ORIGINAL ARTICLE

Effects of Pregnancy on Thyroid Hormone Levels

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ABSTRACT

Objective: Effects of pregnancy on thyroid hormone levels.
Study design: A cross sectional descriptive study was conducted at BMSI Jinnah Postgraduate Medical Centre Karachi.
Patients and methods: A total of 80 subjects ranging b/w 20-40 years of age were randomly selected for this study out of these 20 apparently healthy 20 healthy females and 60 healthy pregnant females were selected these pregnant were further classify on the basis of duration of pregnancy i.e. 1^{st}, 2^{nd} and 3^{rd} trimesters. Clinical detailed were collected then blood samples were drawn by adopting aseptic methods and then serum was analyzed for different tests
Results: Among 80 subjects the age, weight, height and BMI shows non significant ($P>0.05$) difference. The systolic B.P. and RR also shows non significant ($P>0.05$) difference, while diastolic B.P. was significantly decreased during 1^{st}, 2^{nd} trimesters ($P<0.001$), but pulse rate was significantly increased ($P<0.001$) during 1^{st}, 2^{nd} and 3^{rd} trimesters. During 1^{st} trimester no significant difference were found ($P>0.05$) FT_3 in 2^{nd} trimester was significantly reduced as compared with control ($P<0.001$) in these trimester, but no significant difference was observed in FT_4 ($P>0.05$), TSH was also reduced significantly ($P<0.01$). FT_3, FT_4 were significantly reduced, while TSH was significantly increased ($P>0.05$) in 3^{rd} trimester as compared to control. Compare of FT_3, FT_4, TSH and hCG b/w 1^{st}, with 2^{nd} trimester the differences of FT3 and hCG were highly significant ($P<0.001$), FT_4 were significantly decreased ($P<0.05$), while the differences of TSH was not significant ($P>0.05$). The differences of hCG and FT_4 were highly significantly reduced ($P<0.001$) while FT_3 was just significantly reduced ($P<0.05$) when compare b/w 1^{st}, and 2^{nd} trimesters. The differences of hCG and FT_4 were highly significant ($P<0.001$) while FT_3 was just significantly reduced ($P<0.05$) but the TSH of 3^{rd} trimester was significantly increased ($P<0.05$) as compare with 1^{st} trimester. FT_3 was significantly increased ($P<0.05$) and TSH was highly significantly increased ($P<0.001$), however the differences of hCG were non significant ($P>0.05$), where as the FT_4 was significantly reduced b/w 2^{nd} trimester with 3^{rd} trimester.
Conclusion: Concluded that the thyroid hormones are regulated by TSH in non-pregnant women while in pregnancy the thyroid activities are regulated by hCG in addition to TSH.
Key word: Thyroid, pregnancy.

INTRODUCTION

Thyroid is the largest endocrine gland in the body has been found to be essential for the maintenance of normal growth and development of the body (Dillmann, 1996). It has two lobes, each being pear shaped, with its apex being directed upwards as far as the oblique line on the lamina of the thyroid cartilage; while its base lies below at the level of the fourth or fifth tracheal ring. The isthmus which connects the two lobes extends across the midline in front of the second, third, and fourth tracheal rings. A pyramidal lobe is often present, and it projects upward from the isthmus, usually to the left of the midline. A fibrous or muscular band frequently connects the pyramidal lobe to the hyoid bone (Richard, 2000).

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Its functions are regulated primarily, by variations in the circulating level of pituitary thyroid stimulating hormone (TSH). TSH secretion is increased by the thyrotropic releasing hormone (TRH) and inhibited in a negative feedback fashion by circulating free T_3 and T_4. TSH secretion is also inhibited by stress, and in experimental animals it is increased by cold while decreased by warmth. (Figure1). T_3 is also formed in the peripheral tissues by deiodination of T_4. Both hormones are iodine containing amino acids (Ganong, 2000).

Both T_3 and T_4 are synthesized in the colloid by iodination, and condensation of tyrosine molecules bound in peptide linkage in thyroglobulin. Thyroglobulin is synthesized in the thyroid cells and secreted into the colloid by exocytosis of granules, that also contain thyroid peroxidase. The hormones remain bound to thyroglobulin until secreted. When they are secreted, colloid is ingested by the thyroid cells, the peptide bonds are hydrolyzed and free T_3

and T_4 are discharged into the capillaries. Several studies have indicated that thyroglobulin is frequently elevated during pregnancy: the increase in thyroglobulin can be observed as early as the firsttrimester, but by later stages of gestation and particularly near term, is significantly more pronounced. (Torigiani et al., 1969; Rasmussen et al., 1989; and Glinoer, 1999).

