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Research Article

A RANDOMIZED CONTROL TRIAL TO COMPARE THE EFFECTIVENESS OF CLOMIPHENE CITRATE AND LETROZOLE AMONG OVULATORY INFERTILE FEMALES

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Abstract:

Objectives: The objective of this study was to compare the effectiveness of clomiphene citrate and letrozole among ovulatory infertile females.

Material and Methods: We carried out this randomized controlled trial at Jinnah Hospital, Lahore from October 2017 to June 2018 on a total of 224 ovulatory infertile females which were in the age bracket of 18 – 40 years.

Results: We selected women in the age limit of 18 – 40 years which were divided into two main groups Group – A (Clomiphene Citrate) & B (Letrozole) with a respective mean age of (26.72 ± 6.02) years and (26.87 ± 6.33) years. Most dominant age bracket was 18 – 30 years among 148 patients (66.07%). Mean infertility duration was (3.47 ± 2.21) years; for Group – A & B the mean infertility duration was (3.23 ± 2.19) years and (3.68 ± 2.34) years. Group – A efficacy was reported in 19 patients (16.96%) and for Group – B among 37 patients (33.04%) (P -Value = 0.005).

Conclusion: The outcomes conclude that Clomiphene Citrate is less effective than Letrozole in order to achieve pregnancy among ovulatory infertility females.

Keywords: Ovulatory, Letrozole, Infertility, Clomiphene Citrate, Efficacy and Pregnancy.

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INTRODUCTION:

Ovulation is an outcome of maturation process which happens in HPO axis (Hypothalamic Pituitary Ovarian) and it is orchestrated by neuroendocrine cascade which ends in ovaries [1]. Infertile couples face reproductive failure because of an ovulation dysfunction which is prevalent among infertile women from 30% – 40% [2].

Ovulation induction therapy aims at HPO axis which includes oral fertility drugs (Letrozole & Clomiphene Citrate) which can also be amplified through hCG [3, 4]. Other injectable fertility drugs such as Follistim, Gonal-F, Repronex and Menopuror can be managed with in-vitro fertilization or intrauterine insemination. The oral intake of medicines is common all over the world [4, 5].

Clomiphene citrate antagonizes the negative estrogen feedback at hypothalamus with a resultant increase in the stimulation of ovarian through endogenous gonadotropin [6]. Clomiphene drawbacks include poor efficacy, an undesirable profile of side-effects and a relatively higher rate of multiple-pregnancy along with hot flushes and mood changes [6]. Letrozole blocks estrogen synthesis through androgens conversion with an aromatase enzyme activity, it increases the rate of pregnancy by stimulating ovarian and directly affect hypothalamic pituitary ovarian functioning. Aromatase inhibitors have potential advantages over SERM including increased physiological and hormonal endometrium stimulation, reduced rate of multiple pregnancies, the improved profile of side-effects along with rapid clearance, mood signs and few vasomotor [6, 7]. The objective of this study was to compare the effectiveness of clomiphene citrate and letrozole among ovulatory infertile females.

An ovulatory Infertility refers to intercourse without taking contraceptive measures for more than a year and not conceiving even in the presence of a normal diagnosis of pelvic ultrasonography, bilateral normal tubal patency as observed through hysterosalpingography and normal male response.

Effectiveness refers to an onset of pregnancy with a measurement of β -HCG at fifth day after missing first menstrual cycle; Effectiveness is positive in case of

being pregnant with a level of β -HCG as (≥ 5 mlU/ml) at fifth day after missing first menstrual cycle; otherwise, it is negative.

MATERIALS & METHODS:

We carried out this randomized controlled trial at Jinnah Hospital, Lahore from October 2017 to June 2018 on a total of 224 ovulatory infertile females which were in the age bracket of 18 – 40 years. We did not include all those patients who presented a history of pelvic surgery, hyperprolactinemia and hypothyroidism. A random division of patients was made in two groups A & B respectively managed with Clomiphene Citrate (oral dose for five days from third to seventh of a menstrual period for five menstrual cycles) and Letrozole (oral 2.5 mg from third to the seventh day of the menstrual cycle once in a day for five menstrual cycles). We measured the level of β -HCG on the fifth day to confirm pregnancy after first missed a menstrual cycle and documented the effectiveness on a pre-designed Performa.

Data were analyzed through SPSS software. Quantitative variables were presented in Mean and SD values (infertility duration and age). Qualitative variables were presented in frequency and percentage (effectiveness Yes/No). Effectiveness was compared through the Chi-Square Test for both A & B groups (P-Value ≤ 0.05).

