The prevelance of thyroid dysfunction in patient with recurrent miscarriage in first trimester

Written by:

Khansaa Haider Yahya

Noor Amaar Hameed

Mariam Kassem Atia

Aya Haider Jabar

Supervised by:

Dr.Enass Saleh Al-Khayat

بسم الله الرحمن الرحيم

{يرفع الله الذين امنوا والذين أوتوا العلم درجات}

صدق الله العلي العظيم

(سورة المجادلة / اية ١١)

"ALLAH will raise up, to ranks those of you who believe and who have been granted knowledge"

(Al- Mujadalah:11)

Acknowledgment

Everything I am, or ever will be, I owe it " to my mother". My success is because of her, and my failures are because of me. To you mother, and this is just the beginning. & To my biggest supporter, who keeps saying "I am proud of you" in my failures before my successes. To my father. We are forever indebted to our parents, who have always kept me in their prayers.

I would like to thank the chairman of our committee, Dr.Enass Saleh Al-Khayat , for her support, outstanding guidance and encouragement. I would also like to express our gratitude and appreciation to the other members of my instructors.

List of contents

Abstract

The prevelance of thyroid dysfunction in patient with recurrent miscarriage in first trimester.

Purpose :

Thyroid disturbances are common in women during their reproductive years. Thyroid dysfunction interferes with human reproductive physiology, reduces the likelihood of pregnancy and adversely affects pregnancy outcome, thus becoming relevant in the algorithm of reproductive dysfunction. This Review highlights the "gap' in knowledge regarding the contribution of thyroid dysfunction in reproduction.

Literature Reviewed:

Following implantation, the maintenance of the pregnancy is dependent on a multitude of endocrinological events that will eventually aid in the successful growth and development of the fetus. It is estimated that approximately 8-12% of all pregnancy losses are the result of endocrine factors. Autoimmune thyroid disease is present in around 4% of young females and up o 15% are at risk because they are thyroid antibody-positive. There is a strong relationship between thyroid immunity on one hand and infertility, miscarriage , and thyroid disturbances in pregnancy and postpartum, on the other hand. Even minimal hypothyroidism can increase rate of miscarriage and fetal death and may also have adverse effects on later cognitive development at the offspring. Hyperthyroidism during pregnancy may also have adverse consequences Summary: Pregnant women with subclinical hypothyroidism or thyroid antibodies have an increased risk of complications, especially pre-eclampsia, perinatal mortality, and miscarriage. Universal screening for thyroid hormone abnormalities is not routinely recommended at present, but thyroid function must be examined in females with fetal loss or menstrual disturbances Practitioners providing health care for women

should be alert to thyroid disorders as an underlying Etiology for recurrent pregnancy loss. [1]

Objective:

To assess the prevelance of thyroid dysfunction in women with history of recurrent miscarriage in first trimester .

Study design: retrospective cross sectional study .

Setting : AL-Nasiriyah city at May of 2021

Patients and methods :

In this study ,40 women with history of recurrent miscarriage during first trimester 32 cases have normal TSH level while 8 cases have abnormal TSH level which divided into 5 cases hypothyroidism and 3 cases hyperthyroidism

CHAPTER ONE
INTRODUCTION

1.1 Introduction

1.1.1 Definition of miscarriage :

Miscarriage is a spontaneous loss of pregnancy before the fetus reaches viability. ie. gestation age up to 20 weeks or a weight of 500 g. The World Health Organization considers birth weight of 500 g to be used to define visibility in developing countries, where gestational age is not certain . Spontaneous pregnancy loss is often a common occurrence. Large numbers of pregnancies are lost before clinical confirmation, whereas around 15% of all clinically diagnosed pregnancies result in spontaneous abortion, and live births are seen in about 30% of all conceptions . Spontaneous miscarriage is a physical and emotional trauma for the woman as well as for the family, especially when faced with recurrent losses.

1.1.2 Definition of recurrent pregnancy loss :

(RPL) is traditionally referred to as three or more consecutive pregnancy losses before 20 weeks of gestation. (Ectopic, molar, and biochemical pregnancies are excluded.)

