



CODEN [USA]: IAJPB

ISSN: 2349-7750

## INDO AMERICAN JOURNAL OF PHARMACEUTICAL SCIENCES

<http://doi.org/10.5281/zenodo.2556157>
Available online at: <http://www.iajps.com>

Research Article

### COMPARISON OF METFORMIN EFFECTIVENESS AMONG OBESE AND NON-OBESE WOMEN DIAGNOSED WITH PCOS (POLYCYSTIC OVARIAN SYNDROME)

<sup>1</sup>Dr Muhammad Nadeem Butt, <sup>2</sup>Dr Sabir Hussain, <sup>3</sup>Dr. Yasaan Saaqib<sup>1</sup>House Officer, Jinnah Hospital Lahore, <sup>2</sup>Assistant Professor, (Medicine) Ghazi Khan Medical College DGK, <sup>3</sup>House Officer DHQ Teaching Hospital Gujranwala

#### Abstract

**Objective:** This research aimed to evaluate the effectiveness of metformin for PCOS (Polycystic Ovarian Syndrome) second line monotherapy of the patients.

**Methodology:** This case series was conducted on a total of one hundred patients at Jinnah Hospital, Lahore (February to December 2017). We calculated the research sample with Confidence Interval (95%), expected metformin efficacy (29%) and freedom degree (7%) [6]. We included confirmed PCOS patients with clomiphene citrate treatment and any BMI range. Whereas, we did not include the patients with an intake of other than clomiphene citrate and any other known systemic disease. Physical examination history and second menstrual cycle hormonal profile (serum LH, FSH, testosterone, Prolactin and mid-luteal phase progesterone) along with ultrasound of pelvis were also carried out for every patient. Patients started receiving monotherapy of Metformin through an oral dose of (500 mg) per day for a period of one week and for another week the intake of the dose was (1500 mg) every day for a period of six months by non-obese females. We maintained a dose of (200 mg) among two groups obese female groups. During follow up visits after three weeks the researcher assessed the level of Serum Progesterone. Research documented the ovulation after a period of six months of metformin administration. Metformin was effective in the ovulation was at mid-luteal phase on the 21<sup>st</sup> day along with an indication of ovulation having progesterone more than (25 ng/ml). We documented every outcome on a designated proforma and statistical analysis with the help of SPSS software.

**Results:** The research was carried out on one hundred patients who were selected in the age bracket of (20 – 40) years with an average age of (29.47 ± 6.23) years. Further distribution of age bracket was such as 57 patients were in the age bracket of (20 – 30) years and 43 patients were in the age bracket of (31 – 40) years. Metformin effectiveness in PCOS was reported in 63 women: whereas, 37 women reported no effect of metformin. Metformin effectiveness in terms of BMI was such that 12 out of 32 patients were obese (37.5%) and 51 out of 68 patients were non-obese (75%).

**Conclusion:** We conclude that PCOS management is effectively possible by metformin; however, higher efficacy is significant in the PCOS non-obese women.

**Keywords:** Metformin, PCOS (Polycystic Ovarian Syndrome), Effectiveness, Obese and Non-Obese.

#### Corresponding author:

Muhammad Nadeem Butt,

House Officer, Jinnah Hospital Lahore.

QR code



Please cite this article in press Muhammad Nadeem Butt et al., *Comparison Of Metformin Effectiveness Among Obese And Non-Obese Women Diagnosed With Pcos (Polycystic Ovarian Syndrome)*, Indo Am. J. P. Sci, 2019; 06(02).

## INTRODUCTION:

An onset of PCOS is responsible for ovulation, hirsutism and infertility among the females who are at the age of reproductivity [1]. The primary features of PCOS include increased ovarian androgens production and hypothalamic dysfunction. The PCOS occurrence varies in the range of 4% – 23% of the patients [2].

It is a fact that the insulin resistance mechanism is not fully understood. Adipokines alteration may also encompass insulin resistance in obese patients. This mechanism is also not clear in the patients with normal BMI range; however, there is a possibility of the presence of few non-functioning adipose cells [3]. The other possibilities may also include non-functioning beta cells, deficiency of insulin action, hepatic insulin clearance, increased secretion of insulin against diet stimuli [4].

