



## EFFECT OF MYOINOSITOL IN FERTILITY PROFILE OF PCOS PATIENTS

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### Abstract

#### Introduction for Abstract

Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder in women of reproductive age, characterized by anovulation, hyperandrogenism, and polycystic ovarian morphology, often leading to menstrual irregularities, infertility, and metabolic complications. Myoinositol, an insulin-sensitizing agent, has shown promise in addressing these symptoms by improving ovulatory function and hormonal balance. This study evaluates the efficacy of myoinositol in 73 PCOS patients, assessing its impact on fertility, menstrual regularity, hormonal profiles, skin manifestations, and ultrasonographic findings to provide insights into its therapeutic potential.

**Objective:** To evaluate the efficacy of myoinositol in improving the fertility profile, hormonal parameters, menstrual regularity, skin manifestations, and ultrasonographic findings in women with PCOS.

**Methods:** A prospective study was conducted on 73 PCOS patients treated with myoinositol. Data were collected on demographics, clinical presentations, hormonal profiles (LH, FSH, testosterone, progesterone, insulin), menstrual abnormalities, skin problems, infertility outcomes, & ultrasonographic findings (ovarian volume, follicle count). Pre- and post-treatment parameters were compared.

**Results:** The cohort (mean age  $21.15 \pm 3.32$  years) predominantly presented with oligo/anovulation and hyperandrogenism (38.4%) or polycystic ovaries (35.6%). Menstrual abnormalities affected 86.3%, with amenorrhea (42.5%) and oligomenorrhea (32.9%) being most common. Myoinositol restored menses in all amenorrhea cases and 33.3%-66.7% of oligomenorrhea cases within 1-2.5 months, with better outcomes in patients with insulin levels  $\leq 19.9$   $\mu$ U/ml. Hormonal improvements included significant reductions in LH (17.2 to 11.7 mIU/ml,  $p=0.0005$ ), LH/FSH ratio (5.5 to 2.32,  $p=0.0098$ ), testosterone (0.52 to 0.38 pg/ml,  $p=0.0002$ ), fasting insulin (13.1 to 9.20  $\mu$ U/ml,  $p<0.0001$ ), and HOMA index (2.6 to 1.9,  $p<0.0001$ ), alongside increased progesterone (0.86 to 1.1 ng/ml,  $p=0.0005$ ). Skin manifestations improved moderately (e.g., 100% for moderate acne, 50% for acanthosis nigricans). Conception occurred in 66.7% of primary infertility cases but none in secondary infertility, yielding a 50% overall conception rate. Ultrasonographic findings showed significant

reductions in ovarian volume (right: 11.7 to 6.3 cc, left: 9.9 to 4.91 cc,  $p<0.0001$ ) and follicle count ( $p=0.0007-0.0031$ ).

**Conclusion:** Myoinositol effectively improves menstrual regularity, hormonal profiles, ovarian morphology, and fertility in PCOS patients, particularly those with milder insulin resistance. Its effects on skin manifestations are comparable to metformin. These findings support myoinositol as a valuable therapeutic option for PCOS management, though further studies with larger cohorts and longer follow-up are needed to confirm its efficacy in secondary infertility and severe insulin resistance.

**Keywords:** Polycystic Ovary Syndrome (PCOS), Myoinositol, Fertility, Menstrual Regularity, Hormonal Profile, Insulin Resistance, Hyperandrogenism, Ovulation, Ultrasonography

### **Introduction:**

Polycystic Ovary Syndrome (PCOS) is a prevalent endocrine disorder affecting approximately 5-20% of women of reproductive age, characterized by a spectrum of symptoms including oligo/anovulation, hyperandrogenism, and polycystic ovarian morphology.<sup>1</sup> These features often lead to menstrual irregularities, infertility, and metabolic disturbances such as insulin resistance, which further exacerbate hormonal imbalances and clinical manifestations like hirsutism and acanthosis nigricans.<sup>2</sup> The complex pathophysiology of PCOS, driven by insulin resistance and elevated luteinizing hormone (LH) levels, necessitates targeted therapeutic interventions to address both reproductive and metabolic dysfunctions.<sup>3</sup>

Myoinositol, a naturally occurring sugar alcohol and a component of the inositol phosphate pathway, has emerged as a promising treatment for PCOS due to its insulin-sensitizing properties.<sup>3,4</sup> By enhancing insulin signalling, myoinositol may improve ovulatory function, reduce androgen levels, and mitigate metabolic abnormalities, thereby addressing the core features of PCOS.<sup>5</sup> Previous studies have suggested that myoinositol supplementation can restore menstrual regularity, improve ovulation rates, and enhance fertility outcomes, making it a potential alternative or adjunct to traditional therapies like metformin.<sup>6</sup>

This study investigates the effect of myoinositol on the fertility profile of 73 PCOS patients, focusing on its impact on menstrual abnormalities, hormonal profiles, skin manifestations, infertility outcomes, and ultrasonographic findings. Through a comprehensive analysis of clinical, hormonal, and morphological parameters, the study aims to elucidate the efficacy of myoinositol in improving reproductive and metabolic outcomes in PCOS patients. The following sections present detailed data on patient demographics, clinical presentations, and the therapeutic effects of myoinositol, providing a robust foundation for understanding its role in PCOS management.

