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Original Research Article

## To assess ovulation in infertile women using urinary luteinizing hormone surge kits versus transvaginal ultrasonography

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### ABSTRACT

**Background:** The study was conducted to evaluate the efficacy of urinary LH surge kits and TVS to detect ovulation in induced cycles and to compare the ovulation rates by both methods.

**Methods:** Prospective experimental randomized control trial on 72 women with an ovulatory infertility aged 18-35 years, fulfilling the inclusion criteria were given letrozole for ovulation induction. All were randomly divided in two groups. Group 1 woman were asked to check ovulation by urinary LH surge kits and group 2 women were called for follicle monitoring by TVS.

**Results:** Letrozole has no negative effect on endometrium; induced cycle has larger diameter of follicle (median: 22 mm). In induced cycle ovulation occurs later compared to normal cycle (D-16) and half of the women had a BMI more than the recommended WHO criteria (average was 25.28 kg/m<sup>2</sup>). Number of letrozole cycles ( $p=0.2642$ ), dose requirement ( $p=0.0812$ ) and pregnancy rates (10.26% versus 18.19%) were comparable in both groups.

**Conclusions:** TVS is objective, accurate and thus standard modality for ovulation detection. LH surge kit is subjective, having more chances of error but can be used as a good alternative in certain settings like woman of remote area, woman having fear of invasive modality and COVID era woman who are afraid to visit hospital repeatedly.

**Keywords:** LH surge kit, TVS, Ovulation

### INTRODUCTION

Infertility is defined as one year of unprotected intercourse without conception and affects approximately 10-15% of couples. 80-90% of healthy young couples conceive within 1 year, most within 6 months.<sup>1-3</sup> The major causes of infertility are; ovulatory dysfunction (20-40%), Tubal and peritoneal pathology (30-40%), male factor (30-40%), uterine pathology and rest remains unexplained. Ovulatory dysfunction is more in younger than in older couples. The infertility evaluation can be conceptually simplified into confirmation of ovulation, normal female reproductive tract anatomy and normal

semen characteristics. Various methods to detect ovulation are transvaginal ultrasonography (TVS), urinary luteinizing hormone detection, serum progesterone, urinary pregnanediol 3 glucuronide detection, urinary follicular stimulating hormone detection, basal body temperature monitoring, cervical mucus and salivary ferning analysis. An ideal method to detect ovulation should be non-invasive, inexpensive, easily available, easy to use, precise in determining ovulation and precise in determining the fertility window. The fertility window begins approximately 3-5 days (sperm lifespan) before ovulation and continues to a point 1-2 days (oocyte lifespan) after ovulation.<sup>4</sup> Identifying

this window is vital for encouraging or discouraging contraception. By performing ultrasonography, the maximum growth of the dominant follicle and the subsequent decrease in size can be observed, so the time of ovulation, which lies in between, can be determined. Because this time can be clearly defined in this manner, it is recognized as the standard reference examination for ovulation detection and is used mainly in artificial reproductive techniques. Detection of the luteinizing hormone (LH) surge, whether in serum or in urine, is very sensitive and specific for ovulation and provides great accuracy for determining conception capacity. Detection of LH in urine using an over the counter device is much more convenient and less invasive than measuring serum LH level by multiple venipuncture.

Starting from the 10th to 11th day of a new cycle (day 1 is defined as the first day of menstrual bleeding), or 4 days before the estimated ovulation day, women can test their urinary LH once or twice daily. Highly sensitive urinary LH kits detect concentrations as low as 22mIU/ml, while natural LH surge concentration in urine ranges from 20 to 100 mIU/ml.<sup>10</sup> The mean time interval after a positive urinary LH test to follicular rupture detected by sonography was reported to be 20±3 hour (95% CI 14-26) and in a study focused on infertile women, sensitivity, specificity, and accuracy of the urinary LH test to detect ovulation reached 1.00, 0.25, and 0.97, respectively.<sup>5</sup> The U.S. National Academy of Clinical Biochemistry Laboratory Medicine practical guidelines recommend urinary LH test, because a positive result predicts ovulation within 48 hr. Several studies conducted to detect ovulation by urinary LH surge instead of ultrasonography because it is highly accurate, inexpensive, and less invasive.<sup>6-10</sup> Because a positive urinary LH test precedes ovulation, it is theoretically helpful for timed intercourse or intrauterine insemination because the clinical pregnancy rate after a single act of intercourse is highest from a point 2 days before ovulation to the day of ovulation.<sup>11</sup> Thus we thought to see the efficacy of urinary LH surge kits to detect ovulation as it is highly accurate, inexpensive, easy and non-invasive than transvaginal sonography.