1.1.3 Epidemiology

1.1.3.1 Incidence of RPL affects 04-1% of couples . The risk of losing the pregnancy is more in early gestations, mostly in the first trimester. There is 22-57% of risk of miscarriage with pregnancy less than 6 weeks 10)

1.1.3.2 Prevalence of RPL is very uncertain since there is no nationwide registration of miscarriages or RPL in most of the places and many early miscarriages will not be treated in hospitals and are thus not registered. However, from various studies the prevalence of RPL is found to be between 0.6% and 2.3%

1.1.3.3 Risk Factors and Etiology The couple with RPL has main concern for cause and risk of recurrence. Etiologies for RPL. include genetic

abnormalities, endocrine diseases, uterine anomaly. antiphospholipid syndrome (APS), thrombophilia's (heritable or acquired), infections, immunologic abnormalities, and environmental factors. Also increased number of previous miscarriages, maternal age, lifestyle factors, and familiar factors are risk factors for RPL.

1.1.3.4 Number of Previous Miscarriages The risk of future pregnancy losses can be predicted by the obstetric history of women. It has been reported that with every miscarriage, the risk of subsequent pregnancy loss increases . Recurrent miscarriages occur generally at same gestation age in each pregnancy. In epidemiological studies three or more pregnancy losses are being considered for RPL. but clinical evaluation should be considered after two early pregnancies losses .

1.1.3.5 Maternal Age Change in social and lifestyle leads to a trend of delay in child birth, Varies studies show that increasing maternal age is associated with the incidence of miscarriage . The miscarriage rates in women with RPL were almost identical in women -35 years and 36-39 years but increased to 70% in women of age 40-44 years . It shows that the impact of age after 40 years is the strongest prognostic factor in RPL. The age of women with RPL has a role in the findings of Studies of endocrinological and nongenetic immunological biomarkers, With progressing age the ovarian reserve as well as secretion of ovarian steroid hormones will be reduced. Immune parameters such as production of autoantibodies and T helper 2 cytokines are affected both directly by increased maternal age and diminished secretion of ovarian steroids .

1.1.3.5 Lifestyle Factors It has been observed from different epidemiological studies that RPL. is associated with obesity, high intake of caffeine or alcohol daily, use of nonsteroidal anti- inflammatory drugs, and excessive high impact physical exercise. The rate of pregnancy loss is also affected by social class and occupation. These women are at high risk of physical or psychical stress. It is also seen that women with PCOS exhibit an increased rate of miscarriage and RPL, but studies also showed the miscarriage rate in PCOS is not dependent on polycystic

ovarian pathology if obesity is adjusted. Previous history of infertility also has an increased risk of miscarriage .

1.1.3.4 Family History There are studies suggesting that RPL. is increased in first-degree relatives . and Christiansen et al. found the RPL. frequency significantly increased in sisters of RPL . Kolte et al. found in their study a clinical miscarriage rate of 25,3% per pregnancy in siblings of RPL women, which is significantly higher ($p < 0.001$) than the rate of 13.1 in the background population. It is also suggested that most RPL cases are probably caused by several genetic polymorphisms, each contributing only modestly to the total RPL risk, ie, multi- factorial inheritance .

1.1.4 Etiopathogenesis

1.1.4.1 Genetic Causes

Genetic factors comprise approximately 3.5-5% of RPL Etiologies. These include structural chromosomal abnormalities like translocations, insertions, inversions, and mosaicism of which parental balanced and Robertsonian translocations have been reported as common causes of RPL. Monogenic disorder have also been reported as rare causes of repeated pregnancy loss. It is important to evaluate the karyotype of both partners as well as the abortus. Genetic counselling is imperative in such cases by a geneticist or a genetic counsellor, and preimplantation genetic diagnosis or donor gametes can be given as an option .

1.1.4.2 Anatomical Causes

Twelve to sixteen percent of RPL cases are associated with anatomic abnormalities. These include congenital uterine anomalies (incomplete mullerian fusion or septum, uterine artery anomalies, DES exposure, und cervical insufficiency) and acquired anomalies (intrauterine adhesions and uterine fibroids or polyps). Defective vascularization of endometrium leads to improper placentation and finally pregnancy loss. Congenital uterine anomalies are usually also linked with second trimester pregnancy losses. Septate uterus accounts for 76% risk of spontaneous abortion in affected women and it is the commonest uterine anomaly associated with RPL. Other uterine anomalies, like

bicornuate, unicornuate, and didelphous uterus, have very low risk for RPL Intrauterine adhesions result in early pregnancy losses due to its impact on placentation. It is found that RPL. results if there is sub-mucosal fibroid or intramural fibroids more than 5 cm size .

