

# COMPARISON OF LEVELS OF PROLACTIN AND TSH IN PREGNANCY WITH BAD OBSTETRICAL HISTORY AND NORMAL PREGNANT WOMAN

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**Abstract :** Pregnancy is a hypermetabolic state with major physiological alterations affecting all the systems of the body. A healthy woman undergoes many physiological adaptations just for the normal pregnancy. At the neuroendocrinal as well as at the placental level hormonal interaction is mainly responsible for the normal reproductive function. Thus recurrent and early pregnancy loss may be associated with a variety of imbalances and genetic anomalies. The elevated levels of prolactin interfere with the action of gonadotrophins at the ovarian level. Abnormal thyroid functions also cause ovulatory dysfunction and recurrent abortions. So, this study was planned to estimate and compare the levels of Prolactin and TSH in pregnancy with bad obstetrical history and normal pregnant women. A total of 100 females were included out of which 50 were normal pregnant females as controls and 50 pregnant females having history of recurrent abortions as study group attending the Obstetrics and Gynaecology OPD at PGIMS Rohtak. The serum levels of Prolactin and TSH were estimated by chemiluminescent immunoassay on Advia Centaur CP and mean and SD of all the parameters was compared in the groups. Also anti TPO antibody was measured in both the groups on Immulite 1000. Prolactin and TSH levels were found to be significantly elevated in the study group as compared to controls. Four patients also showed an elevated levels of anti TPO antibody. Our findings support the fact that increased TSH and prolactin levels were found in cases having history of abortions and still birth. We conclude that any type of change in the endocrine functions in may affect the pregnancy outcome.

**IndexTerms – Prolactin, TSH, Abortion, Anti TPO antibody.**

## I. INTRODUCTION

Pregnancy is a hypermetabolic state with major physiological alterations affecting all the systems variably including the pituitary thyroid axis, iodine metabolism, immune function and is characterized by production of various hormones by placenta. The extent of changes vary from system to system but no system is unaffected. It is not therefore surprising that thyroid dysfunction arises frequently in relation to pregnancy and the activity of thyroid gland may change during pregnancy.<sup>1</sup> Thus recurrent and early pregnancy loss is a multifactorial problem that may be associated with endocrine dysfunctions, autoimmune disorders, chronic infections, toxins and genetic anomalies. Bad obstetrical history (BOH) is defined as previous history of abortion, missed abortion, intrauterine growth retardation, preterm delivery, still birth, eclampsia malformed baby and pregnancy with any other medical disorders that like diabetes, hypertension, epilepsy that may or may not affect the outcome of pregnancy.<sup>2</sup>

Hyperprolactinemia, the presence of abnormally high levels of prolactin in the blood, is one of the most common endocrine disorder of the hypothalamic-pituitary axis. Many clinical and experimental studies have suggested a close relationship between the hypothalamic-pituitary-thyroid axis, hence thyroid dysfunction can affect the pregnancy outcome in various ways resulting in anovulatory cycles, luteal phase defect, high prolactin (PRL) levels and sex hormone imbalances. The elevated levels of prolactin interfere with the action of gonadotrophins at the ovarian level.<sup>3</sup> Also normal thyroid function is necessary for fertility, pregnancy and to sustain a healthy pregnancy, even in the earliest days after conception. Prevalence of hypothyroidism in the reproductive age group is 2–4% and has been shown to be the cause of infertility and habitual abortion. Hypothyroidism can be easily detected by assessing TSH levels in the blood. It has been found that the most common cause of hypothyroidism in pregnancy is Hashimoto's thyroiditis, whereas Grave's disease is the most common cause of hyperthyroidism in females under 40 years of age.<sup>4</sup> Many infertile women with hypothyroidism had associated hyperprolactinemia due to increased production of thyrotropin releasing hormone (TRH) which is implicated in ovulatory dysfunction. It has been recommended that in the presence of raised PRL, the treatment should be first given to correct the hypothyroidism before evaluating other causes of raised PRL as abnormal thyroid functions also cause ovulatory dysfunction and recurrent abortions.<sup>5</sup>

