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Original article

Comparison of the Efficacy of Inositol-Containing Medication Only *versus* Metformin and Inositol among Libyan Infertile Women with Polycystic Ovarian Syndrome

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Abstract
The polycystic ovarian syndrome (PCOS) is a common endocrinological disorder among females of reproductive age worldwide. The management of PCOs included lifestyle modification, medication, and surgical treatment. This study was conducted to compare the efficacy of inositol-containing medication only versus metformin and inositol among Libyan infertile women with polycystic ovarian syndrome. This study was a randomized controlled trial that enrolled patients at the Infertility Treatment Center in Tripoli, Libya, between January and December 2024. The target sample consisted of 41 Libyan infertile women diagnosed with polycystic ovarian syndrome, who were divided into two groups: 21 patients had received inositol only, while 20 patients had received inositol combined with metformin. All statistical analysis was done using the SPSS Version 21 program. In this study, nearly half of the patients ranged between 25 and 29 years, accounting for 48.8%. Most of them were obese, with an overall percentage was 80.4%. About 22.0% had regular menstrual cycles and 58.5% had hirsutism. 61.0% of patients had primary infertility, while 39.0% of them had secondary infertility. On comparison between two groups in the study a statistically significant results and parameters improvement were reported in most of the hormonal and metabolic determinants in terms of LH, E2, AMH, HbA1C levels in both groups, with additional efficacy in HOMA-IR level for the combined group, but insignificant findings in FSH and prolactin levels. While the opposite finding had found that the inositol-only group had statistically significant results for TSH level. In summary, this study suggested that the combination of inositol treatment with metformin had significant effectiveness and parameter improvement on most of the hormonal and metabolic levels for infertile women with polycystic ovarian syndrome. Therefore, the combination of inositol and metformin therapies appears to offer additional benefits and positive results for optimization of hormonal and metabolic parameters among polycystic ovarian syndrome cases, particularly who seeking fertility advice and expressing obesity.
Keywords. *Polycystic Ovarian Syndrome, PCOS, Inositol, Metformin, Libya.*

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Introduction

The polycystic ovarian syndrome (PCOS) is a common endocrinological disorder among females of reproductive age worldwide. And the estimated prevalence ranges between 2.2% to 26% in different countries according to the demographical characteristics of the population and the criteria settings [1-2]. PCOS is linked to hormonal disturbances in the concentrations of luteinizing hormone (LH), prolactin, estrogen, and serum androgens (testosterone and androstenedione), as well as various metabolic abnormalities such as insulin resistance (IR), impaired glucose tolerance, and lipid abnormalities [3-5]. These disturbances can lead to long-term adverse health outcomes such as type 2 diabetes mellitus, cardiovascular diseases, and endometrial cancer [3,6]. Also, the psychological issues were reported among PCOs cases, which contributed to low self-esteem, mood swings, anxiety, and depression [7]. Additionally, the risk of anovulatory infertility and pregnancy-related complications is well established and evident among PCOS patients [8-10]. PCOS is diagnosed by Rotterdam diagnostic criteria, which are expressed as two of three elements to make the diagnosis via chronic anovulation, biochemical and clinical hyperandrogenism, and polycystic ovaries in ultrasound pictures. There are four different phenotypes (A, B, C, D) of PCOs that have been recognized according to clinical presentations [3,11-14]. The management of PCOs included lifestyle modification, medication, and surgical treatment [4].

Metformin is considered one of most common in insulin-sensitizing agent used in PCOS, it belongs to biguanide derivative antidiabetic agents which decreases gastrointestinal glucose absorption, inhibits gluconeogenesis, and enhances peripheral insulin sensitivity but with persistent use of metformin therapy a common adverse side effects had

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recognized such as gastrointestinal adverse side effects like diarrhea and stomachache [15-16]. In the last two decades, various studies have reported the effectiveness of inositol(s) derivatives in the forms of two stereoisomers, including myo-inositol and D-chiro-inositol, which have been shown to improve pathological conditions and important role in the treatment of PCOS. In the ovary, the D-chiro-inositol is shown to be linked to insulin-mediated androgen synthesis, while the myo-inositol has been found to mediate the uptake of glucose and follicle-stimulating hormone (FSH) signaling [17-28].
For this context, the present study aims to compare the efficacy of inositol-containing medication only versus metformin and inositol among Libyan infertile women with polycystic ovarian syndrome.

