



POLYCYSTIC OVARIAN DISEASE; IMPACT OF METFORMIN ON FERTILITY IN WOMEN

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ABSTRACT... Objectives: To determine the role of metformin in correcting the irregularity of menstrual periods and infertility due to PCO. **Study Design:** Descriptive observational study. **Setting:** Gynecology Department of PUMHS Nawabshah. **Period:** 4th February 2010 up to November 2011. **Patients and methods:** Total 329 patients had selected in this series, based on presence of PCO on ultrasound with 2 or extra following criteria like oligomenorrhea, hirsutism, hyperandrogenism and reversed FSH: LH ratio. Other endocrinal reasons of female infertility as Cushing syndrome, congenital adrenal hyperplasia, hyperprolactinemia and cases thyroid disorder had excluded. After detailed history, Metformin was started with dose of 250mg once a day initially then gradually adjusted to 500mg TD. Weight decreased was encouraged with diet and the exercise. Cases assessed after six months for checking regularity of their menstrual cycle, fertility and the BMI change. Cases those not be success to conceive following 6 months, than the ongoing criteria of clomiphene. Women those failed to conceive after uses of clomiphene citrate, than metformin alone was sustained and fertility had re evaluated on end of 1 year. **Results:** 329 cases had selected. Commonest menstrual irregularity was oligomenorrhea with hypo menorrhoea which is seen in 46% of patients. After six months of metformin treatment 82% cases assessed improvement of menstrual cycle, while 13% still have oligomenorrhea. Results found significant ($P < 0.001$). BMI of all study patients was compared prior and then treatment and significant results were found ($P < 0.001$). After six months for fertility analysis, complete data was available from 117 patients only. Overall fertility rate was 91.1%. **Conclusion:** Metformin is successful treatment of cases having PCOS.

Key words: Polycystic ovaries, fertility, metformin, irregularity of menstrual periods.

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INTRODUCTION

Polycystic ovarian disorder initially described by Stein and Leventhal in 1905, is very important endocrine issue in women with reproductive age.¹ PCO is described by an ovulation, hyperandrogenism and infertility with clinical indications of unpredictable menstrual cycles, acne and hirsutism. Rotterdam symptomatic criteria have incorporated the occurrence of two out of three signs for the finding of PCOS i.e. infrequent or missing ovulation, clinical and/ or biochemical hyperandrogenism and/ or PCO on ultrasound.^{2,3} This disorder, an intricate issue with numerous segments, including conceptive, metabolic and cardiovascular appearances has long term suggestions for the complete duration

of the life.⁴ Typical ovulatory system which incorporates choice of an ovarian follicle which develops in light of suitable secretion of FSH gets to be dominant and ovulates, gets troubled in women having PCOS because of androgens overabundance and hyperestrogenism. Ovarian overproduction of androgen is because of hyperinsulinism and elevated level of the insulin is perceived as imperative highlights of PCOS. Extreme secretion of leptin likewise has been connected with PCOS.⁵ The occurrence of PCOS among youths is assessed to be 11-26 %, ⁶ and around 50 % cases are overweight. Pathophysiology of the PCOS is still indeterminate, while there is proof that both hereditary and environmental variables may assume a part, resulting

ovarian hyperandrogenism and impeded insulin sensitivity.⁷ Above 50% of PCOS cases have the metabolic disorder, including resistance of the insulin, obesity and dyslipidemia.⁸ Even though PCOS is a typical issue, the determination may be overlooked during youthfulness, as unpredictable menses with an ovulatory cycles, acne and obesity are common in women.

Metformin, is the most generally utilized medicine in management for type 2 diabetes around the world. It's essential activity is to restrain hepatic glucose creation, however it additionally expands the affectability of peripheral tissues to insulin. The increment in insulin affectability, which adds to the viability of metformin in the treatment of diabetes, has likewise been indicated in non diabetic ladies with the polycystic ovary syndrome.⁹ In women with the disorder, prolonged treatment with metformin may expand ovulation, enhance menstrual cyclicity, and decrease the level of androgen.¹⁰ Insulin bringing down treatments, for example, metformin can acquire change insulin resistance and ovarian hypergonadism. The purpose of our study was to see role of metformin in correcting the irregularity of menstrual periods and infertility due to PCO.

