

# Frequency of Pregnancy Induced Hypertension (PIH) in Patients Presenting with Hypothyroidism

NAVEEDA ATIF<sup>1</sup>, JAVARIA IMRAN<sup>2</sup>, ERUM ILYAS<sup>3</sup>, SAIRA JAMSHEED<sup>4</sup>, ZAKIA SHAKEEL<sup>5</sup>, ADNAN ANWAR<sup>6</sup>

<sup>1</sup>Senior Registrar, Department of Obstetrician and Gynecology, Sir Syed Medical College and Hospital.

<sup>2</sup>Specialist, Obstetrician and Gynaecologist, Sindh Government Hospital, Korangi, Karachi.

<sup>3</sup>Senior Registrar, Obstetrician and Gynaecologist, Sir Syed Medical College and Hospital.

<sup>4</sup>Associate Professor, Obstetrician and Gynaecologist, Hamdard University Hospital.

<sup>5</sup>Assistant Professor, Obstetrician and Gynaecologist, Liaquat College of Medicine and Dentistry

<sup>6</sup>Associate Professor of Physiology, Hamdard College of Medicine and Dentistry.

Corresponding author: Naveeda Atif, Email: [shizrashahnawaz@yahoo.com](mailto:shizrashahnawaz@yahoo.com)

## ABSTRACT

**Objective:** Preeclampsia is a potentially fatal condition during pregnancy and following delivery. Numerous organs' functions can be influenced by preeclampsia. It is crucial, as this illness may be linked to abnormalities in thyroid function. Therefore, the aim of this study was to assess the frequency of thyroid dysfunction and its association with hypertension in pregnant women.

**Methodology:** This descriptive cross sectional study was conducted at Obstetrics and Gynecology Unit-I, Civil Hospital, Karachi, using a non-probability consecutive sampling technique. The duration of the study was about six months from October 2022 till March 2023. A total of 80 pregnant women who were between the ages of 18 and 40, had gestational ages between 20 and 40 weeks, and had laboratory results that suggested hypothyroidism were included in this study. A chi-square test was applied to evaluate the association between maternal age, parity, gestational age, serum levels of TSH and T4 and pregnancy induced hypertension.

**Results:** The study findings showed that most of the women 33(41.25%) were between 26 to 35 years of age. The mean age of the pregnant women was 29.43±4.64 years. The mean parity was 1.74±0.83 and the mean gestational age was 30.33±5.22 weeks, and the mean duration of hypothyroidism was 4.27±2.06 years. Concerning thyroid parameters, the mean T4 was 5.79±1.21 pmol/L, and the mean TSH was 6.28±2.03 mIU/L. Additionally, there was an insignificant association observed between pregnancy induced hypertension and maternal age, gestational age, parity, and thyroid hormone parameters.

**Conclusion:** This study concluded that alterations in the thyroid function of pregnant women led to pregnancy induced hypertension. Only 25% of hypothyroid pregnant women had gestational hypertension. Furthermore, age, parity, gestational age, and thyroid parameters of pregnant women were insignificantly associated with pregnancy induced hypertension.

**Keywords:** Pregnancy induced hypertension, hypothyroidism, gestational age.

## INTRODUCTION

Preeclampsia is a condition that can have fatal consequences during pregnancy and after giving birth [1]. Preeclampsia is an important health concern that has an affect 2-8% of pregnancies and is a primary reason of morbidity and mortality in mothers and newborns around the world [2, 3]. Preeclampsia was identified in 2017 by the American College of Obstetricians and Gynecologists (ACOG) as having a proteinuria of higher than or equivalent to 300 mg in 24 hours of collection of urine and a blood pressure reading of above 140/90 mmHg at gaps of four hours following the 20th week of gestation [4].

The thyroid gland undergoes entirely typical physiological modifications in pregnancy, and when these changes are not compatible, the thyroid gland becomes dysfunctional. Thyroid hormone levels naturally rise by 40–100% based on the nutritional requirements of both the mother and the fetus [5]. Thyroid Stimulating Hormone (TSH) rises in a healthy pregnancy as a result of an increase in Human Chorionic Gonadotropin (HCG) concentration [6]. While free triiodothyronine and free thyroxine (FT3 and FT4) increase more slowly, total thyroxine (TT4) and total triiodothyronine (TT3) concentrations rise quickly [5]. Only 0.2% of T3 and 0.02% of T4 are free in the serum, whereas the majority of thyroid hormones are protein bound. The majority of thyroid hormones—between 45 and 70 percent bind to thyroxine-binding globulin (TBG), with the remainder bound to albumin and transthyretin [6].

