ORIGINAL RESEARCH

Comparative study on efficacy of Letrozole versus Clomifen Citrate for induction in infertile polycystic ovary syndrome women

Dr. Sannyasi Charan Barman[1], Dr. Pratima Garain[2], Dr. Bonita Sahoo[3], Dr Kajal Kumar Patra[4], Dr Kishore P Madhwani[5]

[1]Assistant Prof., Dept of Gynae and Obstetrics, Bankura Sammilani Medical College, Bankura, West Bengal, India

[2]Associate Prof., Dept of Gynae and Obstetrics, Bankura Sammilani Medical College, Bankura, West Bengal, India

[3]Senior Resident, Dept of Gynae and Obstetrics, Bankura Sammilani Medical College, Bankura, West Bengal, India

[4]Ex-Professor and Head, Dept of Gynae and Obstetrics, Gouri Devi Institute of Medical Science, Durgapur, West Bengal, India

[5]Senior Medical Consultant, Mumbai, Maharashtra, India

Corresponding author
Dr Kajal Kumar Patra
Ex-Professor and Head, Dept of Gynae and Obstetrics, Gouri Devi Institute of Medical Science

ABSTRACT
Background: Polycystic ovary syndrome (PCOS) is defined as the presence of oligo-anovulation and/or hyperandrogenism proven by clinical or laboratory findings and/or polycystic ovary image on ultrasonography. It affects 5-10% of women in the reproductive period and is the most common cause of anovulatory infertility. This study was conducted to identify the efficacy between letrozole versus clomiphene citrate as ovulation induction drug in infertile polycystic ovary syndrome women.
Methods: This retrospective study was conducted in Bankura Sammilani Medical College and Hospital among 98 infertile PCOS pts of 20-35 yrs of age which were selected from outpatient department of Bankura Sammilani Medical College & Hospital after applying inclusion and exclusion criteria and after that data was collected. Statistical data were analysed by using Microsoft Excel and SPSS V.20 software.
Results: Most of the participants of Clomiphene citrate i.e. 53.06% (26) out of 49 belongs to 26 - 29 yrs. of age group. Most of the participants of Clomiphene citrate i.e. 46.94% (23) out of 49 BMI was within normal level. Most of the participant of Clomiphene citrate i.e. 67.35% (33) out of 49 was amenorrhea, whereas 8.16% (4) participants didn't have any problem. Mean value of duration of infertility of participants of Clomiphene citrate group was 3.23, in case of Letrozole group of participants it was 3.20. Most of the participants of Letrozole i.e 75.51% (37) out of 49 ovulation was happened, whereas 24.49% (12) participants ovulation was not happened. Most of the participants of Clomiphene citrate i.e. 75.51% (37) out of 49 was multifollicular, whereas 4.08% (2) participants didn't have any follicle. Participants of Clomiphene citrate i.e. 89.79% (44) out of 49 UPT result was negative, whereas 10.20% (5) participants result was positive.
Conclusions: Compared with CC, its use is associated with thicker endometrium, good ovulation rate and considerable number of pregnancies. So, Clomiphene citrate easily replaced by Letrozole nowadays.

Introduction

Polycystic ovary syndrome, an entity described by Irving F. Stein and Michael L. Leventhalin1953forthefirsttime.[1]Withtheadventofsophisticateddiagnosticmodalitiescoupledwithcontinuedresearchmanynewconceptsofthissyndromehasbeenhighlighted.Polycysticovarysyndrome(PCOS)isthecommonestendocrinopathyresultinginanovulatoryinfertilityinyoungwomen.[2]

The polycystic ovary syndrome, which is diagnosed on the basis of hyperandrogenism, oligo-ovulationwithassociatedoligomenorrhea,andpolycysticovariesonultrasonography,affects 5to10%ofreproductive-agewomenandisthemostcommoncauseofanovulatoryinfertility.[3]Althoughthesyndromeisacomplexreproductive–metabolicdisorder,thehypothalamic–pituitary

axishasbeenthetargetoffirst-lineovulation-inductiontherapy.Clomiphene citrate, a selective estrogen-receptor modulator that antagonizes the negativefeedback of estrogen at the hypothalamus with a consequent increase in ovarian stimulationbyendogenous gonadotropin, hasbeen used for thisindicationfor decades.

Therearemanyclinicalmanifestationsofthesyndrome,andinfertilityduetochronicanovulationisoneofthecommonest.Clomiphenecitrateisalong-standing,standarddrugfor ovulation induction and is still considered as first-line option in PCOS women for morethan40years.[4]

Clomiphene citrate(CC) promotesfollicular development through blocking the negativefeedback of estrogen to the hypothalamus and making the pituitary secrete gonadotropin.Therefore, CC has been used as the traditional first-line medication for inducing ovulation inPCOSwomen,buttheantiestrogeniceffectofCConcervicalmucusandendometrialreceptivity results in low pregnancy rates.[5] Letrozole (LE) was initially applied to treat breastcancer through preventing the conversion of androgens to estrogen and reducing the level ofestrogen in the body. As a result, gonadotropin secretion increases due to blocking estrogen-negativefeedbackofLE,which stimulatesthe developmentofovarianfollicles.[6]