1.1.4.3 Endocrine Causes

Endocrinological causes are implicated for approximately 17-2 of RPL. These include luteal phase insufficiency, androgen disorder, thyroid disorders, und increased serum levels of prolactin, Also metabolic diseases such as polycystic ovarian syndrome (PCOS) and diabetes mellitus are included here Luteal phase defect, characterized by insufficient progesterone production resulting in retarded endometrial development, is thought to be associated with RPL. But there is no accurate test to evaluate the exact effect of LPD on RPL. In women with PCOS, there may be increase in level of luteinizing hormone or androgens or both leading to premature oocytes aging and defect in endometrium maturation . There is correlation between insulin resistance and the resultant hyperinsolinnemia in PCOS and diabetes mellitus with RPL, as there is the decreased in spontaneous pregnancy loss after getting treatment with the insulin sensitizing oral hypoglycaemic agents , Untreated hypothyroidism is clearly related with spontaneous miscarriage and RPL, but the association between antithyroid antibodies and RPL. in euthyroid patients is not established .

1.1.4.4 Thrombotic Causes

Factor V Leiden mutation and mutations in the gene encoding methylene tetrahydrofolate reductase (MTHFR) and prothrombin gene are the most common thrombotic Etiology. The heritable thrombophilia's associated with RPL are increased levels of serum homocysteine, prothrombin promoter mutations, protein C and protein S deficiencies, and antithrombin mutations. Hyperhomocysteinemia and activated protein C resistance are linked with acquired thrombophilia's The proposed mechanism is thought to be thrombosis of spiral arteries, and the intervillous space on the maternal side of the placenta can impair adequate placental perfusion. The resulting abnormalities of the

uteroplacental circulation may cause late fetal loss, intrauterine growth restriction, placental abruption, or preeclampsia .

1.1.4.5 Other Causes

Environmental and occupational exposures to organic solvents, toxins, ionizing radiation, and medications can affect uterine receptivity which may have a role in causation of RPL. However, no strong co-relation has been found between RPL. and occupational factors, stress, or chemicals factors as most evidence in this respect is retrospective Smoking, alcohol, and caffeine addiction are associated with RPL. in a dove-dependent manner, or they also may act synergistically to increase sporadic miscarriages. [2]

1.1.5 Thyroid gland

1.1.5.1 Surgical Anatomy

The normal thyroid gland weighs 20–25 g . The adult thyroid gland is brown in color and firm in consistency and is located posterior to the strap muscles.The thyroid lobes are located adjacent to the thyroid cartilage and connected in the midline by an isthmus that is located just inferior to the cricoid cartilage. The functioning unit is the lobule supplied by a single arteriole and consists of 24–40 follicles lined with cuboidal epithelium. The follicle contains colloid in which thyroglobulin is stored . The arterial supply is rich, and extensive anastomoses occur between the main thyroid arteries and branches of the tracheal and oesophageal arteries . There is an extensive lymphatic network within and around the gland. (3)

1.1.5.2 Physiological Thyroxine

The hormones tri-iodothyronine (T3) and l-thyroxine (T4) are bound to thyroglobulin within the colloid. Synthesis within the thyroglobulin complex is controlled by several enzymes, in distinct steps:

- trapping of inorganic iodide from the blood;
- oxidation of iodide to iodine;

● binding of iodine with tyrosine to form iodotyrosine;

● coupling of monoiodotyrosines and di-iodotyrosines to form T3 and T4.

When hormones are required, the complex is resorbed into the cell and thyroglobulin is broken down. T3 and T4 are liberated and enter the blood, where they are bound to serum proteins: albumin, thyroxine-binding globulin (TBG) and thyroxine-binding prealbumin (TBPA). The small amount of hormone that remains free in the serum is biologically active. The metabolic effects of the thyroid hormones are due to unbound free T4 and T3 (0.03% and 0.3% of the total circulating hormones, respectively). T3 is the more important physiological hormone and is also produced in the periphery by conversion from T4. T3 is quick acting (within a few hours), whereas T4 acts more slowly (4–14 days).

