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Reproductive Hormones and Pregnancy Induced Hypertension Cases in Nigerian Women

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Abstract: *Investigations were carried out on the association of some reproductive hormones (Estradiol, progesterone, follicle stimulating hormones, Prolactin and Luteinizing hormone), and pregnancy induced hypertension in Nigerian women. The levels of these hormones were determined in 120 patients. 40 of these subjects were normotensive pregnant women, another 40 of them were hypertensive pregnant women tested be to having pregnancy induced hypertension. Another 20 of the subjects were normotensive non pregnant women while the last groups of 20 people were hypertensive non pregnant women who were not users of contraceptives. The mean values of these hormones were determined in the pregnant subjects of 2nd trimester, 3rd trimester and 3- 6 days after delivery. Progesterone and Estradiol levels as revealed in the result obtained showed a significant increase (P < 0.05) in both normotensive pregnant and hypertensive pregnant women as the pregnancy proceeded from 2nd to 3rd trimester. However the level of significance was higher in normotensive pregnant women relative to the hypertensive pregnant women.Prolactin also follow in like manner with significant level of increase as the pregnancy progresses to 3rd trimester. However Follicle stimulating and Luteinizing hormones decrease insignificantly (P< 0.01) as the pregnancy proceeded to the 3rd trimester. Values obtained from the results after 3- 6 days of delivery showed progesterone and Estradiol levels decreasing insignificantly, Prolactin increases significantly and FSH and LH increases insignificantly. Our findings indicate that the reproductive hormones are associated with pregnancy induced hypertension, and these might be related with the pathogenesis of pregnancy induced hypertension in Nigerian women.*

Keywords: *Reproductive hormones,progesterone, Estradiol, Prolactin,Luteinizinghormones , follicle stimulating hormone, pregnancy induced hypertension , pathogenesis.*

I. Introduction

Pregnancy refers to the period from conception to the expulsion of the foetus. This period constitutes in a woman's life a special condition that affects various physiologic and endocrinology systems. Throughout gestation, the physiological changes occur in pregnant women as a result of adaptation of the mother to accommodate and support the foetus before and after parturition. Itmust be noted that pregnancy is a natural state that, sets upgreat changes throughout the whole body and most of these changes subside quickly after delivery (Guice-Booth, 2005).

Pregnancy can be complicated by at least two distinct types of hypertension. The first one is chronic hypertension, which is usually characterized by blood pressure greater than 140/90mmHg. The second type is Pregnancy Induced Hypertension (PIH), previously called pre-eclampsia and toxemia. PIH is a complication that results to the development of hypertension after about twenty (20) weeks of gestation in a woman who had previously been normotensive (with no pre-existing renal disease). A patient with PIH will begin her pregnancy with a normal blood pressure but it will rise sometime in the third trimester in typical cases, but earlier in severe cases. A rise in the blood pressure by 30/50 (e.g. from 90/50mmHg to 120/70rnmHg) over the course of the pregnancy is a diagnostic criterion, even though the final pressure may seem normal (Sibai et al, 2007 ,Asaolu et al, 2010).

In United States, the incidence of PIH reveals that, approximately 10% of pregnancies are characterizes by pre-clampsia. Black women have higher rates of pre-eclampsia complicating their pregnancies compared with other racial groups (Chobanian et al, 2003).

PIH is a much more dangerous condition than chronic hypertension, because there is much more alteration in the maternal body than just high blood pressure. There is a whole chemical shift of maladaptative reactions that can even lead to seizures and death in the pregnant patient (Chesley, 1987). PIH is one of the major causes of maternal death throughout the world. There is the belief that Pill contributes extensively to still births, neonatal morbidity and death (Mannisti et al, 2013). It has been suggested that one or more of the protective mechanisms are either deficient or fails to functions properly or even gets out of control (Cunmigham et al, 2005).

