STUDY ON THE RELATIONSHIP BETWEEN THYROID HORMONE LEVELS AND PREECLAMPTIC PREGNANCIES – A CASE CONTROL STUDY

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ABSTRACT

OBJECTIVE: To determine the relationship between thyroid hormone levels and preeclamptic pregnancies.

STUDY DESIGN: A Case Control study.

PLACE AND DURATION: Department of Physiology, Basic Medical Sciences Institute, Karachi in collaboration with the Department of Gynaecology and Obstetrics, Bolan Medical Complex Hospital, Quetta from 1st February, 2015 to 31st January, 2016.

METHODOLOGY: Eighty (80) pregnant subjects (controls and cases) after twenty weeks of conception were included in the study. They were sub-divided into two equal groups. Each group comprised of forty (40) subjects. After detailed history and general physical examination, samples of blood were drawn for the assay of serum thyroid hormone levels.

RESULTS: A highly statistically significant association was found in free thyroxine FT4 (p=0.009). Moreover, no statistically significant association was found in free triiodothyronine (FT3) (p=0.495) and thyroid stimulating hormone (TSH) (p=0.187) between controls and cases. A highly statistically significant association was found in systolic blood pressure (p<0.001) and diastolic blood pressure (p<0.001) between controls and cases. The percentage of urinary protein excretion (UPE) (Nil) was 95% in controls. In addition, UPE (Trace) was 5%. No UPE (1+), UPE (2+) and UPE (3+) were found. On the contrary, UPE (1+) was 32.50% in cases. UPE (2+) was 52.50%. In addition, UPE (3+) was 15% in the cases.

CONCLUSION: Preeclamptic pregnancies are likely to be associated with lower limits of thyroid hormone levels in the last weeks of gestation.

KEYWORDS: Thyroid Hormones, Preeclampsia, Pregnancy, Proteinuria, Hypertension

INTRODUCTION

Pregnancy is linked with profound anatomical, physiological, biochemical and endocrinological alterations that affect multiple organs and systems. The aforementioned changes are momentous to help a woman adapt to the pregnancy state along with aiding fetal growth and survival.¹ It is a period of substantial alterations in blood pressure (BP) which decreases until 18 to 20 weeks after gestation. Afterwards, blood pressure increases until delivery.² Normal changes in thyroid function during pregnancy include a transient suppression of TSH and stimulation of triiodothyronine. Serum total thyroxine (TT4) and total triiodothyronine (TT3) steadily increase during pregnancy to approximately 1.5 times the non pregnant level by mid second trimester.³ The maternal thyroid hormone excess or deficiency can influence maternal and fetal outcomes at all stages of pregnancy.⁴ The levels of thyroid hormone transport proteins (thyroxine binding globulin, albumin and thyroxine binding prealbumin) also undergo remarkable changes during the course of a normal pregnancy. These changes are largely due to increased hepatic synthesis and decreased catabolism by both the liver and to a lesser extent by the renal tubular cells. Thyroxine binding globulin increases by about 2.5 times resulting in corresponding increase in the plasma levels of thyroxine by about 40%-100%. The levels of both T4 and T3 thus gradually increase from conception and reach a plateau by twenty weeks of gestation. They remain unchanged until term. However, the hormones FT4 and FT3 remain within reference limit or slightly raised.⁵ The levels of TSH generally decrease during pregnancy especially in the first trimester. It is largely due to a marked increase in the serum levels of human chorionic gonadotrophin (hCG), which is a placental hormone with alpha (α) chain similar to the alpha chain of TSH. They provide positive interference in TSH estimation.⁶ Preeclampsia is an inimitable multi-system disease to human pregnancy. It is characterized by hypertension and organ system derangement.⁷ It complicates about 2%-10% of pregnancies globally. Maternal Mortality is inexplicably high in Pakistan where 1 in 89 women dies of maternal causes with preeclampsia being one of the major causes.⁸ The etiology of the said disease still remains unknown despite several decades of extensive research.⁹ Gestational hypertension is pondered as one of the major complications of pregnancy and preeclampsia. It affects between 6% and 30% of the pregnant women. It results in a high maternal and perinatal morbidity as well as mortality risk. Its
etiology remains unknown too. Proteinuria remains a significant dysfunction of preeclampsia. The degree of proteinuria may fluctuate widely over 24-hour period due to the circadian variation of urinary albumin excretion. It is also influenced by several factors including contamination, urine specific gravity, pH (potentia hydrogenii), exercise and posture. 

