Publisher homepage: www.universepg.com, ISSN: 2663-7529 (Online) & 2663-7510 (Print)

https://doi.org/10.34104/ejmhs.022.01000110

European Journal of Medical and Health Sciences

Journal homepage: www.universepg.com/journal/ejmhs

Assessment of Biochemical Markers in Polycystic Ovarian Syndrome Patients in the Niger Delta Region, Nigeria

Ezeiruaku Ferdinand Chukwuma[1] and Onitsha Enebrayi Nelson[2]*

[1&2]Department of Medical Laboratory Science, Faculty of Basic Sciences, College of Health Science, Niger Delta University, Wilberforce Island, Bayelsa State, Nigeria.

*Correspondence: brayi4life@gmail.com (Onitsha Enebrayi Nelson, Department of Medical Laboratory Science, Faculty of Basic Sciences, College of Health Science, Niger Delta University, Wilberforce Island, Amassoma, Bayelsa State, Nigeria).

ABSTRACT

Polycystic Ovary syndrome is a chronic endocrine disorder with clinical manifestations of oligomenorrhoea, amenorrhea, hirsuitism, ovarian dysfunction, and multiple ovarian cysts, affecting many women at reproductive age. PCOS is the primary cause of an ovulatory infertility worldwide. This study assessed the concentration of reproductive hormones in polycystic ovarian syndrome patients attending tertiary hospitals in Niger Delta Region, Nigeria. Three hundred and fifty infertile premenopausal women aged 20 to 40 years were recruited; comprising of 250 women presenting complete Rotterdam patients of polycystic ovarian syndrome diagnostic criteria, and 100 apparently healthy women who serve as control. Blood samples were collected and analyzed for reproductive hormone levels using Enzyme linked Immunosorbent Assay. The result showed significantly increased concentration of estradiol, luteinizing hormone, LH/FSH ratio, testosterone, and prolactin levels in the PCOS patients when compared with the control subjects. Progesterone and Follicle stimulating hormone levels were significantly lower in the patients with PCOS than normal subjects. However, there was no significant difference was observed in the serum dehydroepiandrosterone levels. Furthermore, the study revealed that insulin resistance level was significantly (p=0.000) higher in the PCOS patients than the control subjects. The BMI was significantly higher in PCOS patients than control group. The study result showed positive correlation between BMI and insulin resistance, and negative correlation with FSH. The result showed significant positive correlation between estrogen and insulin resistance, Luteinizing hormone, and a negative correlation with LH/FSH ratio. The study affirms that there is an interrelationship between hormones thus, promoting hormonal disorders in polycystic ovarian syndrome patients.

Keywords: Polycystic ovarian syndrome, Reproductive hormones, Insulin resistance, and polycystic ovary.

INTRODUCTION:

Polycystic Ovary Syndrome (PCOS) is a heterogeneous endocrine disorder affecting 20-25% of women of child bearing age (National Institute of Health, 2012).It is defined by the presence of at least two of the Rotterdam criteria: oligo-anovulation, clinical or biological hyperandrogenism, and polycystic ovary (Tarlatzis *et al*., 2010). PCOS is a complex disease characterized with a range of clinical manifestations such as menstrual dysfunction (oligomenorrhea or amenorrhea); hyperandrogenism, infertility, hirsutism, acne, obesity, metabolic syndrome, ovarian dysfunction, and multiple ovarian cysts (Rosenfield and Ehrmann, 2016). It is estimated that nearly one out of every four women has polycystic ovaries (PCO) with a quarter of these women developing symptoms of PCOS (Idrisa, 2005;

Kovacs, 2004). PCOS prevalence varies globally and it's dependent on several factors such as ethnicity, race, environment and the criteria used for the diagnosis of PCOS (Fraser and Kovacs, 2004). According to reports by March *et al*. (2010) and Azziz *et al*. (2004), the prevalence of 2.2%–26% was recorded worldwide among women of child bearing age using the Rotterdam criterion. In Nigeria, two studies by Ugwu *et al.* (2013) and Omokanye *et al.* (2015 10) reported the prevalence of PCOS as 18.1% and 12.2% respectively. Polycystic ovary syndrome (PCOS) is classified by a pattern of hormonal imbalances and metabolic dysregulation, including compensatory hyperinsulinemia, insulin resistance, and dyslipidemia, all of which contribute to the pathogenesis (Diamanti-Kandarakis and Dunaif, 2012).Women of child bearing age with polycystic ovary syndrome and central obesity are predisposed to long-term health ailments, including an ovulation, type 2 diabetes, hyperinsulinemia, endometrial cancer and hypertension (Al-Bayyari, 2018).

