

## ORIGINAL ARTICLE

## THYROID FUNCTIONS IN PREGNANT WOMEN WITH GESTATIONAL HYPERTENSION

Rabia Sattar, Abdul Majeed Cheema\*

Department of Physiology, Sharif Medical and Dental College,

\*Institute of Molecular Biology and Biotechnology, The University of Lahore, Pakistan

**Background:** In normal pregnancy, changes in thyroid function are well acknowledged; however, information about thyroid function in gestational hypertension (GH) is scanty. Hypertensive disorders complicating pregnancy are common and contribute greatly to prenatal and maternal morbidity and mortality in the developing countries. The aim of this study was to investigate thyroid functions in pregnant women with gestational hypertension. **Methods:** This was a case-control study evaluated maternal thyroid hormonal status in 78 (62 hypertensive and 16 normotensive) women with pregnancy of >20 weeks to term, referred to Jinnah Hospital, Lahore. Thyrotropin (TSH), Total thyroxine (tT4) and Total triiodothyronine (tT3) were assayed with ELISA. **Results:** Serum TSH and tT3 were significantly higher in hypertensive pregnant (HP) compared to normotensive pregnant women ( $p=0.002$ ,  $p=0.039$  respectively). Mean serum TSH was  $3.28\pm 0.29$   $\mu\text{IU/ml}$  in normotensive pregnant subjects and  $6.71\pm 1.06$   $\mu\text{IU/ml}$  in HP subjects, whereas mean serum tT3 in normotensive subjects was  $1.22\pm 0.03$   $\text{ng/ml}$  and  $1.31\pm 0.21$   $\text{ng/ml}$  in the HP subjects. There were no significant differences in serum tT4 levels of the subjects. **Conclusion:** Mean serum TSH and tT3 levels were significantly increased without concomitant changes in tT4 in HP compared to normal pregnant women. Raised TSH and tT3 levels might be associated with a risk for occurrence of gestational hypertension.

**Keywords:** Thyroid, Thyroxin, TSH, tT3, tT4, hypertension, Pre-eclampsia, Gestational hypertension

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### INTRODUCTION

Pregnancy is a physiological process. To supply adequate nutrition to the foetus, maternal physiological alterations of different organ systems occur in pregnancy. These alterations are circulatory, metabolic, and hormonal.<sup>1</sup> To meet these challenges of increased metabolic needs during pregnancy, the thyroid adapts through changes in thyroid hormone economy and in regulation of hypothalamic-pituitary-thyroid axis.<sup>2,3</sup> Changes in thyroid functions during normal pregnancy are well-documented, but information about thyroid functions in complicated pregnancy is scanty.<sup>4</sup> Physiological adaptations in pregnancy are found to develop disorders of various natures and significant of these is hypertension.

Pregnancy-associated hypertension has its onset from 20 weeks of gestation. Its characteristics may be hypertension alone, i.e., gestational non-proteinuric hypertension; with proteinuria and multiorgan dysfunction referred as preeclampsia; and additionally to preeclampsia there are seizures that termed as eclampsia.<sup>5,6</sup> Definition has been produced by WHO, American College of Obstetricians and Gynaecologists, and as recommended by the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy.<sup>7-9</sup>

Hypertension complicates up to 10% of all pregnancies and is associated with increased risk of adverse foetal, neonatal and maternal outcomes including preterm birth, intrauterine growth restriction,

perinatal death, acute renal or hepatic failure, ante partum haemorrhage, postpartum haemorrhage and maternal death.<sup>10,11</sup> Hypertensive disorders continue to occur globally, complicating 5–20% of pregnancies. Its incidence varies from 2 to 8% of pregnancies in developed countries reaching 10% or more in developing countries.<sup>9,12</sup> It is the third most common cause of maternal death worldwide.

During pregnancy, there is an increased thyroid hormone demand and increased iodine uptake and synthesis of thyroid hormones. Thyroid activity undergoes many changes during normal pregnancy.<sup>4</sup> Pregnancy is usually associated with mild hyperthyroxinemia, but in gestational hypertension (GH) women have a high incidence of hypothyroidism, i.e., raised TSH.<sup>13,14</sup> The reports of correlated thyroid hormones changes in pregnancy related hypertension certainly indicate that hypertension in pregnancy is found to affect thyroid hormones levels. Thyroid hormones pattern in pregnancy that is already essential for foetal tissues differentiations may be disorderly affected in hypertensive pregnancy. There are reports of thyroid hormones affected by pregnancy hypertension. Maternal thyroid dysfunction during pregnancy has been shown to be associated with a number of adverse outcomes. Elevated maternal TSH has been associated with an increased risk of pre-term birth, placental abruption, foetal death, and impaired neurological development in the child.<sup>15</sup>

Thyroid function in pregnancy has received greater attention compared to gestational hypertension.

Thyroid hormone changes specifically accompanying hypertension have yet to be worked out in Pakistani population.

The present study was carried out to assess thyroid functions in GH. It will enable to understand and address thyroid crises in GH for still better management.

## MATERIAL AND METHODS

The study was conducted in Institute of Molecular Biology and Biotechnology, The University of Lahore, in collaboration with the Jinnah Hospital, Lahore and The School of Biological Sciences, University of the Punjab, after taking permission from the respective head of departments. It include 62 singlet pregnant patients with no history of thyroid disease before and through pregnancy, aged 18–40 years, having diagnosed gestational hypertension, had systolic BP  $\geq 140$  mmHg and diastolic BP  $\geq 90$  mmHg in 20<sup>th</sup> week of pregnancy on two occasions at least 6 hour apart. Gestational age was based on the last menstrual period, confirmed by early pelvic examination, and verified by first trimester or early second-trimester ultrasound. Patients with known history of chronic hypertension, renal disorders, cardiovascular diseases, diabetes, any metabolic disorder that may threat mother or foetus and history of any medication that might affect the thyroid function were excluded from the study. Sixteen normotensive pregnant women were included as controls.

