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Study of Fertility Parameters Amongst PCOS Women Undergoing Successful Ovulation Induction with Clomiphene citrate versus Letrozole

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Abstract

Automation and robotics have significantly transformed in-vitro fertilization (IVF) laboratories by enhancing precision, efficiency, and reproducibility in various procedures. Robotic systems standardize critical tasks such as sperm selection, intracytoplasmic sperm injection (ICSI), and embryo handling, reducing human error and variability. Advanced automation integrates microfluidics and artificial intelligence (AI) for applications such as sperm sorting, time-lapse imaging, and cryopreservation. These innovations enable accurate embryo selection, streamline workflows, and improve patient outcomes. Systems like BLASTO-chip and Magnetic-Activated Cell Sorting (MACS) enhance sperm selection accuracy and fertilization potential. Robotic ICSI minimizes oocyte damage while optimizing injection precision using high-resolution imaging and AI-driven motion control. Automated embryo culture with time-lapse imaging allows continuous monitoring and data-driven decisions, improving implantation success rates. Cryopreservation automation ensures consistency in freezing protocols and safeguards samples via robotic storage systems. Additionally, workflow optimization integrates multiple lab functions, real-time monitoring, and predictive analytics to enhance efficiency and throughput. Challenges, including high costs and integration complexities, limit widespread adoption. Future advancements aim to expand AI applications, integrate omics-based profiling, and enable remote operation for global accessibility. The synergistic application of robotics, AI, and automation holds immense potential to revolutionize IVF practices, enhancing outcomes, reproducibility, and accessibility.

Keywords: Clomiphene Citrate; Letrozole; Ovulation Induction; Infertility; PCOS; IUI

Abbreviations

PCOS: Polycystic ovary Syndrome and IUI: Intrauterine Insemination; OI: Ovulation Induction; GnRH: Gonadotropin stimulating hormone; FSH: Follicle Stimulating Harmone.

Introduction

Among infertile couples, ovulation disorders are a cause of infertility in around 25% of women. Normo-gonadotrophic normo-estrogenic anovulation (World Health Organization

group II anovulation) is the most common anovulatory infertility. Within this group, polycystic ovary syndrome (PCOS) is the most prevalent cause [1,2].

PCOS was first described in 1935 by Stein and Leventhal. It is a complex endocrine disorder, commonly diagnosed in reproductive age women with estimated prevalence of 5% - 15% [3].

The symptoms range from menstrual disorders, infertility, hirsutism to metabolic syndrome.
Diagnostic criteria for PCOS: ROTTERDAM 2003 [4]. Two of three criteria need to be fulfilled.

1. Oligovulation and/or anovulation
2. Clinical and/or biochemical signs of hyperandrogenism
3. Polycystic ovarian morphology

Anovulatory PCOS women are treated with ovulation induction drugs like Clomiphene Citrate (CC) and Letrozole in preference to gonadotropins. CC is a selective estrogen receptor modulator (SERM) [5]. It induces multifollicular development resulting in higher chances of multiple pregnancy. It is mixture of enclomiphene (62%) and zuclomiphene (38%). Clomiphene binds with estrogen receptors which creates pseudo-hypoestrogenic state. Low estrogen level causes negative feedback in hypothalamus resulting in increase in gonadotropin releasing hormone (GnRH) and subsequent FSH. Letrozole is a third-generation aromatase inhibitor. In India, letrozole was approved for ovulation induction from 2006 to 2011 by the Drug Controller General of India (DCGI). Studies from developed world have found that Letrozole was associated with higher live-birth and ovulation rates among infertile PCOS women than CC [6]. In 2016, the American Congress of Obstetricians and Gynecologists recommended that letrozole be considered a first-line therapy for ovulation induction in PCOS patients [7].

Various leading regulatory agencies in world including Canadian health regulator, US FDA, the British medicines and Healthcare products Regulatory Agency (MHRA) issued a warning that Letrozole should not be used for ovulation induction because of the potential for fetal toxicity and malformations. This warning was based on a 2005 study by Biljan and colleagues [8]. Finally, on 12th October, 2011 the use of letrozole was suspended in India by Ministry of Health and Family Welfare due to safer alternatives being available [9]. However, a large study by Tulandi, et al. [10] that included 911 newborns whose mothers had conceived with letrozole demonstrated no difference in the overall rates of malformations or chromosomal abnormalities, when compared to CC. Also study by Forman et al, showed lower malformation rate in Letrozole compared to CC [11]. Thus, on recommendation of Indian Council of Medical Research (ICMR), the Central Government revoked the suspension imposed on the sale and manufacture of Letrozole for infertility treatment in 2017 [12].

The Hospital Infertility Clinic which used CC as the oral ovulogen till December 2017 started using Letrozole as drug of choice from January 2018. Reason for shifting to use Letrozole was that CC is cleared slowly from the body and is detectable in blood for more than a month due to long half-life of approximately 2 weeks. As a consequence, it remains bound to estrogen receptors leading to desensitization of the receptors. CC fails to act on these desensitized receptors in the subsequent treatment cycles (if the treatment cycle needs to be repeated) leading to variability in ovulation rates.