However, clomiphene has certain well-defined disadvantages. Treatment with clomiphene isassociated with discrepancy in ovulation and pregnancy rates. Miscarriage rate is higher thangeneralpopulationand20-25%PCOSwomenareresistanttoclomiphene.Antiestrogenic effect of clomiphene leads to prolonged depletion of estrogen receptors, adversely affectingendometrial growth and development as well as quantity and quality of cervical mucus.[7]Letrozole is an orallyactive aromatase inhibitor, with good potential for ovulation induction.Letrozoleactsbyreducingestrogenproduction byblockingandrogenstoestrogenconversion.
Additionally, it has no adverse effect on endometrium and cervical mucus. InIndia,letrozolewasapprovedforovulationinductionfrom2006to2011bythedrugcontroller general of India (DCGI). Letrozole has been shown to have good ovulation rate inclomiphene-resistantPCOS women.[8]

Endometrial receptivity is critical for embryo implantation, and its impairment has beenproventobeanimportantfactorforinfertility.[9]Inrecentyears,ultrasonicparameters,molecular markers in endometrial tissue and uterine secretions, endometrial microstructure,and hysteroscopy have beenapplied to evaluate endometrial receptivity.[10] The preferredmethodforassessingendometrialreceptivityist ransvaginalultrasound,andmultipleultrasonic indicators havebeenused toassessendometrialreceptivity.[11]

Numerous studies have reported on ovulation and pregnancy rates between LE and CC inPCOS women. An Indian study conducted in the IOG, Madras Medical College from 2007 to2010 by Thiripurasundari G. *et. al.* found letrozole to be more effective than CC in inducingovulation in patients with an ovulatory cycle than CC in terms of monofollicular ovulationandbetterendometrial thickness.[12]

The present study was conducted with the objective to identify the efficacy between letrozole versus clomiphene citrate as ovulation induction drug in infertile polycystic ovary syndrome women.

Methodology

This retrospective study was conducted in Bankura Sammilani Medical College and Hospital among 98 infertile PCOS pts of 20-35 yrs of age which were selected from outpatient department of Bankura Sammilani Medical College & Hospital after applying inclusion and exclusion criteria and after that data was collected.

As this is a comparative study, there were two group. One was Clomiphene Citrate and another was Letrozole. Both groups contain 49 participants
Informed consent was taken from all patients. Patient particulars were noted, medical history and physical examination was undertaken thoroughly.

The data was entered in an excel sheet and the results were written in a tabulated form and then the results of this study were compared with the previous studies results and statistical analysis was done which has found to be significant.

For some decades, Clomiphene citrate has been considered as the first choice of treatment for women having PCOS. CC is known to reduce the uterine receptivity which could be a reason that it results in reducing the likelihood of conception. So in comparison to this letrozole is a relatively better drug than CC.

*Statistical Analysis :*Statistical procedure enables the researcher to reduced, summarized, organized, evaluate, interpret and communicate numerical information. Analysis and interpretation of data were based on the objective of the study. The obtained data were analyzed by using descriptive statistic. The data was tabulated in Microsoft Excel software and analysed with SPSS V.20 software. P value <0.05 was considered as significant.
Ethical considerations- Study was initiated after

obtaining the informed consents from the participants and ethical clearance from the institutional ethical committee.

Results

This area deals with the analysis and interpretation of the collecting data to "A Comparative Study To Evaluate The Efficacy Between Letrozole Versus Clomiphene Citrate As Ovulation Induction Drug In Infertile Polycystic Ovary Syndrome Women." The purpose of analysis is to make the collected data into an intelligible and interpretable form so that the objectives were justified statistically and hypothesis of the research problem were tested

Organizationand presentationof data

The data were organized and presented under the following section in accordance to study objectives
Section A: Findings related to background information of participants.
This section describes the background information of participants depending upon their personal characteristics like age. Findings are depicted in terms of tables and figures with frequency, percentage, mean, standard deviation and standard error.

Table 1: Distribution of participants according to age.   (N- 98)

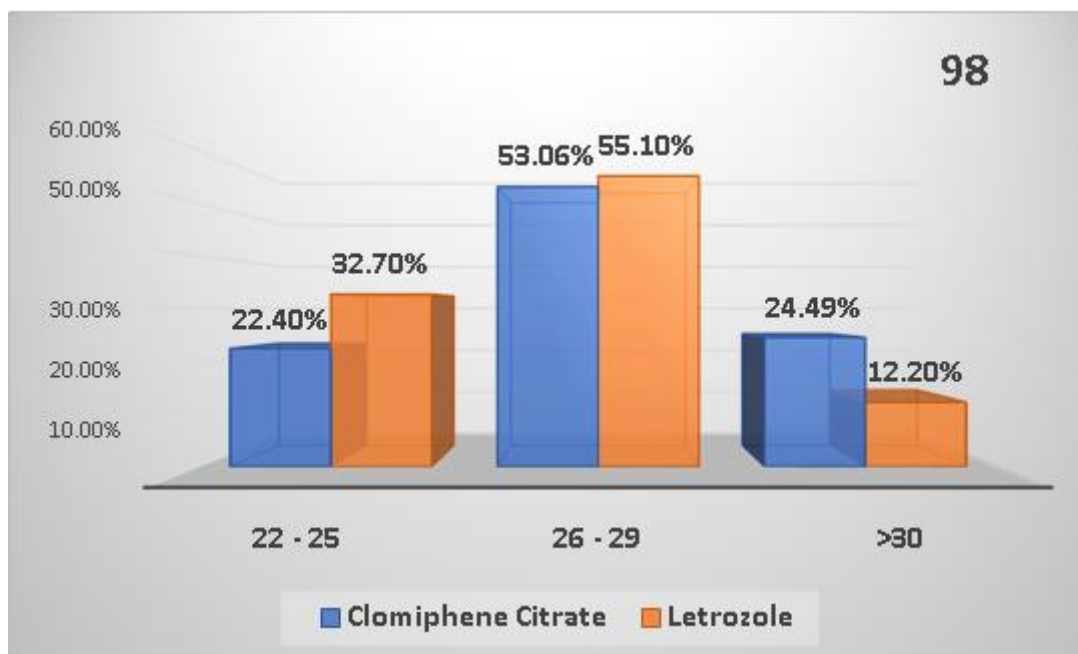| Age (yrs.)	Clomiphene Citrate (n–49)		Letrozole (n–9)	
	Frequency	Percentage(%)	Frequency	Percentage(%)
22 – 25	11	22.4	16	32.7
26 – 29	26	53.06	27	55.1
>30	12	24.49	6	12.2

