

ANALYSIS OF EFFICACY OF METFORMIN AND PIOGLITAZONE IN RESTORING OVULATION AND THEIR EFFECT ON PREGNANCY IN WOMEN WITH POLYCYSTIC OVARIAN SYNDROME

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ABSTRACT

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OBJECTIVE: This study was conducted this study to compare the efficacy of metformin and pioglitazone in restoring ovulation and their effect on pregnancy.

BACKGROUND: Polycystic ovarian syndrome is a prevalent complex condition that affects 5-20% of women of reproductive age. PCOS symptoms include an ovulatory cycle indicators, high serum androgen levels, hirsutism, inflammatory acne, and infertility. Clinical studies have suggested that insulin sensitizers such as metformin (dimethyl biguanide) and pioglitazone are effective in treating PCOS, which is characterized by insulin resistance.

MATERIALS AND METHODS: A Comparative analysis study was conducted using single blind randomization at Gynecology and Obstetrics wards at Civil Hospital, LUMHS Hyderabad from September 2023 to March 2024. 110 patients were divided into two groups A and B (55 in each group). Pioglitazone was given to group A and Metformin was given to group B. The data was entered and analyzed using IBM SPSS version 26.0

RESULTS: Out of the 110 study subjects, 55 patients with PCOS received pioglitazone and 55 patient's metformin. The mean was 32.4 ± 2.56 and 30.7 ± 2.12 years while mean BMI was 25.4 ± 1.61 Kg/m² and 26.7 ± 2.21 Kg/m² in group A and B respectively. 38 (70.37%) of the patient receiving pioglitazone reported to conceive and 16(29.63%) in metformin group. 42 (57.53%) and 31 (42.47%) confirmed ovulation While 12 (24%) and 38 (76%) reported to have pregnancy in pioglitazone group and metformin group respectively.

CONCLUSION: Metformin and pioglitazone both help treat PCOS by decreasing hyperandrogenism, restoring ovulation, and regulating menstrual cycles. Both are interchangeably useful in the treatment of PCOS.

KEYWORDS: PCOS, Metformin, pioglitazone, ovulation

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a prevalent complex condition that affects 5-20% of women of reproductive age [1, 2]. Polycystic ovarian syndrome (PCOS) is the most prevalent endocrine condition in young girls and women of reproductive age, affecting 8-13% of these women [3,]. PCOS is a major public health concern linked to reproductive (menstrual irregularities, sexual orientation, subfertility, and miscarriages), metabolic, and psychosocial issues [3,4].

PCOS symptoms include anovulatory cycle indicators, high serum androgen levels, hirsutism, inflammatory acne, and infertility. It manifests in four distinct phenotypes and is diagnosed using Rotterdam and NIH criteria [2]. Patients with PCOS who are infertile have several difficulties connected to the regulated ovulation stimulation cycle. Increased LH (luteinizing hormone) production and hyperandrogenism are linked to poor oocyte quality, reduced ovulation and pregnancy, and increased abortion. PCOS is caused by a combination of genetic, environmental, and transgenerational factors. Metabolic diseases and obesity are two of the most prevalent signs of PCOS, coupled with reproductive and obstetric issues. PCOS is associated with a variety of metabolic problems, including dyslipidemia, type 2 diabetes, cardiovascular disease, and poor glucose

tolerance. Impaired glucose tolerance, including diabetes mellitus, can occur in all phenotypes [5].

Insulin resistance contributes to infertility. Insulin resistance occurs when the body's cells grow resistant to insulin, the hormone that regulates blood sugar levels. This can cause a rise in blood sugar levels and the development of diseases like diabetes. Insulin resistance can cause infertility by a combination of variables such as obesity, inflammation, and hormonal imbalance. Insulin resistance has been shown in slim women without PCOS to have a negative impact on IVF results [6]. Previously, oestrogen and progesterone were only utilised to treat PCOS. Clinical studies have suggested that insulin sensitizers such as metformin (dimethyl biguanide) and pioglitazone (glitazone/thiazolidinedione) are effective in treating PCOS, which is characterized by insulin resistance [7].