There happens to be an ominous scantiness in availability of latest local data on preeclampsia. The communal influences between preeclampsia and thyroid function linger perplexing. Consequently, the current study was designed to determine thyroid hormone levels in normal and preeclamptic pregnant subjects; in addition to determine the relationship between thyroid hormone levels and preeclamptic pregnancies.

**METHODOLOGY**

The current case control study was carried out in the Department of Physiology, Basic Medical Sciences Institute, Karachi in collaboration with the Department of Gynaecology and Obstetrics, Bolan Medical Complex Hospital (BMCH), Quetta from 1st February, 2015 to 31st January, 2016. The calculated sample was computed to be eighty (80). The sample size was calculated using OpenEpi calculator (version 2.3) from the reference study Raoofi et al. The data was collected by carrying out questionnaire-administered interviews which aimed at acquiring demographic (age and gestational age), anthropometric (weight, height and BMI), laboratory (thyroid profile assay) and other pertinent information.

Inclusion criteria consisted of diagnosed cases of preeclampsia after twenty weeks of conception. Healthy pregnant subjects after twenty weeks of conception. Exclusion criteria consisted of any history or patients of thyroid diseases such as hyperthyroidism or hypothyroidism or thyroid surgery. In addition to consumption of thyroid related medications, chronic illnesses, coronary heart diseases, renal diseases, hepatic diseases and patients with complicated obstetric history.

Preeclampsia was further subdivided into mild preeclampsia and severe preeclampsia as per the specific criteria which have been proposed by the American Congress of Obstetricians and Gynecologists (ACOG). Mild preeclampsia was operationally defined to be a systolic BP of more than 140 mmHg and a diastolic BP of more than 90 mmHg in combination with proteinuria (1+) via two separate measurements obtained at least 6 hours apart. Moreover, severe preeclampsia was operationally defined to be a systolic BP of more than 160 mmHg and a diastolic BP of more than 110 mmHg in combination with proteinuria (≥2+) or substantial evidence of other end-organ dysfunction.

Samples of blood were assayed for hormonal variables including serum FT3, FT4 and TSH by ELISA (enzyme-linked immunosorbent assay) technique, which were analyzed on C (plate reader) Thyroid Cobas e 411 system. Urinary protein excretion was done through dipstick method using samples of urine. Blood pressure was measured by mercury sphygmomanometer. Subjects were asked to lie down in supine position for five (05) minutes. Later their blood pressures were recorded.

Data analysis was done using SPSS (Statistical Package for Social Sciences) version 21. Mean ± SD (Standard Deviation) was calculated for continuous variables like age etc. Frequency/percentage was calculated for categorical variables like UPE etc. T-test was used to analyze continuous variables. Chi square test was used to analyze categorical variables. The P-value of <0.05 was considered to be statistically significant.

**RESULTS**

Eighty (80) pregnant subjects after twenty weeks of conception were included in the study. Comparison of mean serum thyroid profile characteristics of the aforesaid subjects was done as shown in Table I. A highly statistically significant association was found in FT4 (p=0.009) between the controls and cases. Moreover, no statistically significant association was found in Free Triiodothyronine (FT3) (p=0.495) and Thyroid Stimulating Hormone (TSH) (p=0.187) between the aforesaid groups as shown in (Table-I). In addition, A highly statistically significant correlation (p=0.002) was found between FT3 and Urinary Protein Excretion (UPE) as shown in (Table-II). A highly statistically significant association was found in systolic blood pressure (p<0.001) as well as diastolic blood pressure (p<0.001) between controls and cases. The percentage of UPE (Nil) was (95%) in controls. In addition, UPE (Trace) was (5%). Moreover, no UPE (1+), UPE (2+) and UPE (3+) were found. On the contrary, UPE (1+) was (32.50%) in cases. UPE (2+) was (52.50%). In addition, UPE (3+) was (15%). Moreover, no UPE (Nil) and UPE (Trace) were included in the cases.