In Pakistan, the occurrence of PCOS is 17.6% and the obesity rate is also increased with a proportion of (68.5%) and hyperinsulinemia occurrence as (59%). BMI was normal in fourteen percent of the cases, 29.7% cases with BMI (30) and 28.8% cases with BMI in the bracket of (30 – 35) [5]. According to the definition of WHO, overweight and obesity refers to the respective weight of ( $> 25 \text{ kg/m}^2$ ) and ( $> 30 \text{ kg/m}^2$ ) [6]. It is also conjectured that the elevated rate of BMI disturbs the insulin resistance among PCOS patients [7]. Metformin is one of the 2<sup>nd</sup> generation organic compound (biguanide). It aids in the glucose transportation activation and also facilitates the glucose passage into hepatic cells and muscles. Thereby, it also decreases the peripheral insulin resistance and decreases the serum glucose level; however, it does not stimulate the insulin release. It also not contributes to the onset of hypoglycemia when administrated without any other intervention [8].

Previous research studies report on the involvement of 15 out of 17 non-obese women (88%) and 5 out of 17 obese women (29%) ovulated while comparing the significant statistical differences [10].

However, our research aimed to evaluate the effectiveness of metformin for PCOS (Polycystic Ovarian Syndrome) second line monotherapy of the patients. These outcomes will also help the patients of rural areas where PCOS management is not possible due to the non-availability of laparoscopy.

## MATERIAL AND METHODS:

This case series was conducted on a total of one hundred patients at Jinnah Hospital, Lahore (February to December 2017). We calculated the research sample with Confidence Interval (95%), expected metformin efficacy (29%) and freedom degree (7%) [6]. We included confirmed PCOS patients with clomiphene citrate treatment and any BMI range. Whereas, we did not include the patients with an intake of other than clomiphene citrate and any other known systemic disease. Physical examination history and second menstrual cycle hormonal profile (serum LH, FSH, testosterone, Prolactin and mid-luteal phase progesterone) along with ultrasound of pelvis were also carried out for every patient. Patients started receiving monotherapy of Metformin through an oral dose of (500 mg) per day for a period of one week and for another week the intake of the dose was (1500 mg) every day for a period of six months by non-obese females. We maintained a dose of (200 mg) among two groups obese female groups. During follow up visits after three weeks the researcher assessed the level of Serum Progesterone. Research documented the ovulation after a period of six months of metformin administration. Metformin was effective in the ovulation was at mid-luteal phase on the 21<sup>st</sup> day along with an indication of ovulation having progesterone more than (25 mg/ml). We documented every outcome on a designated proforma and statistical analysis with the help of SPSS software.

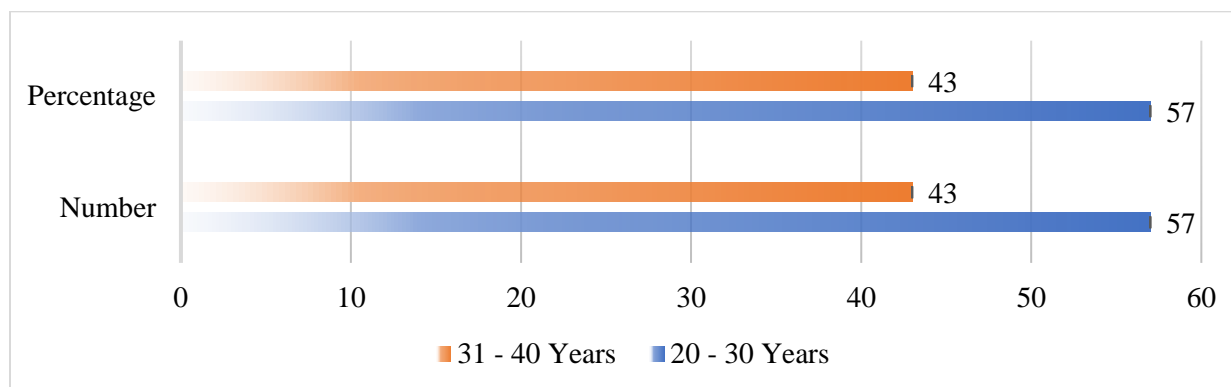
## RESULTS:

