EFFECT OF BODY MASS INDEX ON OVULATION IN NIGERIAN WOMEN WITH POLYCYSTIC OVARIAN SYNDROME UNDERGOING TREATMENT WITH CLOMIPHENE CITRATE: A SONOGRAPHIC STUDY.

E. E EZUGWU[1], A.C. UGWU[1], P.O.MANAFA[2], I.G.EZUGWU[3], M.P.Ogolodom[1]

1. Department of Radiography and Radiological Sciences, Faculty of Health Sciences and Technology, Nnewi Campus Nnamdi Azikiwe University, Anambra State, Nigeria,
2. Department of Medical Laboratory Sciences, Faculty of Health Sciences and Technology, Nnewi Campus Nnamdi Azikiwe University, Anambra State, Nigeria,
3. Prestige Diagnostica LTD, No. 2 Okwudinka Lane, Onitsha, Anambra State, Nigeria

DOI: https://doi.org/10.56293/IJASR.2022.5490

IJASR 2023
VOLUME 6
ISSUE 1 JANUARY - FEBRUARY **ISSN: 2581-7876**

Abstract: Background: Obesity, overweight and elevated BMI are clinical features of PCOS, and between 40-80% of women with PCOS are reported to be overweight or obese. This study aimed to categorize values of patient anthropometric variables such as BMI with change in follicular sizes as determined by sonography following post-CLOMID inducement therapy.

Materials and Methods: This was an experimental cohort study carried out in some selected hospitals in Anambra State, Nigeria, from June 2018 to May 2022.Convenient sampling technique was adopted to select the subjects based on the inclusion criteria, which were women of child bearing age (18 to 45 years) for both groups. Confirmation of patients with PCOS was ascertained with the presence of polycystic ovaries in ultrasound. The ultrasound examinations and anthropometry measurements were carried out on each subject, and data such as BMI, follicular sizes before and post treatment were recorded. The obtained data were subjected to SPSS analysis using both descriptive and inferential statistical tools.

Results: The mean values of the BMI of the participants in the experimental group before and after treatment with clomid were 25.69±5.99 kg/m^2, 25.92±5.55 kg/m^2 respectively, while the mean BMI value for the control group was 23.09±3.41 kg/m^2.There were no statistically significant differences in body mass index, and maximal follicular size in women with failed and successful ovulation in the experimental group before treatment ($p>0.05$). There were statistically significant mean differences in the BMI ($t= 8.75$, $p = 0.001$) and follicular size ($t= 2.04$, $p = 0.04$) of participants in the experimental group after treatment with clomid. There were statistically significant mean differences in the BMI ($t= 2.41$, $p = 0.02$) and follicular size ($t= 4.88$, $p = 0.001$) of participants in the control group after treatment with clomid.

Conclusion: There was higher ovulation failure rate among the overweight and obese subjects in both the experimental and control groups. Also significant increase in mean follicular sizes after clomid inducement in the experimental group was noted. Body mass index has significant negative impacts on ovulation.

Keywords: Body mass index, follicular size, ovaluation, polycystic ovary.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common cause of anovulatory infertility [1,2]. It is a heterogeneous disorder, associated with amenorrhea, infertility, variable levels of hirsutism and obesity in the presence of bilateral enlarged ovaries. The reported prevalence of PCOS ranges from 2.2% to 26% in various countries, depending on the recruitment process of the study population, the criteria used for its definition, and the method used to define each criterion [3]. However two studies in Nigeria reported the prevalence of PCOS as 18.1% and 12.2% respectively, but these studies were based on the Rotterdam criteria [3].

Obesity, overweight and elevated BMI are clinical features of PCOS and between 40-80% of women with PCOS are reported to be overweight or obese [4,5]. Increased accumulation of central fat among women with PCOS was also reported by Dumesic et al [6]. Prolonged exposure to high testosterone level in women with PCOS may modify body fat distribution in this woman [7]. Body mass index (BMI) is a measure of body fat based on height and weight, expressed in Kg/m^2 .Studies have shown that BMI levels correlate with body fat and future health risks [8]. It is an appropriate measure for screening for obesity and its health risks. Elevated body mass index (BMI), increased concentration of serum androgens and insulin are the major features of polycystic ovarian syndrome (PCOS). They cause ovulation failure by suppressing folliculogenesses.