Methods and materials

Study design

This study was a randomized controlled trial.

Study settings and period

The study was conducted at the Infertility Treatment Center in Tripoli, Libya, between January and December 2024.

Study population

The target sample comprised of 41 Libyan infertile women diagnosed by polycystic ovarian syndrome who divided into two groups, 21 patients had received inositol only while 20 patients had received inositol combined with metformin, several hormonal and metabolic parameters had done included follicular stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), antimullerian hormone (AMH), hemoglobin A1C (HbA1C), Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), thyroid stimulating hormone (TSH) and prolactin levels, all parameters performed and standardized according to the laboratory references of the center which measured before and after the therapeutic intervention over 3 months duration.
The patients had been allocated, matched, and underwent randomization to ensure standardization of data that uptaked via a predesigned questionnaire with coding of cases.

Eligibility criteria

The study focuses on Libyan infertile women diagnosed with polycystic ovarian syndrome (PCOS) based on the Rotterdam criteria. These criteria ensure a standardized diagnosis, allowing for a homogeneous study population. Participants must be receiving inositol-based treatment, either as monotherapy or in combination with Metformin, to evaluate the therapeutic effects of these interventions. Additionally, the availability and acceptability of complete biochemical, hormonal, and clinical data are essential for inclusion, as this ensures the reliability and comprehensiveness of the study findings. Conversely, certain exclusion criteria have been established to minimize confounding factors. Women with coexisting endocrine disorders, such as thyroid dysfunction or hyperprolactinemia, are excluded, as these conditions may independently influence reproductive and metabolic outcomes. Similarly, patients using other medications that could affect reproductive or metabolic parameters are excluded to maintain the integrity of the study results. Furthermore, cases with incomplete or missed follow-up data are excluded to ensure that the analysis is based on consistent and fully documented patient records. These criteria collectively enhance the validity and accuracy of the study's conclusions.

Data analysis

All statistical analysis was done using the SPSS Version 21 program. The frequency, percentage, mean, and standard deviation of data results were calculated using descriptive analysis, while comparative analysis between groups was done using a paired t-test for inferential analysis. Differences are considered statistically significant at a P-value of less than 0.05.

Results

Out of 41 Libyan infertile women diagnosed with polycystic ovarian syndrome at the Infertility Treatment Center in Tripoli during the year 2024, the selected patients were divided into two groups. 21 patients had received inositol only, while 20 patients had received inositol combined with metformin to compare their efficacy in hormonal and metabolic

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characteristics. The most frequent age in this study was between 25 and 29 years, accounting for 48.8% (20), followed by 24.4% (10) of them were between 30 and 34 years (Figure 1).

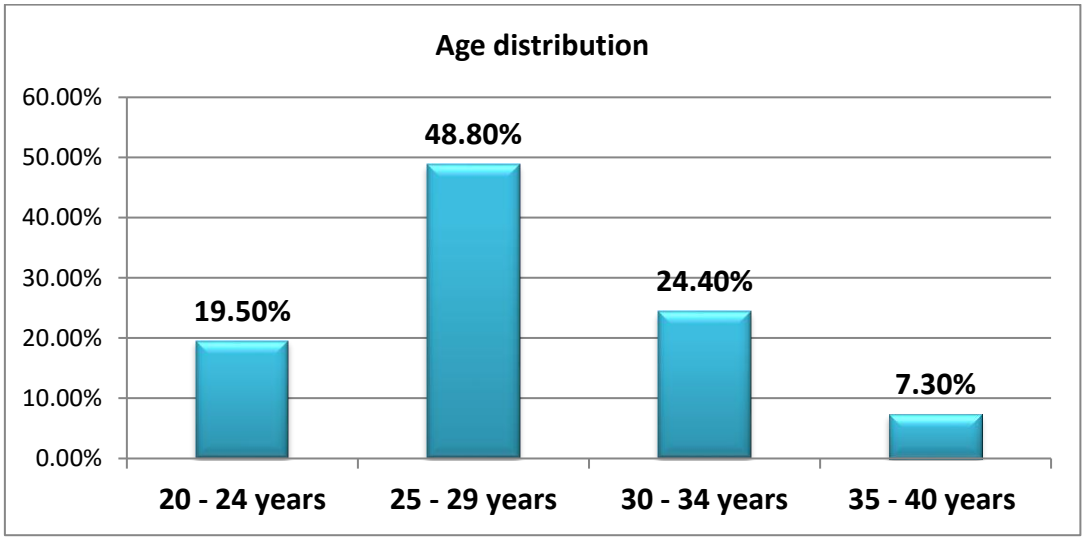

Figure 1. Age distribution, Tripoli, Libya, 2024.

