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Investigation of the Physiological Strongness in Effect of Pregnancy on Thyroid Hormones among Pregnant Women

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Abstract

Background: Pregnancy serves as the thyroid's stress test. Thyroid disorders are quite prevalent among expectant mothers. 10% of expecting mothers have subclinical hypothyroidism. Anemia, low birth weight, and newborn mental damage are all brought on by prenatal hypothyroidism. The results of this study will evaluate mother and fetus outcomes in pregnant women with impaired thyroid function. The purpose of this study is to establish a relationship between decreased thyroid function and adverse consequences on both the mother and the fetus.

Methods: At the private hospital in Babylon City, a prospective study has been conducted. The 198 pregnant participants in this study who were hospitalized to the obstetric ward in the third trimester of a singleton pregnancy provided information. Women were picked without regard to their age, location, or social standing. Women with thyroid disorders, other medical issues, or multiple pregnancies were prohibited. T3 , T4, and TSH were measured as well as the hematological analyses. The conditions that potentially affect either the mother or the fetus were then evaluated in women with abnormal thyroid function tests. Menstrual cycle pattern, previous abortions, family history of thyroid disorders, history of infertility, level of hemoglobin, and fetal expected result were the variables in this study.

Results: Thyroid disorders are prevalent (11% of people have them), with subclinical hypothyroidism, overt hypothyroidism, and subclinical hyperthyroidism affecting 5.6, 3.5, and 1.5% of people, respectively. Anemia was observed in 26.3% of women with subclinical and overt hypothyroidism, and anemia and hypothyroidism were substantially correlated ($p = 0.008$).Hypothyroidism was statistically linked to poor fetal outcomes, including low birth weight (LBW) (31.6%), neonatal intensive care unit (NICU) hospitalization (42.1%), and low APGAR Score (21.1%, $p =0.042$). When compared to women who are euthyroid, the risks of anemia, low birth weight, NICU hospitalizations, and low APGAR score were 4.8, 6.3, 0.14,and 3.64 times greater, respectively, in women with hypothyroidism.

Conclusion: 5.6% of pregnant women had subclinical hypothyroidism throughout the third trimester. Hypothyroidism and anemia, preeclampsia, high cesarean rates,and neonatal morbidities all show significant relationships.

Keywords- Physiological Strongness, Pregnancy, hypothyroidism, Thyroid disorders

Introduction: The stress of pregnancy might result in clinical or subclinical hypothyroidism in women with low thyroid function. The normal value of free thyroxine (fT4) or TSH collected from non-pregnant women differs in pregnancy due to the physiological changes in thyroid function during pregnancy. Thyroxin (T4) and triiodothyronine (T3) output rises by up to 50% during pregnancy, boosting the body's daily requirement for iodine, while thyroid-stimulating hormone (TSH) levels decline, particularly during the first trimester. [1].

Cutoffs are less necessary since Human Chorionic Gonadotrophin (HCG) is thyrotrophic and high levels, especially in the first trimester, might result in low TSH results. Women with low thyroid reserves experience overt sickness as a result of pregnancy stress [2]. Toleration is good if there is enough iodide stored inside the thyroid, but in low-iodide areas, these physiological changes have a significant impact on pregnancy. [3]. Hypothyroidism affects pregnant women often, and detection rates, especially in developing countries like Iraq, have not kept up with the severity of the problem. Early detection and care could minimize the chances of

adverse fetal and mother results in pregnancy, which are frequently found. Hypothyroidism is a simple condition to treat. Two to three percent of pregnant women have overt thyroid dysfunction, ten percent have subclinical thyroid dysfunction, and five to ten percent have autoimmune disease[4, 5].