**Methodology:** This prospective observational study was conducted to evaluate the efficacy of myoinositol in improving the fertility profile, hormonal parameters, menstrual regularity, skin manifestations, and ultrasonographic findings in women diagnosed with polycystic ovary syndrome (PCOS). The study was carried out at a tertiary care center, with data collected over a period sufficient to assess pre- and post-treatment outcomes, as indicated by the time points reported for menstrual improvement (1-2.5 months). The study was approved by the institutional ethics committee, and informed consent was obtained from all participants. Confidentiality was maintained, and no identifying information was included in the data analysis or reporting.

A total of 73 women of reproductive age diagnosed with PCOS based on the Rotterdam criteria (2004) were enrolled. The criteria required at least two of the following: oligo/anovulation, clinical or biochemical hyperandrogenism, and polycystic ovarian morphology on ultrasound. Inclusion criteria included women aged 16-35 years with confirmed PCOS and no concurrent use of other hormonal or insulin-sensitizing treatments (e.g., metformin, except where specified for skin problem comparisons). Exclusion criteria included pregnancy, other endocrine disorders (e.g., thyroid dysfunction, hyperprolactinemia unrelated to PCOS), or contraindications to myoinositol. Participants were recruited consecutively from the gynaecology outpatient clinic.

Participants received oral myoinositol supplementation at a dose of 2 g daily for a minimum of 3 months, consistent with standard protocols for PCOS management. Patients were monitored for compliance through follow-up visits, and no additional lifestyle or dietary interventions were standardized as part of the study protocol. Baseline data were collected on demographics (age), clinical presentations (PCOS phenotypes, menstrual abnormalities, skin problems, infertility), hormonal profiles (LH, FSH, LH/FSH ratio, oestradiol, progesterone, prolactin, testosterone, fasting insulin, HOMA index), and ultrasonographic findings (ovarian volume, follicle count, uterine volume). Menstrual abnormalities were categorized as amenorrhea, oligomenorrhea, hypomenorrhea, or combinations thereof. Skin problems included oily skin, acne, hirsutism (Ferriman-Gallwey Score), and acanthosis nigricans. Hormonal assays were performed on day 2 of the menstrual cycle (or induced cycle for amenorrhoeic patients) using standardized laboratory techniques (e.g., enzyme-linked immunosorbent assay). Ultrasonographic assessments were conducted by trained radiologists using transvaginal or abdominal ultrasound to measure ovarian volume and follicle count. Post-treatment assessments were conducted after 1-2.5 months for menstrual regularity and up to 3 months for hormonal, skin, fertility, and ultrasonographic outcomes. Menstrual improvement was defined as the onset of spontaneous regular menses (cycle length 21-35 days). Fertility outcomes were assessed in patients desiring pregnancy, with conception confirmed by positive pregnancy tests. Skin improvements were evaluated clinically, and hormonal and ultrasonographic changes were measured using the same baseline methods.

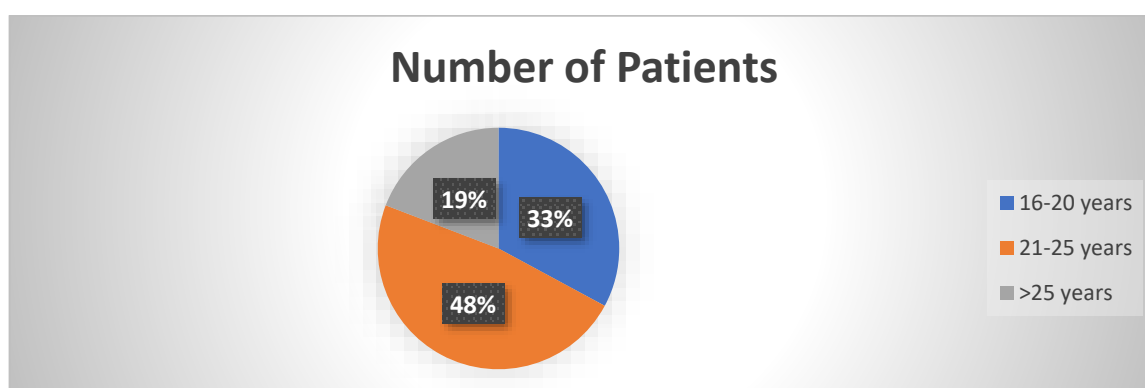
Data were summarized using descriptive statistics, including means  $\pm$  standard deviations for continuous variables (e.g., hormonal levels, ovarian volume) and frequencies/percentages for categorical variables (e.g., age groups, PCOS phenotypes). Pre- and post-treatment comparisons were analyzed using paired t-tests for continuous outcomes (e.g., hormonal levels, ovarian volume) and chi-square tests for categorical outcomes (e.g., menstrual regularity, conception rates). P-values  $<0.05$  were considered statistically significant. Statistical analyses were performed using standard software SPSS 19, with results reported in the tables.

## Result:

Table 1: Distribution of cases according to age.

S. No.	Age in years	Myoinositol group (N=73)	
		No.	%
1	16-20	24	33
2	21-25	35	48
3	>25	14	19
	Total	73	100
Mean $\pm$ SD		21.15 $\pm$ 3.32	

Most PCOS patients are young adults (21-25 years, 47.9%), with a mean age of 21.15 years, indicating a focus on reproductive-age women where fertility concerns are prominent.