Most of the patients suffered from obesity, with an overall percentage was 80.4% (33), which was divided into 34.1% (14) had class II obesity, 26.8% (11) who had class III obesity, and 19.5% (8) who had class I obesity (Table 1).

Table 1. Body mass index measurements distribution, Tripoli, Libya, 2024.

Variables (n = 41)	N	%
Normal (18.5 - 24.9 Kg/m2)	1	2.4%
Overweight (25 - 29.9 Kg/m2)	7	17.1%
Class I Obesity (30 - 34.9 Kg/m2)	8	19.5%
Class II Obesity (35 - 39.9 Kg/m2)	14	34.1%
Class III Obesity (>40 Kg/m2)	11	26.8%

About 22.0% (9) of patients had expressed regular menstrual cycle and 58.5% (24) of them had expressed hirsutism (Table 2).

Table 2. Regular menstrual cycle and hirsutism distribution, Tripoli, Libya, 2024.

Variables (n = 41)	Yes	No
Regular menstrual cycle	22.0% (9)	78.0% (32)
Hirsutism	58.5% (24)	41.5% (17)

About 61.0% (25) of patients had primary infertility, while 39.0% (16) of them had secondary infertility (Figure 2).

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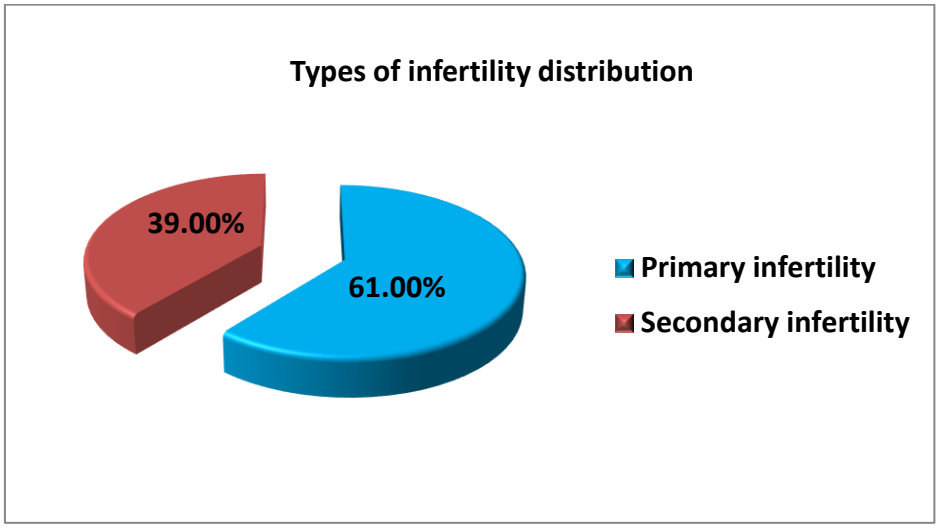

Figure 2. Types of infertility distribution, Tripoli, Libya, 2024.

On comparison between two groups in terms of hormonal assay parameters, the FSH level showed statistical insignificant changes in both groups, but statistically significant and hormonal improvement results were reported in LH, E2, and AMH levels among both groups, particularly in the combined Inositol with Metformin group (Table 3).

Table 3. Hormonal assay parameters distribution, Tripoli, Libya, 2024.

Variables (n = 41)	Inositol only (n = 21)	Inositol with Metformin (n = 20)
FSH level		
Before	6.671 ± 1.821 SD	6.248 ± 1.618 SD
After	6.705 ± 1.408 SD	6.249 ± 1.350 SD
P-value	0.902	0.998
LH level		
Before	9.261 ± 4.669 SD	10.007 ± 5.912 SD
After	6.751 ± 1.900 SD	7.601 ± 3.591 SD
P-value	0.004*	0.006*
E2 level		
Before	36.781 ± 13.642 SD	33.851 ± 15.730 SD
After	51.905 ± 25.699 SD	46.725 ± 14.933 SD
P-value	0.007*	0.005*
AMH level		
Before	4.533 ± 3.135 SD	5.036 ± 2.475 SD
After	3.862 ± 2.071 SD	4.177 ± 1.891 SD
P-value	0.010*	0.001*

*Statistically significant finding = **

On comparison between two groups in terms of Hemoglobin A1C and HOMA-insulin resistance parameters, statistically significant results were documented in both parameters with significant improvement in HOMA-IR level, particularly in the combined Inositol with Metformin group (Table 4).