When the ovum becomes fertilized, a new sequence of events called gestation, or pregnancy, takes place and the fertilized ovum eventually develops into a full term foetus. This period generally lasts 280 days, which can also be counted as nine calendar months plus ten days, or 40 weeks, or then, simply, 10 lunar months (Bijlani, 1997). In pregnancy the placenta forms especially large quantities of oestrogen, progesterone, human chorionic gonadotropin and human chorionic somatotropin which are all essential for a normal pregnancy (Guyton, 2000).

Following implantation, a series of hormonal and metabolic events occur, that help to shield the foetus from unfavorable changes in the maternal environment. Human chorionic gonadotropin (hCG) concentrations rapidly increase ensuring a supply of progesterone necessary for the maintenance of pregnancy before placental production is assured (Kalkhoff et al., 1979; Burrow, 1993).

Due to increased secretion of many hormones during pregnancy, including thyroxine, adrenocortical hormones and the sex hormones, the basal metabolic rate of the pregnant woman increases during the fourth month of gestation, and continues to rise slowly until the eighth month, with a total of 15-20% increase compatible with thyroid hyper function in a nonpregnant women, renal blood flow increases and the glomerular filtration rate may increase by as much as 50% which tends to increase the rate of water and electrolyte excretion in the urine (Ferris, 1988; Burrow, 1993).

During normal pregnancy the changes in maternal thyroid functions can be viewed globally as a balance between hormone requirements and the availability of iodine. The increase in hormone demand is due to three independent factors, that concur to exert stimulatory effects on the thyroid machinery. The first sequence of events begins during the first half of gestation, and is maintained until term. It results from the increase in thyroxine-binding globulin (TBG) levels under the influence of elevated circulating oestrogen concentration. The rapid and marked rise in serum TBG (basal levels increased 2- to 3-fold) is accompanied by a trend towards a reduction in free hormone concentration (both for triiodothyronine (T_3) and thyroxine (T_4), resulting in stimulation of the pituitary-thyroid axis (Glinoer, 1999).

The second sequence of events also takes place transiently during the first trimester, and results from the direct stimulation of the maternal thyroid gland by elevated levels of human chorionic gonadotropin (hCG) (Glinoer et al; 1990).

The third series of events occur throughout gestation, but are mainly active during the second half they are related to modifications in the peripheral metabolism of maternal thyroid hormones (Burrow et al., 1994).

In pregnancy plasma concentrations of total T_3 and T_4 sharply in early pregnancy, and plateau early in the second trimester at concentrations 30-100% greater than pregnancy values (Skjoldebrand et al., 1982; and Guillaume et al., 1985).

Roti et al. (1991) have demonstrated variability in serum free thyroid hormones in pregnant women at term among 10 commercially available methods. Regardless of the method, however, pregnant women, on an average, had lower free hormone concentrations at term than non-pregnant women. Other studies have confirmed that serum free T_3 and T_4 are 25% lower in women at delivery than non-pregnant subjects (Ball et al 1989 Glinoer et al; 1990.

PURPOSE OF STUDY

1. To determine & compare the levels of thyroid hormones (FT3 & FT4) & thyroid stimulating hormone (TSH) during 1^{st} 2^{nd} & 3^{rd} trimesters of pregnant women with the control subjects.
2. To determine & compare the alteration & thyroid hormone levels in relation to change in human chorionic gonadotropic (hCG) hormones during 1^{st} 2^{nd} & 3^{rd} trimesters of the pregnant women.

PATIENTS AND METHODS

A total of 80 subjects ranging between 20-40 years of age were randomly selected for this study. Out of these, 20 apparently healthy non pregnant subjects were selected from the general population of Karachi as controls. Sixty apparently healthy pregnant females were selected from Antenatal Clinic of the Obstetrics and Gynaecology Department of JPMC, Karachi. These subjects were further classified on the basis of duration of pregnancy i.e. first, second and third trimesters. The nature of study was explained and consent was obtained from each one. Patients (Pregnant Women) having liver, renal cardiac diseases, malignancy and those with known h/o of thyroid dysfunctions were excluded from study. Brief biodata, clinical history and physical examination was performed and recorded on proforma designed for this study. Each subject was investigated for B.P, R.R, FT_3, FT_4, TSH and hCG.

