Thyroid Stimulating Hormone Level (TSH) as Possible Indicator for Pre-Eclampsia

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Abstract

Introduction: Hypothyroidism and preeclampsia are associated with endothelial dysfunction. However, there is a rarity of information on the relationship between hypothyroidism in pregnancy, and the risk of preeclampsia. This study aimed to study thyroid hormones as a predictor for preeclampsia in pregnant women.

Patients and Methods: Group of cases: 50 clinically diagnosed pre-eclamptic pregnant women during third trimester, and Group of controls: 50 pregnant women normotensive during third trimester. Data collected through: Questionnaire include demographic, obstetrical, general history, medical and surgical history. Physical (general and pelvic) examination of the patients and laboratory investigation of thyroid function tests, Platelets count, white blood cell count were done to both groups.

Results: The preeclampsia group had significantly higher mean total white blood cell count than the control group, (10.9 ± 4.5), (7.16 ± 2.8), respectively. The mean thyroid stimulating hormone level was significantly higher among cases group (3.01 ± 1.35) than control group (1.9± 0.95). The mean tT3 level was non significantly lower among cases (1.81 ± 0.89) than control group (2.05 ± 1.4). The mean tT4 level was non significantly lower among cases (115.2±61.5) than control group (134.1± 55.52). The cases group had significantly higher percentage of subclinical hypothyroidism 8 (16%) and overt hypothyroidism 3 (6%) than the control group 2 (4%) and 0(0%) respectively.

Conclusions: The results of statistically significant increase in thyroid stimulating hormone levels and non-significant decrease in, tT3, tT4 levels among preeclampsia women indicate careful assessment of the preeclampsia women for thyroid function. The raised TSH levels could be used as predictor of preeclampsia.

Keywords: Thyroid Stimulating Hormone, Pre-eclampsia, Indicator.

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Introduction

Maternal thyroid hormone is essential for fetal development during the first trimester. Universal testing of thyroid-stimulating hormone (TSH) among all women at the preconception stage is controversial, although its selective use in women at high risk of low TSH is well established. [1] Elevated levels of human chorionic gonadotropin (hCG) during the first trimester of pregnancy activate the TSH receptor of the maternal thyroid gland, leading to a mild increase in free thyroxine T4 (FT4) and free triiodothyronine (FT3) levels, and a consequent decrease in maternal TSH [2]. These transient changes are the basis for the lower normal range of TSH levels in pregnancy [3]. Transient subclinical thyrotoxicosis may complicate 10%–20% of pregnancies [4], whereas 0.1%–0.4% of pregnancies are affected by overt hyperthyroidism, most cases of which are attributable to Graves' disease. [5] Low first-trimester TSH poses a clinical dilemma because it can indicate either transient hCG-induced thyrotoxicosis or Graves' disease, which may initially present with similar clinical features [6]. This distinction is important because overt hyperthyroidism in pregnancy can lead to spontaneous abortion, low birthweight, premature labor, stillbirth, pre-eclampsia, and heart failure [7]. By contrast, subclinical thyrotoxicosis of pregnancy is not associated with adverse outcomes [8]. Additionally, medical treatment of early pregnancy thyrotoxicosis poses risks for both mother and fetus; thus, anti-thyroid drugs should be used selectively in this setting [9].

Patients and Methods

A case control study carried out in Salahadeen general hospital/ gynecology outpatient clinic, during the period 1st January 2022 to 1st July 2022. A convenient sample was randomly selected and divided in to 2 groups: Group of cases: 50 clinically diagnosed preeclamptic pregnant women during third trimester (28-40 weeks), Group of controls: 50 pregnant women normotensive during third trimester (28-40 weeks). Informed consent was taken from women included in the study. Both groups informed about the study aims and informed about the results of their tests.

The inclusion criteria were age of 18–40 years, & without

history of thyroid disease before and through pregnancy. The exclusion criteria include the following: Patients with known history of chronic hypertension, renal disorders, cardiovascular diseases, diabetes, any metabolic disorder that may threat to mother or fetus and history of any treatment that might disturb the thyroid function. Patients were included from outpatient clinic and hospital admission those fulfilling the inclusion criteria. Data collected through: A- Questionnaire: consists of demographic questions, age, contain information about obstetrical and general history, medical and surgical history.

B- Physical examination of the patient: general and pelvic examination, Blood pressure. Lab investigation include: thyroid function tT3,tT4, TSH, Platelets count, white blood cell count.

