IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 20, Issue 8 Ser.11 (August. 2021), PP 13-19
www.iosrjournals.org

Study of thyroid function and dysfunction during pregnancy in tertiary center of central India

Sachdeva Payasvi[1], Tamrakar Seema[2], Yadav Gayatri[3], Kachhawa Kamal[4], Naz Sabiha[5], Tripathi Rashmi[6]

[1] *Associate Professor, Department of Biochemistry, LNMC & JK Hospital, Bhopal, India*
[2] *Associate Professor, Department of Biochemistry, Rishiraj College of Dental Sciences, Bhopal, India*
[3]*Assistant Professor, Department of Biochemistry, LNMC & JK Hospital, Bhopal, India*
[4]*Assistant Professor, Department of Biochemistry, Government Medical College, Datia, India*
[5]*Assistant Professor, Department of Gynecology LNMC & JK Hospital, Bhopal, India*
[6]*Assistant Professor, Department of Biochemistry, MIMS, Bhopal, India*
Corresponding Author: Mrs. Seema Tamrakar
Department of Biochemistry
LNMC & JK Hospital Bhopal MP

Abstract
Introduction: *During pregnancy thyroid is hyper stimulated, resulting in changes in thyroid hormone concentrations. Normal thyroid function is important for mother and growing fetus in the course of pregnancy. This article discusses the changes in thyroid physiology that occur during pregnancy Trimester-specific intervals are especially important during pregnancy when thyroid insufficiency may be associated with adverse obstetric outcome and fetal neuro developmental deficits. Appropriate management results in improved outcomes, demonstrating the importance of proper diagnosis and treatment.*
Aim: *Investigate of thyroid profile level first and third tri-mester of normal and hypothyroidism pregnant women.*
Material and Method: *The present study included total 150 cases attended ANC Clinic at the department of Gyne LNMC & J K Hospital was screened for the study. Level of Total T_3, Total T_4 and TSH estimated by Immunoassay Enzyme Linked Fluorescent Assay (ELFA) method.*
Result: *T3 level in 1st and 3rd trimester of normal antenatal women difference was significantly increased and level of T3 for hypothyroidism antenatal women in 1st and 3rd trimester difference was significantly increased. T4 level in 1st and 3rd trimester of normal antenatal women difference was slightly increased, and level of T4 for hypothyroidism antenatal women 1st and 3rd trimester difference was significantly increased. TSH level in 1st and 3rd trimester of normal antenatal women difference was significantly increased, and level of TSH for hypothyroidism antenatal women in 1st and 3rd trimester difference was significantly decreased.*
Conclusion *Thyroid activity undergoes many changes during normal pregnancy; in our study found significant increased in TT_4, TT_3, and TSH in 1st and 3rd trimester of normal antenatal women. Thyroid dysfunction is common in pregnancy. Proper diagnosis and care of thyroid dysfunction in the pre-pregnancy, pregnancy and post-pregnancy periods are important to reduce the risk of complications.*
Key words*: Pregnancy, Total T_3, Total T_4, TSH.*

Date of Submission: 10-08-2021 Date of Acceptance: 25-08-2021

I. Introduction

Pregnancy is a time period of exceptional hormonal changes and metabolic demands which bring about composite results on thyroid function **[1–3].** The Thyroid hormone is needed for fetal growth and improvement. Until the fetus synthesizes its own thyroid hormones, it is dependent on the T4 hormone that passes through the placenta from the mother **[4, 5].** During pregnancy marked modifications in thyroid characteristics, like the increase in thyroxin-binding globulin (TBG), the impact of human chorionic gonadotropin (HCG) on the maternal thyroid, and alteration in iodine requirement **[1].** An increase in total T4 and total T3 in early pregnancy is due to accelerated serum TBG in pregnancy **[6, 7-9].** Also, reference degrees for the thyroid-stimulating hormone TSH are decreased due to cross-reactivity of the alpha subunit of human chorionic gonadotropin with the TSH receptor **[10, 11].** Thyroid disease in being pregnant may be accompanied through both maternal and fetal complications. Hypothyroidism in pregnancy is associated with premature birth, fetal cardiac complications, and low birth weight, increased frequency of cesarean delivery, placental

