

Original paper**Thyroid Dysfunction during Pregnancy****Zahraa Abdulaali Mohammad Hassan<sup>^</sup>, Ula Salah Jumaa<sup>^\*</sup>**<sup>^</sup>*University of Kufa/Collage of medicine /department of physiology /Najaf/Iraq***Abstract**

**B**ackground: Pregnancy is the time of hormonal changes which may result in endocrine disorders. Thyroid disorders are common clinical problem during pregnancy in which subclinical hypothyroidism is the most common thyroid disorders. Maternal thyroid dysfunction may result in short-term and long-term harm to the mother and child.

**Objective:** To study the prevalence of thyroid disorder during pregnancy and to follow the correlation between (TSH, FT3, and FT4) with BMI

**Materials and Method:** A cross sectional study involved 120 pregnant women in second and third trimester (apparently normal) between (19-42) years.

The participants were collected randomly from outpatient unit of Al-Zahraa teaching hospital in AL-Najaf AL-Ashraf, detailed history and data for pregnant women were recorded (including maternal age, gestational age, medical history of thyroid disease and history of abortion and infertility). Pregnant women with history of thyroid disease were excluded from the study. Serum TSH, FT3 and FT4 were measured for all pregnant women participated in study

**Results:** The prevalence of thyroid disorder during pregnancy was 20.8% out of which 20(16.6%) had SCH and 2(1.6%) had OH. Hyperthyroidism detected in 3(2.5%) pregnant women all of them had subclinical hyperthyroidism. and there was a positive correlation between TSH, FT3 with BMI and negative correlation of FT4 with BMI, also maternal age don't affect thyroid function status significantly (p value > 0.05).and there was no significant relation between thyroid disorder and history of abortion or infertility (p value > 0.05)

**Conclusion**

There is a high prevalence of hypothyroidism during pregnancy and the majority is subclinical hypothyroidism. BMI was correlated positively with TSH and FT3 and negatively with FT4.

**Key words:** pregnancy, thyroid dysfunction, BMI, TSH, FT3, FT4

**Introduction**

Pregnancy is the time of hormonal alternations, which may result in endocrine disorders that lead to adverse outcome to the mother and fetus. Thyroid dysfunction is common endocrinological disorder during pregnancy<sup>(1)</sup>

Pregnancy is a stressful condition on thyroid gland which is greater in iodine deficient areas, thyroid dysfunction during pregnancy either hypothyroidism or hyperthyroidism. Hypothyroidism is common during pregnancy which is either subclinical that is more prevalent or overt

hypothyroidism or isolated hypothyroxinemia while hyperthyroidism is uncommon during pregnancy usually caused by Graves' disease or gestational Transient hyperthyroxinemia (due to stimulation of thyroid gland by hCG which act as TSH agonist so that increase level of TSH)<sup>(2)</sup>

Prevalence of thyroid dysfunction in USA for SCH and OH is 9% and 3% respectively<sup>(3)</sup> and for overt hyperthyroidism in pregnancy was estimated about 0.4% and 1.7% for subclinical hyperthyroidism<sup>(4)</sup>

\*for correspondence Email: drulasalah@gmail.com

In normal pregnancy thyroid gland tends to adapt its structure and function through changes in metabolism of thyroid hormone, iodine uptake, and regulation of the hypothalamic-pituitary-thyroid axis to reach an increased functional requirements of pregnant women. Decreased thyroidal storage may result in thyroid insufficiency<sup>(5)</sup>

Thyroid dysfunction in pregnancy is associated with adverse maternal and fetal outcome, the detrimental effects of thyroid dysfunction may extend beyond pregnancy and delivery to affect neurodevelopment of child<sup>(6)</sup>, pregnant women with thyroid dysfunction are at higher risk of pregnancy complications such as placental abruption, threatened abortion, postpartum hemorrhage, preterm labor and preeclampsia. The fetal complications such as low-birth-weight, intrauterine growth retardation, neonatal deaths, preterm delivery, neonatal hypothyroidism, and still birth<sup>(7)</sup>