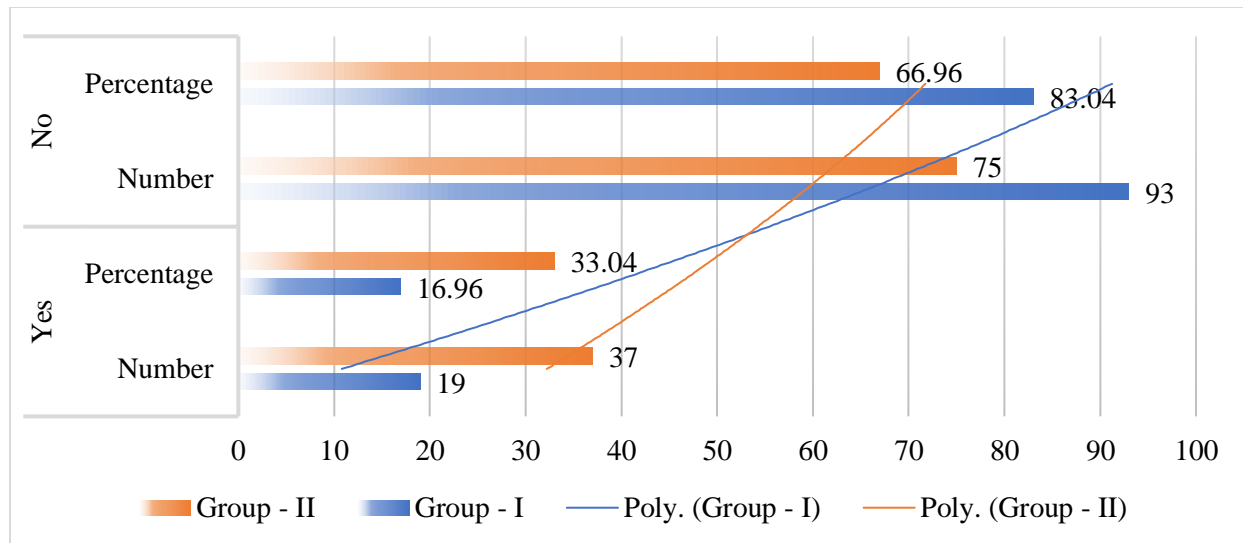
RESULTS:

We selected women in the age limit of 18 – 40 years which were divided into two main groups Group – A (Clomiphene Citrate) & B (Letrozole) with a respective mean age of (26.72 ± 6.02) years and (26.87 ± 6.33) years. Most dominant age bracket was 18 – 30 years among 148 patients (66.07%). Mean infertility duration was (3.47 ± 2.21) years; for Group – A & B the mean infertility duration was (3.23 ± 2.19) years and (3.68 ± 2.34) years. Group – A efficacy was reported in 19 patients (16.96%) and for Group – B among 37 patients (33.04%) (P-Value = 0.005). Detailed outcomes are presented in Table – I (Group Wise Efficacy) and Table – II (Age and Infertility Comparison).

In terms of efficacy, Group – A there were 19 (16.96%) patients for “Yes” and 93 (83.04%) for “No”; whereas, Group – B there were 37 (33.04%) were “Yes” and 75 (66.96%) for “No”.