The thyroid gland is one of the body organs whose activity is disturbed by hypertension [7]. Generally, not all investigations came to the same conclusions. For instance, despite rising TSH levels in one study, women with preeclampsia had relatively stable T3 and T4 levels [8]. Similarly, the outcomes of two trials showed no discernible differences in TSH, TT4, or TT3 levels between preeclamptic and healthy pregnant women [4,9]. According to American Thyroid Association (ATA) recommendations, there is no connection between preeclampsia and alterations in thyroid function testing [10]. According to certain research, preeclamptic

pregnant women were more likely than normal pregnant women to experience an elevation in TSH and low T4 levels [9].

A number of health-related impacts on mothers and babies have been linked to maternal thyroid hormones, which are vital for preserving systemic homeostasis. Numerous investigations have demonstrated a link between hypertensive diseases and thyroid dysfunction [11,12]. In China, persistent hypertension, gestational hypertension (GH), preeclampsia, and eclampsia are some of the hypertensive illnesses of pregnancy, with a predicted incidence of 4% to 11% among pregnant women [13]. A significant contributor to maternal and newborn morbidity and mortality is GH. According to one observational study, mothers with hypothyroidism have a higher risk of GH [14]. Further researches, however, have found less convincing links between GH and milder types of maternal thyroid dysfunction [15].

Pregnant women frequently experience thyroid problems. In accordance with earlier studies, the overall incidence of subclinical or overt hyperthyroidism during pregnancy ranges from 0.1-0.4%. Approximately 2.5 percent of people have hypothyroidism, of which 0.2-0.3% have clinical hypothyroidism, 2-3% have subclinical hypothyroidism, and 1% to 2% have hypothyroxinemia [16].

One of the recognized reasons of hypertension is hypothyroidism. Untreated overt and subclinical hypothyroidism are both linked to a number of negative effects on the mother and fetus [17,18]. Negative neonatal results are not more likely to occur in treated hypothyroid patients than in healthy pregnant women, but preeclampsia risk may be higher [19]. According to research by Medici M et al. [20], biochemical hyperthyroidism during early pregnancy but not hypothyroidism is linked to a higher risk of hypertensive problems. Hence, more research is still needed to determine the connections between thyroid dysfunction and preeclampsia-related pregnancy outcomes. Preeclampsia with an early onset at < 34 weeks of pregnancy is known to have an increased risk of placental malfunction [21], and it has also been shown to increase the risk of cardiovascular [22], respiratory, renal, neurological, hepatic, and other comorbidities [23]. Thyroid

hormones were, however, tested in the majority of earlier investigations before 20 weeks of gestation.

According to international scientific society recommendations, a maternal age of more than 30 years is also a risk indicator for hypothyroidism in pregnancy, and thyroid function screening is advised [24]. Nonetheless, there isn't much research that specifically addresses the connection between maternal thyroid function and GH.

It is imperative to comprehend the prevalence of thyroid dysfunction in pregnancy to conduct community-based assessments safely. In Pakistan, there is a dearth of data available on pregnancy-induced hypertension and thyroid abnormalities during pregnancy. Therefore, the objective of this study was to assess the frequency of thyroid dysfunction and its association with hypertension in pregnant women in their 2<sup>nd</sup> and 3<sup>rd</sup> trimesters.

**METHODOLOGY**

This descriptive cross sectional study was conducted at Obstetrics and Gynecology Unit-I, Civil Hospital, Karachi, using a non-probability consecutive sampling technique. The Ethical Review Committee of the Civil Hospital gave ethical approval of this study. The duration of the study was about six months, from October 2022 till March 2023. A total of 80 pregnant women who were between the ages of 18 and 40, had gestational ages between 20 and 40 weeks (determined by history and ultrasound scan), were alive, had singleton pregnancies on USG, were of any parity, and had laboratory results that suggested hypothyroidism were included in this study. Mothers who had a serious illness were excluded from the study, including those with diabetes (as determined by a blood glucose test), chronic hypertension, ischemic heart disease, renal disease, multiple gestations, ectopic pregnancies found on ultrasound, patients taking thyroxin or other medications that affect thyroid function, and patients with a history of pituitary tumors that secrete TSH.