Triiodothyronine has an important role in regulation of energy expenditure and thermogenesis and also it has an essential role in the metabolism of carbohydrate and lipid, food intake and fatty acids oxidation so thyroid hormone is involved in normal metabolic alternations during pregnancy<sup>(8)</sup>. Even mild degree of maternal obesity (BMI more than 23 kg/m<sup>2</sup>) is considered a risk factor for thyroid disorders, especially in iodine-deficient areas.<sup>(9)</sup> Patients with thyroid dysfunction characterized by alternations in body weight and the level of TSH is positively correlated with BMI<sup>(10)</sup>

## Material and Method

The study is a cross sectional involved 120 pregnant women in second and third trimester (apparently normal), their ages range between (19-42) years and their BMI range between (21.2-50.78) kg/m<sup>2</sup>

The participants were collected randomly from outpatient unit of Al-Zahraa teaching hospital in AL-Najaf AL-Ashraf during the time from January 2017 to July 2017.

Pregnant women with history of thyroid disease were excluded from this study.

Data for pregnant women involved in our study were included age, gestational age, medical history of thyroid disease, history of abortion and infertility

Gestational age was estimated depend on the last menstrual period (LMP) and ultrasound was performed when the LMP was uncertain.

Body mass index was estimated by dividing pregnant's weight in kilograms by the square of height in meter.

BMI formula = weight (kg)/height (m)<sup>2</sup>

Height was measured by measuring tape while weight was measured by using mechanical scale when the pregnant standing in erect position without shoes. According to WHO guideline and BMI values people are classified into:

BMI values used during pregnancy is the same that is used in non-pregnant women<sup>(12, 13)</sup>

Five milliliters of blood sample was collected from each participant following standard laboratory procedure. The blood sample was left for about 15-30 minutes at room temperature for clotting then centrifuged at 3000 rpm for 3-5 minutes for serum separation. The serum was transferred into disposable tube for storage at (-10 C) to be used later for hormonal analysis.

TSH, FT3 and FT4 were measured by Mini Vitic Immunoassay Diagnostic Assay System (mini VIDAS) method, the kits were supplied by BioMe'rieux ® France.

Normal reference range of TSH in second and third trimester<sup>(14)</sup> were (0.2 to 3.0 mU/L), (0.3 to 3.5 mU/L) respectively. On other hand, the normal reference level of FT3, FT4 in the second and third trimester<sup>(15, 16)</sup> were (3-5.5 pmol/L) (9-15.4 pmol/L) respectively.

Statistical analysis was performed by using SPSS version 20. In which number with percentages as descriptive statistics were used. For analysis Pearson correlation coefficient and chi square was used.

## Results

### Demographical study

A total 120 pregnant women were included in this study. Table 2 summarized the demographic characteristics of these pregnant women. Their ages were ranged between (19-42) years with mean  $\pm$  SD ( $32 \pm 5.8$ ) and their BMI range between (21.2-50.7) with mean  $\pm$  SD ( $33.6 \pm 5.3$ )

### Prevalence of thyroid disorder during pregnancy

In this study of total 120 pregnant women between second and third trimester gestational age, 25(20.8%) pregnant women had thyroid dysfunction in which 22(18.3%) pregnant women had hypothyroidism out of which 20(16.6%) had SCH and 2(1.6%) had OH. Hyperthyroidism detected in 3(2.5%) pregnant women all of them had subclinical hyperthyroidism as in table 2. In this study all pregnant women with thyroid disorder

were asymptomatic and their detection based on laboratory test.

### Effect of maternal age on thyroid function during pregnancy

There was statistically no significant relation between thyroid disorder and maternal age (p value  $>0.05$ ) as shown in table 3.

### The correlation between TSH and BMI

When we study the relation between TSH and BMI there was significant positive correlation between TSH and BMI in which serum TSH was higher among pregnant women with higher BMI as demonstrated in figure 1

### The correlation between FT4 and BMI

When we study the relation between TSH and BMI there was significant negative correlation between FT4 and BMI in which higher values of serum FT4 were associated with lower BMI as shown in figure 2.

