112

No. of hypertension =12

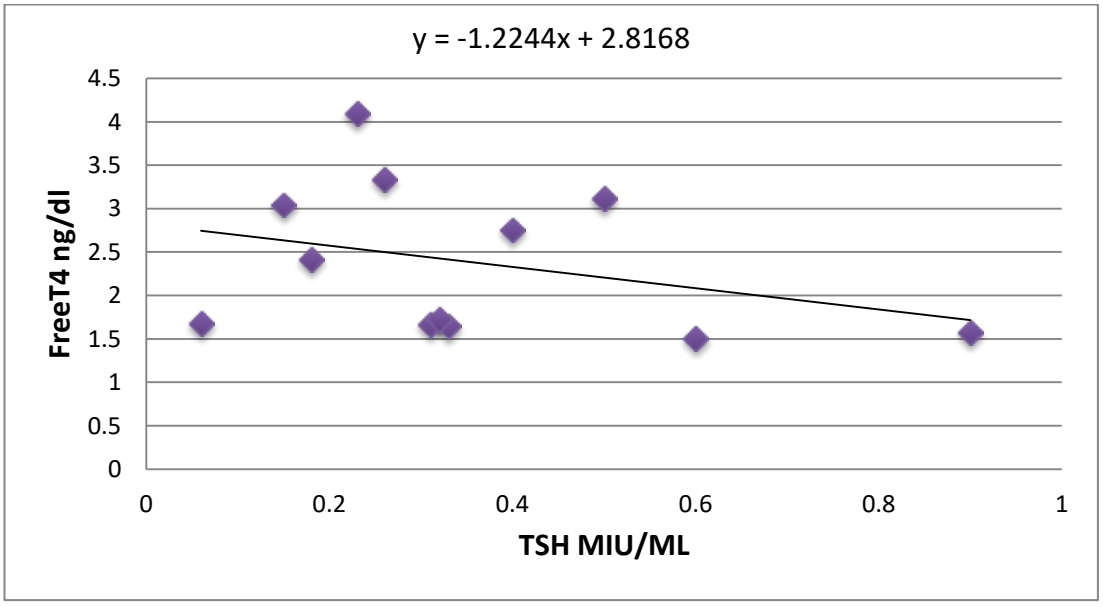

Figure (3.9.B) A: Negative correlation of TSH concentration and FreeT4 concentration in hyperthyroid pregnant women with thyroid hypertension (r =0.319).

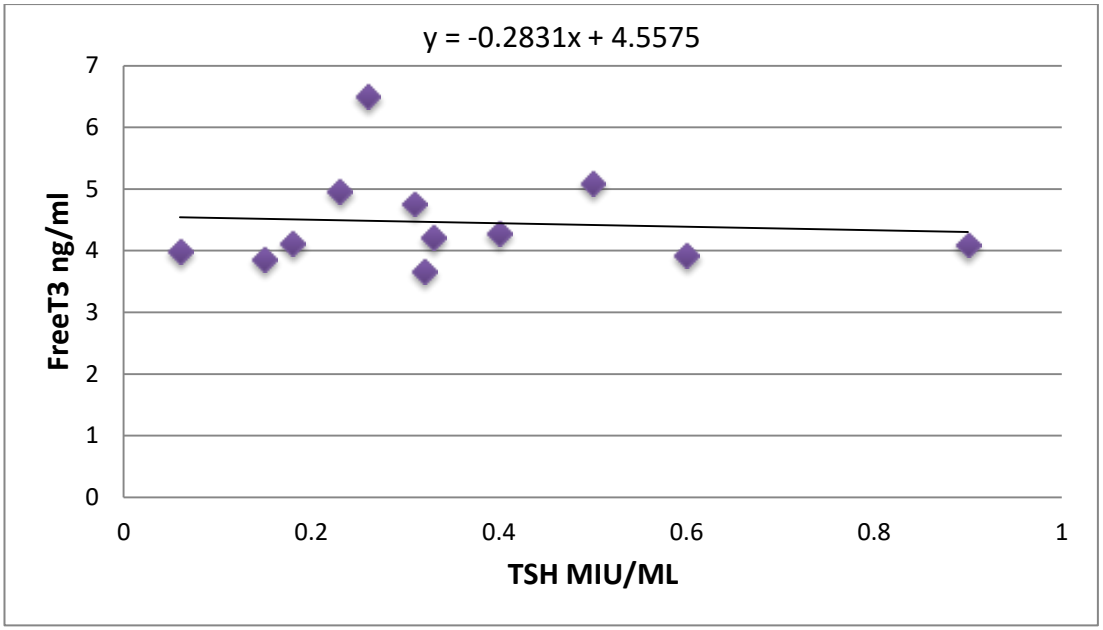

Figure (3.9.B) B: Negative correlation of TSH concentration and FreeT3 concentration in hyperthyroid pregnant women with thyroid hypertension

(r = 0.082) .

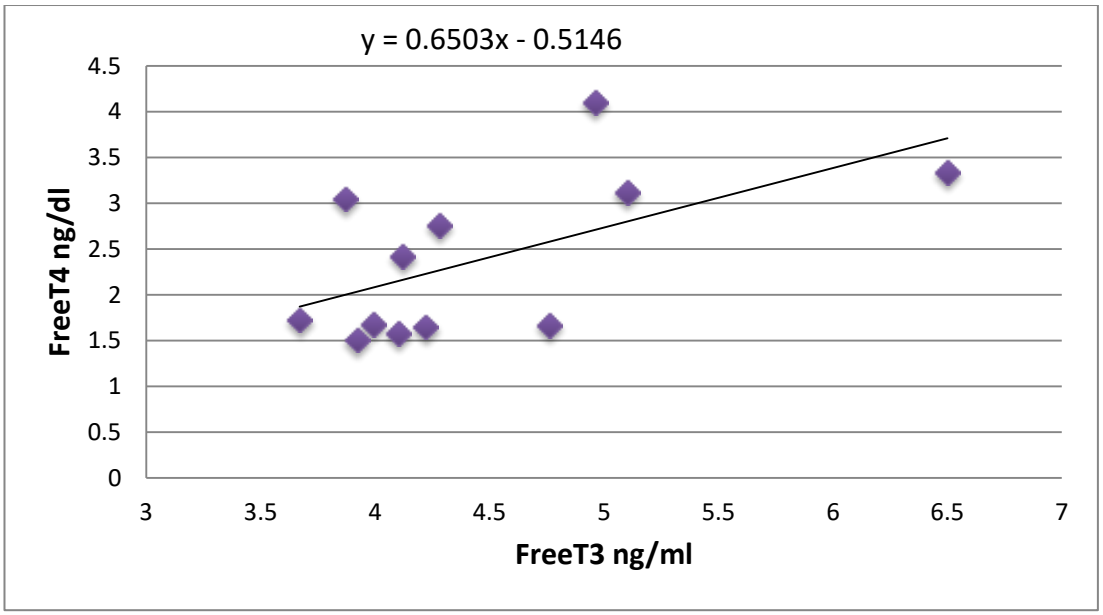

Figure (3.9.B) C: Positive correlation of free T3 concentration and free T4 concentration in hyperthyroid pregnant women with thyroid hypertension

(r = 0.583).

3.10 Levels of thyroid hormones for pregnant women with diabetes

3.10.A Hormonal test pregnant women with diabetes in hypothyroidism

The results of the thyroid hormones test in the blood serum of diabetic women showed significant differences, $P < 0.05$ when compared with the control groups, where the results indicated a significant increase in TSH, ($P = 0.019$) and in FreeT4 hormone ($P = 0.012$), FT3 ($P=0.006$) . As shown in Table (3.10.A).

Table 3.10.A: Levels of thyroid hormone in pregnant women with diabetes in hypothyroidism compared to the control group

Parameter	Diabetes	Control	P value
TSH (µIU/ml)	4.895 ± 0.325*	1.992±1.112	0.006
FreeT4(ng/dl)	0.382 ± 0.119*	1.061±0.206	0.012
FreeT3 (ng/ml)	1.287 ± 0.088*	2.496±0.396	0.019

No. of diabetes=10

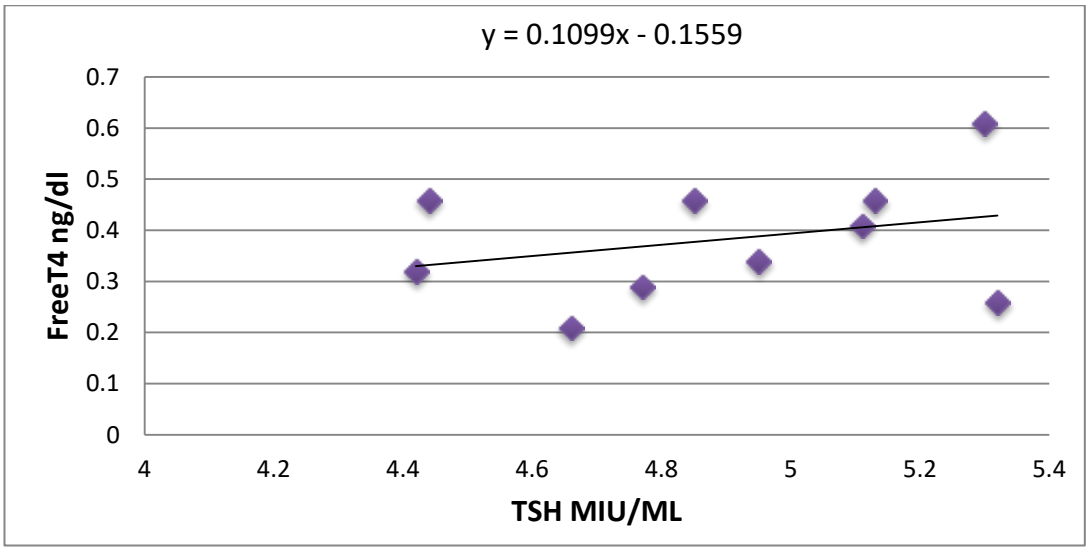

Figure (3.10.A) A: Positive correlation of TSH concentration and FreeT4 concentration in hypothyroidism pregnant women with diabetes mellitus (r = 0.298).

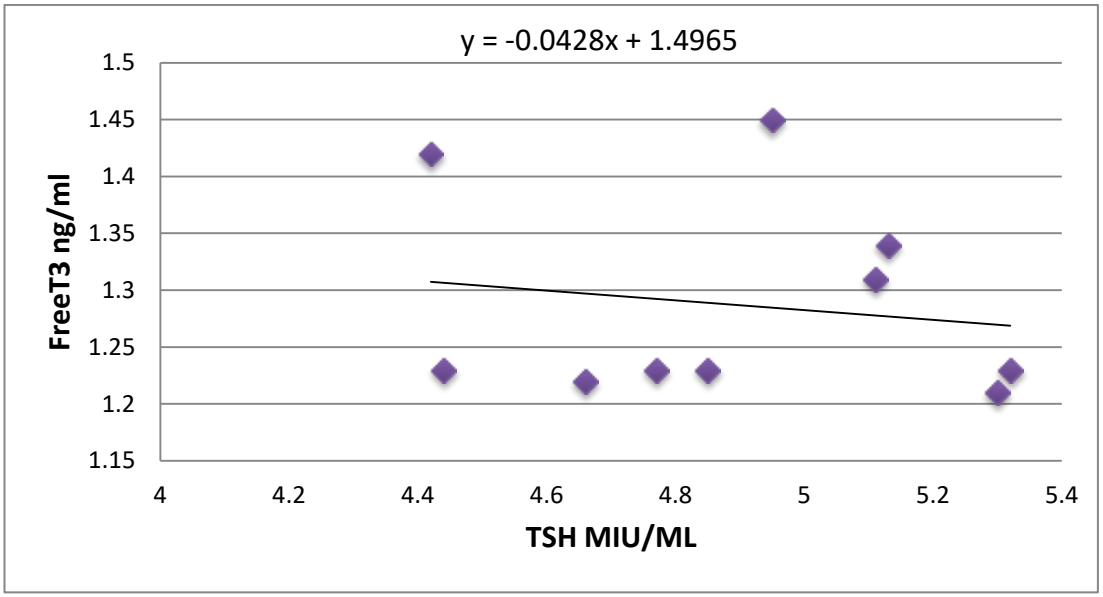

Figure (3.10.A) B: Negative correlation of TSH and FreeT3 concentrations in hypothyroidism pregnant women with diabetes mellitus (r = 0.156).