The etiology of PCOS is complex and certain factors such as genetic, environmental and lifestyle factors may contributes to its development, but the exact underlying defect remains unknown. However, it is commonly linked to insulin resistance resulting to hyperandrogenism, dyslipidemia and other metabolic disturbances (Lee *et al*., 2010 13; Karabulut *et al*., 2012). Hyperandrogenism alters ovarian steroidogenesis and folliculogenesis, resulting to anovulation (Lee *et al*., 2010). Other possible etiological factors of PCOS include; disorders of the hypothalamic-pituitary-ovarian axis (HPO) and patient`s genetic predisposition, which varies geographically (Chen *et al*., 2008; Sharif *et al*., 2019; Igwegbe *et al*., 2013).

Polycystic ovarian syndrome (PCOS) is diagnosed by clinical or laboratory investigations revealing the existence of irregular menstrual cycles, oligo/anovulation, elevated total and free testosterone levels (hyperandrogenaemia), and the presence of polycystic ovaries on transvaginal scan as recognized at the European Society of Human Reproduction and Embryology (ESHRE)/American Society of Reproductive Medicine (ASRM) consensus meeting in Rotterdam2003 recorded by ESHRE/ASRM, 2004. The diagnosis was based on the above criteria fulfilling sufficient specificity and sensitivity to define the ovarian morphology in PCOS as the presence of twelve (12) or more follicles measuring 2 to 9 mm in diameter and increased of ovarian volume (>10cm3) (Balen *et al*., 2003). The USA National Institute of Health (NIH) and the Androgen Excess Society (AES) are two other criteria used for the diagnosis of PCOS, accounting for the different prevalence assessments of PCOS in the past (Vaduneme and Chidi, 2019).Over the years, the diagnosis has been contentious; however, the Rotterdam criteria require that at least two (2) of the three (3) above characteristics for a widely accepted diagnosis of PCOS are maintained and patient-specific phenotypes are identified for each patients with PCOS, as this has implications for early and late PCOS complications (Akpata *et al*., 2018; Palomba *et al*., 2015).

PCOS is a clinical syndrome characterized by a range of endocrine, reproductive, and metabolic abnormalities that can be severe in some patients but only cause minor symptoms in others. In different patients, the major clinical symptoms of hyperandrogenism and an ovulatory cycle, termed as the typical phenotype in PCOS, occur in varied rates (Setji and Brown, 2007, Pembe *et al*., 2009; Palomba *et al*., 2015). Biochemically, hyperandrogenism is defined as an increase in male steroid hormones such as testosterone and androstenedione (DHEAS) (Chen *et al*., 2006). It is presented as free androgen index, which is calculated from low serum levels of sex hormone binding globulin (SHBG) in PCOS women. The alteration in reproduction system presents as oligomenorrhea, amenorrhea, or dysfunctional uterine bleeding which is connected with an ovulation and resultant infertility (Maharaja and Amod, 2009; Yan-min *et al*., 2010).

The Serum/plasma levels of reproductive hormones of the Hypothalamo-Pituitary-Ovarian (HPO) axis may be disturbed in polycystic ovary syndrome (PCOS) patients. This disruption is responsible for two other endocrine manifestations of PCOS such as elevated serum LH leading to an increased LH/FSH ratio in some patients (Vaduneme and Chidi, 2019). The studies of Obuna *et al*. (2012) and Baqai *et al.* (2010) found that PCOS can influence the response to ovulation inducers (drugs) and may also lead to early miscarryage in infertile women. However, the presence of polycystic ovaries (PCO) has not been shown to have a substantial impact on fertility in women. This study is

designed to assess some biochemical markers of polycystic ovary syndrome patients attending different Health Facilities in the Niger Delta Region of Nigeria.

MATERIALS AND METHODS:

Study Area

This research was carried out in two (2) States (Bayelsa and Rivers States) in the Niger Delta Region of Nigeria. The samples for the study were collected from women that attended the Department of Gynaecology and Obstetrics in some Tertiary Health Institutions in the region: University of Port Harcourt Teaching Hospital (UPTH) Port Harcourt, Niger Delta University Teaching Hospital (NDUTH) Okolobiri, Federal Medical Centre (FMC) Yenagoa, Bayelsa State, and other tertiary health centres in the Niger Delta Region.