**Table1.** World Health Organization (2010) "BMI Classifications" <sup>(11)</sup>.

Classification	BMI range (kg /m <sup>2</sup> )
Normal weight	From 18.5-24.9
Overweight	From 25-30
Obese	$>30$

**Table2.** Sociodemographic characteristics of studied pregnant women.

Variable	Frequency	Percent	
Age/years	15-25	22	18.3
	26-35	64	53.3
	36-45	34	28.3
Gestational age	Second trimester (14-26 week)	35	29.2
	Third trimester (27-40 week)	85	70.8
BMI Kg/m <sup>2</sup>	normal weight	6	5.0
	Overweight	21	17.5
	Obese	93	77.5
History of abortion	Negative	70	58.3
	Positive	50	41.7
History of Infertility	Negative	92	76.7
	Positive	28	23.3
Gestational diabetes	Positive	39	32.5
	Negative	81	67.5
	Total	120	100.0

**The correlation between FT3 and BMI**

When we study the relation between TSH and BMI there was positive significant correlation between FT3 and BMI in which FT3 increased with higher BMI as shown in Figure 3

**Relation between thyroid disorders and history of abortion:**

In our population study there was no significant relation between history of

abortion and thyroid disorders (p value >0.05) .as in table 5

**Relation between thyroid disorders and history of infertility:**

The result of present study showed there was no significant relation between history of infertility and thyroid disorder (pvalue >0.05)

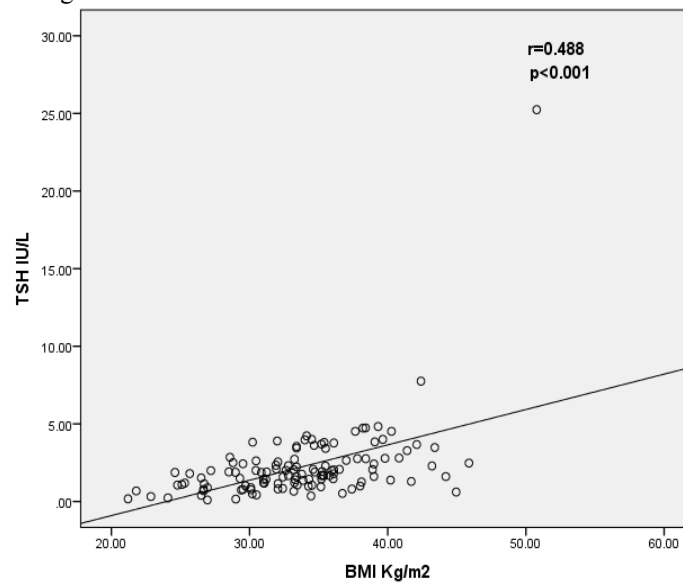
**Table 3.** Prevalence of thyroid disorder during pregnancy

Thyroid function status	Frequency	Percent	Clinical presentation	
Euthyroid	95	79.2		
Hyperthyroidism	3	2.5	Overt	0
			Subclinical	3
Hypothyroidism	22	18.3	Overt	2
			Subclinical	20
Total	120	100.0		

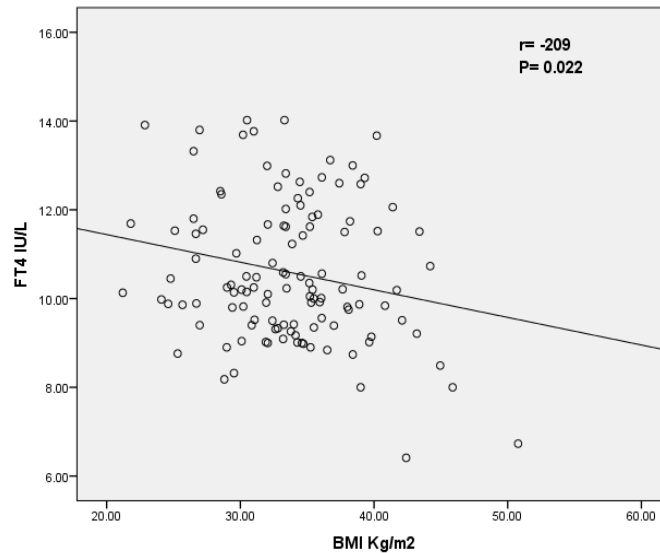
**Table 4.** Effect of maternal age on thyroid function during pregnancy

