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Thyroid Dysfunction & Pregnancy

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Pregnancy, Thyroid dysfunction, thyroid hormones

Abstract

Thyroid disorder is the second most common endocrine disorder in pregnancy, after diabetes. The increased prevalence of thyroid disorders makes it necessary to start universal screening of pregnant women for thyroid disorders which would help in the early identification and rectification of thyroid disorders in pregnant women. Further, early screening and treatment of thyroid disorders would prevent to a large extent the incidence of thyroid disorders in the newborns, which is one of the leading causes of mental retardation.

1. INTRODUCTION

Pregnancy is a period of life in which a lot of physiological changes occur in body. Various complex hormonal changes also occur. When some endocrine disorders occur along with pregnancy, then the adverse outcomes can be immense[1].
Thyroid disorder is found to be most commonly occurring endocrine disorder in pregnancy after

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diabetes. In context to gender, thyroid diseases are four to five times more commonly observed in women in contrast to men [2] (primarily in gestational period). According to thyroidologist, pregnancy is a prolonged bodily condition in which a number of events occur that can modify thyroid function. Furthermore these events occur at varied times in pregnancy, so it is difficult to interpret the complications arising from it [3].

Thyroid disease has highly significant maternal and fetal implications. Children born to untreated or undertreated mother has a deep impact on future intellective growth of the child. Thyroid disease is increasing the risk of miscarriage, premature birth, preeclampsia and increased fetal mortality. [4]

The primary function of the cells of the thyroid follicles is synthesis of thyroid hormones that is thyroxine or L- tetraiodothyronine or T4 and L-triiodothyronine or T3 [5].The secretion of these thyroid hormones is stimulated through hypothalamus pituitary thyroid axis. Thyrotropin releasing hormone (TRH)secreted from the Hypothalamus in brain stimulate the release of thyrotropin or thyroid stimulating hormone (TSH) from the anterior pituitary [6]. Negative feedback mechanism regulates the release of TSH from the anterior pituitary. Thyroid hormones, T_3 and T_4 hormones travel in blood stream as bound to thyroxine binding proteins and reach their target sites[6].

Thyroid gland is perceptibly altered in case of normal pregnancy which occurs throughout gestation. These modifications are important so that the maternal thyroid gland could meet the demands of pregnancy and these modifications have much more importance in first trimester as the fetus thyroid is able to make enough thyroid hormones only after 20 weeks of gestation so it is completely dependent on maternal TH hormones in this duration[7].

In pregnancy there is increased production of thyroid hormones binding proteins, majorly TBG, that is thyroid binding globulin as a result of estrogen stimulation. TBG has prolonged half life in pregnancy due to increased sialylation of TBG during gestational period. Also, affinity of TBG for thyroid hormones increases [8].

The production of hormones by thyroid gland expands by 50% in pregnancy. This is a direct consequence of elevated levels of TBG. T3 and T4 levels, both are known to be elevated in pregnancy. Therefore, non-pregnancy reference intervals cannot be used in pregnancy as they can mislead on the detectionof thyroid disorder and can hence result in delay in treatment of thyroid disorder during pregnancy [9].

There is also an increased degradation of THs by A placental hormone, type 3 iodothyroninedeiodinase, causes increased degradation of Thyroid hormones. This further necessitates the production of increased levels of thyroid hormones by thyroid gland of the mother [10].

β-hCG (Human Chorionic Gonadotropin) share the similarity in structure with TSH (Thyroid Stimulating Hormone).Hence, it has a stimulatory effect of on thyrocyteswhich induces causes a transient increase in free T4 levels which ultimately cause TSH suppression.The level of thyroglobulin, that is the precursor protein for thyroid hormones is also controlled by β-hCG secreted in pregnancy. Some studies have reported that TG levels are increased in pregnancy. Increase in TG is associated with transient thyroid stimulation by hCG because of its thyrotrophic action [11].

As iodine is most important element required for thyroid hormone synthesis, In small level iodine deprived areas, the thyroid gland is unable to achieve the required adjustments in pregnancy and the pathological condition develop. Complications severity increases with decrease in iodine intake. The most visible consequence is goiter in mother and fetus. These alterations can be prevented by iodine supplementation if detected early [12].

For mother, pregnancy is known to act as strong goitrogenic stimulus, even in areas where there is only moderate iodine deficiency. Maternal goiter formation can be a result of continuous glandular stimulation that occurs during pregnancy. Fetal thyroid is also affected by the maternal thyroid disorder as goitrogenesis has been seen in fetus of mothers with thyroid disorder [13].

Considering variations in the maternal thyroid economy during pregnancy, use of normal reference range for pregnant women can mislead

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on the diagnosis and treatment of thyroid disorder during pregnancy, hence trimester specific reference has been established. In thyroid disease during pregnancy, maternal thyroid gland is not able to cope with all the situations and there is excessive or insufficient release of thyroid hormones. Thyroid autoimmunity is also reported to be associated with increased premature delivery and cases of abortion. Measuring levels of autoantibody can therefore act as marker to diagnose women who have probability of getting hypothyroidism in pregnancy. Hence, women positive for thyroid autoantibody should be monitored closely and given possible treatment [14].