The research was carried out on one hundred patients who were selected in the age bracket of (20 – 40) years with an average age of ( $29.47 \pm 6.23$ ) years. Further distribution of age bracket was such as 57 patients were in the age bracket of (20 – 30) years and 43 patients were in the age bracket of (31 – 40) years as shown in Table – I. Metformin effectiveness in PCOS was reported in 63 women: whereas, 37 women reported no effect of metformin as shown in Table – II. Metformin effectiveness in terms of BMI was such that 12 out of 32 patients were obese (37.5%) and 51 out of 68 patients were non-obese (75%) as shown in Table – III.

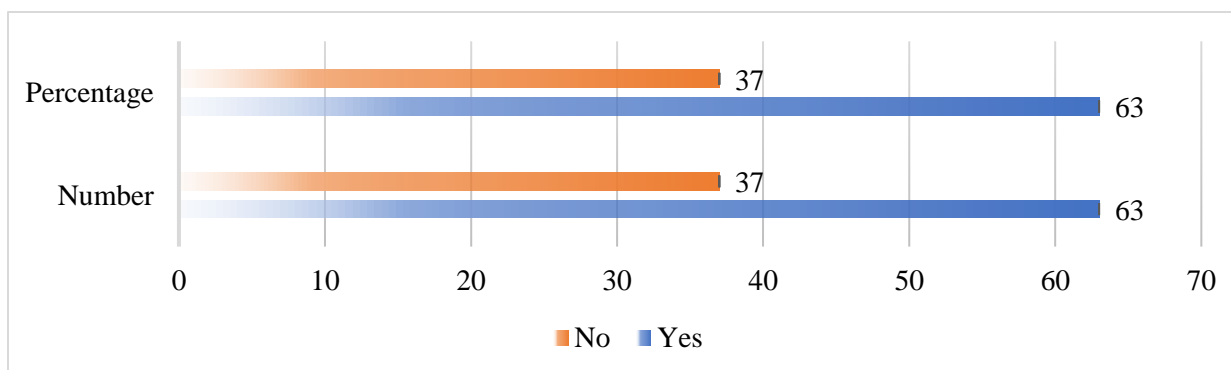
Detailed outcomes are available in the given tabular and graphical presentation below (Table – I, II and III).

**Table – I: Age Distribution**

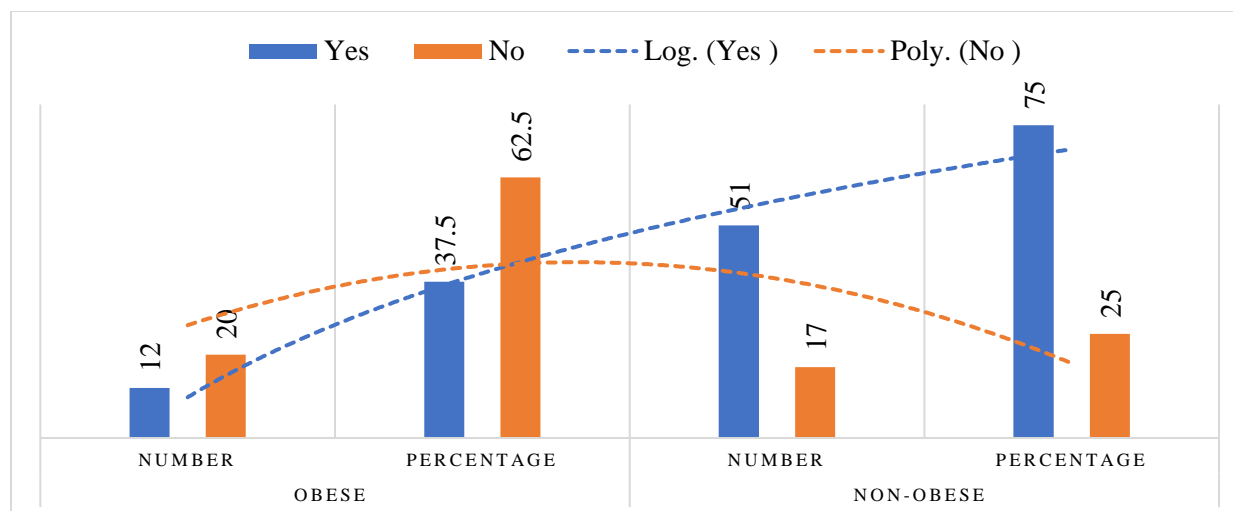
Age	Number	Percentage
20 – 30 Years	57	57
31 – 40 Years	43	43