complications, preeclampsia, and gestational hypertension, perinatal morbidity-mortality, and cognitive dysfunction. In hyperthyroidism throughout pregnancy complications such as stillbirth, abortion, premature birth, preeclampsia, heart failure, and thyroid storm may develop **[12–15].** The incidence of hypothyroidism in being pregnant is around 2.5% in step with western literature. There are few reviews of the occurrence of hypothyroidism for the duration of being pregnant from India with quotes starting from 4.8% to 11% **[16, 17].** The incidence of hyperthyroidism in pregnant women has been stated to be about 0.2%; the main cause is Graves disease **[18].**

Appropriate treatment of thyroid disease during pregnancy is essential in preventing adverse maternal and fetal outcomes. In this article, I tried to summarize the possible adverse outcomes of hypothyroidism mother and fetus during gestation. It also sheds light on the right management of these conditions to keep away from such complications.

II. Materials & Method

This was an observational prospective study conducted at Clinical Biochemistry LNMC in associated with the department of Obstetrics and gynecology, LNMC & J. K. Hospital Bhopal, the present study included total 150 cases attended ANC Clinic at the department of Obstetrics and gynecology, LNMC & J. K. Hospital from May 2019 onwards, were screened for the study.

Study comprised of two groups of patients.

Group - A 150 antenatal patients of 1st trimester of pregnancy.

Group - B 150 same antenatal patients of 3rd trimester of pregnancy.

Sample collection and processing:

Pregnant women were taken from 20-35 years of age group. 3 to 5 ml venous blood sample were taken using a tube that contained clot activator from the pregnant women, and then centrifuged to be assayed on the same day. Estimation for TSH, Total T3, and T4 was done using the immunoassay Enzyme Linked Fluorescent Assay (ELFA) technique, using commercially available kits by Mini vidas analyzer system.

INCLUSION CRITERIA

Antenatal patients of 1st and 3rd trimester of pregnancy.

EXCLUSION CRITERIA

Antenatal patients of 2nd trimester & thyroid disease. And Antenatal patients suffering from asthma / hypertension / DM / any other systemic disease.

Trimester- specific visits were planned as follows:

• First trimester of pregnancy: 8–10 weeks
• Third trimester of pregnancy: 30–32 weeks.

Ethics

Study was approved by the Ethical committee of institutes. Informed consent was obtained from all patients

STATICAL ANALYSIS

Statistical analysis was done by Graph Pad Prism version 5. Analysis was done by Anova followed by Tukey test. $p<0.05$ was considered as statistically significant.

III. Results:

Table1: Serum Tri iodothyronine (T3) level at 1st and 3rd trimester in Normal antenatal and hypothyroidism Antenatal Women

Groups	Pregnant women -1st trimester (normal) Mean ±SD	Pregnant women -3rd trimester (normal) Mean ±SD	Pregnant women -1st trimester (Hypothyroidism) Mean ±SD	Pregnant women – 3rd trimester (Hypothyroidism) Mean ±SD	P value (<0.001)
Serum T3 (ng/dl) Level	125.4 ± 7.241	144.1± 11.09**	67.58 ± 2.50**,$$	113.3 ± 6.41$$,##	<0.001

** < 0.001 – comparison with 1st trimester (normal)
$$ < 0.001 – comparison with 3rd trimester (normal)
< 0.001 – comparison with 1st trimester (Hypothyroidism)

