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Association of Body Mass Index with Hypothalamus-Pituitary-Ovarian Axis Hormones in Infertile Women in the Niger Delta Region, Nigeria

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Abstract

Background: Infertility is well-known global health problem that has significant impacts on an individual, families and communities. Many modifiable lifestyle risk factors increase the risk of women to several reproductive disorders. **Aim**: This study established the relationship between obesity and Hypothalamic-Pituitary-Ovarian (HPO) axis hormones in infertile women in the Niger Delta Region, Nigeria. **Methodology**: Six hundred and twenty-six (626) women aged 18 - 40 years comprising of 513 obese infertile women and 113 non obese women who served as control were recruited for the study. Anthropometric measurements were taken and Body Mass Index was calculated. A non-fasting venous blood sample was collected from the women and analyzed for serum Estrogen, Luteinizing Hormone (LH), Follicle Stimulating Hormone (FSH), Progesterone, Inhibin B, and Prolactin using Enzyme linked immunosorbent assay method. **Results**: In the present study, the Body Mass Index of women with primary (1˚) infertility is significantly ($p < 0.05$) higher than secondary (2˚) infertility women. Whereas, women with 2˚ infertility were older and have a higher height than women with 1˚ infertility. The result revealed that serum estrogen, luteinizing hormone, follicle stimulating hormone and prolactin levels were significantly ($p < 0.05$) higher in the obese infertile women, while inhibin B and progesterone levels were significantly ($p < 0.05$) reduced in the obese infertile women compared to the control subjects. However, women with 1˚ infertility have a significantly higher LH and FSH levels than the 2˚ infertility women. Furthermore, the study revealed that hyperestrogenism is the most prevalent gonadal disorder in women with primary infertility and secondary infertility. The BMI of infertile women suffer-

ing Hyperestrogenism is significantly higher than any other female gonadal disorder. The result also showed that there is statistically significant positive correlation between BMI and Hypogonadism, Hypogonadotropic and Amenorrhoea in obese infertility women. While, no significant correlation between BMI and Hypergonadism and Hypergonadotropic was observed. Furthermore, there was a positive correlation between BMI and Hypothalamus-Pituitary Ovarian hormones, as BMI showed a positive correlation with LH, FSH, Estrogen, progesterone, and prolactin in women with primary and secondary infertility, while Inhibin B showed a negative correlation with BMI. **Conclusion**: There is a relationship between BMI and Hypothalamus-Pituitary Ovarian hormones, signifying that obesity could affect female reproduction and directly impact ovarian function. Therefore, body weight maintenance should be considered as a first line of management of Hypothalamus-Pituitary Ovarian hormonal related infertility.

Keywords

Body Mass Index, Hypothalamus-Pituitary Ovarian Axis, Infertility, Obesity and Female Reproductive Hormones

1. Introduction

Infertility remains a well-known public health concern that is connected to medical, psychosocial and economics burdens [1] [2]. It is a global disease that affects an average of 8% to 12% of married couples across the globe [2]. Infertility prevalence in sub-Saharan Africa is apparently 30.0% [3], and in Nigeria, the prevalence rate of infertility is recorded as 10% - 30% among couples [3] [4]. Infertility is one of the most common reasons for women seeking gynaecological consultation from medical expertise [5] [6]. Infertility is of two types; primary and secondary infertility. A demographic health surveys by Mascarenhasc *et al.* [7] reported that the overall rate of primary infertility ranged between 0.6% - 3.4% and 8.7% - 32.6% for secondary infertility. Its etiology in Nigeria was found to be mainly related to post infectious causes; sexually transmitted infections, post abortal and puerperal sepsis [8].

Obesity is recognized as a global problem that causes a huge economic burden, where it is estimated that obesity will add 48 - 66 billion dollars in related health care expenditures by the year 2030 [9]. Globally, its incidence has continually escalated for the past two decades despite efforts in confronting it [10]. The World Health Organization estimated that approximately one (1) billion people worldwide are overweight and that over 600 million adults of this population are obese [11] [13]. Majority of this population is made up of women of reproductive age [12] [13]. According to World Health Organization, obesity is defined as body mass index of ≥30 kg/m^2 [14]. In Nigeria, the prevalence of obesity ranged from 8.1% to 22.2%, with overweight people accounting for 20.3% to 35.1% of the population [15]. It is well-known fact that obesity is a key player

in the pathogenesis of a multitude of morbid disorders including cardiovascular disease, diabetes, hypertension, dyslipidemias, obstructive sleep apnea and related consequences [16] [17] [18] [19].