To the best of the authors' knowledge, there is no study that evaluates the role of obesity on follicular growth in PCOS patients following clomid inducement therapy in our setting. This study sought to match or categorized values of patient anthropometric variables such as BMI with change in follicular sizes as determined by sonography following post- CLOMID inducement therapy.

MATERIALS AND METHODS

This was an experimental cohort study carried out in the Obstetrics and Gynecology Department of General Hospital, Onitsha, and other selected hospitals in Anambra State, Nigeria from June 2018 to May 2021. The study population was made up of all fertility challenged women due to polycystic ovarian syndrome, who were undergoing treatment and women with no history of reproductive or thyroid hormone insufficiency at the aforementioned selected hospitals during the period of this study. A total sample size of 100 was determined using the formula for a finite population described by Taro Yemani (1967) as cited by Colditz et al [9] was used as shown bellow.

n= N/1+N (e)^2, Where n= Minimum sample size, N= Population under study, **e**= Error margin, which may have values (010, 0.05, or 0.01), Whereas N= 2000 (The population for the two years under consideration), Using error margin, **e**= 0.10, and **n** = 93.5 and this was increased to 100 in order to increase the validity of the study.

After obtaining ethical approvals for this study from the Human Research and Ethical Committees of both Anambra State Ministry of Health, Awka (MH/AWK/M/321/390) a convenient sampling technique was adopted to select the subjects based on the inclusion criteria, which were women of child bearing age (18 to 45 years) for both groups .The experimental group include only subjects with PCOS whereas the control group include subjects with no history of reproductive and thyroid hormone abnormality. Subjects with reproductive hormone abnormality and history of hysterectomy/oophorectomy were excluded from this study. Confirmation of patients with PCOS was ascertained with the presence of polycystic ovaries in ultrasound [10].

The weight of each subject was measured with a Hana standard recalibrated weighing balance that weighs between 0-120Kg. To do this, the weighing balance was placed on a plane ground and the subjects were made to stand on it in Frank fort's position. Before the measurement, subjects were instructed to remove all heavy objects such as bags and shoes. Height of each subject, in meter was measured using a standard metre rule with subject in Frank fort position and bare footed. The body mass index (BMI) values were later derived from the weight and height measurement with formula of BMI= weight (Kg)/ height (m^2).

The ultrasound examinations were performed by the researchers using standard scanning techniques as described by Sanders [11] on ultrasound scanner (Mindray-DCN3, Mindray Electronic Instrument Company Limited, Jiangsu, China, 2014) with adjustable frequency between 6 -10MHz. Measurement of follicular size was made by taking two orthogonal diameters (d1 and d2) at the largest follicle plane on real-time 2D image of the follicle that will be obtained. This was determined by placing calipers at the inner follicle borders. Each 2D follicular diameter was examined two times consecutively during the examination and the mean follicular diameter obtained. Mean follicular diameter was obtained using the formula, d1+d2/2. The average value from three measurements for each follicle was used for statistical analysis [12].

Statistical analysis was carried out using the Statistical Package for social sciences Version 22.0 (SPSS Inc., Chicago Illionis). Mean distribution for the age, BMI and follicular sizes of the test and control groups were presented in tables. Independent t-test was used to compare the BMI and maximal follicular size between women with polycystic ovary before clomid treatment and healthy control. Chi-square test was used to determining the differences in

distribution of women with polycystic ovary before clomid treatment and healthy control across different categories of body mass index, and maximal follicular size.

RESULTS:

The mean values of the BMI of the participants in the experimental group before and after treatment with clomid were 25.69±5.99 kg/m², 25.92±5.55 kg/m² respectively, while the mean BMI value for the control group was 23.09±3.41 kg/m²(Table 1).

There were statistically significant mean differences in the follicular size across the various BMI classes in the experimental group before (F= 2.094, p= 0.11) and after (F=1.39, p= 0.25) treatment and in the control group (F=2.15, p= 0.10)(Table 2).