**Table – II:** Metformin Efficacy

Efficacy	Number	Percentage
Yes	63	63
No	37	37

**Table – III:** Comparison of Obese and Non-Obese Patients

Efficacy	Obese		Non-obese	
	Number	Percentage	Number	Percentage
Yes	12	37.5	51	75
No	20	62.5	17	25



### DISCUSSION:

Various authors have made their efforts in the investigation of metformin effectiveness on females diagnosed with PCOS. Metformin effectively reduces the levels of testosterone and it also regularizes the menstrual. It also improves fertility within a few weeks of intake along with weight loss. Although, metformin is not a weight rearing agent even than it reduces the weight of the females when utilized. Another trial conducted on placebo revealed better effects of metformin over placebos as it induces ovulation among PCOS affected women. Metformin efficacy has been shown in the obese women; whereas, women with normal weight are less benefitted from metformin effects.

In this research, patients started receiving monotherapy of Metformin through an oral dose of (500 mg) per day for a period of one week and for another week the intake of the dose was (1500 mg) every day for a period of six months by non-obese females. We maintained a dose of (200 mg) among two groups obese female groups. In order to reduce the adverse gastrointestinal effects, we advised women to take the dose before taking meals with a gradual increase in the quantity of the dose. An author confirmed that an increased dose of (850 mg) thrice a day in obese women does not produce the required outcomes with related benefits [9].

Our research aimed to evaluate the effectiveness of metformin for PCOS (Polycystic Ovarian Syndrome) second line monotherapy of the patients. These outcomes will also help the patients of rural areas where PCOS management is not possible due to the non-availability of laparoscopy.

The research was carried out on one hundred patients who were selected in the age bracket of (20 – 40)

years with an average age of  $(29.47 \pm 6.23)$  years. Further distribution of age bracket was such as 57 patients were in the age bracket of (20 – 30) years and 43 patients were in the age bracket of (31 – 40) years. Metformin effectiveness in PCOS was reported in 63 women: whereas, 37 women reported no effect of metformin. Metformin effectiveness in terms of BMI was such that 12 out of 32 patients were obese (37.5%) and 51 out of 68 patients were non-obese (75%). Similar outcomes are also presented in a research conducted by Kumari AS, according to her outcomes 15 out of 17 non-obese women (88%) ovulated and 5 out of 17 obese women (29%) ovulated [10]. According to the outcomes presented by Tan S et al. 59% of non-obese PCOS affected women gained regularity in the menstrual cycle than 50% obese PCOS affected women [11]. Few other authors wither failed to establish any relation or found no difference for insulin resistance among obese and non-obese women [12 – 15]. It is clear that PCOS aggravates with an onset of obesity and treatment also reduces the weight of the women [11, 16]. Another author also reported improvement in the menstrual cycle, enhanced ovulation frequency and endocrine profile among PCOS affected women [17]. It also reduces the metabolic syndrome and CVD risk among patients. Metformin also reduces the hunger in the course of hypoglycemia and weight loss is also common which reduces moderately [18]. These outcomes are not in agreement with the outcomes of this particular research.

Cynthia R reported the effectiveness of metformin among overweight and normal weight obese women; furthermore, it is also effective for non-obese T2DM patients [19].

**CONCLUSION:**

We conclude that PCOS management is effectively possible by metformin; however, higher efficacy is significant in the PCOS non-obese women.