RESULTS

Comparision of age, weight, height and BMI between control (non-pregnant) and pregnant females during trimesters. Non significant (P>0.05) differences were observed. The systolic BP and R.R were not significant b/w control and pregnant females (P>0.05), while diastolic B.P. was significantly decreased during 1st and 2nd trimester (P<0.001), but pulse rate was significantly increased during 1st, 2nd and 3rd trimesters of pregnancy (P<0.001). During 1st trimester no significant difference were found (P>0.05), FT_3 in 2nd trimester was significantly reduced as compare with control (P<0.001), but no significant difference was observed in FT_4 (P>0.05). TSH was also reduced significantly. FT_3 FT_4 were significantly reduced (P<0.05) and (P<0.001), while TSH was significantly increased (P<0.05) in 3rd trimester as compare to control.

When comparison of FT_3, FT_4, TSH and hCG b/w 1st and 2nd trimester, the difference of FT_3 and hCG were highly significant (P<0.001), FT_4 were significantly decreased, (P<0.05) while the TSH were non significant (P>0.05)

Comparision of FT_3, FT_4, TSH and hcg b/w 1st and 3rd trimester, the difference of FT4 and hcg were highly significantly reduced (P<0.001) while FT_3 was just significantly reduced (P<0.05) in 3rd trimester as compare to 1st trimester, while TSH of 3rd trimester was significantly increased (P<0.05) as compared with 1st trimester.

Comparison of FT_3, FT_4, TSH and hcg b/w 2nd and 3rd trimester, the FT_3 was significantly increased (P<0.05) and TSH was highly significantly increased (P<0.001). But the difference of hcg was non significant (P>0.05), where as the FT_4 was significantly reduced (P<0.05) b/w 2nd and 3rd trimester.

Table 1: Anthropometric parameters between control (non-pregnant females) and pregnant females at 1st 2nd and 3rd trimesters. (The values are expressed as mean±SEM)

Parameters	Control	1st trimester	2nd trimester	3rd trimester
Age (Years)	28.35± 1.19	27.90 ± 1.20	26.50 ± 1.13	27.75 ± 1.12
Weight (Kg)	49.85±1.23	51.55 ± 1.09	49.15 ± 1.21	50.65 ± 0.90
Height (cm)	159.75 ± 1.21	158.25 ± 1.65	157 ± 1.76	159.62 ± 1.17
Body mass index (BMI)	19.45 ± 0.37	20.45 ± 0.51	19.67 ± 0.53	19.47 ± 0.32

N.S = Non Significant (P > 0.05).

Table 2; Cardiorespiratory parameters between control (non-pregnant females) and pregnant females at 1st 2nd & 3rd trimesters. (The values are expressed as mean±SEM)

Parameters	Control	1st trimester	2nd trimester	3rd trimester
Systolic Blood Pressure (mmHg)	116.25± 1.57	116.50 ± 1.26	117.0 ± 1.32	117.75 ± 1.28
Diastolic blood Pressure (mmHg)	74.50 ± 1.45	64.25 ± 0.90**	67.00 ± 1.11**	72.25 ± 1.33**
Pulse rate (Per minute)	73.90 ± 0.34	80.20 ± 0.44**	82.10 ± 0.73**	83.30± 0.67**
Respiratory rate (Per minute)	16.00 ± 0.29	16.30 ± 0.22	16.04 ± 0.24	16.06 ± 0.24

*P < 0.05 shows significant difference. < 0.001 shows highly significant difference.

Table 3: FT_3 FT_4 and TSH between control (non-pregnant females) and pregnant females at 1st 2nd & 3rd trimesters. (The values are expressed as mean±SEM)

Parameters	Control	1st trimester	2nd trimester	3rd trimester
FT_3 (pg/ml)	2.96± 0.03	3.1 ± 0.12	2.39 ± 0.07**	2.64 ± 0.10*
FT_4(ng/dl)	1. 40 ± 0.04	1.49 ± 0.05	1.30 ± 0.06	1.11 ± 0.03**
TSH (mIU/1)	1.40 ± 0.03	1.2 ± 0.12	1.12 ± 0.09*	1.70 ± 0.10*

*P < 0.05 Shows significant difference. 0.001 shows highly significant difference.