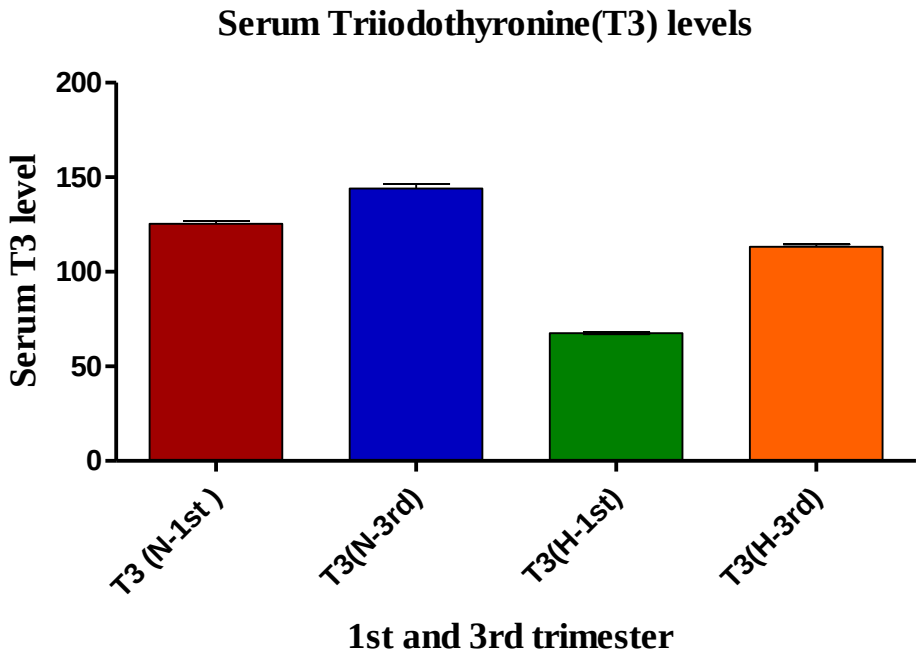

Figure1: Serum T3 Level of normal antenatal and hypothyroidism antenatal women

Table 1:

❖ Serum Triiodothyronine (T3) value 125.4 (ng/dl) in the 1st trimester in normal antenatal women and T3 value 144.1(ng/dl) in 3rd trimester in normal antenatal women, difference was significant.

❖ Although, in Serum Triiodothyronine (T3) value 67.58 (ng/dl) in 1st trimester in hypothyroidism antenatal women significantly decreased compared to T3 value125.4 (ng/dl) in 1st trimester in normal antenatal women.

❖ In comparison of serum Triiodothyronine (T3) value 113.3 (ng/dl) in 3rd trimester in hypothyroidism antenatal women increased as compared to serum Triiodothyronine (T3) value 67.58 (ng/dl) in 1st trimester in hypothyroidism antenatal women, difference was statistically significant.

❖ However, serum Triiodothyronine (T3) value 113.3 (ng/dl) in 3rd trimester in hypothyroidism antenatal women significantly decreased compared to serum Tri iodothyronine (T3) value 144.1(ng/dl) in 3rd trimester in normal antenatal women

Table 2: Serum Thyroxin (T4) level at 1st and 3rd trimester in Normal antenatal and hypothyroidism Antenatal Women

Groups	Pregnant women - 1st trimester (normal) Mean ±SD	Pregnant women -3rd trimester (normal) Mean ±SD	Pregnant women -1st trimester (Hypothyroidism) Mean ±SD	Pregnant women -3rd trimester (Hypothyroidism) Mean ±SD	P value (<0.001)
Serum T4 (ug/dl) Level	10.19 ± 1.007	10.32 ± 0.977	3.461 ± 0.2532**$$	8.63 ± 0.4981**$$##	<0.001

** < 0.001 – comparison with 1st trimester (normal)
$$ < 0.001 – comparison with 3rd trimester (normal)
< 0.001 – comparison with 1st trimester (Hypothyroidism)