Pregnant women who presented to the Unit-I obstetrical OPD, met the eligibility requirements, and had hypothyroidism were enrolled after receiving proper written consent. The researcher recorded information on name, age, gestational age, parity, and residence on a proforma. Pregnancy-related hypertension was identified based on a clinical examination, and blood pressure was monitored using a sphygmomanometer that was in good working order. Before 20 weeks of pregnancy, GH was classified as having a systolic blood pressure of  $\geq 140$  mmHg and/or a diastolic blood pressure of  $\geq 90$  mmHg with normal blood pressure. Between weeks 21 and 38 of pregnancy, blood samples were taken at the outpatient clinic. Electrochemiluminescence immunoassays were used to test thyroid hormone parameters, including the levels of thyroid-stimulating hormone (TSH) and free thyroxine (FT4), According to manufacturer's instructions. Patients were monitored to look for the development of PIH at 24, 28, 34, 36, and 38 weeks until childbirth.

All data was entered and analyzed using SPSS version 19. Mean and standard deviation were used to express continuous variables such as the mother age, parity, gestational age, blood pressure, and serum TSH and T4 levels. Frequency and percentages used to express categorical variables, such as the pressure of pregnancy-induced hypertension. A chi-square test was applied to evaluate the association between maternal age, parity, gestational age, serum levels of TSH and T4, and pregnancy induced hypertension. A p-value of  $\leq 0.05$  was taken as statistically significant.

**RESULTS**

A total of 80 pregnant women with hypothyroidism were involved in this study. The frequency of pregnancy induced hypertension among pregnant women presenting with Hypothyroidism was observed in 20(25.0%) women, and 60(75.0%) women had no pregnancy induced hypertension, as shown in Fig. 1.

The mean age of the pregnant women was 29.43 $\pm$ 4.64 years. The mean parity was 1.74 $\pm$ 0.83 and the mean gestational age was 30.33 $\pm$ 5.22 weeks, and the mean duration of hypothyroidism was 4.27 $\pm$ 2.06 years, as shown in Table I.

Descriptive statistics of blood pressure revealed that the mean Systolic blood pressure of the pregnant women was 131.25 $\pm$ 11.01 mm Hg, and the mean diastolic blood pressure was 84.36 $\pm$ 7.06 mm Hg. Concerning thyroid parameters, the mean T4 was 5.79 $\pm$ 1.21 pmol/L, and the mean TSH was 6.28 $\pm$ 2.03 mIU/L, as shown in Table II.

Out of 80 pregnant women, 37(46.25%) had primiparity and 43(53.73%) had multiparity, wherein 11(29.7%) primiparous women had pregnancy induced hypertension while 9(20.9%) multiparous women had PIH, with an insignificant association observed among them (p=0.365). Most of the women 33(41.25%) were between 26 to 35 years of age; 21(26.25%) women were between 31 to 35 years, 18(22.50%) women were  $\leq$  25 years, and only 8(10.0%) women were  $>$ 35 years, Furthermore, it was observed that the rate of PIH had an insignificant relationship among different age groups (p=0.292). Concerning gestational age, 13(31%) women had PIH and 29(69%) had no PIH in 21 to 32 weeks, whereas 7(18.4%) women had PIH and 31(81.6%) had no PIH in 33 to 38 weeks, with an insignificant association observed among them (p=0.196). Around 11(24.4%) women had  $\leq$  5 pmol/L T4 and 9(25.7%) women had  $>$  5 pmol/L T4 with an insignificant difference noticed among them (p=0.896). Around 9(19.6%) women had 4.6-5.9 mIU/L TSH and 11(32.4%) women  $\geq$  6 mIU/L TSH, with an insignificant difference noticed among them (p=0.192), as shown in Table III.

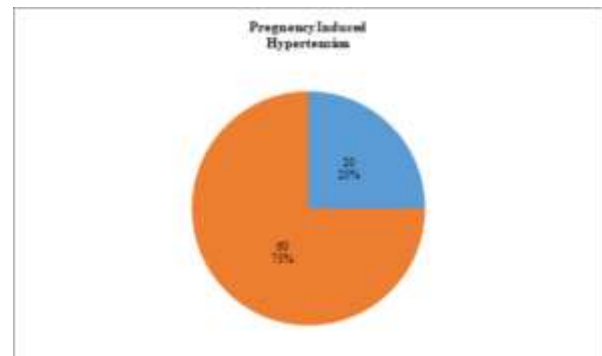


Fig. 1: Frequency of Pregnancy Induced Hypertension among pregnant women presenting with Hypothyroidism.