Fig.2 and table 1 depicted that most of the participants of Clomiphene citratei.e. 53.06% (26) out of 49 belongs to 26 - 29 yrs. of age group. Whereas 22.4% (11) participants belong to 22
25 yrs. of age group. This table and graph also depicted that most of the participants of Letrozole i.e. 55.1% (27) out of 49 belongs to 26 - 29 yrs. of age group. Whereas 12.2% (6) participantsbelong to >30 yrs. of age group

Table 2: Distribution of participants according to BMI.   (N- 98)

BMI	Clomiphene Citrate (n–49)		Letrozole (n–49)	
	Frequency	Percentage(%)	Frequency	Percentage(%)
18.5– 24.9	23	46.94	13	26.53
25– 29.9	22	44.9	34	69.39
30– 39.9	4	8.16	2	4.08

Table2depictedthatmostoftheparticipantsofClomiphenecitrate
i.e.46.94%(23)outof49BMIwaswithinnormallevel.Whereas   8.16%(4)participantsBMIwas   within30–39.9 kg/m^2.Table and This graph also depicted that most of the participant of Letrozole i.e.69.39% (34) out of 49 BMI were within 25 – 29.9 kg/m^2. Whereas 4.08% (2) participantsBMIwerewithin 30– 39.9 kg/m^2.

Table 3: Distribution of BMI of participants in terms of mean and Standard Deviation (SD) and Standard Error (SE). (N–98)

Variables	Types oftreatment	Mean	StandardDeviation(SD)	StandardError(SE)
	ClomipheneCitrate	25.61	2.001	0.285
BMI	Letrozole	26.13	1.79	0.25

Data given in table 3 depicted that mean value of BMI of participants of Clomiphene citrate group was 25.61, Standard Deviation was ± 2.001 and Standard Error was 0.285in case of Letrozole group of participants mean value of BMI was 26.13, Standard Deviation was ±
1.79 and Standard Error was 0.25

Table 4: Distribution of participants according to Menstrual History.   (N– 98)

MenstrualHistory	Clomiphene Citrate (n–49)		Letrozole (n–49)	
	Frequency	Percentage (%)	Frequency	Percentage (%)
Oligomenorrhea	12	24.49	22	44.9
Amenorrhea	33	67.35	14	28.6
Nocomplaints	4	8.16	13	26.5

Table 4 depicted that most of the participant of Clomiphene citratei.e. 67.35% (33) out of 49 was amenorrhea. Whereas 8.16% (4) participants didn't have any problem. This table also depicted that most of the participants of Letrozole i.e. 44.9% (22) out of 49 was oligomenorrhea. Whereas 26.5% (13) participants didn't have any problem.

Table 5: Distribution of participants according to Duration of infertility. (N– 98)

Duration ofinfertility(yrs.)	Clomiphene Citrate (n–49)		Letrozole (n–49)	
	Frequency	Percentage (%)	Frequency	Percentage (%)
1 – 3	27	55.1	37	75.51
>3– 6	22	44.9	12	24.49

Table 5 depicted that most of the participants of Clomiphene citrate i.e. 55.1% (27) out of 49 duration of infertility was within 1 – 3 yrs. Whereas 44.9% (22) participants duration of infertility was within >3 – 6 yrs. This table also depicted that most of the participants of Letrozole i.e. 75.51% (37) out of 49 duration of infertility was within 1 – 3 yrs. Whereas 24.49% (12) participants duration of infertility was within >3 – 6 yrs.

Table 6: Distribution of duration of infertility of participants in terms of mean and Standard Deviation (SD) and Standard Error (SE). (N– 98)

Variables	Types of treatment	Mean	Standard Deviation (SD)	Standard Error (SE)
	Clomiphene Citrate	3.23	1.05	0.15
Duration ofinfertility	Letrozole	3.20	3.32	0.47

Data given in table 6 depicted that mean value of duration of infertility of participants of Clomiphene citrate group was 3.23, Standard Deviation was ± 1.05 and Standard Error was 0.15.in case of Letrozole group of participants mean value of duration of infertility was 3.20, Standard Deviation was ± 3.32 and Standard Error was 0.47.