The blood sample was immediately transferred to plane serum vials and kept for 30 min to clot, and centrifuged at 3,000 rpm for 10 min. The clear serum was pipetted out in three separate 1.5 ml vials. The processed samples were stored at -20 °C until used for hormone assays. Laboratory work was performed at The School of Biological Sciences, University of the Punjab; and Pathology Laboratory of Jinnah Hospital Lahore. Serum TSH, tT3 and tT4 levels were estimated with ELISA.

Patients from outdoor and hospital admission fulfilling the inclusion criteria were included in this research after taking a written informed consent that was approved by the Human Research Ethics Committee of The University of Lahore. Detailed history and examination was done. Data was recorded on a questionnaire and analyzed using SPSS-17. The significance of differences between the groups was analyzed by independent *t*-test and one way ANOVA, and  $p < 0.05$  was considered statistically significant.

## RESULTS

In the present study the thyroid gland activity was compared among the 62 hypertensive pregnant and 16 comparable control pregnant. Thyroid gland function was assessed by assaying TSH, tT3 and tT4. In this study hypertensive pregnant had significantly raised

TSH and tT3 levels, as compared with pregnant normotensives.

The average concentration of TSH in normotensive pregnant subjects was  $3.28 \pm 0.29$   $\mu$ U/ml. The mean value of TSH in HP subjects was found  $6.71 \pm 1.06$   $\mu$ U/ml. In hypertensive subjects TSH level was 104.26% greater than the normotensive subjects and the difference is statistically highly significant ( $p = 0.002$ ). The mean tT3 in normotensive subjects was  $1.22 \pm 0.03$  ng/ml whereas it was  $1.31 \pm 0.21$  ng/ml in the HP subjects. In HP subjects tT3 level was 7.3% greater than the normotensive pregnant subjects and the difference is statistically significant ( $p = 0.039$ ). The average concentration of tT4 in non-hypertensive subjects was  $13.96 \pm 1.35$   $\mu$ g/dl. In HP subjects the value was  $14.22 \pm 0.7$   $\mu$ g/dl. There had not been a noticeable difference between the groups. (Table-1).

**Table-1: TSH, tT3 and tT4 in control and hypertensive pregnant subjects (Mean $\pm$ SEM)**

Parameters	Controls	Gestational hypertensives	<i>p</i>
TSH ( $\mu$ U/ml)	$3.28 \pm 0.29$	$6.71 \pm 1.06$	0.002*
tT3 (ng/ml)	$1.22 \pm 0.03$	$1.31 \pm 0.21$	0.039*
tT4 ( $\mu$ g/dl)	$13.96 \pm 1.35$	$14.22 \pm 1.35$	0.876

\*Significant

## DISCUSSION

Gestational hypertension is one of the leading causes of maternal death and a major contributor of maternal and perinatal morbidity. Even after a decade the conclusion of Duley<sup>10</sup> is still valid that the understanding of pregnancy associated hypertension has so far remain enigmatic and have unknown aetiology, unique to pregnancy. Thyroid adaptations are considered to be one of the probable causes.

Thyroid function and its associated hormones had shown alterations in the hypertensive pregnancy of the present study compared to the controls. In the HP group TSH was more than 100% and tT3 was highly significant statistically without any related change in tT4. Kumar<sup>1</sup> studied maternal thyroid hormone status in GH and found TSH levels significantly increased but without concomitant changes in free T3 and T4, in GH compared to normal pregnancy. In another study of Dhananjaya<sup>16</sup> evaluated increase in TSH levels could be used as a predictor of gestational hypertension however, T3 and T4 levels were within the normal limits.

Total T3 values were significantly increased in hypertensive pregnancy group when compared with the healthy control. There is possibility that TSH is potentiating peripheral production of tT3 through deiodination of total tT4. This assessment is not supported from the response of no significant effect on tT4 levels in the present study. Normally tT4 levels rise in the blood from about 6–12 weeks, and peak by mid-gestation; reverse changes are seen with TSH<sup>17</sup> such

increases in pregnancy have been attributed partly to the high levels of oestrogen and to the weak thyroid stimulating effects of human chorionic gonadotropin (hCG) that acts like TSH. With the thyroid hormone secretion being boosted, TSH levels are suppressed<sup>18</sup> later in pregnancy; decreasing hCG levels may lead to a reduced thyroid hormone release and in higher TSH concentrations, mainly in the second half of gestation.<sup>19</sup> All above reports proclaim that rise in thyroxine tends to lower TSH in pregnancy.

The elevation of TSH and tT3 in the present study are the adaptations in hypertensive state of pregnancy which require further investigation and understanding. Other studies have reported variedly on this parameter. Asmehan<sup>20</sup> studied the correlation between thyroid-related hormones and HP and found serum TSH and tT3 levels were significantly increased in HP women compared with healthy pregnant ones without concomitant change in T4 in HP. Increase in tT3 and TSH without any effect on tT4 is largely on the pattern as observed in the present study.

## CONCLUSION

To avoid complications and timely management of gestational hypertension, identification of altered thyroid hormones and thyroid screening during pregnancy might be very helpful. Further studies on large scale are needed for thyroid function in gestational hypertension.

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## Address for Correspondence:

**Dr Rabia Sattar**, Assistant Professor, Department of Physiology, Sharif Medical and Dental College, Lahore, Pakistan.  
**Cell:** +92-323-4450000  
**Email:** rabia.ahsan100@gmail.com

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