Anti-thyroid peroxidase (anti-TPO) antibodies are specific to thyroid peroxidase which is a 105kDa glycoprotein that catalyzes iodine oxidation and thyroglobulin tyrosyl iodination reactions in the thyroid gland. Anti-TPO antibodies are the most common anti-thyroid autoantibody, present in approximately 90% of Hashimoto's thyroiditis, 75% of Graves' disease and 10-20% of nodular goiter. Also, 10-15% of normal individuals can also have high level anti-TPO antibody titres.<sup>6</sup> High serum antibodies are found in active phase chronic autoimmune thyroiditis. Thus, an antibody titer can be used to assess disease activity in patients that have developed such antibodies. They are believed to cause thyroid cell damage by complement activation and antibody dependent cell cytotoxicity.<sup>7</sup>

Measurement of TSH and PRL is routinely done as while investigating the females with bad obstetrical history, this study was planned with the objective of estimation and comparison of the levels of prolactin and TSH in pregnancy with bad obstetrical history and normal pregnant females along with measurement of anti-TPO antibody in all the subjects.

### Methodology:

A total of hundred females were included out of which 50 were pregnant females having previous history of normal pregnancy as controls between the age of 18-40 years (Group –I), and 50 pregnant females having bad obstetrical history as study group between the age of 18-40 years (Group- II ), attending the Obstetrics and Gynaecology OPD at PGIMS Rohtak. We checked for the inclusion and exclusion criteria.

Inclusion Criteria: For controls, women between age of 18-40 years with uneventful pregnancy and for bad obstetrical history females having previous history of abortion, missed abortion, preterm delivery, intrauterine growth retardation, malformed baby, still birth, pregnancy induced hypertension and abruptio placentae were identified as study group. We also included females with intrauterine pregnancy with either an empty gestational sac or a gestational sac containing an embryo or fetus without fetal heart activity within the first 10- 12 weeks of gestation.

Exclusion Criteria: Chronic illness like TB and anatomical pathology and females on treatment for hypothyroidism or hyperthyroidism.

Blood was collected on 3<sup>rd</sup> day of cycle under all aseptic precautions and was analysed for routine investigations The serum levels of prolactin and TSH were estimated by chemiluminescent technique on Advia Centaur CP and mean and SD of all the parameters was compared in the groups. Also anti TPO antibody was measured in both the groups on Immulite 1000.

### Results:

In the present study the mean age in the two groups was comparable. Also the routine investigations like Hemoglobin, TLC, DLC, ESR, blood sugar ,blood urea and serum creatinine were within the reference range and comparable in both the groups. It was also observed that the subjects in control group were gravida1 to gravida 3 and in study group were gravida 2 to gravida 5. The mean level of Prolactin among control group was  $15.38 \pm 1.68$  ng/mL while among Group II was  $48.52 \pm 14.03$  ng/mL (Table-I). Statistical analysis showed that the difference in the mean values in the Group I and Group II was significant ( $p < 0.05$ ). The mean level of TSH among Group I was  $1.27 \pm 0.69$  mIU/L while among Group II was  $1.78 \pm 0.81$  mIU/L (Table-II). Statistical analysis showed that the difference in the mean values in the Group I and Group II was found to be significant ( $p < 0.05$ ). In the BOH group three patients were having very high prolactin levels and three other patients were having increased TSH levels along with history suggestive of hypothyroidism. No case of hyperthyroidism was found. Four patients also showed an elevated levels of anti TPO antibody ( $>35$  IU/mL) in the study group whereas the control group showed the normal levels for the same. (Table-III). However we could not establish any correlation between prolactin and TSH levels.

### Discussion:

Factors responsible for recurrent pregnancy loss are multiple and endocrine dysfunction is one of them. Prolactin is essential for female reproduction and commonly measured in women with recurrent abortion, as elevated prolactin levels are associated with ovulatory dysfunction. High prolactin levels also interfere with the normal production of other hormones, such as oestrogen and progesterone. This can change or stop the release of an egg from the ovary or can also lead to irregular or missed periods. However, some women have high prolactin levels without experiencing any symptoms.<sup>8</sup> Prolactin also called lactogenic hormone has role in puberty, breast development, pregnancy and lactation. Elevated levels of prolactin interfere with the action of gonadotrophins at the ovarian level ultimately leading to abortions and preterm delivery.<sup>9</sup> Samal et al studied association between hyperprolactinemia and reproductive function and concluded that

abnormal prolactin secretion leads to miscarriage and recurrent abortions.<sup>10</sup> Bussen et al studied the serum concentration of prolactin in patients with history of recurrent abortions and found that prolactin levels were significantly raised.<sup>11</sup> As per our study prolactin levels were found to be significantly elevated in the study group when it was compared with control, hence we also submit that there is potential role of prolactin in abortions.

