Vol 4 | Issue 2 | 2014 | 119-122.

e-ISSN 2248 – 9142
print-ISSN 2248 – 9134

International Journal of
Current Pharmaceutical & Clinical Research

www.ijcpcr.com

# USAGE OF METFORMIN IN POLYCYSTIC OVARIAN DISEASE IN A TERTIARY CARE CENTER

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**ABSTRACT**

The basic etiology behind the anovulation associated with PCOS is mainly insulin resistance and hyperinsulinemia. The strong association between hyperinsulinemia and anovulation would suggest that a reduction of insulin concentrations could be of great importance. Weight loss for the obese can reverse this situation as mentioned above but for those who fail to lose weight or are of normal weight but hyperinsulinemic, an insulin sensitizing agent such as Metformin is indicated. So this study was aimed to find out the usage of Metformin in PCOD and its outcome. A descriptive study was planned out. The protocol was approved by Institutional Human Ethics Committee. 100 was the estimated sample size. All outpatients who were taking Metformin for PCOD were included. The data was collected retrospectively. Details on marriage, usage of Metformin and its outcome and usage of concurrent medications were recorded using case record form. The collected data was analysed statistically. Metformin was widely used drug for PCOD. It has induced fertility in24.4% of women with PCOD and 50% of Clomiphene resistant patients. It has induced follicular maturation and reduced size of cysts in 36.6% of married women and 55.6% of unmarried women. No adverse reactions were recorded for the use of Metformin. So it is safe drug and has no reports on teratogenicity.

**Key words:** Metformin, PCOD/PCOS, Outcome, Tertiary care center.

## INTRODUCTION

World health Organisation has defined infertility as the inability to achieve pregnancy after one year of unprotected sexual intercourse. Hanostia reports infertility is a disease. Infertility problem can result in dissolution of marriages. Infertility is automatically assigned to be the women's fault in most societies In India about 10 million couples in the age group 18-40 years of age are infertile. 70-80% can be treated with routine treatment (The New Indian Express, August 2000). The most common cause of infertility among women is polycystic ovarian disease/syndrome (PCOD/PCOS). PCOS is a hormonal disorder characterized by excessive androgen production which is the most common cause of anovulation leading to infertility. Although women who have PCOS can experience any varieties of symptoms, the classic ones are anovulation, obesity, and hirsute.

The basic etiology behind the anovulation associated with PCOS is mainly insulin resistance and hyperinsulinemia [1,2]. The strong association between hyperinsulinemia and anovulation would suggest that a reduction of insulin concentrations could be of great importance. Weight loss for the obese can reverse this situation as mentioned above but for those who fail to lose weight or are of normal weight but hyperinsulinemic, an insulin sensitizing agent such as Metformin is indicated. However the indications for the administration of Metformin to anovulatory women with PCOS in anovulation induction program have widened as it seems to

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be difficult to predict which individuals will respond well this medication [2]. Metformin is an oral biguanide, well established for the treatment of hyperglycemia that does not cause hypoglycemia in normoglycaemic patients. The sum total of its actions is to decrease insulin levels as a consequence lowering circulating total and free androgen levels with a resulting improvement of the clinical sequalae of hyperandrogenism.

There are now large numbers of studies published on the effect of Metformin in a dose of 1500-2550 mg/day in women with PCOS. The vast majority of these studies have demonstrated a significant improvement in insulin concentrations, insulin sensitivity and serum androgen concentrations accompanied by decreased Luteinizing Hormone (LH) [3]. The restoration of regular menstrual cycles by Metformin has been reported in large majority of patients and ovulation has occurred in 78%-96% of patients [4,5]. Clomiphene resistant infertile patients have well responded with Metformin compared to placebo [6-8]. There were more mature oocytes, embryos cleaved, increased fertilization and clinical pregnancy rates in the Metformin group [9]. These later would seem to confirm that both obese and insulin resistant women with PCOS have much greater tendency to a multifollicular response. Metformin lowers insulin, testosterone and glucose levels both in obese and nonobese patients [10,11]. The evidence so far is encouraging concerning the efficacy and safety of Metformin as a single agent or in combination with Clomiphene citrate or gonadotropins for induction of ovulation [12]. Not only Metformin seem to be safe when continued throughout pregnancy but also decrease the high miscarriage rate usually associated with PCOS [13,14]. Metformin reduces risk of gestational diabetes in PCOS [15]. So this study was aimed to find out the usage of Metformin in PCOD and its outcome.