A few examples of maternal problems are miscarriage, anemia, preeclampsia, gestational hypertension, placental abruption, premature delivery, an increase in Caesarean sections, and postpartum hemorrhage. The fetal-pituitary-thyroid axis may suffer negative effects from the method of birth. Preterm delivery, neonatal respiratory distress syndrome, low birth weight (LBW), perinatal morbidity and mortality, increased NICU hospitalization, neuropsychological impairment, and cognitive impairment are all fetal outcomes that can occur from thyroid dysfunction. The brain development of the growing fetus depends on thyroid hormone. If congenital hypothyroidism is not diagnosed and treated right away, children who have it will experience significant cognitive, neurological, and developmental problems. A study [6] found that children born to pregnant women with hypothyroidism had lower IQ scores than those born to pregnant women without hypothyroidism. For these reasons, it's essential to create screening methods for early detection and the beginning of effective therapy, as well as suitable strategies to pinpoint women who are susceptible to these adverse consequences. Due to disagreements over trimester-specific reference ranges in various demographic contexts and the dearth of studies in developing countries, the study is highly relevant. Because issues to mother and fetus due to thyroid abnormality in pregnancy, this study aims to determine the frequency of thyroid disorders in pregnant women, maternal and fetus outcomes in a hospital in Babylon city.

Methodology: This is an observational research done at private hospitals in Babylon. For other obstetric purposes, we recruited 198 third-trimester prenatal women with singleton pregnancies who were admitted to the obstetric ward. Every residents and people of all socioeconomic status provided informed permission. Women who were known to have thyroid disorders, had numerous pregnancies, were on medication, or had any pre-existing medical conditions including diabetes mellitus, heart illness, or pulmonary disease were not allowed to participate. results of hematological tests and T3, T4, TSH estimation done. Maternal and fetal problems were then evaluated in patients with an abnormal thyroid profile. The primary study variables included infertility, history of thyroid diseases, repeated abortions, menstruation history, mean T3, T4, TSH levels, haemoglobin levels, and mother and fetal outcome. To determine the relationship between thyroid abnormalities and other clinical parameters such menstrual rhythm, infertility, family history of thyroid condition, and miscarriage, a univariate analysis was carried out. TSH was estimated using the Enhanced Chemiluminescence technique. Then, when TSH levels were abnormal, estimates of free T3 and free T4 were made. The American Pregnancy and Thyroid Association recommended the following cutoff values for TSH: first trimester: 0.1- 4.0mIU/L, second trimester: 0.2-4.5mIU/L, third trimester: 0.3 -5mIU/L[7]. Normal free T4 and free T3 levels range from 0.7 to 1.8 ng/dl and 1.7 to 4.2 pg/ml, respectively[8]. Patients were thought to have subclinical hypothyroidism (SCH) if their fT4 levels were normal but their TSH levels were high, overt hypothyroidism if their fT4 levels were low but their TSH levels were high, subclinical hyperthyroidism if their fT4 levels were high but their TSH levels were low [9].

Preeclampsia, gestational hypertension (blood pressure over 140/90 without protein in the urine after 20 weeks gestation), oligohydramnios (amniotic fluid index 5), a history of miscarriage, anemia (Hb value less than 10 g/dl), preterm delivery (delivery before the end of 37 weeks of gestation), and a higher rate of LBW (neonatal birth weight less than 2.5 kg) are all signs The SPSS Version 25 statistical package for the social sciences was used to manage and analyze the data. The category variables in the study were evaluated using the Pearson chi-square test. Calculations of risk factor relationships were performed using binary logistic regression[11]. The test was regarded as significant only when the p value was less than 0.05. The study's design was approved by the institution's Scientific and Ethical Committee [12]. They were all also given an explanation of the study's approach and the information that would need to come from each participant. It received written consent[13].