Thyroid function status	Age/years			Total	P value
	15-25	26-35	36-45		
Euthyroid	19(86.4%)	47(73.4%)	29(85.3%)	95(79.2%)	0.521
Hyperthyroidism	0(0.0%)	2(3.1%)	1(2.9%)	3(2.5%)	
Hypothyroidism	3(13.6%)	15(23.4%)	4(11.8%)	22(18.3%)	
Total	22(100.0%)	64(100.0%)	34(100.0%)	120(100.0%)	

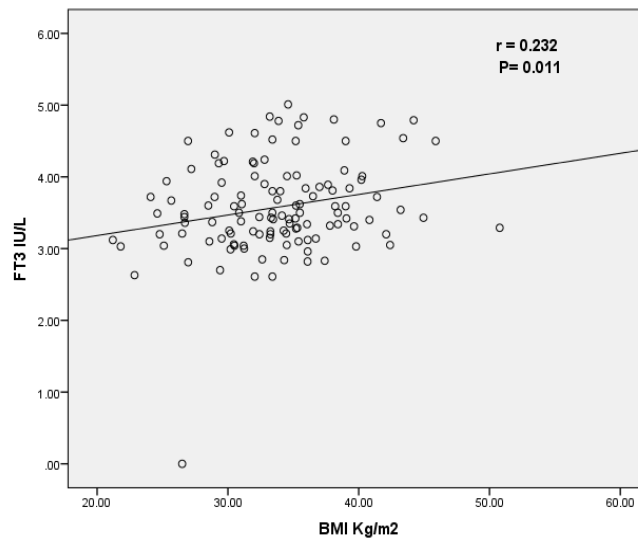
P value ≥0.05 regarded significant.



**Figure 1.** Correlation between TSH and BMI



**Figure 2.** Correlation between FT4 and BMI



**Figure 3.** Correlation between FT3 and BMI

**Table 5.** Relation between thyroid disorders and history of abortion.

Thyroid function status	History of abortion		Total	P value
	Negative	positive		
Euthyroid	55(57.9%)	40(42.1%)	95(100.0%)	0.952
Hyperthyroidism	2(66.7%)	1(33.3%)	3(100.0%)	
Hypothyroidism	13(59.1%)	9(40.9%)	22(100.0%)	
Total	70(58.3%)	50(41.7%)	120(100.0%)	

p value >0.05

**Table 6.** Relation between thyroid disorders and history of infertility.

Thyroid function stats	Infertility		Total	P value
	Negative	Positive		
Euthyroid	74(77.9%)	21(22.1%)	95(100.0%)	0.803
Hyperthyroidism	2(66.7%)	1(33.3%)	3(100.0%)	
Hypothyroidism	16(72.7%)	6(27.3%)	22(100.0%)	
Total	92(76.7%)	28(23.3%)	120(100.0%)	

p value >0.05

## Discussion

Thyroid dysfunction can lead to impairment of fertility in both sex and can affect the outcome of pregnancy<sup>(17)</sup>.

Subclinical hypothyroidism is the consequence of normal physiological alternations that happen during pregnancy and exceed the adaptation abilities of the pregnant woman. When pregnant woman who has decreased thyroidal storage or has developed early insulin resistance SCH may be occurred.<sup>(18)</sup>

In current study the prevalence of overt hypothyroidism (OH) during pregnancy is 1.6% and subclinical hypothyroidism is 16.6% while Hyperthyroidism is detected in (2.5%) all of them are subclinical hyperthyroidism