Table 4: Hemoglobin A1C and Homa-insulin resistance parameters distribution, Tripoli, Libya, 2024.

Variables (n = 41)	Inositol only (n = 21)	Inositol with Metformin (n = 20)
HbA1C level		
Before	5.297 ± 0.423 SD	5.455 ± 0.587 SD
After	5.110 ± 0.383 SD	5.105 ± 0.379 SD

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P-value	0.000*	0.003*
HOMA-IR level		
Before	4.910 ± 1.185 SD	5.424 ± 1.006 SD
After	3.021 ± 0.925 SD	2.852 ± 0.504 SD
P-value	0.000*	0.000*

*Statistically significant finding = **

On comparison between two groups in terms of thyroid stimulating hormone and prolactin parameters, the TSH level showed statistically significant improvements in the Inositol only group while statistically insignificant changes in Inositol with Metformin group, but statistically insignificant results of prolactin level in both groups (Table 5).

Table 5: Thyroid-stimulating hormone and prolactin parameters distribution, Tripoli, Libya, 2024.

Variables (n = 41)	**Inositol only (n = 21)**	**Inositol with Metformin (n = 20)**
TSH level		
Before	1.851 ± 0.605 SD	1.650 ± 0.652 SD
After	1.751 ± 0.551 SD	1.566 ± 0.390 SD
P-value	0.008*	0.492
Prolactin level		
Before	19.656 ± 5.778 SD	17.632 ± 6.075 SD
After	18.238 ± 6.924 SD	16.880 ± 6.211 SD
P-value	0.156	0.419

*Statistically significant finding = **

Discussion

The polycystic ovary syndrome (PCOS) is a common and complex endocrinopathy globally with a wide range of endocrine and metabolic disorders such as hyperinsulinemia, insulin resistance, hyperlipidemia, obesity, type 2 diabetes mellitus, cardiovascular diseases, and a high risk of infertility, miscarriages, and pregnancy complications [1, 14, 29-32].

The present study assessed 41 Libyan infertile women who were diagnosed with polycystic ovarian syndrome, which was divided into two groups: 21 patients had received inositol only, while 20 patients had received inositol combined with metformin to compare their efficacy in hormonal and metabolic characteristics.

Our results found that most of the hormonal and metabolic parameters in terms of LH, E2, AMH, and HbA1C levels had significantly improved in both groups, with an additional improvement effect for HOMA-IR level among the combination group. These findings were consistent with several studies, which showed significant hormonal improvement and reduction of hyperandrogenism features of polycystic ovarian syndrome cases in combined therapy [33-37]. Additionally, metformin, as a classical insulin sensitizer, is well established in various studies to be an effective therapy among PCOS cases to improve menstrual cycles, reduce insulin resistance and androgen excess, as identified in the current study, where the HOMA-IR became significantly improved with the use of metformin in the combined group [38-39]. But the Fruzzetti et al study had shown that the HOMA-IR level significantly improved with just use of myoinositol supplementation [40].

The limitation of the study was a small sample size, but the strength of the study was an appropriate study design and assessment of laboratory parameters.

Conclusion

In summary, this study suggested that the combination of inositol treatment with metformin had significant effectiveness and parameter improvement on most of the hormonal and metabolic levels for infertile women with polycystic ovarian syndrome. Therefore, the combination of inositol and metformin therapies appears to offer additional benefits and positive results for optimization of hormonal and metabolic parameters among polycystic ovarian syndrome cases, particularly who seeking fertility advice and expressing obesity.

Ethical approval

This study was ethically approved by the Infertility Treatment Center to use the relevant data for study purposes while maintaining confidentiality throughout the research process.

Conflict of interest

There is no conflict of interest among the authors regarding the study publication.