Hence thyroid dysfunction including hyperthyroidism and hypothyroidism require close monitoring in pregnancy.Hypothyroidism is much common in pregnancy than hyperthyroidism. [15]A close relationship has been observed in hypothyroidism and reduced fertility.Thyroid dysfunction varies according to region and is reported to 4.5% prevalent in western countries and 11 % in India[16].The significant association between pregnancy and thyroid function has been recognized only in last few years. As hypothyroidism and goitrogenesis has been observed in normal women living in geographical areas with iodine restriction, this gives a clue that pregnancy serve as a goitrogenic stimulus.

Although hCG has indirect effect on thyroid functioning but it is no doubt a thyroid-regulating hormone in pregnancy. [17] Thyroid disorders like goiter formation, hyperthyroidism, autoimmune thyroid disease and subclinical hypothyroidism have been found to affect a significant number of pregnant women. These differences can be due to population specific factors such as ethnicity and Body Mass Index. Hence it is very necessary to compare the results with a correct reference interval for every population rather than just relying on universal cut off. Reference interval is different for different range of BMI in pregnant women. Hence BMI index of every woman under study should be measured and taken into consideration[18].

2. DISCUSSION

Thyroid gland is a butterfly shaped structure which has two lobes joined in the midline by thin tissue called isthmus [19].It receives blood supply from the superior thyroid arteries (arising from the external carotids) and the inferior thyroid arteries (arising from the subclavian arteries) [20]. Thyroid gland constitutes a number of follicles which are encapsulated by fibrous capsule layer[21]Follicles are the functional unit of the thyroid gland. Follicles are spherical cells which enclose a proteinaceous material called colloid. Colloid consists primarily of thyroid hormone precursor protein thyroglobulin [22].

3. THYROID HORMONES SYNTHESIS AND REGULATION

The primary function of the cells of the thyroid follicles is synthesis of thyroid hormones that is thyroxine or L- tetraiodothyronine(T4) and L-triiodothyronine (T3) [23].The release of thyroid hormones is stimulated through hypothalamus pituitary thyroid axis. Thyrotropin releasing hormone (TRH) from the Hypothalamus stimulates the release of thyrotropin or thyroid stimulating hormone (TSH) from the anterior pituitary.

TSH further binds to TSH receptor which is present on the follicular cells. This in turn stimulates the release of thyroglobulin which is an inactive protein into the follicle lumen as colloid [24].

Sodium Iodide (NaI)co-transporter is an energy dependent transporterthrough which dietary iodide ion travel from blood stream intothe thyroid follicle cells or thyrocytes [25].

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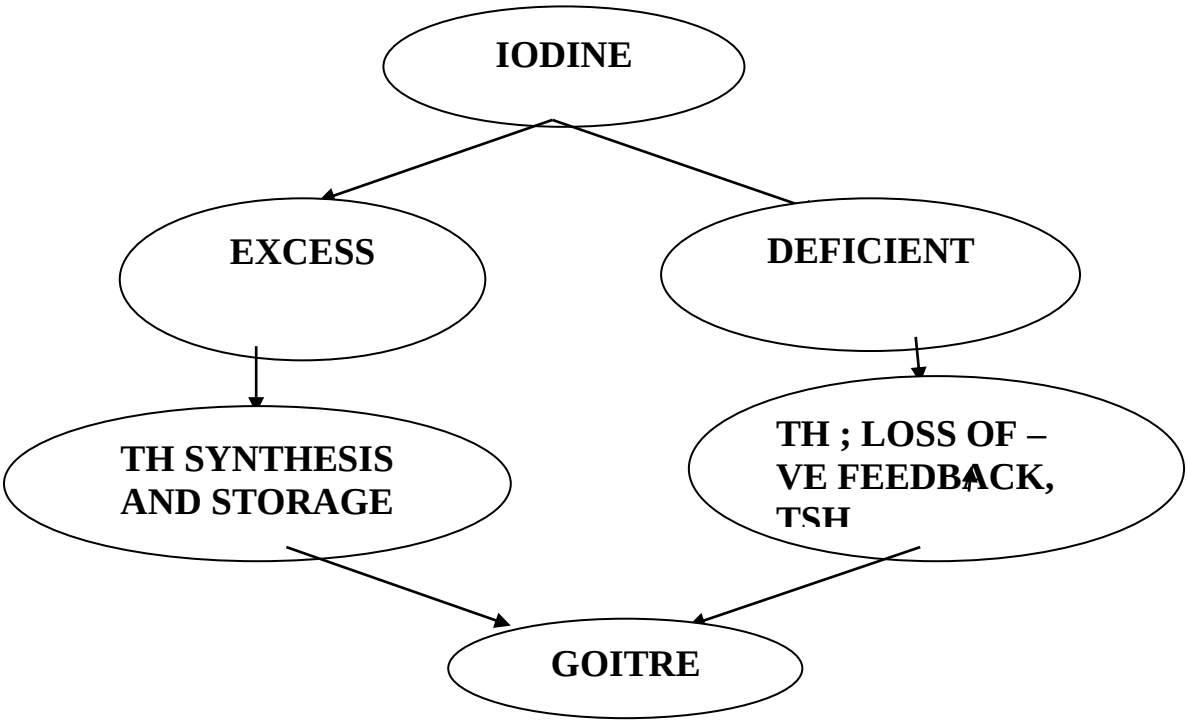