Prevalence of thyroid disorders during pregnancy is variable in different regions and different studies , the results of present study were comparable with prospective study conducted in North Spain that demonstrated the prevalence of SCH and OH was 13.7% and 1.6% respectively <sup>(19)</sup> . A study done by Casey et al (2006) <sup>(20)</sup> who found the prevalence of subclinical hyperthyroidism was 1.7%. A large prospective study in United Kingdom by Vaidya et al (2007)<sup>(21)</sup> was demonstrated the prevalence of OH and SCH were 1 % and 1.5% respectively and prevalence of subclinical hyperthyroidism was 5.6%

A study conducted in north India demonstrated high prevalence of thyroid disorder during pregnancy about 26.1 % in which (21.5%) women had SCH and (1.3%) of women had OH while (0.4%) of women had overt hyperthyroidism and (3.3%) of the women had subclinical hyperthyroidism<sup>(22)</sup>.

A cross sectional study reported by Yassae et al (2014) <sup>(23)</sup> in Tehran –Iran found the prevalence of SCH and OH were 4.15 % and 0.5% respectively .

In current study, the results showed that there was non-significant relation between maternal age and thyroid function status Our results are in agreement with study

done by Rijal *et al.*, (2011)<sup>(24)</sup> who reported that the difference was not significant between women with different age groups and thyroid function status. A study conducted in Iran by Saki et al (2014)<sup>(25)</sup> also reported the same findings, another study demonstrated there was non-significant difference in maternal age between pregnant with OH and euthyroid pregnant women <sup>(26)</sup>

In contrast to our results , Kubavat et al (2015) <sup>(27)</sup> found was an increased in the incidence of thyroid dysfunction with increased maternal age , also another study demonstrated there was a positive association between SCH and an increased in maternal age<sup>(28)</sup>.

In the present study, both TSH & FT3 levels were significantly correlated positively with BMI while FT4 serum level had a negative correlation with BMI

These results agree with study which reported that levels of TSH and FT3 had a positive correlation with BMI but FT4 had a negative correlation with BMI <sup>(29)</sup>

While Knudsen *et al* (2005)<sup>(30)</sup> found that there was a positive significant relation between BMI and TSH and the higher level of serum FT4 was associated with lower BMI, but there was no significant association between serum FT3 and BMI

A cross sectional study done by Kumar (2017) <sup>(31)</sup> who studied the correlation of TSH, FT3 and FT4 in healthy pregnant women with normal thyroid function with BMI in each trimester, result were shown that TSH level was significantly positively correlated with BMI during first and second trimester of pregnancy. FT4 level had significant negative correlation with BMI in second and third trimester of pregnancy while there is no significant correlation between BMI and FT3 level in any trimesters.

Another study by Ali *et al* (2016) <sup>(32)</sup> was reported that FT3 and FT4 levels were negatively correlated with BMI and no significant correlation of TSH with BMI

The correlation between TSH and thyroid hormones with BMI might be explained by

an increased secretion of leptin by adipose tissue in obese individual, leptin affects hypothalamic pituitary thyroid axis through up regulation of TRH which lead to increase TSH secretion, also leptin increases deiodinase activity that causes an increased in conversion of T4 into T3, the increased level of FT3 and TT3 leads to an increased the energy expenditure, Therefore, these alternations in TH levels in obese subjects are an adaptive process to weight gain. An increased energy expenditure decreases the energy that is available to be converted into fat which results in avoidance of accumulation of energy as fat<sup>(33)</sup>

There was no significant relation between history of abortion and thyroid function status in present study this may be due to recent diagnosis of thyroid dysfunction in our selected patient.

Our results were in agreement with another results which demonstrated a non-significant difference in history of abortion in women with hypothyroidism and euthyroid women<sup>(34)</sup>. A study reported by Cleary-Goldman *et al* (2008)<sup>(35)</sup> who found that history of abortion was non statistically significant in pregnant with SCH, also Ozdemir *et al*(2013)<sup>(36)</sup> has been reported that pregnant women with history of abortion have no statistical difference among women with hypothyroidism and euthyroid pregnant women.