The female reproductive physiology is a complex interaction between neuroendocrine and endocrine signaling affecting the hypothalamus, the pituitary gland and the ovaries [20]. Obesity has a negative influence on reproductive potential due to physiological alterations in the Hypothalamic-Pituitary-Ovarian (HPO) axis [21]. It causes various hormonal changes in the reproductive system, making it difficult to manage infertility [22]. Ovulatory disorders connected with increasing body weight are known to contribute not just to subfertility, but also to early pregnancy losses [13] [23]. Detrimental impacts of an excess body mass index (BMI) on the outcomes of infertility treatments are also increasingly known, due to impaired response to ovarian stimulation, resulting in higher rates of cycle cancellation, lower yields of mature oocyte and lower chances for live birth are seen in association with obesity in infertile women undergoing in vitro fertilization (IVF) [24] [25].

Several researchers have associated obesity with a variety of reproductive and obstetric complications, including irregular menstruation, infertility, miscarriage, endometrial hyperplasia and cancer as well as poor obstetrical and perinatal outcomes [7] [26]. The reduction in obesity-related infertility is due to the effects of different steps of each stage, such as the implantation stage, which begins with follicle selection, due to the imbalance between the hypothalamus-pituitary-ovarian axis [27] [28]. A study by Chang [29] reported that the complex hormonal balance of the hypothalamic-pituitary-gonadal axis is affected by an individual's body mass index (BMI). Jain *et al.* [30] also documented evidence of alterations in the hypothalamic-pituitary-gonadal axis (HPO) in premenopausal years in morbidly obese women compared to women of a normal body mass index (BMI).

Physiological redundancy of the gonadotropin releasing hormone (GnRH) causes disruption of the normal secretion of luteinizing hormone (LH) and follicle stimulating hormone (FSH), which is involved in a number of reproductive disorders in women [31]. Measurements of hormones such as estrogen, progesterone, prolactin, luteinizing hormone, follicle stimulating hormone and thyroid stimulating hormones give diagnostic values for the evaluation of women fertility function [30] [31] [32]. In the Niger Delta Region in Nigeria, studies evaluating the association of obesity with Hypothalamus-Pituitary-Gonadal Axis hormones in obese infertile women are lacking. Therefore, this study evaluated the association of body mass index with hormones of the pituitary-gonadal axis among infertile women in the Niger Delta Region, Nigeria.

2. Materials and Methods

2.1. Study Area

This is a cross-sectional study carried out in two states in the Niger Delta Region

(Bayelsa, and Rivers States), Nigeria. Blood samples were collected from obese infertile and non-obese fertile women that attended the gynaecological clinics of the University of Port-Harcourt Teaching Hospital (UPTH) Port-Harcourt Rivers State, Niger Delta University Teaching Hospital (NDUTH) Okolobiri, and Federal Medical Centre (FMC), Yenagoa, Bayelsa State.

2.2. Study Population

A total of six hundred and twenty-six (626) subjects aged 18 to 40 years; comprising of 513 infertile women with a BMI > 30 kg/m^2 and 113 non obese fertile women, also with a BMI < 25 kg/m^2 who served as control were recruited for the study. The duration of the study was between May, 2014 and June, 2018. Subjects were grouped into primary infertility (297) and secondary infertility (216) women with Body Mass Index (BMI) of >30.0 kg/m^2 and without any known medical/hormonal complications, and on any medications (oral contraceptives or steroid hormones in the last 3 months) were included for the study. Other inclusion criteria were women whose partners had normal semen count gotten from the medical history. Excluded from the study were women with known medical/hormonal problems and on medications, and whose spouses were known to have low semen count. Subjects were asked to complete a structured questionnaire that contained information about age, time period of infertility, and whether primary or secondary infertility. Causes of infertility were extracted from the patient's folder.