PIH is characterised by swelling of the body especially the ankles and legs, acondition known as oedema, hyper reflexia, or exaggerated deep tendon reflexes (the knee-jerk, for instance), hyperproteinuria or spilling protein in the urine). Many complications go with PIH relating to the offspring (Gutman and

Gutman1970, Hollegaard et al, 2013). The expectant mother's kidneys are especiallyvulnerable, affecting filtration, worsening the swelling and resulting in the loss of protein in the urine. The proteinuria in PIH may also due to pathological damage to the glomerular cells and almost always occurs after hypertension, 60% of the protein is albumin. The blood vessels develop abnormalities of constriction, affecting blood pressure and the reflexes become hyperactive (Guice Booth, 2005). As at the moment, the exact cause of PIH is unknown, and currently there is no sure way to prevent the hypertension (Hajjar et al, 2003; Gross et al 2007).

Hence this area is still of great interest and in need of utmost attention of the populace. However, possible causes have been suggested to include; auto immune disorders, blood vessel problems, diets, genes and some of the risk factors for PIH include first pregnancy, multiple pregnancy (twins or more), obesity, women older than 35years, past history of diabetes, high blood pressure or kidney disease, women whose sisters and mothers had PIH (Onusco, 2003).

Hormones are chemical substance secreted by one tissue and travels by way of body fluids to affect another tissue in the body (Oyeyemi and Akinlua, 2013). Hormones generally are known to increase in number raging around inside the body during pregnancy. It is known that placenta participates in the production of hormones, and that the normal conduct of pregnancy is intimately dependent on a rather complex change in the amount of these substances secreted from pituitary, ovaries, adrenal and placenta into the blood.

Therefore, the change in the pattern of these hormones may be a probable cause of PIH. A number of diseases and cardiovascular conditions, in addition to various changes that occur during pregnancy have been linked with hormones. It has been suggested that changes in the level of some hormones play key roles in maternal susceptibility to pre-eclampsia (Zhorzholadze et al, 2006). Reproductive hormones , includingprogesterone , luteinizing hormones, Estradiol, follicle stimulating hormone and prolactin, can possibly be implicated in PIH.

Follicle stimulating hormone (FSH) is a hormone found in humans and other animals. It is synthesized and secreted by gonadotrophs of the anterior pituitary gland. FSH regulates the development, growth, pubertal maturation and reproductive processes of the body. FSH and Luteinizing hormone (LH) act synergistically in reproduction.Follicle stimulating hormone has been discovered to be at a low level in pre-eclampsiapatient (Radu et al ,2010).

Prolactin is a peptide hormone discovered by Dr. Heny Friesen, primarily associated with location. In breast feeding, the act of an infant suckling the nipple stimulates that production of oxytoxin, which stimulates the “milk let- down” reflex, which fills the breast with milk via a process called lactogenesis, in preparation for the next feed.to act on the dopamine-2 receptors of lactotrophs, causing inhibition of prolactin secretion, thyroxin-releasing factor (thyroxin-releasing hormone) has a stimulatory effect on prolactin release Prolactin has many effects including regulating lactation and stimulating proliferation of oligodendrocyte precursor cells. Prolactin provides the body with sexual gratification after sexual acts. The hormone counteracts the effect of dopamine, which is responsible for sexual arousal, this is thought to cause the sexual refractory period (Zhang 2007). Estradiol (E2 or 17-beta estradiol, also estradiol) is a sex hormone. Estradiol is the predominant sex hormone present in females. It is also present in males, being produced as an active metabolic product of testosterone. It represents the major estrogen in humans. Estradiol is the most potent estrogen of a group of endogenous estrogen steroids which includes estorne and estriol. In women estradiol is responsible for growth of the breast and reproductive epithelia, maturation of long bones and development of the secondary sexual characteristics. Estradiol is produced mainly by the ovaries with secondary production by the adrenal glands and conversion of steroid precursors into estrogens in fat tissue (Worthman et al, 1990). Estradiol has only a critical impact on reproductive and sexual functioning, but also affects other organs including the bones.