References

1. Bozdag G, Mumusoglu S, Zengin D, Karabulut E, Yildiz BO. The prevalence and phenotypic features of polycystic ovary syndrome: a systematic review and meta-analysis. Hum Reprod. 2016 Dec;31(12):2841-55.
2. Alaswad N, Elmabrouk A, Abugdera E. Knowledge and awareness about polycystic ovarian syndrome among Libyan females. AlQalam J Med Appl Sci. 2024 Aug 10:755-62.
3. Teede HJ, Misso ML, Costello MF, Dokras A, Laven J, Moran L, Piltonen T, Norman RJ; International PCOS Network. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Fertil Steril. 2018 Aug;110(3):364-79.
4. Noor AL, Abofaed M, Alqeeyadi H, Alshahrani M, Alsherif E. Prevalence and dietary management of polycystic ovary syndrome among Libyan women attending Tripoli Infertility Center. AlQalam J Med Appl Sci. 2024 Jan 20:74-81.
5. Abdalla A, Alzowam R, Alkilani D, Altwer T. Prevalence of polycystic ovarian syndrome in Alkhoms City, Libya: a cross-sectional study. AlQalam J Med Appl Sci. 2025 Mar 8:408-14.
6. Aghil M, El-Megrabi R, Alfaghi H, Alrakhees R. The relationship between insulin resistance and polycystic ovary syndrome in Libyan women. Khalij-Libya J Dent Med Res. 2025 Jul 12:159-64.
7. Barry JA, Kuczmierczyk AR, Hardiman PJ. Anxiety and depression in polycystic ovary syndrome: a systematic review and meta-analysis. Hum Reprod. 2011 Sep;26(9):2442-51.
8. Vander Borght M, Wyns C. Fertility and infertility: definition and epidemiology. Clin Biochem. 2018 Dec;62:2-10.
9. Joham AE, Palomba S, Hart R. Polycystic ovary syndrome, obesity, and pregnancy. Semin Reprod Med. 2016 Mar;34(2):93-101.
10. Balen AH, Morley LC, Misso M, Franks S, Legro RS, Wijeyaratne CN, et al. The management of anovulatory infertility in women with polycystic ovary syndrome: an analysis of the evidence to support the development of global WHO guidance. Hum Reprod Update. 2016 Nov;22(6):687-708.
11. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Hum Reprod. 2004 Jan;19(1):41-7.
12. Guastella E, Longo RA, Carmina E. Clinical and endocrine characteristics of the main PCOS phenotypes. Fertil Steril. 2010 Dec;94(7):2197-201.
13. Legro RS, Arslanian SA, Ehrmann DA, Hoeger KM, Murad MH, Pasquali R, et al. Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2013 Dec;98(12):4565-92.
14. Azziz R, Carmina E, Chen Z, Dunaif A, Laven JS, Legro RS, et al. Polycystic ovary syndrome. Nat Rev Dis Primers. 2016 Aug 11;2:16057.
15. Baillargeon JP, Iuorno MJ, Nestler JE. Insulin sensitizers for polycystic ovary syndrome. Clin Obstet Gynecol. 2003 Jun;46(2):325-40.
16. Renato P. Metformin in women with PCOS, Pros. Endocrine. 2015 Mar;48(2):422-6.
17. Genazzani AD, Battaglia C, Malavasi B, Strucchi C, Tortolani F, Gamba O. Metformin administration modulates and restores luteinizing hormone spontaneous episodic secretion and ovarian function in nonobese patients with polycystic ovary syndrome. Fertil Steril. 2004 Jan;81(1):114-9.
18. Lord JM, Flight IHK, Norman RJ. Metformin in polycystic ovary syndrome: systematic review and meta-analysis. BMJ. 2003 Oct 25;327(7421):951-3.
19. Pasquali R, Gambineri A. Insulin-sensitizing agents in polycystic ovary syndrome. Eur J Endocrinol. 2006 Jun;154(6):763-75.
20. Gerli S, Mignosa M, Di Renzo GC. Effects of inositol on ovarian function and metabolic factors in women with PCOS: a randomized double blind placebo-controlled trial. Eur Rev Med Pharmacol Sci. 2003 Nov-Dec;7(6):151-9.
21. Gerli S, Papaleo E, Ferrari A, Di Renzo GC. Randomized, double blind placebo-controlled trial: effects of myo-inositol on ovarian function and metabolic factors in women with PCOS. Eur Rev Med Pharmacol Sci. 2007 Sep-Oct;11(5):347-54.
22. Iuorno MJ, Jakubowicz DJ, Baillargeon JP, et al. Effects of D-chiro-inositol in lean women with the polycystic ovary syndrome. Endocr Pract. 2002 Nov-Dec;8(6):417-23.
23. Nestler JE, Jakubowicz DJ, Reamer P, Gunn RD, Allan G. Ovulatory and metabolic effects of D-chiro-inositol in the polycystic ovary syndrome. N Engl J Med. 1999 Apr 29;340(17):1314-20.
24. Unfer V, Carlomagno G, Dante G, Facchinetti F. Effects of myo-inositol in women with PCOS: a systematic review of randomized controlled trials. Gynecol Endocrinol. 2012 Jul;28(7):509-15.