MATERIAL & METHODS

Descriptive study had conducted at PUMHS Nawabshah from 4th Feb. 2010 up to November 2011 in gynae department. 329 cases were selected. Inclusion criteria were based on presence of PCO on ultrasound with 2 or extra of following criteria as oligomenorrhea, hirsutism, hyperandrogenism and reversed FSH: LH ratio. Other endocrinal reasons of female infertility including Cushing syndrome, congenital adrenal hyperplasia, hyperprolactinemia and thyroid disorder had excluded. Tubal patency and semen analysis was also confirmed. Demographic data and detailed history was noted on self made proforma. Detailed history regarding menstrual cycle, past obstetric, drug usage was also noted. Point by point examination was completed in all cases along with BMI. Relevant investigations were carried out and metformin was started with dose of 250mg once a day initially then gradually adjusted to 500mg 3 per day. Weight decrease

had encouraged by diet and the exercise. Cases were evaluated after six months for checking their menstrual cycle regularity, fertility and change in BMI. Cases those not be success to conceive following 6 months, than clomiphene citrate according to procedure. Women who failed to conceived after clomiphene citrate, than metformin alone was sustained and fertility had re evaluated on end of 1 year. All information was entered and analyzed on SPSS 17.0 version. Chi-square test and paired t test used where appropriate.

RESULTS

Total 329 women integrated in this series. Commonest menstrual irregularity was oligomenorrhea with hypo menorrhea found in 46% cases, followed by oligomenorrhea in 23.7% cases. After six months of metformin treatment 82% cases had gated correction of menstrual cycle, while 13% still have oligomenorrhea. A significant difference found ($P < 0.001$) (Table-I).

BMI of all study cases was compared previously and then the treatment and results found significant ($P < 0.001$) (Table-I).

After six months for fertility analysis, complete data was available from 117 patients only. After six months on only metformin, 53% cases had conceived, while 21.1% cases conceived after addition of clomiphene citrate, 17% patients conceived after 1 year while 15.3% patients had failed to conceive ($P < 0.001$). Overall fertility rate was 91.1% (Table-I).

DISCUSSION

Results of our study show that metformin improves the menstrual cycle irregularities in 82% of patients. Study conducted by Essah et al,¹¹ also found that metformin is highly effective in normalizing the menstrual cyclicity in women with PCO, especially with a treatment duration of six months or longer. Comparable results found in the series of Tariq N.¹² Another study conducted by Ara Hassan J, found that metformin is very valuable in the management of regularity of menses, ovulation and the pregnancy in cases with PCO.¹³

Variables	Before treatment percentage (%)	After treatment percentage (%)	Chi – square (p–value)
Menstrual Cycle (N=329)			
Normal cycles	21.4	82	< 0.001
Oligo/Hypomenorrhoea	46	06	
Oligomenorrhoea	23.7	13	
Amenorrhoea	6.3	1.4	
BMI (n=329)			
<25	34.3	36	< 0.001
25-30	37	46	
30-35	18	16	
>35	15	10	
Fertility (N=117)			
Conceived < 6 months	NIL	53	< 0.001
Conceived at 1 year	NIL	21.1	
conceived > 1 year	NIL	17	
Not conceived	100%	15.3	

Table-I. Comparison between pre and post treatment outcome

In PCO, reduction of obesity through diet, metformin and the exercise are important. In our study, results showed that patients in increased BMI moved to lower BMI after six months of treatment. Similar results stated by Norman RJ.¹⁴

Insulin resistance category increase to hyperandrogenism through consequential an ovulation is commonest pathogenetic mechanism in PCOS.¹⁵ Resistance of insulin develop not only in the women obesity with PCOS, where it may be expecting since obesity is often linked to resistance of insulin, but also in 50% of normal weight women with PCOS.¹⁶ The drug clomiphene citrate and gonadotrophins mostly used in PCOS for the ovulation induction, but understanding mechanism of this pathogenesis has given a new track to the PCOS treatment with insulin sensitizing drugs, giving promising results and significantly higher success rates of ovulation and pregnancy¹⁷ as compared with clomiphene citrate.^{17,18} In these medicines metformin widely utilized being safe and lacking teratogenic effects.¹⁹

In our study, 53% women conceived after six months of metformin therapy, while an additional

21.1% conceived after addition of clomiphene citrate.

Imtiaz et al²⁰ studied the role of metformin in ovulation induction and subsequent conception in Pakistani patients of PCOS having hyperinsulinemia and shows similar results. Similar results were obtained in another study which stated that after 6 month treatment of metformin, regularity of menses got in 86% women and mostly women were ovulating at 6 months.²¹ Study conducted by Kocak I shows that metformin significantly improves the rates of insulin resistance, ovulation and the pregnancy in infertile women.²²

The association of insulin resistance contributing to an ovulation has led to the novel and promising therapy of administering insulin sensitizing agents to women with PCOS in order to restore ovulation and enhance fertility.²³ Hence, early diagnosis and management should be offered to women having PCOS quite than waiting for the full blown presentation of PCOS.

CONCLUSION

We concluded that metformin is very success full treatment of PCOS cases. It is a useful adjuvant

to lifestyle adjustment in overweight and obese patients with PCO.



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AUTHORSHIP AND CONTRIBUTION DECLARATION

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