The pituitary–thyroid axis Synthesis and release of thyroid hormones from the thyroid is controlled by thyroid stimulating hormone (TSH) from the anterior pituitary. Secretion of TSH depends upon the level of circulating thyroid hormones and is modified in a negative feedback manner. In hyperthyroidism TSH production is suppressed, whereas in hypothyroidism it is stimulated. Regulation of TSH secretion also results from the action of thyrotrophin-releasing hormone (TRH) produced in the hypothalamus.

Thyroid-stimulating antibodies A family of IgG immunoglobulins bind with TSH receptor sites (TRAbs) and activate TSH receptors on the follicular cell membrane. They have a more protracted action than TSH. (16–24 versus 1.5–3 hours) and are responsible for virtually all cases of thyrotoxicosis not due to autonomous toxic nodules. Serum concentrations are very low but their measurement is not essential to make the diagnosis.

Serum thyroid hormones Serum TSH TSH levels can be measured accurately down to very low serum concentrations with animmunochemiluminometric assay. Interpretation of deranged TSH

levels depends on knowledge of the T3 and T4 values. In the euthyroid state, T3, T4 and TSH levels will all be within the normal range. Florid thyroid failure results in depressed T3 and T4 levels, with gross elevation of TSH. Incipient or developing thyroid failure is characterised by low normal values of T3 and T4 and elevation of TSH. In toxic states, the TSH level is suppressed and undetectable . T3 toxicity (with a normal T4) is a distinct entity and may only be diagnosed by measuring T3, although a suppressed TSH in the presence of normal T4 suggests the diagnosis.

Thyroid autoantibodies Serum levels of antibodies against thyroid peroxidase (TPO) and thyroglobulin are useful in determining the cause of thyroid dysfunction and swellings. Autoimmune thyroiditis may be associated with thyroid toxicity, failure or euthyroid goiter. Levels above 25 units/mL for TPO antibody and titres of greater than 1:100 for antithyroglobulin are considered significant, although a proportion of patients with histological evidence of lymphocytic (autoimmune) thyroiditis are seronegative. The presence of antithyroglobulin antibody interferes with assays of serum thyroglobulin, with implications for follow-up of thyroid cancers. TSH receptor antibodies (TSH-Rab or TRAB) are often present in Graves' disease. They are largely produced within the thyroid itself. (3)

The thyroid gland during pregnancy hCG may suppress thyroid-stimulating hormone (TSH) in early pregnancy because they share a common α-subunit. The thyroid remains normally responsive to stimulation by TSH and suppression by tri-iodothyronine (T3). There is a threefold rise in the thyroid's clearance of iodine, allowing the absolute iodine uptake to remain within the non-pregnant range. Thyroid-binding globulin concentrations double during pregnancy, but other thyroid-binding proteins do not increase. Overall, free plasma T3 and thyroxine (T4) concentrations remain at the same levels as outside pregnancy (although total levels are raised) and most pregnant women are euthyroid. Free T4 may fall in late gestation .Calcitonin, another thyroid hormone, rises during the first trimester, peaks in the second and falls thereafter, although the changes are not large. It may contribute to the regulation of 1,25 dihydroxyvitamin D. (4)

The thyroid gland enlarges in up to 70% of pregnant women; this varies according to iodine intake. Iodine uptake by the thyroid is increased threefold, urine excretion increases, and iodothyronines are transferred to the fetus, thus plasma inorganic iodide levels in the mother decrease . Concentrations of thyroid-binding globulin double in pregnancy (70). Concentrations of total tri-iodothyronine (T3) and thyroxine (T4) are increased in very early pregnancy then decrease to the non-pregnant range. T3, T4, and TSH do not cross the placental barrier and therefore have no direct effect on fetal thyroid function.(5)