Results: 22 (11%) of the 198 women who had thyroid function tests for abnormalities. As can be seen from the prevalence of subclinical hypothyroidism, overt hypothyroidism, and subclinical hyperthyroidism being 5.6% (n = 11), 3.5% (n = 7), and 1.5% (n = 3), respectively, during pregnancy, subclinical hypothyroidism is more common. One sample exhibited a high TSH and a barely above-average T4 level. In order to calculate risk

factors, hypothyroidism was included, with 19 serving as the denominator. The mean serum TSH values in women with subclinical hypothyroidism, overt hypothyroidism, and subclinical hyperthyroidism were 8.02 1.25 mIU/ml, 11.92 5.34 mIU/ml, and 0.07 0.03 mIU/ml, respectively. The mean serum fT3 levels in women with subclinical hypothyroidism, overt hypothyroidism, and subclinical hyperthyroidism were 2.920.454 pg/ml, 1.58 0.66 pg/ml, and 4.160.40 pg/ml, respectively. The mean serum fT4 values in women with subclinical hypothyroidism, overt hypothyroidism, and subclinical hyperthyroidism, respectively, were 1.090.30, 0.360.24, and 1.20.10 ng/dl. (Table 1). The 22 dysfunctional women had a history of abnormal menstrual cycles in 22.7% of them, infertility treatments in 4.5%, thyroid disease in 4.5% of their families, and multiple miscarriages in 4.5% of them. None of these characteristics were significantly linked to the occurrence of thyroid disease (p values of 0.655, 0.217, 0.079, and 0.752) respectively(Table 2). Anaemia affected 26.3% of the women with hypothyroidism, and there was a statistically significant (p = 0.008) correlation between the two conditions. 15.8% of women had preeclampsia, and there was a statistically significant correlation (p = 0.041) between the presence of hypothyroidism and preeclampsia. 5.3% of hypothyroidism cases resulted in preterm births, however there was no connection between the two conditions. In 10.5%of women with hypothyroidism who had a significant correlation with oligohydramnios (p = 0.072) and cesarean delivery (p = 0.012), cesarean delivery occurred. Baby LBW was present in 31.6% of births, and there was a substantial (p = 0.001) link between LBW and hypothyroidism. For a Apgar score, acutoff value of 5 was used as a sign of fetal hypoxia. It was strongly linked (p =0.042) that 4 (21.1%) of the 19 hypothyroid women gave birth to infants with lowApgar scores. 42.1% of NICU admissions were strongly correlated with hypothyroidism (p 0.000). Women with hypothyroidism are 4.8 times more likely than women with euthyroidism to develop anemia (95% CI = 1.5-15.8). It is likely that hypothyroidism could make anemia worse. Women with hypothyroidism have a 6.3-fold increased risk of having LBW kids than women with euthyroidism (95% CI = 2.03-19.5). Babies born to women with hypothyroidism had a 0.14 times (95% CI = 0.048-0.39) and 3.6 times (95% CI = 1.04-12.7) higher risk of NICU and Apgar score admission than babies born to women with euthyroidism, respectively (Table 3).

Table 1 :Frequency of thyroid conditions in the third trimester of pregnancy.

Thyroid Status	No.	%	TSH (mIU/L)	Mean fT4 (ng/dl)	Mean fT3 (pg/ml)
			Mean ±S.D		
Subclinical hypothyroidism	11	5.6	8.02 ± 1.25	1.09 ± 0.30	2.92 ± 0.45
Overt hypothyroidism	7	3.5	11.92 ± 5.34	0.36 ± 0.24	1.58 ± 0.66
Subclinical hyperthyroidism	3	1.5	0.07 ± 0.03	1.2 ± 0.10	4.1 ± 0.40

Table 2: Thyroid disease prevalence and related risk factors.

Risk factors	No. (%)	P. value
Irregular menstrual rhythm	5(22.7)	0.650
Family history of thyroid disorder	1(4.5)	0.079
History of infertility treatment	1(4.5)	0.216
Miscarriage	1(4.5)	0.752

Table 3: correlation between maternal and fetal risk variables in hypothyroid women