2.3. Sample Collection and Preparation

Blood samples were collected from the obese and non-obese women that attend the fertility clinics. About 5.0 ml of a single non-fasting venous blood was collected from the ante-cubital region on day 2 or 3 of the menstrual cycle from the subjects via venipuncture between 8:00 AM and 11:00 AM, to control for diurnal variations (24) and dispensed into plain containers. The blood sample was allowed to clot properly and centrifuged at 1500 rpm for 5 minutes using bench centrifuge, and serum separated and stored frozen at −20˚C until analysis. The measurement of the hormones was done within 7 days of sample collection. Detail of the study was explained to the women and informed consent was gotten from the women before samples and anthropometric indices were collected. Institutional ethical clearance was gotten from the research ethical committee of the various hospitals.

2.4. Analytical Methods

Body Mass Index: obesity status of the subjects was confirmed after collecting their height and weight to calculate their Body Mass Index (BMI). The BMI was calculated by dividing the weight of the women by their height in meters squared. The height was measured with a Standiometer, the subject standing erect without shoes, leg forming a V-shape and the back against a wall. This was recorded in

meters to one decimal point. The body weight was measured using a known-weight standardized weighing scale; the women stood on the scale without shoes and the weight was recorded in kilogram to one decimal point.

Analysis of Hormones: The serum progesterone, estrogen, inhibin, follicle stimulating hormone, luteinizing hormone and Prolactin assays was done using AB Diagnostics, Abia hormone ELISA kits from Halomedicals, Germany [33].

2.5. Statistical Analysis

Data generated from this study were analyzed statistically using SPSS package, version 23 and presented as mean ± standard deviation. Analysis of Variance (ANOVA) and student's t-test were used to test difference in mean values. 95% confidence level at $P < 0.05$ was used and considered significant.

3. Results

3.1. Baseline Characteristics of Obese Infertile Women and Control Group

Result from Table 1 showed that out of 513 obese infertile participants, women with cases of primary infertility were more compared with secondary infertility (297 vs 216 subjects) respectively. Women with 2˚ infertility were older statistically, with an average age in years of 33.10 ± 6.06 compared with 1˚ infertility with an average age of 29.33 ± 5.77. However, when compared with the control, the infertile obese women were older than the control (28.94 ± 5.52), and was statistically significant ($p = 0.001$). The mean height in meters of obese women with 2˚ infertility (1.57 ± 0.59) was significantly ($p = 0.047$) higher compared with 1˚ infertility (1.49 ± 0.53). The Body Mass Index (BMI) of women with primary (1˚) infertility and secondary (2˚) infertility were significantly ($p = 0.000$) higher compared with the control group. However, BMI of the participants with primary infertility was higher than those with secondary infertility.

3.2. Comparison of Reproductive Hormones in Obese Women (BMI > 30 kg/m^2) with Primary (1˚) and Secondary (2˚) Infertility and Control Group

Result from the study, (Table 2) shows that serum level of inhibin B in the obese women with 1˚ and 2˚ infertility were significantly ($p = 0.000$) reduced compared with the control group (3.91 ± 1.93 and 4.58 ± 2.83 vs 6.15 ± 3.10) respectively. Serum progesterone level was also significantly ($p = 0.038$) reduced in the obese women with primary and secondary infertility compared with the control group (0.55 ± 0.27 and 0.61.04 ± 0.29 vs 0.71 ± 0.36) respectively. The mean values of Follicle Stimulating Hormone (10.15 ± 30.37 and 10.56 ± 4.01 vs 7.55 ± 3.91), Luteinizing hormone (8.57 ± 3.04 and 7.28 ± 3.12 vs 6.33 ± 3.06), Estrogen (19.55 ± 5.83 and 23.90 ± 6.18 vs 14.55 ± 9.03) and prolactin (23.53 ± 9.15 and 25.60 ± 8.40 vs 15.76 ± 6.89) of the obese infertile women with primary and secondary infertility were significantly ($p < 0.05$) elevated compared with the

Table 1. Mean ± SD of baseline characteristics of obese infertile women and control group.