Metformin operates primarily by inhibiting hepatic gluconeogenesis, although it also inhibits intestinal glucose absorption while increasing glucose uptake and consumption. Metformin medication is frequently accompanied with side symptoms such as indigestion, nausea, vomiting, stomach cramps, and diarrhoea, which may need treatment withdrawal. Glitazones are PPAR- γ agonists. These receptors mediate signalling pathways linked with adipocyte

proliferation and the transcription of pro-inflammatory genes. PPAR- γ controls lipid metabolism in the liver [8]. We conducted this study to compare the efficacy of metformin and pioglitazone in restoring ovulation and their effect on pregnancy.

MATERIAL AND METHODS

Subsequent to obtaining the ethical approval a comparative analysis study was conducted to at Gynecology and Obstetrics wards at Civil Hospital, LUMHS Hyderabad from September 2023 to March 2024. 110 Patients aged between 18 years to 45 years polycystic ovary syndrome were inducted in the study. Using single blind randomization, the patients were divided into two groups A and B (55 in each group). Pioglitazone was given to group A and Metformin was given to group B. However, we excluded the patients who reported any chronic comorbid condition like liver disease, history of ischemic heart disease or hypothyroidism chronic renal failure. All the patients included in both groups went through pelvic ultrasound scan and hormonal profile (serum FSH, testosterone, LH, Prolactin, and mid-luteal progesterone) at the start of the study.

We gave Pioglitazone 30 mg (OD) to the

patients in group A and Metformin 850mg (BD) for 12 weeks. The follow-up ultrasound scan was obtained after the completion of the mentioned drugs. Using the TVS (transvaginal scan) three follow-ups were recorded until transvaginal scan detected the ovulation. We discontinued the medication for patients who ovulated or conceived. However, the medicines were maintained for 6 months if patients' failed to ovulate. We evaluated the effectiveness after 06 months of treatment.

The obtained data was entered and analyzed using IBM SPSS version 26.0. All the quantitative variables were reported in mean & SD while qualitative variables were reported in frequency & percentage. The chi square test of association was employed to evaluate the strength of association between the variables.

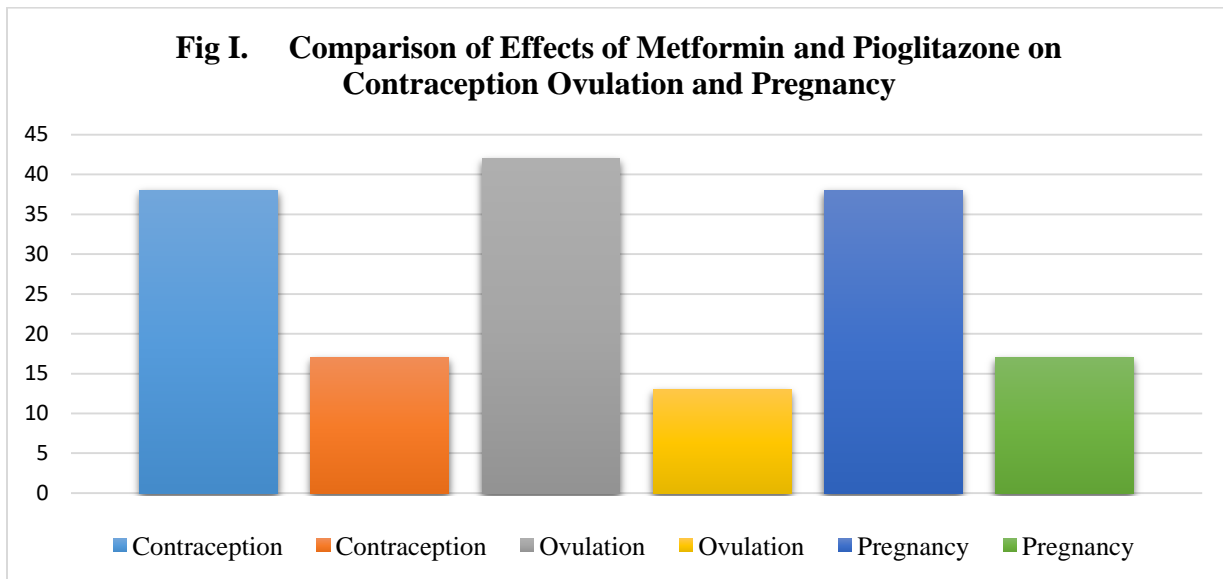
RESULTS

According our findings, the mean was 32.4 ± 2.56 and 30.7 ± 2.12 years while mean BMI was 25.4 ± 1.61 Kg/m² and 26.7 ± 2.21 Kg/m² in group A and B respectively. The mean duration since the disease was 4.43 ± 0.96 years and 3.62 ± 1.12 years in group A and B. Table I

