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COMPARISON OF OUTCOME OF CLOMIPHENE CITRATE ALONE AND IN COMBINATION WITH PIOGLITAZONE FOR INDUCTION OF OVULATION IN INFERTILE WOMEN WITH POLYCYSTIC OVARIAN SYNDROME

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ABSTRACT

Introduction: *Polycystic ovarian syndrome (PCOS) is a common endocrine condition and a primary contributor to infertility in women of reproductive age. Clomiphene citrate (CC) serves as a primary intervention for ovulation induction; yet, its effectiveness may be constrained in certain cases.*

Objectives: *To compare the outcome of ovulation induction in clomiphene citrate (CC) alone and combined treatment with CC and pioglitazone in terms of mean maximum follicle size among infertile women with PCOS.*

Material and Methods: *This randomized controlled trial was conducted at the Gynecology and Obstetrics Department, DHQ Teaching Hospital Rawalpindi, from August 2024 to February 2025. A total of 274 married women with PCOS and infertility were enrolled and randomized into two groups: Group A (CC alone, n=137) and Group B (CC + pioglitazone, n=137). Ultrasonographic folliculometry was performed until mature follicles were detected. Inj. hCG (10,000 IU) was given intramuscularly when at least one follicle ≥18 mm was formed in either ovary. Mean maximum follicle size was recorded over three menstrual cycles. Data were analyzed using SPSS.*

Results*: The mean maximum follicle size was significantly larger in Group B (21.48 ± 2.26 mm) compared to Group A (18.53 ± 3.31 mm, p<0.001). Subgroup analyses confirmed the superiority of the combined treatment across age, BMI, residential status, duration of marriage, and type of infertility.*

Conclusion*: The combination of pioglitazone with CC markedly improves follicular development in infertile patients with PCOS. This combination provides a relatively economical and attainable treatment approach, especially advantageous for resource-constrained environments. Additional research is required to assess long-term effects and safety profiles.*

Keywords: *PCOS, Infertility, Follicle Size, Ovulation, Clomiphene Citrate, Pioglitazone*

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a highly heritable, complicated polygenic, multifactorial condition, constituting the most prevalent endocrine-metabolic illness among women of reproductive age. Diagnosis is

usually diagnosed by the application of the Modified Rotterdam criteria.[1,2] Recent research indicate that PCOS affects 5-15% of pre-menopausal women worldwide.[3] The prevalence of PCOS in South Asian women, particularly Pakistani women, is significantly higher at 52% compared to the white population, which ranges from 20% to 25% in the UK.[4] Several factors have been recognized as contributing to the pathophysiology of PCOS, including environmental toxicants, oxidative stress, epigenetics, nutrition, insulin resistance, hyperandrogenism, inflammation, and obesity.[5] Numerous short- and long-term health complications are associated with PCOS, including metabolic, cardiovascular, and reproductive concerns, all of which affect a woman's identity and health-related quality of life (QoL).[6]

Recent statistics indicate that infertility impacts around 8-12% of couples globally, with PCOS being one of the most prevalent underlying reasons of infertility among these women.[7] Ovulation problems account for roughly 25% of infertility cases in couples, with polycystic ovary syndrome (PCOS) being the predominant cause of anovulatory infertility, representing about 70% of all instances.[8] The management of subfertility linked to PCOS often focuses on lifestyle modifications, surgical interventions, assisted reproductive technologies, and pharmacological treatments such as metformin, thiazolidinedione, clomiphene citrate, letrozole, and pioglitazone.[9]

The cyclical pathogenic interplay of insulin resistance, hyperinsulinemia, and hyperandrogenism, along with hypothalamic-pituitary dysfunction, exacerbates ovarian dysfunction, potentially leading to anovulation and infertility in women with PCOS. Consequently, the primary objective in managing PCOS is to reduce androgen levels and improve ovarian responsiveness to gonadotropins. Clomiphene citrate (CC) is extensively utilized as the primary therapy for anovulatory PCOS. CC exerts an antiestrogenic action via binding to estrogen receptors in the brain. This triggers a pulse of gonadotropin-releasing hormone that prompts gonadotropin release from the anterior pituitary gland.[10] Recently, peroxisome proliferator-activated receptor (PPAR) like pioglitazone has been emerged as an effective alternative to metformin for treating PCOS especially among those who were not-responded to metformin. Additionally, now studies are being conducted to evaluate the effectiveness of added pioglitazone instead of metformin with CC for treating infertility among women with PCOS (11,12).[11,12]