Table 1: Descriptive Statistics of pregnant women (n=80).

Variables	Mean $\pm$ Std. Deviation	95% Confidence Interval for Mean		Median (IQR)
		Lower Bound	Upper Bound	
Age (Years)	29.43 $\pm$ 4.64	28.39	30.46	29(7)
Parity	1.74 $\pm$ 0.83	1.55	1.92	2(1)
Gestational Age (Weeks)	30.33 $\pm$ 5.22	29.16	31.49	30(10)
Duration of Hypothyroidism	4.27 $\pm$ 2.06	3.81	4.735	4(3)

Table 2: Descriptive Statistics of Blood Pressure and Thyroid Profile.

Variables	Mean $\pm$ Std. Deviation	95% Confidence Interval for Mean		Median (IQR)
		Lower Bound	Upper Bound	
Systolic blood pressure SBP (mmHg)	131.25 $\pm$ 11.01	128.79	133.70	130(16.8)
Diastolic blood pressure DBP (mmHg)	84.36 $\pm$ 7.06	82.79	85.93	80(10)
T4(pmol/L)	5.79 $\pm$ 1.21	5.52	6.06	5(1)
TSH(mIU/L)	6.28 $\pm$ 2.03	5.8356	6.74	5.8(1.39)

Table 3: The association of the frequency of pregnancy-induced hypertension among pregnant women presenting with Hypothyroidism by Age Groups, Parity, Gestational Age, T4, and TSH.

Variables	Pregnancy Induced Hypertension			p-value	
	Yes	No	Total		
Age groups	≤ 25 Years	7(38.9%)	11(61.1%)	18(22.50%)	0.292
	26 to 30 Years	6(18.2%)	27(81.8%)	33(41.25%)	
	31 to 35 Years	4(19.0%)	17(81.0%)	21(26.25%)	
	>35 Years	3(37.5%)	5(62.5%)	8(10.0%)	
Parity	Primiparity	11(29.7%)	26(70.3%)	37(46.25%)	0.365
	Multiparity	9(20.9%)	34(79.1%)	43(53.75%)	
Gestational Age(weeks)	21 to 32	13(31.0%)	29(69.0%)	42(52.5%)	0.196
	33 to 38	7(18.4%)	31(81.6%)	38(47.5%)	
T4 (pmol/L)	≤5 pmol/L	11(24.4%)	34(75.6%)	45(56.25%)	0.896
	>5 pmol/L	9(25.7%)	26(74.3%)	35(43.75%)	
TSH (mIU/L)	4.6-5.9	9(19.6%)	37(80.4%)	46(57.5%)	0.192
	≥6	11(32.4%)	23(67.6%)	34(42.5%)	

**DISCUSSION**

The circulation of maternal thyroid hormone is crucial to regulating systemic homeostasis and has been linked to a variety of adverse health outcomes in both pregnant women and young babies [25]. According to some authors, pregnant women who have thyroid dysfunction also tend to have high blood pressure and hypertensive diseases [11]. Changes in thyroid function can have anegative effect on a number of organ systems and increase the risk of hypertensive pregnancy problems [26]. As a result, this study showed the relationship between thyroid parameters and pregnancy-induced hypertension in pregnant women.

A cross-sectional study evaluated 200 women, including 150 pregnant hypertensive women, 25 non-hypertensive pregnant women, and 25 non-pregnant non-hypertensive women. According to the study's findings, hypertensive pregnant women are substantially older than non-hypertensive pregnant women and non-pregnant non-hypertensive women (p<0.001). When the ages of non-hypertensive pregnant women and non-pregnant non-hypertensive women were compared, there was no discernible difference (p > 0.05). When compared to pregnant women who were not hypertensive, the serum TSH was considerably greater in the hypertension group (p 0.035). When the thyroxine (T4) levels of pregnant women with hypertension and pregnant women without hypertension were evaluated, there was no discernible difference (p > 0.05) [27]. The present study was inconsistent with the above-reported study and revealed that there was an insignificant association observed between the age groups and hypertension and non-hypertension induced by pregnancy in pregnant women (p=0.292). Additionally, an insignificant difference was also observed in TSH (p=0.192) and T4 level (p=0.896) and PIH.