Iodide ion is oxidized to iodine by thyroperoxidase enzyme in the presence of hydrogen peroxide, H_2O_2. (Autoantibodies to thyroid peroxidase are a common cause of hypothyroidism).Then thyroglobulin is iodinated on tyrosine residues. Then coupling of iodothyroninesoccur to form L-Thyroxine or tetraiodothyronine and L-Triiodothyronine [4,2]. Therefore, Iodine is a very important component of thyroid hormones constituting 65% of the mass of T_4 and 58% of the mass of T_3[25].Two diiodotyrosyl residues form T_4 and diodotyrosyl and one monoiodotyrosyl combine to form T_3.The release of thyroid hormone is under regulation by negative feedback loop. Increased level of THs majorly T_3 inhibit the release of Thyroid Stimulating Hormone in turn suppressing secretion of thyroid hormones by thyroid gland.T_3 and T_4 hormones travel in blood stream as bound to thyroxine binding proteins and reach their target sites. T_4 makes up 90 percent of the THs but T_3 is highly bioactive as compared to T_4[25].

4. FUNCTIONS OF THYROID HORMONES

Thyroid hormones increases Body Mass Ratio, body temperature, gluconeogenesis, glucose absorption lipolysis and proteolysis. Thyroid hormones elevate stroke volume and heart rate thus causing upsurged cardiac output which shows that thyroid hormones affect heart also. Thyroid hormones also help in bone maturation and hence overall growth. These hormones are also necessary for central nervous system (CNS) development. Para follicular cells are also present in the thyroid gland which secrete calcitonin hormone. This hormone is important for calcium homeostasis [26].

5. THYROID GLAND DISORDERS

Thyroid gland disorders are one of the common endocrine gland disorders in India. Thyroid gland is affected by environmental factors because of its dependency on dietary Iodine further increase the subject with thyroid disorders. Some common thyroid disorders are listed below.

6. HYPOTHYROIDISM-

Hypothyroidism is one of the very common thyroid related pathologies. Hypothyroidism is a condition of decreased production of thyroid hormones. It can be because of several reasons some of which are listed below:

- Iodine restriction or Iodine-deficient diet
- surgical removal of the thyroid gland

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- Radio ablation of the thyroid gland (done to treat hyperthyroidism)
- Malignancy or tumor of the thyroid gland
- Medications, e.g. lithium
- Loss of upstream signaling because pituitary or hypothalamic disorder (secondary and tertiary hypothyroidism respectively).
- Autoimmunity (one the most common cause of hypothyroidism). Autoimmunity is because of antibodies which attack self-thyroid gland constitutents. Examples of such autoantibodies are antithyroglobulin and antithyroid peroxidase (ATPO). Thyroid peroxidase enzyme is required for converting iodide into iodine for synthesis of thyroid hormones in the follicle [26,27].

The severity of signs and symptoms varies with delay in diagnosis and age of onset of hypothyroidism .

7. HYPERTHYROIDISM

Increased concentration of thyroid hormones in blood is called hyperthyroidism. Hyperthyroidism can be due to several reasons. Some of them are listed below:

- Hyper functional adenoma
- Thyroid malignancy
- Increased TSH secretion from pituitary adenoma (secondary hyperthyroidism)
- Thyroid damage from radiation
- Trauma or stress
- External thyroid hormone ingestion
- Grave's disease (responsible for about 85% cases of hyperthyroidism). Grave's disease occur because of development of autoantibodies to the TSH receptors present on the follicular cells This results in perpetual stimulation of follicular cells resulting in release of thyroid hormones[28].

Increased thyroid hormones inhibit TSH release; hence TSH levels are low in hyperthyroidism. Myxedema, coma, congenital hypothyroidism, carcinoma of the thyroid, multinodular goiter, Hashimoto thyroiditis are some of the other major disorders of the thyroid gland [29].

8. THYROID GLAND DEVELOPMENT:

Thyroid gland which is a type of endocrine gland is first to develop in fetus during pregnancy. Development starts approximately at 3rd week of gestation. First and second pharyngeal pouches present near the base of the tongue act as precursor for development of thyroid gland in fetus. A diverticular overgrowth develops from the primitive pharynx. Thyroid is still attached to tongue by thyroglossal duct during migration. Thyroid solidifies during migration and follicular element of the thyroid differentiates [30].