## METHODS

This prospective experimental randomized control study was conducted in the department of obstetrics and gynaecology, LLRM medical college and associated SVBP Hospital from May 2019 to June 2020 comprising of 72 women aged 18-35 years. With an ovulatory infertility, fulfilling the inclusion criteria. An informed consent was obtained from each woman. Ethical clearance was taken from the institutional ethical committee.

### Inclusion criteria

An ovulatory infertile women, normal semen analysis, age 18-35 years, no other gynaecological pathology,

normal bilateral tubal patency, not a known case of any medical or surgical illness.

### Exclusion criteria

Women with uterine or adnexal pathologies, hyperthyroidism or hypothyroidism, male factor infertility, previous history of any surgeries related to genital tract. Ovulation induction was done by letrozole (2.5-7.5 mg from day 2 or 3) in all enrolled cases. They were randomly allocated in 2 groups by chit method. group 1 those who picked LH surge kit chit were asked to check ovulation by urinary LH surge kits in the morning sample from day 12, till the test is positive. If it is not positive even by day 25, test was stopped and cycle was considered an ovulatory and group 2 those who picked TVS chit were called for follicle monitoring by TVS from day 11-12, every alternate day till rupture of follicle. If no dominant follicle was seen by day 25, the cycle was considered an ovulatory. Both groups were advised for timed intercourse after the urinary LH surge test is positive or ovulation about to occur on TVS (follicle size around 20±2 mm). In an ovulatory cycles letrozole dose was sequentially raised maximum up to 7.5 mg as necessary. Primary outcome was ovulation as denoted by urinary LH surge in group 1 and follicle rupture on TVS in group 2, secondary outcome was dose of letrozole needed for ovulation, conception rate and determination of day of ovulation with follicular size. Descriptive results were presented in the form of proportions/percentages for categorical variables and median/interquartile range along with mean and standard deviation for continuous data. Fisher Exact test/Chi square test was used for the comparison of proportions (categorical variables). Continuous variables were compared using the Mann Whitney test or student t test (independent group/unpaired data) after testing for normalcy of data, p<0.05 was considered significant.

## RESULTS

Out of total 72 women, ovulation induction was diagnosed using LH surge kits in 39 women (54.17%) and using TVS in 33 women (45.83%) (Table 1).

**Table 1: Sample size distribution.**

Parameters	N	%
<b>Total sample size of patients</b>	72	100.00
<b>Number with LH surge kits</b>	39	54.17
<b>Number with TVS</b>	33	45.83

The mean age of the study population was 26.9 years in group 1 and 26.85 years in group 2 (Table 2). The mean BMI of the study population was 25.28 kg/m<sup>2</sup>. Most of the women in both the groups were nulliparous (87.50% in group 1 and 84.48% in group 2) housewives (94.8% in group 1 and 81.81% in group 2) having mean duration of the marriage 5.35 years. Duration of infertility was 4.32 years in LH surge group and 4.7 years in TVS group;

p=0.7743. Primary infertility was noted 71.79% in group 1 and 72.72% in group 2.

