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Hypothyroidism in miscarriage abortion during second trimester regarding on the ABO- Rh blood system

Nasreen Kader Kamel *

Department of Drugs and Toxicology, College of pharmacy, Kirkuk University, Iraq.

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Abstract

The spontaneous loss of conception before 20-21weeks of gestation called miscarriage, and thyroid dysfunction acts as risk factor for recurrent abortion for negative R uses of goiter pregnancy. The Study aimed to investigate the hypothyroidism goiter state in miscarriage abortion during second trimester reliance upon blood groups and R uses system.

Material& Methods:135 subjects was carried out in prospective study at Kirkuk teaching hospital, since from April to first of July 2021 .The study included 45 cases of miscarriage abortions, while 45 was healthy control pregnancy and study constituted 45 women with goiter hypothyroidism of same fertility age ranged at 27- 40 years determined hormones level (T4 (thyroxin), T3 (triiodothyronine), TSH (thyroid stimulating hormone), LH (luteinization hormone), Prolactin (PRL) by ELISA method, and blood groups antigen due to reaction with antibody serum pregnancy and abortion by using slide test method. Questionnaire was complete taken for all women, such as metabolic, chronic diseases and endocrine disorder.

Results: The mean T4 level in cases of recurrent abortion was (119.21±1.98 mmol/l), while in control group was (4.78±0.76ng/dl) during second trimester in negative R uses groups, the mean level of LH in negative R uses group in recurrent abortion cases was (9.91±1.23 mu/l),, while in control group was (6.41±1.18 mmol/l) during second trimester for negative Ruses group, and the level of T3 was (17.21±1.42 mmol/l) in miscarriage abortion while in control group was (1.56±0.5 ng/dl) during second trimester at $p<0.05$. Identifications of blood groups and Ruses factor in healthy pregnant was (30 women Rh+) and (15 women Rh_) when (17 blood group A, 13 blood group B), while in miscarriage abortion was (18 women Rh+) and (27womenRh_), when (11 blood group A, 20 blood group B).

Conclusion: The hypothyroidism goiter pregnancy repressed LH and prolactin highly level during miscarriage abortion lead to outcome of pregnancy under lowering level of T4, TSH suppression in negative Ruses with blood group B at age ranged about 27- 40years thru second trimester after 21 weeks ago of the gestation.

Keywords: T4; TSH; LH; miscarriage; Goiter hypothyroidism; Second trimester; R uses factor

1. Introduction

The miscarriage abortion has been more complication of second trimester after 24 weeks for some blood groups, unrelenting for antigen and antibody interaction should be risk factor for recurrent abortion, and incompatibility of the blood groups may be affected both pregnancy and fetus (1), so the main cases lead to abortion both fetal and parental, while the mother and father with incompatibility blood groups lead to experiences spontaneous miscarriage abortion and inducing the stillbirth became more frequently for amongst abortion fetus within normal karyotype state (2),

* Corresponding author: Nasreen Kader Kamel
Department of Drugs and Toxicology, College of pharmacy, Kirkuk University, Iraq..