Differentiation of left and right lobe of thyroid also occurs in the 5th week of gestation. By the seventh week of gestation thyroid reaches its final destination in the neck. By the 10th week of gestation, thyroglossal duct degenerates, then cellular differentiation and maturation occurs and thyroid become functionally mature by 12th week of gestation [31].Thyroid then starts forming little amount of thyroid hormones but the enough amount of thyroid hormones start to release at 20th week of gestation. So, mainly in the first trimester of pregnancy, fetus development is dependent on maternal thyroid which it receives through placenta [32].

9. PREGNANCY AND THYROID GLAND

A number of physiological changes occur in maternal thyroid gland in pregnancy to release more TH to meet maternal and fetal needs. Human chorionic gonadotropin levels are high during the first trimester of pregnancy and HCG acts as TSH as alpha subunit of hCG is similar to TSH. Hence levels of TSH are reduced in first trimester of pregnancy under the influence of hCG. According to previous studies TSH upper limit has been defined to be approximately 2.5IU/L during the first trimester [33].

As estrogen levels increase rapidly during pregnancy which in stimulate synthesis of thyroxine binding globulin in liver increasing the

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levels of thyroxine binding globulin in blood in pregnancy[34]. Estrogen mediated prolongation of half life of TBG also occur increasing half life of TBG from 15 minutes to 3 days just a week after gestation[35].Availability of iodide is decreased because of increased renal clearance of iodide and fetal uptake.

Physiological Changes	Thyroid-related consequences
Increased renal I- clearance	Increased 24-hr RAIU
Reduced plasma Iodine and placental Iodine delivery to the fetus	In Iodine deficient mother, reduced T4, elevated TSH, and goitre formation
High O_2 consumption by fetoplacental unit, heavy uterus	Increased Basal metabolic rate
High hCG in first trimester of pregnancy	free T_4 and T_3 above normal,

Table - Effects of pregnancy on thyroid gland [36, 37]

Intact thyroid gland in a healthy pregnant woman will be able to supply the hormone according to need but any disorder in thyroid will result in improper supply of hormones to the child and can have drastic effects like miscarriages, prenatal mortality and affect on neurological development of the fetus**[38].** According to a study done by Haddow et. al, a 7-point IQ deficit is found in children who are born to mother with thyroid disorder as compared to children born to mother with normal thyroid function [39]

10. DETECTION OF THYROID DISORDER IN PREGNANCY

Thyroid disorder can be diagnosed by measuring the level of thyroid related hormones most promising of which is TSH.According to most recent endocrinology guidelines, reference value in first trimester of pregnancy for TSH is 0.1-2.5µIU/L. and 0.2- 3.0 mIU/L in the second and third trimesters of pregnancy [40].Along with TSH, levels of FT4 and FT3 should be measured so as to prevent misdiagnosis due to changes in levels of thyroxine binding globulin[41]. Besides this, detection of autoantibodies (e.g. autoantibodies to thyroid peroxidase enzyme) should also not be ignored[42].

11. PREGNANCY AND HYPOTHYROIDISM

Clinical and subclinical hypothyroidism is found be present in approximately 2.5% of the pregnant women [43] but, Subclinical hypothyroidism would have a prevalence of 50% if universal screening of pregnant women would have been done. Indian thyroid society guidelines have suggested that universal screening of pregnant women for thyroid disorders should be norm [44] .Clinical hypothyroidism (CH) is a condition of free T4 levels below normal accompanied by increased levels of TSH, that is TSH levels higher than 10 mIU/L. Its incidence ranges from 0.3 to 0.5% in pregnant women[45].

Subclinical hypothyroidism (SCH): A person is said to be suffering from subclinical hypothyroidism if he has increased TSH (> 4.5mIU/L) but T_4 levels are within the normal range. Population, region, age, sex and race are major factors in deciding the prevalence of subclinical hypothyroidism in an area. Its prevalence ranges from 3 to 17% in the adult population. Its frequency is higher in women and elderly people. Prevalence among pregnant women is reported to be between 2% and 4%[46].Impaired nerve cell differentiation, inadequate CNS development, increased risk of perinatal defects, low birth weight babies, and neurological defect have been observed in fetus who do not get sufficient amount of maternal thyroid hormones especially during first trimester of pregnancy. “Placental abruption and increased risk of preterm birth, spontaneous abortion, gestational hypertension and severe preeclampsia” are some of the complications which a pregnant women with

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hypothyroidism face[47].

12. Pathophysiology

Triiodothyronine is known to upregulateReelin. Reelin is glycoproteinaceous in nature. It is involved in the signaling of neuronal migration in the cortex, hippocampus and cerebellum. Hypothyroidism is thus associated with decreased reelin levels which can result in aberrant neuronal migration[48].