Table I Descriptive Statistics in the Study

Study Variables	Mean	SD	P-value
Age			
Group A (Pioglitazone)	32.4	±2.56	0.26
Group B (Metformin)	30.7	±2.12	
BMI			
Group A (Pioglitazone)	25.4	±1.61	0.12
Group B (Metformin)	26.7	2.21	
Duration of Disease (years)			
Group A (Pioglitazone)	4.43	±0.96	0.08
Group B (Metformin)	3.62	±1.12	

The comparison of effects of metformin and pioglitazone on contraception ovulation and pregnancy is depicted in figure I.



Out of the 110 study subjects, 55 patients with PCOs received pioglitazone and 55 patient's metformin. 38 (70.37%) of the patient receiving pioglitazone reported to

conceive compared to the 16(29.63%) in metformin group, 42 (57.53%) of the patient receiving pioglitazone confirmed ovulation compared to the 31 (42.47%) in metformin

group. While 12 (24%) of the patient receiving metformin reported to have

pregnancy compared to the 38 (76%) in pioglitazone group. Table II

Table II Comparison of effects of Metformin and Pioglitazone on Contraception Ovulation and Pregnancy

Study Variable	Study group (n=110)				P-Value
	Pioglitazone (n=55)		Metformin (n=55)		
	n	%	n	%	
Conception					
Yes	38	70.37	16	29.63	0.08
No	17	30.36	39	69.64	
Ovulation					
Yes	42	57.53	31	42.47	0.23
No	13	35.14	24	64.86	
Pregnancy					
Yes	38	76.00	12	24.00	0.03**
No	17	28.33	43	71.67	

** denotes significant findings

DISCUSSION

This study aimed to examine the effectiveness and therapeutic benefits of metformin and pioglitazone in women with PCOS. When fully exhibited phenotypically, PCOS is defined by metabolic abnormalities associated with insulin resistance and hyperandrogenism [9]. Insulin resistance is related with fasting hyperinsulinemia and an impaired response to oral glucose in around 30% of lean and 70% of obese PCOS women [10]. Our study was conducted to assess the effectiveness of metformin and pioglitazone in reducing hyperinsulinemia and hyperandrogenism, and thus in

regularising menstrual cycles, improving clinical and biochemical hyperandrogenism, and restoring ovulation in the context of our Pakistani population's local, ethnic, socioeconomic, and environmental influences. Patients with PCOS who were age and BMI matched were recruited for the study in both groups. After treatment, both groups showed a significant reduction in fasting blood sugar levels and fasting insulin levels. Similar results were found in a number of other studies [11,12].

In one research, women on metformin had a lower BMI than those taking pioglitazone. An Indian study conducted in 2016 by Shahebrahimi K. revealed a significant

CONFLICT OF INTEREST

The authors declared no any conflict of interest

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AUTHORS' CONTRIBUTION

Authors 1 and 3 Collected the data, 4 and 6 entered and analyzed the data, 2 drafted the manuscript and 5 critically analyzed the draft

decrease in waist circumference in the metformin group but no significant change in the pioglitazone group; a similar observation was noted by Romualdi et al. and other investigators. Ovulation rates were significantly improved in both groups in our study; comparable results of improvement in ovulatory function have been observed in earlier studies indicating equal efficiency of both medications in recovering ovulation [13,14]. However, in her study, Razzaq M found pioglitazone to be more efficient than metformin for ovulation induction in PCOS [14-17].

In our study, both drugs were found to be equally effective in reducing clinical and biochemical hyperandrogenemia, restoring ovulation, and regulating the menstrual cycle; however, metformin was found to be more effective in weight loss than Pioglitazone. It is advised that both medicines be used in PCOS after considering physician recommendations, patient tolerance, and drug compliance. Metformin, as a category B medicine, can be maintained during pregnancy due to the potential effects of reducing first trimester pregnancy losses in PCOS women.

CONCLUSIONS

Metformin and pioglitazone are both beneficial in treating PCOS by lowering hyperandrogenism, restoring ovulation, and regulating menstrual periods. Both are beneficial in the treatment of PCOS and can be used as an alternate treatment in individuals who are unable to tolerate or do not respond to one or the other

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