Study Population

This is a cross-sectional study carried out on three hundred and fifty (350) patients aged 20 to 40 years, comprising of two hundred and fifty (250) women presenting complete Rotterdam patients of polycystic ovarian syndrome (PCOS) diagnostic criteria (oligo-/amenorrhea; clinical and/or biochemical signs of HA; polycystic ovaries detected by ultrasound); and one hundred (100) apparently healthy women (with normal menstruating cycles) that served as control. The study was conducted for a period of two (2) years from November, 2019 and September, 2021.

Sampling and Sample Selection

A non-probability purposive sampling was used. Inclusion Criteria include; Patients presenting with menstrual abnormalities, subfertility, hirsuitism and obesity (BMI>25kg/m^2) acanthosis nigricans and acne; ovarian volume more than 7.5cm3 on ultrasonography and Age 20-40 years. Additional inclusion criteria were: women without other known endocrine disorders; absence of drug administration over 3 months preceding the study, (including oral combined contraceptives); and informed consent of the patient.

The exclusion criteria were: patients receiving treatment for polycystic ovarian disease; mental illnesses; inherited syndromes and congenital malformations; hyperprolactinemia; congenital dysfunction of the adrenal cortex; thyroid disorders; Cushing syndrome and disease; tumors of the pelvic organs.

Data Collection Procedure

A total of two hundred and fifty (250) cases of polycystic ovarian syndrome as diagnosed on ultrasound were selected from outpatient department (OPD) of various selected tertiary health institutions. An informed consent was collected from PCOS patient's included in the study. History of patient was taken at presentation regarding name, age, address, marital status, symptoms (menstrual disturbances, sub fertility, obesity and excessive hair growth), severity, duration and any previous treatment was obtained. These cases were examined for height, weight, body mass index ((BMI >25kg/m^2), hirsutism, acne, acnthosis nigricans, breast examination (galactorrhoea).

Sample Collection and Preparation

About 5.0ml of a single non-fasting venous blood was collected from the antecubital region from the subjects via venipuncture between 8:00AM and 11:00 AM, to control for diurnal variations and dispensed into plain containers. The blood sample was allowed to clot properly and centrifuged at 1500rpm for 5minutes using bench centrifuge, and serum separated and stored frozen at −20˚C until the time of assay. The blood samples were investigated for LH, FSH, estrogen, progesterone testosterone, DHEAS, Insulin resistance and prolactin levels within seven (7) days of sample collection.

Ethical Clearance

The essence and details of the study was explained to the subjects (both test and control group) and consent gotten before sample collection. Institutional ethical approval was gotten before the sample collection was performed from the institution research ethical committee.

Analytical Methods

The measurement of Height and body weight was done using standard procedures with a stadiometer and scales, respectively. BMI was calculated using the formula BMI = Body weight (kg)/height (m2). The serum progesterone, estrogen, follicle stimulating hormone, luteinizing hormone and Prolactin assays were analyzed using AB Diagnostics, Abia hormone ELISA kits from Halomedicals, Germany (Amballi *et al*., 2003). The principle is based on the solid phase enzyme linked Immunosorbent assay. The components of the ELISA kit were specifically designed to analyze

estradiol, progesterone, estrogen, testosterone, DHEAS, FSH, LH and prolactin. Insulin resistance was assayed using homeostasis model assessment (HOMA-IR) method and calculated using the formula (HOMA-IR) = FPI X FPG/22.5 (Bakari and Onyemelukwe, 2009).

Data Analysis Procedure

The results of this investigation were input into the SPSS package, version 23, and displayed as mean and standard deviation. The difference in mean values was tested using the student's t-test. The 95 percent confidence level (P<0.05) was used and considered significant.