1.1.5.3 Thyroid abnormalities and recurrent pregnancy loss

1.1.5.3.1 Hypothyroidism

Hypothyroidism complicates up to 3% of pregnancies, of which 0.3–0.5% is overt and 2.0–2.5% is subclinical hypothyroidism. When iodine intake is sufficient, the most common cause of hypothyroidism during pregnancy is chronic autoimmune thyroiditis whereas a smaller proportion is due to iatrogenic causes including surgery to treat thyroid cancer or nodules or radioactive iodine ablation to treat hyperthyroidism. Pregnant women or women planning pregnancies are diagnosed with overt hypothyroidism when they have elevated TSH levels with low free T4 concentrations, preferably defined with pregnancy-specific reference intervals. However, pregnant women with TSH over 10 mIU/l are always diagnosed with overt hypothyroidism, irrespective of free T4 concentrations. Subclinical hypothyroidism is diagnosed when TSH is elevated but less than 10 mIU/l and fT4 concentrations are normal.(6,9)

Overt and subclinical hypothyroidism as well as increases in maternal TSH concentrations have been associated with increased risk of miscarriages/fetal losses,hypertensive disorders of pregnancy,placental abruptions,preterm birthand poor neurological development in the offspring.Overt hypothyroidism has also been associated with maternal anemia and postpartum hemorrhage,(7) and subclinical hypothyroidism with cesarean sections,(11) gestational diabetes breech

presentation,infants being small for gestational age,(8) fetal distress,neonates needing intensive care treatmentand respiratory distress syndrome.However, some studies have found no association between adverse perinatal outcomes and hypothyroidism.

Due to the well-established associations between overt hypothyroidism and adverse pregnancy outcomes, overt hypothyroidism should be promptly treated to attempt to mitigate these known risks.(6,9) However, there is debate about whether to treat all women with subclinical hypothyroidism. Two different strategies are proposed: to treat everyone (9) or to treat women with subclinical hypothyroidism and positive thyroid antibodies.(6)Up to 40% of women with positive thyroid antibodies develop hypothyroidism during or immediately after pregnancy, but most studies evaluating the association between subclinical hypothyroidism and pregnancy outcomes have been cross-sectional and based on first trimester measures of thyroid function. Therefore, more information is needed to determine whether hypothyroidism detected in the first trimester will progress, which factors predict disease progression, and if some women switch from hypothyroidism to euthyroidism as pregnancy continues.

1.1.5.3.2 Hyperthyroidism

Hyperthyroidism occurs in 0.1–1.0% of all pregnancies and is diagnosed when TSH concentrations are low or suppressed along with elevated fT4 or free triiodothyronine (in overt disease) or with normal thyroid hormone levels (in subclinical disease). Graves' disease, an autoimmune condition characterized by stimulation of the thyroid gland by TSH receptor antibodies (TRAbs), is the most common cause of hyperthyroidism among fertile-aged women.(6) Other reasons include toxic multinodular goiter, toxic adenoma, thyroiditis or struma ovarii. As untreated Graves' disease can lead to ovulatory dysfunction and infertility, a new-onset of Graves' is thought to be rare in pregnancy.A more common condition, gestational (transient) hyperthyroidism, occurs in up to 1–3% of all pregnancies and is probably due to the physiologic

thyroidal stimulation by high human chorionic gonadotropin levels in early pregnancy. Notably, up to 50% of women with hyperemesis gravidarum (severe nausea and vomiting in early pregnancy) have transient hyperthyroidism.(6,9)

Distinguishing between new-onset or recurring Graves' disease in pregnancy and gestational hyperthyroidism may be difficult. Symptoms associated with Graves' disease (goiter or eye symptoms) as well as previous history of thyroid disease help in differentiating between Graves' disease and gestational hyperthyroidism, as gestational hyperthyroidism is more common among women without history of thyroid diseases. Elevated TRAb titers are rarely present in gestational hyperthyroidism, so their presence can help confirm Graves' disease in pregnancy.(6,9)

Hyperthyroidism is associated with increased risk of pregnancy complications, including miscarriages, preeclampsia, low birth weight or fetal growth restriction and maternal cardiac dysfunction, with risks increasing with poorer hyperthyroidism control. However,gestational hyperthyroidism has not been associated with adverse pregnancy outcomes.(10)

Autoimmune Thyroiditis

Approximately 11–15% of all fertile aged women have positive thyroid antibodies, either thyroid peroxidase antibodies (TPO-Abs) or thyroglobulin antibodies (TG-Ab), which act as a marker of silent autoimmune thyroiditis. Up to 20–40% of all women with positive thyroid antibodies develop hypothyroidism during pregnancy or immediately postpartum, and generally women with autoimmune thyroiditis have higher TSH concentrations at baseline. Notably, TPO-Ab and TG-Ab concentrations decrease as pregnancy progresses, so false-negative findings regarding thyroid autoimmunity are possible in late gestation.