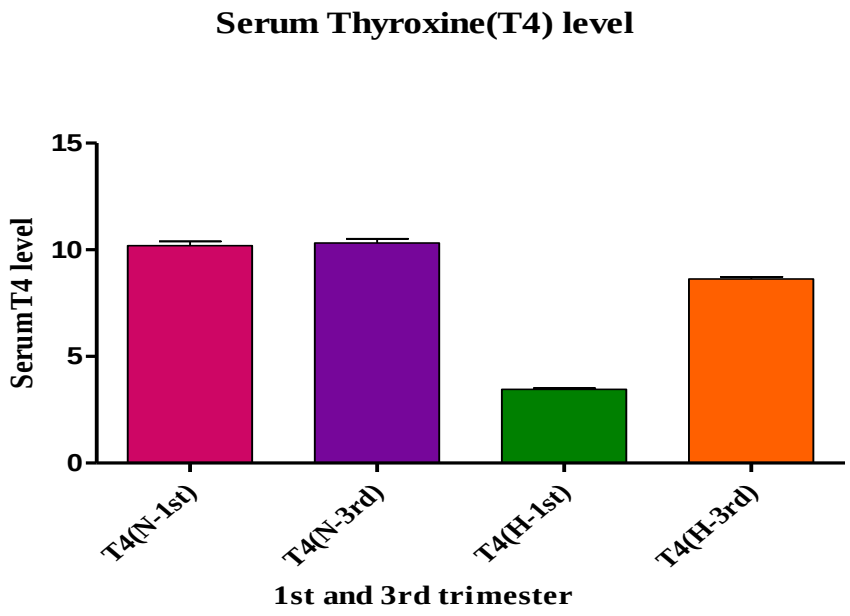

Figure2: Serum T4 Level normal antenatal and hypothyroidism antenatal women.

Table 2:

❖ Serum Thyroxin (T4) value 10.19 (ug/dl) in the 1st trimester of normal antenatal women and T3 value 10.32 (ug/dl) in 3rd trimester of normal antenatal women, difference was slightly increased.

❖ Although, in Serum Thyroxin (T4) value 3.461 (ng/dl) in 1st trimester of hypothyroidism antenatal women significantly decreased compared to T4 value10.19 (ng/dl) in 1st trimester of normal antenatal women.

❖ In comparison of serum thyroxin (T4) value 8.63 (ng/dl) in 3rd trimester of hypothyroidism antenatal women increased as compared to serum thyroxin (T4) value 3.461 (ng/dl) in 1st trimester of hypothyroidism antenatal women, difference was statistically significant.

❖ However, serum thyroxin (T4) value 8.63 (ug/dl) in 3rd trimester in hypothyroidism antenatal women significantly decreased compared to serum thyroxin (T4) value 10.32 (ug/dl) in 3rd trimester in normal antenatal women

Table 3: Serum TSH level at 1st and 3rd trimester in Normal antenatal and hypothyroidism Antenatal Women

Groups	Pregnant women - 1st trimester (normal) Mean ±SD	Pregnant women -3rd trimester (normal) Mean ±SD	Pregnant women -1st trimester (Hypothyroidism) Mean ±SD	Pregnant women - 3rd trimester (Hypothyroidism) Mean ±SD	P value (<0.001)
Serum TSH (ulU/ml) Level	1.546 ± 0.4330	1.759± 0.4066	5.513± 0.5087**$$	2.497± 0.3719**$$##	<0.001

** < 0.001 – comparison with 1st trimester (normal)
$$ < 0.001 – comparison with 3rd trimester (normal)
< 0.001 – comparison with 1st trimester (Hypothyroidism)