One of the vascular pathologic effects of hypothyroidism has been discovered to be endothelial cell dysfunction, which serves as a pathophysiological component of gestational hypertension [28]. According to another study, a higher maternal serum TSH level (more than 10 mIU/L) was linked to a higher chance of stillbirth [29]. In contrast to the previously mentioned study, the current investigation found that maternal blood TSH levels of ≥ 6 mIU/L were associated with pregnancy-induced hypertension in 11 (32.4%) pregnant women.

Numerous studies [20,30] only examined the first trimester and left out other preeclampsia forms [31]. Another study evaluated different types of preeclampsia depending on severity and age at gestation and assessed thyroid hormones in women with gestational hypertension in the second trimester of pregnancy [32]. Additionally, their findings agreed with those of other second-trimester research. Similarly, a study involving 6031 women revealed that there was no appreciable difference in the risk of developing preeclampsia compared to normal pregnant women after adjustment of the thyroid hormones with proper therapy in women with hypothyroidism in the first trimester. Nevertheless, the risk of preeclampsia was 2.18 times higher for women if hypothyroidism developed during the third trimester. As far as the present study is concerned, hypertension was observed at gestational age at the end of second and third trimesters. It was seen that 13(31.0%) pregnant women had hypertension at 21 to 32

weeks and 7(18.4%) had hypertension at 33 to 38 weeks, with an insignificant difference noticed among them (p=0.196).

This prospective cohort study assessed the relationships between early-pregnancy maternal thyroid hormone levels and gestational hypertension (GH). They discovered, in line with other studies [26], that hypothyroidism, subclinical hypothyroidism, and elevated TSH levels were linked to an increased risk of GH [25]. The present study was not similar to the above-reported studies and revealed that only 20(25.0%) pregnant women with hypothyroidism reported gestational hypertension. However, an insignificant association was observed among pregnant women with and without PIH.

Our research has several restrictions. Because of the limited sample size and single centre design of this investigation, the sensitivity and specificity of the findings were not entirely sufficient. We are currently unable to identify whether thyroid dysfunction in the second half trimester or in the third trimester has a bigger impact on maternal and fetal pregnancy outcomes due to the limited size of our study. Undoubtedly, further research is required to better understand the relationship between thyroid disease and newborn outcomes. The findings imply that, even if thyroid function is normal during the first trimester, thyroid function monitoring during the second trimester is important. Therefore, thorough thyroid hormone assessment during the entire pregnancy and prompt therapy are crucial to lowering the risk of preterm birth and reduced birth weight. Therefore, the need for infant critical care units will decline, as will the burden on families and society as a whole. Thyroid dysfunction should be treated as soon as feasible to prevent negative pregnancy outcomes, hence, it may be beneficial to evaluate thyroid hormone levels in women with preeclampsia in all three stages.

**CONCLUSION**

This study concluded that alterations in the thyroid function of pregnant women led to pregnancy induced hypertension. Only 25% of hypothyroidpregnant women had gestational hypertension. Furthermore, age, parity, gestational age, and thyroid parameters of pregnant women were insignificantly associated withpregnancy induced hypertension. For the purposes of timely treatment and diagnosis and to enhance pregnancy outcomes, it may be frequent to evaluate thyroid function in pregnant hypertensive women. Consequently, if a diagnosis is obtained, thyroid conditions that manifest during pregnancy may be effectively treated. In addition, it is very likely that this illness will have major health effects on the mother and the newborn child.