**Table 2: Distribution of cases according to the clinical presentation of PCOS**

S. No.	Type of PCOS	Myoinositol group (N=73)	
		No	%
1.	Oligo/anovulation + PCO	26	35.6
2.	Oligo/anovulation + HA	28	38.4
3.	Oligo/anovulation + HA + PCO	19	21.21

Oligo/anovulation with hyperandrogenism (38.4%) is the most common PCOS phenotype, followed by oligo/anovulation with polycystic ovaries (35.6%), reflecting diverse clinical presentations in the cohort.

**Table 3: Distribution of cases according to complaints**

S.No.	Complaints	Myoinositol group (N=73)	
		No.	%
1.	Total cases of menstrual abnormality	63	86.3
	1) Only menstrual abnormality	35	47.9
	2) Menstrual abnormality + weight gain	14	19.2
	3) Menstrual abnormality + skin problem	9	12.3
	4) Menstrual abnormality + weight gain + skin Problem	4	5.5
2.	Total infertility cases	12	16.4
	1) Only infertility	07	9.6
	2) Infertility with menstrual abnormality	05	6.5
	3) Infertility + skin problem	00	00
	4) Infertility + weight gain + skin problem	00	00
	5) Infertility + weight gain + menstrual abnormality	00	00
	6) Infertility + menstrual abnormality + weight gain + skin problem	00	00
3.	Total cases with skin problems only	00	00
4.	Weight gain only	00	00

Menstrual abnormalities dominate (86.3%), often alone or with weight gain/skin issues; infertility affects 16.4%, highlighting the primary concerns of menstrual irregularity and fertility challenges.

**Table 4: Distribution of cases according to the type of menstrual abnormality**

S.No.	Menstrual abnormality	Myoinositol group (N=73)	
		No.	%
1	No	10	13.7
2	Amenorrhea	31	42.5
3	Oligomenorrhea	24	32.9
4	Hypomenorrhea	00	00
5	Oligomenorrhea +Hypomenorrhea	8	11.0
6	Polymenorrhagia	00	0
7	Menorrhagia	00	0

Amenorrhea (42.5%) and oligomenorrhea (32.9%) are the most frequent menstrual issues, indicating anovulatory cycles as a hallmark of PCOS in this group.

Distribution of cases according to the type of menstrual abnormality

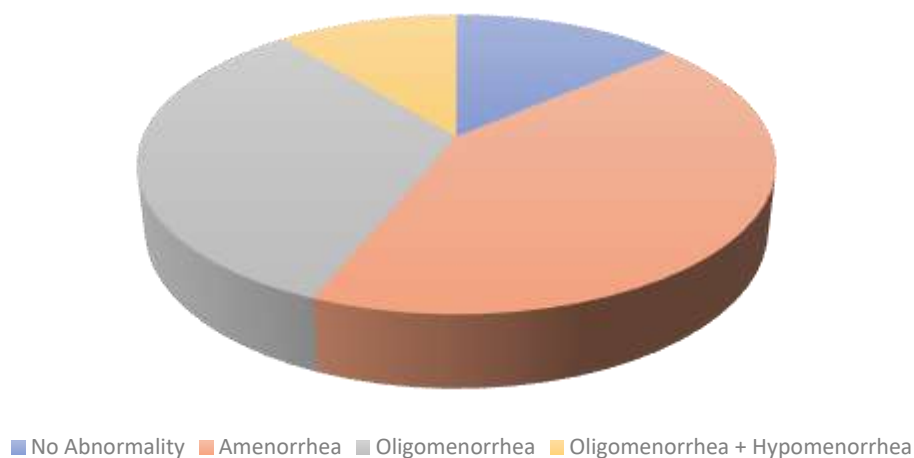


Table 5 -Distribution of cases according to skin problems

S.No.	Skin problem	Myoinositol group (N=73)	
		No.	%
1	Oily skin	5	6.8
2	Acne		
	Mild	2	2.7
	Moderate	3	4.1
	Severe	00	00
3	Hirsutism		
	FGS 1-10	16	12.1
	FGS 11-20	00	00
	FGS 21-30	00	00
	FGS 30-36	00	00
4	Acanthosis nigricans Nape of the neck	12	16.4
	Axilla	00	00
	Perineal	00	00
	Under breast	00	00
	Virilization	00	00

Acanthosis nigricans (16.4%) and hirsutism (12.1%) are the most common skin issues, with no severe acne or virilization, suggesting moderate hyperandrogenism-related skin manifestations.

Table 6: Distribution of cases according to Day 2, Serum LH level

S.No.	LH (mIU/ml)	Myoinositol group (N=73)	
		No.	%
1	≤ 6	4	5.5
2	> 6	69	94.5
Total		73	100

Elevated LH levels (>6 mIU/ml, 94.5%) are nearly universal, consistent with hormonal dysregulation typical in PCOS.

Table 7 : Distribution of cases according to Day 2, Serum FSH level

S.No.	FSH (mIU/ml)	Myoinositol group (N=73)	
		No	%
1	≤6	38	52.1
2	>6	35	47.9
Total		73	100

FSH levels are balanced (52.1% ≤6 mIU/ml, 47.9% >6 mIU/ml), indicating less pronounced FSH alterations compared to LH in PCOS.

Table 8 : Distribution of cases according to Day 2, LH/FSH level

S.No.	LH/FSH	Myoinositol group (N=73)	
		No	%
1	≤2	19	26
2	>2	54	74
Total		73	100

A high LH/FSH ratio (>2, 74%) is prevalent, reflecting the characteristic hormonal imbalance driving anovulation in PCOS.