Table – I: Group Wise Efficacy

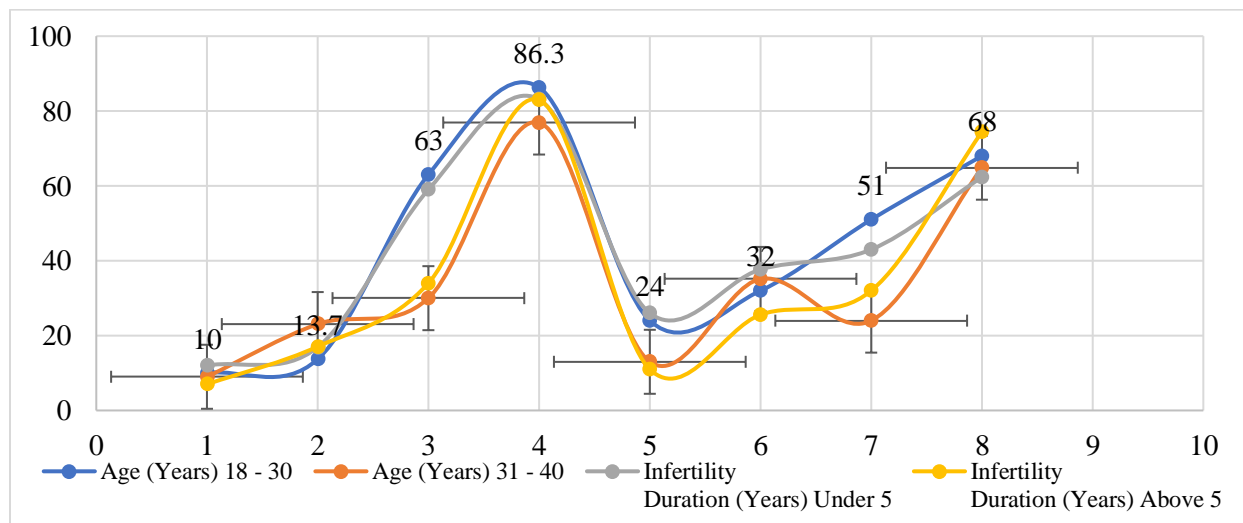
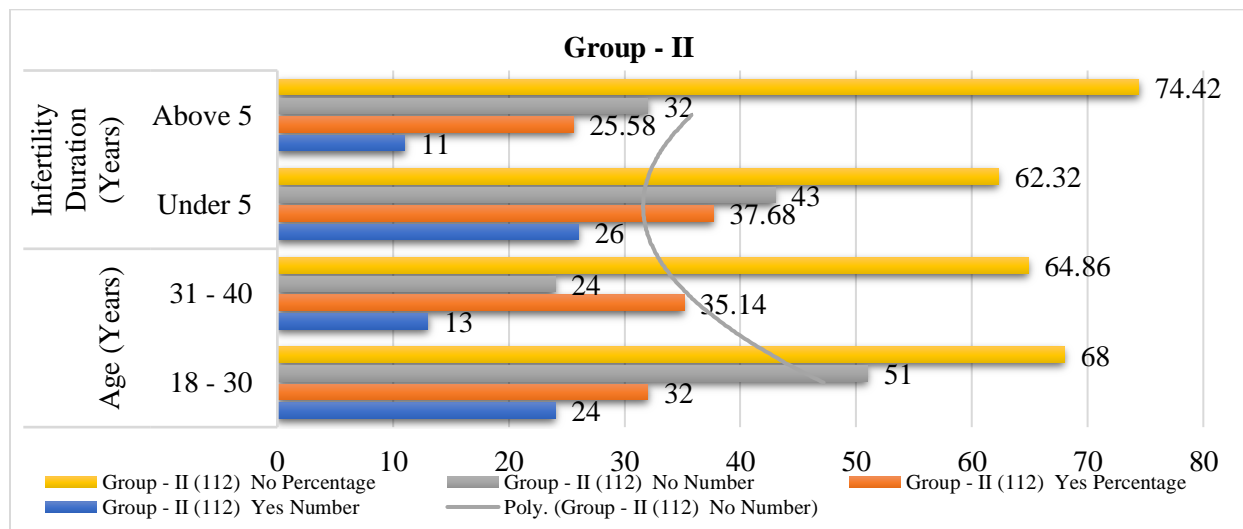
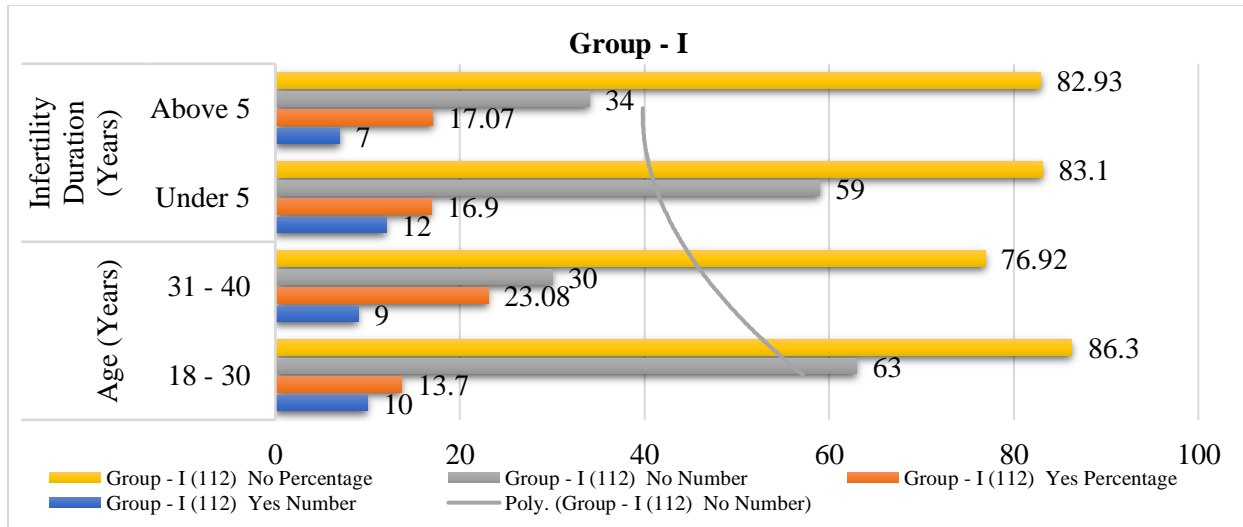
Efficacy	Yes		No		P-Value
	Number	Percentage	Number	Percentage	
Group – A	19	16.96	93	83.04	0.005
Group – B	37	33.04	75	66.96	