Few studies have shown that pregnancy is associated with significant and reversible changes in maternal thyroid physiology that may cause confusion in the diagnosis of thyroid abnormalities. However TSH is the most sensitive indicator of hypothyroidism, which is associated with the broad range of reproductive disorders ranging from infertility to recurrent abortions, which can be explained by presence of thyroid hormone receptors in human oocytes. TSH also affects fertility by altering the metabolism of oestrogen and decreasing SHBG production. Both pathways may result in abnormal feedback at pituitary. Also patients with autoimmune diseases are having T cells in blood and thyroid gland which may cause pregnancy loss.<sup>12</sup>

Abalovich et al reported that outcome of pregnancy was abortion in 60% of hypothyroid patients, premature delivery in 20% and term delivery in another 20% which clearly indicated that hypothyroidism is associated with bad obstetrical history. The incidence of pregnancy loss was very low in treated hypothyroid women having normal thyroid indices but markedly increased in women with elevated TSH levels.<sup>13</sup> Casey et al reported that the pregnancies in women with subclinical hypothyroidism were 3 times more likely to be complicated by placental abruption as compared with healthy pregnant women.<sup>14</sup>

Kennedy et al reported that thyrotoxicosis may occur about 1 in 2000 pregnancies and is commonly due to Graves' disease where thyroid is stimulated by autoantibodies directed at the TSH receptor. However as the symptoms of thyrotoxicosis and normal pregnancy are overlapped the thyrotoxicosis may be missed unless it is borne in mind.<sup>15</sup>

Guan et al in found that in the pregnancy group the prevalence of hyperthyroidism was lower than that of hypothyroidism. It was concluded that hypothyroidism accounts for most of the thyroid diseases during pregnancy.<sup>16</sup>

In our study no case of hyperthyroidism was found that may be due to low prevalence of hyperthyroidism in pregnancy and a relatively small study group. Our study revealed that thyroid function disorders play a role in causing BOH, and as the prevalence of hypothyroidism in women of reproductive age group is quite high, therefore TSH levels should be measured as a routine screening tests in all the pregnancies irrespective of outcome.

Anti TPO antibodies are identified more frequently in females with recurrent pregnancy loss. The presence of these antibodies is non specific being present in upto 20% of biochemically euthyroid pregnant women.<sup>17</sup> Studies have shown an evidence of alteration in cytokine expression by peripheral T lymphocytes in women positive for thyroid antibodies. The presence of thyroid autoantibodies might be a marker of underlying subtle alteration in thyroid reserve which could be associated with reduced adaptation to the physiological changes of pregnancy. It was also postulated that during pregnancy some modification of immunoregulatory pathways occurs which may lead to autoimmune thyroiditis to euthyroid pregnant females.<sup>18</sup>

In our study only 8% of patients had elevated anti TPO antibodies and they were clinically hypothyroid and also mean TSH level was higher than pregnant women negative for anti-TPO antibody. Thus the thyroid antibodies detected in early pregnancy seem to predict pregnancy complications.

### Conclusion:

Our findings support the fact that increased TSH levels were found in cases having history of abortions and still birth. A change in the endocrine factors due to subtle disturbances in hypothalamic- pituitary- thyroid axis may cause increased prolactin or disturbed thyroid function that may lead to change in hormonal milieu of body and may affect the pregnancy outcome. Anti- TPO antibodies if detected in females with recurrent abortions can be helpful for further treatment plan and follow up.

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Table I : Comparison of Prolactin levels in normal controls and Pregnancy with BOH.

Group	No. of cases	Prolactin ng/mL	Mean±SD	p value
Controls-I	50	11.36-17.5	15.38±1.68	<0.05
Pregnancy with BOH-II	50	13.5-154.2	48.52±14.03	

Table II : Comparison of TSH levels in normal controls and Pregnancy with BOH

Group	No. of cases	TSH (mIU/mL)	Mean±SD	p value
Controls-I	50	0.35-4.10	1.27±0.69	<0.05
Pregnancy with BOH-II	50	0.48-22.10	1.78±0.81	

Table III: Levels of anti-TPO antibody in study group.

Group-II	Anti-TPO antibody (IU/mL)	No. of individuals	%
Pregnancy with BOH	<35	46	92
Pregnancy with BOH	>35	4	8