Outcome No.(%)	95% CI	Odds Ratio	p value
Anemia	1.50–15.8	4.88	0.008

5(26.3)			
Preeclampsia 3(15.8)	1.06–19.22	4.52	0.041
Preterm 1(5.3)	0.253–22.54	2.39	0.447
Oligohydramnios 2(10.5)	0.034–1.15	0.19	0.072
Caesarean section 5(26.3)	1.38–14.39	4.48	0.013
Low birth weight (LBW) 6(31.6)	2.04–19.55	6.3	0.001
Low Apgar Score 4(21.1)	1.05–12.71	3.65	0.040
NICU admission 8(42.1)	0.049–0.390	0.15	0

Discussion: After diabetes, thyroid disease is the endocrine condition that affects women of reproductive age most frequently. Based on a range of factors, there are significant regional differences in the prevalence of thyroid problems during pregnancy and their consequences on the mother and fetus. The amount of iodine in table salt and how much is consumed might vary from region to region; hence, geography may play a role in the prevalence of thyroid problems. The issues surrounding fetomaternal outcomes and abnormal thyroid function in this context are covered in this paper.

Risk factors: Risk factors: Thyroid disease causes abnormal sex hormone levels, elevated prolactin (PRL) levels, and irregular ovulatory cycles. According to various authors [14], all of these variables may cause delay pregnancy and irregular menstrual cycles. 4.5% of the women in the current study who had hypothyroidism had previously had infertility treatment, compared to (3.8 to 4.0)% of these women in previous investigations [15& 16]. We found that the menstrual rhythm was irregular in 22.7% of hypothyroid women. Iodine is organized and oxidized by the thyroid peroxidase (TPO) enzyme, which also produces the fT4 and fT3 hormones [17]. A glycoprotein called thyroglobulin (TG) serves as a substrate for the production and storage of thyroid hormones [18]. Both antibodies and hypothyroidism are symptoms of autoimmune thyroid diseases. A widespread immune system activation and transplacental antibody transfer that results in fetal rejection are thought to be the causes of the recurrent miscarriage that is linked to thyroid autoimmunity [19, 20]. There is a significant risk of miscarriages, preterm births, gestational diabetes, postpartum thyroiditis, and lifelong hypothyroidism associated with thyroid peroxidase (TPO) or thyroglobulin antibodies[21–23]. The miscarriage rate among women with hypothyroidism in the current study was 4.5%, which is comparable to earlier studies' findings, which reported rates of 5.6and 5.0% [8, 15]. Clinical obstetric issues are particularly relevant to pregnancy-related hypothyroidism. First-degree relatives of people with Hashimoto's thyroiditis-related hypothyroidism have a nine-fold greater risk of developing the condition compared to the general population. [24]. 4.5% of women with hypothyroidism had a family history of thyroid illness, which is comparable to the incidence of 12.7% reported in other research [8]. No statistically significant correlation between thyroid problem and any clinical obstetrical and gynecological aspects, such as miscarriage, irregular menstruation, a family history of thyroid disease, or infertility, was found in this investigation (Table 2).

Association of thyroid disease and anemia with maternal and fetal outcome:

The heme-dependent enzyme thyroid peroxidase is impaired by iron shortage, which limits thyroid hormone synthesis and can lower levels of tT3 and tT4 in the blood. Hypothyroidism may be cured with iron replacement [25]. Anemia was found in 26.3% of the women with hypothyroidism in the current study (p = 0.008), although 4.2% of the women with hypothyroidism were found to have anemia by other authors [26]. According to one study, iron deficiency caused anemia to occur in up to 60% of hypothyroid women [27,28]. Pre-eclampsia:

Preeclampsia in hypothyroidism may be caused by contraction of blood vessels in the smooth muscle in the arteries of body and renal, which can increase peripheral vascular resistance, diastolic pressure, and impaired tissue perfusion [29, 30]. Proteinuria, which is known to cause an increase in the excretion of thyroxine and thyroid binding globulins, can be a sign of thyroid dysfunction. Rare instances of proteinuria that is severe enough to cause thyroxine and thyroid- binding globulin losses that cannot be replaced by the body have been documented [31–33].