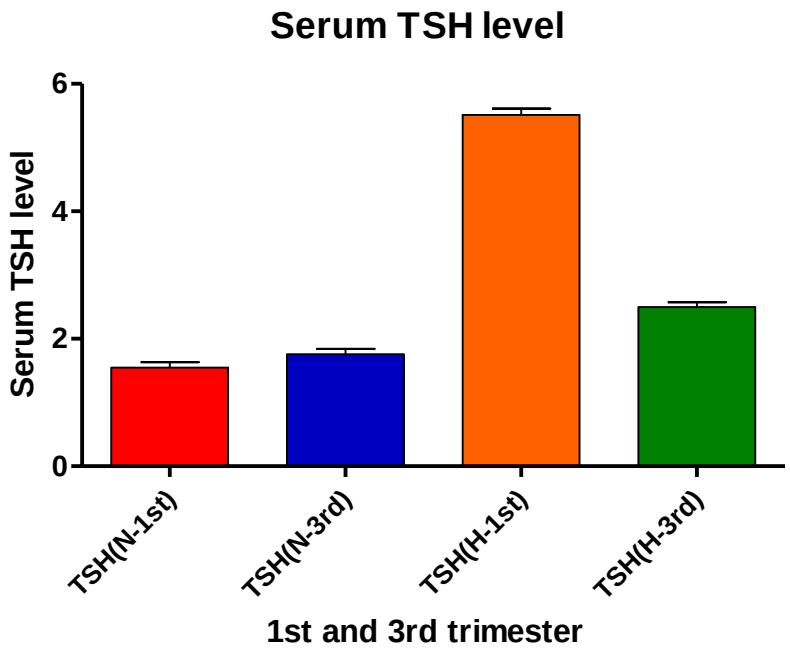

Figure3: Serum TSH Level of normal antenatal women and hypothyroidism antenatal women.

Table 3:

❖ Serum TSH value 1.546 (ulU/ml) in the 1st trimester of normal antenatal women and T3 value 1.759 (uIU/ml) in 3rd trimester in normal antenatal women, difference was significantly increased.

❖ Although, in Serum TSH value 5.513 ulU/ml in the 1st trimester in hypothyroidism antenatal women significantly increased, compared to TSH value 1.546 (ulU/ml) in 1st trimester in normal antenatal women.

❖ In comparison of serum TSH value 2.497 (ulU/ml) in 3rd trimester of hypothyroidism antenatal women significantly decreased, as compared to serum TSH value 5.513 (ulU/ml) in 1st trimester in hypothyroidism antenatal women, difference was statistically significant.

❖ However, serum TSH value 2.496 (ng/dl) in 3rd trimester in hypothyroidism antenatal women significantly increased, compared to serum TSH value 1.759 (uIU/ml) in 3rd trimester in normal antenatal women

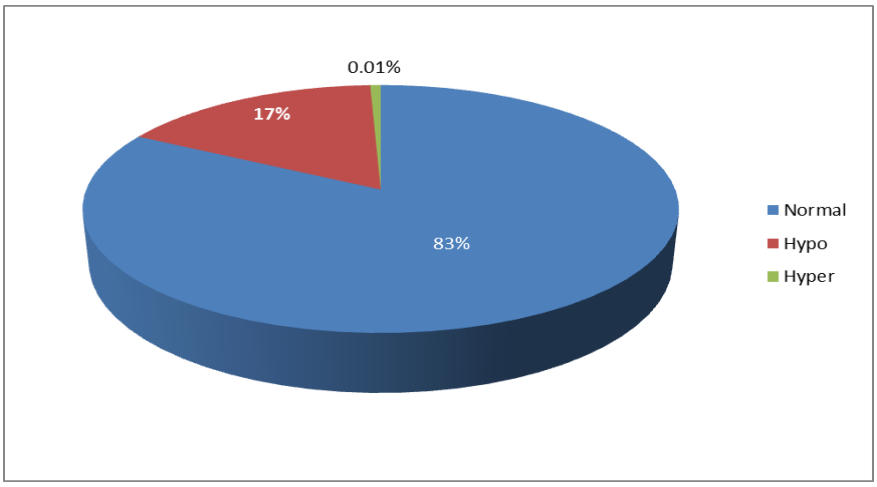

Figure 4: Percentage Distribution Thyroid profile

In our study found 83% Normal antenatal Women and 17% Hypothyroidism antenatal women and 0.01% Hyperthyroidism antenatal women.