Hypothyroidism is associated with reduced expression of "*Egr-1*, *Arc*, *Erk* and *Bndf"* in the child's hippocampus.*EGR-1 is* a transcription factor that is involved in the *Long-term potentiation* process. [49].

13. PREGNANCY AND HYPERTHYROIDISM

Hyperthyroidism has been reported to be3.3% prevalently in Indian pregnant women.

14. Causes of hyperthyroidism

"Graves' disease, Transient gestational hyperthyroidism, Toxic multinodular goiter, Single toxic adenoma, Subacute thyroiditis, Trophoblastic tumor, Iodide induced hyperthyroidism, Struma ovarii, Thyrotropin receptor activation" [50].According to certain reports if only the hisk groups are analyzed for thyroid disorder then one third of the affected person will be missed out of diagnosis.[51]As a result of this a large number of pregnant women with thyroid disorder will enter second and third trimester of pregnancy without being diagnosed. Hence it becomes very important to analyze the levels of various thyroid related hormones in early pregnancy so as to prevent the irreversible damage to fetus. [52].

Thyroid disorders are very commonly observed in female in reproductive age. It is the second most frequent endocrine disorder after (DM) diabetes mellitus [53]. To date, there is not much study done on thyroid function in pregnancy in central India. Hence, exact data is not known about the prevalence of thyroid dysfunction in pregnancy.

The geographic location is a very important factor in deciding the prevalence of thyroid dysfunction because Iodine levels in salt in different regions vary and also the consumption of salt vary [54]. First trimester value shall be analyzed more criticallly because these are much more important than second and third trimester values as it has immense role in preventing thyroid complications later on [55]. Maternal thyroid disorder in early pregnancy is known to influence fetal development and pregnancy outcome. It can lead to premature birth, fetal mortality, hypertension and low infant birth weight [56].It can negatively affect fetal brain development and can cause mental retardation [57]. The most appropriate test for diagnosing thyroid dysfunction is estimating TSH levels as it is more sensitive parameter than FT4 and FT3 levels [58]. TPOAb measurement is also considered when examining thyroid disorder because these Abs are majorly responsible for autoimmune disorder of thyroid [59].

According to studies done by *Wang et al*. case finding strategy for screening thyroid problems can results in missing many cases of hyperthyroidism and hypothyroidism [60].Hence universal screening of pregnant women should be done to prevent adverse outcomes on fetal of maternal thyroid dysfunction. If thyroid disorder will be diagnosed early than proper treatment can be given on time and fetal outcomes of thyroid dysfunction can be prevented.

One hundred and forty two pregnant women selected for the study were evaluated for thyroid function and autoimmunity by ECLIA method. ECLIA has been found to highly sensitive technique for diagnosing thyroid dysfunction [61].

In the studies done by *Pietro et al*. it was observed that hypothyroidism is much more commonly observed in pregnancy as compared to hyperthyroidism [62].1 of the pregnant women were found to have hyperthyroidism as they had TSH levels less than normal and high FT4 levels[63].According to previous studies SCH is known to be present 1-2% of all pregnancies but this is older estimate of prevalence and based on region, assay, and trimester-specific TSH cut-offs for the diagnosis [64].

Endocrinology studies done recently suggest much higher prevalence of any kind of hypothyroidism in pregnant women "(12.3% Finnish, 15.5% American to 35.3% South American)".This is in accordance with studies done by Jacob J. who

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suggested that SCH in the first trimester of pregnancy would be having prevalence of more than 50% in pregnant women of Northern population if universal screening in pregnancy was done [65].

Exposure to much higher intakes of dietary iodine in North India can be a major reason of subclinical hypothyroidism because according to studies done by *Grewal et al.* 72% of the pregnant women have more than required intake of Iodine in first trimester of pregnancy [66].

A significant number of Indian populations is found to have autoantibodies to thyroid peroxidase [67]. These antibodies increase the risk of complications in pregnancy like miscarriage, preterm delivery, placental abruption etc. [68]In a study done by *Haddow et. al*. which suggested that hCG cause suppression of TSH release[69].

Thyroid disorder is found to be 33.09% prevalent in high risk groups as compared to 17.6 % in non - high risk groups. Thyroid disease is found to me more common in patients who have some family member suffering from thyroid disease thyroid or have they themselves suffered from thyroid disorder. The results are in accordance with study done by Wang et al. which reported that high risk groups are more prone to develop thyroid disease. Hence, its adverse effects need to be prevented by universal screening and early replacement by levothyroxine [70].

According to a study conducted in 2021 by Harshvardhan et al., thyroid insufficiency affected 51.4% of pregnant women. With elevated TSH levels but normal FT4 levels, subclinical hypothyroidism was discovered in 40.9% of the pregnant women. In pregnant women, hyperthyroidism is far less common than hypothyroidism.[71]

15. CONCLUSION

Hypothyroidism is diagnosed to be much more common that hyperthyroidism in pregnant women and subclinical hypothyroidism is a major public health burden in Northern Indian population. Adverse outcomes of thyroid disorder and treatment should be analyzed in the child so that possible treatment strategies can be adopted. Patients can be tested for presence of antibodies to TSH receptor and genomic study of pregnant women diagnosed with autoimmune disorder can be done.

