



COMPARISON OF EFFECTIVENESS OF STANDARD VS LONG LETROZOLE PROTOCOL FOR OVULATION INDUCTION IN WOMEN WITH PCOS



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Introduction

The polycystic ovarian syndrome (PCOS) is a heterogeneous group of disorders which comprises of significant metabolic, reproductive and endocrine dysfunctions.¹ Anovulation due to PCOS is multifactorial and its pathophysiology revolves around the insulin resistance and reduced expression of sex hormone binding globulin.² The ESHRE criteria for the diagnosis of PCOS, also known as Rotterdam criteria includes

1. Oligo or anovulation.

2. Clinical and/or biochemical signs of hyperandrogenism.
3. Polycystic ovaries on ultrasound.

According to ESHRE letrozole should be used as first line for anovulation.⁵ Letrozole is a selective, reversible competitive inhibitor of the aromatase enzyme.

Letrozole has been used in different doses for ovulation induction and while a short course is routinely used, it is debated that a longer duration may achieve better results avoiding need of Gonadotrophin injections.⁷

Objective

To compare the effectiveness of standard dose Letrozole with long dose Letrozole protocol for induction of ovulation in women with PCOS.

Method

STUDY DESIGN:

Prospective randomized comparative study

PLACE OF STUDY:

Sir Ganga Ram Hospital, Lahore, Pakistan

DURATION OF STUDY:

One year 23/07/2023 to 22/06/2024

SAMPLE SIZE:

Sample size of 174 was calculated with 5 % margin of error and 95% confidence interval by expecting 13% of PCOS effecting females. Each group will have 87 participants.

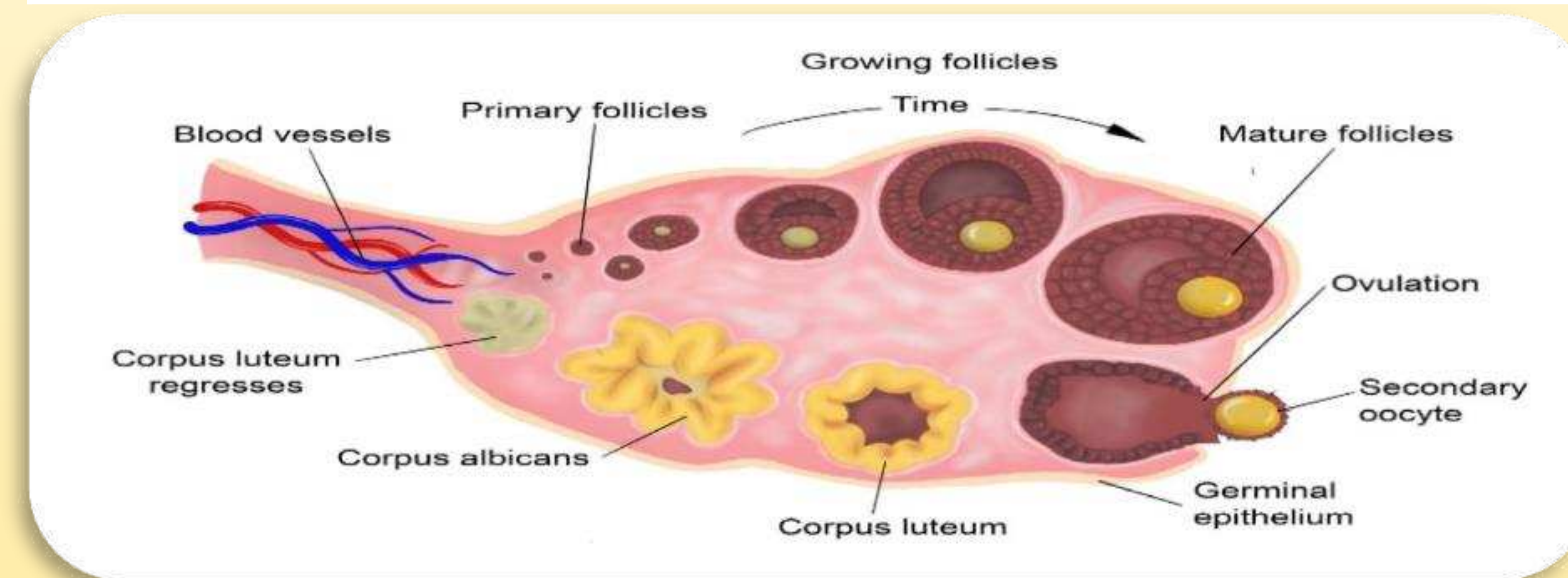
Selection Criteria

INCLUSION CRITERIA:

Women of 18-35 years of age. Subfertility for one year or more.
Diagnosed case of PCOS on biochemical/ultrasound.

EXCLUSION CRITERIA:

Women with evidence of tubal blockage on HSG/laparoscopy.
If husband had abnormal semen analysis
Other coexistent cause of infertility like endometriosis or fibroid etc



Data Collection

All patients were advised metformin and life style modification for 3 months before the start of ovulation induction in both groups

Group A (standard protocol) Letrozole 2.5 mg was given daily (Day 2–6).

- If follicle ≥ 18 mm on Day 10 $\rightarrow$ HCG 5000 IU given intramuscularly and couple advised to have intercourse after 24 to 35 hours. If no menstruation after 2 weeks serum bhcg checked for positive pregnancy.
- If follicle 14–16 mm $\rightarrow$ rescan on Day 12; if ≥ 18 mm $\rightarrow$ HCG given.
- If no follicle > 10 –11 mm, then in next cycle Letrozole 5mg given (Day 2–6)
- If still no response, then Letrozole 7.5 mg in third cycle for same 5 days was given. If still no mature follicle $\rightarrow$ treatment failure.

Group B (Long Letrozole protocol):

- Letrozole 2.5 mg daily (Day 2–10). TVS on Day 10, if follicle ≥ 18 mm $\rightarrow$ HCG 5000 IU given, If no mature follicle, then in next 2 cycles Letrozole 5 mg (Day 2–10) is given with TVS on day 10 and 12 to see mature follicle. If still no response $\rightarrow$ treatment failure.

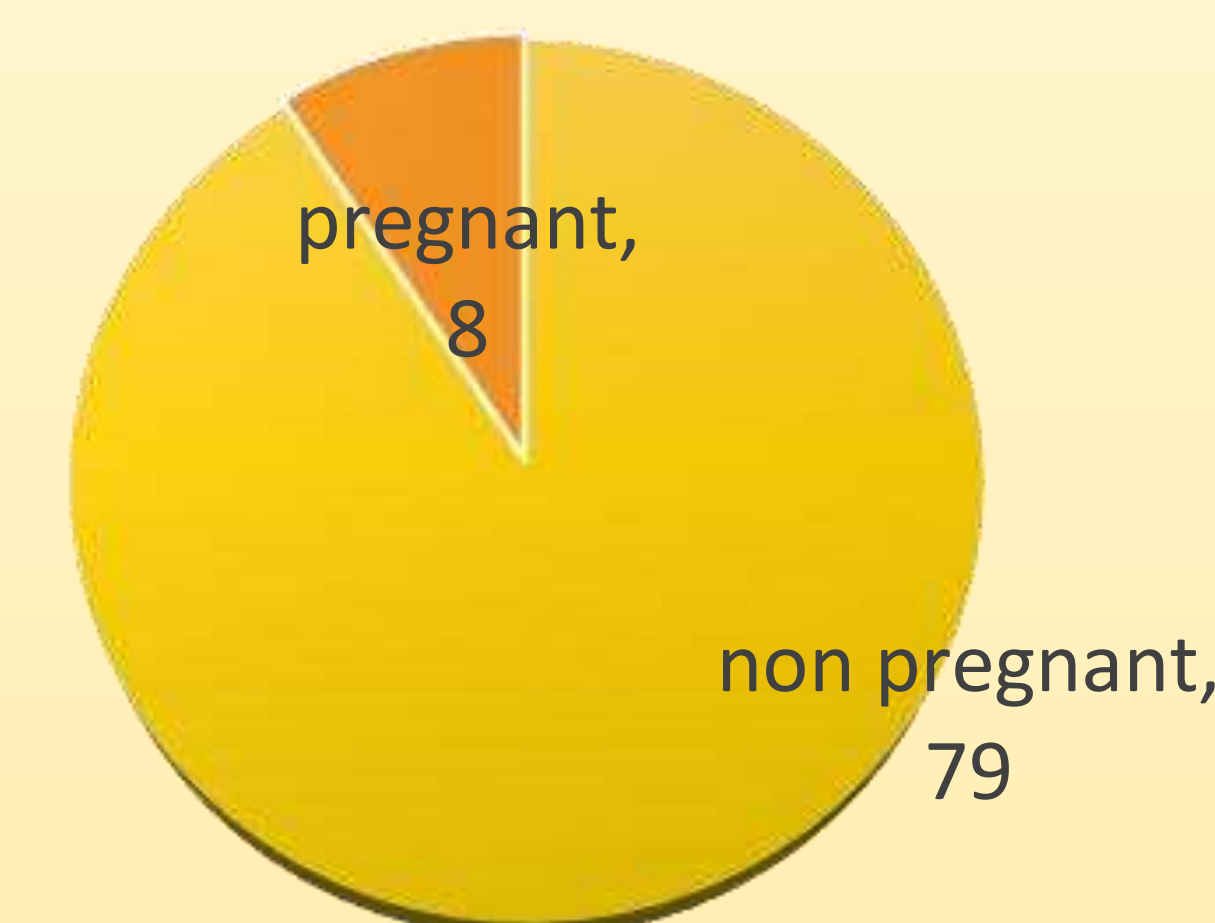
Outcomes: • Primary: 1–2 mature follicles (18–22 mm) on day 12.