IV. Discussion

This study aimed to evaluate thyroid function level during first and third trimester of pregnancy in an observational prospective study in Bhopal region of India. Iodine is the most important part of the thyroid hormones, triiodothyronine (T3) and thyroxin (T4), make by the thyroid gland. T3 is the active thyroid hormone, around 80% of T3 is created from the deiodination of T4 in the liver, muscle, and other tissues. Starting in early pregnancy, increased maternal estradiol levels result in increased sialylation and glycosylation of TBG in the liver [19, 20]. This decreases the peripheral metabolism of TBG to bring about approximate 1.5–2 folds sustained upwards in serum TBG ranges comparison to euthyroid non-pregnant women [1, 21]. There by developing an increased amount for T3 and T4 production during pregnancy. Serum HCG is a glycoprotein produced basically through the placenta and peaks at the end of the first trimester of pregnancy. It binds to the TSH receptor on the thyroid cellular membrane and is a weak stimulator, resulting in elevated secretion of T4 and T3 and partial suppression of serum TSH. Due to the effects of HCG, the lower range of serum TSH is decreased in pregnancy [8, 22]. Although the decrease limit for serum TSH in pregnant women should be lower than in the non-pregnant population expert opinion has advocated the following trimester-specific recommendations for TSH reference ranges during pregnancy: 0.1–2.5 mIU/L (first trimester), 0.2–0.3 mIU/L (second trimester), and 0.3–3.0 mIU/L (third trimester) .[11,23].

In our study found Serum T3 and T4 level in 1st and 3rd trimester of normal antenatal women difference was significant (<0.001) and hypothyroidism antenatal women 1st and 3rd trimester level of T3 and T4 difference was significantly increased (< 0.001). Serum TSH level in the 1st and 3rd trimester in normal antenatal women difference was significant (< 0.001). Serum TSH level in 1st and 3rd trimester in hypothyroidism antenatal women statically significant (< 0.001). TSH level in the 1st and 3rd trimester in normal antenatal women difference was significant (< 0.001), same findings according to by. [22] Total T4 and T3 concentrations significantly increased due to increases in TBG level. [1] Thyroid activity undergoes numerous changes at the time of normal pregnancy including a remarkable increase in serum TBG, thyroglobulin, total T4, and total T3, an increase in renal iodide clearance and stimulation of the thyroid by hCG, [2]. T3 was significantly higher in the 1st to third. [24-26] Total T3 and T4 levels increase starting in early pregnancy, due to the increased TBG levels. [27,28] TSH significantly increased by. [29] During pregnancy, reference ranges for the thyroid-stimulating hormone (TSH) are decreased because of the cross-reactivity of the alpha subunit of human chorionic gonadotropin with the TSH receptor. [10] TSH significantly increased in Chinese women. [30] TSH value increased in the first trimester to third trimester in normal pregnant women, difference was found statistically significant and total T3 and T4 increased in the first trimester to third trimester, difference was found statistically significant (< 0.001). Similar finding according to my study. [31] TSH levels decreased during the first trimester and then increased significantly ($P < 0.05$) in the second and third trimester, this result similar to our study.

Serum thyroid stimulating hormone concentration is the initial and most authentic test for assessing thyroid function during pregnancy [33]. Hypothyroidism indicates insufficient production of thyroid hormones by the thyroid gland and can be primary-abnormality in the thyroid gland itself or secondary/central-as a result of hypothalamic or pituitary disease. Maternal hypothyroidism is the most common thyroid dysfunction in pregnancy. In our study, hypothyroidism pregnant women was found (17%), 1st trimester hypothyroidism pregnant women value of TSH 5.513 ± 0.5087 and 3rd trimester was 2.497 ± 0.3719, result found significantly decreased and total T3 and T4 significantly increased in 1st to 3rd trimester of hypothyroidism pregnant women. Significant result and improved outcome found proper management and require good collaboration between the obstetrician and endocrinologist. In other studies trimester specific data not found in hypothyroidism pregnant women.

V. Conclusion

Physiologic changes associated with pregnancy require an increased availability of thyroid hormones by 40% to 100% to meet the needs of mother and fetus during pregnancy. Thyroid activity undergoes many changes during normal pregnancy including significant increased in serum, TT_4, TT_3, and TSH. Different studies have showed that thyroid dysfunction is common in pregnancy. The major causes for this dysfunction are hormonal and metabolic changes during pregnancy leading to profound alterations of the biochemical parameters of the thyroid function. Thyroid disease usually affects females of the reproductive age group and caring for these women during pregnancy requires careful monitoring of both the mother and the fetus. Appropriate diagnosis, care and management of thyroid dysfunction in the pre-pregnancy, pregnancy and post-pregnancy periods are important to minimize the risk of complications.