There were no statistically significant differences in body mass index, and maximal follicular size in women with failed and successful ovulation in the experimental group before treatment (p>0.05). Nevertheless, those with successful ovulation had significantly lower body mass index (24.66±7.20kg/m²). The mean values of the BMI (30.90±3.14kg/m²) and follicular size (27.91±5.10kg/m²) of those with failed ovulation in the experimental group after treatment were higher than that of those with successful ovulation. There were statistically significant mean differences in the BMI (t= 8.75, p = 0.001) and follicular size (t= 2.04, p = 0.04) of participants in the experimental group after treatment with clomid (Table 3). In the control group, those with failed ovulation had mean BMI and follicular size of 25.64±6.57kg/m² and 30.56±23.74kg/m² respectively. There were statistically significant mean differences in the BMI (t= 2.41, p = 0.02) and follicular size (t= 4.88, p = 0.001) of participants in the control group after treatment with clomid (Table 3).

Table 1. Mean values of body mass index of women with polycystic ovary and healthy control

Variable	Mean±SD		
	Before clomid	**After clomid**	**Control**
Body mass index (kg/m²)	25.69±5.99	25.92±5.55	23.09±3.41

Table 2: Analysis of Variance comparing follicular sizes at ovulation among test (before and after treatment) and control group with different body mass indices

Group	Class	follicular size Mean±SD	F	P
Test (before)	Underweight	25.00	2.094	0.11
`	Normal weight	20.96±8.74		
	Overweight	24.72±8.26		
	Obese	25.88±9.41		
Test (after)	Underweight	27.00	1.39	0.25
`	Normal weight	25.59±4.89		
	Overweight	27.44±4.66		
	Obese	27.68±4.85		
Control	Underweight	25.00	2.15	0.10
`	Normal weight	24.64±4.53		
	Overweight	22.17±3.00		
	Obese	26.80±5.85		

Table 3: Body mass index and maximal follicular size of women with and without polycystic ovary who had successful and failed ovulation

Variable	Mean±SD		T	P
	Failure	Success		
Women with polycystic ovary before clomid treatment				
Body mass index	26.39±4.77	24.66±7.20	1.39	0.17
Max. Follicular size	23.38±10.26	22.59±3.52	0.39	0.70
Women with polycystic ovary after clomid treatment				
Body mass index	30.90±3.14	23.24±4.63	8.75	0.001*
Max. Follicular size	27.91±5.10	25.86±4.59	2.04	0.04*
Control Group				
Body mass index	25.64±6.57	22.84±2.87	2.41	0.02*
Max. Follicular size	30.56±23.74	23.74±3.65	4.88	0.001*

DISCUSSION

Polycystic ovarian syndrome is the most common endocrine disorder responsible for subfertility among the young adult [2]. The prevalence of PCOS is increasing and as high as 15-20[13]. Safe and effective ovulation induction is important for women with WHO group II anovulation and Clomiphene citrate has been used for ovulation induction since 1960s[14]. In this study, women with PCOS had significantly higher BMI than their healthy counterpart (control group). This finding is in harmony with the findings of the studies carried out by Dumesic et al[6], Al-Shattawi et al[15] and Doh et al [16] ,which also reported high BMI among subjects with PCOS. According to Doh et al[16], they hypothesized that PCOS and obesity act synergistically and independently resulting in insulin resistance (IR). In Dumesic et al [6] study, they noted that dual-energy X-ray absorptiometry have revealed increased accumulation of central fat in women with PCOS.