Groups	Control Mean ± S.D	Primary (1˚) Infertility Mean ± S.D	Secondary (2˚) Infertility Mean ± S.D	P-value
Number	113	297	216	-
Age (years)	28.94 ± 5.52	29.33 ± 5.77	33.10 ± 6.06	0.001*
Height (m)	1.52 ± 0.67	1.49 ± 0.5 3	1.57 ± 0.59	0.047*
Weight (kg)	51.82 ± 7.42	83.40 ± 8.65	81.91 ± 8.02	0.000*
BMI (kg/m^2)	22.43 ± 2.17	33.37 ± 3.09	31.66 ± 3.05	0.001*

*represent $p < 0.05$ statistically significant, BMI (Body Mass Index).

Table 2. Mean values of reproductive hormones in obese women (BMI > 30 kg/m^2) with primary (1˚) and secondary (2˚) infertility with respect to control group.

Parameters	Control Mean ± S.D	Primary Infertility Mean ± S.D	Secondary Infertility Mean ± S.D	P-value
Inhibin B	6.15 ± 3.10	3.91 ± 1.93	4.58 ± 2.83	0.000*
FSH	7.55 ± 3.91	11.15 ± 30.37	10.56 ± 4.01	0.015*
LH	6.33 ± 3.06	8.57 ± 3.04	7.28 ± 3.12	0.027*
E2	14.55 ± 9.03	19.55 ± 5.83	23.90 ± 6.18	0.000*
PROG	0.71 ± 0.36	0.55 ± 0.27	0.61.04 ± 0.29	0.038*
PRL	15.76 ± 6.89	23.53 ± 9.15	25.60 ± 8.40	0.000*

Key: FSH (Follicle stimulating hormone); LH (Luteinizing Hormone); E2 (Estorgen); PROG (Progesterone); $p < 0.05$ = statistically significant; $p > 0.05$ = Not statistically significant. One-way Analysis of variance (ANOVA) was used.

control group respectively. However, all the analyzed hormones were found to be elevated in the women with secondary infertility compared with the primary infertility.

3.3. Comparison of the Frequency Distribution of Reproductive Disorders in Obese Women of Primary (1˚) Infertility and Secondary (2˚) Infertility with Body Mass Index (BMI)

Results from Table 3 shows that the percentage of obese women with infertility and secondary infertility who suffered from hypoestrogenisim (32.32% vs 24.54%), Hyperestrogenism (68.01% vs 70.73%), Hypergonadism (7.07% vs 6.48%), Hypergonadotropic (15.82% vs 19.90%), Hypogonadotropic (10.44% vs 15.74%) and Amenorrhoea (13.80% vs 10.65%). The study revealed that obese women with primary infertility and secondary infertility suffer more from hyperestrogenism 202 (68.01%) and 154 (70.73%) than any other gonadal disorders. The result also showed that the Body Mass Index (BMI) of women with secondary infertility suffering from Hypoestrogenism, Hyperestrogenism, Hypergonadism, Hypogonadism and Amenorrhoea (37.37 kg/mg^2, 33.56 kg/mg^2, 35.05

Table 3. Comparison of the frequency distribution of reproductive disorders in obese women of primary (1˚) infertility and secondary (2˚) infertility with body mass index (BMI).

Endocrine disorders	1˚ Infertility (% Abnormal) n = 297	BMI (kg/mg^2)	2˚ Infertility (% Abnormal)	BMI (kg/mg^2) n = 216	P-value
Hypoestrogenism	96 (32.32%)	32.75	53 (24.54%)	33.56	P < 0.05*
Hyperestrogenism	202 (68.01%)	36.20	153 (70.73%)	37.37	P < 0.05*
Hypergonadism	21 (7.07%)	33.06	14 (6.48%)	35.05	P < 0.05*
Hypogonadism	83 (27.95%)	32.45	67 (31.02%)	33.17	P < 0.05*
Hypergonadotropic	47 (15.82%)	31.95	42 (19.90%)	31.50	P > 0.05
Hypogonadotropic	31 (10.44%)	35.52	34 (15.74%)	34.25	P < 0.05*
Amenorrhoea	41 (13.80%)	34.83	23 (10.65%)	35.02	P < 0.05*

p < 0.05 = statistically significant; p > 0.05 = not statistically significant. T-test was used to compare the two groups.