RESULTS:

Results from **Table 1** in the current study revealed significantly (p=0.000) higher values for body weight (68.39 ± 2.59 vs 70.18 ± 1.87) and BMI (22.17 ± 0.75 vs 27.81 ± 0.87) in the Polycystic Ovarian Syndrome patients compared with the control group. Also, no significant differences was observed in age (34.89 ± 4.90 vs 35.80 ± 5.40) and in height (1.61 ± 0.02 vs 1.62 ± 0.25) of women with PCOS compared with the control group. Results from **Table 2** shows that the mean serum concentration of estradiol (E2) in the PCOS patients is significantly (p=0.014) higher than the controls (29.26± 3.52 vs 48.22 ± 14.44). The mean serum concentration of progesterone (3.94 ± 2.11 vs 2.63 ± 1.30; (p=0.010) and Follicle Stimulating Hormone (FSH) (11.10 ± 5.27 vs 8.01± 3.34 p=0.017) in the patients with PCOS was significantly lower than the control group. Serum level of Luteinizing Hormone (LH) in the patients with PCOS was significantly higher when compared with the control group (10.79 ± 23.49 vs 19.25 ± 7.08; p=0.029). The mean value of LH/FSH ratio (1.31 ± 0.39 vs 2.00 ± 1.08) and testosterone (0.88 ± 0.17 vs 1.15 ± 0.39) was significantly higher (p=0.000 and p=0.005 respectively) in the PCOS patients compared to the control. Serum dehydroepiandrosterone (DHEAS) showed no signifycant difference (p=0.298) in the subjects. The mean serum level of prolactin was significantly (p=0.000) higher in the PCOS patients compared with the control group (12.81± 4.47 vs 23.95 ± 8.32). Results from **Table 3** shows that the mean values of Insulin Resistance was significantly (p=0.000) higher in the PCOS patients compared to the control group (1.50± 0.51 versus 2.96 ± 1.39). Results from **Table 4** shows a significant positive correlation between Body Mass Index (BMI) and insulin resistance (IR) with a correlation coefficient of r=0.386 (P=0.015). BMI showed a non-significant positive correlation with estrogen, progesterone, Luteinizing Hormone, LH/FSH ratio, testosterone, dehydroepiandrosterone and prolactin.

However, there was a non-significant negative correlation between BMI and FSH levels with a correlation coefficient of r=0.562 (P=0.731). Data from **Table 5** revealed that there was significant positive correlation between estrogen and insulin resistance (IR) and Luteinizing hormone (LH). Follicle Stimulating Hormone (FSH), testosterone, dihydroepiandrosterone (DHEAS) and prolactin (PRL) showed a non-significant positive correlation with estrogen levels. However, the study shows a negative correlation between estrogen and LH/FSH ration in the polycystic ovarian syndrome patients (Allagoa *et al.,* 2021).

Table 1: Comparison of the Anthropometric Characteristics of Polycystic Ovarian Syndrome (PCOS) women and Control Subjects.

Groups	Control (n=100) (Mean±S.D)	Women with PCOS (n=250) (Mean±S.D)	t-value/P-value
Age (Yrs)	35.89±4.90	34.80±5.40.416	.681^{NS}
Height (M)	1.61±0.02	1.62±0.252.908	.371^{NS}
Weight (Kg)	68.39±2.59	70.18±1.874.452	.000*
BMI (Kg/m^2)	22.17±0.75	27.81±0.875.406	.000*

Key *= represent P < 0.05 was statistically significant; NS=Not statistically significant (P>0.05); Values are the mean ± SD. Abbreviations: kg/m^2 = kilogram per meter squared; BMI= body mass index; Kg= Kilometer; Yrs= Years. Student t-test was used.

Table 2: Comparison of Reproductive Hormone levels of Women with Polycystic Ovary Syndrome (PCOS) and Controls.

Parameters	Control (n=100) (Mean±S.D)	Women with PCOS (n=250) (Mean±S.D)	t-value/P-value
E2 (Pg/ml)	29.26 ± 3.52	48.22 ± 14.44 - .831	.014*
PROG (ng/ml)	3.94 ± 2.11	2.63 ± 1.30 - 2.78	.010*
LH (U/L)	10.79 ± 23.49	19.25 ± 7.08-785	.029*
FSH (U/L)	11.10 ± 5.27	8.01± 3.342.544	.017*
LH/FSH	1.31 ± 0.39	2.00 ± 1.084.099	.000*
TESTOS (ng/ml)	0.88 ± 0.17	1.15 ± 0.393.025	.005*
DHEAS (nmol/L)	1.17 ± 0.36	3.90 ± 1.321.062	.298^{NS}
PRL (ng/ml)	12.81± 4.47	23.95 ± 8.328.164	.000*

Key: E2 (Estradiol); PROG (Progesterone); FSH (Follicle stimulating hormone); LH (Luteinizing Hormone); LH/FSH (LH/FSH ratio); TESTOS (Testosterone); DHEAS (dehydroepiandrosterone); PRL (Prolactin). * represent p<0.05 is statistically significant; p>0.05=Not statistically significant.