Also due to antiestrogenic effect on cervix, it alters the permeability properties of cervical mucus. CC leads to estrogen receptor depletion and decrease blood supply to the endometrium and further reduces conception rate. Hence, our infertility clinic started using Letrozole as treatment of choice.

Aims and Objectives

1. To compare the fertility parameters of PCOS women undergoing successful ovulation induction with CC versus letrozole which are namely
2. Number of women who became pregnant (Urine Pregnancy Test positive)
3. Number of follicles ruptured
4. Endometrial thickness in millimeters at the time of IUI
5. Adverse events reported

Materials and Methods

Retrospective analysis: Retrospective analysis of patients diagnosed with PCOS who came for infertility treatment at our Hospital ART Center and underwent successful ovulation induction with CC or with Letrozole from Jan 2017 to December 2018 in the clinic was carried out. CC was used for ovulation induction for women with PCOS from January 2017 to December 2017. From January 2018 – Dec 2018, Letrozole was used as drug of choice for women with PCOS for ovulation induction.

Sample Size: Data available on IUI register maintained at ART Centre for PCOS women undergoing ovulation induction with CC in 2017 was 75 and for induction with letrozole in 2018 was 160. Therefore, total number of participants were 235.

Inclusion criteria:

- Infertile women between 21-40 years
- Diagnosis of PCOS according to the Rotterdam criteria
- Participants having ≤3 follicles at time of HCG trigger and IUI performed

- Minimum criteria for IUI: TMSC (Total motile sperm count) ≥5 million/ml in post wash semen sample

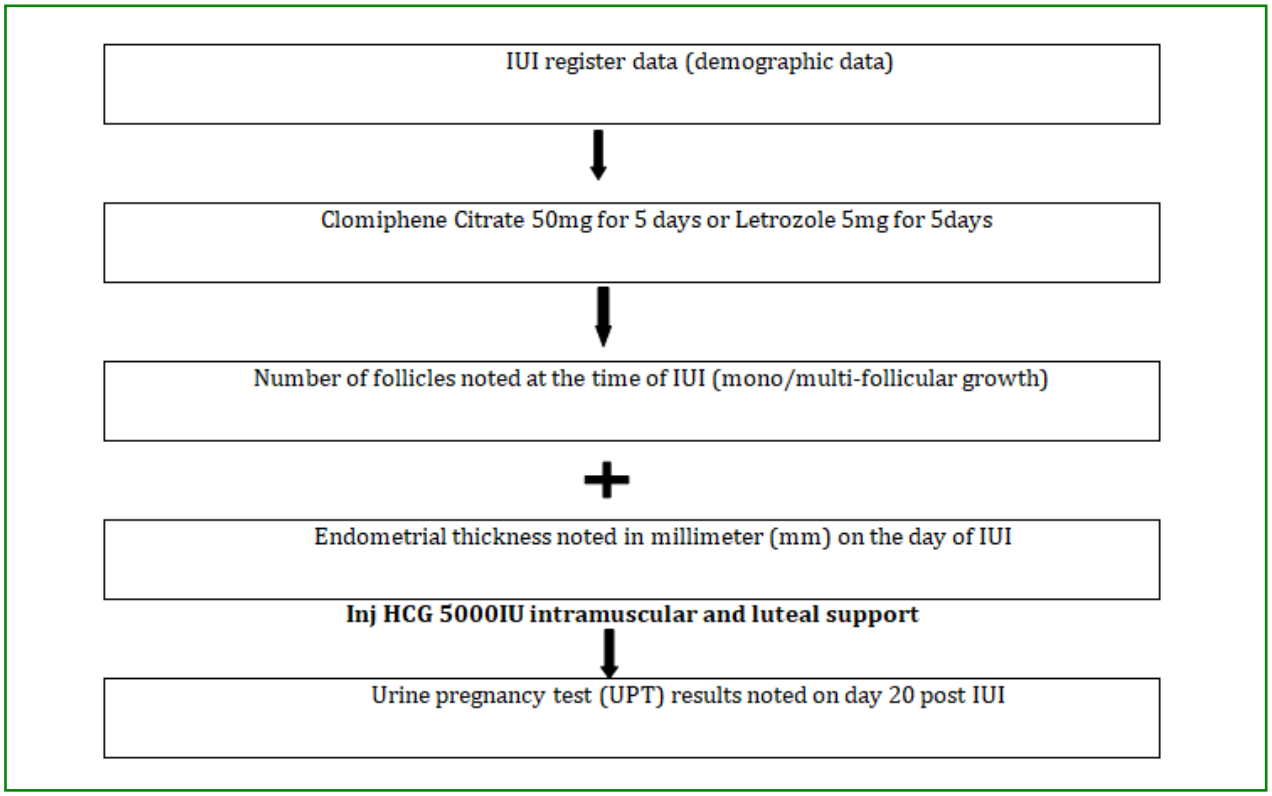
Exclusion Criteria:

- Disordered TSH, prolactin, fasting insulin levels and abnormal blood sugar level
- Any other factor contributing to infertility: Adenomyosis, endometriosis, genital Koch's, pelvic inflammatory disease, fibroid
- Any ovarian cyst
- All patients with luteinized unruptured follicle

Treatment Method Used: There were 75 patients who received CC 50mg/day on day 2-6 of menstrual cycle in January 2017-December 2017 and 160 patients who received Letrozole 5mg/day on day 2-6 of menstrual cycle in January 2018-December 2018. Serial monitoring of follicles and endometrial thickness was done by transvaginal ultrasonography.

The endometrial thickness and number of ruptured follicles were noted on day of IUI. Post procedure luteal phase support was given. Urine pregnancy test was done on day 20 post IUI.

Procedure followed:



Variables Recorded in IUI Register:

- Age of husband and wife
- Married since (in years)
- Trying to conceive (in years)
- Stimulation with: clomiphene citrate or letrozole
- Trigger injection: Human Chorionic Gonadotropin
- Endometrial thickness (in mm on day of IUI)
- Number of follicles ruptured
- Pre-wash sperm and post wash sperm count and motility
- Urine pregnancy test [20 days post IUI]
- Serious adverse events reported

Statistical Analysis: Data were analysed using SPSS V15.0 (Statistical Package for Social Sciences, Version 15.0) package. Data was given as Mean, SD and N for continuous data and Number and Percentage for categorical data. Comparison of means between 2 groups were carried out by Student's unpaired t-test for numerical normal data. Fisher Exact Probability tests and Chi square tests were applied to compare percentages for categorical data between 2 groups. 95 % Confidence Intervals were calculated for Absolute difference and Rate ratio. All statistical tests were two tailed. Alpha (α) Level of Significance was taken as $P<0.05$.

Results and Observation: Variables such as age of partners, duration of infertility, treatment given, number of attempts of IUI, endometrial thickness are given in Mean ± SD (Table1). Whereas pregnancy positive is denoted in number and percentage % (Table 2). No OHSS was recorded in either groups.

Variables	CLOMIPHENE CITRATE (N= 75)	LETROZOLE (N= 160)	Significance & P Value
Age of female partner (Years)	27.96 ± 3.61	27.90 ± 3.68	NS, P=0.9
Age of male partner (Years)	32.26 ± 4.05	32.21 ± 4.14	NS, P=0.9
Years of marriage (Years)	5.14 ± 3.55	4.89 ± 3.09	NS, P=0.5
Trying to conceive since/Duration of infertility (years)	4.58 ± 3.31	4.42 ± 3.05	NS, P=0.7
Endometrial thickness on day of IUI (mm)	7.83 ± 1.50	8.42 ± 1.49	S, P=0.005
NO. of ruptured follicles	1.24 ± 0.548 (n=75)	1.03 ± 0.22 (n=160)	S, P=0.0001
No of attempts of IUI	1.14 ± 0.39 (n=75)	1.23 ± 0.49 (n=160)	NS, P=0.1

Table 1: Comparison between Clomiphene Citrate and Letrozole groups.

Variables	Clomiphene Citrate (N= 75)	Letrozole (N= 160)	Test Value, Significance & P Value
UPT Positive	Yes= 9(12.0%)	Yes= 23(14.4%)	
	No=66(88.0%)	No= 137(85.6%)	F=0.39, DF=1, NS, P=0.39

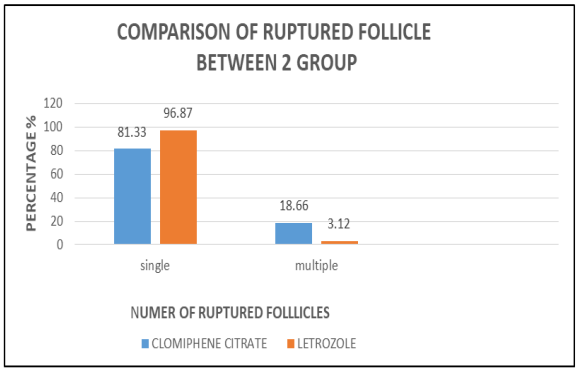
Table2: Comparison of positive UPT between two group.