kg/mg^2, 33.17 kg/mg^2 and 34.83 kg/m^2 respectively) were significantly (p < 0.05) higher than those with primary infertility (37.37 kg/mg^2, 32.75 kg/mg^2, 33.06 kg/mg^2, 32.45 kg/mg^2 and 34.83 kg/mg^2) respectively. While, the BMI of women with secondary infertility suffering from Hypergonadotropic (31.50 kg/m^2) was slightly lower than those with primary infertility (35.52 kg/m^2).

3.4. Correlation of Body Mass Index (BMI) with Hormones in Women with Primary (1˚), Secondary (2˚) and Reproductive Disorders

Results from Table 4 shows that FSH (+0.313), LH (+0.095), E2 (+0.397), Progesterone (+0.296) and Prolactin (+0.432) levels in obese women with primary infertility showed a positive correlation with Body Mass Index (BMI). Whereas, Inhibin B (−0.289) shows a negative correlation with BMI. Results from Table 5 shows that FSH (+0.305), LH (+0.056), E2 (+0.433), Progesterone (+0.379) and Prolactin (+0.511) levels in obese women with secondary infertility showed a positive correlation with Body Mass Index (BMI). Whereas, Inhibin B (−0.312) shows a negative correlation with BMI.

3.5. Correlation of Body Mass Index (BMI) with Hormones in Women with Reproductive Disorders

Results from Table 6 shows that Hypogonadism (+0.472), Hypogonadotropic (+0.368) and Amenorrhoea (+0.257) in obese infertility women showed a statistically significant positive correlation with BMI. There is no correlation between BMI and Hypergonadism and Hypergonadotropic in infertile obese women.

4. Discussion

The prevalence of infertility in Nigeria is increasing steadily and has been seen as

Table 4. Pearson correlation of body mass index (BMI) with hormones in women with primary (1˚) infertility.

Parameter	Inhibin B	FSH	LH	E2	PROG	PRL
R-value	−0.289	+0.313	+0.095	+0.397	+0.296	+0.432
P-value	0.674	0.542	0.036*	0.667	0.203	0.511

+ = positive correlation, − = negative correlation, Pearson correlation was used.

Table 5. Pearson correlation of body mass index (BMI) with reproductive hormones in women with primary (2˚) infertility.

Hormones	Inhibin B	FSH	LH	E2	PROG	PRL
R-value	−0.312	+0.305	+0.056	+0.433	+0.379	+0.511
P-value	0.145	0.741	0.036*	0.582	0.083	0.267

+ = positive correlation, − = negative correlation, Pearson correlation was used.

Table 6. Pearson correlation of body mass index (BMI) with reproductive disorders in infertile obese women.

Hormonal Disorders	Hypergonadism	Hypogonadism	Hypergonadotropic	Hypogonadotropic	Amenorrhoea
BMI (Kg/m^2)	−0.312	+0.472	+0.056	+0.368	+0.257
P-value	0.257	0.001*	0.735	0.042*	0.001*

+ = positive correlation, − = negative correlation, Pearson correlation was used.

a public health concern that has significant impacts in individual, families and communities. Many adjustable lifestyle factors may affect the possibilities of conception in women. Among these lifestyle risk factors, Body Mass Index is considered as one of the important component that predisposes women to infertility. The present study investigated the association of Body Mass Index with Hypothalamic-Pituitary-Ovarian (HPO) axis hormones in infertile women in the Niger Delta Region, Nigeria. Data from the current study showed that out of the 513 women recruited for the study, women with primary (1˚) infertility were 297, while those with secondary (2˚) infertility were 216. This suggests that primary (1˚) infertility is more common than secondary (2˚) infertility among the obese women. This is consistent with previous reports by Goynumer *et al.* [34] and Mesbahi and colleagues [35], which documented that primary (1˚) infertility is more common among women than secondary (2˚) infertility. The study also indicates that women with secondary (2˚) infertility were older compared with those Primary (1˚) infertility. This finding concurs with Seth *et al.* 36 and states the independent role of age in the physiology of fertility in women37.The average height of obese women with secondary (2˚) infertility was higher compared with primary (1˚) infertility [36] [37]. The Body Mass Index (BMI) of obese infertile women was significantly higher than the control group as shown in (**Table 1**). However, the BMI of women with 1˚ infertility is slightly higher than 2˚ infertility women. This is in consonance with previous findings by Raque-Bogdan *et al.* [38] and Friis *et al.* [39] who reported that fertility declines with increasing