25. Nestler JE, Unfer V. Reflections on inositol(s) for PCOS therapy: steps toward success. Gynecol Endocrinol. 2015 Jul;31(7):501-5.
26. Nestler JE, Jakubowicz DJ, de Vargas AF, Brik C, Quintero N, Medina F. Insulin stimulates testosterone biosynthesis by human thecal cells from women with polycystic ovary syndrome by activating its own receptor and using inositolglycan mediators as the signal transduction system. J Clin Endocrinol Metab. 1998 Jun;83(6):2001-5.
27. Unfer V, Carlomagno G, Papaleo E, Vailati S, Candiani M, Baillargeon JP. Hyperinsulinemia alters myoinositol to d-chiroinositol ratio in the follicular fluid of patients with PCOS. Reprod Sci. 2014 Jul;21(7):854-8.
28. Carlomagno G, Unfer V, Roseff S. The D-chiro-inositol paradox in the ovary. Fertil Steril. 2011 Jun;95(8):2515-6.
29. Lizneva D, Suturina L, Walker W, Brakta S, Gavrilova-Jordan L, Azziz R. Criteria, prevalence, and phenotypes of polycystic ovary syndrome. Fertil Steril. 2016 Jul;106(1):6-15.
30. Rees DA, Jenkins-Jones S, Morgan CL. Contemporary reproductive outcomes for patients with polycystic ovary syndrome: a retrospective observational study. J Clin Endocrinol Metab. 2016 May;101(4):1664-72.
31. Bruyneel A, Catteau-Jonard S, Decanter C, et al. Polycystic ovary syndrome: what are the obstetrical risks? Gynecol Obstet Fertil. 2014 Feb;42(2):104-11.
32. Fauser BC, Tarlatzis BC, Rebar RW, et al. Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. Fertil Steril. 2012 Jan;97(1):28-38.e25.
33. Gudović A, Bukumirić Z, Milincic M, Pupovac M, Andjić M, Ivanovic K, et al. The comparative effects of myo-inositol and metformin therapy on the clinical and biochemical parameters of women of normal weight suffering from polycystic ovary syndrome. Biomedicines. 2024 Feb 2;12(2):349.
34. Rashid R, Mir SA, Kareem O, Ali T, Ara R, Malik A, et al. Polycystic ovarian syndrome-current pharmacotherapy and clinical implications. Taiwan J Obstet Gynecol. 2022 Jan;61(1):40-50.
35. Garzia E, Galiano V, Marfia G, Navone S, Grossi E, Marconi AM. Hyperandrogenism and menstrual imbalance are the best predictors of metformin response in PCOS patients. Reprod Biol Endocrinol. 2022 Jan 8;20(1):6.
36. Merviel P, James P, Bouée S, Le Guillou M, Rince C, Nachtergaele C, et al. Impact of myo-inositol treatment in women with polycystic ovary syndrome in assisted reproductive technologies. Reprod Health. 2021 Jan 12;18(1):13.
37. Bonnet F, Scheen A. Understanding and overcoming metformin gastrointestinal intolerance. Diabetes Obes Metab. 2017 Apr;19(4):473-81.
38. Diamanti-Kandarakis E, Christakou CD, Kandaraki E, Economou FN. Metformin: an old medication of new fashion: evolving new molecular mechanisms and clinical implications in polycystic ovary syndrome. Eur J Endocrinol. 2010 Feb;162(2):193-212.
39. Rena G, Hardie DG, Pearson ER. The mechanisms of action of metformin. Diabetologia. 2017 Sep;60(9):1577-85.
40. Fruzzetti F, Perini D, Russo M, Bucci F, Gadducci A. Comparison of two insulin sensitizers, metformin and myo-inositol, in women with polycystic ovary syndrome (PCOS). Gynecol Endocrinol. 2017 Jan;33(1):39-42.