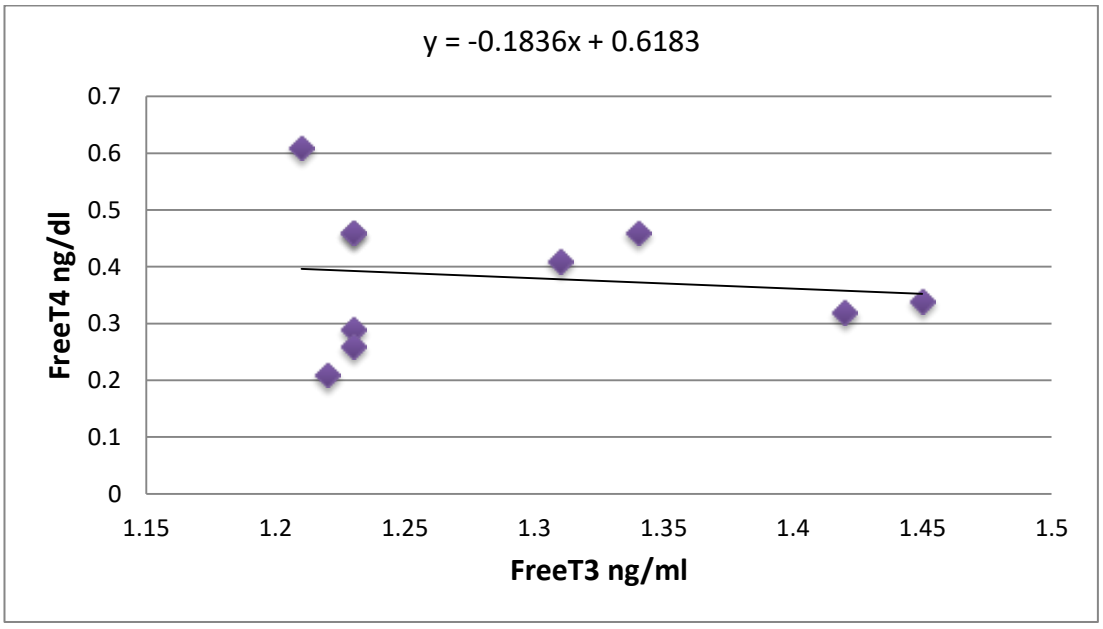

Figure (3.10.A) C: Negative correlation of FreeT3 and FreeT4 concentrations in hypothyroidism pregnant women with diabetes mellitus (r = 0.136).

3.10.B Hormonal test pregnant women with diabetes in hyperthyroidism

The results of the thyroid hormones test in the blood serum of diabetic women showed significant differences, $P < 0.05$ when compared with the control groups, where the results indicated a significant increase in TSH, FT4 hormone ($P = 0.001$) and no significant difference in FreeT3 hormone, as is It is shown in Table (3.10.B).

Table (3.10.B): Levels of thyroid hormone in pregnant women with diabetes in hyperthyroidism compared to the control group

Parameter	Diabetes	Control	P value
TSH(µIU/ml)	0.201 ± 0.211*	1.992±1.112	0.001
FreeT4(ng/dl)	2.408 ± 0.612*	1.061±0.206	0.001
FreeT3 (ng/ml)	4.422 ± 0.458*	2.496±0.396	NS

No. of Diabetes =15

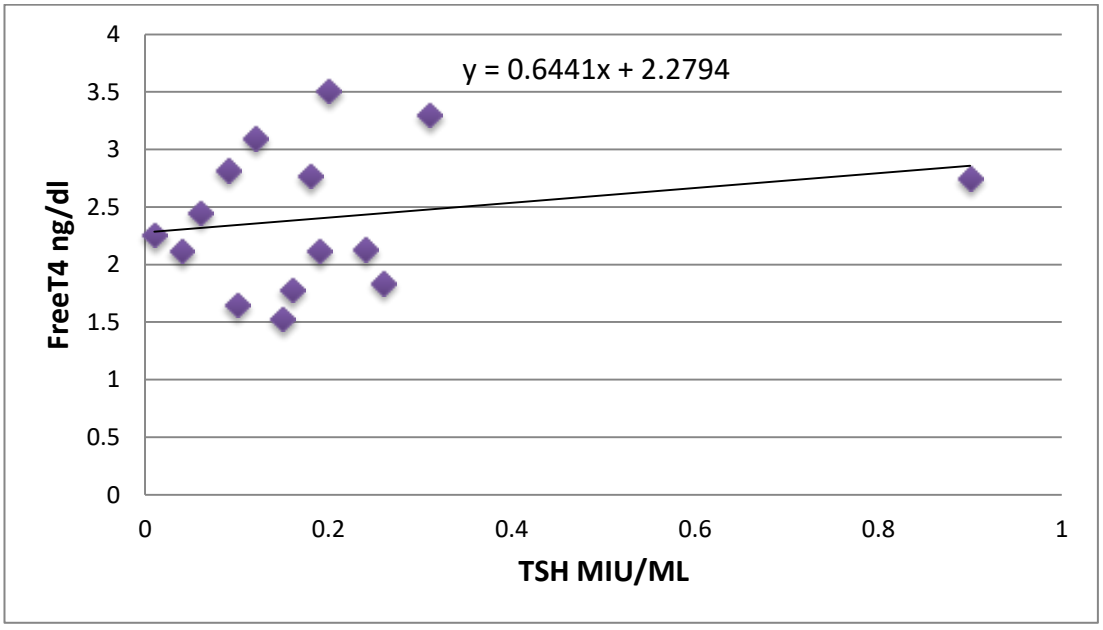

Figure (3.10.B) A: Positive correlation of TSH concentration and FreeT4 concentration in hyperthyroid pregnant women with diabetes (r = 0.222).

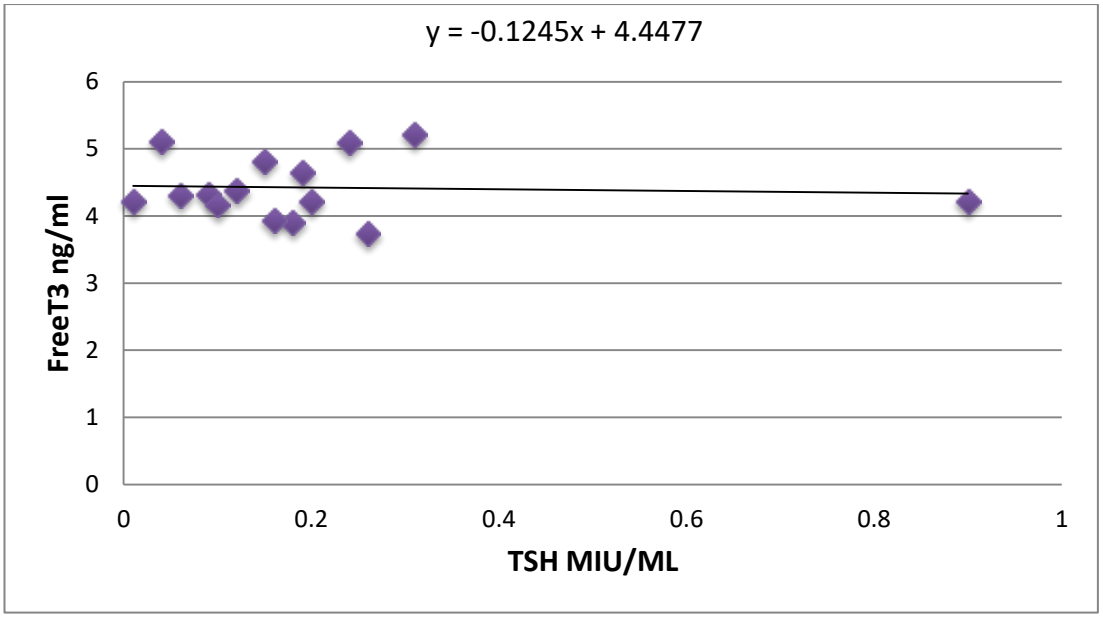

Figure (3.10.B) B: Negative correlation of TSH and FreeT3 concentrations in hyperthyroid pregnant women with diabetes (r = 0.057).

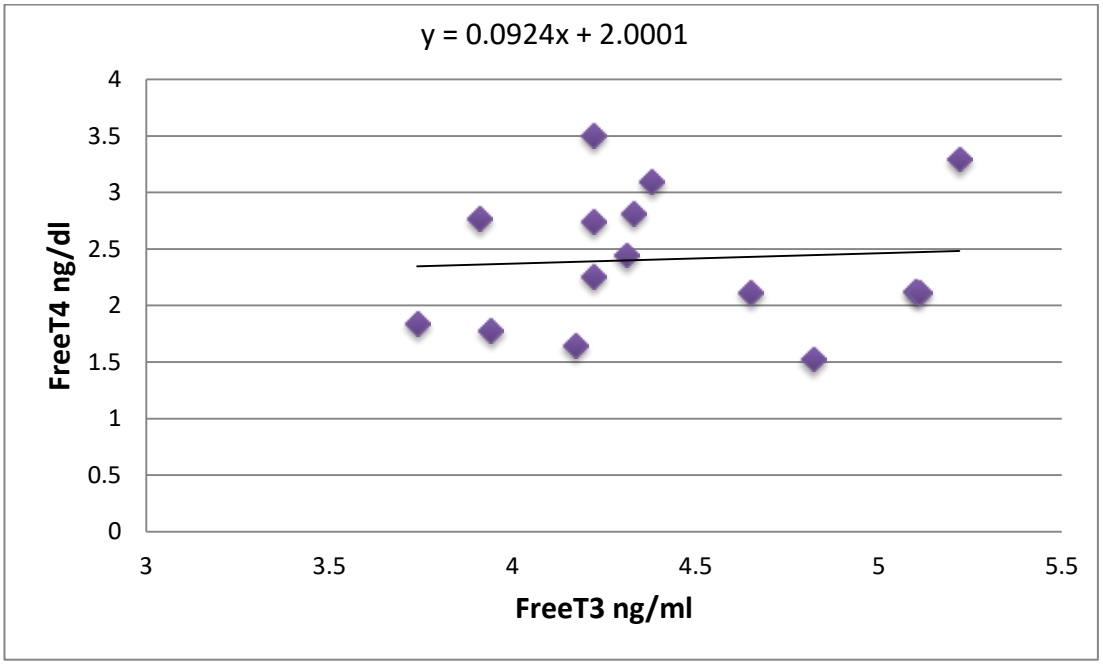

Figure (3.10.B) C: Positive correlation of FreeT3 and FreeT4 concentrations in hyperthyroid pregnant women with diabetes (r = 0.069).

3.11 Levels hormonal parameters for pregnant women with intrauterine growth restriction (IUGR).

3.10.A Hormonal test pregnant women with IUGR in hypothyroidism

The results of thyroid hormones test in the serum of women with intrauterine growth restriction (IUGR) showed a statistically significant difference $P < 0.05$ when compared with the control groups, where the results indicated a significant increase in thyroid hormones FT3, FT4 ,TSH ($P = 0.001$) with the control group as shown in Table (3.11.A).