Both A and B groups included 112 infertile females. The age comparison was made for two age categories including 18 – 30 years and 31 – 40 years; whereas, infertility duration was measured in years having two categories of under five years and above five years.

Table – II: Comparison of Age and Infertility Duration

Efficacy			Age (Years)		Infertility Duration (Years)	
			18 – 30	31 – 40	Under 5	Above 5
Group – A (112)	Yes	Number	10	9	12	7
		Percentage	13.7	23.08	16.9	17.07
	No	Number	63	30	59	34
		Percentage	86.3	76.92	83.1	82.93
Group – B (112)	Yes	Number	24	13	26	11
		Percentage	32	35.14	37.68	25.58
	No	Number	51	24	43	32
		Percentage	68	64.86	62.32	74.42
P-Value			0.008	0.247	0.006	0.342



DISCUSSION:

The objective of this study was to compare the effectiveness of clomiphene citrate and letrozole among ovulatory infertile females. We selected women in the age limit of 18 – 40 years which were divided into two main groups Group – A (Clomiphene Citrate) & B (Letrozole) with a respective mean age of (26.72 ± 6.02) years and (26.87 ± 6.33) years. Most dominant age bracket was 18 – 30 years among 148 patients (66.07%). Mean infertility duration was (3.47 ± 2.21) years; for Group – A & B the mean infertility duration was (3.23 ± 2.19) years and (3.68 ± 2.34) years. Group – A efficacy was reported in 19 patients (16.96%) and for Group – B among 37 patients (33.04%) (P-Value = 0.005). According to a research conducted by Ibrahim, the rate of pregnancy for Letrozole group was (23.07%); whereas, the rate of pregnancy for Clomiphene Citrate group was (10.68%) [8].

In another research Group A, B & C were respectively treated with Clomiphene, Tamoxifen and Letrozole. In terms of an overall rate of ovulation was reported in 60 females (73.4%), further subdivision showed that Clomiphene treated patients were 39 in Group – A (78%), tamoxifen-treated patients were 24 in Group – B (68%) and letrozole-treated patients were 37 in Group – C (74%). Respective rate of pregnancy was 32 in Group – A (64%), 20 in Group – B (40%) and 25 in Group – C (50%) [9].

According to Atay V, Letrozole treated group showed better outcomes about the rate of pregnancies than the rate of pregnancies of Clomiphene Citrate treated group [10]. Bayar U found no significant difference in the rate of pregnancies for both the medications wither Letrozole or Clomiphene Citrate [11]. Kar reported 60.78% rate of ovulation in Clomiphene citrate treated group and 73.08% rate of ovulation for Letrozole treated group which is not statistically significant (P-Value = 0.39) [6]. Roy also found Letrozole as a significant initiator of pregnancy than Clomiphene citrate (43.8% versus 26.4% respectively) [12]. The outcomes presented by Hussain are also similar to our research as pregnancy rate achieved by Letrozole was 25.3% which is higher than the pregnancy rate of Clomiphene citrate 16% [13].

CONCLUSION:

The outcomes conclude that Clomiphene Citrate is less effective than Letrozole in order to achieve pregnancy among ovulatory infertility females. Therefore, the use of Letrozole as mainstream therapy for ovulatory infertile female's is recommended in order to attain maximum pregnancies.

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