Section B: Findings related to obstetrical information of participants.
This section describes the obstetrical information of participants like parity. Finding were depicted in terms of tables and figures with frequency, percentage, mean, standard deviation, standard error and chi - square.

Table 7: Distribution of participants according to parity. (N– 98)

PARITY	Clomiphene Citrate (n–49)		Letrozole (n–49)	
	Frequency	Percentage (%)	Frequency	Percentage (%)
P_{0+0}	35	71.43	36	73.47
P_{1+0}	3	6.12	3	6.12
P_{0+1}	7	14.29	8	16.33
P_{0+2}	3	6.12	2	4.08

P_{0+3}	1	2.04	0	0

Table 7 depicted that most of the participants of Clomiphene citrate i.e. 71.43% (35) out of 49 were primipara. Whereas 2.04% (1) participants parity were P0+3. This table also depicted that most of the participants of Letrozole i.e. 73.47% (36) out of 49 were primipara. Whereas 4.08% (2) participants parity were P0+2

Section C: Findings related to result of infertility treatment.
This section describes the result of infertility treatment of participants like ovulation, number of dominant follicles, size of dominant follicle, endometrial thickness and UPT result. Findings are depicted in terms of tables and figures with frequency, percentage, mean, standard deviation, standard error and chi – square.

Table 8: Distribution of participants according to Ovulation. (N– 98)

Ovulation	Clomiphene Citrate (n–49)		Letrozole (n–49)	
	Frequency	Percentage (%)	Frequency	Percentage (%)
YES	24	48.98	37	75.51
NO	25	51.02	12	24.49

Table 8 depicted that most of the participants of Clomiphene citrate i.e. 51.02% (25) out of 49 ovulations was not happened. Whereas 48.98% (24) participant's ovulation was happened.
This table also depicted that most of the participants of Letrozole i.e 75.51% (37) out of 49 ovulations was happened. Whereas 24.49% (12) participant's ovulation was not happened.

Table 9: Distribution of participants according to Number of dominant follicle. (N– 98)

Number ofDominantFollicle	Clomiphene Citrate (n–49)		Letrozole (n–49)	
	Frequency	Percentage (%)	Frequency	Percentage (%)
Monofollicular	10	20.40	36	73.47
Multifollicular	37	75.51	11	22.45
Nil	2	4.08	2	4.08

Table 9 depicted that most of the participants of Clomiphene citrate i.e. 75.51% (37) out of 49 was multifollicular. Whereas 4.08% (2) participants didn't have any follicle. This table graph also depicted that most of the participants of Letrozole i.e 73.47% (36) out of 49 was monofollicular. Whereas 4.08% (2) participants didn't have any follicle

Table 10: Distribution of participants according to Size of dominant follicle. (N– 98)

Sizeof Dominant Follicle	Clomiphene Citrate (n–49)		Letrozole (n–49)	
	Frequency	Percentage (%)	Frequency	Percentage (%)
10X10	1	2.04	0	0
11X10	2	4.08	4	8.16
12X10	3	6.12	0	0
12X11	2	4.08	3	6.12
13X10	1	2.04	0	0
13X11	5	10.20	0	0
13X12	0	0	1	2.04
14X12	3	6.12	1	2.04
15X13	3	6.12	2	4.08
16X13	1	2.04	0	0
16X14	2	4.08	1	2.04
17X15	2	4.08	0	0
18X18	0	0	1	2.04
19X18	0	0	2	4.08
20X18	5	10.20	5	10.20
20X20	1	2.04	1	2.04
21X17	1	2.04	0	0
21X18	2	4.08	4	8.16
21X19	0	0	1	2.04
21X20	2	4.08	6	12.24

22X20	2	4.08	3	6.12
22X21	1	2.04	0	0
23X21	3	6.12	5	10.20
23X22	1	2.04	0	0
24X22	2	4.08	3	6.12
24X23	1	2.04	1	2.04
25X23	1	2.04	5	10.20
25X24	1	2.04	0	0
26X24	1	2.04	0	0

Table 10 depicted that most of the participants of Clomiphene citrate i.e. 10.20% (5) out of 49 size of dominant follicle was 20X18. Whereas most of the participants of Letrozole i.e 12.24% (6) out of 49 size was 21X20. Size of dominant follicle of letrozole group was higher than Clomiphene citrate.

Table 11: Distribution of participants according to Endometrial thickness. (N– 98)

Endometrialt hickness	Clomiphene Citrate (n–49)		Letrozole (n–49)	
	Frequency	Percentage (%)	Frequency	Percentage (%)
5.3–7.4	33	67.35	18	36.73
>7.4	16	32.65	31	63.27

Table 11 depicted that most of the participants of Clomiphene citrate i.e. 67.35% (37) out of 49 endometrial thickness was within 5.3 – 7.4. Whereas 32.65% (16) participants endometrial thickness was >7.4. This table also depicted that most of the participants of Letrozole i.e 63.27% (31) out of 49 endometrial thickness was >7.4. Whereas 36.27% (18) participants endometrial thickness was 5.3 – 7.4

Table 12: Distribution of Endometrial Thickness of participants in terms of mean and Standard Deviation (SD) and Standard Error (SE). (N– 98)

Variables	Types of treatment	Mean	Standard Deviation (SD)	Standard Error (SE)
EndometrialThi ckness	Clomiphene Citrate	6.898	0.902	0.12
	Letrozole	7.59	1.01	0.14

Data given in table 12 depicted that mean value of endometrial thickness of participants of Clomiphene citrate group was 23.38, Standard Deviation was ± 2.53 and Standard Error was 0.185.in case of Letrozole group of participants mean value of endometrial thickness was 22.73, Standard Deviation was ± 2.40 and Standard Error was 0.18.