## METHODOLOGY

A descriptive study was planned out. The protocol was approved by Institutional Human Ethics Committee. 100 was the estimated sample size. All outpatients who were taking Metformin for PCOD were included. The data was collected retrospectively. Details on marriage, usage of Metformin and its outcome and usage of concurrent medications were recorded using case record form. Personal details like, name, Date of Birth, telephone number and address were not taken. Patient details were kept confidential. The collected data was analysed statistically.

## RESULTS

- Out 110 patients using Metformin 10 patients were Clomiphene resistant.
- Out of these PCOD patients 82% were married and 18% were unmarried ( Figure 1).
- Out of the married PCOD patients 24.4% became pregnant, 36.6% attained follicular maturation but not became pregnant and 39 % patients were lost to follow up (Figure 2)
- Among unmarried PCODs 55.6% attained follicular maturation and 44.4% were lost to follow up (Figure 3)
- Among Clomiphene resistant patients, when Metformin was added 50% became pregnant and 50% were lost to follow up ( Figure 4)
- It was also found that 40.9% have received Metformin alone, 27.2% have received it in combination with progestin, 22.7% have received in combination with Mefenamic acid and remaining 9.2% have received Metformin in combination with Mefenamic acid and Progestin (Figure 5)
- No adverse reactions were recorded for the use of Metformin.