therefore lead to premature birth during repeated delivery of the abnormal newborn when the stillbirth has more frequent of mother and father due to incompatible blood group ABO antigens (3). Some study showing the relationship between blood groups in the recurrent miscarriage abortion during incompatible ABO and Rh uses system then causing intra uterine fetal death and severe fetal hemolytic anemia occurring (4).The abnormalities' LH levels lead to releasing early luteinization with follicular atresia for controlling of ovarian stimulation, and Highly LH levels lead to premature secretory transformation of the endometrium due to bellowing the occurrence of implantations, there for lead to lowering the pregnancy rate (5). Thyroid disorders involving thyroid hormone levels within the thyroid gland abnormalities, such as Nutrient deficiency iodine cause lead to endemic goiter condition (6), therefore, the thyroid hormones has multifunctional effects due to infertility and birth defects, so the blood investigations through thyroid profile by ultrasonography and required with FNAC (fine needle aspiration cytology techniques) for Blood grouping pregnancy have been categorized four different groups according on them blood groups, therefore (7), they were divided into some categories depended on their thyroid hormone levels was labeled as abnormal states with hypothyroidism condition (8).The human chorionic gonadotrophic (hCG) has been thyrotrophic activity and owing to subunit homology within thyroid stimulating hormone (TSH) which was suppressing during the first trimester of pregnancy (9), If hCG levels is highly elevated lead to the TSH responses to thyrotrophic releasing hormone and reducing in the first trimester and returns to normal state after this time in second trimester (10), While thyroid binding globulin increases in the first 2 weeks of pregnancy and reaches plateau level during 20 weeks ago, Therefore, the increasing production of total T3 (tri-iodothyronine)and T4 (thyroxin) after 20 weeks induced in this cases (11). Through this time the Glomerular Filtration Rate increased of pregnancy resulting an increased renal loss of iodide molecule (12), which is essential substance for thyroid hormone synthesis and the thyroid compensates lead to increasing the proportion of iodide for taken up from blood stream, so the relative background iodide deficiency occurring increased and these changes may be resulting the enlargement of the thyroid gland during pregnancy called (thyroid goiter) (13) .There for, the hyper metabolic rate of normal pregnancy makes clinical assessment of thyroid functions have been needed to be checked biochemically examination for all trimester (14), so the physiological changes of pregnancy lead to soften about 50 per cent of plasma volume expansion obtain, and the decreasing the levels of TSH within rising level of T4 concentration in the first trimester of normal healthy pregnancy induced the following due to the false of T4 levels within advancing effects of the gestation and induced the most marked effect during third trimester of normal pregnancy (15) .The firstly prevalent cause of hypothyroidism in some pregnancy is chronic autoimmune thyroiditis (Hashimoto's thyroiditis) but the other causes including endemic iodine deficiency and must be prior for radioactive iodine therapy (16), while untreated hypothyroidism in pregnancy produced increasing the risk for adverse pregnancy complications incidence and inducing detriment the of effects on fetal neurocognitive development degree and increasing the risk rate for premature birth state within low birth weight and miscarriage rate will be increased then lead to the fetal deaths at greater than 22 weeks of gestation (17), or at least 1 preterm birth (<35 weeks) during sever preeclampsia occurring and placental insufficiency has been incidence, because thyroid hormones have been impact on oocytes at the level of the granulosa cell within luteal cells that interfere with normal ovulation in pregnancy (18), Therefor, the Low T4 levels exert a positive feedback effect mechanism on thyroid releasing hormone (TRH), so the high concentrations in TRH have been associated with high prolactin (PRL) levels and lead to highly PRL levels altering the stimulation of gonadotropin releasing hormone (GnRH) for inducing highly LH levels in the serum within interference normal ovulation (19), Therefore, the hypothyroidism condition inducing some complication in pregnancy which is closely associated with an ovulation and infertility cases (20).

The aim of study to assessment the maternal thyroid hormones level in pregnancy with history of recurrent miscarriage abortion in second trimester according on Blood groups and Rh uses typing comparing within pregnancy without history of miscarriage abortion.

2. Patients and Methods

2.1. Study design

By prospective case control study and Settings at the Al-Kirkuk city from April to first of July 2021, so the study included pregnancy attending obstetrics and gynecology unit at Kirkuk teaching hospital and pediatric dispensary in Kirkuk city.

2.2. Subjects' collection

135 pregnancies were included in this study They divided into three groups: Study group :45 pregnant women with history of recurrent miscarriage abortion in the second trimester with gestational age ranged (21) Weeks. Control group :45 pregnant women without history of miscarriage with gestational state and age ranged (21) Weeks.

2.3. Goiter group

45 pregnant women without history of miscarriage abortion with gestational age ranged (21) weeks, and the detailed history due to the general physical examination had been carried out in all the pregnant women.