Table 13: Distribution of participants according to UPT result.   (N– 98)

UPTResult	Clomiphene Citrate (n–49)		Letrozole (n–49)	
	Frequency	Percentage (%)	Frequency	Percentage (%)
Positive	5	10.20	9	18.37
Negative	44	89.79	40	81.63

Table 13 depicted that most of the participants of Clomiphene citrate i.e. 89.79% (44) out of 49 UPT result was negative. Whereas 10.20% (5) participants result was positive. This table also depicted that most of the participants of Letrozole i.e 81.63% (40) out of 49 UPT result was negative. Whereas 18.37% (9) participants result was positive

Section D: Findings related to Adverse effect of treatment.
This section describes the adverse effect of treatment like nausea, vomiting, headache, blurring of vision, twin pregnancy and OHSS. Findings are depicted in terms of tables and figures with frequency and percentage.

Table 14: Distribution of participants according to Adverse effect. (N– 98)

Adverseeffect	Clomiphene Citrate (n–49)				Letrozole (n–49)			
	Yes		No		Yes		No	
	F	P (%)	F	P (%)	F	P (%)	F	P (%)
Nausea	8	16.33	41	83.67	3	6.12	46	93.87
Vomiting	8	16.33	41	83.67	5	10.20	44	89.79
Headache	6	12.24	43	87.76	6	12.24	43	87.76

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Blurringof vision	2	4.08	47	95.91	0	0	0	0
Twin pregnancy	3	6.12	46	93.87	0	0	0	0
OHSS	0	0	47	95.91	0	0	0	0

Table 14 depicted that most of the participants of Clomiphene citrate i.e. 16.33% (8) out of 49 suffered from nausea, another 16.33% (8) out of 49 suffered from vomiting, 12.24% (6) h suffered from headache, 6.12% (3) have twin pregnancy, 4.08% (2) suffered from blurring of vision and no one suffered from OHSS. This also depicted that most of the participants of Letrozole i.e 6.12% (3) out of 49 suffered from nausea, 10.20% (5) out of 49 have suffered from vomiting, 12.24% (6) suffered from headache

Section E: Findings related to association between infertility treatment and selected variables.

This section describes association between infertility treatment and selected variables of participants.

In order to find out the association between infertility treatment and selected variables (BMI, Duration of infertility, ovulation, no. of dominant follicle, size of dominant follicle endometrial thickness and pregnancy rate) the following hypothesis was formulated.

H1: There is significant association between BMI and infertility treatment at 0.05 level of significance.

To test research hypothesis following null hypothesis was formulated.

H01: there is no significant association between BMI and infertility treatment at 0.05 level of significance.

H2: There is significant association between duration of infertility and infertility treatment at
0.05 level of significance.

To test research hypothesis following null hypothesis was formulated.

H02: there is no significant association between duration of infertility and infertility treatment at 0.05 level of significance.

H3: There is significant association between Ovulation and infertility treatment at 0.05 level of significance.

To test research hypothesis following null hypothesis was formulated.

H03: there is no significant association between ovulation and infertility treatment at 0.05 level of significance

H4: There is significant association between size of dominant follicle and infertility treatment at 0.05 level of significance.

To test research hypothesis following null hypothesis was formulated.

H04: There is no significant association between size of dominant follicle and infertility treatment at 0.05 level of significance.

H5: There is significant association between no. of dominant follicle and infertility treatment at 0.05 level of significance.

To test research hypothesis following null hypothesis was formulated.

H05: There is no significant association between no. of dominant follicle and infertility treatment at 0.05 level of significance.

H6: There is significant association between endometrial thickness and infertility treatment at
0.05 level of significance.

To test research hypothesis following null hypothesis was formulated.

H06: There is no significant association between endometrial thickness and infertility treatment at 0.05 level of significance.

H7: There is significant association between pregnancy rate and infertility treatment at 0.05 level of significance.

To test research hypothesis following null hypothesis was formulated.

H07: There is no significant association between pregnancy rate and infertility treatment at
0.05 level of significance.

Table 15: Chi square value shows the association between infertility treatment and selected variables. (N–98)

SelectedVariables	x^2	Df	Pvalue
BMI	60.086(S)	42	0.035
Durationofinfertility	18.87(S)	10	0.042
Ovulation	98.00(S)	3	<0.001
Sizeofdominant follicle	98.00(S)	40	<0.001
No.ofdominant follicle	29.431(S)	3	<0.001
Endometrialthickness	35.6	35	0.440
Pregnancyrate	47.361(S)	1	<0.001

S=Significant

Data presented in table 15 indicates that the association between BMI and treatment of infertility Chi square value was 60.086 which is significant at the level of 0.035. So, p value is lower than 0.05.

So there was association between BMI and treatment of infertility. So the null hypothesis is rejected and research hypothesis is accepted.

This table also indicates association between duration of infertility and treatment of infertility. Chi square (X2) value is 18.87 which was found to be statistically significant at the level 0.042 because it p value less than 0.05 level of significance.