Table (3.11.A): Levels of thyroid hormone in pregnant women with intrauterine growth restriction (IUGR) in hypothyroidism compared to the control group

Parameter	IUGR	Control	P value
TSH (µIU/ml)	4.891 ± 0.279*	1.992±1.112	< 0.001
FreeT4(ng/dl)	0.386 ± 0.121*	1.061±0.206	< 0.001
FreeT3 (ng/ml)	1.386 ± 0.144*	2.496±0.396	< 0.001

No. of Intrauterine growth restriction (IUGR)=25

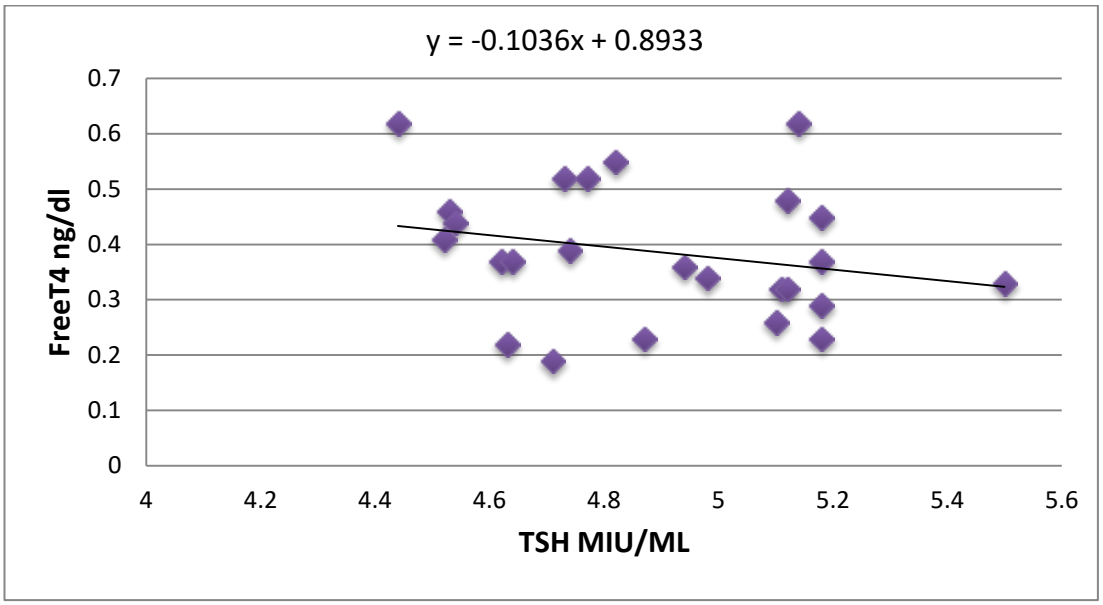

Figure (3.11.A) A: Negative correlation of TSH concentration and FreeT4 concentration in hypothyroidism pregnant women with IUGR (r = 0.24) .

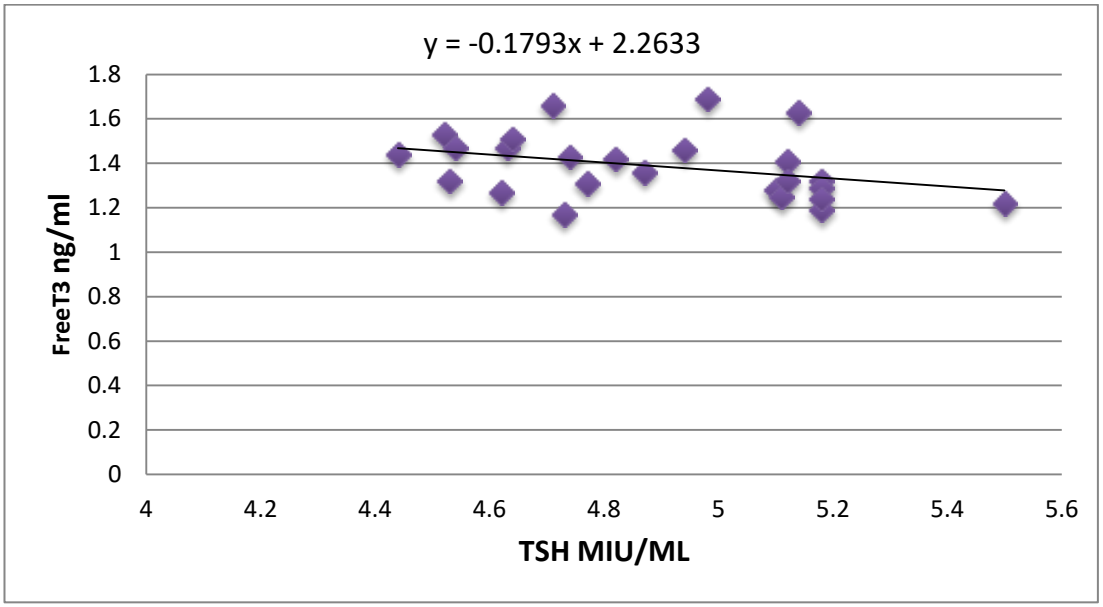

Figure (3.11.A) B: Negative correlation of TSH concentration and FreeT3 concentration in hypothyroidism pregnant women with IUGR (r = 0.348).

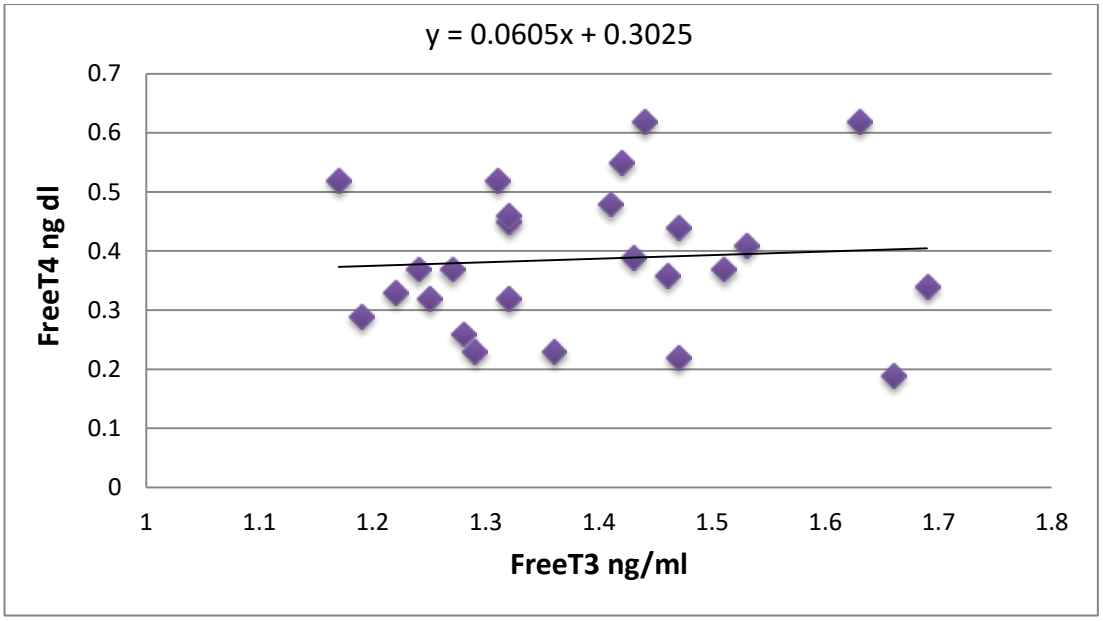

Figure (3.11.A) C: Positive correlation of FT3 concentration and FreeT4 concentration in hypothyroidism pregnant women with hypothyroidism (r = 0.072) .

3.11.B Hormonal test pregnant women with IUGR in hyperthyroidism

The results of thyroid hormones test in the serum of women with intrauterine growth restriction (IUGR) showed a statistically significant difference $P < 0.05$ when compared with the control groups, where the results indicated a significant increase in thyroid hormones (0.009) FT4 and TSH ($P = 0.024$) And there was no significant difference in ft3 hormone with the control group as shown in Table (3.11.B).

Table (3.11.B): Levels of thyroid hormone in pregnant women with intrauterine growth restriction (IUGR) in hyperthyroidism compared to the control group

Parameter	IUGR	Control	P value
TSH (µIU/ml)	0.202 ± 0.079*	1.992±1.112	0.024
FreeT4(ng/dl)	2.770 ± 0.384*	1.061±0.206	0.009
FreeT3 (ng/ml)	4.580 ± 0.482*	2.496±0.396	NS

No. of Intrauterine growth restriction (IUGR)=5

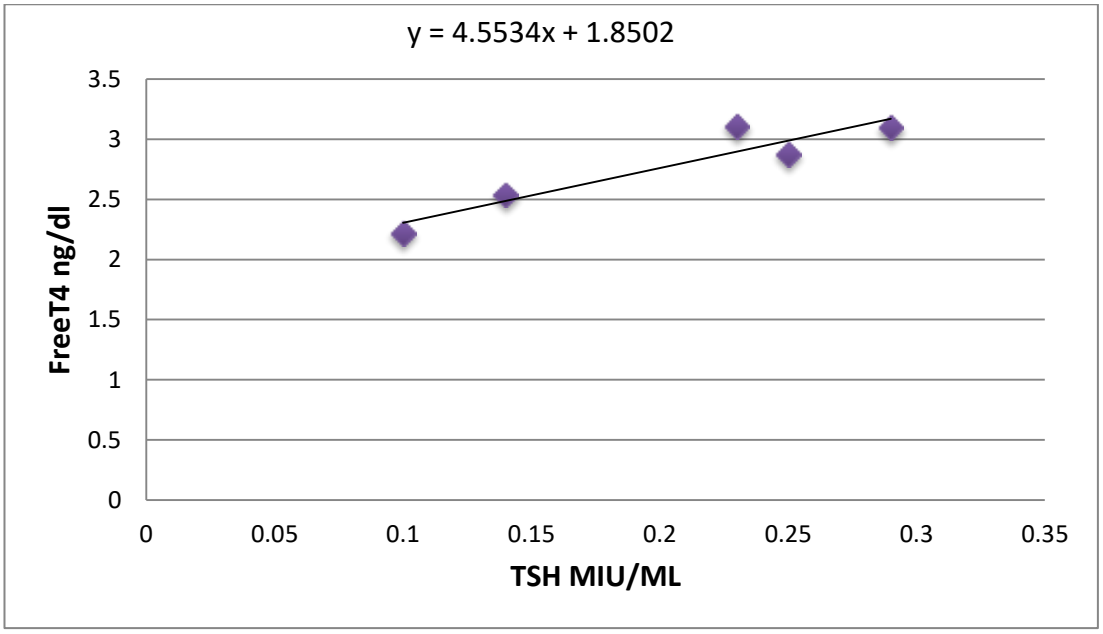

Figure (3.11.B) A: Positive correlation of TSH concentration and FreeT4 concentration in hyperthyroid pregnant women with IUGR (r = 0.937).

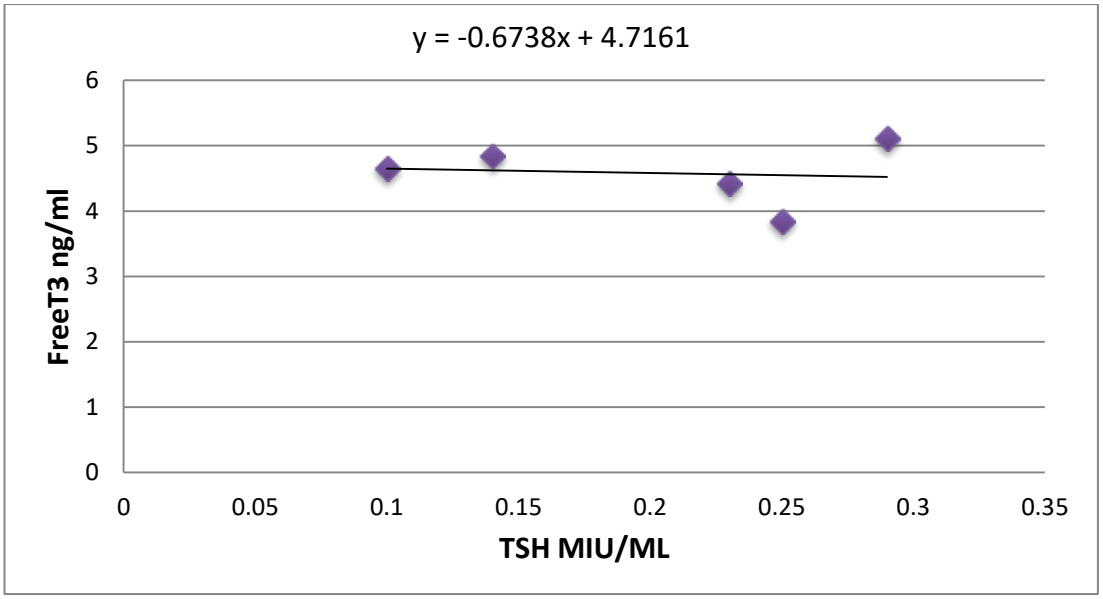

Figure (3.11.B) B: Negative correlation of TSH concentration and FreeT3 concentration in hyperthyroid pregnant women with IUGR (r = 0.111).