Findings from this study also showed no statistically significant difference in follicular size between individuals across different body mass indices in any of the groups (test group before and after treatment and control group, indicating that BMI had no significant influence whatsoever in the follicular size of the groups. This is further supports a previous work that concluded that oocyte recovery rate from follicles >15mm is unrelated to patient's BMI [17]. Those with successful ovulation had significantly lower BMI in the experimental group and this is also similar with that of the control group in this study. This reduction in BMI in both the women that underwent clomiphene citrate treatment and control group with successful ovulation explains the finding from a previous study that obese women with PCOS are more likely than thin women with PCOS to suffer from anovulation[18]. Popova et al [19], found that lean women with PCOS treated with metformin had menstrual function (55%) and ovulation (45%) restored more often than obese women with PCOS (only one patient (7%) responded to the treatment), P = 0.018. There was no change in BMI and waist circumference in both groups. They concluded that treatment with metformin 1700 mg daily was more effective in lean than in obese women with PCOS. Its efficacy was independent of the initial surrogate markers of resistance to insulin [19].

There were no statistically significant differences in body mass index, and maximal follicular size in women with failed and successful ovulation in the experimental group before treatment ($p>0.05$). Nevertheless, those with successful ovulation had significantly lower body mass index .Those with failed ovulation in the experimental group after treatment had higher BMI than those with successful ovulation in the same group. There were statistically significant mean differences in the BMI and follicular size of participants in the experimental group after treatment with clomid. In the control group, those with failed ovulation had higher mean values of BMI and follicular size when compared with those with successful ovulation in the same group. There were statistically significant mean differences in the BMI and follicular size of participants in the control group after treatment with clomid. This reduced BMI in this present study may necessarily not be due to clomiphene citrate treatment but rather those with lower BMI had successful ovulation after using clomiphene citrate seeing that the control group had successful ovulation with low BMI. This entails successful ovulation could be dependent on low BMI. This is further supported by a previous study where increased body mass index was seen to be associated with ovulatory subfertility and anovulatory infertility [20]. Another study was conducted to compare the ovulation and pregnancy

rates in response to metformin therapy in lean and obese women with PCOS. Comparison between lean and obese women was found to be statistically significant. Metformin monotherapy is very effective in improving the ovulation and pregnancy rates in lean women with PCOS as compared with obese women [21]. Though this present study use clomiphene citrate and not metformin but both clomiphene citrate and metformin are considered first line of treatment for PCOS and sometimes they are used together hence a previous study concluded that overweight women with PCOS are less likely to respond to the pharmacological induction of ovulation [18].

CONCLUSION

There was higher ovulation failure among the overweight and obese subjects in both the experimental and control groups and also significant increase in mean follicular sizes after clomid inducement in the experimental group. Therefore, we concluded that BMI has significant negative impacts on ovulation.

Conflict of interest: None declared among the authors in this study.

Acknowledgement

We most specially thank the head of obstetrics and Gynecology department, general hospital, Onitsha, Dr Ebele Okeke for the support she rendered throughout the period of this project. Also appreciated is the management of Prestige Diagnostica LTD for their great assistance during this project. The technical staff members of both establishments are also immensely appreciated for their commitment of time and energy until the completion of this research work.