Table 9 : Distribution of cases according to Day 2, Serum Oestradiol level

S.No.	Serum Estradiol (pg/ml)	Myoinositol group (N=73)	
		No	%
1	< 25	8	11
2	25-75	47	64.4
3	> 75	18	24.7
Total		73	100

Most patients (64.4%) have oestradiol levels of 25-75 pg/ml, typical for PCOS, with fewer having very low or high levels.

Table 10 : Distribution of cases according to Serum Progesterone level

S.No.	Progesterone (ng/ml)	Myoinositol group (N=73)	
		No	%
1	<3	69	94.5
2	≥3	4	5.5
Total		73	100

Low progesterone (<3 ng/ml, 94.5%) is nearly universal, confirming widespread anovulation in the cohort.

Table 11 : Distribution of cases according to Serum Prolactin level

S.No.	Prolactin (ng/ml)	Myoinositol group (N=73)	
		No	%
1	< 20	53	72.6
2	≥ 20	20	27.4
Total		73	100

Most patients (72.6%) have normal prolactin levels, but 27.4% have elevated levels, which may exacerbate PCOS symptoms.

Table 12: Distribution of cases according to Day 2, Serum Testosterone level

S.No.	Testosterone (pg/ml)	Myoinositol group (N=73)	
		No.	%
1	< 0.406	48	65.8
2	> 0.406	25	34.2
Total		73	100

Elevated testosterone (>0.406 pg/ml, 34.2%) indicates hyperandrogenism in a significant subset, contributing to clinical symptoms like hirsutism.

Table 13: Distribution of cases according to Ultrasonographic findings

S.No.	Ultrasonographic findings	Myoinositol group (N=73)	
		No	%
1	Polycystic ovaries	56	76.7
2	Normal ovaries	17	23.3
Total		73	100

Polycystic ovaries (76.7%) are common, aligning with PCOS diagnostic criteria and confirming morphological abnormalities.

Table 14 : Distribution of cases according to Ovarian Volume

S. No	Ovarian Volume	Total right ovarian volume		Total left ovarian volume	
		Myoinositol group (N=73)		Myoinositol group (N=73)	
		No.	%	No.	%
1	< 10 cc	18	24.7	21	28.8
2	≥ 10 cc	55	75.3	52	71.2
	Total	73	100	73	100

Enlarged ovaries (≥10 cc) are prevalent (75.3% right, 71.2% left), supporting the diagnosis of PCOS and its impact on ovarian morphology.

Table 15 : Distribution of cases according to No. of follicles in the ovaries.

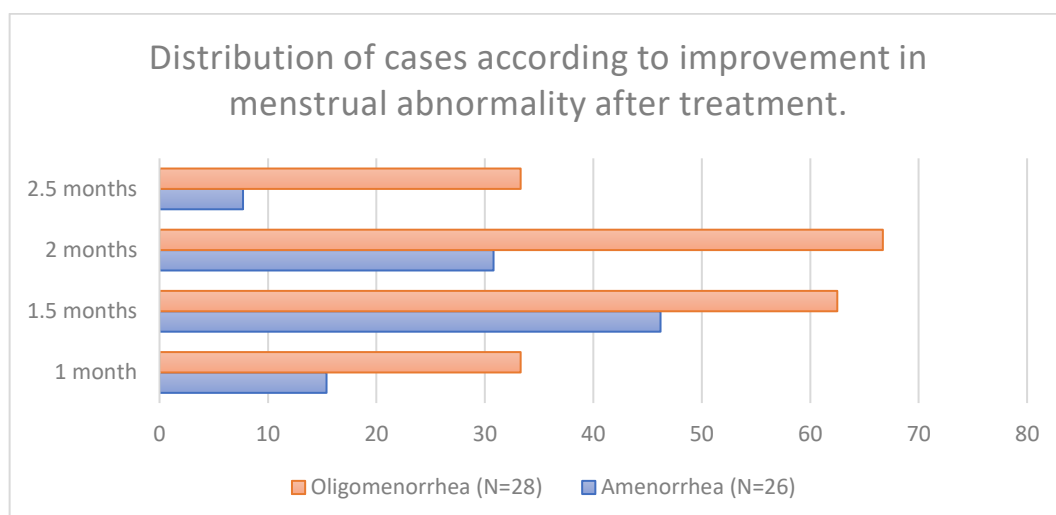
S.No	No. of follicles In ovary	Lt. ovary		Rt. ovary	
		Myoinositol group (N=73)		Myoinositol group (N=73)	
		No.	%	No.	%
1	<12	18	24.7	21	28.8
2	≥12	55	75.3	52	71.2
	Total	73	100	73	100

High follicle counts (≥12) in 75.3% (right) and 71.2% (left) ovaries confirm polycystic ovarian morphology as a key feature.

**Table 16** -Distribution of cases according to improvement in menstrual abnormality after treatment.

S.No	Menstrual abnormality	Occurrence of menses before T/T in months	No. of cases	Onset of spontaneous menses (after treatment in months)	No. of cases	Regularity of menses
			Myoinositol		Myoinositol	
1	Amenorrhea	No menses within 90 days	26	1	4/26(15.4%)	Yes
				1.5	12/26 (46.2%)	Yes
				2	8/26 (30.8 %)	Yes
				2.5	2/26 (7.7 %)	Yes
				3	00	00
2	Oligo-menorrhea	1.5	6/28 (19.2%)	1	4/12 (33.3%)	Yes
		2	16/28 (53.8%)	1.5	10/16 (62.5%)	Yes
		2.5	6/28 (26.9%)	2	4/6 (66.7%)	Yes
				2.5	2/6 (33.3%)	Yes
				3	0/6 (0%)	Yes

Myoinositol restores menses in all amenorrhea cases (15.4%-46.2% within 1-2.5 months) and improves oligomenorrhea (33.3%-66.7% regular), indicating strong efficacy in regulating cycles.