Thyroid antibody positivity has been associated with increased risk for miscarriages, perinatal mortality and preterm birth. TPO-Ab positivity in euthyroid women is associated with placental abruptions, very early

preterm delivery, neonatal respiratory distress and externalizing problems, for example, attention problems and aggressive behavior, in children. However, most of these studies evaluated thyroid function only once during pregnancy, so the effect of hypothyroidism as the underlying reason for these associations cannot be ruled out.

The effect of levothyroxine treatment among TPO-Ab-positive euthyroid women to reduce miscarriages has been studied in a few trials, with generally encouraging results. In one trial, risk for preterm delivery risk was also reduced. Among women undergoing in vitro fertilization, the pregnancy and delivery rates of TPO-Ab-positive and -negative women are generally similar and levothyroxine treatment of TPO-Ab-positive women did not improve delivery outcomes.However, women undergoing assisted reproduction with TPO-Ab positivity and miscarriage had higher prepregnancy TSH than those with successful pregnancies. Overall, these studies suggest that the association between TPO-Ab positivity and adverse outcomes might be influenced by the presence of hypothyroidism, so levothyroxine might be improving pregnancy outcomes by addressing hypothyroidism rather than a direct effect related to antibody status. More studies with longitudinal follow-up are needed to demonstrate whether thyroid autoimmunity is associated with adverse outcomes in women who are euthyroid throughout pregnancy.(12,13,14)

CHAPTER TOW

PATIENTS AND MTHODS

Objective:
To assess the prevelance of thyroid dysfunction in women with history of recurrent miscarriage in first trimester .

Study design: retrospective cross sectional study .

Setting : AL-Nasiriyah city at May of 2021

Patients and methods :
In this study ,40 women with history of recurrent miscarriage during first trimester 32 cases have normal TSH level while 8 cases have abnormal TSH level which divided into 5 cases hypothyroidism and 3 cases hyperthyroidism

Inclusion criteria

1. Gestational age (7-12)Week

2. History of recurrent miscarriage 3-6 in 1st trimester for study group

Exclusion criteria

1. Multiple pregnancy

2. Patient with chronic medical problem like hypertension ,diabetes

3. cigarette smoking.

4. patient on chronic use of drug .

5. pathological cause of pregnancy loss such as cervical incompetence ,fibroid or congenital anomalies of uterus .

All the participants were subjected to the following :

1. They were told about the nature of the study and only those who agreed to participate in the study were included .Verbal consent was obtained from all pregnant women in the study .

2. The demographic characteristics of each patient were assessed including maternal age ,parity ,no. of miscarriage and gestational age(7-

12)weeks .was calculated from the first day of LMP and confirmed by early ultra sound scan .

3. Full history and physical examination were done to all participants .

4. body mass index was calculated to all patients by dividing the weight of the participant in kilogram over the square of the height in meters .

5. An abdominal ultrasound examination was done to all patients to confirm the gestational age ,viability ,to exclude multiple pregnancy and any pathological abnormalities such as fibroid.