• Secondary: pregnancy (serum β -hCG positive), prevention of OHSS

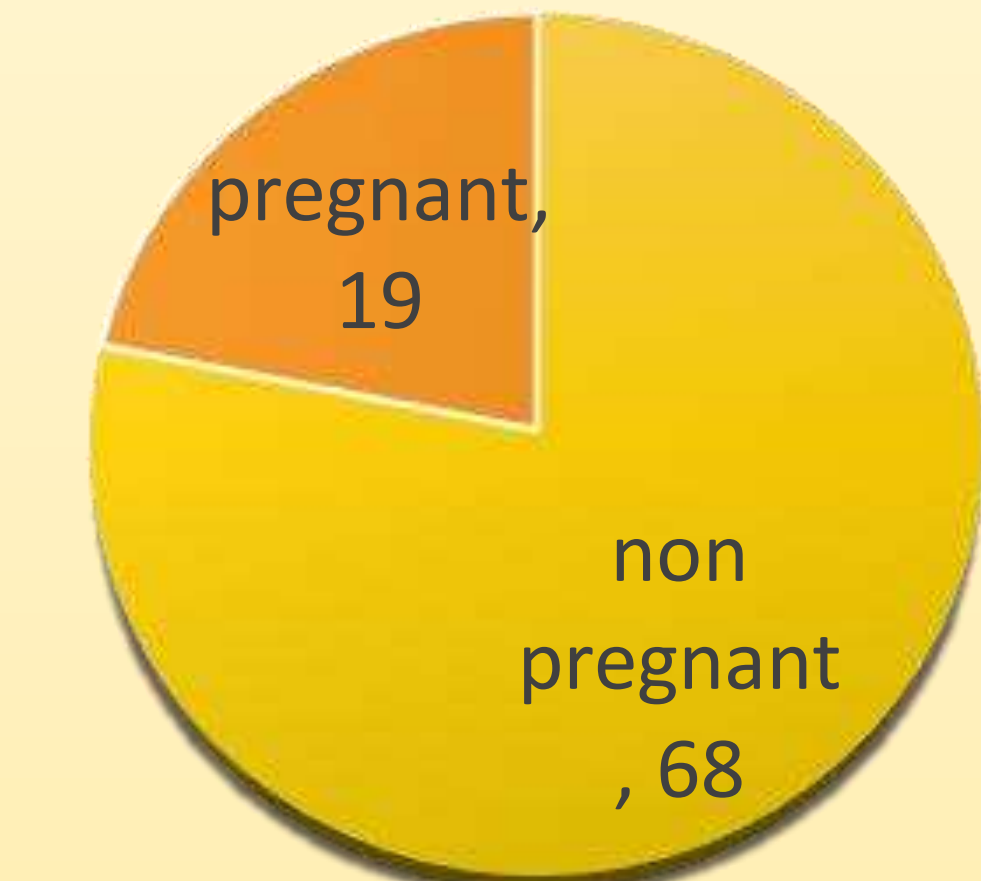
Analysis

The data was entered and analyzed using SPSS 24.0. Mean $\pm$ SD was given for quantitative variables (age, gestational age, BMI, duration of infertility). Frequency and percentage were calculated. Independent 't' test was applied to compare ovulation in both groups taking $p \leq 0.05$ as significant.

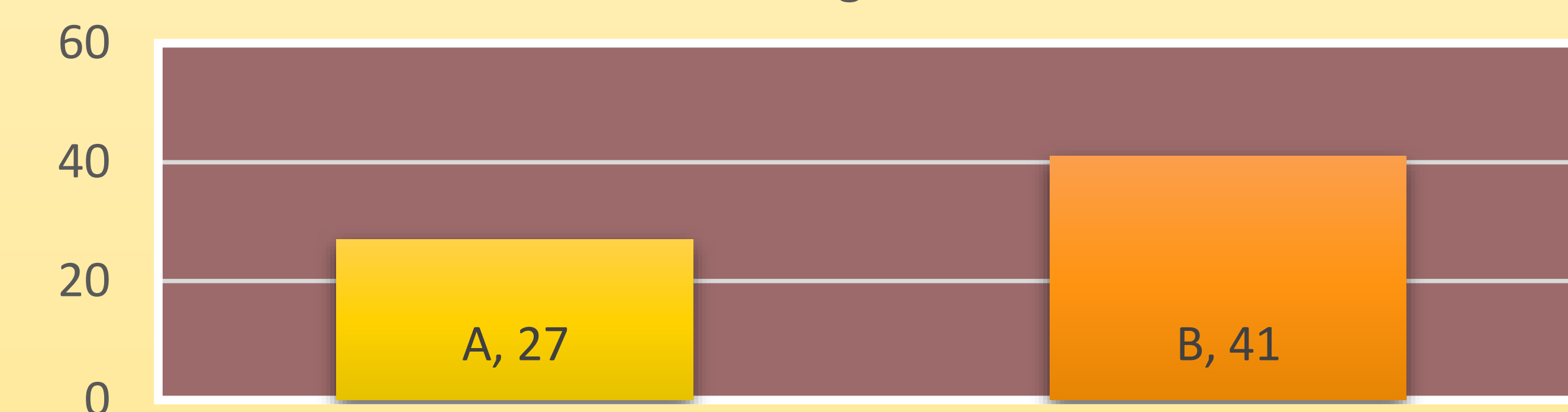
Pregnancy in short protocol A



Pregnancy in long protocol B



Ovulating Patients



Results & Conclusion

The mean size of the dominant follicle on day 12 was 18 ± 3.69 in long protocol which was greater than the other group 14.61 ± 3.49 mm
The number of ovulating patients was greater in extended letrozole group (47.12 % versus 31.0%). $P < 0.001$
Pregnancy occurred in 19 women (21.8%) in long protocol and only 8 (10.3%) in short protocol.

There was not a single case of ovarian hyperstimulation syndrome seen in both groups and these regimes were cost effective as no gonadotrophins were used.

Utilization and outcome: Extended dose Letrozole is more effective in PCOS women compared to conventional standard dose protocol in terms of mature follicles, ovulation rate, pregnancy rate and no serious side effects.