BIBLIOGRAPHY

1. Carney LA, Quinlan JD, West JM. Thyroid disease in pregnancy. American family physician. 2014 Feb 15;89(4):273-8.
2. Morganti S, Ceda GP, Saccani M, Milli B, Ugolotti D, Prampolini R, Maggio M, Valenti G, Ceresini G. Thyroid disease in the elderly: sex-related differences in clinical expression. Journal of endocrinological investigation. 2005 Jan 1;28(11 Suppl Proceedings):101-4.
3. Mahadik K, Choudhary P, Roy PK. Study of thyroid function in pregnancy, its feto-maternal outcome; a prospective observational study. BMC Pregnancy and Childbirth. 2020 Dec;20(1):1-7.
4. 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.
5. Mullur R, Liu YY, Brent GA. Thyroid hormone regulation of metabolism. Physiological reviews. 2014 Apr;94(2):355-82.
6. Visser TJ. Regulation of thyroid function, synthesis and function of thyroid hormones. Thyroid Diseases Endocrinology. Springer, Cham. 2018:1-30.
7. Alemu A, Terefe B, Abebe M, Biadgo B. Thyroid hormone dysfunction during pregnancy: A review. International Journal of Reproductive BioMedicine. 2016 Nov;14(11):677.
8. Leung AM. Thyroid function in pregnancy. Journal of trace elements in medicine and biology. 2012 Jun 1;26(2-3):137-40.
9. Rajput R, Singh B, Goel V, Verma A, Seth S, Nanda S. Trimester-specific reference interval for thyroid hormones during pregnancy at a Tertiary Care Hospital in Haryana, India. Indian journal of endocrinology and metabolism. 2016 Nov;20(6):810.
10. Ahmed RG. Maternal-fetal thyroid interactions. In the thyroid hormone. 2012 Jul 18:125-56.
11. Kennedy RL, Darne J. The role of hCG in regulation of the thyroid gland in normal and

ISSN: 2309-5288 (Print)
ISSN: 2309-6152 (Online)
CODEN: JCLMC4
Journal of Coastal Life Medicine

abnormal pregnancy. Obstetrics and gynecology. 1991 Aug 1;78(2):298-307.
12. Chung HR. Iodine and thyroid function. Annals of Pediatric Endocrinology & Metabolism. 2014 Mar;19(1):8.
13. Glinoer D, Lemone M. Goiter and pregnancy: a new insight into an old problem. Thyroid. 1992;2(1):65-70.
14. Prummel MF, Wiersinga WM. Thyroid autoimmunity and miscarriage. European Journal of Endocrinology. 2004 Jun 1;150(6):751-6.
15. Cignini P, Cafà EV, Giorlandino C, Capriglione S, Spata A, Dugo N. Thyroid physiology and common diseases in pregnancy: review of literature. Journal of prenatal medicine. 2012 Oct;6(4):64.
16. Bjoro T, Holmen J, Krüger O, Midthjell K, Hunstad K, Schreiner T, Sandnes L, Brochmann H. Prevalence of thyroid disease, thyroid dysfunction and thyroid peroxidase antibodies in a large, unselected population. The Health Study of Nord-Trondelag (HUNT). European journal of endocrinology. 2000 Nov 1;143(5):639-47.
17. Yassaee F, Farahani M, Abadi AR. Prevalence of subclinical hypothyroidism in pregnant women in Tehran-Iran. International journal of fertility & sterility. 2014 Jul;8(2):163.
18. Korevaar TI, Medici M, de Rijke YB, Visser W, de Muinck Keizer-Schrama SM, Jaddoe VW, Hofman A, Ross HA, Visser WE, Hooijkaas H, Steegers EA. Ethnic differences in maternal thyroid parameters during pregnancy: the Generation R study. The Journal of Clinical Endocrinology & Metabolism. 2013 Sep 1;98(9):3678-86.
19. Beynon ME, Pinneri K. An overview of the thyroid gland and thyroid-related deaths for the forensic pathologist. Academic forensic pathology. 2016 Jun;6(2):217-36.
20. https://www.niddk.nih.gov/health-information/endocrine-diseases/pregnancy-thyroid-disease.
21. https://www.slideshare.net/drcfng/thyroid-gland.
22. Lee J, Yi S, Kang YE, Kim HW, Joung KH, Sul HJ, Kim KS, Shong M. Morphological and functional changes in the thyroid follicles of the aged murine and humans. Journal of pathology and translational medicine. 2016 Nov;50(6):426.
23. http://www.biosciencenotes.com/thyroid-gland-and-thyroid-hormones.
24. Szkudlinski MW, Fremont V, Ronin C, Weintraub BD. Thyroid-stimulating hormone and thyroid-stimulating hormone receptor structure-function relationships. Physiological reviews. 2002 Apr 1;82(2):473-502.
25. Bizhanova A, Kopp P. The sodium-iodide symporter NIS and pendrin in iodide homeostasis of the thyroid. Endocrinology. 2009 Mar 1;150(3):1084-90.
26. Carvalho DP, Dupuy C. Thyroid hormone biosynthesis and release. Molecular and cellular endocrinology. 2017 Dec 15; 458:6-15.
27. Canaris GJ, Steiner JF, Ridgway EC. Do traditional symptoms of hypothyroidism correlate with biochemical disease? Journal of general internal medicine. 1997 Sep;12(9):544-50.
28. Brent GA. Mechanisms of thyroid hormone action. The Journal of clinical investigation. 2012 Sep 4;122(9):3035-43.
29. Gaitonde DY, Rowley KD, Sweeney LB. Hypothyroidism: an update. South African Family Practice. 2012 Sep 1;54(5):384-90.
30. Reid JR, Wheeler SF. Hyperthyroidism: diagnosis and treatment. American family physician. 2005 Aug 15;72(4):623-30.
31. Nilsson M, Fagman H. Development of the thyroid gland. Development. 2017 Jun 15;144(12):2123-40.
32. Pekonen F, Alfthan H, Stenman UH, Ylikorkala O. Human chorionic gonadotropin (hCG) and thyroid function in early human pregnancy: circadian variation and evidence for intrinsic thyrotropic activity of hCG. The Journal of Clinical Endocrinology & Metabolism. 1988 Apr 1;66(4):853-6.
33. Guillaume J, Schussler GC, Goldman J, Wassel P, Bach L. Components of the Total Serum Thyroid Hormone Concentrations during Pregnancy: High Free Thyroxine and Blunted Thyrotropin (TSH) Response to TSH Releasing Hormone in the First Trimester. The Journal of Clinical Endocrinology & Metabolism. 1985 Apr 1;60(4):678-84.
34. 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.
35. Gahlawat P, Singh A, Nanda S, Kharb S. Thyroid dysfunction in early pregnancy and spontaneous abortion. Biomedical and Biotechnology Research Journal (BBRJ). 2017 Jan 1;1(1):81.