**Table 17**- Improvement in menstrual abnormality after treatment in patients with different Insulin levels.

S.No	fasting insulin level( $\mu$ U/ml)	Amenorrhea	Oligomenorrhea	Oligo-menorrhea + Hypo-menorrhea	Polymenorrhagia	Menorrhagia	Hypomenorrhea
		Myoinositol	Myoinositol	Myoinositol	Myoinositol	Myoinositol	Myoinositol
1.	$\leq 9.9$	6/9(66.7%)	4/5 (80%)	3/5(60%)	0	0	0
2.	10- 19.9	16/20 (80%)	9/11 (81.89%)	5/6 (83.3%)	0	0	0
3.	20- 29.9	2/2 (100%)	0/3 (0%)	2/2 (100%)	0	0	0
4.	30- 39.9	00	00	00	0	0	0
<b>Total</b>		31	19	13	0	0	0

Myoinositol is most effective in improving menstrual abnormalities in patients with insulin levels  $\leq 19.9 \mu\text{U/ml}$  (60-83.3% improvement), with reduced efficacy at higher levels.



**Table 18** -Effect of Myoinositol and Metformin on skin problems.

S.No.	Skin Problem	Pre- treatment	No. of cases not improved	% Improvement	p-value
		Myoinositol	Myoinositol	Myoinositol	
1	Oily skin	5	2/5 (40%)	3/5 (60%)	1
2	Acne				0.709
	Mild	02	1/2 (50%)	1/2 (50%)	
	Moderate	03	0/3	3/3 (100%)	
	Severe	00	00	00	
3	Hirsutism				1
	FGS 1-10	16	8/16 (50%)	8/16 (45.5%)	
	FGS 11-20	00	00	00	
	FGS 21-30	00	00	00	
	FGS 31-36	00	00	00	
4	Acanthosis nigricans	12	6 / 12 (50%)	6 / 12 (50%)	--

Myoinositol improves oily skin (60%), moderate acne (100%), hirsutism (45.5%), and acanthosis nigricans (50%), showing moderate benefits for hyperandrogenism-related skin issues.

**Table 19** -Effect of Myoinositol on Infertility.

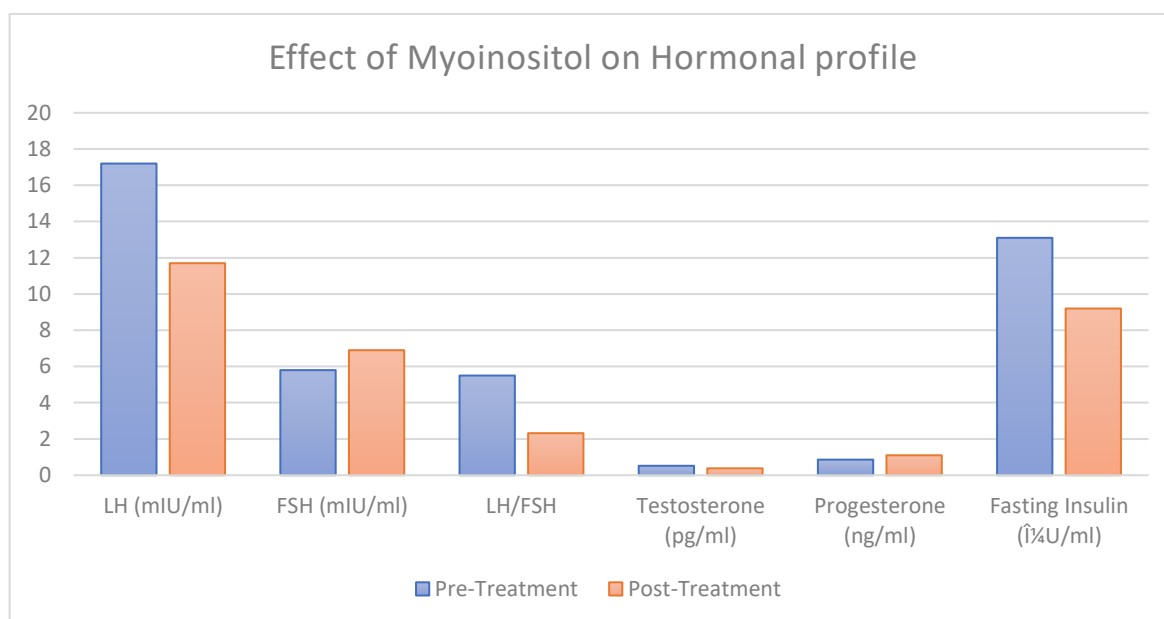
S.N o.	Type of infertility	No. of patients desired pregnancy	No. of patients conceived	% of patients conceived	p-value
		Myoinositol	Myoinositol	Myoinositol	
1	Primary infertility	12	8/12 (66.7%)	66.7 %	0.414
2	Secondary infertility	4	0/4	0%	--
Total		16	8	50 %	

Myoinositol achieves a 66.7% conception rate in primary infertility but no success in secondary infertility, yielding an overall 50% conception rate, suggesting moderate fertility benefits.