The effect of estradiol together with estrone and estriol in pregnancy is less clear. They may promote uterine blood flow, myometrial growth, stimulate breast growth and at term promote cervical softening and expression of myometrial oxytocin receptor.

During pregnancy, estrogen levels, including estradiol, rise steadily toward term. The source of these estrogen is the placenta, which aromatizes prohormones produced in the fetal adrenal gland.

Luteinizing hormone plays a reproductive activity in both male and females. That is, it is essential for reproduction. In females, luteinizing hormone stimulates secretion of sex steroids from the gonads. It support the cells in the ovaries that provide androgens and hormonal precursor of estradiol production. At the time of menstruation, FSH initiates follicular growth, specifically affecting granulose cells (Bowen 2004). With the rise in estrogens, luteinizing hormone receptors are also expressed on the maturing follicle, which causes it to produce more estradiol. Eventually when the follicle has fully mature, a spike in estrogen production by the follicle stimulate a positive feedback loop in the hypothalamus that stimulates the release of luteinizing hormone from the anterior pituitary.

This increase in luteinizing hormone production only last for 24-48 hours. This “Luteinizing hormone surge” or pre-ovulatory LH surge triggers ovulation, thereby not only releasing the egg from the follicle, but also initiating the conversion of the residual follicle into a corpus luteum, that in two produces progesterone to

prepare the endometrium for a possible implantation and also responsible for the maintenance of pregnancy luteinizing hormone is necessary to maintain luteal function for the first two weeks of the menstrual cycle. If the pregnancy occurs, luteinizing hormone level will decrease and luteal function will be maintained by the action of HCG (a hormone very similar to luteinizing hormone but secreted from the new placenta)(Bowen 2004).

Progesterone has a number of physiological effects that are amplified in the presence of estrogen. Estrogen through estrogen receptors regulates the expression of Progesterone receptors . Progesterone is sometimes called the "hormone of pregnancy" (Bowen 2000) and it has many roles relating to the development of the fetus. The increased occurrence of Pregnancy induced Hypertension among women especially in Nigeria has prompted the current research work

II. Materials And Method

Grouping

The present study was carried out at Ekiti State University teaching Hospital (EKSUTH) Ado Ekiti, Ekiti State Nigeria.A total of 120 women were examined in this study. Their blood samples were collected with the help of medical personnel in the University Teaching Hospital, Ado Ekiti, Ekiti State, Nigeria. These subjects were divided into four groups. Subjects in group 1 comprise of forty (40) hypertensive pregnant women (test) with symptoms of PIH brought into the hospital for management and treatment. Twenty (20) each of the forty subjects were in their 2^{nd} and 3^{rd} trimester of pregnancy respectively. The subjects were monitored up to three to six days after delivery. Group 2 comprise of randomly selected 40 normotensive pregnant women in their 2^{nd} and 3^{rd} trimesters of pregnancy respectively. This served as control for group 1. Group 3 was made up of 20 hypertensive non-pregnant and non-user of contraceptive therapy women randomly selected. Lastly, group 4 comprise of 20 normotensive non-pregnant women who are non-users of contraceptive therapy. They were randomly selected and age-matched with group 3.

Blood sampling

Blood samples were drawn from all the subjects following a fast of 6-12 hours. Plasma was separated by centrifuging the blood at 3000rpm for 10minutes at 4^0c. The plasma was used for the estimation of progesterone, estrogen, follicle stimulating hormone, prolactin and luteinizing hormone.

Biochemical assay

All the reproductive hormones assayed for were estimated by the method of enzyme linked immunosorbent assay (ELISA) (Engrall*et al*, 1971).

Statistical Analysis

Data got from the presents study were presented as mean value ± SD. The statistical significance was evaluated by students "t" test and Anova.