Another studies<sup>(37-39)</sup> have been reported that history of abortion was significantly higher in hypothyroid than euthyroid pregnant women which not agreement with this study.

The association between thyroid dysfunction and an increased risk of abortion might be explained by the role of TH in the maintenance of pregnancy through stimulation of the production and secretion of progesterone, E2, hCG ( $\alpha$ , $\beta$ ) and hPL by placenta<sup>(40)</sup>

Our results were shown non-significant relation between history of infertility and thyroid function status.

The finding of this study agreed with Poppe *et al* (2002)<sup>(41)</sup> who was reported that thyroid dysfunction either hypothyroidism or hyperthyroidism was not significantly frequent in infertile women than euthyroid women but the prevalence of positive TPO-Ab was significantly higher than in control groups.

Our study disagreed with study reported by Abalovich *et al* (2007)<sup>(42)</sup> who found a high prevalence of SCH among infertile women. Pushpagiri (2015)<sup>(43)</sup> has been observed that the prevalence of hypothyroidism was higher in women with infertility than euthyroid infertile women.

The possible cause of relation between thyroid dysfunction and infertility can be explained that the TH is important for normal reproductive function, thyroid dysfunction can cause disruption of the menstrual cycle also hypothyroidism can change the function of the oocytes. Normal TH concentration seems to be important for oocyte maturation as well as low level of TH decrease the levels of sex hormone-binding globulin<sup>(44)</sup> the decreased level of SHBG leads to decreased plasma concentrations of both total testosterone and E2 also in patient with hypothyroidism there is an increased in prolactin level because of an increased in TRH secretion<sup>(45)</sup>

## Reference

1. Parham M; Asgarani F; Bagherzadeh M; Ebrahimi G; Vafaeimanesh J; Thyroid function in pregnant women with gestational diabetes: Is screening necessary?. *Thyroid Research Practice*. 2013;12:3–7.
2. Lazarus JH ;Thyroid function in pregnancy. *British Medical Bulletin*.2011;97: 137–148.
3. Casey BM ; Dashe JS; Wells CE; McIntire DD; Byrd W; Leveno KJ; et al. Subclinical Hypothyroidism and Pregnancy outcomes. *Obstetrics & Gynecology*. 2005; 105:239–245.
4. Casey BM; Dashe JS; Wells CE; McIntire DD; Byrd W; Leveno KJ, et al. Subclinical hyperthyroidism and pregnancy outcomes. *Obstetrics & Gynecology*. 2006;107:337-341.
5. Diéguez M ; Herrero A ; Avello N; Suárez P; Delgado E; Menéndez E; Prevalence of thyroid dysfunction in women in early