Pre-eclampsia was seen in 15.8% of the women in the current study who had hypothyroidism ($p = 0.041$). These results are agreement with other studies findings that preeclampsia occurs in 14.7% of women with overt hypothyroidismand 13.6% of women with SCH [15, 34].

Delivery by C-section :

Another result was a higher rate of cesarean deliveries, which were seen in 26.3% ($p = 0.012$) of hypothyroid women. 22.9% of deliveries by cesarean section were reported by other authors to be made by hypothyroid mothers [34]. The accompanying pregnancy problems, such as gestational diabetes, blood pressure disorders, and premature birth, may be the cause of the higher risk of cesarean delivery. Further research is needed to determine whether otherwise uncomplicated hypothyroidism affects the risk of cesarean delivery [35– 37]. According to some investigators, hypothyroidism is significantly correlated with preeclampsia ($p = 0.001$), premature delivery ($p = 0.001$), and placenta abruption ($p = 0.03$) [38]. In this study, oligohydramnios (10.5%) and premature delivery (5.3%) were found to occur less frequently in women with hypothyroidism. These results echo those from prior studies [20, 27].

Fetal results :

Because preeclampsia and hypothyroidism are linked, low birth weight is also linked to hypothyroidism. Reduced fetal thyroxine may interfere with the fetal pituitary's ability to produce fetal growth hormone, the maturation of the vascular system, and the maintenance of cardiovascular homeostasis in utero [39–41]. These factors are responsible for the observed lower newborn birth weight in children born to moms who had their hypothyroidism poorly controlled at the time of delivery or in the third trimester. In this study, 31.6% of women with hypothyroidism had LBW, compared to 20% in a different study [42]. Thyroid disorder had a 42.1% NICU admission rate, which is comparable to the rates of 46.6 and(42)% [10, 42]. In comparison to another study's findings of 20%, 21.1% of babies born to hypothyroid mothers had low Apgar scores [15]. Contrary to one report's findings [38], We couldn't find any proof that fetal hypothyroidism causes intrauterine mortality. Hypothyroidism was observed to be significantly associated with LBW ($p = 0.001$) and NICU hospitalization ($p = 0.000$), which is similar to the study by Gupta HP et al. [38]. The results lead us to the conclusion that thyroid function analysis and diagnosis are essential from a clinical standpoint. The question of whether routine prenatal screening is more economical than targeted screening is still up for debate. Current recommendations recommend targeted TSH screening for expectant women who are at high risk for thyroid disease.[7]. Additionally, recommendations emphasize TPO antibodies positive and negative women. It states that TPO Abs positives at first trimester cutoff TSH 2.5 mU/L and more have a higher risk of miscarriage. Levothyroxine treatment at 9 weeks of gestation is recommended by authors in an RCT [43]. Additionally, they show that thyroxin therapy only improves unfavorable pregnancy outcomes in TPO Abs-positive women with mild hypothyroidism (defined as a TSH > 2.5 mU/L). The Task Force recommends that asymptomatic women with elevated TSH (2.5 mU/L) in the first trimester have their TPO Abs evaluated. We did not check the TPOAbs status of the study participants in this study. According to our sample size ($n = 198$), the study is 80.7% powered for the evaluation of the result across 8 independent variables, which is sufficient.

Implications: As TSH, T4 and T3 readings are tracked during the third trimester of pregnancy, the body of knowledge will expand. The strong correlation between hypothyroidism and a range of harmful consequences for both mother and fetus serves as additional evidence for the necessity of routine thyroid function testing throughout pregnancy. Limitations Due to the small sample size and inconsistent TSH estimation technique, we are unable to submit accurate TSH, T4, and T3 values for the third trimester of pregnancy.

Conclusion: According to current study's findings, thyroid impairment is highly prevalent in pregnancy (11%) in Babylon province where women are more likely to have subclinical hypothyroidism. The association between preeclampsia, pregnancy anemia, increased cesarean delivery, the presence of LBW neonates, decreased Apgar score, and a high rate of NICU hospitalization is the study's key finding.

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