So there is association between duration of infertility and treatment of infertility. So the research hypothesis is accepted and null hypothesis is rejected.

This table also indicates association between ovulation and treatment of infertility. Chi square (X2) value is 98.00 which was found to be statistically significant at the level <0.001 which is less than 0.05 level of significance.

So there is association between ovulation and treatment of infertility. So the research hypothesis is accepted and null hypothesis is rejected.

This table also indicates association between size of dominant follicle and treatment of infertility. Chi square (X2) value is 98.00 which was found to be statistically significant at the level <0.001 which is less than 0.05 level of significance.

So there is association between size of dominant follicle and treatment of infertility. So the research hypothesis is accepted and null hypothesis is rejected.

This table also indicates association between no. of dominant follicle and treatment of infertility. Chi square (X2) value is 29.431 which was found to be statistically significant at the level <0.001 which is less than 0.05 level of significance.

So there is association between no. of dominant follicle and treatment of infertility. So the research hypothesis is accepted and null hypothesis is rejected.

This table also indicates association between endometrial thickness and treatment of infertility. Chi square (X2) value is 35.6 which was found to be statistically not significant because it p value more than 0.05 level of significance.

So there is no association between endometrial thickness and treatment of infertility. So the research hypothesis is rejected and null hypothesis is accepted.

This table also indicates association between pregnancy rate and treatment of infertility. Chi square (X2) value is 47.361 which was found to be statistically significant at the level <0.001 which is less than 0.05 level of significance.

So there is association between pregnancy rate and treatment of infertility. So the research hypothesis is accepted and null hypothesis is rejected

Discussion
*FINDINGS RELATED TO BACKGROUND INFORMATION-
Age:

In present study most of the participants of clomiphene citrate 53.06% (26) out of 49 belongs to 26-29 years of age group, the age group remains the same in case of most of the patients treated with letrozole.

Study conducted by Sahu M. *et. al.*[8] The mean age was 27.34 ±04.38 years in study group and 27.16 ± 4.14 years in control group. Accordingto Nambiar SS.*et.al*[13] It was noted that in the clomiphene group 28.1% were below or equal to 24 years of age, 53.1% between 25 years and 29 years and 18.8% more than or equal to 30 years of age. In the letrozole group 33.7% were less than or equal to 24 years of age, 45.2% between 25 years and 29 years and 21.2% more than or equal to 30 years of age. The p value was 0.822 hence no significant difference in the age distribution of patients in either group

BMI:

In present study most of the participants of clomiphene citrate i.e 46.94% (23) out of 49 BMI was within normal level. Whereas most of the participants of letrozolei.e.69.39% (34) out of 49 was within 25-29.9kg/m2. The mean value of BMI of participants of clomiphene citrate group was 25.61Standard deviation was± 2.001 and standard error was 0.285. In case of letrozole group of participants mean value of BMI was 26.13. The standard deviation was ± 1.79 and standard error was 0.25. Chi square value was 60.086 which was significant at the level of 0.035. So p value is lower than 0.05. So there was association between BMI and treatment of infertility.

In study conducted by Sahu M. *et. al.*[8] The mean BMI in group letrozole was 26.20 with SD of 2.0628 and the mean BMI in group clomiphene was 26.09 with SD of± 2.1366. Both the groups are comparable with respect to BMI with p value 0.809 (>0.05) not significant. Study conducted by JainS.*et.al*[14] the mean BMI was 22.90± 2 kg/m2in study group and 23.062± 04 kg/m2in control group. Difference were not statistically significant. Accordingto Khakwani M.*et. al.*[15] Among 70patientsmost of the patients 52 (66.7%) were having BMI less than 25 kg/m2. The overall mean BMI was 23.74± 2.96. This is almost similar to present study

Duration of infertility :

In this study, most of the participants of clomiphene citrate i.e. 55.1% (27), the duration of infertility was within 1-3 years. Whereas 44.9% (22) participants, the duration of infertility was within >3-6 years. Most of the participants of letrozolei.e. 75.51%

(37) out of 49 duration of infertility was within 1-3 years. Whereas 24.49% (12) participant's duration of infertility was within >3-6 years. Mean value of duration of infertility of participants of clomiphene citrate group was 3.23 standard deviation was ± 1.05 and standard error was 0.15. In case of letrozole group of participants, mean value of duration of infertility was 3.20, standard deviation was ±3.32 and standard error was 0.47. Chi square value was 18.87 which was found to be statistically significant at the level 0.042 (p<0.05). So there is association between duration of infertility and treatment of infertility.

In study conducted by Sahu M. *et. al.*[8] the mean duration of infertility in group letrozole is 2.89 years and in group clomiphene is 2.93 years with p value was 0.819 (0.05), which was not significant. Both the groups are comparable with respect to mean duration of infertility. Accordingto JainS.*et.al*[14] the mean duration of infertility was 4.58± 2.68 yrs for letrozole group and 5.62±3.47 years in clomiphene group. The duration of infertility in different categories among the two groups were not statistically significant (p>0.05).