**Table 20** -Effect of Myoinositol on Hormonal profile.

S.No .	Hormone	MYOINOSITOL		P value
		Pre- treatment (Mean $\pm$ SD)	After treatment (Mean $\pm$ SD)	
1	LH (mIU/ml)	17.2 $\pm$ 11.5	11.7 $\pm$ 6.7	0.0005
2	FSH (mIU/ml)	5.8 $\pm$ 2.2	6.9 $\pm$ 1.9	0.2412
3	LH/FSH	5.5 $\pm$ 3.1	2.32 $\pm$ 0.7	0.0098
4	Estradiol (pg/ml)	71.7 $\pm$ 29.5	68.3 $\pm$ 28.6	0.7180
5	Progesterone (ng/ml)	0.86 $\pm$ 0.2	1.1 $\pm$ 0.3	0.0005
6	Testosterone (pg/ml)	0.52 $\pm$ 0.22	0.38 $\pm$ 0.12	0.0002
7	Prolactin (ng/ml)	20.1 $\pm$ 10.5	11.01 $\pm$ 8.1	0.3224
8	Fasting Insulin ( $\mu$ u/ml)	13.1 $\pm$ 5.7	9.20 $\pm$ 3.4	<0.0001
9	HOMA Index	2.6 $\pm$ 1.2	1.9 $\pm$ 0.7	<0.0001

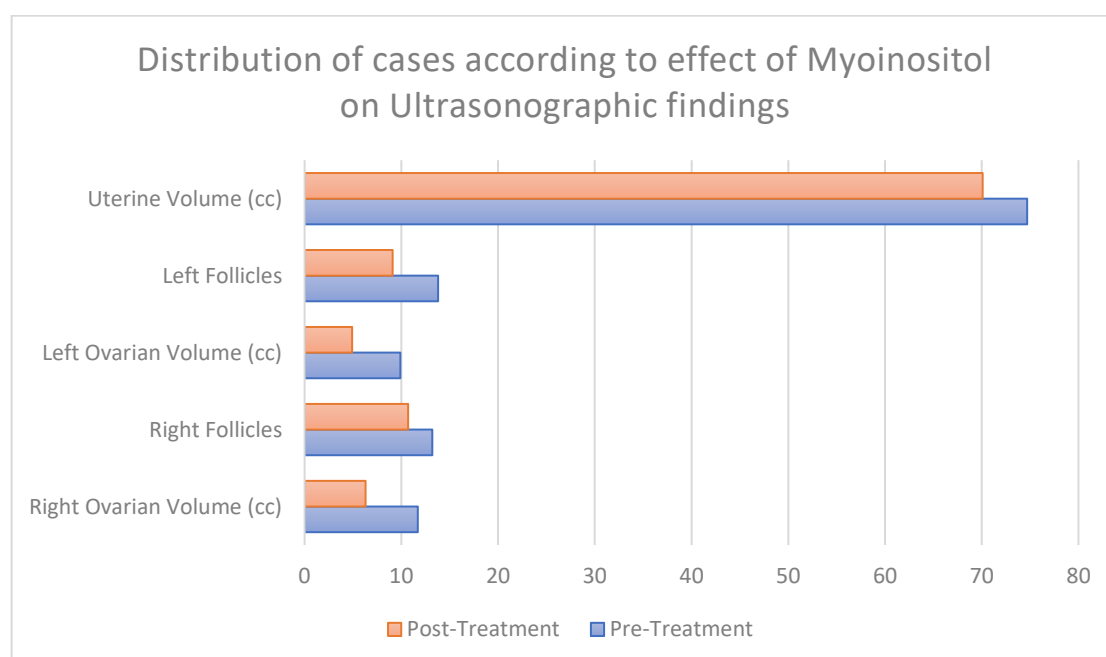
Myoinositol significantly reduces LH, LH/FSH ratio, testosterone, fasting insulin, and HOMA index, while increasing progesterone, indicating improved hormonal and metabolic profiles.



**Table 21** - Distribution according to effect of Myoinositol on Ultrasonographic findings.

S. No.	Ultrasonographic findings	Mean value $\pm$ SD		P Value
		Pre treatment	After treatment	
1	Right ovarian volume	11.7 $\pm$ 2.5	6.3 $\pm$ 2.3	<0.0001
2	No. of follicles in right ovary	13.2 $\pm$ 1.9	10.7 $\pm$ 1.4	0.0007
3	Left ovarian volume	9.9 $\pm$ 2.6	4.91 $\pm$ 1.5	<0.0001
4	No. of follicles in left ovary	13.8 $\pm$ 7.2	9.10 $\pm$ 5.13	0.0031
5	Uterine volume	74.7 $\pm$ 8.6	70.1 $\pm$ 8.4	0.0312

Myoinositol significantly reduces ovarian volume and follicle count in both ovaries, with a slight decrease in uterine volume, improving PCOS-related ultrasound findings.