RESULTS

The mean age of the cases was 28.5 ± 4.2 in comparison to the control group (26.6 ± 5.8), this relation was statistically significant(P value < 0.05), as shown in table 3.1. Most of the cases and controls were from rural area 26(52%), 29(58%), this relation was statistically not significant (P value > 0.05). Most of the cases 2ndry school education 17(34%), and control had 1ry education 17(34%), this relation was statistically not significant (P value > 0.05).

Most of the cases and controls were housewife 36(72%), 38(76%), this relation was statistically not significant (P value > 0.05). Most of the cases Primigravida 24(48%), in comparison to control group 11(22%), this relation was statistically significant (P value < 0.05). Most of the cases Nulliparous 30(60%), in comparison to control group 14(28%), this relation was statistically significant (P value < 0.05). As shown in table 1.

Table 1. The general characteristics of cases and controls

General characteristics	**Cases**		**Controls**		
	Frequency	**Percent**	**Frequency**	**Percent**	**P value**
Age (mean± SD)	28.5 ± 4.2		26.6 ± 5.8		<0.05 *S
Residence					
Urban	24	48	21	42	>0.05 NS
Rural	26	52	29	58	
Education					
Illiterate	11	22	12	24	>0.05 NS
1ry	15	30	17	34	
2ndry	17	34	13	26	
College	7	14	8	16	
Job					
Employed	14	28	12	24	>0.05 NS
Housewife	36	72	38	76	
Gravidity					
Primigravida	24	48	11	22	< 0.05 S*
2_4	22	44	24	48	
>4	4	8	15	30	
Parity					
Nulliparous	30	60	14	28	< 0.05 S*
1_3	15	30	17	34	
> 3	5	10	19	38	

The classification of preeclampsia patient according to the severity show that 24(48%) of the patient were mild cases of preeclampsia and 26 (52%) of them were sever preeclampsia, as shown in figure 3.1.

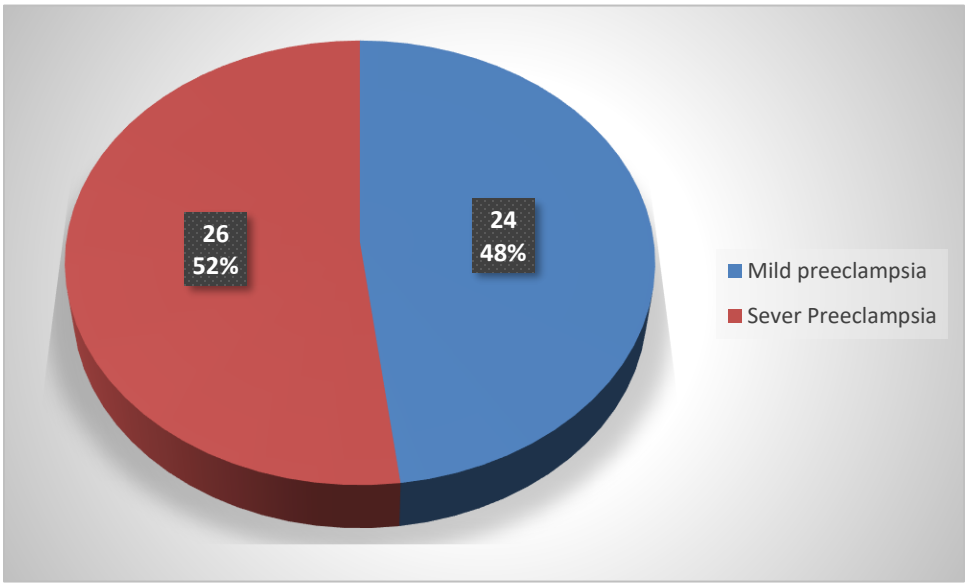

Figure 3.1. Classification of preeclampsia patient according to severity

The Maternal and neonatal outcome represent that most of the cases delivered by Caesarean section (C/S) 28(56%), in comparison to control group 15(30%), this relation was statistically significant (P value < 0.05). the cases had preterm labour 14 (28%),higher than the control group 4(8%), this relation was statistically significant (P value < 0.05). the cases had low birth weight 11 (22%),higher than the control group 3(6%), this relation was statistically significant (P value < 0.05). As shown in table 2.