Statistical test used:

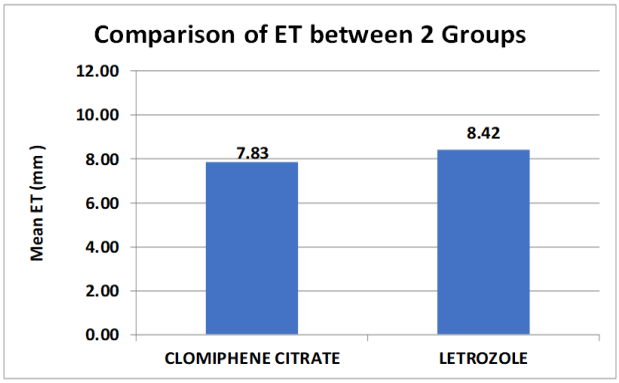
- Student's unpaired t test
- Fisher Exact Probability Test (F)

Number Of Ruptured Follicle	Clomiphene Citrate (N=75)	Letrozole (N=160)	Chi Square Test, P Value, Significance
Single Follicle	61(81.33%),	155(96.87%),	Chi Square Test 16.59, P=0.00004, Significant
Multiple Follicle	14(18.66%)	5(3.12%)	

Table 3: Comparison of number of follicles ruptured in percentage (%) between Clomiphene citrate and Letrozole group.



Graph 1: Comparision of ruptured follicle between 2 groups.

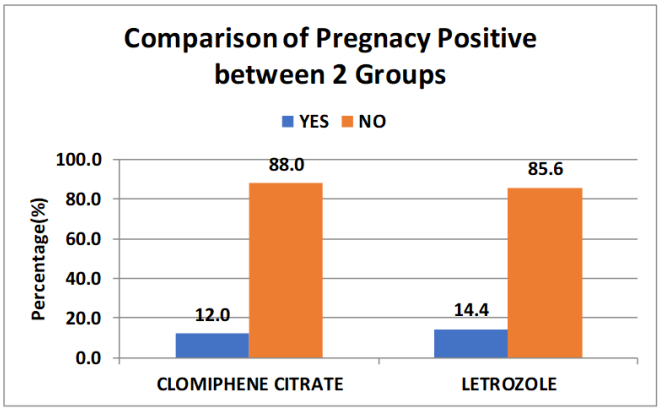


Graph 2: Comparision of ET between 2 groups.

Graph 4 indicates that the mean endometrial thickness in letrozole group was higher compared to that in clomiphene group which was statistically significant (8.42mm vs 7.83mm respectively, p value=0.005).

Variables	Cclomiphene Citrate (N= 75)	Letrozole (N= 160)	Absolute Difference Between Groups (95% Ci)	Rate Ratio In Letrozole (95% Ci)	P Value
(Upt Positive)	9(12.0%)	23(14.4%)	2.4 (-3.74,11.94)	1.2 (0.54,2.83)	0.39

Table 4: Comparison of results of urine pregnancy test between CC and Letrozole groups.

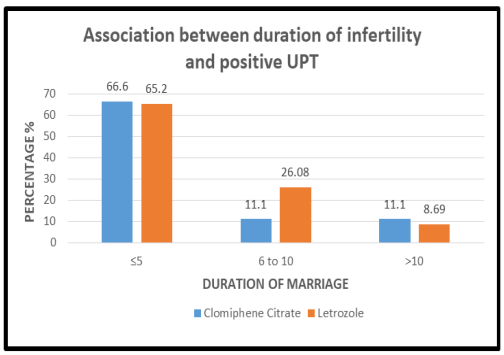


Graph 3: Comparision of pregnancypositive between 2 groups.

Table 4 and Graph 5 shows that UPT positive rate was 12% and 14.4% in CC and Letrozole group respectively which was statistically insignificant. Thus, the pregnancy rates were similar in both the groups.

Variables	Cclomiphene citrate (n= 75)		Letrozole (n= 160)	
Duration of infertility	Upt positive	Upt negative	Upt positive	Upt negative
≤5 (n=185)	7(77.7%)	62(93.9%)	15(65.21%)	101(73.72%)
6 TO 10 (n=37)	1(11.1%)	2(3.03%)	6(26.08%)	28(20.43%)
>10 (n=13)	1(11.1%)	2(3.03%)	2(8.69%)	8(5.83%)
TOTAL=235	9(100.0%)	66(100%)	23(100.0%)	137(100%)
Chi sq.test,_DF,	Chi square stat=2.81,		Chi square stat=0.74,	
significance	p value 0.2, NS, DF=2		p value 0.6 ,_NS, DF=2	

Table 5: Association between duration of infertility and urine pregnancy test results between two groups.



Graph 4: Association between duration of infertility and positive UPT.

Table 5 and graph 6 shows more patient conceived within 6 years of marriage. Later on, conception rate showing decreasing trend.

There was no statistically significant difference when a correlation was done between duration of marriage and UPT positive. This suggest there no association between duration of infertility and pregnancy test positive result.

Retrospective analysis of patients diagnosed with PCOS who came for infertility treatment at our Hospital ART Center and underwent successful ovulation induction with Clomiphene Citrate or with Letrozole from Jan 2017 to December 2018 in the clinic was carried out.