References

[1]. Glinoer D. The regulation of thyroid function in pregnancy: pathways of endocrine adaptation from physiology to pathology. Endocrine reviews. 1997 Jun 1;18(3):404-33.

[2]. Fantz CR, Dagogo-Jack S, Ladenson JH, Gronowski AM. Thyroid function during pregnancy. Clinical Chemistry. 1999 Dec 1;45(12):2250-8.

[3]. Abalovich M, Amino N, Barbour LA, Cobin RH, De Groot LJ, Glinoer D, Mandel SJ, Stagnaro-Green A. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society Clinical Practice Guideline. The journal of clinical Endocrinology & Metabolism. 2007 Aug 1;92(8_supplement):s1-7.

[4]. Negro R, Mestman JH. Thyroid disease in pregnancy. Best Practice & Research Clinical Endocrinology & Metabolism. 2011 Dec 1;25(6):927-43.

[5]. American College of Obstetricians and Gynecologists. ACOG practice bulletin. Clinical management guidelines for obstetrician-gynecologists. Number 37, August 2002.(replaces practice bulletin number 32, November 2001). Thyroid disease in pregnancy. Obstetrics and gynecology. 2002 Aug;100(2):387-96.

[6]. Versloot PM, Elst JS, Van Der Heide D, Boogerd L. Effects of marginal iodine deficiency during pregnancy: iodide uptake by the maternal and fetal thyroid. American Journal of Physiology-Endocrinology and Metabolism. 1997 Dec 1;273(6):E1121-6.

[7]. Shankar P, Kilvert A, Fox C. Changing thyroid status related to pregnancy. Postgraduate medical journal. 2001 Sep 1;77(911):591-2.

[8]. Kasper D, Harrison TR. Harrison's principles of internal medicine. Vol. 1. McGraw-Hill, Medical Publishing Division; 2005.

[9]. Zigman JM, Cohen SE, Garber JR. Impact of thyroxine-binding globulin on thyroid hormone economy during pregnancy. Thyroid. 2003 Dec 1;13(12):1169-75.

[10]. De Groot L, Abalovich M, Alexander EK, Amino N, Barbour L, Cobin RH, Eastman CJ, Lazarus JH, Luton D, Mandel SJ, Mestman J. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. The Journal of Clinical Endocrinology & Metabolism. 2012 Aug 1;97(8):2543-65.

[11]. Stagnaro-Green A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R, Nixon A, Pearce EN, Soldin OP, Sullivan S. American Thyroid Association Taskforce on Thyroid Disease During Pregnancy and Postpartum. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid 2011; 21: 1081.;125.

[12]. Baloch Z. Guidelines Committee, National Academy of Clinical Biochemistry. Laboratory medicine practice guidelines. Laboratory support for the diagnosis and monitoring of thyroid disease. Thyroid. 2003;13(1):3-126.

[13]. Mandel SJ, Cooper DS. The use of antithyroid drugs in pregnancy and lactation. The Journal of Clinical Endocrinology & Metabolism. 2001 Jun 1;86(6):2354-9.

[14]. Tekin YB, GÜVEN ES. Gebelikte tiroid hastalıkları ve neonatal sonuçları. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi. 2014 Dec 12;11(4):150-3.

[15]. Casey BM, Leveno KJ. Thyroid disease in pregnancy. Obstetrics & Gynecology. 2006 Nov 1;108(5):1283-92.

[16]. Nambiar V, Jagtap VS, Sarathi V, Lila AR, Kamalanathan S, Bandgar TR, Menon PS, Shah NS. Prevalence and impact of thyroid disorders on maternal outcome in Asian-Indian pregnant women. Journal of thyroid research. 2011 Mar 9;2011.

[17]. 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. Archives of gynecology and obstetrics. 2010 Feb;281(2):215-20.

[18]. Lazarus JH. Thyroid disease in pregnancy and childhood. Minerva endocrinologica. 2005 Jun 1;30(2):71-87.

[19]. AIN KB, MORI Y, REFETOFF S. Reduced clearance rate of thyroxine-binding globulin (TBG) with increased sialylation: a mechanism for estrogen-induced elevation of serum TBG concentration. The Journal of Clinical Endocrinology & Metabolism. 1987 Oct 1;65(4):689-96.