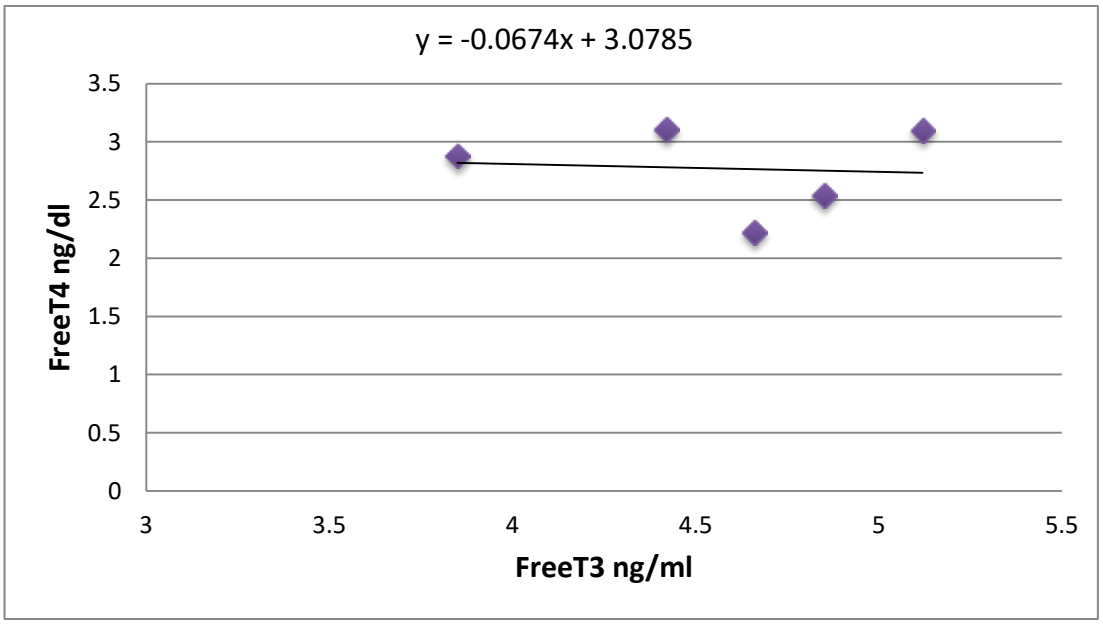

Figure (3.11.B) C: Negative correlation of FT3 concentration and FreeT4 concentration in hyperthyroid pregnant women with IUGR (r = 0.0842) .

3.12 Levels of biochemical and hormonal parameters of recurrent miscarriage, hypertension, diabetes and IUGR pregnant women

Hormones

All thyroid hormone tests and biochemical criteria showed no statistically significant differences between pregnant women with risk factors when comparing the factors between them. As it all test results were higher than the significant level (P = 0.05) .As showed in the table below (3.12). Comparing the risk factors among them, a significant difference was found between abortion and intrauterine growth restriction, and a difference between hypertension and intrauterine growth restriction, as well as a significant difference was found when comparing diabetes and intrauterine growth restriction.

Table (3.12) :The relationship between levels of biochemical and hormonal parameters in pregnant women with risk factors

Parameter	Group A with B	P value	Group A with C	P value	Group A with D	P value	Group B with C	P value	Group B with D	P value	Group C with D	P value
Age	30.65±6.76 30.25±7.513	NS	32.375±6.54 30.645±6.76	NS	26.67±6.0 30.645±6.76	NS	30.25±7.513 32.375±6.54	NS	30.25±7.513 26.67±6.079	NS	26.67±6.079 32.375±6.54	NS
Gestational age	2.58±0.765 2.62±0.659	NS	2.5±0.722 2.58±0.765	NS	2.54±0.767 2.58±0.765	NS	2.62±0.659 2.5±0.722	NS	2.62±0.659 2.54±0.767	NS	2.54±0.767 2.5±0.722	NS
TSH (μIU/ml)	4.3143±2.51905 3.3123±2.47752	NS	4.3143±2.51905 2.0784±2.36112	NS	4.3143±2.51905 4.1100±1.79592	NS	3.3123±2.47752 2.10784±2.36112	NS	3.3123±2.47752 4.1100±1.79592	0.001	2.0784±2.36112 4.1100±1.79592	0.002
Free T4(ng/dl)	0.9813±1.20037 1.1663±1.15357	NS	0.9813±1.20037 1.5980±1.11822	NS	0.9813±1.20037 0.7837±0.921219	0.040	1.1663±1.15357 1.5980±1.11822	NS	1.1663±1.15357 0.7837±0.92121	0.052	1.5980±1.11822 0.7837±0.92121	0.048
FreeT3 (ng/ml)	2.0177±1.54204 2.5443±1.66298	NS	2.0177±1.54204 3.1684±1.6074	NS	2.0177±1.54204 1.9187±1.60746	0.011	2.5443±1.66298 3.1684±1.6074	NS	2.5443±1.66298 1.9187±1.60746	<0.001	3.1684±1.6074 1.9187±1.60746	0.001

Group A: No. of recurrent miscarriage =30

Group B: No. of hypertension=30

Group C: No. of diabetes=25

Group D: No. of intrauterine growth restriction (IUGR) =30

3.13 Age distribution of pregnant women with risk factors

The results of the current paper present that the ages of patients with risk factors ranged between (15-43) years, and they were divided into three age groups (15-24), (25-34) and (35-43). Women with intrauterine growth-restricting factor were more prevalent in the age group (15-24) years with an average of 13.9%, while women with recurrent miscarriage factor were more prevalent in the age group (25-34) with a mean of 12.1% and in the group (35-43) Pregnant women with a hypertensive factor were the most prevalent in this age group at 13%. As shown in the table below (3.13).

Table (3.13): the numbers and percentages of pregnant women with risk factors distributed according to the age group.

Age	Recurrent abortion	Hypertension	diabetic	IUGR	Total
15-24 %	4 3.5%	6 5.2%	4 3.5%	16 13.9%	30 26.18%
25-34 %	14 12.1%	9 7.8%	8 6.9%	9 7.8%	40 34.8%
35-43 %	12 10.4%	15 13%	13 11.3%	5 4.4%	45 39.1%
Total number	30	30	25	30	115
Total %	26%	26%	22%	26%	100%

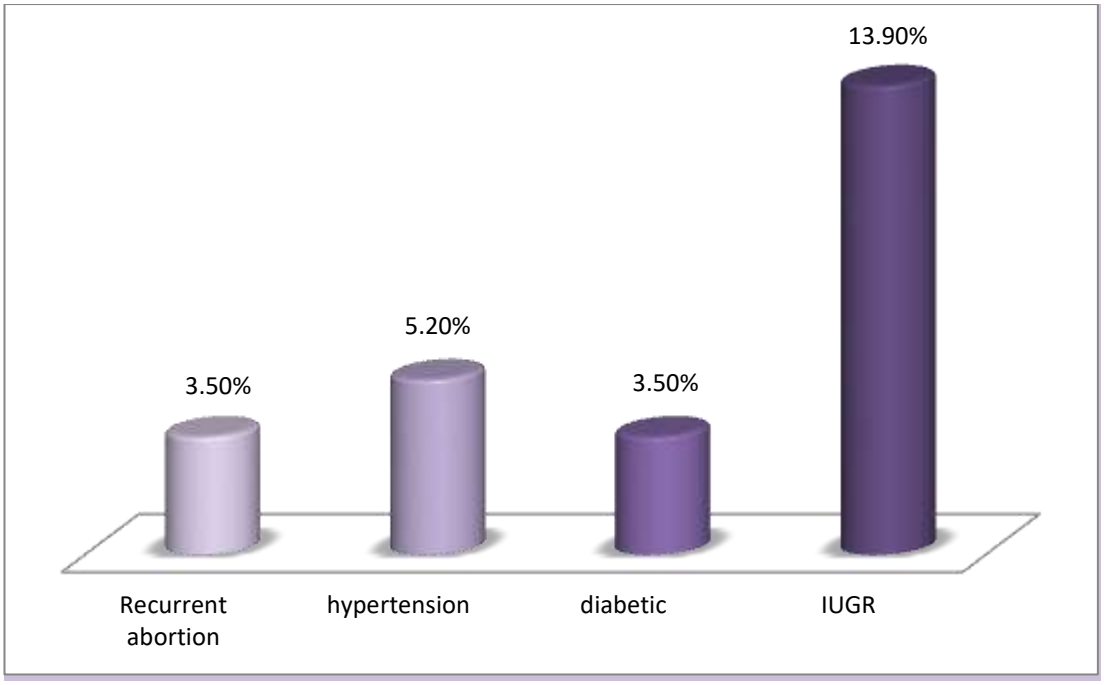

Figure (3.12) A: Percentage distribution of pregnant women with risk factors in the age group (15-24) years.

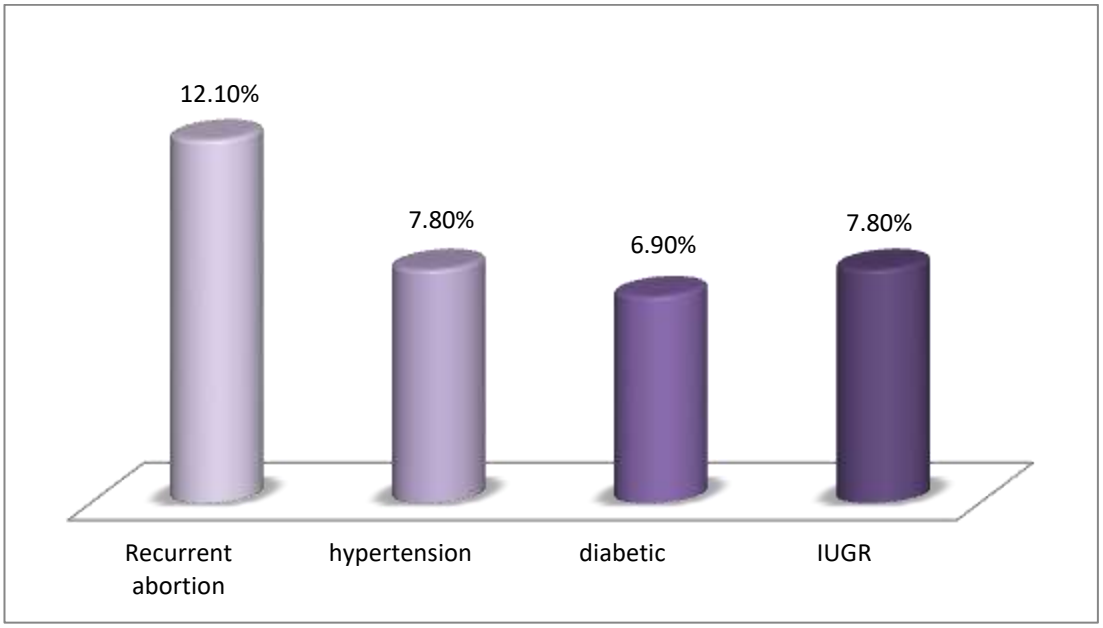

Figure (3.12) B: Percentage distribution of pregnant women with risk factors in the age group (25-34) years

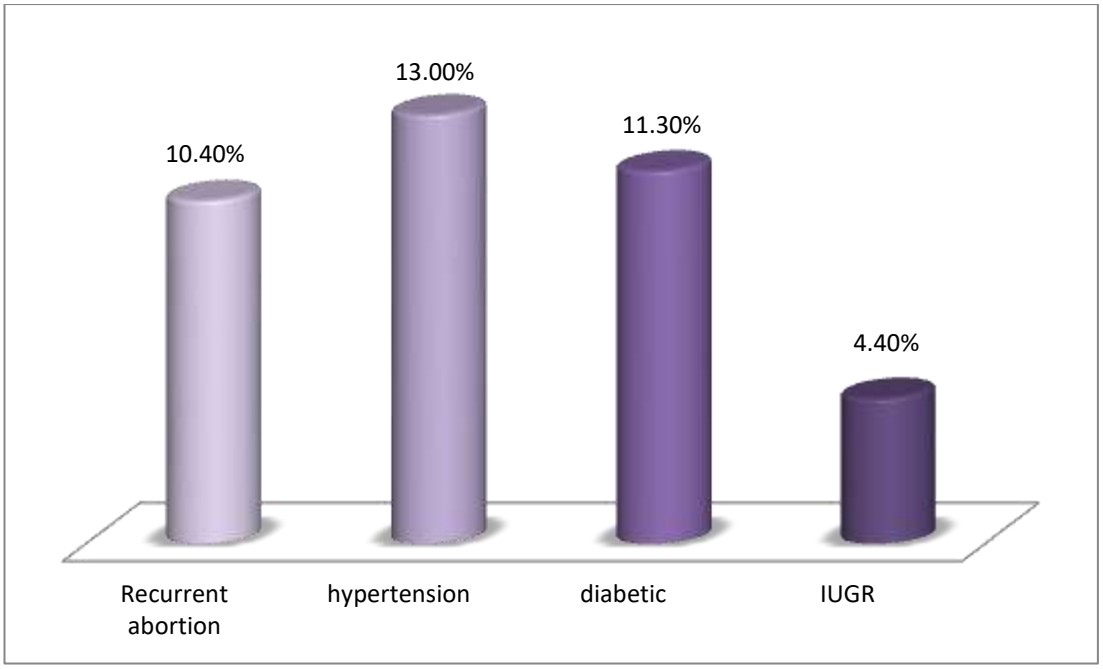

Figure (3.12) C: Percentage distribution of pregnant women with risk factors in the age group (35-43) years.