Clomiphene Citrate was used for ovulation induction for women with PCOS from January 2017 to December 2017. From January 2018 – Dec 2018, Letrozole was used as drug of choice for women with PCOS for ovulation induction.

Study Design: Retrospective Observational Analysis of past 2 years
[1st January2017- 31st December 2018]

Sample Size: Data available on IUI register maintained at ART Centre for PCOS women undergoing ovulation induction with CC clomiphene citrate in 2017 was 75 and for induction with letrozole in 2018 was 160. Therefore, total number of participants were 235.

Inclusion Criteria:

- Infertile womenAge between 21-40 years
- At least 1year of infertility2
- Diagnosis of PCOS according to the Rotterdam criteria
- Participants having ≤3 follicles at time of HCG trigger and IUI performed
- Minimum criteria for IUI: TMSC (Total motile sperm count) ≥5 million/ml in post wash semen sample

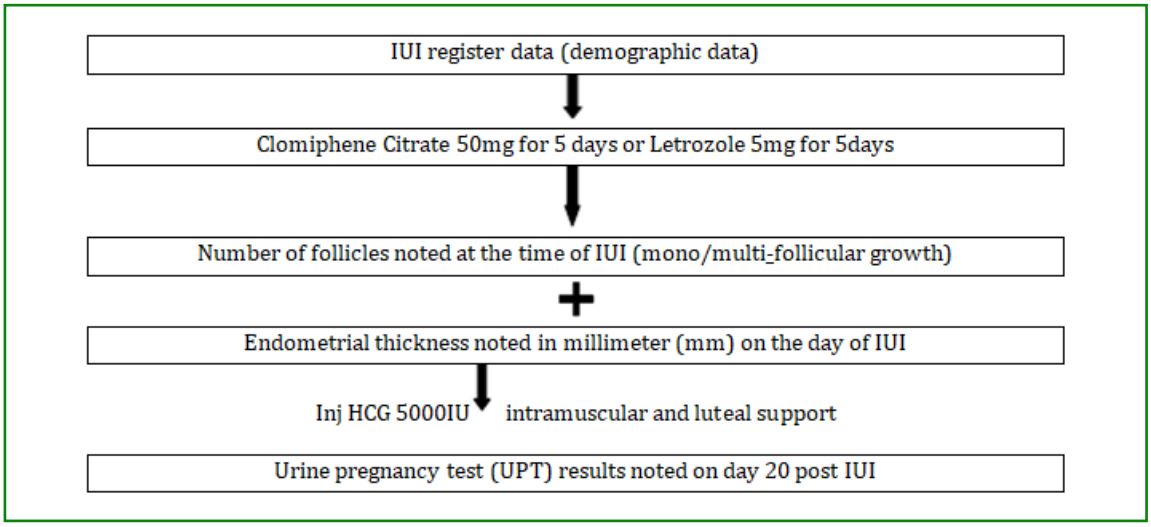
Exclusion Criteria:

- Disordered TSH , prolactin, fasting insulin levels and abnormal blood sugar level
- Any other factor contributing to infertility: Adenomyosis, endometriosis, genital Koch's, pelvic inflammatory disease, fibroid
- Any ovarian cyst
- All patients with luteinized unruptured follicle

Treatment Method used: There were 75 patients who received Clomiphene Citrate 50mg/day on day 2-6 of menstrual cycle in January 2017- December 2017 and 160 patients who received Letrozole 5mg/day on day 2-6 of menstrual cycle in January 2018-December 2018. Serial monitoring of follicles and endometrial thickness was done by transvaginal ultrasonography.

The eOptimum size of endometrial thickness and number of ruptured follicles were noted on day of IUI. Post procedure luteal phase support was given. Urine pregnancy test was done on day 20 post IUI.

Procedure followed:



Variables recorded in IUI register:

- Age of husband and wife
- Married since (in years)
- Trying to conceive (in years)
- Stimulation with: clomiphene citrate 50mg [od] or letrozole 5mg[od] for a five day period
- Trigger injection: Human Chorionic Gonadotropin (HCG) 5000IU intramuscular
- Endometrial thickness (in mm on day of IUI)
- Numbero of follicles ruptured
- Pre-wash sperm and post wash sperm count and motility
- Urine pregnancy test [20 days post IUI]
- Serious adverse events reported or documented

Statistical Analysis: Data were analysed using SPSS V15.0 (Statistical Package for Social Sciences, Version 15.0) package. Data was given as Mean, SD and N for continuous data and Number and Percentage for categorical data. Comparison of means between 2 groups were carried out by Student's unpaired t- test for numerical normal data. Fisher Exact Probability tests and Chi square tests were applied to compare percentages for categorical data between 2 groups. 95 % Confidence Intervals were calculated for Absolute difference and Rate ratio. All statistical tests were two tailed.

Alpha (α) Level of Significance was taken as P<0.05.