REFERENCES

1. Perales-Puchalt A, Legro R.S. Ovulation induction in women with polycystic ovary
2. syndrome Steroids. 2013; 78 (8): 767-772
3. Wafa, Y.A.E.S, Labib, M.M., Fatah, A.G.K.A.E. Role of Letrozole Versus Clomiphene Citrate in Induction of Ovulation in Patients with Polycystic Ovarian Syndrome. Journal of Gynecology & Reproductive Medicine. 2017; 1(1):2-6.
4. Akpata, C.B., Uadia, P.O, Okonofua, F.E. Prevalence of Polycystic Ovary Syndrome in Nigerian Women with Infertility: A Prospective Study of the Three Assessment Criteria. Open Journal of Obstetrics and Gynecology.2018; 8, 1109-1120.
5. Hind, A.B., Laurel, S., May, A.B., Helena, R., Yueqin, Z., and Sergio, O. Polycystic ovary syndrome , body mass index and outcome of assisted reproductive technologies. Reproductive Biomedicine online. 2009; 18(6): 856- 863.
6. Sussan S. Obesity and polycystic ovary syndrome. Obese management. 2007; 3(2): 69-73.
7. Dumesic, D.A., Akopians, A. L., Madrigal, V. K., Ramirez, E., Margolis, D. J., Sarma, M. K.,Thomas, A. M., Grogan, T. R., Haykal, R., Schooler, T. A., Okeya, B. L., Abbott, D. H. and Chazenbalk, G. D. Hyperandrogenism Accompanies Increased Intra-Abdominal Fat Storage in Normal Weight Polycystic Ovary Syndrome Women, The Journal of Clinical Endocrinology & Metabolism, 2016; 101 (11): 4178–4188, https://doi.org/10.1210/jc.2016-2586.
8. Sam, S. Obesity and polycystic ovary syndrome. Obesity Management. 2007; 3 (2): 69-73
9. Lewis, C., McTigur, K. Burke, L., Poiviev, P., Eckel, R., Howard, B. Mortality, health outcomes and body mass outcome in the overweight range: A Science Advisory from the American Heart Association. 2009; 119: 201-203.
10. Colditz, G.A., Brewer T.F., Berkey C.S. Efficacy of BCG Vaccine in prevention of Tuberculosis. Meta – analysis of the published data. Journal of American Medical Association. 1994; 271 (9): 698-702.
11. Rotterdam ESHRE/ASHRM-Sponsored PCOS consensus workshop group Reviewed consensus on Diagnostic criteriaand long -term health risk related to polycystic ovary syndrome. Fertility and Sterility.2004; 81:19-25.
12. Sander RC, Winter TC. Clinical Sonography: A Practical Guide (Clinical Sonography: A
13. Practical Guide (Sanders)) 4th edition Lippincott Williams & Wilkins; 2006.
14. Ping, P, Xiaoli, C., Yu, L., Qingxue, Z., Xiaomiao, Z., Madafeitom, M.A., Bodombossou, D, Dongzi ,Y. PLOS . 2013. https://doi.org/10.1371/journal.pone.0077095

15. Moran, L. and Teede, H. Metabolic features of the reproductive phenotypes of polycystic ovary syndrome. Human Reproduction Update. 2009; 15(4):477-88.
16. Zeba, D., Biswas, R., Fatema, K., Khair, M. A., Zesmin, F. and Sharifa, J. Letrozole or Clomiphene Citrate for Induction of Ovulation in Patients with Polycystic Ovarian Syndrome: A Prospective Randomized Trial. Faridpur Medical College Journal 2018; 13 (2): 78-81.
17. Al-Shattawi SSM, Al-Jumili, EF, Al-Azzam MA. The effect of hypercytokinemia in the Pathogenesis of Polycystic Ovary Syndrome in Iraqi Women. Indian Journal of Public Health Research and Development. 2019;10(2):768DOI: 10.5958/0976-5506.2019.00387.5
18. Doh E, Mbanya A, Kemfang-Ngowa JD, Dohbit S, Tchana-Sinou M, Foumane P, et al. The relationship between adiposity and insulin sensitivity in african women living with the polycystic ovarian syndrome: a clamp study. *Int J Endocrinol.* 2016:9201701. doi: 10.1155/2016/9201701
19. Orvieto, R., Mohr-Sasson, A., Aizer, A, and Nuhum, R.. Do follicles of obese patients yield competent oocytes/embryos.Gynecology and Obsterics Investigation.2020; 85(3): 1-4.
20. Al-Azemi M, Omu FE, Omu AE. The effect of obesity on the outcome of infertility management in women with polycystic ovary syndrome. Archives of gynecology and obstetrics. 2004; 270:205–210
21. Popova, P.V., Ivanova, L.I., Karonova, T.L., Grineva, E.N. Ovulation induction by metformin in lean and obese women with polycystic ovary syndrome. Endocrinology. 2011; 26: p90
22. Pandey, S., Pandey, S., Maheshwari, A. and Bhattacharya, S. The impact of femaleobesity on the outcome of fertility treatment. Journal of Human Reproductive Science. 2020; 3 (2): 62-67
23. Kumari, A.S., Haq, A., Jayasundaram, R., Abdel.Wareh, L, O., Al HAIJA, S.A., Alvares, M., Metformin monotherapy in lean women with polycystic ovary syndrome. ReproductionBiomedicine Online. 2005; 10:100-4