3.14 Levels of Educational state pregnant women with thyroid disorder and the control group

The results of the research showed that there were statistically significant differences in the academic achievement of pregnant women. As in table (3.14).

Table (3.14): Levels of Educational state pregnant women with thyroid disorder and the control group

Eductional State	Patient	Control	Total	P.V
primary	58 50%	14 28%	72 44%	0.00
secondary	23 20%	10 20%	33 20%	0.02
tertiary	10 9%	6 12%	16 10%	0.32
collage	24 21%	20 40%	44 26%	0.55
Total%	115 100%	50 100%	165 100%	0.03

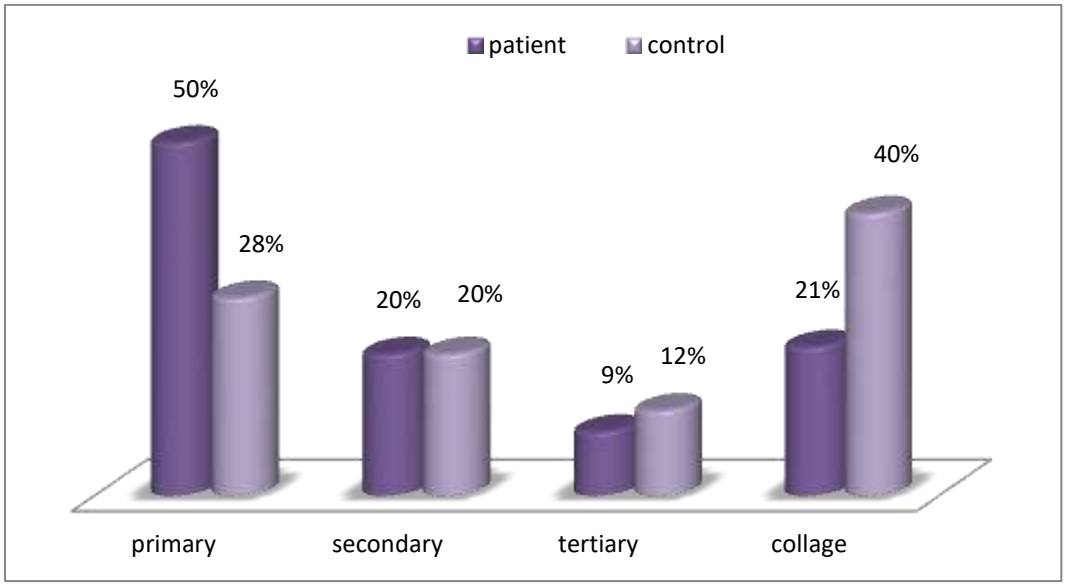

Figure (3.13): Percentage distribution of educational attainment in pregnant women

3.15 The effect of the economic situation on the financial income of pregnant women

Table (3.15): Levels of economic Situation pregnant women with thyroid disorder and the control group

Economic Situation	Patient	Control	Total	P.V
Low	30 26%	6 12%	36 23%	0.00
Medium	53 46%	27 54%	80 48%	0.00
High	32 28%	17 34%	49 29%	0.03
Total%	115 100%	50 100%	165 100%	0.15

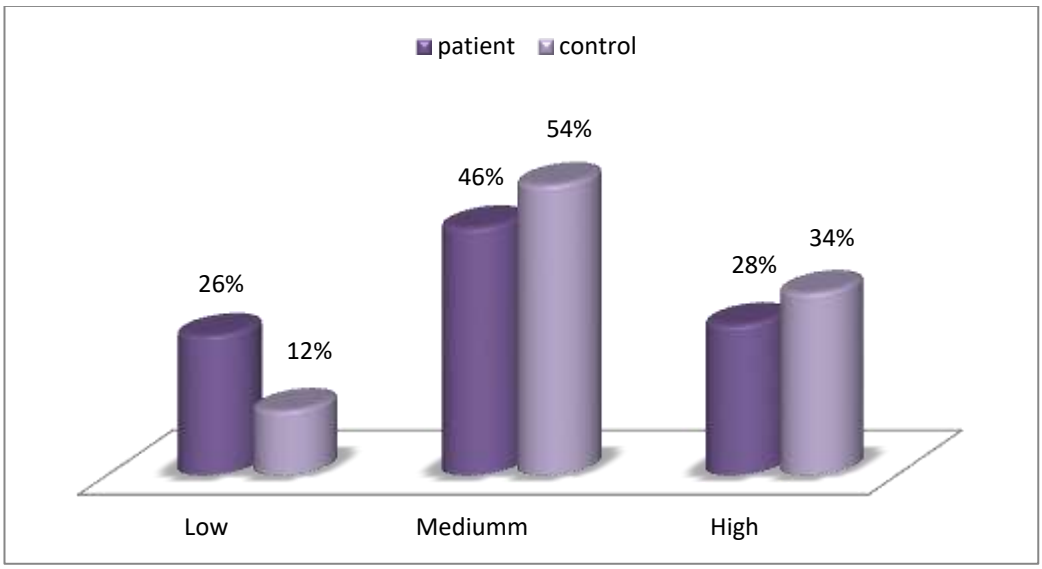

Figure (3.14): Percentage distribution of economic Situation in pregnant women.

CHAPTER FOUR

Discussion

4.1 Mechanisms of physiological changes in thyroid function during pregnancy

Preparation of the thyroid gland begins early in the first trimester by B-HCG, which shares some structural analogy with TSH. There is also an estrogen-mediated increase in circulating levels of circulating thyroid-binding globulin (TBG) during pregnancy by 2-3 times that of serum TBG concentrations. TBG is one of several proteins that transport thyroid hormones in the blood with a high affinity for thyroid hormone T4, increases in serum after a few weeks of pregnancy and is stable during mid-gestation. The mechanism for this increase in TBG includes both the increased hepatic synthesis of TBG and persistence by estrogen in Formation of TBG that increases the half-life from 15 minutes to 3 days to fully form TBG [(80)] .elevated levels of TBG lead to lower concentrations of free T4 which results in increased pituitary secretion of TSH, thus enhancing production and secretion of TH. the net effect of elevated TBG synthesis is to force a new balance of free and restricted thyroid hormones, thereby dramatically increasing total T3 and T4 .The increased demand for TSH is reached at about 20 weeks of gestation and persists until term [(81)]. changes in iodine metabolism, a prerequisite for the synthesis of thyroid hormones, reflect an increased demand for iodine, and a pregnancy-related significant increase in iodine clearance by the kidneys and maternal iodide withdrawal from the fetus during pregnancy .There is an increase in urinary iodine excretion due to an increase in glomerular filtration and a decrease in renal tubular reabsorption. In addition maternal iodine is actively transported to the fetal placental unit this contributes to a state of relative iodine deficiency [(12)]. another factor is the effect of HCG secreted by the human placenta.

Thyroid stimulation in response to HCG thyroid activity bypasses the normal procedure for the thyroid-pituitary-thyroid feedback system TSH that can bind and transmit signals from TSH receptors on thyroid epithelial cells until the end of the first trimester of pregnancy.

When HCG levels reach their peak, a large part of the thyroid stimulating activity is from HCG, during which time TSH levels in the blood drop. The thyroid-stimulating activity of HCG actually causes some women to develop transient hyperthyroidism [(33)]. The possible source of TH for the fetus is its own fetal thyroid and the mother's thyroid gland. Human fetuses acquire the ability to synthesize thyroid hormones approximately in the first trimester of pregnancy. Current evidence from several types indicates that there is significant transport of thyroid hormones across the placenta, and the placenta also contains deiodinases that can convert T4 to T3 [(83)].Protecting the pregnant mother and the infant is a priority in health, because these groups are often vulnerable to disease and death. Thyroid dysfunction is a common complication of pregnancy and contributes significantly to maternal and fetal morbidity and mortality.

4.1.1 Body Mass Index (BMI)

The BMI levels of pregnant patients showed a significant increase ($P = 0.01$) when compared with the control group as shown in Table (3.1).

The role of the endocrine glands in the human body is highlighted by the secretion of many hormones, and these hormones are chemical messengers produced by the glands in the endocrine system. And through their secretion into the bloodstream, these hormones control the main bodily functions. Starting from fertility and passing through hunger

and reaching emotions and moods Therefore, it occupies a great importance in the human body, especially in pregnant women. The thyroid gland is one of the endocrine glands that secretes T3, T4 and these hormones regulate metabolism, growth and body temperature. There are many diseases that affect the thyroid gland and affect its function, causing weight gain, and this increase contributes through a complex relationship between the thyroid gland and glands other endocrine disorders and diseases that affect them and body weight. A high or low BMI is an indication of a thyroid disorder. Overweight and obesity [84,85] .Has become a major health problem worldwide and is also associated with poor pregnancy outcomes.

The of the study indicated that there was a significant increase in body mass index in pregnant women with thyroid disorders compared to healthy pregnant women with normal thyroid gland.

These results point to several interpretations:

First: The decrease in thyroid hormones leads to weight gain because the body cannot metabolize and burn fat properly, so fat and fluid accumulate, causing an increase in body mass .the effect of the insulin hormone when insulin resistance occurs, sugar accumulates in the blood and this may lead to weight gain and type 2 diabetes [86].

Second: The reasons of the inverse relationship between thyroid hormones, cortisol, estrogen and leptin, weight gain occurs. Where the hormone cortisol is secreted from the adrenal gland and when a person is depressed, stressed or tense, its secretion increases in the body, and its main function is to reduce stress levels by increasing blood sugar. Because of the stress and anxiety that a pregnant woman experiences, the body becomes in a constant state of tension, and this leads to an

increase in cortisol, as it urges the body to store fat and fluids more, which causes an increase in weight and high blood pressure.While estrogen, the main female sex hormone, when it is out of balance, estrogen leads to weight gain. When estrogen levels rise the cells that produce insulin are put under stress, and this makes the body resistant to insulin, leading to high blood sugar. In women, estrogen becomes less and less late in age, and in order to compensate for this deficiency. The body begins to look for other sources to produce this hormone .One of these sources is fat cells, where when the level of estrogen decreases, the body begins to convert all available energy sources into fats to increase the level of glucose in the body [87]. While the hormone leptin maintains the balance of energy levels in the body by keeping hunger under control .But when you eat food rich in sugar, the excess amount of fructose turns into fat that is deposited in the liver, abdomen and other areas of the body. It is these fat cells that secrete leptin , and because of the inverse relationship between it and thyroid hormones, when high levels of leptin weaken the body's sensitivity to it this means that the brain stops receiving notifications that the body does not need to eat. Therefore , the desire to eat more food increases without feeling full or knowing when to stop eating, which leads to weight gain .while the opposite happens in patients with hyperthyroidism [88] .

4.1.1 Personal family history of thyroid disease

The levels of personal family history factor with thyroid disease showed a significant increase ($P < 0.001$) when compared with the control group. As shown in Table No. (3.2).

Family history is an important risk factor that increases the risk of developing thyroid disease. It is slightly larger if anyone nearby has a female (mother, sister, daughter) with thyroid disease.

A family history of goiter, especially during childhood, may result in nontoxic goiter (papillary thyroid carcinoma), an independent thyroid nodule that is a separate mass of the thyroid gland whose independent or normal function is to control the pituitary gland[33] .Studies (Harach and Williams et al) indicate that a number of morphological subtypes of follicle-derived thyroid tumors have been identified in families with goiter, indicating a genetic predisposition for the development of these particular types of tumors [89,90]. Besides the risk of developing a family history of congenital hypothyroidism, where there is a deficiency of thyroid hormones at birth due to the absence of thyroid tissue and genetic defects in the biosynthesis of thyroid hormones, hypothyroidism occurs more commonly in infants and permanent abnormalities occur It is one of the most common causes of mental retardation. Most children with congenital hypothyroidism do not show a clear clinical manifestation of hypothyroidism at birth. This may result from persistent neonatal thyroid function due to overexpression of deiodinases through compensatory mechanisms in target organs or in thyroid hormones. It is received from breast milk [91]. A family history of any autoimmune disease increases the risk of autoimmune thyroid diseases, such as Graves' disease and Hashimoto's disease, and this is what the study found by (Munkner and Bettmann et al) [92,93].therefore, pregnant women who have a family history of thyroid disease are more likely to develop thyroid dysfunction.