**REFERENCES**

1. Popovski N, Nikolov A. Practice Bulletin of the American College of Obstetrics and Gynaecologists 2019 on Magement of Hypertensive Disorders in Pregnancy-A Short Review of the Current Recommendations. *Biomed J Sci Tech Res.* 2019;23(2):17198–201.
2. Sadek A, Baban R, Al-Habib, M, Khazaali E. Serum vitamin D3 levels in pregnant women with preeclampsia at third trimester of pregnancy. *Baghdad J BiochemApplBiol Sci.* 2021;2(03):131–7.DOI: <https://doi.org/10.47419/bjbabs.v2i03.42>.
3. Nasser NA, Baban RS, Al-Habib MF, Jameel RA. The association between urinary placental protein 13 and soluble fms-like tyrosine kinase-1 in preeclamptic women in the third trimester of pregnancy. *Baghdad Journal of Biochemistry and Applied Biological Sciences,* 2020;1(01):49-55. doi: bjbabs.v1i01.31
4. Sattar R, Ahmed E, Abbasi SQ. Thyroid Hormones Pattern in Preeclampsia. *Ann King Edward Med Univ Lahore Pakistan.* 2018;24(S):863–6.
5. Alemu A, Terefe B, Abebe B, Biadgo B. Thyroid hormone dysfunction during pregnancy: A review. *Int J Reprod Biomed.* 2016 Nov;14(11):677-686.
6. Chowdhary S, aara S, Nazeer M., Allaqban, M. Thyroid Function Tests in Preeclampsia. *Int J Med SciClin Invention.* 2018;5(03):3606–9.<https://doi.org/10.18535/ijmsci/v5i3.09>
7. Sadiq AM, Yousif MG, Mohammed FA, Aladly SH, Hameed HH. Subclinical hypothyroidism with preeclampsia. *Res J Pharm BiolChem Sci.* 2016;7(3):1536–44.