Results and Observation: Variables such as age of partners, duration of infertility, treatment given, number of attempts of IUI, endometrial thickness are given in Mean ± SD (Table1). Whereas pregnancy positive and adverse events (ovarian hyperstimulation syndrome) is denoted in number and percentage % (Table 2). No OHSS was recorded in either groups.

Variables	Clomiphene citrate (n= 75)	Letrozole (n= 160)	Significance & P value
Age of female partner (Years)	27.96 ± 3.61	27.90 ± 3.68	NS, P=0.9
Age of male partner (Years)	32.26 ± 4.05	32.21 ± 4.14	NS, P=0.9
Years of marriage (Years)	5.14 ± 3.55	4.89 ± 3.09	NS, P=0.5
Trying to conceive since/Duration of infertility (years)	4.58 ± 3.31	4.42 ± 3.05	NS, P=0.7
Dose (mg)	50.00 ± 0.00	5.00 ± 0.00	NA1
Duration (Days)	5.00 ± 0.00	5.00 ± 0.00	NA1
Inj.HCG IM given (5000IU)	5000.00 ± 0.00	5000.00 ± 0.00	NA1
USG FINDING Endometrial thicknessT on day of IUI (mm)	7.83 ± 1.50	8.42 ± 1.49	S, P=0.005
No. of ruptured Follicles	1.24 ± 0.548 (n=75)	1.03 ± 0.22 (n=160)	S, P=0.0001
NO. OF ATTEMPTS OF IUI	1.14 ± 0.39 (n=75)	1.23 ± 0.49 (n=160)	NS, P=0.1

NA 1= Not Applicable, NS = Not Significant

Table 6: Comparison between Clomiphene Citrate and Letrozole groups.

Statistical test used: student unpaired t test used

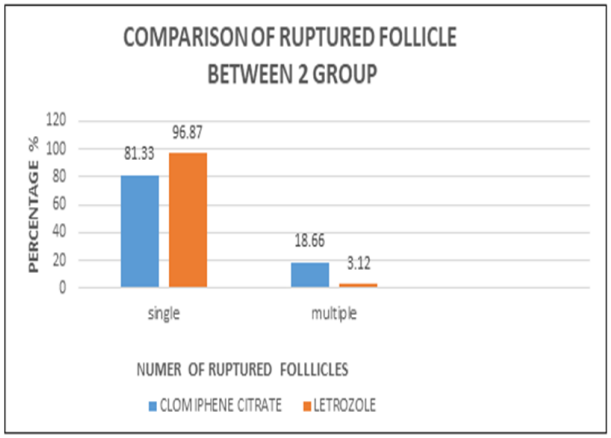
Variables	Clomiphene citrate (n= 75)	Letrozole (n= 160)	Test value, Significance & P value
UPT Positive	YES= 9(12.0%)	YES= 23(14.4%)	F=0.39, DF=1, NS, P=0.39
	NO=66(88.0%)	NO= 137(85.6%)	
OHSS	YES= 0(0.0%)	YES= 0(0.0%)	NA2
	NO=75(100.0%)	NO= 160 (100.0%)	

Table 7: Comparison of positive UPT and OHSS between two group.

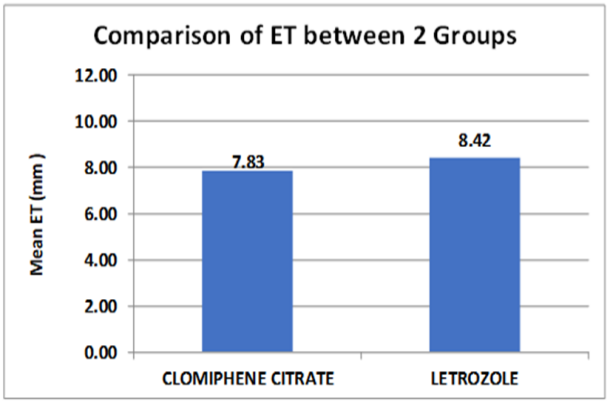
Statistical test used:
Student's unpaired t test
Fisher Exact Probability Test (F)

Number of Ruptured Follicle	Clomiphene citrate (n=75)	Letrozole (n=160)	Chi square test, P value, Significance
Single Follicle	61(81.33%),	155(96.87%),	Chi square test 16.59, P=0.00004,
Multiple Follicle	14(18.66%)	5(3.12%)	significant

Table 8: Comparison of number of follicles ruptured in percentage (%) between Clomiphene citrate and Letrozole group.



Graph 5: Comparison of ruptured follicle between 2 group.