4.2 Levels of biochemical and hormonal parameters for pregnant women with thyroid disorders

Women patients were divided into hypothyroidism and hyperthyroidism.

4.2.1 Hypothyroidism

Hypothyroidism is more common in females of childbearing age. It is common in pregnancy with an expected prevalence of 75% for overt hypothyroidism[94].Iodine deficiency causes most cases of hypothyroidism in pregnant women worldwide, while Hashimoto's disease is the leading cause of hypothyroidism in appropriate parts of the world. A cross-sectional study by (Lafranchi et al) found that the prevalence of subclinical hypothyroidism was 4.3% and pronounced hypothyroidism was 20.8% according to internationally approved criteria effects of hypothyroidism on the foetus are commonly observed, such as low birth weight, impaired brain development, intrauterine death, neonatal dyspnoea, and preterm delivery [95,96]. A study reported by (Wilson et al) showed that infants born to TPO-negative mothers had a significantly smaller head circumference, lower brain weight and lower brain-to-body ratio than those born to TPO-negative mothers, which correlated with higher head circumference and risk of miscarriage and early delivery [97] .

4.2.2 Thyroid hormones

The results in our study indicated increased TSH, with decreased T3 and T4. As shown in Table (3.3.A), these results can be explained by:

The cause of the hormone elevation in response to low levels of T3 and T4 may be because the lack of hormones stimulates the pituitary gland to secrete TSH [98]. Or because of Hashimoto's disease, and this is

consistent with the results of (Jensovsky et al) which is an autoimmune thyroid disease caused by the presence of antibodies that are produced and present in the blood serum of patients with this disease. These antibodies are called thyroid-suppressive immunoglobulin (TPO) antibodies[(99)] .Where these bodies attack and then destroy the tissues and receptors of the thyroid gland, because these bodies have the ability to bind to TSH receptors located on the membranes of thyroid cells and thus reduce the effectiveness of TSH in stimulating the growth of the thyroid gland and the synthesis of its hormones [(100)].

4.2.3 The risk of hypothyroidism on the health of the foetus and the mother

Uncontrolled hypothyroidism during pregnancy can lead to preeclampsia, anaemia, miscarriage, low birth weight and stillbirth [(101)]. A study by Casey et al et al. found that the risk of placental abruption and the risk of preterm birth complications was reported to be three times greater in the mother with hypothyroidism [(102)]. Since TSH is essential for foetal brain and nervous system development, uncontrolled hypothyroidism, especially during the first three months of pregnancy, can affect the baby's growth and development [(103)].

4.2.4 Treatment of hypothyroidism during pregnancy

Hypothyroidism is treated with synthetic TH called LT4 thyroxin, which matches natural T4.Pregnant women with pre-existing hypothyroidism need to increase the pre-pregnancy dose of T4 to maintain normal thyroid function. Thyroid function should be monitored every 6 to 8 weeks during pregnancy. Synthetic T4 is safe and necessary for the well-being of the foetus if the mother has hypothyroidism [(104)]. Asymptomatic pregnant

women should be routinely screened for hypothyroidism and patients with subclinical hypothyroidism should be treated to ensure a healthy pregnancy [105]. A prospective pilot study found that treatment of hypothyroidism with LT4 reduces the risk of adverse maternal and foetal outcomes [106]. Dietary supplements such as iodine a very important mineral for the mother during pregnancy because the thyroid gland uses iodine to make its hormones. During pregnancy, the baby gets iodine from the mother's diet, and the mother needs more iodine when she is pregnant [107]. Choosing iodized salt (I-) over regular salt and prenatal vitamins containing (I-) will ensure nutritional supplementation [108].

4.2.5 Hyperthyroidism

When hyperthyroidism is a pathological process in which thyroid hormones are produced and secreted, while the term thyrotoxicosis refers to an excess of thyroid hormones in the circulatory system [109]. It can occur in about 1% of the population and up to 40% of pregnancies [33]. A previous study by Wang et al found that the prevalence of hypothyroidism was 10.2%, hyperthyroidism 1.8%, and hypothyroidism 7.5% [110].There are two causes of hyperthyroidism such as the traditional causes that occur in the general population and other causes during pregnancy. Hyperthyroidism may result from inflammatory thyroid disease, pregnancy-related complications (such as hyperemesis gravid arum), the presence of thyroid tissue, or from other sources of thyroid hormones [114].Histological effects of hyperthyroidism include rapid metabolism, inhibition of serum TSH, lowering of cholesterol, increased bone turnover, and decreased bone density with increased risk of osteoporosis and fractures [111,112].The (Marvisi et al) study found that hyperthyroidism is closely associated with lower TSH values and increased pulmonary

artery pressure, leading to severe pulmonary hypertension [113]. In the first trimester of pregnancy.

4.2.6 Hormones in hyperthyroidism

The results of this research indicated low TSH, with elevated T3 and T4. As shown in Table (3.3.B). These results can be explained by:

This may be due to a defect in TSH that regulates thyroid hormones, and this increased stimulation by inappropriate TSH secretion may be due to TSH-secreting pituitary tumours affecting the synthesis and secretion of elevated thyroid hormones .Or because type III deiodinase is produced by the placenta and this enzyme that converts T4 to rT3 and T3 to T2. Which has a very high activity during the life of the foetus [114] .Or due to Graves' disease and this is consistent with the findings (Biondi et al) is an autoimmune disease caused by thyroid-stimulating antibodies, sometimes called TSHR Abs, which are able to stimulate the thyroid gland, leading to increased production of thyroid hormones and an increase Stimulating the growth of the thyroid gland [115].

4.2.7 The risks of hyperthyroidism on the health of the foetus and the mother

Uncontrolled hyperthyroidism in pregnancy can lead to congestive heart failure, preeclampsia, hypertension in late pregnancy, thyroid storm, diabetes, miscarriage, premature delivery, placental abruption and low birth weight [116].

In new-borns, hyperthyroidism can lead to an increased heart rate, which can lead to heart failure, and sometimes an enlarged thyroid gland that can press on the windpipe and interfere with breathing [117].

Independent production of thyroid hormones and maternal hyperthyroidism may result .Inappropriate to foetal and neonatal hyperthyroidism due to trans placental transfer of stimulatory TSHR Abs [118,119]. Hyperthyroidism in new-borns occurs in about 1% of babies born to mothers with GD. Hypothyroidism is often not observed in new-borns of mothers with Graves' disease, and this may result from trans placental transfer of ant thyroid drugs circulating in the mother. Suppression of the hypothalamic-pituitary-thyroid axis from the transfer of thyroid hormones to the mother [120] .Thyroid storm produces the most severe manifestations of untreated hyperthyroidism and may cause infection and diabetes [121].

Toxic thyroid periodic paralysis is another uncommon problem of hyperthyroidism. It is a reversible disorder characterized by severe muscle weakness and hypokalaemia, episodes of periodic paralysis caused by hypokalaemia caused by trans cellular shift rather than the entire body's potassium depletion [122].

4.2.8 Treatment of hyperthyroidism during pregnancy

Maternal and foetal outcomes are directly related to the control of hyperthyroidism during pregnancy, mild hyperthyroidism, where the TSH is low but the FT4 is normal, does not require treatment.

Severely elevated thyroid hormones are treated with anti-thyroid drugs (beta-blockers, methimazole). The drugs cross the placenta in small amounts and can reduce the production of thyroid hormones for the foetus. Therefore, the lowest possible dose should be used to avoid hypothyroidism in the child. Medicines have harmful effects in some people, such as allergic reactions and patients with low white blood cells, which can reduce a person's resistance to infection and liver failure

in rare cases [123]. However, if the pregnant woman is unable to tolerate anti-thyroid drugs or cannot undergo radioactive iodine treatment, she may become a candidate to undergo thyroid surgery, although this procedure is not an option except for a few cases [124].

4.3 Levels of biochemical and hormonal factors of pregnant women with thyroid disease with a risk factor for recurrent abortion

There were significant differences in thyroid hormones in women with recurrent abortion compared to the control group.Table (3.4)

Abortion: The spontaneous loss of a foetus before it becomes viable and occurs at a rate of 15-20%, a spontaneous abortion is defined as the loss of a foetus weighing less than 500 grams, which equates to approximately 20-22 weeks of gestation. It is one of the most common complications after preterm birth [125].While known as recurrent spontaneous abortion (RSA), or anti-abortion, it is the loss of two or more clinically recognized consecutive pregnancies before the 20th week of gestational age. A study by (Jauniaux et al) found that post-HCG pregnancy loss occurs .Elevated serum B-HCG serum but prior to ultrasound examination or histological verification is defined as a biochemical loss occurring before the sixth week of gestation .Positive ultrasound examination or histological evidence of intrauterine pregnancy [126]. RSA is a multifactorial disorder caused by genetic factors or filters, endocrine damage, cervical shortening, thrombosis, polycystic ovary syndrome, obesity, luteinizing hormone (LH) or autoimmune disorders [127].Parental chromosomal abnormalities, thyroid hormones are essential for brain development during foetal life and early after birth. Low availability of maternal thyroid hormones may lead to

irreversible brain damage with consequent neurological abnormalities. Thyroid hormones also affect the eggs at the level of the follicular cells and the corpus luteal, which interferes with normal ovulation.

4.3.1 Hormones in recurrent abortion

4.3.1.1 In hypothyroidism

There is an increase in TSH levels and a decrease in both FT4 and FT3 thyroid hormone levels. Table (3.8.A).

These results point to several explanations by the reasons:-

First: Untreated hypothyroidism during pregnancy increases the risk of negative pregnancy complications.one such complication is recurrent miscarriage, in which the decrease in thyroid hormones is due to non-pituitary stimulation of thyroid hormone secretion and this is consistent with a study by (Glinoer et al) [12]. The increase in TSH indicates that the thyroid hormones (TH) in the circulation are not high enough to stop the stimulation of the hypothalamus to release TRH to the anterior pituitary gland to give the stimulation and secretion of TSH, thus the thyroid hormones are not sufficient to meet the needs of the mother and foetus resulting to termination of pregnancy [128,129].

Second: Because of the lack of iodine which reduces the biosynthesis of thyroid hormones, and thus the lack of food that reaches the foetus through the placenta which increases the failure of pregnancy.

Third: chronic autoimmune thyroiditis.

The association between miscarriage and autoimmune thyroid disease significantly affects pregnancy, and the relative risks of

miscarriage are three times higher in women with autoimmune thyroid disease than in healthy controls [130].

With the presence of thyroid antibodies, miscarriage may be associated with a reduced ability of thyroid function to adequately adapt to pregnancy-related changes because thyroid function reserves may be insufficient to meet the demand that occurs during pregnancy [131]. And chronic autoimmune infections are chronic diseases so that the body considers the thyroid gland and the hormones it secretes (T3, T4, TSH) dangerous to the body, so the body manufactures antibodies that target and attack thyroid cells and thus work to destroy them. Thyroid antibodies often appear when lymphocytes are present in the target organ [132]. Studies (Dantas et al) have shown that women with recurrent miscarriages have an increased number of T lymphocytes in the endometrium [133].These lymphocytes produce antibodies that target three different thyroid proteins

1- Thyroid peroxidase antibodies.

2- Antibody to thyroglobulin.

3- Antibodies to thyroid hormone.

These antibodies increase the incidence of thyroid dysfunction, miscarriage (pregnancy failure) and extension of postpartum thyroiditis [134].

4.3.1.2 In hyperthyroidism

While the results of the study indicated a decrease in the level of TSH and an increase in FT4 and FT3.Table (3.8.B)

These results point to two important reasons:

First: autoimmune thyroiditis, whereby antibodies to the thyroid gland stimulate the production of T3, T4 hormones increasingly more than the needs of the mother and foetus, these antibodies may cross the placenta and that the foetus sometimes has a rapid heart rate, which leads to failure pregnancy [135].