6. Every patient had under gone the following investigations in the form of :

1. Complete blood count

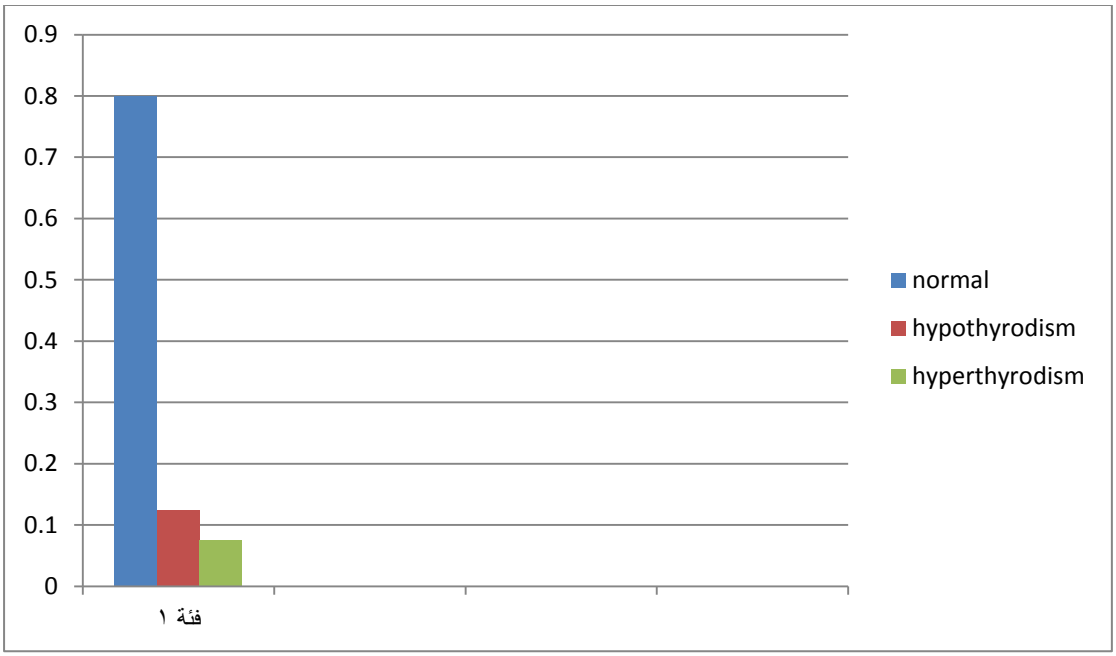
2. Thyroid function test .(Thyroid stimulating hormone)

CHAPTER THREE
RESULTS

Prevelance of patient with thyroid dysfunction=number of patient with recurrent miscarriage and thyroid dysfunction / total number of patient with recurrent miscarriage

PREVELANCE = 8/40

= 0.2



		Number	Percent
Gravida	1	Zero	Zero
	٢	Zero	Zero
	3	11	27.5
	4/+	29	72.5
Parity	0	8	20
	1	6	15
	2	9	22.5
	3	8	20
	4/+	9	٢٢,٥

Distribution of study group according to gravida and parity

CHAPTER FOUR

CONCLUSION and DISCUSSION

Conclusion :

1-The TSH levels were found to be normal in miscarriage women .

compared with healthy pregnant women. The feedback mechanism

of thyroid-pituitary glands is profound or not properly works in

recurrent miscarriage women..

2-Most of women with recurrent misscarge were with euthyroid.

Discussion

Preconception or early pregnancy screening for thyroid dysfunction has been proposed but is not widely accepted. However, measurement of thyroid function and should certainly be considered in those who are at high risk of thyroid disease and in those whose pregnancy is otherwise high risk. In women at reproductive age, hypothyroidism can be reversed by thyroxine therapy to improve fertility and avoid the need for use of assisted reproduction technologies. Accordingly, TSH determination is warranted for all women planning pregnancy or those already pregnant. Women with thyroid dysfunction at early gestation stages should be treated with l-thyroxine to avoid pregnancy complications.. none Furthermore, it was recently shown that thyroxine administration to pregnant women with positive thyroid auto antibodies and a history of recurrent abortions may improve the final outcome. Regarding prevention of miscarriage, there are few studies showing that thyroxine treatment may be effective in reducing the number of miscarriages when given during the early stages of pregnancy. Further studies are required with a greater number of women in order to reach definitive conclusions. At present, routine screening and treatment of autoimmune thyroid disease in euthyroid pregnant women is not .warranted

To date, there is a lack of well-designed randomized clinical trials to elucidate this controversy. Subclinical and overt forms of hypothyroidism are associated with increased risk of pregnancy-related morbidity, for which thyroxine therapy can be beneficial. Suboptimal

iodine status affects a large proportion of the world's population, and pregnancy further depletes iodine stores. There is controversy surrounding the degree to which iodine should be supplemented and the duration of supplementation. The practicing clinician needs to be aware of the thyroid changes which accompany pregnancy. Future research, within the setting of clinical trials, should focus on the potential health gain of identification, and effect of treatment, of thyroid disease on pregnancy outcome

References

1-1. Kennedy RL. Malabu UH, Jarrod G, Nigam P, Kannan K, Rane A. Thyroid function and pregnancy: Before, during and beyond. J Obstet Gynnecol 2010,30: 774-83.