**REFERENCES:**

1. Vrbikova J, Cibula D, Dvorakova K, Stanicka S, Sindelka G, Hill M, Fanta M, Vondra K, Skrha J. Insulin sensitivity in women with polycystic ovary syndrome. *J Clin Endocrinol Metab* 2004; 89:2942–5.
2. Vanky E, Kjøtrod S, Salvesen KA, Romundstad P, Moen MH, Carlsen SM. Clinical, biochemical and ultrasonographic characteristics of Scandinavian women with PCOS. *Acta Obstet Gynecol Scand* 2004; 83:482–6.
3. Crosignani PG, Colombo M, Vegetti W, Somigliana E, Gessati A, Ragni G. Overweight and obese anovulatory patients with polycystic ovaries: parallel improvements in anthropometric indices, ovarian physiology and fertility rate induced by diet. *Hum Reprod* 2003; 18:1928–32.
4. Schultes B, Oltmanns KM, Kern W, Fehm HL, Born J, Peters A. Modulation of hunger by plasma glucose and metformin. *J Clin Endocrinol Metab* 2003; 88:1133–41.
5. Tan S, Hahn S, Benson S, Dietz T, Lahner H, Moeller LC, Schmidt M, Elsenbruch S, Kimmig R, Mann K, Janssen O E. Metformin improves polycystic ovary syndrome symptoms irrespective of pre-treatment insulin resistance. *Eur J Endo* 2007; 157:669-76.
6. Cynthia R, Lynda M, Molyneaux RN, Maria I, Stephen M, Twigg MD. Long-Term Efficacy of Metformin Therapy in Nonobese Individuals with Type 2 diabetes. *Diabetes Care* 2006; 29:2361–4.
7. Vahratian A. Prevalence of overweight and obesity among women of childbearing age. *Matern Child Health J*.2009;13(2):268-73.
8. Lord J, Thomas R, Fox B, Acharya U, Wilkin T. The effect of metformin on fat distribution and the metabolic syndrome in women with polycystic ovary syndrome – a randomized, double-blind, placebo-controlled trial. *BJOG*.2006;113:817-24.
9. ASRM Practice Committee. Use of insulin-sensitizing agents in the treatment of polycystic ovary syndrome. *Fertil Steril*2008;90(Suppl 3): S69-S73.
10. Harborne L, Fleming R. A randomized study comparing dose of metformin in obese women with polycystic ovary syndrome. *Fertil Steril*2002;78 Suppl 1:34.
11. Kumari AS, Haq A, Javasundaram R, Abdel-Wareth LO, Haija SA. Metformin monotherapy in lean women with polycystic ovary syndrome. *Reprod BiomedOnline*.2005;10(1):100-4.
12. Dunaif A, Segal KR, Futterweit W, Dobrjansky A. Profound peripheral insulin resistance, independent of obesity, in polycystic ovary syndrome. *Diabetes* 1989; 38:1165–74.
13. Ovesen P, Møller J, Ingerslev HJ, Jørgensen JO, Mengel A, Schmitz O, Alberti KG, Møller N. Normal basal and insulin-stimulated fuel metabolism in lean women with the polycystic ovary syndrome. *J Clin Endocrinol Metab* 1993; 77:1636–40.
14. Dale PO, Tanbo T, Vaaler S A, Byholm T. Body weight, hyperinsulinemia, and gonadotropin levels in the polycystic ovary syndrome: evidence of two distinct populations. *Fertil Steril* 1992; 58:487–91.
15. Haq F, Khalid R, Nuru T, Rizvi J. “Does continuous use of Metformin throughout pregnancy improve pregnancy outcome in women with polycystic ovarian syndrome? *Obstet Gynecol Res*. 2008;34(5):832-7.
16. Khan U, Gibson E. Polycystic Ovary Syndrome in Adolescents. *J Pediatr Adolesc Gynecol* 2007; 20:101-4.
17. Carmina E, Orio F, Palomba S. Evidence for altered adipocyte function in polycystic ovary syndrome. *Eur J Endocrinol*. 2005; 152:389-94.
18. Ehrmann DA, Liljenquist DR, Kasza K. Prevalence and predictors of the metabolic syndrome in women with polycystic ovary syndrome.
19. Haq F, Aftab O, Rizvi J. Clinical, biochemical and ultrasonographic features of infertile women with the polycystic ovarian syndrome. *J Coll Phys Surg Pak*. 2007;17(2):76-80.