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Original Research Article.

A Comparative Study of Serum Prolactin in Pregnancy Induced Hypertension and Normal Pregnant Females in Second Trimester of Pregnancy

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ABSTRACT

Background: Hypertension disorder of pregnancy affects up to 8% of all gestations. Pregnancy induced Hypertension (PIH) is defined as hypertension that develops for first time in pregnancy after 20 weeks of gestation. Pathophysiological placental abnormalities are seen consistently by increasing secretion of hormone Prolactin. Prolactin (PRL) is a polypeptide hormone primarily secreted by the anterior pituitary gland, whose levels increases physiologically during pregnancy. The imbalance between the isoforms of prolactin causes PIH.

Method: The present study was conducted on 50 healthy pregnant controls and 50 clinically established pregnancy induced hypertensive subjects. Serum Prolactin was measured by Enzyme Linked Fluorescent Assay Method. For analyzing the Data, Statistical software Epi info was used. The results were revealed in mean ± standard deviation. Comparisons of cases and control groups were done by applying unpaired t-test.

Results: Serum Prolactin was significantly higher in pregnancy induced hypertensive subjects as compared with healthy pregnant control subjects.

Conclusion: Abnormally high serum Prolactin in PIH Subjects is a dreaded complication of pregnancy. Serum Prolactin should be included in routine investigation.

Keywords: Pregnancy Induced Hypertension, Prolactin, Placental Abnormalities.

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INTRODUCTION

Pregnancy is a physiological process but needs strict monitoring throughout gestational period to circumvent perilous complications like pregnancy induced hypertension (PIH), gestational diabetes etc. Pregnancy induced hypertension is defined as blood pressure ≥ 140/90 on two occasions, at least 6 hours apart and proteinuria of ≥ 300mg/24 hours or ≥ 1+ dipstick after 20 weeks of gestation in previous normotensive women.[1]

Hypertensive disorders during pregnancy are classified into four categories as recommended by The National High Blood Pressure Education Program Working Group in pregnancy: [2]

I. Chronic Hypertension
II. Preeclampsia-eclampsia
III. Preeclampsia superimposed on chronic hypertension
IV. Gestational hypertension (transient hypertension of pregnancy or chronic hypertension identified in the later half of pregnancy).

Prolactin (PRL) is a polypeptide hormone primarily secreted by the anterior pituitary gland. A substantial increment in serum PRL levels physiologically occurs during pregnancy. Pregnancy induced hypertension (PIH) is the most common medical complication of pregnancy, whose incidence has continued to increase worldwide. It is associated with significant maternal morbidity and mortality, accounting for about 50,000 deaths worldwide annually[3,4] and risk is very high in Indian women.[5] WHO estimates that one woman die every minute due to the complications of hypertensive disorders of pregnancy (HDP).[6] Pregnancy induced hypertension is a disease influencing 5-10% of all pregnancies and PIH is identified in 3.9% of all pregnancies.[7] Although the best known biological functions of PRL are linked to lactation and reproduction, this hormone has been also associated with other physiological processes, including angiogenesis.[8] Because abnormal angiogenesis is an essential component of the

pathogenesis of preeclampsia and considering that PRL has pro- and antiangiogenic effect. PRL might be the potent biomarker for pregnancy as predictors for PIH.

Prolactin is synthesized in brain, placenta, amnion, deciduas, uterus, and epithelium of lactating mammary gland.[9] In addition to milk production Prolactin has more than 300 biological activities.[10] Hence it is also called "omnipotin" or "versatilin".[11] Prolactin is coded by a single gene on chromosome 6.[12] Prolactin contains four long α-helices arranged in anti- parallel fashion.[13] Prolactin undergoes splicing and forms variants.[14] Most common variants are 14, 16 and 22-kDa. The gene coding for prolactin receptor is located on chromosome 5.[15]

Prolactin performs various functions like mammogenesis, lactogenesis, galactopoesis, maintenance of corpus luteal function, psychological effects etc. it exhibits a circadian rhythm with highest levels during sleep and highest during waking period. Its secretion is regulated by suckling, stress, increased estrogen. Of the various isoforms of prolactin, 23-kDa is the most predominant one and comprises about 90% of prolactin. This isoform promotes angiogenesis. The other isoform 16 and 14-kDa are antiangiogenic. The imbalance between the two causes PIH.[16]

The objective of present study is to compare levels of serum prolactin during 20-26 weeks of pregnancy between normal and PIH pregnant women and to investigate the clinical utility of maternal Serum Prolactin level as predictors for PIH in early second trimester.