ISSN: 2309-5288 (Print)
ISSN: 2309-6152 (Online)
CODEN: JCLMC4
Journal of Coastal Life Medicine

36. Lazarus J. Thyroid regulation and dysfunction in the pregnant patient. Endotext [Internet]. 2016 Jul 21.
37. Feingold KR, Anawalt B, Boyce A, Chrousos G, Dungan K, Grossman A, Hershman JM, Kaltsas G, Koch C, Kopp P, Korbonits M. Thyroid Regulation and Dysfunction in the Pregnant Patient--Endotext.
38. Burrow GN, Fisher DA, Larsen PR. Maternal and fetal thyroid function. New England Journal of Medicine. 1994 Oct 20;331(16):1072-8.
39. Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, O'Heir CE, Mitchell ML, Hermos RJ, Waisbren SE, Faix JD. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. New England Journal of Medicine. 1999 Aug 19;341(8):549-55.
40. Shan ZY, Chen YY, Teng WP, Yu XH, Li CY, Zhou WW, Gao B, Zhou JR, Ding B, Ma Y, Wu Y. A study for maternal thyroid hormone deficiency during the first half of pregnancy in China. European journal of clinical investigation. 2009 Jan;39(1):37-42.
41. Zarghami N, Rohbani-Noubar M, Khosrowbeygi A. Thyroid hormones status during pregnancy in normal Iranian women. Indian Journal of Clinical Biochemistry. 2005 Jul;20(2):182-5.
42. De Leo S, Pearce EN. Autoimmune thyroid disease during pregnancy. The Lancet Diabetes & Endocrinology. 2018 Jul 1;6(7):575-86.
43. Teng W, Shan Z, Patil-Sisodia K, Cooper DS. Hypothyroidism in pregnancy. The lancet Diabetes & endocrinology. 2013 Nov 1;1(3):228-37.
44. Dave A, Maru L, Tripathi M. Importance of Universal screening for thyroid disorders in first trimester of pregnancy. Indian journal of endocrinology and metabolism. 2014 Sep;18(5):735.
45. Kostoglou-Athanassiou I, Ntalles K. Hypothyroidism-new aspects of an old disease. Hippokratia. 2010 Apr;14(2):82.
46. Casey BM, Dashe JS, Wells CE, McIntire DD, Byrd W, Leveno KJ, Cunningham FG. Subclinical hypothyroidism and pregnancy outcomes. Obstetrics & Gynecology. 2005 Feb 1;105(2):239-45.
47. Sahay RK, Nagesh VS. Hypothyroidism in pregnancy. Indian journal of endocrinology and metabolism. 2012 May;16(3):364.
48. Nazarpour S, Tehrani FR, Simbar M, Azizi F. Thyroid dysfunction and pregnancy outcomes. Iranian journal of reproductive medicine. 2015 Jul;13(7):387.
49. Moog NK, Entringer S, Heim C, Wadhwa PD, Kathmann N, Buss C. Influence of maternal thyroid hormones during gestation on fetal brain development. Neuroscience. 2017 Feb 7; 342:68-100.
50. Grigoriu C, Cezar C, Grigoras M, Horhoianu I, Parau C, Vîrtej P, Lungu A, Horhoianu V, Poiana C. Management of hyperthyroidism in pregnancy. Journal of medicine and life. 2008 Nov 15;1(4):390.
51. Moleti M, Di Mauro M, Sturniolo G, Russo M, Vermiglio F. Hyperthyroidism in the pregnant woman: maternal and fetal aspects. Journal of clinical & translational endocrinology. 2019 Jun 1; 16:100190.
52. Kobaly K, Mandel SJ. Hyperthyroidism and pregnancy. Endocrinology and Metabolism Clinics. 2019 Sep 1;48(3):533-45.
53. Hage M, Zantout MS, Azar ST. Thyroid disorders and diabetes mellitus. Journal of thyroid research. 2011 Oct;2011.
54. Chiovato L, Magri F, Carlé A. Hypothyroidism in context: where we've been and where we're going. Advances in therapy. 2019 Sep;36(2):47-58.
55. 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.
56. Zhou M, Wang M, Li J, Luo X, Lei M. Effects of thyroid diseases on pregnancy outcomes. Experimental and therapeutic medicine. 2019 Sep 1;18(3):1807-15.
57. Nazarpour S, Ramezani Tehrani F, Simbar M, Azizi F. Pregnancy outcomes in pregnant women with hypothyroidism (A review Article). The Iranian Journal of Obstetrics, Gynecology and Infertility. 2014;17(126):17-26.
58. Sheehan MT. Biochemical testing of the thyroid: TSH is the best and, oftentimes, only test needed–a review for primary care. Clinical medicine & research. 2016 Jun 1;14(2):83-92.
59. Fröhlich E, Wahl R. Thyroid autoimmunity: role of anti-thyroid antibodies in thyroid and extra-thyroidal diseases. Frontiers in immunology. 2017 May 9;8:521.
60. Wang W, Teng W, Shan Z, Wang S, Li J, Zhu L, Zhou J, Mao J, Yu X, Li J, Chen Y. The prevalence