**Figure 1: Usage of Metformin in PCOD in %**

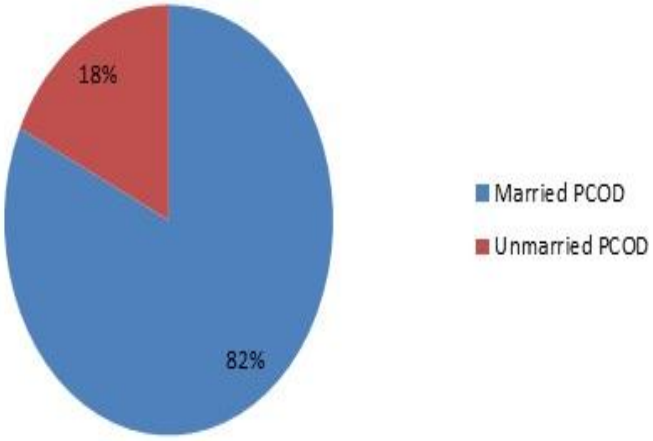



**Figure 2: Outcome of Metformin therapy in married PCOD in %**

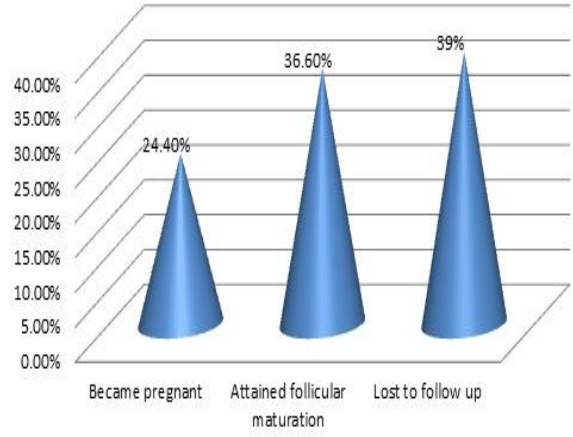


**Figure 3: Outcome of Metformin therapy among unmarried PCOD in %**

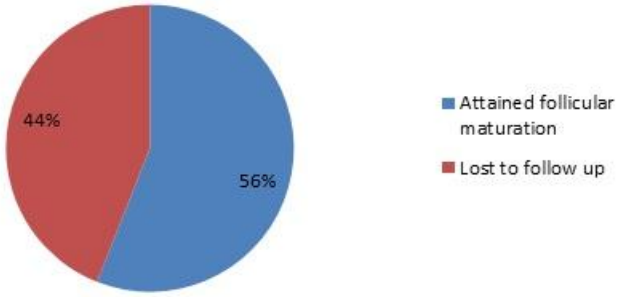



**Figure 4: Outcome of Metformin theraphy in clomiphene resistant PCOD in %**

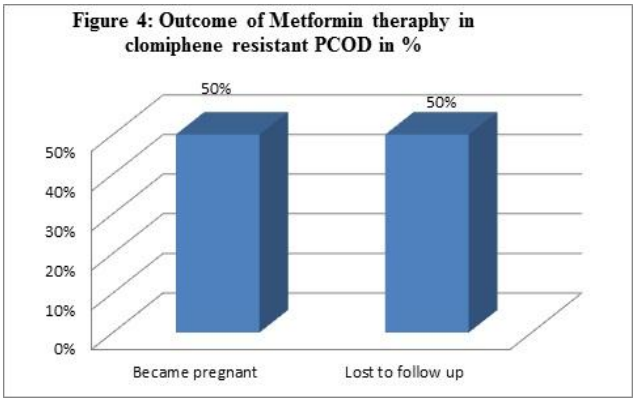
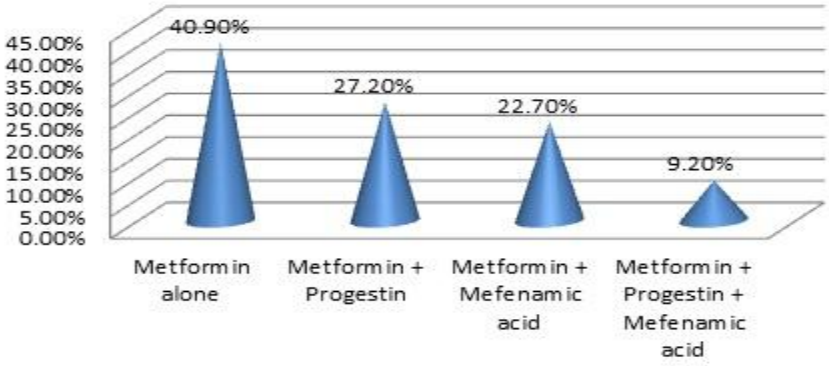



**Figure 5: Pattern of usage of Metformin with other drugs in %**




**DISCUSSIONS**

- Metformin was prescribed to 10 patients who were Clomiphene resistant. They were diagnosed as primary infertility. Since Clomiphene can be given only for three cycles, those who were not became pregnant were given Metformin.
- Out of the married PCOD patients 24.4% became pregnant, 36.6% attained follicular maturation but not became pregnant and 39 % patients were lost to follow up (Figure 2). This shows that Follicular maturation has taken place in almost all patients who have been treated with Metformin. 39% of patients were lost to follow up. It is quiet common in PCOD patients since they will be consulting many physicians.
- Among unmarried PCODs 55.6% attained follicular maturation and 44.4% were lost to follow up (Figure 3). Once again it was proved that almost all patients who have taken Metformin have attained follicular maturation and regularization of menstruation.
- Among Clomiphene resistant patients, when Metformin was added 50% became pregnant and 50% were lost to follow up (Figure 4). This also proves the efficacy of Metformin in infertility. 50% were lost to follow up which was also quiet common scenario in infertility patients. They will be consulting multiple doctors to become pregnant early.
- It was also found that 40.9% have received Metformin alone, 27.2% have received it in combination with progestin, 22.7% have received in combination with Mefenamic acid and remaining 9.2% have received Metformin in combination with Mefenamic acid and Progestin (Figure 5). Progestin will be commonly added to Metformin if the cycles are irregular. Mefenamic acid is given for patients having intense abdominal pain during menstruation.
- No adverse reactions were recorded for the use of Metformin. So it is safe drug and has no reports on teratogenicity.

**CONCLUSION**

- Metformin was widely used drug for PCOD.
- It has induced fertility in24.4% of women with PCOD and 50% of Clomiphene resistant patients.
- It has induced follicular maturation and reduced size of cysts in 36.6% of married women and 55.6% of unmarried women.
- No adverse reactions were recorded for the use of Metformin. So it is safe drug and has no reports on teratogenicity.

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