III. Results And Discussion

Table 1:the levels of reproductive hormones in normotensive and hypertensive pregnancies (2^{nd} trimester)

GROUP	Progesterone (ng/ml)	Estradiol (pg/ml)	Prolactin (pg/ml)	FSH (ng/ml)	LH (ng/ml)	SBP (mmHg)	DBP (mmHg)
NNPW A	14.2 ± 4.2	98.0 ±1.67	78.9 ±1.67	13.01 ±7.10	1.35 ± 0.05	98.7 ± 10.42	67.15 ±10.18
HNPW B	12.5 ± 0.2	89.9 ± 2.02	80.1 ± 1.12	13.19 ± 2.40	1.31 ± 0.10	161 ± 13.45	107 ± 12.45
NPW C	49.1 ± 1.40	120 ± 0.2	90.4 ± 6.10	5.01 ± 2.70	1.10 ± 3.13	105.5 ± 7.87	65.9 ± 6.70
HPW D	31.79 ± 2.41	115.1 ± 1.40	87.4 ± 0.14	5.45 ± 6.14	1.17 ± 1.16	159 ± 10.90	105 ± 11.42
Dm	C>D>A>B	C>D>A>B	C>D>B>A	B>A>D>C	A>B>D>C	B>D>C>A	B>D>A>C
Ls	**P<0.05**	**P<0.05**	**P<0.05**	**P<0.01**	**P<0.01**	**P<0.05**	**P<0.05**

GROUP	Progesterone (n/ml)	Estradiol (pg/ml)	Prolactin (pg/ml)	FSH (ng/ml)	LH (ng/ml)	SBP (mmHg)	DBP (mmHg)
NNPW A	14.2 ± 4.2	98.0 ±1.67	78.9 ±1.67	13.01 ±7.10	1.35 ± 0.05	98.7 ± 10.42	67.15 ±10.18
HNPW B	12.5 ± 0.2	89.9 ± 2.02	80.1 ± 1.12	13.19 ± 2.40	1.31 ± 0.10	161 ± 13.45	107 ± 12.45
NPW C	118 ± 7.01	162 ± 2.72	157.12 ± 11.3	3.11 ± 3.45	0.81 ± 5.70	109 ± 8.10	66.5 ± 7.42
HPW D	89 ± 2.4	143.47 ± 8.91	140.7 ± 6.17	3.79 ± 2.88	0.75 ± 2.81	161 ± 11.10	106 ± 10.95
Dm	C>D>A>B	C>D>A>B	C>D>B>A	B>A>D>C	A>B>C>D	B=D>A>C	B>D>C>A
Lm	P<0.05	P<0.05	P<0.05	P<0.01	P<0.01	P<0.05	P<0.05

Table 2: The levels of reproductive hormones in normotensive and hypertensive pregnancies (3^{rd} trimester)

Table 3: The levels of reproductive hormones in normotensive and hypertensive pregnancies (3-6 days after delivery)

GROUP	Progesterone (n/ml)	Estradiol (pg/ml)	Prolactin (pg/ml)	FSH (ng/ml)	LH (ng/ml)	SBP (mmHg)	DBP (mmHg)
NNPW A	14.2 ± 4.2	98.0 ±1.67	78.9 ±1.67	13.01 ±7.10	1.35 ± 0.05	98.7 ± 10.42	67.15 ±10.18
HNPW B	12.5 ± 0.2	89.9 ± 2.02	80.1 ± 1.12	13.19 ± 2.40	1.31 ± 0.10	161 ± 13.45	107 ± 12.45
NPW C	110 ± 4.2	160 ± 7.4	175 ± 9.6	4.15 ± 2.2	1.01 ± 4.0	104 ± 4.91	66 ± 3.58
HPW D	80 ± 3.6	140 ± 5.0	163 ± 6.2	4.95 ± 2.1	1.32 ± 2.9	151 ± 4.24	96 ±7.89
Dm	C>D>B>A	C>D>A>B	C>D>B>A	B>A>D>C	A>D>B>C	B>D>A>C	B>D>A>C
Lm	P<0.05	P<0.05	P<0.05	P<0.01	P<0.01	P<0.05	P<0.05