Infertility among women with PCOS is managed with various treatment regimens around the globe and published literature on these treatment regimens showed mixed results based on geo-ethnic variations. In our setting, such women are treated with CC alone and in combination with insulin sensitizers like metformin or pioglitazone, whichever is considered suitable by the consultant gynecologist and selection of treatment is most of the time evidence based. However, no study has been done to date that assessed the effectiveness of either treatment regimen among our local patients. Moreover, there are few studies around the globe that compared the outcome of CC alone and in combination with pioglitazone. So, a present study is planned to decide whether the combination between CC and pioglitazone is better than CC alone in induction of ovulation in infertile women due to PCOS of our local population. The treatment with better results would be preferred in the future that would eventually help to reduce the overall morbidity and improve the quality of life in these patients.

MATERIAL AND METHODS

This randomized controlled trial was conducted at Gynecology and Obstetrics Department, DHQ Teaching Hospital Rawalpindi from 8th August 2024 to 8th February 2025. All married women who presented with PCOS as well as complaint of infertility as per our operational definition with age between 16-40 years and having normal serum prolactin (<25 ng/mL or 25 µg/L) & absence of galactorrhea (milk production from the breast unrelated to pregnancy or lactation) were enrolled for the study. Female with thyroid abnormalities, menstrual dysfunction, uterine or tubal abnormalities and hypersensitive to CC or pioglitazone were excluded from the study. Women with abnormal serum Prolactin Levels (>25ng/ml) or presence of galactorrhea (milk production from the breast unrelated to pregnancy or lactation) and those who were already taking certain medications like metformin, aromatase inhibitors, tamoxifen or gonadotropins were also excluded. The sample size was calculated using WHO sample size calculator taking level of significance as 5% and power of test as 80% and using Amirian et al's study as reference

where it was seen that the maximum follicle size in the CC alone group was smaller when compared to the combination treatment group (16.6 ± 2.7mm versus 17.5 ± 2.6mm, p-value=0.055).[13] The sample size comes out to be 274 patients (137 in each group).

Baseline ultrasonography was performed by the trainee researcher under the supervision of a consultant gynecologist, and the required laboratory tests (Sex Hormones, TFTs, Semen Analysis of the male partner, etc.) were advised before starting the treatment. The patients were assigned to two groups, A and B, using computer-generated random numbering. The allocation sequence was concealed from the researcher enrolling and assessing participants in sequentially numbered, sealed, and stapled envelopes that were kept with the nurse, and the envelopes were opened only after the enrolled participants completed all baseline assessments, at which time the intervention was allocated. Group A received 50 mg clomiphene citrate alone in the first menstrual cycle, 100 mg clomiphene citrate alone in the second menstrual cycle, and 150 mg clomiphene citrate alone in the third menstrual cycle, taken daily from the third to the seventh day of menstruation. Group B patients received 50 mg clomiphene citrate plus 30 mg pioglitazone in the first menstrual cycle, 100 mg clomiphene citrate plus 30 mg pioglitazone in the second menstrual cycle, and 150 mg clomiphene citrate plus 30 mg pioglitazone in the third menstrual cycle, taken daily from the third to the seventh day of menstruation. Transvaginal ultrasound (TVS) monitoring (Folliculometry) was performed on all patients on days 9–16 of the cycle (on alternate days) until mature follicles were detected. Inj. hCG (10,000 IU) was given intramuscularly when at least one follicle ≥18 mm was formed in either ovary. Enrolled women were advised to have intercourse throughout 24–36 hours after the hCG injection. Ovulation signs were monitored 2 days (48 hours) after hCG injection administration. Once the TVS findings confirmed ovulation as per the operational definition, the women were followed up for three months.