Table 2: The maternal and neonatal outcomes

maternal and neonatal outcomes	**Cases**		**Controls**		
	Frequency	**Per cent**	**Frequency**	**Per cent**	**P value**
Mode of delivery					
C/S	28	56	15	30	< 0.05 S*
Vaginal delivery	22	44	35	70	
Gestational age					
Preterm	14	28	4	8	< 0.05 S*
Term	36	72	46	92	
Intrauterine death					
Yes	1	8	0	0	>0.05 NS
No	49	92	50	100	
Birth weight					
Normal	39	78	47	94	< 0.05 S*
Low	11	22	3	6	

*significant, C/S Caesarean section

The cases group had higher mean systolic blood pressure than the control group, (145.4±7.6), (115± 5.43), respectively, this relation was statistically significant as shown in table 3.4. The cases group had higher mean systolic blood pressure than the control group, (96.8±4.6), (80±5.9), respectively, this relation was statistically significant as shown in table 3.

Table 3: The systolic and diastolic blood pressure among cases and controls

Blood pressure	**Cases**	**Control**	**P(t)**
Systolic BP	145.4±7.6	115± 5.43	<0.05(30.3)*
Diastolic BP	95.8±4.6	80±5.9	<0.05(15.8)*
*significant, BP: blood pressure			

The cases group had lower mean platelet count ($\times 10^3/\mu L$) than the control group, (160.2± 42.4), (191.8 ± 35.24), respectively, this relation was statistically significant as shown in table 3.5. The cases group had higher mean Total WBC ($\times 10^3/\mu L$) than the control group, (10.9 ± 4.5), (7.16 ± 2.8), respectively, this relation was statistically significant, as shown in table 3.4

Table 3: The mean platelet and WBC count among cases and controls

	Cases	**Control**	**P(t)**
platelet count ($\times 10^3/\mu L$)	160.2± 42.4	191.8 ± 35.24	<0.05(6.3)*
Total WBC ($\times 103/\mu L$)	10.9 ± 4.5	7.16 ± 2.8	<0.05(4.9)*
*significant, WBC: white blood cell count			

The mean thyroid stimulating hormone (TSH) level was

higher among cases (3.01 ± 1.35) than control group (1.9± 0.95), this relation was statistically significant (P value < 0.05), as shown in table 3.5. The mean tT3 level was lower among cases (1.81 ± 0.89) than control group (2.05 ± 1.4), this relation was statistically not significant (P value < 0.05), as shown in table 3.5. The mean tT4 level was lower among cases (115.2±61.5) than control group (134.1± 55.52), this relation was statistically not significant (P value < 0.05), as shown in table 5.

Table 5: The mean thyroid hormones among cases and controls

	Cases	Control	P(t)
TSH	3.01 ± 1.35	1.9± 0.95	<0.05(4.7)
tT3	1.81 ± 0.89	2.05 ± 1.4	> 0.05(1.02)
tT4	115.2±61.5	134.1± 55.52	>0.05(1.6)
*significant, TSH: thyroid stimulating hormone			

The subclinical hypothyroidism was found among 8(16%) of the cases in comparison to 2(4%) of the control group, and overt hypothyroidism found among 3(6%) of the cases in comparison to 0(0%) of the control group, the normal thyroid function was found among 39(78%) of the cases in comparison to 48(96%) of the control group, this relation was statistically significant (X2=7.5, df=2, P value= < 0.05) as shown in figure 3.2.