Table 3: Comparison of Insulin Resistance in Polycystic Ovary Syndrome (PCOS) Patients and Control.

Groups	Control (n=100) (Mean±S.D)	Women with PCOS (n=250) (Mean±S.D)	t-value/P-value
Insulin Resistance	1.50±0.51	2.96 ± 1.39 4.710	.000*

Key: *= represent significant; Values are the mean ± SD.

Table 4: Correlation analysis between Body Mass Index and Insulin Resistance, Female Reproductive Hormones among Patients with Polycystic Ovarian Syndrome.

IR	E2	PROG	LH	FSH	LH/FSH	TESTOS	DHEAS	PRL
BMI (Kg/m^2)	+0.386	+0.245	+ 0.691	+0.471-0.562	+0.142	+0.454	+0.612	+0.653
P-value	0.015*	0.672	0.221	0.322-0.745	0.531	0.124	0.243	0.316

Key: BMI (Body Mass Index); IR (Insulin Resistance); E2 (Estradiol); PROG (Progesterone); FSH (Follicle stimulating hormone); LH (Luteinizing Hormone); LH/FSH (LH/FSH ratio); TESTOS (Testosterone); DHEAS (dehydroepiandrosterone); PRL (Prolactin). * represent p<0.05 is statistically significant; p>0.05=Not statistically significant.

Table 5: Correlation coefficients between Estrogen (E2) and other female Reproductive Hormones and Insulin Resistance among Women with Polycystic Ovarian Syndrome.

IR	PROG	LH	FSH	LH/FSH	TESTOS	DHEAS	PRL
E2 (pg/ml)	+0.782	+0.674	+0.790	+0.194-0.263	+0.127	+0.159	+0.454
P-value	0.001*	.543	0.002*	0.374- 0.561	0.634	0.241	0.134

Key: BMI (Body Mass Index); IR (Insulin Resistance); E2 (Estradiol); PROG (Progesterone); Follicle stimulating hormone; Luteinizing Hormone; LH/FSH (LH/FSH ratio); TESTOS (Testosterone); DHEAS (dehydroepiandrosterone); PRL (Prolactin). * represent p<0.05 is statistically significant; p>0.05=Not statistically significant.

DISCUSSION:

Polycystic Ovary Syndrome (POS) is the most frequent heterogeneous endocrine disorder in premenopausal women and the leading cause of an ovulatory infertility in women of childbearing age (Vaduneme and Chidi, 2019). It is usually manifested with oligomenorrhoea, amenorrhoea, hirsuitism, acne, obesity, metabolic syndrome, ovarian dysfunction, & multiple ovarian cysts.