DEFINITIONS

Polycystic Ovarian Syndrome (PCOS): was diagnosed, by the consultant gynecologist with at least three years of teaching experience, among all the infertile women at the time of presentation to the hospital using the Modified Rotterdam criteria, which requires the presence of two of the following three criteria:

- Hyperandrogenism (Clinical signs: acne, hirsutism, male pattern alopecia or biochemical: Total testosterone >70 ng/dL)
- Ovulatory dysfunction (<9 menstrual cycles per year or >35 days between cycles)
- Ultrasonographic findings showing presence of 12 or more follicles in each ovary measuring 2-9 mm in diameter, and/or increased ovarian volume (>10 ml)

Infertility: was defined as the women not being able to get pregnant (conceive)after one year (or longer) of unprotected sex despite having a normal semen analysis of report in male partner.

Induction of ovulation: will be determined in all the enrolled women taking either therapy after 48 hours of Inj. HCG (10,000 IU) administration and will be measured as maximum follicle size.

RESULTS

A total of 274 infertile women with PCOS were enrolled for this study and divided equally in two groups: Group A (Clomiphene Citrate alone) and Group B (Clomiphene Citrate combined with Pioglitazone), with 137 participants in each group. The mean age and BMI of participants was 27.97 ± 5.52 years and 24.08 ± 5.46 kg/m2 respectively, with no significant difference between the groups. Detailed analysis of quantitative analysis in both groups including age, BMI, time since marriage and number of mature follicles are presented in table 1. The majority of participants were aged <30 years (60.2%), had a BMI ≤25 kg/m² (59.1%), and were married for <5 years (59.5%). Urban participants predominated in Group B (91.2%) compared to Group A (65.0%). Primary infertility was more common in Group B (62.8%) than in Group A (54.7%). Detailed descriptive analysis of qualitative demographic and clinical variables is presented in table 2.

The mean maximum follicle size was significantly greater in Group B (21.48 ± 2.26 mm) compared to Group A (18.53 ± 3.31 mm) ($p < 0.001$). Stratified analysis revealed that women aged <30 years in Group B had a

mean follicle size of 21.46 ± 2.43 mm, significantly larger than Group A (18.60 ± 3.51 mm) ($p < 0.001$). Similar results were observed for women aged ≥30 years. On the other hand, among participants with BMI ≤25 kg/m², the mean follicle size was 21.57 ± 2.27 mm in Group B, compared to 18.31 ± 3.19 mm in Group A ($p < 0.001$). A similar trend was seen for those with BMI >25 kg/m². Furthermore, urban participants in Group B had a mean follicle size of 21.43 ± 2.27 mm, significantly larger than Group A (18.12 ± 3.06 mm) ($p < 0.001$). Rural participants showed similar trends. Women married ≤5 years in Group B exhibited larger mean follicle sizes (21.35 ± 2.29 mm) than Group A (18.68 ± 3.45 mm) ($p < 0.001$) and among women with primary infertility, Group B had a mean follicle size of 21.50 ± 2.33 mm, compared to 18.13 ± 2.92 mm in Group A ($p < 0.001$). Similarly, secondary infertility showed a significant difference favoring Group B (table 3 and table 4). These findings indicated that the Clomiphene Citrate in combination with Pioglitazone results in significantly larger mean maximum follicle size compared to Clomiphene Citrate alone across all demographic and clinical subgroups.

Table 1: Demographic & clinical profile of the quantitative variables among both groups of the study population (Mean ± SD) n=274 Patients

Variable *Mean ± SD*	**Group A (Clomiphene) n=137**	**Group B (Clomiphene plus Pioglitazone) n=137**	**Total N=274**
Age (Years)	27.47 ± 5.54	28.47 ± 5.48	27.97 ± 5.52
BMI (kg/m^2)	24.19 ± 5.49	23.98 ± 5.46	24.08 ± 5.46
Number of Years Since Marriage	4.12 ± 2.20	3.88 ± 1.84	4.00 ± 2.02
Number of Mature Follicles	10.99 ± 4.46	12.44 ± 4.57	11.71 ± 4.57

Table 2: Frequency and percentages of various demographic & clinical variables among both groups of the study population (n=274 Patients)