Second: Increased serum human placental gonadotropin levels. HCG is a glycoprotein produced primarily by the placenta and peaks at the end of the first trimester of pregnancy. HCG can stimulate the thyroid gland by binding to the thyrotropin receptor TSH of the thyroid cell membrane during pregnancy because of its structural similarity to TSH [136]. This leads to an increase in the secretion of thyroid hormones and a decrease in TSH in the blood. Elevated human placental gonadotropin levels in pregnant women are considered a sign of miscarriage. This is consistent with a study conducted by (Fantz et al).

4.4 Levels of biochemical and hormonal parameters of pregnant women with thyroid disease with risk factor hypertension

The results of the study indicated that there were significant differences in thyroid hormones compared to the control group .Table (3.5).

Hypertension during pregnancy which is diagnosed as high blood pressure, systolic 140 mm Hg and diastolic 90 mm Hg without proteinuria after 20 weeks of pregnancy .The thyroid gland directly affects all parts of the body, especially the heart, kidneys, and liver .The relationship of the thyroid gland to pressure and the strength of the heart rate is influenced by its secretions and when there is an imbalance in the

thyroid gland, it causes heart problems or makes existing heart conditions worse hypertension during pregnancy is associated with a wide range of maternal and foetal complications and is a common factor during pregnancy . A study by (Klein et al) found that high blood pressure during pregnancy is of great importance because it causes 16% of maternal deaths worldwide [137]. This factor has been associated with an increased risk of morbidity and mortality in mothers and children, not only during pregnancy but also after pregnancy [138,139].Several studies (Ashoor et al, Mannisto et al, Wilson et al) have demonstrated an association and an increased incidence of hypertension in mothers with hypothyroidism and hyperthyroidism [140,141,142,143]. Even slight differences in thyroid function can have important implications for pregnancy complications, including hypertension during pregnancy [144,145].

4.4.1 Hormones in hypertension

4.4.1.1 In hypothyroidism

A significant increase in the level of TSH and a decrease in the thyroid hormones FT3 and FT4. Table (3.9.A).

These results indicate that pregnant women who have a risk factor for gestational hypertension suffer from hypothyroidism .the mechanism by thyroid hormones may influence the onset of high blood pressure during pregnancy, From the study (Danzi et al) that investigated the cardiovascular effects of thyroid dysfunction. Whereas, hypothyroidism has been shown to be associated with increased cardiac contractility and increased systemic vascular resistance [146]. And endothelial dysfunction leading to endothelial-derived vasodilatation characterized by a decrease

in nitric oxide [147,148] .Leading to hypertension as well as ventricular hypertrophy leading to heart failure which leads to maternal death pregnant woman [149,150,151] .

4.4.1.2 In hyperthyroidism

A decrease in the level of TSH and an increase in FT3 and FT4. Table (3.9.B).

These findings suggest that women who have a risk factor for gestational hypertension have hyperthyroidism. In hyperthyroidism the heart beats stronger and faster, an arrhythmia in the heart can lead to high blood pressure and atrial fibrillation, which is an irregular heartbeat in the two upper chambers of the heart. The combination of a strong heartbeat and high blood pressure may lead to chest pain or angina [152]. High levels of thyroid hormones can cause endothelial dysfunction, which is known to play a pivotal role in the physiology of high blood pressure during pregnancy [123]. Studies (Burggraaf et al, Cesareo et al) have shown that patients with Graves' hyperthyroidism have reduced protective mechanisms against endothelial damage and thus show signs of endothelial cell activation and dysfunction [153,154,155,156].

4.5 Levels of biochemical and hormonal factors in pregnant women with thyroid disease with diabetes mellitus risk factor

There were significant differences in thyroid hormones compared to the control group. Table (3.6)

Gestational diabetes is an abnormal condition that affects the human body and involves an error in carbohydrate metabolism due to a

deficiency or absence of insulin secreted by the beta cells of the pancreas and as a result the body cannot use sugar (glucose) normally and was first discovered during pregnancy [157]. Glucose is a form of sugar that provides energy and can be obtained from food and the liver stores glucose. Blood glucose levels are controlled by the hormone insulin, a polypeptide hormone made up of amino acids secreted by the beta cells of the pancreas. The function of insulin is to transport glucose into the cells of the body to lower the level of sugar in the blood. Any imbalance in the production and use of insulin leads to diabetes [158,159]. The thyroid gland plays a vital role in helping to regulate balance and maintain the level of glucose in the blood, and gestational diabetes is more common in women who suffer from thyroid diseases [160,161]. Thyroid hormones regulate gluconeogenesis in the liver and glucose uptake in the intestine and surrounding tissues [162].In addition, it modulates messenger RNA and protein expression of glucose transporters secreting pathways that accelerate glycogenolysis and modulating circulating levels of insulin and counter regulatory hormones [163,164] .Thyroid disorders are linked to insulin resistance and changes in carbohydrate metabolism, which leads to diabetes. Another cause of insulin resistance is genetic causes. Insulin resistance may spread in the same family and is more common in cases of consanguineous marriage. Excessive intake of sugars, fats and soft drinks, in addition to psychological stressors and lack of sleep [123]. Glucose is transported in the mother's blood through the placenta to the foetus to provide energy. High blood sugar in the mother leads to high blood sugar in the foetus as well. In response to high levels of glucose, the foetus produces large amounts of insulin, which leads to problems in the excessive growth of the foetus and low blood sugar levels after birth [165].

4.5.1 Hormones in diabetes

4.5.1.1 In hypothyroidism

The results of the study indicated a significant decrease in thyroid hormones FT3 and FT4 and a decrease in the level of TSH in women with gestational diabetes as a risk factor. Table (3.10.A)

These results point to several reasons by the explanations:

First: women with hypothyroidism develop insulin resistance, and this resistance is caused by a reduced need to use insulin. The reason for this decrease is due to the refusal to enter the insulin into the cells through the insulin receptor, so the cell sends a signal to the pancreas to manufacture more insulin (its function is to transport sugar into the cells). Insulin builds up sugar in the blood, which leads to type 2 diabetes [(166)] .Or because of obesity, where the need to use glucose in the cells and muscles decreases due to the accumulation of fat in them, so the insulin receptor on the cells works to refuse the entry of insulin and because of incorrect nutrition of the pregnant mother and the decrease in the need to use glucose inside the cells leads to the accumulation of fat, which leads to diabetes from type 2 [(167)].

Second: autoimmune diseases of the thyroid gland, where the immune system attacks the pancreas and destroys the insulin-producing cells, and this leads to type 1 diabetes in pregnant women with Hashimoto's disease.

4.5.1.2 In hyperthyroidism

A decrease in the level of the hormone TSH and a significant increase in the hormones FT3, FT4 in women with the risk factor of gestational diabetes.in table (3.10.B).

This is due to the inverse relationship between thyroid hormones and insulin. When the thyroid hormones rise, the effectiveness of insulin decreases in reducing the level of sugar in the blood, and this leads to an increase in the level of sugar in the blood and the development of type 2 diabetes [168] .Or due to an autoimmune disease of the thyroid gland, which causes type 1 diabetes by attacking the antibodies of the cells responsible for insulin production in the pancreas. [169]

4.6 Levels of biochemical and hormonal parameters of pregnant women with thyroid disease with a risk factor for intrauterine growth restriction (IUGR) .

The results of the study indicated that there were significant differences in thyroid hormones compared to the control group. Table (3.7)

The environment in which the foetus develops is important for its long-term growth, maturation, health and neurodevelopment after birth. Several hormones including oestrogen, progesterone, insulin growth factor, and thyroid hormones carefully regulate foetal growth and metabolism during pregnancy by controlling the supply of nutrients that cross the placenta. In addition to foetal synthesis and hormones that regulate foetal growth, their regulation by the placenta plays a major role in the weakness and maturation of the developing brain. The growth of the foetus depends on several factors related to the mother, foetus and

placenta, especially the genetic background, nutrients, oxygen supply to the foetus, maternal nutrition, various growth factors and hormones [170]. Sub-optimal foetal growth is a major factor in disturbed brain development and many neurodevelopmental disorders of motor and cognitive impairment have their origins in the prenatal period [171,172]. Specifically, intrauterine growth restriction, defined as the inability of the foetus to reach its genetically determined size, is closely related to neurodevelopmental deficiency. Children exposed to IUGR are at high risk not only for neonatal death and cerebral palsy [173] .But also for other neurodevelopmental diseases including mental retardation and a wide range of learning difficulties and developmental behavioural disorders associated with the emergence of neuropsychiatric disorders later in life [174,175]. Many of these neurodevelopmental disorders are associated not only with the detrimental effect of brain development but also with the injury of the developing brain with intrauterine growth hyperplasia. Hormonal balance plays an important role in foetal growth, maturation, childbirth, new born adaptation and brain development [176] .Hormones act as maturational and nutritional signals that control tissue growth and differentiation and interact closely with the uterine environment. Hormonal imbalances due to placental abnormalities or chronic prenatal stress not only impair foetal maturation and development, but may also lead to intra partum and perinatal complications, psychological distress syndrome, abnormal blood sugar regulation, and pituitary axis response [33].

Thyroid hormones are necessary for the normal growth and development of the foetus, and even the presence of minor disorders in the state of the thyroid gland of the mother during pregnancy leads to an imbalance in the neurological development of the foetus [177,81,178] .

Because the effects of the thyroid condition affect the foetus at a time before the development of the thyroid gland in the foetus .Maternal thyroid function can affect growth in two different ways. Thyroid hormones influence the regulation of both human trophoblastic cell proliferation and differentiated function [179].

4.6.1 Hormones in Intrauterine growth restriction IUGR)

4.6.1.1 In hypothyroidism

A significant increase in the level of TSH and a significant decrease in the thyroid hormones FT4 and FT3 in women with hypothyroidism with intrauterine growth restriction factor. Table (3.11.A).

These results point to several reasons.

First: The foetus during the first trimester does not have a thyroid gland, so it depends on the thyroid hormones of the mother, and when there is a decrease in the levels of FT3 and FT4 of the mother, this leads to the passage of small amounts. From it through the placenta to the foetus, and this deficiency causes intellectual disability failure to thrive and foetal size restriction. This means that these hormones are not enough to meet the needs of both the mother and foetus [180].

Second: The T3 hormone plays a role in the development of the function of the placenta, as a deficiency of this hormone leads to the placenta insufficiency and its inability to provide the foetus's needs for nutrients and transport the oxygen necessary for its growth. Any defect in the supply of hormones to the foetus through the placenta .This abnormality in the placenta leads to physical disability, low infant

weight, and delay in neurodevelopment and this is consistent with a study conducted by (Nicolaides et al) [181].

Third: Autoimmune Thyroiditis: Thyroid autoimmunity can disrupt the normal adaptation of the immune system of the foetus and the mother unit, and may cause premature birth, resulting in low birth weight. Thyroid peroxidase antibodies destroy thyroid tissue. Thyroid hormones are necessary for the growth and maturation of foetal tissues, and this causes intrauterine growth retardation and this is consistent with a study by (Glinoer et al) [182,183].

4.6.1.2 In hyperthyroidism

The presence of a decrease in the level of TSH and an increase in the thyroid hormones FT3 and FT4 in women with hyperthyroidism with a risk factor for intrauterine growth restriction. Table (3.11.B).

It is due to an autoimmune disorder of the thyroid gland, in which abnormal thyroid antibodies lead to increased production of thyroid hormones, and these antibodies may cross the placenta and stimulate the thyroid gland in the foetus. As a result, the foetus sometimes has a fast heart rate and is not growing normally. The thyroid gland in the foetus may enlarge to form a goitre .Rarely, the goitre is so large that it makes swallowing difficult for the foetus and causes too much fluid to build up in the membranes surrounding the foetus (hydrocephalus) which leads to the onset of early labour and obstruction in the foetus. The neurological and physical development of the foetus is consistent with a study by (Leung et al) [184,185].

4.7 Levels of biochemical and hormonal parameters of risk factors pregnant women

There were significant differences between intrauterine growth restriction factor, abortion, growth restriction, hypertension and diabetes mellitus. Table (3.12).

Intrauterine growth restriction is a term used to describe a condition in which the foetus does not grow as quickly as it should in the womb, and the new-borns are smaller than normal during pregnancy and weigh less for their gestational age [(186)]. The reason for intrauterine growth restriction may be due to problems that occur in the placenta that prevent it From providing the foetus with adequate food and oxygen, which sometimes leads to miscarriage of the foetus. Poor placental function occurs due to high arterial blood pressure in the mother and severe malnutrition in the mother.