age and Body Mass index.

The level of reproductive hormones for obese infertile women with 1˚ infertility and 2˚ infertility as compared with the control group, are shown in (**Table 2**). The concentration of estrogen, luteinizing hormone, follicle stimulating hormone and prolactin was significantly ($p < 0.05$) higher in the obese infertile women compared with the control group. While, inhibin B and progesterone levels was significantly ($p < 0.05$) reduced in the obese infertile women compared to the control subjects. The increase in LH and FSH levels could be attributed to the fact that FSH stimulates several follicles to mature and LH stimulates ovulation by causing the dominant follicle to rupture and release its eggs into the fallopian tube for implantation [39] [40]. High LH and FSH levels increase ovarian testosterone production, alter oestrogen production, and causes abnormalities with ovulation. The reduction in inhibin B and progesterone could be linked to the obesity, which can stimulate the Hypothalamic-Pituitary Gonadal axis (HPG) by increasing free estrogen levels because of increased conversion of androgens to estrogens in adipose tissue. Elevated estrogen reduces Gonadotropin Releasing Hormone (GnRH) by the negative response, thus, the affected HPG axis create anovulatory or abnormal cycle and hence lowers the levels of progesterone hormone [40]. This finding is consistent with previous the report by Farah and Zena [41] who reported a significant decrease in inhibin B and progesterone levels in obese women. The elevated prolactin level could be attributed to the fact that hyperprolactinemia negatively influence fertility potential by obstructing the pulsatility of GnRH and thus hindering ovarian function [42]. A high prevalence of obesity has been significantly associated with hyperprolactinaemia, and the nexus between hyperprolactinemia and increased body weigh has been reported.

Furthermore, women with 1˚ infertility have a slightly higher Luteinizing hormone and Follicle Stimulating Hormone levels than the 2˚ infertility women, while estrogen, inhibin B and prolactin levels were slightly higher in the women with 2˚ infertility than 1˚ infertility women. Elevated LH and FSH concentrations are primary features of women with polycysticovarian syndrome [43]. The primary function of luteinizing hormone (LH) is the regulation of production of androgen in the theca interna, while follicle stimulating hormone (FSH) is responsible for the regulation of the growth and maturation of ovarian follicles, and stimulation of the aromatization of androgens to estrogens [44]. The elevated level of Luteinizing Hormone and Follicle Stimulating Hormone observed in the women with primary infertile is indicative of a possible primary ovarian failure and poor pregnancy outcomes [45] [46]. The estrogen level in women with 2˚ infertility was slightly higher than 1˚ infertility women. This could be attributed to obesity, which is connected with sex hormone imbalance and low level of sex hormone-binding globulin (SHBG). The exact cause of infertility among the obese women appears to be the absence of long anovulation due to hyperandrogenism caused by obesity [47] [48].