Variable *Frequency (%)*	Group A (Clomiphene) n=137	Group B (Clomiphene plus Pioglitazone) n=137	Total N=274
Age Groups			
<30 Years	85 (62.0%)	80 (58.4%)	165 (60.2%)
≥30 Years	52 (38.0%)	57 (41.6%)	109 (39.8%)
BMI Groups			
≤25 kg/m^2	81 (59.1%)	81 (59.1%)	162 (59.1%)
>25 kg/m^2	56 (40.9%)	56 (40.9%)	112 (40.9%)
Time Since Marriage			
<5 Years	79 (57.7%)	84 (61.3%)	163 (59.5%)
≥5 Years	58 (42.3%)	53 (38.7%)	111 (40.5%)
Residential Status			
Rural	48 (35.0%)	12 (8.8%)	60 (21.9%)
Urban	89 (65.0%)	125 (91.2%)	214 (78.1%)
Type of Infertility			
Primary	75 (54.7%)	86 (62.8%)	161 (58.8%)
Secondary	62 (45.3%)	51 (37.2%)	113 (41.2%)
Menstrual Cycle			

Variable *Frequency (%)*	Group A (Clomiphene) n=137	Group B (Clomiphene plus Pioglitazone) n=137	Total N=274
Age Groups			
<30 Years	85 (62.0%)	80 (58.4%)	165 (60.2%)
≥30 Years	52 (38.0%)	57 (41.6%)	109 (39.8%)
First	37 (27.0%)	42 (30.7%)	79 (28.8%)
Secondary	70 (51.1%)	73 (53.3%)	143 (52.2%)
Third	30 (21.9%)	22 (16.1%)	52 (19.0%)

Table 3: Comparison of clomiphene citrate alone and in combination with pioglitazone for mean maximum follicle size among infertile women with PCOS (n=274)

Study Groups	N	Mean Maximum Follicle Size	± Std. Deviation	*p*-value (Independent Sample *t*-Test)
Group A (Clomiphene) n=137	137	18.53	3.31	
Group B (Clomiphene plus Pioglitazone) n=137	137	21.48	2.26	

Table 4: Comparison of clomiphene citrate alone (CC) and in combination with pioglitazone (CC+ Pioglitazone) for mean maximum follicle size among infertile women with PCOS (stratification on the basis of age, BMI, residential status, time since marriage and type of infertility)

Study Confounders		Study Groups	N	Mean	± Std. Deviation	*p*-value (Paired sample *t*-Test)
Age (Years)	< 30	Clomiphene Citrate	85	18.60	3.51	0.000
		Clomiphene Citrate Plus Pioglitazone	80	21.46	2.43	
	≥ 30	Clomiphene Citrate	52	18.42	2.98	0.000
		Clomiphene Citrate Plus Pioglitazone	57	21.51	2.03	
BMI (Kg/m^2)	≤ 25	Clomiphene Citrate	81	18.31	3.19	0.000
		Clomiphene Citrate Plus Pioglitazone	81	21.57	2.27	
	> 25	Clomiphene Citrate	56	18.86	3.48	0.000
		Clomiphene Citrate Plus Pioglitazone	56	21.36	2.27	
Residential Status	Rural	Clomiphene Citrate	48	19.29	3.63	0.017
		Clomiphene Citrate Plus Pioglitazone	12	22.00	2.22	
	Urban	Clomiphene Citrate	89	18.12	3.06	0.000
		Clomiphene Citrate Plus Pioglitazone	125	21.43	2.27	
Time Since Marriage	≤ 5	Clomiphene Citrate	79	18.68	3.45	0.000
		Clomiphene Citrate Plus Pioglitazone	84	21.35	2.29	
	> 5	Clomiphene Citrate	58	18.33	3.12	0.000
		Clomiphene Citrate Plus Pioglitazone	53	21.70	2.22	
	Primary	Clomiphene Citrate	75	18.13	2.92	0.000

Type of Infertility		Clomiphene Citrate Plus Pioglitazone	86	21.50	2.33	
	Secondary	Clomiphene Citrate	62	19.02	3.69	0.000
		Clomiphene Citrate Plus Pioglitazone	51	21.45	2.18	