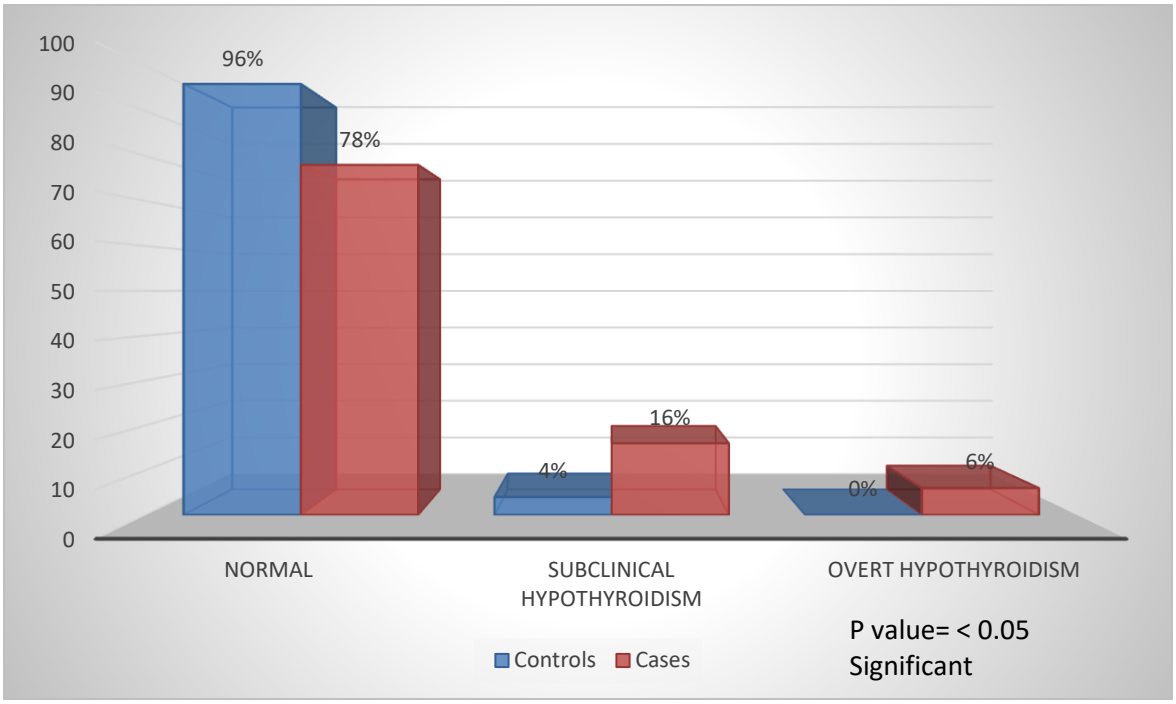

Figure 2: Distribution of cases & controls according to thyroid function status

Discussion

The mean age of the cases was significantly higher among cases (28.5 ± 4.2) in than the control group (26.6 ± 5.8), this goes with Majeed BA et al 2020 in Iraq [10] the mean age of PE patient (29.47 ± 6.32) were significantly higher than control group. Sheen JJ et al 2020 found that the proportion of women with preeclampsia aged 15 to 24 years decreased from 42.3% in 1998 to 30.1% in 2014, while preeclampsia among those 30 to 54 years increased from 32.9 to 43.7%, With a changing demographic profile of preeclampsia, older women accounted for an increasing proportion of preeclampsia and related adverse outcomes. [11] Also Hussein YA, and ALEzzi J 2018[12] *f*ound that predominant age group among PE women was 20-29 years (51.6%). A study in Japan documented that pregnancy of maternal age more than 40 years is highly accompanied by adverse maternal outcomes like pre-eclampsia, severe eclampsia, cesarean section and placenta previa and age effect differs according to conception way and parity. [13] Most of the cases primigravida 24(48%), in comparison to control group 11(22%) this goes with Hussein YA, and ALEzzi J 2018 [12] found (51.7%) was primigravida. Most of the cases Nulliparous 30(60%), in comparison to control group 14(28%), this goes with Kongwattanakul K, et al 2018 [14] found that 49.8%) of PE patient were nulliparous. The Maternal and neonatal outcome represent that most of the cases delivered by Caesarean section 28(56%), in comparison to control group 15(30%), this goes with Majeed BA et al 2020 in Iraq[10] found that the cesarean section delivery was

significantly the most common adverse maternal outcome of pre-eclampsia (p<0.001; OR=9.1). also Hussein YA, and ALEzzi J 2018 [12] found a highly significant association between CS delivery mode and PE (71%) of PE patient delivered by Caesarean section. van der Tuuk K et al 2015 [15] in Netherlands reported that in women with pre-eclampsia, the cesarean section risk is predicted. In current study the cases had preterm labour 14 (28%), higher than the control group 4(8%), this goes with Hussein YA, and ALEzzi J 2018 [12] found (65%) of PE pregnant had preterm labour. The cases had low birth weight 11 (22%),higher than the control group 3(6%), this goes with Parra-Pingel PE et al 2017 [16] found that low birth weight was (43.9%) among PE pregnant. Venkatesh KK et al [17] found that fetal growth restriction among PE women was (7%). The cases group had lower mean platelet count ((160.2± 42.4) $\times 10^3/\mu L$) than the control group, (191.8 ± 35.24$\times 10^3/\mu L$), this goes with previous studies done by Sitotaw C et al 2018 [18] found the the mean ± SD platelet count (PTC) was significantly lower in PE group (158.38 ± 42.71 × 103/μL) comparedto the control group (194.05 ± 45.59 × 103/μL). Alisi PN et al 2014 [19] found significant decrease in platelate cont among PE women.In contrary Çintesun E, et al 2018 found that no significant diffrence in the platelate count between control and PE group while meanplatelate volume was significantly higher among PE group [20] In this study, we observed statistically significant elevated leukocyte count in PE group (10.9 ± 4.5), as compared to the control group (7.16 ± 2.8). Similar findings have been reported by Sitotaw C ET AL 2018[18] found the mean ± SD white blood cell count (WBC) was significantly higher in PE group (10.71 ± 3.49× 103/μL) compared to the control group (8.18 ± 2.05× 103/μL). This may be due to an exaggerated inflammatory response in PE than healthy pregnancy, and that Activated leukocytes are responsible for the vascular dysfunction associated with preeclampsia[21] The mean thyroid stimulating hormone (TSH) level was significantly higher among cases (3.01 ± 1.35) than control group (1.9± 0.95). this findings goes with Muraleedharan N 2017 found that [22], TSH was significantly high in PE (3.76 ± 1.55) than controls (2.30 ± 0.94 mIU/L). Sattar R et al 2018 [23] found that the average concentration of TSH in normotensive pregnant group was (3.28 ± 0.29 μIU/ml). The mean value of TSH in preeclamptic group was found 6.56±1.88 μIU/ml that was observed 100% higher in PE but all the increases were statistically not significant. Murmu AK et al 2018 [24] found that TSH of the PE and control group was 2.407±0.171mIU/L and I.5±0.954mIU/L respectively.