2.4. Inclusion criteria has been taken about

Gestational age (21)Weeks and History of recurrent miscarriage abortion 2-3 in 2st trimester for study groups, while the Exclusion criteria incorporates: youngish pregnancy and age ranged 27-40 years, so the pregnancy without chronic medical problem like hypertension, thyroid disorder, diabetes, unary tract infection, and the cigarette smoking has not be taken, when the pregnancy and all subjects not be chronic using of drugs, therefore, the pathological causes of pregnancy must be reducing such as cervical incompetence and congenital anomalies of the uterus and endometrium .volume of 5mL blood was plucked from the venous blood, and serum was separated by centrifugation mechanism for routine investigations and measuring total T3 and thyroxin (T4) for each group with TSH levels were estimation in maternal blood by chemiluminescence instrument (21). All the subjects were followed every 5weekly till 21weeks and the outcome was noted in terms of an embryonic pregnancy with missing abortion within spontaneous abortion for continuation of pregnancy.

- Blood group divided by blood type was classified four groups A, B, AB, O according to the agglutination within anti monoclonal reagent
- Hormone investigation by estimation the level of T3, T4, TSH, LH was evaluated by using minivans apparatus through the appropriated kit protocol type VIDAS for T3 and BioMerieux SA/France within VIDAS for T4 BioMerieus SA/France (22). The level of serum LH concentration for abortion group was examination with ROC analysis and prolactin estimated by ELISA method for normal and goiter pregnancy (23).

2.5. Statistical analysis

Data was collected were presented as mean ±standard deviation when the Statistical Package for the Social Sciences (SPPSS) analysis due to covariance (ANOVA) was applied of the data for all women by a comparison of the variables between them and using the Student's-test for Pregnancy and abortion.

3. Results

Table 1 Thyroid hormones level In normal pregnancy (n=45) for Rh ruses system

	T3 (mmol/l)		T4 (mmol/l)	TSH (mIU/l)	LH mmol/l	PR mmol/l
First trimester	Rh+	3.60±0.2	5.68±1.7	2.56±0.96	15.30±1.55	2.58±1.64
	Rh_	1.24±0.1	3.11±0.88	1.97±0.74	12.82±1.23	2.97±1.92
Second trimester	Rh+	3.15±0.5	5.98±1.88	2.68±1.18	7.81±1.85	3.43±1.97
	Rh_	1.56±0.5	4.78±0.76	1.65±0.19	6.41±1.18	3.77±0.99
Third trimester	Rh+	5.89±1.32	6.13±1.78	3.85±1.29	3.93±1.84	4.23±1.55
	Rh_	3.73±0.7	5.23±0.99	1.48±0.97	2.96±1.93	9.73±1.56

Table 2 Thyroid hormones level in goiter hypothyroidism pregnancy (n=45) for Rh uses system

	T3 (mmol/l)		T4 (mmol/l)	TSH (mIU/l)	LH (mmol/l)	PRL (mmo/l)
second trimester	Rh+	3.18±0.7	1.55±0.62	3.88±1.97	7.28±1.68	11.32±3.77
	Rh_	1.15±0.8	1.34±0.18	1.64±0.15	9.68±1.84	19.47±3.96

Table 1 shows the variables acquirement during the three stages of pregnancy, Basal prolactin levels in the second trimester (3.77±0.99mmol/l) and third trimester (9.73±1.56mmol/l)were higher than those estimation in the first trimester (2.97±1.92mmol/l), and there is no significant difference between second and third trimester, The mean LH

level in control group was (6.41±1.18mmol/l)has negative Rh system and high level groups was (7.81±1.85mmol/l)has positive Rh system during second trimester of normal pregnancy group, so the Table 1 shows the levels of LH for both Rh+ and Rh- (15.30±1.55mmol/l, 12.82±1.23mmol/l) in first trimester for control groups compared with hypothyroidism miscarriage abortion (7.94±2.4, 9.91±1.23mmol/l), the level of TSH slightly decreased in second trimester (1.65±0.19mIU/l) and third trimester (1.48±0.97mIU/l) than that in first trimester (1.97±0.74mIU/l), and amongst 135 women diagnosed with thyroid hormones level normally in serum was formed by women with "A " blood group, and " B" blood groups with O blood group being least common, show Table 4.