Table 4: FT_3 FT_4, TSH and hCG between 1st trimester with 2nd trimester. (The values are expressed as mean±SEM)

Parameters	1st trimester	2nd trimester	P value
FT_3 (pg/ml)	3.10 ± 0.12	2.39 ± 0.07**	P <0.001
FT_4 (ng/dl)	1.49 ± 0.05	1.30 ± 0.06*	P <0.05
TSH (mIU/1)	1.20 ± 0.12	1.12 ± 0.09$^{N.S}$	P >0.05
hCG (IU/1)	121.90 ± 6.76	60.95 ± 9.59**	P <0.001

*P < 0.05 Shows significant difference. 0.001 shows highly significant difference.

P >0.05 shows non-significant.

Table 5: FT_3 FT_4, TSH and hCG between 1st trimester with 3rd trimester. (The values are expressed as mean ±SEM)

Parameters	1st trimester	3rd trimester	P value
FT_3 (pg/ml)	3.10 ± 0.12	2.64 ± 0.10*	P <0.05
FT_4 (ng/dl)	1.49 ± 0.05	1.11 ± 0.03**	P <0.001
TSH (mIU/1)	1.20 ± 0.12	1.70 ± 0.10*	P <0.05
hCG (IU/1)	121.90 ± 6.76	52.0 ± 4.66**	P <0.001

*P < 0.05 Shows significant difference. 0.001 shows highly significant difference.

Table 6: FT_3 FT_4, TSH and hCG between 2nd trimester with 3rd trimester. (The values are expressed as mean±SEM)

Parameters	2nd trimester	3rd trimester	P value
FT_3 (pg/ml)	2.39 ± 0.07	2.64 ± 0.10*	P <0.05
FT_4 (ng/dl)	1.30 ± 0.06	1.11 ± 0.03*	P <0.05
TSH (mIU/1)	1.12 ± 0.09	1.70 ± 0.10**	P <0.001
hCG (IU/1)	60.95 ± 9.59	52.0 ± 4.66*	P >0.05

*P < 0.05 Shows significant difference. 0.001 shows highly significant difference.
P > 0.05 shows non-significant

DISCUSSION

Following implantation a series of hormonal and metabolic events occur, human chorionic gonadotropin (hCG) concentration rapidly increased ensuring a supply of progesterone necessary for the maintenance of pregnancy (Kalkhoff etal; 1979, Burrow, 1993).

Pregnancy is a hypermetabolic state, it is the demand of fetus which may have ill effects on mothers health to carry out its vital functions like growth and development. The thyroid functions of mother are normally increased to fulfill the demand of fetus (mori etal; 1988,). In pregnancy the alterations in thyroid hormones is the direct consequence of increase TBG. Total T3 and T4 levels increased during first of pregnancy. Levels of T4 rise sharply b/w 6-12 weeks and progress more slowly thereafter, but stabilized in midgestation and serum T3 rises more progressive (Hotelling and Sherwood; 1971). In this study it was observed that thyroid activity during 1st trimester reflected by a decreased in circulating concentration of TSH the origin of increased maternal thyroid function is almost certainly stimulation of TSH receptors by hCG . This increase of thyroid activity in 1st trimesters has been reported earlier by a investigators (Guillaume etal; 1985 and Balbio etal; 1991). Maternal blood volume increases by 40% above non-pregnant values due to hormonal changes and venous detention that occurs when the vascular capacity of the uterus increases. Stroke volume, cardiac output and heart rate increase in pregnant women and systemic resistance is decreased (Mc Auntly etal; 1988). In this study no statistically significant differences were observed in respiratory rate and systolic blood pressure. Diastolic blood pressure has been decreased while an increased was noted in peripheral resistance. This increase in PR and decrease in DBP have been reported earlier by some other researchers as well (Alistair & Kevin, 1998, Campbill, 2000). In view of the data obtained and reported studies it is conceivable that the thyroid hormones are regulated by TSH in non-pregnant women while in pregnancy the thyroid activities appears to be regulated by hCG in addition to TSH.

CONCLUSION

In view of the reported studies and results, it is conceivable that thyroid functions are regulated by TSH in non-pregnant women, while in pregnancy the thyroid activities are regulated by hCG in addition to TSH.

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