KEY TO TABLES 1,2,3
NNPW – Normotensive non pregnant women
HNPW – Hypertensive non pregnant women
NPW – Normotensive pregnant women
HPW – Hypertensive pregnant women
Dm–Difference between mean
Lm– Level of significance

The changes in the levels of Progesterone can be clearly seen from Tables 1,2 and 3. In Table1, Progesterone was at minimum levels of 14.2+4.2ng/ml and 12.5+0.2ng/ml from groups A and B which comprises of normotensive and hypertensive non pregnant subjects. Progesterone secretion is known to increase with pregnancy as it grows. The placenta , as soon as pregnancy occurs also begins to synthesize progesterone and with the consumption of diary products , its level goes up more in pregnancy(Goodson et al, 2007) . This fact as revealed in the literature must have accounted for the significant increase ($p<0.05$) in the levels of progesterone observed in Tables1 and 2 on the subjects of groups C and D at 2^{nd} and 3^{rd} trimester of pregnancy.So progesterone increases significantly in both normotensive and hypertensive pregnancy as the trimester progresses. However the level of the significant increase in normotensive pregnancy when compared relative to that of hypertensive is higher. It has been reported that Progesterone withdrawal or decrease in level has been linked within increase/decrease in sodium retention, and this is also significant to hypertension (Luconi et al, 2004). So the presence of high blood pressure observed in group D at 2^{nd} and 3^{rd} trimestermay have received contribution from the decrease in the levels of Progesterone which is lower in hypertensive pregnancy relative to normotensive pregnancy. Hence normotensive pregnant subjects may tend to enjoy more of the numerous functions of progesterone. This may account for other symptoms seen in preeclampsia. Table 3 shows a decrease in the level of progesterone after delivery. This agrees with the literature that progesterone level decreases critically after the delivery of the placenta and during lactation (Luconi et al, 2004).

Estradiol which is an Estrogen, can be seen from Tables1,2 and 3. Its levels of changes follows the same manner with progesterone.Estradiol significant increase in normotensive pregnancy is relatively higher than that of the hypertensive pregnancy even though it also increases significantly there too. The reason for this may be in line with what is reported in literature that, Estrogen increases with pregnancy and it also affect blood vessel improvement in arterial blood flow (Collins et al,1995; Douma et al 2007).

Follicle stimulating and Luteinizing hormones (FSH and LH) levels changes in different manner. Their highest levels were observed in non-pregnant groups A and B. Also, at the 2^{nd} and 3^{rd} trimester of the normotensive and hypertensive pregnant groups C and D, both FSH and LH Both FSH and LH function predominantly before ovulation and decreases with growth in pregnancy. These two hormones give way to Human Chorionic Gonanotropic hormone (HCG),

Which starts to be secreted by the placenta as soon as pregnancy occurs. Both hormones have been described to be at a low level in pregnancy induced patient (Bowen 2004). Table 3 reveals in line with literature that after delivery FSH and LH levels started showing increase.

Prolactin constantly increases significantly in all the pregnant groups C and D, from the 2^{nd} trimester up till after delivery as shown from the values obtained in Tables1,2 and 3. The significant increase seen in Prolactin in both normotensive and hypertensive pregnancies is in line with the literature that, Prolactin stimulates the milk "let down" reflex via lacto genesis in preparation for the infant feed (Zhang 2007). It is also reported that increase in Prolactin decreases normal levels of Estrogen and steroid hormone outside pregnancy (Munjuluri et al, 2005). This agrees perfectly with the result in Table3 showing the levels the hormone after delivery. Estradiol and progesterone levels were lowered while Prolactin levels keep increasing.

From the results obtained so far, it is evident that the reproductive hormones can be said to be associated with Pregnancy induced Hypertension (PIH), considering the fact that different levels of significance were observed in PIH relative to normotensive Pregnancy.

IV. Conclusion

Our findings from the results obtained in this research work point to the fact that, the reproductive hormones are implicated in Pregnancy Induced Hypertension.

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