The mean tT3 level was non significantly lower among cases (1.81 ± 0.89) than control group (2.05 ± 1.4), and the mean tT4 level was lower among cases (115.2±61.5) than control group (134.1± 55.52), this goes with Sattar R et al 2018 [23] who found that Mean FT3 in PE was (2.12±0.55) and in controls was (2.43 ± 0.47 pg/ml). FT4 in cases was 1.16±0.24 and in controls was 1.33± 0.27 ng/dL, suggestive of hypothyroidism, and he found that the risks for hypothyroidism increase with the severity of PE. Murmu AK et al 2018 [24] found that The mean fT3 of the study group and control group were 1.422±0.621 pg/ml and 1.604±0.63 pg/ml respectively. Zhang Y et al 2017 [25] found that after normalization of the thyroid hormoneswith appropriate treatment in women developing hypothyroidism in the first trimester, there was no significant difference in the risk of developing preeclampsia compared with the normal pregnant women, and if the women developed hypothyroidism in the third trimester, they still had a 2.18-fold higher risk of developing preeclampsia [25]. It has been suggested that the reduced concentration of t3 and t4 levels might be explained by the loss of protein and protein bound hormones. Since t3 is mostly the product of peripheral conversion of t4, the involvement of organs such as liver and kidney contributes to low level of t3. [25]

Nwabudike P et al 2022 [26] found that the mean triiodothyronine (T3) among hypertensive pregnant women was observed to be non-significantly higher (1.02 ± 0.85) than non-hypertensive pregnant women(1.64 ± 0.08). was also observed in thyroxine (T4) levels when hypertensive pregnant women and non-hypertensive pregnant women were compared. The subclinical hypothyroidism was found among 8(16%) of the cases in comparison to 2(4%) of the control group, and overt hypothyroidism found among 3(6%) of the cases in comparison to 0(0%) of the control group, the normal thyroid function was found among 39(78%) of the cases in comparison to 48(96%) of the control group. This goes with Murmu AK et al 2018 [24] found that 42 % of preeclampsia had hypothyrodism. This findings goes with Deshpande S 2015 [89] who found that that preeclampsia group have chance of higher TSH (>4.8 mIU/L) by 2.19 times, and 20% had subclinical hypothrodism and 3% had overthypothyrodism that preeclampsia group have chance of higher TSH (>4.8 mIU/L) by 2.19 times. Gui J et al 2020 found that 12 % of those with sever preeclampsia had subclinical hypothyrodism and 9.4 % had overt hypothyrodism [27] Hypothyroidism has been shown to have various vascular pathogenic effects, including endothelial cell dysfunction [28] which is also a pathophysiological basis of gestational hypertension Worldwide, iodine deficiency is the most common cause of hypothyroidism, however, in iodine-sufficient countries like the United States, the most common cause is autoimmune thyroiditis or Hashimoto's thyroiditis [29]. Marginal dietary iodine deficiency is one of the most common causes of isolated hypothyroxinemia [30].

Conclusions and Recommendations

The cases group had significantly higher percentage of subclinical hypothyroidism (16%) and overt hypothyroidism (6%) than the control group (4%) and (0%) respectively. The results of statistically significant increase in thyroid stimulating hormone levels and non-significant decrease in, tT3, tT4 levels among preeclampsia women indicate careful assessment of the preeclampsia women for thyroid function.

The raised TSH levels could be used as predictor of preeclampsia.

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