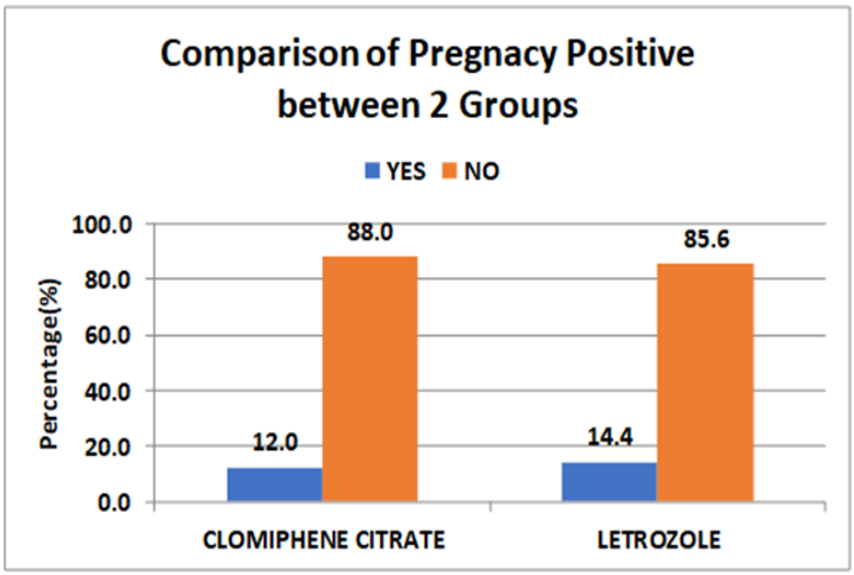


Graph 6: Comparison of ET between 2 groups.

Graph 4 indicates that the mean endometrial thickness in letrozole group was higher compared to that in clomiphene group whichand this was statistically significant (8.42mm vs 7.83mm respectively, p value=0.005). The mean endometrial thickness were 7.83mm with clomiphene citrate and 8.42mm with Letrozole.

Variables	CC	LETROZOLE	Absolute Difference between Groups (95% CI)	Rate Ratio in LETROZOLE	P value
	(n= 75)	(n= 160)		(95% CI)	
(UPT positive)	9(12.0%)	23(14.4%)	2.4 (-3.74,11.94)	1.2 (0.54,2.83)	0.39

Table 9: Comparison of results of urine pregnancy test between CClomiphene Citrate and Letrozole groups.



Graph 7: Comparison of pregnancy positive between 2 groups.

Table 4 and Graph 5 shows that UPT positive rate was seen in 12% and 14.4% patients in CClomiphene and Letrozole group respectively which. However this was statistically insignificant. Thus, the pregnancy rates were similar in both the groups.

Variables	Cclomiphene Citrate (n= 75)		Letrozole (n= 160)	
Duration of Infertility	UPT Positive	UPT Negative	UPT Positive	UPT Negative
≤5 (n=185)	7(77.7%)	62(93.9%)	15(65.21%)	101(73.72%)
6 TO 10 (n=37)	1(11.1%)	2(3.03%)	6(26.08%)	28(20.43%)
>10 (n=13)	1(11.1%)	2(3.03%)	2(8.69%)	8(5.83%)
TOTAL=235	9(100.0%)	66(100%)	23(100.0%)	137(100%)
Chi sq.test,_DF,	Chi square stat=2.81,		Chi square stat=0.74,	
significance	p value 0.2, NS, DF=2		p value 0.6 ,_NS, DF=2	

Table 10: Association between duration of infertility and urine pregnancy test results between two groups.

The table 5 and graph 6 shows more patient conceived within 6 years of marriage. Later on, conception rate showing decreasing trend. There washas no statistically significant difference when a correlation was done between duration of marriage and UPT positive. This suggest there no association between duration of infertility and pregnancy test positive result.

Results and Discussion

Nearly 75% of women with PCOS presents with infertility. It is important to counsel patients regarding the role of lifestyle modification and weight reduction in the treatment of infertility in addition to pharmacological treatment.

Clomiphene has remained the first line drug for ovulation induction for the last 50 years [13]. However, Cochrane review 2018 and international PCOS guidelines 2018 both concluded that letrozole is drug of first choice for ovulation induction (OI) in anovulatory PCOS [14]. Letrozole gives better live birth and pregnancy rates in anovulatory PCOS women, compared to CC.

After applying inclusion and exclusion criteria, 235 participants with PCOS undergoing ovulation induction were analysed in our study, 75 in Clomiphene group and 160 in Letrozole group.

The patients in both groups were well matched for their baseline parameters

Present study shows that the mean age of the patients was 27.9 years. Majority of the patients were aged 28 years. Age is an important factor for prediction of spontaneous conception in both untreated patients and patients undergoing infertility treatment. Fertility in women peaks between 20 to 24 years, decreases till the age of 30 and then declines progressively . In our study, 90% of patients with UPT positive were less than 35 years of age and 75% patients were less than or equal to 30 years of age. There was a decline in conception rate by 50% between ages of 31 years and 35 years (75% in the age <30 years and 25% between ages 31 to 35 years). A French study showed that conception rates in insemination cycles were highest in patients less than 30 years, with 16% decline between 31 to 35 years [16]. Cumulative conception rates in a British study were 20-35% lower in women over age 30 in insemination cycles [17]. There is no association in our study between age and pregnancy rate amongst two groups.