Accordingto Khakwani M.*et. al.*[15] the overall mean duration of infertility was found to be 2.62± 0.74 years. Accordingto Nambiar SS.*et.al.*[13] it was noted that in clomiphene group the duration of marital life prior to commencement of the study was less than or equal to 2 years in 39.6%, between 2 years and 4 years in 21.9%, between 4 years and 6 years in 17.7%, more than or equal to 6 in 20.8% with a mean +standard deviation of 4.1 + 2.7 compared to 40.4%, 25%, 17.3%, 17.3%, respectively in letrozole group with a mean + standard deviation of 4.1 + 3.2. The p value was 0.984, hence no significant difference in the distribution between the two groups.

Inmystudy, mostoftheparticipantofClomiphenecitratei.e.67.35%(33)outof49hadamenorrhea.WhereasmostoftheparticipantofLetrozole i.e.44.9%(22)outof49hadoligomenorrhea.

*FINDINGSRELATED TORESULTOFINFERTILITYTREATMENT
Ovulati on rate :
In the present study most of the participants of clomiphene citratei.e. 51.02% (25) ovulation was not happened whereas 48.98% (24) participant's ovulation was happened. Most of the participants of letrozole i.e. 75.51% (37) out of 49 ovulation happened. Whereas 24.49% (12) participant's ovulation not happened. Chi square value is 98.00 which is found to be statistically significant at the level <0.001 (<0.05). So there was association between ovulation and treatment of infertility.

Study conducted by Sahu M.*et.al*[8] in his study out of 50 patients in letrozole group 38 patients ovulated accountingto 76% which was similar to the present study. Out of 50 patients in clomiphene group 26 patients ovulated accounting to 52%. By applying chi square tests, chi square value is 6.250 and p value was 0.012 (<0.05) which is significant. This shows that there was statistically significant difference in ovulation induction rate treated between the group of patients with letrozole and clomiphene.

Study conducted by JainS.et.al[48] Letrozole was given during 218 cycles of 50 patients ovulation occurred in 178 (81.65%) cycles which was suggested by rupture of dominant follicle. In the control group, clomiphene citrate was given in 232 cycles of 50 patients and ovulation occurred in 152 (65.51%) cycles. In this case, ovulation rate in letrozole group was more and statistically highly significant (p<0.01) as comparedto clomiphene.

In another study by NambiarSS.*et.al.*[13] in the clomiphene group 7.3% achieved no ovulation, 22.9% achieved ovulation in the first cycle, 35.4% in the second cycle, 28.1% in the third cycle and only 6.3 % in thefourth cycle. In the letrozole group, 1.9% achieved no ovulation, 22.1% in   the first cycle, 47.1% in the secondcycle, 26.0% in the third cycle and only 1.9 % in the fourth cycle. Over all 2.03+1.03 ovulations occurred in the clomiphene group against 2.07 + 0.85 in the letrozole group, with a p value of 0.787 which was Statistically insignificant.

No.andsizeof follicles :
In the present study, most of the participant of Clomiphene citrate i.e. 75.51% (37) was multifollicular. Whereas most of the participants of Letrozole i.e 73.47% was monofollicular. Chisquarevalue was29. 431 which wasfound to bestatisticallysignificantatthe level <0.001 which islessthan 0.05 levelofsignificance. So therewasassociationbetweenno. ofdominantfollicle andtreatmentofinfertility.Most of theparticipantofClomiphenecitratei.e.10.20% (5) sizeof dominantfollicle was20x18, whereasmostof theparticipantof letrozolei.e.12.24% (6) size was21x20. Sothe size ofdominantfollicle ofletrozolegroup washigherthan Clomiphene citrate.Chi square(X2) valueis 98.00 which was found to bestatisticallysignificant at the level <0.001whichwaslessthan 0.05levelofsignificance. So,therewasassociation betweensize of dominantfollicle and treatment of infertility.

According toSahu M. *et. al.*[8] Inletrozolegroup ,81.25%ofthecasesdevelopedsingle follicleand18.75%of the casesdevelopedmultiplefollicle. Inclomiphenegroup, 32.65%of the cases developedsingle follicleand67.34%of the cases developed multiplefollicles. By applyingchisquare tests

thevalue was 23.66 and pvalue (<0.05) which is highlysignificant.Sofromtheabovestudiesletrozoletreated cases had better monofollicularovulationratesascomparedtoclomiphenegroup.

Accordingto JainS.*et.al*[14] Inthisstudy,letrozole out of 208 cycles, 178 (85.57%) cycle had 1 no. offollicles. Mean noof follicles in thisstudygroupwas1.17±0.47.Inthe control group outof 216 cycles, 120 (55.55%) cycleshad2no. offollicles. Meanno. of follicles inthe control groupwas1.90±0.77. So no. offolliclesin letrozolegroupas compared toclomiphenegroupwas less andstatisticallysignificant(p<0.001).

Accordingto Nambiar SS.*et.al*[13] Whencompared for the totalnumberoffolliclesmorethanorequalto 14 mm seenin the clomiphenegroup,amean +standarddeviationof 2.54 + 0.77 was seencomparedto1.39 ± 0.53in theletrozolegroup. This hada*p*value 0<0.01, hencestatisticallysignificant.Theclomiphenegroup had astatisticallysignificantincreaseinthetotal number offollicles morethanorequalto14mm,i.e.,significantmultifolliculardevelopment.About 60.2% ofpatientsinthe letrozolegroupshowedmonofolliculardevelopmentcompared toonly9.4%intheclomiphenegroup;whereasmultifolliculardevelopmentwas seen in 90.6%patients in the clomiphene groupcompared to 39.8%oftheletrozolegroup.The*p* value was 0.000. Hence, monofollicular developmentwasfoundtobeveryhighlystatisticallysignificant inthe letrozolegroup, which is one of its majoradvantages.