- pregnancy: Does it increase with maternal age?. *Clinical Endocrinology*. 2016; 84:121–126.
6. Okosieme OH; Lazarus JH; Thyroid dysfunction in pregnancy: Optimizing fetal and maternal outcomes. *Expert Review of Endocrinology and Metabolism*. 2010; 5:521-529.
  7. Ajmani SN; Aggarwal D; Bhatia P; Sharma M; Sarabhai Vi; Paul M.; Prevalence of overt and subclinical thyroid dysfunction among pregnant women and its effect on maternal and fetal outcome. *Journal of Obstetrics and Gynecology of India*. 2014; 64:105–110.
  8. Biondi B .Thyroid and obesity: An intriguing relationship. *Journal of Clinical Endocrinology and Metabolism*. 2010; 95:3614–3617.
  9. Gowachirapant S; Melse-Boonstra A , Winichagoon P, Zimmermann MB. Overweight increases risk of first trimester hypothyroxinaemia in iodine-deficient pregnant women. *Maternal and Child Nutrition*. 2014; 10:61–71.
  10. Nyrrnes A; Jorde R; Sundsfjord J; Serum TSH is positively associated with BMI. *International Journal of Endocrinology and Metabolism*. 2006; 30:100-105.
  11. Wilkes S; Murdoch A; Obesity and female fertility: a primary care perspective. *J Fam Plann Reprod Health Care*. 2009; 35: 181–185.
  12. Addo VN; Body Mass Index, Weight Gain during Pregnancy and Obstetric Outcomes. *Ghana Medical Journal*. 2010; 44:64–69.
  13. Shub A; Huning E YS; Campbell K J; Mc Carthy E A; Pregnant women’s knowledge of weight, weight gain, complications of obesity and weight management strategies in pregnancy. *BMC Research Notes*. 2013; 6: 278.
  14. Garber JR; Cobin RH; Gharib H; Hennessey JV; Klein I; Mechanick JI et al. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. *Endocrine practice* . 2012;18:988–1028.
  15. Cotzias C; Wong SJ; Taylor E; Seed P; Girling J; A study to establish gestation-specific reference intervals for thyroid function tests in normal singleton pregnancy. *European Journal of Obstetrics Gynecology and Reproductive Biology*. 2008; 137:61–66.
  16. Almomin A; Mansour A; Sharief M; Trimester-Specific Reference Intervals of Thyroid Function Testing in Pregnant Women from Basrah, Iraq Using Electrochemiluminescent Immunoassay. *Diseases*. 2016; 4: p.20.
  17. Dittrich R; Beckmann MW; Oppelt PG, Hoffmann I; Lotz L; Kuwert T; et al. Thyroid hormone receptors and reproduction. *Journal of Reproductive Immunology*. 2011; 90: 58–66.
  18. Toulis KA; Stagnaro-Green A; Negro R; Maternal Subclinical Hypothyroidism and Gestational Diabetes Mellitus: A Meta Analysis. *Endocrine practice*. 2014; 20:703-714.
  19. Aguayoa A; Graua G; Velaa A; Aniel-Quirogab A; Espadac M; Martula P; et al . *Journal of Trace Elements in Medicine and Biology*. 2013; 27:302–306.
  20. Casey BM; Dashe JS; Wells CE; McIntire DD; Byrd W; Leveno KJ; et al. Subclinical hyperthyroidism and pregnancy outcomes. *Obstetrics & Gynecology*. 2006;107:337-341.
  21. Vaidya B; Anthony S; Bilous M; Shields B; Drury J; Hutchison S., et al. Detection of thyroid dysfunction in early pregnancy: Universal screening or targeted high-risk case finding?. *Journal of Clinical Endocrinology and Metabolism*. 2007; 92:203–207.
  22. Rajput R; Goel V; Nanda S; Rajput M ; Seth S; Prevalence of thyroid dysfunction among women during the first trimester of pregnancy at a tertiary care hospital in Haryana. *Indian Journal of Endocrinology and Metabolism*. 2015; 19: 416-419.
  23. Yassaee F; Farahani M; Abadi AR; Prevalence of subclinical hypothyroidism in pregnant women in Tehran-Iran. *International Journal of Fertility and Sterility*. 2014; 8:163–166.
  24. Rijal, B; Shrestha, R; Jha B; Association of thyroid dysfunction among infertile women visiting infertility center of Om Hospital, Kathmandu, Nepal. *Nepal Medical College journal*. 2011 ;13:247–249.
  25. Saki F; Dabbaghmanesh MH; Ghaemi SZ; Forouhari S; Omrani GR; Bakhshayeshkaram M; Thyroid function in pregnancy and its influences on maternal and fetal outcomes. *International Journal of Endocrinology and Metabolism*. 2014; 12:1–7.
  26. Hirsch D; Levy S; Nadler V; Kopel V; Shainberg B; Toledano Y; Pregnancy outcomes in women with severe hypothyroidism. *European Journal of Endocrinology*. 2013; 169:313–320.
  27. Kubavat K; Patel A; Patel HL; High Prevalence of Thyroid Dysfunction Among Pregnant Women in Ahmedabad City , *International Journal of Advanced Research*. 2015 ; 3:676–682.
  28. Sannaboraiah A; Upadhyaya R ; Garag S; Krishnappa S; Subclinical hypothyroidism in pregnancy and outcomes .*International Journal of Reproduction, Contraception, Obstetrics and Gynecology*. 2017; 6:1215-1221.
  29. De Pergola G; Ciampolillo A ; Paolotti S; Trerotoli; Giorgino R; Free triiodothyronine and thyroid stimulating hormone are directly associated with waist circumference, independently of insulin resistance, metabolic