MATERIAL AND METHODS

This study was designed to evaluate all pregnant women between the gestational age of 20-26 weeks who were normotensive and non-proteinuric in first trimester for rise in prolactin level, and who were visited Ante-natal clinic of Obstetrics and Gynaecology department of S.N. Medical College, Jodhpur from January 2015 to December 2015.

Inclusion Criteria

Those with known gestational age of second trimester between 20-26 weeks are selected in this study, irrespective of parity.

Exclusion Criteria

Women with hypertension diagnosed before 20 weeks of gestation (before pregnancy), Women with multiple pregnancy, Pregnant women with diabetes mellitus, Ultrasonography proved congenital malformations; Women with Liver and Renal failure were excluded.

The study was approved by the Institutional Ethics Committee of S.N. Medical College, Jodhpur.

After taking informed consent, all eligible (fit under inclusion and exclusion criteria) pregnant women were enrolled. We closed our enrolment after taking 50 eligible candidates in each group. We got pregnancy induced hypertensive eligible candidate along with 50 eligible healthy pregnant by the end of December 2015 and April 2015 respectively. So all enrolled eligible pregnant women were divided into two groups on the basis of clinical examinations and biochemical investigations:

Group 1: Healthy pregnant females (50 in number)

Group 2: Pregnancy Induced Hypertension females (50 in number)

Collection and Analysis of Blood Samples

After an overnight fast 10-12 hours, about 10ml venous sample was drawn under aseptic conditions from median cubital vein and transferred in a plain vial and the sample was allowed to clot. The serum was separated from the clotted sample by centrifugation at 3000rpm for 10 minutes and the serum Prolactin was estimated from the separated serum.

BIOCHEMICAL ANALYSIS

Method: Enzyme Linked Fluorescent Assay Method.[17]

Principle: The assay principle combines an enzyme immunoassay sandwich method with a final fluorescent detection (ELFA).

The Solid Phase Receptacle (SPR), serves as the solid phase as well as the pipetting device for the assay. Reagents for the assay are ready-to-use and pre-dispensed in the sealed reagent strips. All of the assay steps are performed automatically by the instrument. The sample is taken and transferred into the well containing alkaline-phosphatase-labelled anti-prolactin conjugate. The antigen binds to the antibodies coated on the SPR and to the conjugate forming a "sandwich".

During the final detection step, the substrate (4-Methyl-umbelliferyl phosphate) is cycled in and out of the SPR. The conjugate enzyme catalyzes the hydrolysis of this substrate into a fluorescent product (4–Methyl–umbelliferone), the fluorescence of which is measured at 450 nm. The intensity of the fluorescence is proportional to the concentration of prolactin present in the sample.

At the end of the assay, results were automatically calculated by the instrument in relation to calibration curve stored in memory, and then printed out.

Calculation: Once the assay was completed, results were analyzed automatically by the computer. Results were calculated automatically by the instrument in relation to the calibration curve stored in memory (4-parameter logistic model) and the concentrations were expressed in ng/ml.

Range: The measurement range of the VIDAS Prolactin kit is: 0.5-200ng/ml. Table 1 represents the reference values of Prolactin among normal menstruating women, menopausal women and men.

Data Analysis

Data were analyzed using Epi-info software. Mean and standard deviation was calculated and mean Prolactin values in both groups were compared using t test.