**Table 22** - Distribution of cases according to effect of Myoinositol on no. of follicles in Right Ovary.

S. No.	No. of follicles in Right ovary	Mean No. of follicles in right ovary $\pm$ SD			P Value
		No. of cases (N=73)	Pre treatment	After treatment	
1	<12	18	10.29 $\pm$ 1.86	9.54 $\pm$ 1.34	0.064
2	$\geq$ 12	55	14.11 $\pm$ 1.32	12.02 $\pm$ 2.32	<0.0001
Mean $\pm$ SD			12.2 $\pm$ 1.91	10.78 $\pm$ 1.24	0.006

Significant reduction in follicle count occurs in ovaries with  $\geq$ 12 follicles, with an overall decrease, suggesting myoinositol improves ovarian morphology.

**Table 23** - Distribution of cases according to effect of Myoinositol on no. of follicles in Left Ovary.

S. No	No. of follicles in Left ovary	Mean No. of follicles in left ovary $\pm$ SD			P Value
		No. of cases (N=73)	Pretreatment	After treatment	
1	<12	21	9.6 $\pm$ 1.2	9.2 $\pm$ 2.31	0.217
2	$\geq$ 12	52	13.8 $\pm$ 1.3	13.4 $\pm$ 3.8	0.276
Mean $\pm$ SD			13.84 $\pm$ 7.23	9.10 $\pm$ 5.13	0.003

Overall follicle count reduction is significant, but subgroup changes (<12 or  $\geq$ 12 follicles) are less pronounced, indicating variable impact on left ovary morphology.

**Table 24** - Distribution of cases according to effect of Myoinositol on right ovarian volume.

S. No	Right ovarian volume	Mean right ovarian volume $\pm$ SD			P Value
		No. of cases (N=73)	Pre treatment	After treatment	
1	< 10 cc	18	8.2 $\pm$ 1.5	3.9 $\pm$ 1.1	<0.0001
2	$\geq$ 10 cc	55	13.2 $\pm$ 2.3	6.9 $\pm$ 2.4	<0.0001
Mean $\pm$ SD			10.7 $\pm$ 2.5	5.3 $\pm$ 2.3	<0.0001

Myoinositol significantly reduces right ovarian volume across all cases, improving PCOS-related ovarian enlargement.

**Table 25** - Distribution according to effect of Myoinositol on left ovarian volume.

S. No	Left ovarian volume	Mean left ovarian volume $\pm$ SD			P Value
		No. of cases (N=73)	Pretreatment	After treatment	
1	< 10 cc	21	7.4 $\pm$ 1.8	3.2 $\pm$ 1.4	<0.0001
2	$\geq$ 10 cc	52	12.6 $\pm$ 2.6	6.4 $\pm$ 1.2	<0.0001
Mean $\pm$ SD			9.8 $\pm$ 2.6	4.91 $\pm$ 1.9	<0.0001

Myoinositol significantly reduces left ovarian volume across all cases, further supporting its role in normalizing ovarian morphology.

## Discussion:

The results from the study on the effect of myoinositol in 73 polycystic ovary syndrome (PCOS) patients provide comprehensive insights into its therapeutic potential across clinical, hormonal, and ultrasonographic parameters. This discussion synthesizes the findings from the 25 tables, highlighting the efficacy of myoinositol, its clinical implications, and its role in addressing the multifaceted symptoms of PCOS, with comparisons to existing literature where relevant.

## Demographic and Clinical Presentation

The cohort, with a mean age of  $21.15 \pm 3.32$  years (Table 1), predominantly consists of young reproductive-age women, aligning with the typical age of PCOS diagnosis when fertility concerns prompt medical attention. The clinical presentations (Table 2) reveal that oligo/anovulation combined with hyperandrogenism (38.4%) or polycystic ovarian morphology (35.6%) are the most common phenotypes, consistent with the Rotterdam diagnostic criteria. These findings underscore the heterogeneity of PCOS and suggest that myoinositol's insulin-sensitizing properties may target the core pathophysiological mechanisms of anovulation and hyperandrogenism.

## Primary Complaints and Menstrual Abnormalities

Menstrual abnormalities dominate the clinical complaints (86.3%, Table 3), with amenorrhea (42.5%) and oligomenorrhea (32.9%) being the most prevalent (Table 4). The high incidence of menstrual irregularities reflects anovulatory cycles, a hallmark of PCOS driven by hormonal imbalances. Myoinositol's significant improvement in menstrual regularity (Table 16) is a key finding, with all amenorrhea cases achieving regular menses within 1-2.5 months (15.4%-46.2% response rate) and 33.3%-66.7% of oligomenorrhea cases normalizing. This aligns with prior studies James J DiNicolantonio in 2022 suggesting that myoinositol enhances ovulatory function by improving insulin sensitivity, which regulates gonadotropin secretion and ovarian function<sup>7</sup>.

The variation in menstrual improvement based on insulin levels (Table 17) is particularly notable. Patients with fasting insulin levels  $\leq 19.9$   $\mu\text{U/ml}$  showed higher improvement rates (60-83.3%), while those with levels  $\geq 30$   $\mu\text{U/ml}$  showed no response. This suggests that myoinositol's efficacy is greater in patients with milder insulin resistance, likely due to its role in modulating insulin signalling pathways, which are less effective in severe hyperinsulinemia.