2. Abbassi-Ghonavoti M Thyroid autoantibodies and pregnancy . outcomes. Clin Obstet Gynecol 201154:499-505

3. Kaprpara A. Krassas GE Thyroid autommunity and miscarriage Hormones Athens 2008:7:294-302

4: Twig G, Shinn A, Amital H, Shoenteld Y Pathogenesis of infertility and recurrent pregnancy lose in thyroid autoimmunity Autoimmun2012 38 275-81

5. Poppe K, Velieniers B, Glinoer D. The role of thyroid autoimmunity in fertility and pregnancy. Nat Clin Pract Endocrinol Metab 2008,4394-405.

2_Recurrent Pregnancy Loss
edited by Sumita Mehta, Bindiya Gupta

3- SHORT PRACTICE of SURGERY Bailey & Love's chapter 50

4- Ramsay ID (1998) The thyroid gland. In: Chamberlain G & Broughton Pipkin F (eds) Clinical Physiology in Obstetrics,3rd edn.

5- Oxford: Blackwell Science Ltd, 374–84.Oxford Textbook of Obstetrics and Gynecology . P117. Chapter 8

- Aboul-Khair SA, Crooks J, Turnbull AC, Hytten FE. The physiological changes in thyroid function during pregnancy. Clin Sci 1964;27:195–207.

-7 Man EB, Reid WA, Hellegers AE, Jones WS. Thyroid function in human pregnancy. 3. Serum thyroxine-binding prealbumin (TBPA) and thyroxine-binding globulin (TBG) of pregnant women aged 14 through 43 years. Am J Obstet Gynecol 1969;103:338–47.

6-Stagnaro-Green A, Abalovich M, Alexander E et al. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid 21(10), 1081–1125 (2011).

7-Sahu MT, Das V, Mittal S, Agarwal A, Sahu M. Overt and subclinical thyroid dysfunction among Indian pregnant women and its effect on maternal and fetal outcome. Arch. Gynecol. Obstet. 281(2), 215–220 (2010).

8-Schneuer FJ, Nassar N, Tasevski V, Morris JM, Roberts CL. Association and predictive accuracy of high TSH serum levels in first trimester and adverse pregnancy outcomes. J. Clin. Endocrinol.Metab. 97(9), 3115–3122 (2012).

9-De Groot LJ, Abalovich M, Alexander EK et al. Management of thyroid dysfunction during pregnancy and postpartum: an endocrine society clinical practice guideline. J. Clin. Endocrinol. Metab. 97(8), 2543–2565 (2012).

10-Millar LK, Wing DA, Leung AS et al. Low birth weight and preeclampsia in pregnancies complicated by hyperthyroidism. Obstet. Gynecol. 84(6), 946–949 (1994).

11-Davis LE, Leveno KJ, Cunningham FG. Hypothyroidism complicating pregnancy. Obstet. Gynecol. 72(1), 108–112 (1988).

12-Glinoer D, Riahi M, Grun JP, Kinthaert J. Risk of subclinical hypothyroidism in pregnant women with asymptomatic autoimmune thyroid disorders. J. Clin.Endocrinol. Metab. 79(1), 197–204 (1994).

13-Negro R, Formoso G, Mangieri T et al. Levothyroxine treatment in euthyroid pregnant women with autoimmune thyroid disease: effects on obstetrical complications. J. Clin. Endocrinol. Metab. 91(7), 2587–2591 (2006).

14-Thangaratinam S, Tan A, Knox E et al. Association between thyroid autoantibodies and miscarriage and preterm birth: meta-analysis of evidence. BMJ 342, d2616 (2011).