Table 3 Thyroid hormones level in hypothyroidism miscarriage abortion (n=45)for Rh ruses system

	T3 (mmol/l)		T4 (mmol/l)	TSH (mIU/l)	LH (mmol/l)
Abortion week (21 week of pregnancy)	Rh+	3.58±1.18	1.85±0.68	3.93±1.62	7.94±2.4
	Rh_	17.21±1.42	119.21±1.98	1.82±0.34	9.91±1.23

Table 4 Blood groups &Rh ruses system in normal pregnancy &hypothyroidism current abortion after21 week

Blood groups	healthy pregnancy	Rh+	Rh_	current abortion	RH+	RH_
A	17	13	4	11	4	7
B	13	9	4	20	7	13
AB	8	5	3	5	1	4
O	7	3	4	9	6	3
Total	45	30	15	45	18	27

The table 1 showing highly increased in T4 in normal pregnancy during third (5.23±0.99mmol/l) and second trimester (4.78±0.76mmol/l) than that in first trimester (3.11±0.88mmol/l) and level of T3 increased in third trimester (3.73±0.7mmol/l) and second trimester (1.56±0.5mmol/) than that in first trimester (1.24±0.1mmol/l)

Table 2 shows the highly decreased in the level of T4 in second trimester (1.34±0.18mmol/l) for hypothyroidism goiter pregnant than that normal healthy pregnant (4.78±0.76mmol/l), and T3 level in second trimester (1.15±0.8mmol/l) for goiter hypothyroidism pregnancy than that of normal healthy (1.56±0.5mmol/l), while the TSH in second trimester for goiter hypothyroidism is slightly decreased (1.64±0.15mIU/l)than normal control (1.65±0.19mIU/l), but this table showing highly elevation of level of LH (9.68±1.84mIU/l)in goiter hypothyroidism than that of normal control (5.43±1.18mIU/l), and highly increased in the concentration of prolactin (19.47±3.96mmol/l)in goiter hypothyroidism than that healthy pregnant (3.77±0.99mmol/l)during second trimester in the negative Rh system.

Table 3 shows the highly decreased in the level of T3 (17.21±1.42mmol/l) and T4 (119.21±1.98mmo/l) in recurrent abortion than that of healthy pregnant, and the level of TSH remain normal ranged approximately in miscarriage abortion after 21 weeks of pregnancy, but this table estimated highly level of LH (9.91±1.23mmol/l)in current abortion. Table 4 determined the blood groups and Rh uses factor for healthy and miscarriage hypothyroidism abortion, Rh+ in healthy pregnant (30 subjects) is more than that in recurrent abortion (18 subjects), but the Rh_ in miscarriage abortion (27 subjects)is more than that healthy pregnant (15 subjects) and blood group B in miscarriage abortion was (20 subjects) but in healthy group was (13)while blood group A in miscarriage abortion was (11)but in healthy group was (17)**.**

4. Discussion

There is a significantly association between T4, T3 and TSH with an abortion rate in study group and goiter hypothyroidism group at last weeks of second trimester compare with healthy pregnancy and elevated circulation LH hormone in the state of abortion mainly in second trimester for negative Rh uses system than positive Rh uses groups, show Table 1and Table 2, and this result agree with (24).