[20]. Pittas AG, Lee SL. Evaluation of thyroid function. Handbook of diagnostic endocrinology. 2003:107-29.

[21]. Mandel SJ, Spencer CA, Hollowell JG. Are detection and treatment of thyroid insufficiency in pregnancy feasible?. Thyroid. 2005 Jan 1;15(1):44-53.

[22]. Glinoer D, NAYER PD, Bourdoux P, Lemone M, Robyn C, STEIRTEGHEM AV, Kinthaert J, Lejeune B. Regulation of maternal thyroid during pregnancy. The Journal of Clinical Endocrinology & Metabolism. 1990 Aug 1;71(2):276-87.

[23]. Mannisto T, Surcel HM, Ruokonen A, Vaarasmaki M, Pouta A, Bloigu A, Järvelin MR, Hartikainen AL, Suvanto E. Early pregnancy reference intervals of thyroid hormone concentrations in a thyroid antibody-negative pregnant population. Thyroid. 2011 Mar 1;21(3):291-8.

[24]. Soldin OP, Hilakivi-Clarke L, Weiderpass E, Soldin SJ. Trimester-specific reference intervals for thyroxine and triiodothyronine in pregnancy in iodine-sufficient women using isotope dilution tandem mass spectrometry and immunoassays. Clinica Chimica Acta. 2004 Nov 1;349(1-2):181-9.

[25]. Soldin OP, Tractenberg RE, Hollowell JG, Jonklaas J, Janicic N, Soldin SJ. Trimester-specific changes in maternal thyroid hormone, thyrotropin, and thyroglobulin concentrations during gestation: trends and associations across trimesters in iodine sufficiency. Thyroid. 2004 Dec 1;14(12):1084-90.

[26]. Soldin OP, Tractenberg RE, Soldin SJ. Differences between measurements of T4 and T3 in pregnant and nonpregnant women using isotope dilution tandem mass spectrometry and immunoassays: are there clinical implications?. Clinica chimica acta. 2004 Sep 1;347(1-2):61-9.

[27]. Sapin R, d'Herbomez M, Schlienger JL. Free thyroxine measured with equilibrium dialysis and nine immunoassays decreases in late pregnancy. Clinical laboratory. 2004 Jan 1;50(9-10):581-4.

[28]. Lee RH, Spencer CA, Mestman JH, Miller EA, Petrovic I, Braverman LE, Goodwin TM. Free T4 immunoassays are flawed during pregnancy. American Journal of Obstetrics and Gynecology. 2009 Mar 1;200(3):260-e1.

[29]. Thevarajah M, Chew YY, Lim SC, Sabir N, Sickan J. Determination of trimester specific reference intervals for thyroid hormones during pregnancy in Malaysian women. Malays J Pathol. 2009 Jun 1;31(1):23-7.

[30]. Zhang J, Li W, Chen QB, Liu LY, Zhang W, Liu MY, Wang YT, Li WY, Zeng LZ. Establishment of trimester-specific thyroid stimulating hormone and free thyroxine reference interval in pregnant Chinese women using the Beckman Coulter UniCel™ DxI 600. Clinical Chemistry and Laboratory Medicine (CCLM). 2015 Aug 1;53(9):1409-14.

[31]. Almomin AM, Mansour AA, Sharief M. Trimester-specific reference intervals of thyroid function testing in pregnant women from Basrah, Iraq using electrochemiluminescent immunoassay. Diseases. 2016 Jun;4(2):20.

[32]. Kachhawa P, Sinha V. Assessment of thyroid dysfunction, dyslipidemia and oxidative stress in hypertensive end stage chronic renal disease patients in a teaching hospital in Western Uttar Pradesh. Asian Journal of Medical Sciences. 2019 Aug 9;10(5):13-8.

[33]. Glinoer D, Spencer CA. Serum TSH determinations in pregnancy: how, when and why?. Nature Reviews Endocrinology. 2010 Sep;6(9):526.