8. Thanna RC, Nigoskar S. Association of TSH (Thyroid Stimulating Hormone) with Preeclampsia as a Diagnostic Indicator. *Int J Health Sci Res.* 2015;5(6):107–10.
9. Khadem N, Ayatollahi H, VahidRoodsari F, Ayati S, Dalili E, Shahabian M, et al. Comparison of serum levels of Tri-iodothyronine (T3), Thyroxine (T4), and Thyroid-Stimulating Hormone (TSH) in preeclampsia and normal pregnancy. *Iran J Reprod Med.* 2012 Jan;10(1):47-52.
10. Alexander EK, Pearce EN, Brent GA, Brown RS, Chen H, Dosiou C, et al. 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. *Thyroid.* 2017;27(3):315–89.
11. Ramtahal R, Dhanoo A. Subclinical hypothyroidism causing hypertension in pregnancy. *J Am Soc Hypertens* 2016; 10(9): 691–693.
12. Han Y, Mao LJ, GeXet, Huang K, Yan SQ, Ren LL, al. Thyroid autoantibodies in pregnancy are associated with hypertensive disorders of pregnancy: Ma'anshan Birth Cohort Study. *ClinEndocrinol (Oxf).* 2018; 88(6): 928–925.
13. Zhu YC, Yang HX, Wei YM, Zhu WW, Meng WY, Wang YQ, et al. Analysis of correlation factors and pregnancy outcomes of hypertensive disorders of pregnancy - a secondary analysis of a random sampling in Beijing, China. *J Matern Fetal Neonatal Med* 2017; 30(6): 751–754. DOI: 10.1080/14767058.2016.1186161.
14. Männistö T, Mendola P, Grewal J, Xie Y, Chen Z, Laughon SK. Thyroid diseases and adverse pregnancy outcomes in a contemporary US cohort. *J ClinEndocrinolMetab.* 2013 Jul;98(7):2725-33. doi: 10.1210/jc.2012-4233.
15. Mannisto T, Vaarasmaki M, Pouta A, Hartikainen AL, Ruokonen A, Surcel HM, et al. Thyroid dysfunction and autoantibodies during pregnancy as predictive factors of pregnancy complications and maternal morbidity in later life. *J ClinEndocrinolMetab* 2010; 95(3): 1084–1094.
16. Dulek H, Vural F, Aka N, Zengin S. The prevalence of thyroid dysfunction and its relationship with perinatal outcomes in pregnant women in the third trimester. *North ClinIstanb.* 2019 Sep 2;6(3):267-272. doi: 10.14744/nci.2018.51422.
17. Kumru P, Erdogdu E, Arisoy R, Demirci O, Ozkoral A, Ardic C, et al. Effect of thyroid dysfunction and autoimmunity on pregnancy outcomes in low risk population. *Arch Gynecol Obstet.* 2015;291(5):1047–1054. doi: 10.1007/s00404-014-3533-9.
18. Shinohara DR, Santos TDS, de Carvalho HC, Bahls LC, Akimoto LS, Alessi SM, et al. Pregnancy complications associated with maternal hypothyroidism: a systematic review. *ObstetGynecolSurv.* 2018;73(4):219–230. doi: 10.1097/OGX.0000000000000547.
19. Wolfberg AJ, Lee-Parritz A, Peller AJ, Lieberman ES. Obstetric and neonatal outcomes associated with maternal hypothyroid disease. *J Matern Fetal Neonatal Med.* 2005;17(1):35–38. doi: 10.1080/14767050400028642.
20. Medici M, Korevaar TI, Schalekamp-Timmermans S, Gaillard R, de Rijke YB, Visser WE, et al. Maternal early-pregnancy thyroid function is associated with subsequent hypertensive disorders of pregnancy: the generation R study. *J ClinEndocrinolMetab.* 2014;99(12):E2591–E2598. doi: 10.1210/jc.2014-1505.
21. Li XL, Guo PL, Xue Y, Gou WL, Tong M, Chen Q. An analysis of the differences between early and late preeclampsia with severe hypertension. *Pregnancy Hypertens.* 2016;6(1):47–52. doi: 10.1016/j.preghy.2015.12.003.
22. Veerbeek JH, Hermes W, Breimer AY, van Rijn BB, Koenen SV, Mol BW, et al. Cardiovascular disease risk factors after early-onset preeclampsia, late-onset preeclampsia, and pregnancy-induced hypertension. *Hypertension.* 2015;65(3):600–606. doi: 10.1161/HYPERTENSIONAHA.114.04850.
23. Lisonkova S, Sabr Y, Mayer C, Young C, Skoll A, Joseph KS. Maternal morbidity associated with early-onset and late-onset preeclampsia. *Obstet Gynecol.* 2014;124(4):771–781. doi: 10.1097/AOG.0000000000000472.
24. De Groot L, Abalovich M, Alexander EK, Amino N, Barbour L, Cobin RH, et al. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. *J ClinEndocrinolMetab* 2012; 97: 2543–2565.
25. Lai H, Zhan ZY, Liu H. Association between thyroid hormone parameters during early pregnancy and gestational hypertension: a prospective cohort study. *J Int Med Res.* 2020 Feb;48(2):300060520904814. doi: 10.1177/0300060520904814.
26. Akram FH, Johanssen B, Mollerstrom G, Landgren BM, Stavreus-Evers A, Skjöldebrand-Sparre L. Incidence of subclinical hypothyroidism and hypothyroidism in early pregnancy. *J. Women Health* 2017; 26(11): 1231–1235.
27. Nwabudike P, Emokpae MA. Thyroid Dysfunction among Hypertensive Pregnant Women in Warri, Delta State, Nigeria. *Medicines.* 2022; 9(4):29. <https://doi.org/10.3390/medicines9040029>.
28. Zhang Y, Dai X, Yang S, Zhang C, Han M, Huang HF, Fan J. Maternal low thyroxin levels are associated with adverse pregnancy outcomes in a Chinese population. *PLoS One.* 2017 May 23;12(5):e0178100. doi: 10.1371/journal.pone.0178100.
29. Korevaar TIM, Medici M, Visser TJ, Peeters RP. Thyroid disease in pregnancy: new insights in diagnosis and clinical management. *Nat Rev Endocrinol.* 2017;13(10):610–622. doi: 10.1038/nrendo.2017.93.
30. Hernandez M, Lopez C, Soldevila B, Cecenarro L, Martínez-Barahona M, Palomera E, et al. Impact of TSH during the first trimester of pregnancy on obstetric and foetal complications: usefulness of 2.5 mIU/L cut-off value. *ClinEndocrinol (Oxf)* 2018;88(5):728–734. doi: 10.1111/cen.13575.
31. Procopciuc LM, Caracostea G, Hazi G, Nemeti G, Stamatian F. D2-Thr92Ala, thyroid hormone levels and biochemical hypothyroidism in preeclampsia. *GynecolEndocrinol.* 2017;33(2):136–140. doi: 10.1080/09513590.2016.1240774.
32. Gui J, Xu W, Zhang J. Association between thyroid dysfunction and perinatal outcomes in women with gestational hypertension: a retrospective study. *BMC Pregnancy Childbirth.* 2020; 20: 119. doi: 10.1186/s12884-020-2805-6.