The presence of a chronic disease in the mother, such as type 1 diabetes or disorders of the immune system, is one of the main factors for poor placental function and its impact on the development of the foetus. Preeclampsia is one of the well-known reasons for the cessation of the growth of foetuses inside the womb.

4.8 The effect of body mass index (BMI) on levels of biochemical parameters of pregnant women with risk factors

They were classified into three groups, those with a BMI(≤25 Kg /m2) normal weight were classified as group A and the number of this group in patients was 20 and in control 9, and those with a BMI of(> 25-30 Kg/m2) overweight were classified as group B. The number of users

of this group was 35 patients and control 21, while those over (>30Kg/m2) obese as group C, the number of this group in patients was 60 and in control 20.Table (3.1).

Hypothyroidism is a pathological condition that leads to insufficient production of thyroid hormones, upsetting the normal balance of chemical reactions in the body. Delaying treatment for a long time can cause a number of health problems such as obesity. A low metabolic rate in a patient with hypothyroidism is generally associated with weight gain and excess fat accumulation. Most of the excess weight gained in thyroid patients is due to fluid retention within the body. Hypothyroidism may also affect kidney function, increasing fluid retention in the body. Also, weight gain caused by hypothyroidism is usually excessive [(187)]. As for hyperthyroidism, obesity is reversed, and the patient becomes thin despite eating it in large quantities. The reason for this is hormonal imbalance, which is an increase in the thyroid gland's secretion of its hormones as a result of hyperthyroidism. Hyperthyroidism can speed up the body's metabolic rate, which leads to weight loss, although the appetite or the amount of food eaten remains unchanged from normal [(188)].

BMI results appeared no significant differences in the factor of hypertension and diabetes when comparing BMI groups, while the results showed no significant differences in the factor of recurrent miscarriage when comparing the normal factor, overweight and obesity in addition to being statistically significant in intrauterine growth restriction when comparing normal and overweight . Events occurring in utero are known to have long-term effects on disease risk later in life [(189)]. Although there are strict recommendations for overweight and obese pregnant women to reduce weight gain, women who were

overweight before pregnancy are more likely to exceed recommendations and have a higher risk of complications [(190)]. Maternal obesity is associated with an increased risk of perinatal mortality and genetic disorders. The most common complications are foetal death in utero, genetic disorders, miscarriage, and intrauterine growth restriction [(191)]. A study by (Armitage et al) found that hyperglycaemia and increased levels of free fatty acids and amino acids lead to permanent changes in appetite control, neuroendocrine functioning or energy metabolism, leading to a risk of obesity (with risks of cardiovascular disease). bloody later in life [(192)]. Health problems and affect the regularity of the menstrual cycle and the amount of ovulation with each menstrual cycle. Where fatty tissue stores male and female hormones and leads to a disturbance in the menstrual cycle and affects the fertility of women, as there are many cases in which women delay pregnancy due to polycystic ovaries and the most important causes of obesity or pregnancy, it does not continue because of the poor quality of the egg leading to abortion onset of pregnancy overweight and obesity during pregnancy lead to an increase in all pregnancy complications, as obesity increases the rate of miscarriage and leads to an increase in insulin resistance during pregnancy [(193)] .Thus the emergence of gestational diabetes, which is more common in obese women, and obesity also increases the rates of preeclampsia .Hypertension and urine albumin Preeclampsia is one of the diseases associated with obesity, and all these factors due to obesity double the risk of miscarriage. A recent study between obesity and exposure to repeated miscarriages found that an obese pregnant woman was 60% more likely to miscarry again than normal-weight pregnant women [(194)]. As for intrauterine growth restriction factor, obese mothers have been linked to poor brain development and behavioural changes in children. Mothers who are

overweight and who are prone to obesity are more likely to have a child with developmental delays and children are more likely to have ADHD, lack focus, and have difficulty with organizational feelings [195]. Maternal obesity poses a great health risk to the foetus, and its impact increases according to the degree of obesity. An unbalanced diet during pregnancy contributes not only to abnormal foetal development and the subsequent increase in neonatal morbidity and mortality, but also to increased morbidity during childhood, adolescence and adulthood. Because of the difficulties in recognizing and monitoring these foetuses, both before and after birth, and because of the increased mortality and morbidity associated with intrauterine growth restriction (IUGR), it remains a serious multidisciplinary problem [196] .A systematic effort to lose weight is necessary to avoid the transmission of obesity from one generation to the next. Achieving this goal is likely to result in a drastic reduction in foetal and neonatal morbidity and mortality and improved follow-up outcomes and future pregnancies.

4.9 Age distribution of pregnant women with risk factors

The ages of patients with risk factors ranged between (15-43) years, and they were divided into three age groups (15-24), (25-34) and (35-43).

Women with intrauterine growth-restricting factor were most prevalent in the age group (15-24) years with a rate of 13.9%, while women with recurrent miscarriage factor were most prevalent in age group (25-34) with a mean of 12.1% and in group (35-43) Pregnant women with a hypertensive factor were the most prevalent in this age group at 13%. As shown in the table below (3.13). Most age-related thyroid disorders are hypothyroidism, which is more common in older

women, while hyperthyroidism is more common in younger women. Intrauterine growth restriction occurs in the age group (15-24). This is due to changes in hormones, especially female hormones (estrogen and progesterone) or due to poor nutrition, and the weight of the expectant mother, these factors further restrict intrauterine growth during this age group.

While a woman's age greatly affects fertility and pregnancy, a gradual decline in a woman's fertility rate occurs as she gets older. And due to environmental factors, unhealthy diet and obesity problems, all this increases miscarriage complications .Blood pressure usually increases with age because the body's ability to absorb the force of contraction decreases. Additionally, an individual's specific blood volume may contribute to high blood pressure [72].Or because the blood vessels become stiffer with age, and when this happens, the pressure rises, which is common in older pregnant women.

4.10 Levels of Educational state pregnant women with thyroid disorder and the control group

There are significant differences in the levels of educational attainment of pregnant women. As shown in Table (3.14).

Education for women brings personal benefit in several aspects, the most important of which is raising health awarenesss [197] . As the educated woman possesses sufficient awareness and keenness to protect herself before pregnancy and protect the fetus during pregnancy and after childbirth by adhering to periodic reviews in consulting a doctor and taking vaccinations and not taking drugs without consulting from In

order to complete pregnancy and avoid exposure to negative pregnancy results. Education for a woman makes her aware of how to deal with and protect her child, as well as protect herself from many complications that occur during pregnancy [198].

4.11 The effect of the economic situation on the financial income of pregnant women

The levels of the financial status of the pregnant woman with thyroid disorder and the control group were divided into three levels, namely, low, medium, and high financial status.Figure (3.15).

One of the most important factors related to medical outcomes is financial status.[199] When financial income is low, medical care is not enough, and in light of the recent great recession during which many families have been in financial distress, the decline in average family income and high unemployment rate has led to the deterioration of the financial situation. Especially among pregnant women because this leads to negative results.Low-or middle-income women are less likely to receive antenatal care, resulting in poor outcomes during pregnancy such as miscarriage, premature birth, preeclampsia, gestational diabetes, and death [200]. This is due to the lack of health care required in hospitals. In order to address this problem, it is necessary to secure good health care and a medical assistance system for people with limited income to avoid harm to the pregnant woman or foetus, which affects the psychological and social status of the family and society [201,202].

CHAPTER FIVE

Conclusions and Recommendations

CONCLUSIONS

1. A relationship between thyroid hormones and pregnancy, where there was a significant difference in TSH, FT4 and FT3 compared to the control group.
2. Hypothyroidism leads to an increase in TSH and a significant decrease in FT3 and FT4 hormones compared to the control group by 75%.
3. Hyperthyroidism leads to a significant decrease in TSH and a significant increase in FT3 and FT4 compared to the control group by 40%.
4. The relationship between thyroid disease and risk factors, as the prevalence of recurrent miscarriage was 22%, hypertension 18%, diabetes mellitus 10%, and intrauterine growth restriction 25% in the case of hypothyroidism, while the prevalence was.. Of the miscarriages, recurrent hyperthyroidism was 8%, hypertension 12%, diabetes mellitus 15%, and intrauterine growth restriction 5%.
5. There is an effect of the factor of repeated abortion on weight gain and obesity in pregnant women with hypothyroidism.
6. The incidence of growth restriction factor in pregnant women with hypothyroidism was higher in the age group 15-24 years by 13.9%, and the rate of recurrent miscarriage 12.1% which is the highest in the age group 25-34 years while hypertension was 13%. , which is highest in the 35-43 age group.
7. Relationship between intrauterine growth restriction, recurrent miscarriage, diabetes and hypertension in pregnant women with hypothyroidism.

5.1 Recommendations

A study of thyroid function during pregnancy is recommended in the following cases:

1- Thyroid hormones in pregnant women who have chronic thyroid dysfunction.
2- Women with autoimmune disorders of the thyroid gland.
3- Relationship between placental abruption and thyroid disease.
4- Parathyroid glands for pregnant women who have pressure associated with pregnancy.

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الخلاصة

صُممت هذه الدراسة للتحقيق في العلاقة بين هرمونات الغدة الدرقية والحمل ، وكذلك مدى انتشار وتأثير اختلال وظائف الغدة الدرقية لدى النساء الحوامل مع وجود عوامل خطر للإجهاض المتكرر ، وتقييد النمو داخل الرحم ، وارتفاع ضغط الدم ومرض السكري الذي يحدث أثناء الحمل. تم اخذ 115 حامل من النساء المصابات بعوامل الخطر موزعة على فترات مختلفة من الحمل ، وتراوحت أعمارهن بين 15-43 سنة ، و 50 امرأة حامل طبيعية تتراوح أعمارهن بين 15-43 سنة كمجموعة ضابطة. أجريت هذه الدراسة في مستشفى النسائية والتوليد في كربلاء خلال الفترة (ايلول) 2020/9/1 الى (آذار) 2021/3/1 حيث تم قياس هرمونات الغدة الدرقية TSH، FT4، FT3 باستخدام جهاز Mini Vedas لمصل النساء الحوامل. أظهرت نتائج الدراسة أن هناك علاقة بين هرمونات الغدة الدرقية والحمل ، وجد فرق معنوي في TSH و FT4 و FT3 مقارنة بالمجموعة الضابطة ، أدى قصور الغدة الدرقية إلى زيادة في هرمون TSH وانخفاض كبير في هرمونات FT4،FT3. مقارنة بالمجموعة الضابطة بنسبة 75٪ ، بينما أدت الزيادة في هرمونات الغدة الدرقية (فرط نشاط الغدة الدرقية) الى انخفاضًا معنويًا في TSH وزيادة معنوية في FT3 و FT4 مقارنة بالمجموعة الضابطة بنسبة 40٪. كما وجدت علاقة بين قصور الغدة الدرقية وفرط نشاط الغدة الدرقية مع عوامل الخطر ، حيث بلغ انتشار الإجهاض المتكرر 22٪ ، وارتفاع ضغط الدم 18٪ ، وداء السكري 10٪ ، وتقييد النمو داخل الرحم 25٪ في قصور الغدة الدرقية ، بينما كان انتشار الإجهاض المتكرر في فرط نشاط الغدة الدرقية. 8٪ ، ارتفاع ضغط الدم 12٪ ، السكري 15٪ ، تقييد النمو داخل الرحم 5٪ ، كما أظهرت نتائج الدراسة تأثير الإجهاض المتكرر على زيادة الوزن والسمنة. ووجد أن نسبة حدوث عامل تقييد النمو كانت أعلى في الفئة العمرية 15-24 سنة بنسبة 13.9٪ ، ومعدل الإجهاض المتكرر 12.1٪ هو الأعلى في الفئة العمرية 25-34 سنة بينما كان ارتفاع ضغط الدم 13٪. ، وهي الأعلى في الفئة العمرية 35-43. وكذلك وجود علاقة بين تقييد النمو داخل الرحم والإجهاض المتكرر والسكري وارتفاع ضغط الدم.

وزارة التعليم العالي والبحث العلمي

جامعة كربلاء

كلية التربية للعلوم الصرفة

قسم الكيمياء

تأثير هرمونات الغدة الدرقية على الحوامل في محافظة كربلاء

رسالة

مقدم لكلية التربية للعلوم الصرفة ، جامعة كربلاء ،مقدمة في طلب جزئي للحصول على درجة الماجستير في الكيمياء الحيوية

أعدت بواسطة

رباب سلمان الخفاجي

(بكالوريوس كيمياء جامعة كربلاء 2017-2018)

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