Meanendometrialthickness
In presentstudy mostof theparticipantsofClomiphenecitratei.e.67.35% (37) endometrial thicknesswas within5.3-7.4, whereas32.65% (16) participant'sendometrial thicknesswas >7.4.Most of theparticipantsof letrozolei.e. 63.27% (31) out of 49endometrialthickness was>7.4 whereas36.27% (18) participant'sendometrial thicknesswas5.3-7.4. Meanvalue ofendometrial thicknessofparticipantsofClomiphene citrategroup was23.38,standarddeviationwas ±2.53andstandarderrorwas 0.185 incase ofletrozolegroupof participantsnst meanvalue ofendometria lthickness was 22.73,standarddeviationwas ±2.40andstandarderrorwas 0.18.

Studyconducted by Sahu M.*et.al*[8] the meanendometrialthickness inletrozolegroupwas8.29mmwithaSDof ±0.7836. In Clomiphenegroup the meanendometrial thickness was7.18 mmwitha SD of ±0.7259 pvalueobtained was <0.05, highlysignificant.

Study conducted by Khakwani M.*et. al.*[15] themeanendometrialthicknesswas noted tobe 8.11.5 mminhalf of the pts whoreceivedtabletrozoleand6.8±1.9mminrest of the ptstreatedwithdrugclomiphenecitrate andthedifferenceturnedtobestatisticallysignificant.

Study conducted by NambiarSS.*et.al*[13] reveal that The meandifferenceachieved inendometrialthicknesswiththeuseofthedrugswas3.03 in the clomiphenegroupand3.64intheletrozole group.The*p*value was 0.024 which was highlystatisticallysignificant

PregnancyRate :
In thepresentstudy, mostof theparticipantsofClomiphenecitrate i.e.89.79% (44) out of49 UPTresult wasnegative,whereas10.20% (5)participantsresult waspositive. Most of theparticipantsofLetrozolei.e.81.63% (40) out of49UPT resultwasnegative,and18.37% participantsresult waspositive. Chisquarevalue is47.361 which wasfound to bestatisticallysignificantatthe level <0.001 which islessthan 0.05 levelofsignificance. So thereis associationbetweenpregnancyrate andtreatmentof infertility

According toSahu M. *et. al.*[8] the pregnancyggrouptabulationshowsthatinletrozolegroup, 24%ofcasespregnancyoccurred and inclomiphenegroup12%ofcasespregnancyoccurred. By applyingChisquaretestspvalue0.118(>0.05) was notsignificant. Thisshowsthatletrozoletreated pts hadbetter Pregnancy rates thanclomiphene but it was notstatisticallysignificant.

Accordingto JainS.*et.al*[14] 48% pts conceivedinstudy group whileincontrolgroup16%conceived.Analmost three fold increase in pregnancy ratewasobservedptswho receivedletrozolecompared to those who received Clomiphenecitrate, this difference was statisticallysignificant(p<0.05).

Accordingto Nambiar SS.*et.al.*[13] In the clomiphenegroup, 30.2%patientsachievedpregnanc in1–2 cycles, 62.55%in3–4 cyclesand7.3% in 5–6 cycleswithamean + standarddeviationof3 +1.01whencomparedto30.8%,66.3% and 2.9%respectivelyintheletrozolegroupwithamean +standarddeviation of 2.92+ 0.89. The *p*valuewas 0.566,againnot statisticallysignificant.

The present study which was conducted at Bankura Sammilani Medical College andHospital,

there was association between BMI and infertility treatment outcome. From theabovestudies aswefound thatLetrzoleismoreeffective inobesePCOSwomenwhereasCC is more effective in normal BMI patients. This finding similar to our study. Letrozole hasbetter monofollicular development whereas CC has better multifollicular development whichwas found in the present study. So our study almost coincides with the study conducted byJain S.*et.al* and Sahu M. *et.al*. Letrozole has better ovulation and pregnancy outcome than CCwhich was found in the present study, which was similar to those studies of Jain S. *et. al.* andSahuM. *et. al.*[8]

Conclusion:

For the last 40 years, the first line of treatment for anovulation in infertile women has beenclomiphene. The choice of CC was appropriate because the drug was highly effective ininducing ovulation in selected patients with the advantages of being orally administered,relatively safe and inexpensive. In contrast, alternative treatments usually involved parenteralgonadotropins that were significantly more complicated and uncomfortable to administer,expensive and associated with more frequent and serious complications. However, CC wasalsofoundtohaveadverseeffects,especiallyinthefor mofcommonantiestrogenicendometrialandcervicalmu couschangesthatcouldpreventpregnancyinthefaceofsu ccessfully induced ovulation. Aromatase inhibitors are a new group of drugs to join thearsenaloffertilitytreatments.Theyareorallyadminist ered,easytouseandrelativelyinexpensive, with minor side effects. Based on the evidence reviewed above, these oralagent's aromatase inhibitor letrozole seems to be efficient for ovulation induction. But afterconducting this study, author believes that advantages of using of letrozole will be more thanCC. Because ovulation rate was higher than Clomiphene citrate. Major advantage of letrozoleforovulationinductionwasmono-follicularovulation.

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