DISCUSSION

Infertility is frequently stigmatized among our local community, resulting in considerable mental and social distress for affected women.[13] This study presents a straightforward and efficacious therapeutic approach, providing hope to several women and families facing infertility associated with PCOS. Furthermore, the results support increased awareness and early intervention, which may alleviate the long-term consequences of untreated PCOS. This study examined the impact of Clomiphene Citrate (CC) alone and in conjunction with Pioglitazone on the average maximum follicle size in infertile women diagnosed with PCOS. The findings indicated that the incorporation of Pioglitazone with CC markedly enhanced follicular development, as reflected by an increased mean maximum follicle size across all demographic and clinical categories. These findings have significant implications for enhancing treatment methods for PCOS-related infertility, especially in resource-constrained environments such as ours. The markedly increased follicle size in the combination therapy group (21.48 ± 2.26 mm) over the CC-alone group (18.53 ± 3.31 mm) underscores the synergistic impact of Pioglitazone with Clomiphene. Pioglitazone, an insulin-sensitizing drug, presumably augments the ovulatory response by ameliorating insulin resistance, a critical element in the pathophysiology of PCOS. Stratified analysis reinforces the validity of this conclusion, demonstrating constant advantages of the combination therapy regardless of age, BMI, residential situation, duration of marriage, or type of infertility. This corresponds with the results of a research by Amirian et al., which indicated an increased follicle count with the addition of pioglitazone, although no significant variation in total ovarian stimulation and pregnancy rates.[14] The follicle size was compared between infertile women with PCOS treated with CC alone and in conjunction with pioglitazone. The results indicated that the maximum follicle size in the CC-only group was smaller than that of the combination treatment group (16.6 ± 2.7mm versus 17.5 ± 2.6mm, p-value=0.055).[14] While our results did not explicitly address pregnancy outcomes, research by Abuelghar et al.[15] indicated no notable enhancement in pregnancy rates when pioglitazone was combined with clomiphene in overweight women with PCOS. Comparable results were also noted in an additional trial that evaluated clomiphene combined with pioglitazone vs clomiphene alone. The disparity in menstrual cycles across groups in your study aligns with prior data indicating that response patterns often stabilize after the second cycle of ovulation induction with combination treatments. Research conducted by Kar and Sanchita[16] indicates same patterns of escalating reactions over cycles, however diminishing after the third cycle. The study had several characteristics, notably the inclusion of 274 individuals, which enhances the reliability and generalizability of the findings among comparable groups. The subgroup analysis enhances the results by illustrating the effectiveness of the combination therapy across diverse demographic and clinical attributes. This study primarily focuses on a group where PCOS is frequently underdiagnosed or poorly treated due to insufficient resources and knowledge. The results support the implementation of a cost-efficient and accessible combination treatment in resource-limited environments. Notwithstanding these merits, our study also possesses certain shortcomings. The data was sourced from a singular healthcare institution, perhaps limiting its applicability to wider populations. Our study did not evaluate pregnancy rates or live birth outcomes, which are essential indicators of infertility treatment efficacy. The study did not assess the cost-effectiveness of the combo treatment, a crucial factor in resource-constrained environments. The study did not thoroughly investigate the potential adverse effects of Pioglitazone, which may affect its acceptability and adherence.

This study's importance is its potential to impact infertility care procedures in resource-limited environments. In low-income nations, where sophisticated infertility treatments such as in-vitro fertilization (IVF) may be prohibitively expensive, it is essential to optimize oral pharmacological medications. Pioglitazone is an affordable and readily accessible medication that can augment the effectiveness of CC, offering a viable option to more intrusive and expensive treatments. Moreover, PCOS is a common but little acknowledged contributor to infertility within our local demographic.[17] The research fills a significant void in the literature by offering

evidence-based suggestions specifically designed for women in these contexts. This is especially pertinent in rural regions, where healthcare resources are limited, and women frequently encounter delays in diagnosis and treatment.