The study diagnosed the interaction between ABO, Rh blood selection and miscarriage abortion during lowering T3, T4, TSH in Rh negative typing and A, B blood group system with many other factors (25), such as morphological, acrosome and endocrine disorder could be lethal to the conception and may be observed in the recurrent abortion, and this study agree with other research's (26), but the study diagnosed the Rh type has been risk factor in some cases of miscarriage abortion in goiter groups ($p<0.05$) (27), and lowering TSH level about 3-4 mu/l in this group, show Table 3 while the T3&T4 also slightly decreased concentration in this cases and normal pregnancy have been hyperthyroidism according to iodine intake as sample size immunological response under hormones level variation in value such as LH, and this result agree with other reported (28), prolactin (PRL) have been important role in the reproductive impairment and directly associated to the thyroid gland efficiency which is most cases responses for miscarriage and infertility age ranged, therefore any increased in prolactin levels lead to baby lost at last week of second trimester in negative Ruses system, and this result accepted with (29)show table2. The relation between thyroid dysfunctions and gonadal secretion in all trimester lead to menstrual irregularities for infertility and miscarriage morbidity rate increased if untreated Hypothyroidism due to the receptors of thyroid hormones are expressed in the endometrium uterus and ovary has been more stimulus to obtain multiple cumulus-oocyte complexes for inducing the estradiol hormone level become more highly level in this cases than that normal pregnancy during second trimester and lead to decreased level of LH for inducing an hypothalamic effects with pituitary thyroid hormone doses due to could be impairment thyroid hormones level, this result agree with (30)show table2 .In miscarriage women with lowering level of iodine in the serum for negative Rh blood typing is history marker for development the hypothyroidism goiter cases and lead to impairment the scores has been most complication in second trimester in this cases and induced the placental abortion for postpartum hemorrhage in negative Ruses mothers and normalized serum TSH, and accepted with (31)show table3.T4&T3 in second trimester during last week (21 weeks) in goiter Hypothyroidism groups lead to lowering ranged compared to normal groups and TSH levels slightly different than control group in blood group A & AB with Rh – lead to incompatibility problem could be inducing the antigen with antibody interaction and then lead to disrupt implantation during goiter hypothyroidism and inducing premature delivery which was seen in Rh negative mother and mostly recurrent abortion compare with positive Rh mother without any abortion within completely fertilization and accedes with (32)show table3, therefore, the blood system antigens and Rh antibody will be response for fertilization and fetal lost, show table 4 .In second trimester the TSH return to the normal ranged in healthy pregnancy and remain stable during this trimester, this study agree with (33), but small number of pregnancy has been less than in T4, T3 level during gestation (32), while in goiter and present hypothyroidism has been important for iodine estimation in the urine at the last week of second trimester, and accepted with (34), and lead to highly level of LH in miscarriage abortion for goiter pregnancy than control normal pregnancy and not significantly relation between gonadotrophic hormones and thyroid hormones (35), therefore LH has been risk factor for lowering hormone thyroxin of goiter group (36), because The increased secretion of LH more than>10 ng/dl after 20-21 weeks of pregnancy lead to significantly increased in the recurrent abortion in goiter hypothyroidism when T4 lowering and TSH is more than 6mu/l due to significantly increased in prolactin levels and making the stillbirth has been adverse effects on fetus with maternal outcome, which is agree with (37), so the highly level of LH with prolactin could be risk factor for miscarriage conception due to inhibition progesterone secretion and lead to the luteal phase defecting, and this result agree with (38).T4 levels was changed during all trimester, and there is increased T4 secretion and requirement due to increased iodine uptake by mother for synthesis hormone T4, this result agree with (39) ;after increased the liver production of thyroxin binding globulin (TBG) within decreasing the amount of T4 and then pass to the fetus due to placenta transferring of T4 and during second half of pregnancy after 21 weeks and stimulated to increasing the function of thyroid gland for physiological demands of pregnancy and Fetus when placental mother growth were affected by thyroid dysfunction in early pregnancy, agree with (40). In this study the mean value of T3 and T4 when comparable with normal pregnancy was not significantly differences in the first trimester respectively (41)show table1, while the difference in the mean TSH value in the three groups was found to be insignificantly differences, and disapproved with (42), and the levels of T3 and T4 in recurrent abortion found significantly lower value than that in normal pregnant may be due to the present study groups has been included within a history of abortion, but in hypothyroidism pregnancy showing a strong association between TSH levels with abortion rate, which is agree with (43), and some study have been reported a significantly decreased in T4andT3 and level of TSH in goiter pregnancy groups than that in healthy pregnant, could be the indicating of the existence the feedback mechanism for the TSH and T4 secretion in this groups (44), and this report agree with present study.

5. Conclusion

The level of TSH was significantly increased in second trimester in women who had miscarriage abortion as compared with healthy groups and which is associated with abortion in goiter groups, while the highly level of T4in hypothyroidism may be reduced the risk factor of miscarriage abortion in blood group AB for both groups goiter and hypothyroidism women compared with blood group O has higher significantly abortion: therefore, the incompatibility ABO system between mother and fetus maybe risk factor for miscarriage abortion.

Compliance with ethical standards

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Statement of informed consent

The information was intending for provided the general advice for practitioners not should be relied on the substitute to proper assessment and respect the particular circumstances for each cases and patient .The clinical management would be responsible for the needing all individual and patient and this information has been prepared for regarding the information available at each time.

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