Obesity has a negative influence on reproductive potential due to its physio-

logical alterations in the Hypothalamic-Pituitary-Ovarian (HPO) axis [21]. Obesity has been reported to cause fluctuations in peripheral steroid sex hormone-thereby making it difficult to manage infertility [22]. In the present study, the percentage of women with primary infertility and secondary infertility who suffered from various gonadal disorders; hypoestrogenisim (32.32% vs 24.54%), Hyperestrogenism (68.01% vs 70.73%), Hypergonadism (7.07% vs 6.48%), Hypergonadotropic (15.82% vs 19.90%), Hypogonadotropic (10.44% vs 15.74%) and amenorrhoea (13.80% vs 10.65%) respectively as shown in (**Table 3**). The study observed that obese women with primary infertility and secondary infertility suffer more from hyperestrogenism 202 (68.01%) and 154 (70.73%) than any other gonadal disorders. The high predominance of hyperestrogenism in obese infertile women could be attributed to the fact that obesity is linked with high estrogen levels, as would be expected from androgen aromatization in adipocytes [48]. It may also be due to a sex hormone imbalance and low levels of sex hormone-binding globulin (SHBG), which can increase the target tissue's exposure, to free estrogen [49].

In addition, the Body Mass Index (BMI) of women with 1˚ infertility suffering from Hypoestrogenism (32.75 kg/mg^2), Hyperestrogenism (36.20 kg/mg^2), Hypergonadism (33.06 kg/mg^2), Hypogonadism (32.45 kg/mg^2), Hypergonadotropic (35.52 kg/m^2) and amenorrhoea (34.83 kg/mg^2) as shown in (**Table 3**). While, the BMI of women with 2˚ infertility suffering from Hypoestrogenism (33.56 kg/mg^2), Hyperestrogenism (37.37 kg/mg^2), Hypergonadism (35.05 kg/mg^2), Hypogonadism (33.17 kg/mg^2), Hypergonadotropic (31.50 kg/m^2) and amenorrhoea (34.83 kg/m^2) as shown in (**Table 3**). This results suggests that the BMI of women with 2˚ infertility is significantly ($p < 0.05$) higher than those with 1˚ infertility. The study also showed that infertile women suffering Hyperestrogenism have higher BMI than any other female gonadal disorder. This could be due to the fact that obese women exhibit defective estrogen receptors, leading to decreased T-estrogen-binding globulin, increased clearance of androgenic hormones, and elevated estrogen production rates, which may respond to the high concentrations of estrogen in obese women.

The results of the current study also revealed that there was a correlation between Body Mass Index (BMI) and infertility hormones as shown in (**Table 4** & **Table 5**). This affirms that obesity is a sign that increases the risk factors of infertility in women. From the result, BMI showed a positive correlation with luteinizing hormone, follicle stimulating hormone, Estrogen, progesterone, and prolactin in women with primary and secondary infertility, while Inhibin B showed a negative correlation with BMI in both primary and secondary infertility. The positive correlation between prolactin and Body Mass Index in infertile women is not yet clear, but it could be due to the stimulation of lipogenesis or to the dysregulation of the dopaminergic tone of the central nervous system [50].

Furthermore, the present study also showed that there is statistically significant positive correlation between BMI and Hypogonadism, Hypogonadotropic

and Amenorrhoea in obese infertility women. This confirms the findings of Yunhui *et al.* [51] and Labban, [52] which reported that BMI is positively associated with Amenorrheoa and Hypogonadism. However, the study observed no correlation between BMI and Hypergonadism and Hypergonadotropic in infertile obese women.

5. Conclusion

In conclusion, the study reviewed that there's a positive correlation between BMI and the hormones of the hypothalamic-pituitary-target organ axis. BMI is a preventable risk factor for infertility and precautionary measures to manage it may be an effective method of reducing the risk of infertility and other associated disorders. Thus, change of lifestyle towards reducing body weight might help in controlling obesity and subsequently infertility for women who are trying to conceive.

Author's Contribution

Both authors contributed to the design of the work. The design and interpretation of the results and review was performed by Prof. Ezeiruaku Ferdinand Chukwuma and Onitsha Enebrayi Nelson. Data acquisition and analysis, and literature review was performed by Onitsha Enebrayi Nelson. Both authors were involved in the statistical interpretation and case analysis. Both authors read and gave final approval of the manuscript for publication.

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Ethical Approval

Ethical approval was given by the ethical and research committee of the University of Port-Harcourt Teaching Hospital (UPTH) Port-Harcourt Rivers State, Niger Delta University Teaching Hospital (NDUTH) Okolobiri, and Federal Medical Centre (FMC), Yenagoa, Bayelsa State.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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