This study evaluated the levels of reproductive hormones and insulin resistance in women with Polycystic Ovarian Syndrome in the Niger Delta Region, Nigeria. Results from current study revealed no significant differences (p>0.05) observed in the age and height of women with PCOS compared with the control (**Table 1**). This concurs with the previous studies by Chukwunonso *et al*. (2018) and Oyebanji *et al*. (2018), which reported a non-significant difference in the age and height of PCOS subjects compared with normal subjects. Overweight or obesity is diagnosed in approximately 60–80 percent of women having Polycystic Ovarian Syndrome (Moran *et al*., 2012). A high BMI raises the chance of reproductive problems. Obesity reduces reproductive capacity due to physiological changes in the Hypothalamic-Pituitary-Ovarian (HPO) axis, resulting in menstruation and ovulation abnormal ities, as well as infertility (Suturina *et al*., 2017; Kaur *et al*., 2018). In the present study, the weight and BMI of the women having PCOS was significantly (p=0. 000) higher than the control as shown in (**Table 1**). This is consistent with the findings of Mariya *et al*. (2020), which documented that many women suffering from PCOS were over-weight or obese. Estradiol (E2) is the most biologically active form of estrogen. It is a major female sex steroid hormone that is thought to play a vital role in the regulation of menstrual female reproductive cycles. In our findings, the serum concentration of estradiol (E2) is significantly (p=0.014) higher in the women having PCOS than the control group (**Table 2**). This finding is in consonance with the works of Oyebanji *et al*. (2018) and Khmil *et al.* (2020), which reported an elevated serum estradiol levels in PCOS patients compared with control, and contradicts the work by Hashemi *et al*. (2016) who reported an increased Estradiol (E2) levels in PCOS women. This elevation in Estradiol (E2) levels could be attributed to reduced sex hormone-related globulin levels (Dumitrescu *et al*., 2015). Progesterone is an endogenous steroid sex hormone involved in variety of female reproductive physiology such as pregnancy, menstrual cycle, and embryogenesis (De-Groot *et al*., 2015). Results from this study revealed that serum progesterone level was significantly (p=0.010) reduced in the PCOS patients as compared to the control subjects. This finding corresponds with Vaduneme and Chidi, (2019) and Hussein and Alalaf, (2013), which reported low progesterone levels in women suffering Polycystic Ovarian Syndrome. The reduction in progesterone level could be associated to hyperinsulinemia and/or insulin resistance which is reported as a possible cause of the progesterone deficiency in PCOS. Reduced progesterone level may results to failure of the ovaries to release eggs, resulting to anovulation.

Irregularities of the Hypothalamic-Pituitary-Ovarian (HPO) Axis has been implicated in PCOS, and disruption in the pulsatility of gonadotrophin releasing hormone (GnRH) results in the relative rise in LH to FSH release (Alnakash *et al.,* 2007). LH and FSH are glycolproteinhormones produced by the anterior pituitary in response to gonadotropin releasing hormone (GnRH) from the hypothalamus (Stamatiades and Kaiser, 2018). They are primarily involved in sexual development and reproductive process in both male and female body system (Barbieri, 2014). The serum level of luteinizing hormone (LH) was significantly (p=0.029) greater in PCOS patients, whereas FSH was significantly (p=0.017) lower in PCOS patients compared to the control group in the current study (**Table 2**). Decreased FSH level may causes follicular atresia of the ovaries resulting to an abrupt development of anovulation (Sampurna *et al.,* 2017). High LH levels cause the theca cells of the ovaries to produce more androgens. Therefore, high LH levels and low FSH levels can lead to loss of menstrual cycles, infertility, decreased sex drive, vaginal dryness, and osteoporosis, which can lead to a tendency to develop fractures and thus, PCOS (Nas *et al*., 2020; Oyebaiji *et al*., 2018).

LH and FSH are the anterior pituitary hormones that control ovarian physiology in female reproductive system. In normal physiological system, the serum concentration of FSH is higher than LH. However, in PCOS, the serum concentration of LH is higher than FSH causing overproduction of ovarian androgen and ovulatory dysfunction (Clamn *et al*., 2002). Results in this study showed that the serum level of LH/FSH ratio was significantly (p=0.000) elevated in the PCOS subjects compared with the control subjects (**Table 2**). This is similar to the previous study of Yue and colleagues, (2017) which reported an increased LH level and LH/FSH ratio in women suffering from PCOS when compared with control subjects. This increase in LH/FSH ratio could be related to the patho-

logical secretion of gonadotropin (gonadotropin-releasing hormone) which upregulates the transcription of the LH β-subunit through the FSH β-subunit, which results to a higher LH/FSH ratio in PCOS patients. Dehydroepiandrosterone sulfate (DHEAS) is a prehormone produced by the adrenal cortex and converted into DHEA. In the present study, the level of DHEAS was higher in PCOS patients than in controls, however, no significant difference (p = 0.298) was observed (p = 0.298) (**Table 2**). This concurs with the works of Khan *et al* (2021) who documented a significantly elevated DHEAS levels in the PCOS patients. Hyperandrogenemia, or high serum testosterone levels, has been linked to menstrual cycle irregularities and negative metabolic conditions in premenopausal women, including insulin resistance, central obesity, dyslipidemia, and chronic inflammation, all of which may predispose them to other metabolic disorders (Marilyn and Richardson, 2003). Our findings revealed a significant (p=0.005) elevation of serum testosterone levels in PCOS patients compared with controls as shown in (**Table 2**). This result is in consonance with previous works by Mariya *et al.* (2020); Khan *et al*. (2021) and Oyebanji *et al.* (2018), which documented that women with PCOS demonstrated a significant elevation in serum total Testosterone levels. Prolactin is a hormone secreted from anterior pituitary gland whose primary function is the production of milk (lactation) in reproductive females (Muhjah, 2020). Abnormally high serum androgen level has been demonstrated in PCOS patients which results in ovulatory failure and increased infertility (Al-Hindawi, 2018). Apostolos, (2018) reported an increased serum prolactin level in PCOS patients. This study revealed a significantly (p=0.000) higher prolactin level PCOS patients when compared with the control subjects (**Table 2**).