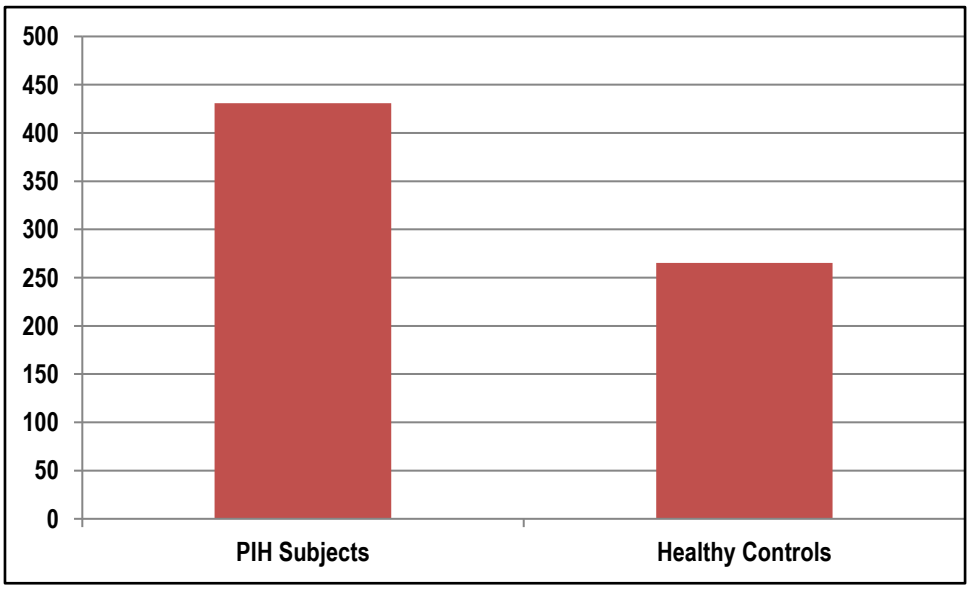
Table 1: Reference Value

GROUP	≤ 5 ng/ml	5-35 ng/ml	≥ 35 ng/ml
Normal menstruating women	2.6%	93.4%	4.0%
Menopausal women	3.3%	93.5%	3.2%
Men	2.5%	93.2%	4.3%

Table 2: Statistical analysis of Serum Prolactin among the Group studied

S.N.	Statistical analysis	Group compared Non PIH v/s PIH
1.	t- value	12.63
2.	p – value	<0.01
3.	Statistical significance	Highly Significant

Fig 1: Mean Serum Prolactin (ng/ ml) of subjects studied



RESULTS

The mean age of study subjects among normal healthy pregnant women was 23.05±2.64 and the mean age of PIH patients was 23.08±2.54. On comparison both the groups were comparable.

Figure 1 illustrates the graph of Mean ± SD levels of Prolactin of PIH subjects (430.79±14.53) as compared with healthy pregnant controls (265.17 ± 19.62). In the same way, Table 2 illustrates statistical analysis of Prolactin with t-value (12.63) and were significantly high (p <0.01) in PIH subjects when compared with healthy pregnant controls.

DISCUSSION

The present study was being conducted on 50 healthy pregnant controls and 50 clinically established pregnancy induced hypertensive subjects attending Ante Natal Clinic. The aim of this study was to find out the correlation of serum prolactin levels during 20-26 weeks of pregnancy as predictors for PIH in second trimester of pregnancy. In present study statistically significant difference was found between the mean values of Serum Prolactin among PIH and Normal Healthy pregnant females. Similar result was obtained by Schock H et al.[18]

In similar study, Nandini et al reported that serum prolactin was significantly higher in pregnancy induced hypertensive subjects (433.43 ± 13 ng/ml) as compared to healthy pregnant control subjects (266.395 ± 153 ng/ml). They found that prolactin is produced by placenta and decidua, the isoform of prolactin 23 kDA is angiogenic and 16 kDA is anti-angiogenic. The imbalance between the two leads to increased anti-angiogenic portion. This leads to development of PIH. Alternate mechanism is renal damage which leads to reduced clearance of various substances like urate and prolactin. They elucidated that 16kDA was significantly higher in PIH subjects rather than healthy control subjects.[19]

A similar rise in serum Prolactin level was reported by Masumoto A et al (2010) ($p<0.05$)[20] and Abdulah S A et al (2010) ($P<0.001$).[21] Masumoto A et al suggested that anti-angiogenic PRL fragments in the placenta may be present only in the PIH cases.

To conclude, the present study gives us an idea that abnormally high serum prolactin in PIH subjects is a dreaded complication of pregnancy. There has been a constant endeavour to identify the risk involved in pregnancy and if possible, its prediction. If prediction is possible, prevention will follow naturally.

The present study indicates an increased risk of PIH in pregnant women with elevated serum prolactin in second trimester (20-26 weeks). As yet there is no practical, acceptable and reliable screening test for PIH. Serum Prolactin seems to be good and early predictors for the development of PIH and should be included in routine investigation in second trimester of pregnancy.

The study needs to be more comprehensive with large samples collection in larger population for further evaluation and deep research in this field.

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