CONCLUSION

This study highlights the significant benefit of combining Clomiphene Citrate with Pioglitazone for improving follicular growth in infertile women with PCOS. The findings have substantial implications for resource-limited countries, offering a cost-effective, accessible, and scalable approach to managing a common yet challenging condition. However, future studies should focus on long-term outcomes, cost-effectiveness, and the safety profile of this combination therapy to further strengthen its utility in clinical practice.

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REFERENCES

Azziz R. Polycystic Ovary Syndrome. Obstet Gynecol. 2018;132(2):321-36.

Smet ME, McLennan A. Rotterdam criteria, the end. Australas J Ultrasound Med. 2018;21(2):59-60.

Hallajzadeh J, Khoramdad M, Karamzad N, Almasi-Hashiani A, Janati A, Ayubi E et al. Metabolic syndrome and its components among women with polycystic ovary syndrome: a systematic review and meta-analysis. J Cardiovasc Thorac Res. 2018;10(2):56-69.

Azhar A, Abid F, Rehman R. Polycystic Ovary Syndrome, Subfertility and Vitamin D Deficiency. J Coll Physicians Surg Pak. 2020;30(5):545-6.

Escobar-Morreale HF. Polycystic ovary syndrome: definition, aetiology, diagnosis and treatment. Nat Rev Endocrinol. 2018;14(5):270-84.

Sadeghi HM, Adeli I, Calina D, Docea AO, Mousavi T, Daniali M, et al. Polycystic Ovary Syndrome: A Comprehensive Review of Pathogenesis, Management, and Drug Repurposing. Int J Mol Sci. 2022;23(2):583-6.

F Borght MV, Wyns C. fertility and infertility: Definition and epidemiology. Clin Biochem. 2018;62:2-10.

Cunha A, Póvoa AM. Infertility management in women with polycystic ovary syndrome: a review. Porto Biomed J. 2021;6(1):e116-9.

Teede HJ, Misso ML, Costello MF. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Fertil Steril. 2018;110:364–79.

Takasaki A, Tamura I, Okada-Hayashi M, Orita T, Tanabe M, Maruyama S, et al. Usefulness of intermittent clomiphene citrate treatment for women with polycystic ovarian syndrome that is resistant to standard clomiphene citrate treatment. Reprod Med Biol. 2018;17(4):454-8.

Gul HM, Ather S, Ain QU. Comparison of Efficacy of Clomiphene Citrate Alone and with Glucophage for Treatment of Infertility in Polycystic Ovarian Syndrome. J Soc Obstet Gynaecol Pak. 2022;12(3):272-5.

Cao C, Qi Y, Fang D, Yu Y. Clinical study on polycystic ovary syndrome treated with Diane-35 and Pioglitazone. Am J Transl Res. 2021;13(11):12742-9.

Sana M, Abdullah M, Sana F. Link Between Psychological Stress and Female Infertility? Call for Increased Research in India and Pakistan. *J Psychosexual Health*. 2024;6(3):297-298.

Amirian M, Shariat Moghani S, Jafarian F, Mirteimouri M, Nikdoust S, Niroumand S, et al. Combination of pioglitazone and clomiphene citrate versus clomiphene citrate alone for infertile women with the polycystic ovarian syndrome. BMC Womens Health. 2021;21(1):302-6.

Abuelghar, Wessam M., Osama S. Elkady, and Ahmed A. Khamees. "Clomiphene Citrate Alone, in Combination with Metformin or in Combination with Pioglitazone as First Line Therapy in Induction of Ovulation in Infertile Women with Polycystic Ovary Syndrome, a Randomized Controlled Trial." Middle East Fertility Society Journal 18, no. 3 (2013): 135-141.

Kar S, Sanchita S. Clomiphene citrate, metformin or a combination of both as the first line ovulation induction drug for Asian Indian women with polycystic ovarian syndrome: A randomized controlled trial. J Hum Reprod Sci. 2015;8(4):197-201.

Rizvi M, Islam MA, Aftab MT, Naqvi AA, Jahangir A, Ishaqui AA, et al. Knowledge, attitude, and perceptions about polycystic ovarian syndrome, and its determinants among Pakistani undergraduate students. PLoS One. 2023 May 25;18(5):e0285284.