However, it contradicts the works of Vaduneme and Chidi, (2019) and Hussein and Alalaf, (2013). Hyperprolactinemia may influence fertility in women by inhibiting GnRH secretion by its inhibitory action on GnRH neurons, or by affecting the pituitary gland and decreasing gonadotropin production, resulting in ovulatory failure (Ursula, 2012).

Insulin resistance is a state in which a given concentration of insulin produces an attenuated biological response (Cefalu, 2001). High levels of insulin may be a factor in the inflammation and other metabolic complications associated with PCOS. Although insulin resistance is not part of the diagnostic criteria for PCOS, its importance in the pathogenesis of PCOS cannot be determined. PCOS is connected to insulin resistance independent of total or fat free body mass. Data from the present study shows that the mean value of Insulin Resistance was significantly (p=0.000) higher in the PCOS patients (**Table 3**).This elevation in insulin resistance could be attributed to abnormalities in pituitary gonadotropin secretion, excessive stimulation of IGF-I receptors, excessive activity of 17α-hydroxylase, an enzyme that regulates conversion of 17-hydroxy-progesterone into androstenedione, as well as diminished synthesis of insulin-like growth factor binding protein 1 (IGF-BP1). Results from **Table 4** showed a significant positive correlation between Body BMI and insulin resistance with a correlation coefficient of r=0.386 (P=0.015). BMI showed non-significant positive correlation with estrogen, progesterone, LH, LH/FSH ratio, testosterone, dehydroepiandrosterone and prolactin. However, BMI and FSH shows a non-significant negative correlation between with a correlation coefficient of r=0.562 (P=0. 731). Our finding is consistent with the work of Jayashree and colleagues, (2019) which documented that insulin resistance showed a significant positive correlation with BMI. It also concurred with Zaheera, (2020) which reported that BMI did not significantly correlate with LH, FSH, or prolactin (P>0.05). Our finding also confirmed the work by Kiddy *et al.* (1990) who a negative correlation between BMI and FSH levels in PCOS. Furthermore, a significantly positive correlation was observed between estrogen and insulin resistance and LH. While, a negative correlation was observed between estrogen and LH/FSH ration in women with PCOS.

CONCLUSION:

This study showed higher levels of estradiol (E2), LH, LH/FSH ratio, testosterone, hydroepiandrosterone and prolactin levels in PCOS patients. Furthermore, it revealed that the level of progesterone and FSH was lower in the patients with PCOS than normal subjects. This study has showed that estradiol (E2), LH, FSH, LH/FSH ratio, testosterone, prolactin, & progesterone were implicated in PCOS patients. The study also

revealed that insulin resistance level was higher in the women than the control subjects. Insulin resistance had a strong positive correlation with BMI, but FSH had a substantial negative correlation. The result also showed significant positive correlation between estrogen and insulin resistance, Luteinizing hormone, and a negative correlation with LH/FSH ratio.

ACKNOWLEDGEMENT:

We sincerely thank the management and staff of University of Port Harcourt Teaching Hospital (UPTH) Port Harcourt, Niger Delta University Teaching Hospital (NDUTH) Okolobiri, and Federal Medical Centre (FMC) Yenagoa, Bayelsa State for creating an enabling environment in the course of this work. We also appreciate all the staff of De-Integrated Medical Laboratory Port-Harcourt, Rivers State.

CONFLICTS OF INTEREST:

There is no conflict of interest regarding to the publication of this article.

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Citation: Ezeiruaku FC., and Onitsha EN. (2022). Assessment of biochemical markers in polycystic ovarian syndrome patients in the Niger Delta region, Nigeria. *Eur. J. Med. Health Sci.*, **4**(4), 100-110. https://doi.org/10.34104/ejmhs.022.01000110