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<th>TABLE – I: COMPARISON OF MEAN SERUM THYROID PROFILE CHARACTERISTICS OF SUBJECTS (N=80)</th>
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<td><strong>Controls (n=40)</strong></td>
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<td>FT3 (ng/mL)</td>
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<th>TABLE – II: CORRELATION BETWEEN THYROID PROFILE AND UPE CHARACTERISTICS OF SUBJECTS (N=80)</th>
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DISCUSSION

We found mean FT3 levels to be slightly higher in controls when compared with preeclamptic subjects. Although, there was no statistically significant difference. Dhananjaya et al,\textsuperscript{11} witnessed that the thyroid hormones levels were within the normal ranges. They did not find any statistically difference in the aforesaid levels between normal women and preeclampsics. In disagreement with the results of our study, Rathore et al,\textsuperscript{12} found that in preeclamptic pregnancies; mean serum TT4 and FT4 were non-significantly higher while TT3 and FT3 were significantly lower than that of normal pregnancies. The prevailing disparity in the aforesaid results pertaining to mean FT3 levels could be due to reduced extra thyroidal conversion of T4 to T3. Furthermore, the titers of FT3 are significantly related to decreased plasma albumin concentration in preeclampsia. So, it has been suggested that reduced concentration of thyroid hormones in preeclampsia may be due to the loss of protein and protein-bound hormones in the urine.

We found higher mean FT4 levels in controls when compared with preeclamptic subjects, which were found to be 10.09 and 8.75 respectively. A highly statistically significant difference was found between the above-mentioned groups. In line with the results of our study, Raoofi et al,\textsuperscript{14} found that levels of FT4 in the preeclamptic pregnancies were less than normal pregnancies. On the contrary, results of Khadem,\textsuperscript{13, 15} didn’t support the aforesaid results. This could be due to the qualitative and not quantitative measurement. Since disparity in severity of underline causes and risk factors of preeclampsia lead to variation in results.

We found slightly higher mean TSH levels in controls when compared with preeclamptic subjects. Although, there was no statistically significant difference between the above-mentioned groups. In accordance with the results of our study, Ayub et al,\textsuperscript{13} found similar results. On the contrary, Dhananjaya et al,\textsuperscript{11} found that the mean difference in TSH levels was elevated in cases than controls. In addition, the said difference was statistically significant.

We correlated thyroid profile and UPE between the two study groups. We found that serum FT3 had a positive correlation with UPE. Moreover, serum FT4 had a negative correlation with UPE. In addition, serum TSH had a positive correlation with UPE. A highly statistically significant correlation was found between FT3 and UPE. The aforesaid discrepancy in results could be due to variations in geographical areas, races and diet. Moreover, the contributory association in the abovementioned alterations in thyroid profile could also be manifested by the course of thermogenesis. Thyroid hormones augment thermogenesis all the way through a boost in cellular activity to generate adenosine triphosphate. The exact mechanism of which has yet not been identified.

We found mean systolic and diastolic blood pressures were too high in preeclamptic subjects as compared to controls. A highly statistically significant difference was found in systolic as well as diastolic blood pressures between the above-mentioned study groups. Similar results were found by Siddiqui,\textsuperscript{17} as well as Pennington et al,\textsuperscript{18}. It might be due to rise in the levels of low density lipoproteins (LDL) in addition to the levels of elevated total lipid profile. Moreover, the available literature pertaining to UPE was scarce in literature review.

CONCLUSION

Preeclamptic pregnancies are likely to be associated with lower limits of thyroid hormone levels in the last weeks of gestation.

RECOMMENDATIONS

The bulk of complications thanks to preeclampsia are able to be avoided through the provision of well-timed and useful investigations. Thyroid profile assay in addition to UPE ought to be opted as obligatory routine investigations after twenty weeks of gestation. Large scale, multicentre and multi ethnic studies ought to be carried out which are able to probe at molecular/genetic levels to evaluate the idiopathic mechanisms involved in preeclampsia. For determination of UPE, urinary protein collection of twenty four hours urinary in addition to serum albumin ought to be employed as mandatory parameters. Optimizing delivery system (health care) to avert and cure pregnant women with preeclampsia happens to be an indispensable measure towards scheming the fatal menace.
CONTRIBUTION OF AUTHOR:
Muhammad Alam Mengal: Principal investigator/researcher.
Abdul Shakoor Memon: The conception, design and analysis of the data.
Mahwash Mengal: Collection and assembly of data in addition to critical revision of the manuscript for important intellectual content.
Syed Azhar Hussain Zaidi: Drafting of the manuscript and statistical expertise.

REFERENCES