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of thyroid disorders during early pregnancy in China: the benefits of universal screening in the first trimester of pregnancy. European Journal of Endocrinology. 2011 Feb 1;164(2):263-8.

61. Sarkar R. TSH comparison between chemiluminescence (Architect) and electrochemiluminescence (Cobas) immunoassays: an Indian population perspective. Indian journal of clinical biochemistry. 2014 Apr 1;29(2):189-95.
62. Cignini P, Cafà EV, Giorlandino C, Capriglione S, Spata A, Dugo N. Thyroid physiology and common diseases in pregnancy: review of literature. Journal of prenatal medicine. 2012 Oct;6(4):64.
63. Cooper DS. Subclinical hypothyroidism. New England Journal of Medicine. 2001 Jul 26;345(4):260-5.
64. Hennessey JV, Espaillat R. Subclinical hypothyroidism: a historical view and shifting prevalence. International journal of clinical practice. 2015 Jul;69(7):771-82.
65. Jacob JJ. Subclinical hypothyroidism in the first trimester of pregnancy in North India. Indian journal of endocrinology and metabolism. 2013 Oct;17(Suppl1): S160.
66. Grewal E, Khadgawat R, Gupta N. Assessment of iodine nutrition in pregnant north Indian subjects in three trimesters. Indian journal of endocrinology and metabolism. 2013 Mar;17(2):289.
67. Koulouri O, Gurnell M. How to interpret thyroid function tests. Clinical medicine. 2013 Jun;13(3):282.
68. Balucan FS, Morshed SA, Davies TF. Thyroid autoantibodies in pregnancy: their role, regulation and clinical relevance. Journal of thyroid research. 2013 Jan 1;2013.
69. Haddow JE, McClain MR, Lambert-Messerlian G, Palomaki GE, Canick JA, Cleary-Goldman J, Malone FD, Porter TF, Nyberg DA, Bernstein P, D'Alton ME. Variability in thyroid-stimulating hormone suppression by human chronic gonadotropin during early pregnancy. The Journal of Clinical Endocrinology & Metabolism. 2008 Sep 1;93(9):3341-7.
70. 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):25
71. Harshvardhan, Tomo, S.,Rawat, A., Aggarwal, J. The Increased Prevalence of Thyroid Dysfunction in First Trimester Pregnancy in a Tertiary Care Centre and the Significance of Universal Screening;2021.Journal of Datta Meghe Institute of Medical Sciences University, Volume 16, Issue 3, July-September 2021, Pages 457-461.