The patients in this study presented with 2 to 15 years of infertility. Majority of the patients presented with 3-6 years of infertility. The average duration of infertility in CC group and Letrozole group was 5.14 ± 3.55 years and 4.89 ± 3.09 years respectively. Current study showed most of the women conceived within 6 years . There is no association in our study between pregnancy rate and duration of infertility between two groups. Duration longer than 10 years showed an exponential decrease in conception rates according to a study by Dechanet C, et al. [18]. Similar findings were reported by Wilkes S, et al. [19]. A meta-analysis of similar studies performed by van Loendersloot LL, et al. [20] has confirmed the importance of the duration of infertility in patients undergoing infertility treatment.

The cycles were monitored using ultrasonographic folliculometry to determine the serial follicular growth, occurrence of ovulation and endometrial thickness at the time of IUI was documented. This study shows mean number of ruptured follicles in CC were 1.24 as opposed to 1.03 in Letrozole group which is statistically significant (p<0.0001). In the present study amongst Clomiphene induced cycles, single follicle ruptured was noted in 81.33% and multiple follicle ruptured was noted in 18.66%. In Letrozole-induced cycles, single follicle ruptured was noted in 96.87% while multiple follicle ruptured was noted in 3.12 %. There is significant difference in the number of ruptured follicles between two groups (p=0.000) with more follicles in the clomiphene group. In our study, the greater number of ruptured follicle in the Clomiphene group did not result

in increased pregnancy rate. Sabnam et al. conducted comparative study on CC versus Letrozole for ovulation induction in PCOS. About 60.2% patients in letrozole showed monofollicular development compared to only 9.4% in clomiphene group. This study showed that inspite of greater number of follicles in Clomiphene group, the number of pregnancies achieved was marginally higher in Letrozole group, but the difference was not statistically significant. However, the comparative study by Zeinalzadeh et al. [21] Bayar et al. did not show any significant difference in the number of mature follicles between two groups.

In this study, endometrial thickness was significantly higher in Letrozole group. The mean endometrial thickness of cycles induced by CC and Letrozole was 7.83 mm and 8.42 mm respectively which was statistically significant (P=0.005). The cause of endometrial thickening in patients receiving Letrozole is due to improved vascularisation as compared to CC [22]. Also CC can cause inadequate endometrial thickness because it has negative effect on the quality or quantity of cervical and endometrial mucosa. The recommended follicular phase endometrial thickness, which is positively associated with pregnancy outcome is 7 mm [23,24]. Past research found no pregnancy occurred when endometrial thickness was less than 6 mm [25]. Study by Adel F et al. and Sabnam et al., showed endometrial thickness was significantly higher in letrozole group, as compared to the clomiphene group similar to some other studies [26]. However, some studies like the study by Chakravarty and Angel show that there is no significant difference in endometrial thickness between two group.

In this study, the pregnancy rate in patients induced with CC and letrozole was 12% and 14.4% respectively which was not statistically significant . A positive urine pregnancy test done on 20 day post IUI were taken into account. A review by Kamath and Requena did not show any significant difference in the pregnancy rates per patient when Clomiphene or Letrozole was used as a first-line agent. The conception rates varied widely in numerous studies carried out comparing Clomiphene and Letrozole in various protocols. However, the study by Amer and Roy showed that pregnancy rates were statistically significantly higher in letrozole group as compared to clomiphene group.

In the present study which is a retrospective study, live pregnancy rate and teratogenic effects of the two drugs was not studied as data is available only till urine pregnancy test result on day 20 post IUI.

Minor side effects such as hot flushes, fatigue, nausea, headache were not recorded in the IUI register. Only serious events such as ovarian hyperstimulation syndrome as an adverse event in view of morbidity and mortality was recorded. In our Infertility Clinic, IUI was not performed if the number of follicles is >3 in order to prevent an adverse event like OHSS. That could be the reason for no OHSS event in our study groups.

Reported OHSS rates in the literature for women with PCOS who conceive after IVF are up to7.5% compared to women without PCOS being in the order of 2.7%. Study by Yun et al. showed the prevalence of OHSS being significantly lower in the Letrozole compared to CC group (1.5% vs. 10.3%, p=0.003). But Cochrane Syst Rev by Franic et al. in 2018 showed OHSS rates are similar with Clomiphene and Letrozole (0.5%).

Conclusions

Letrozole shows monofollicular growth and rupture whereas Clomiphene shows multi follicular rupture.

The endometrial thickness on day of IUI was statistically better in the Letrozole group (8.42 mm) as compared to Clomiphene (7.83 mm).

Both the multi-folliculogenesis in CC induced cycle and increased endometrial thickness in Letrozole induced cycle did not translate into higher pregnancy rates. Pregnancy rate in both the groups were comparable (12% with clomiphene as against 14.4% with Letrozole).

No severe adverse event of OHSS was noted in both groups.

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