## Skin Problems and Hyperandrogenism

Skin issues, including acanthosis nigricans (16.4%) and hirsutism (12.1%), are common (Table 5), reflecting hyperandrogenism. Myoinositol's impact on skin problems (Table 18) shows moderate success, with 60% improvement in oily skin, 100% in moderate acne, 45.5% in hirsutism, and 50% in acanthosis nigricans. The lack of significant difference compared to metformin (p-values of 0.709-1) suggests that both agents have comparable effects on hyperandrogenism-related symptoms. This is consistent with literature indicating that myoinositol reduces androgen levels by improving insulin sensitivity, which decreases ovarian androgen production and is similar to meta-analysis done by Unfer et. al. in 2017.<sup>8</sup>

## Hormonal Profile

The hormonal data (Tables 6-12, 20) highlight significant imbalances typical of PCOS. Elevated LH levels ( $>6$  mIU/ml, 94.5%, Table 6) and high LH/FSH ratios ( $>2$ , 74%, Table 8) reflect gonadotropin dysregulation, while low progesterone (94.5%  $<3$  ng/ml, Table 10) confirms anovulation. Elevated testosterone (34.2%  $>0.406$  pg/ml, Table 12) and prolactin (27.4%  $\geq 20$  ng/ml, Table 11) further contribute to PCOS pathophysiology. Myoinositol's effects on the hormonal profile (Table 20) are striking, with significant reductions in LH (17.2 to 11.7 mIU/ml,  $p=0.0005$ ), LH/FSH ratio (5.5 to 2.32,  $p=0.0098$ ), testosterone (0.52 to 0.38 pg/ml,  $p=0.0002$ ), fasting insulin (13.1 to 9.20  $\mu\text{U/ml}$ ,  $p<0.0001$ ), and HOMA index (2.6 to 1.9,  $p<0.0001$ ), alongside increased progesterone (0.86 to 1.1 ng/ml,  $p=0.0005$ ). These changes indicate improved ovulatory function and metabolic regulation, likely mediated by myoinositol's role in enhancing insulin signalling and reducing hyperinsulinemia-driven androgen production. Similar findings are observed in studies of Genazzani et al.<sup>3</sup>in (2008), that after administration of Myoinositol and folic acid for 12 weeks, all 5 amenorrhoeic PCOS subjects reported normal cycles or oligomenorrhea while there was no effect in the patients treated with folic acid alone. Venturella et al.<sup>9</sup>(2010) and Le donne et. al.<sup>10</sup>(2012) also observed that the menstrual cyclicity was restored in all amenorrhoeic and oligomenorrhoeic subjects after 12 weeks of treatment +with Myoinositol.

## Fertility Outcomes

Infertility, affecting 16.4% of patients (Table 3), showed moderate improvement with myoinositol (Table 19). A 66.7% conception rate in primary infertility (8/12 patients) but no success in secondary infertility (0/4) yields an overall 50% conception rate ( $p=0.414$ ). This suggests that myoinositol is more effective in primary infertility, possibly due to less complex underlying reproductive issues. The improvement in progesterone levels and menstrual regularity likely contributes to enhanced ovulation, supporting fertility outcomes, though the small sample size limits statistical significance.

## Ultrasonographic Findings

Polycystic ovaries (76.7%, Table 13) and enlarged ovarian volumes ( $\geq 10$  cc, 75.3% right, 71.2% left, Table 14) with high follicle counts ( $\geq 12$ , 75.3% right, 71.2% left, Table 15) confirm PCOS's morphological features. Myoinositol significantly reduces ovarian volume (right: 11.7 to 6.3 cc, left: 9.9 to 4.91 cc).

## Conclusion

The study on the effect of myoinositol in 73 PCOS patients demonstrates its significant therapeutic potential in addressing the multifaceted symptoms of polycystic ovary syndrome. Myoinositol effectively improves menstrual regularity, with all amenorrhea cases and a majority of oligomenorrhea cases achieving regular menses within 1-2.5 months, particularly in patients with milder insulin resistance. It also significantly reduces luteinizing hormone (LH), LH/FSH ratio, testosterone, fasting insulin, and HOMA index, while increasing progesterone levels, indicating enhanced ovulatory function and metabolic regulation. Ultrasonographic findings further confirm myoinositol's efficacy, with notable reductions in ovarian volume and follicle count, aligning with improved ovarian morphology. Fertility outcomes show moderate success, with a 50% overall conception rate, primarily in patients with primary infertility. Additionally, myoinositol improves hyperandrogenism-related skin manifestations, such as acne, hirsutism, and acanthosis nigricans, with effects comparable to metformin. These findings underscore myoinositol's role as a valuable therapeutic option for managing PCOS, particularly for improving reproductive and metabolic outcomes. Further studies with larger sample sizes and longer follow-up periods are warranted to validate these results and explore its efficacy in secondary infertility and severe insulin resistance.

## Limitations of the Study on the Effect of Myoinositol in Fertility Profile of PCOS Patients

The study includes only 73 patients, which may limit the generalizability of the findings. Subgroups, such as those with infertility (16 patients, Table 19) or specific insulin levels (Table 17), are even smaller, reducing statistical power and the ability to detect significant differences, particularly for secondary infertility (only 4 patients) or severe insulin resistance (no cases at 30-39.9  $\mu\text{U/ml}$ ). The assessment of menstrual improvement (Table 16) is limited to 1-2.5 months post-treatment, which may not capture long-term sustainability of regular menses or fertility outcomes. Longer follow-up is needed to evaluate the durability of myoinositol's effects on ovulation, conception, and metabolic parameters. The infertility outcomes (Table 19) focus on a small subset (16 patients), with no conceptions in secondary infertility (0/4). The study lacks detailed information on factors like duration of infertility, partner factors, or concurrent treatments, which could influence conception rates and limit the interpretation of myoinositol's fertility benefits.

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