- parameters and blood pressure in overweight and obese women. *Clinical Endocrinology*. 2007 ;67: 265–269.
30. Knudsen N; Laurberg P; Rasmussen LB; Bülow I; Perrild H; Ovesen L ,et al. Small differences in thyroid function may be important for body mass index and the occurrence of obesity in the population. *Journal of Clinical Endocrinology and Metabolism*.2005;90:4019–4024.
  31. Kumar S; Chiinngaihlun T; Singh MR; Punyabati O ;Correlation of Body Mass Index (BMI) with Thyroid Function in Euthyroid Pregnant Women in Manipur, India. *Journal of Clinical and Diagnostic Research*. 2017; 11:13-15.
  32. Ali EA; Abdullahi H; Rayis DA; Adam I; Lutf MF; Effect of gestational diabetes mellitus on maternal thyroid function and body mass index. *F1000Research*. 2016; 5:1746.
  33. Reinehr T; Obesity and thyroid function. *Molecular and Cellular Endocrinology*. 2010; 316:165–171.
  34. Feldthusen AD; Pedersen PL; Larsen J; Toft Kristensen T; Ellervik C; Kvetny J; Impaired fertility associated with subclinical hypothyroidism and thyroid autoimmunity: The danish general suburban population study. *Journal of Pregnancy*. 2015;2015:6pages.
  35. Cleary-Goldman J; Malone FD; Lambert-Messerlian G; Sullivan L; Canick J; Porter TF; Maternal thyroid hypofunction and pregnancy outcome. *Obstetrics and Gynecology*. 2008; 112:85–92.
  36. Ozdemir H; Akman I; Coskun S; Demirel U; Turan S; Bereket A et al. Maternal Thyroid Dysfunction and Neonatal Thyroid Problems. *International Journal of Endocrinology*. 2013; 2013:6pages.
  37. Gahlawat P; Singh A ; Nanda S; Kharb S; Thyroid Dysfunction in Early Pregnancy and Spontaneous Abortion . *Biomedical and Biotechnology Research Journal* . 2017;1:81-84.
  38. Brown S; Miscarriage and Its Management. *Seminars in Reproductive Medicine* . 2008; 26: 391–400.
  39. Wang L ; Shao YY; Ballock RT; Thyroid hormone-mediated growth and differentiation of growth plate chondrocytes involves IGF-1 modulation of ??-catenin signaling. *Journal of Bone and Mineral Research*. 2010; 25:1138–1146.
  40. Maruo T; Matsuo H; Mochizuki M; Thyroid hormone as a biological amplifier of differentiated trophoblast function in early pregnancy. *Acta endocrinologica*. 1991;125:58–66.
  41. Poppe K ; Glinoe D; Van Steirteghem A; Tournaye H; Devroey P; Schiettecatte J, et al. Thyroid Dysfunction and Autoimmunity in Infertile Women . *THYROID*. 2002;12: 997-1001.
  42. Abalovich M; Mitelberg L; Allami C; Gutierrez S; Alcaraz G; Otero P, et al. Subclinical hypothyroidism and thyroid autoimmunity in women with infertility. *The journal of Gynecological Endocrinology*. 2007; 23:279–283.
  43. Pushpagiri N; Gracelyn LJ; Nagalingam S ; Prevalence of subclinical and overt hypothyroidism in infertile women. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*. 2015; 4:1733–1738.
  44. Budenhofer BK; Ditsch N; Jeschke U; Gärtner R; Toth B; Thyroid dysfunction in normal and disturbed pregnancy. *Archives of Gynecology and Obstetrics*. 2013; 287:1–7.
  45. Unuane D; Tournaye H; Velkeniers B, Poppe K; Endocrine disorders & female infertility. *Best Practice and Research: Clinical Endocrinology and Metabolism*. 2011 ;25:861–873.