**Table 2: Demographic parameters.**

Demographic parameters		Overall	LH surge kit group	TVS group	P value
<b>Age related parameters</b>	Mean	26.88	26.90	26.85	0.6947
	SD	4.23	3.76	4.79	
	Median	27.00	27.00	26.00	
	Quartile 1	24.00	25.00	24.00	
	Quartile 3	29.25	29.50	29.00	
<b>BMI related parameters</b>	Mean	25.28	25.57	24.93	0.5597
	SD	3.89	4.33	3.34	
	Median	24.55	24.88	23.90	
	Quartile 1	22.60	22.86	22.60	
	Quartile 3	27.78	27.65	27.70	
<b>Occupation</b>	Housewife	64 (88.88)	37 (94.87)	27 (81.81)	0.0811
	Parlour	1 (1.38)	0	1 (3.03)	0.2770
	Tailor	3 (4.16)	1 (2.56)	2 (6.06)	0.4620
	Teacher	4 (5.55)	1 (2.56)	3 (9.09)	0.2313
	Total	72	39	33	-
<b>Parity status</b>	Zero/Nulliparous	63 (87.50)	35 (89.74)	28 (84.48)	0.5068
	Parity 1	5 (6.94)	2 (5.12)	3 (9.09)	0.5119
	Parity 2	3 (4.16)	2 (5.12)	1 (3.03)	0.6604
	Parity 3	1 (1.38)	0	1 (3.03)	0.2770
	Total	72	39	33	-
<b>Duration of marriage ( years)</b>	Mean	5.35	5.06	5.68	0.9616
	SD	3.93	2.71	5.03	
	Median	5.00	5.00	5.00	
	Quartile 1	3.00	3.00	3.00	
	Quartile 3	6.00	6.00	7.00	
<b>Duration of infertility (years)</b>	Mean	4.49	4.32	4.70	0.7743
	SD	3.08	2.44	3.73	
	Median	4.00	4.00	3.00	
	Quartile 1	2.00	3.00	2.00	
	Quartile 3	6.00	6.00	6.00	
<b>Status of infertility</b>	Primary	52 (72.22)	28 (71.79)	24 (72.72)	0.9305
	Secondary	20 (27.78)	11 (28.21)	9 (27.28)	
	Total	72	39	33	

The duration of menstrual cycle was higher in the TVS group compared to the LH surge kit group (32.48 vs. 30.23 days; p=0.4191), menstrual flow duration was slightly higher in the TVS group, but the difference was not statistically significant (p=0.6049) (Table 3). Most of the women in the study had normal menstrual flow character (p=0.6608). Fifteen women had dysmenorrhea with a higher proportion in TVS group compared to the LH Kits surge group (21.22 vs. 20.52), but the difference was not statistically significant (p=0.9423). The proportion of patients in LH surge kit group (10.26) with dyspareunia was higher compared to the TVS Group (3.04) but again the difference was not statistically significant (p=0.2333).

The median number of letrozole cycles given to the study was 1 with a mean of 1.75 (Table 4). The median number

of cycles were same across both the groups, but the mean number of cycles were higher in the TVS Group compared to the LH surge kit group (1.91 vs. 1.62; p=0.2642). Most of the cases ovulate in first cycle (57%), followed by second cycle (19%), third cycle (17%) and fourth cycle (7%). The LH surge kit group had a higher proportion of women receiving only one or two cycles (61.53% for one cycle and 20.51% for two cycles). The TVS group however had a higher proportion of women receiving three or more cycles (24.24% for three cycles, 9.09% for four cycles). Although the results were comparable. Most of the women in the study received 2.5 mg letrozole. The TVS Group had a higher proportion of women receiving higher dose (5 mg) of the letrozole in the study (39.40% receiving 5mg in TVS compared to 20.51% in the LH surge kit group; p=0.0812). Most of the women in the study received 2.5 mg letrozole dose.

The TVS Group of women had a higher proportion of women receiving higher dose (5 mg) of the letrozole in

the study (39.40% receiving 5mg in TVS compared to 20.51% in the LH surge kit group) ( $p=0.0812$ ).

**Table 3: Menstrual characteristics.**

Menstrual characteristics		Overall	LH surge kit group	TVS group	P value
Cycle duration related parameters	Mean	31.26	30.23	32.48	0.4191
	SD	7.63	3.22	10.68	
	Median	30.00	30.00	30.00	
	Quartile 1	30.00	30.00	30.00	
	Quartile 3	30.50	30.00	32.00	
Menstrual flow duration related parameters	Mean	4.82	4.77	4.88	0.6049
	SD	1.76	1.91	1.60	
	Median	4.50	4.00	5.00	
	Quartile 1	4.00	4.00	4.00	
	Quartile 3	5.00	5.00	6.00	
Menstrual flow character	Normal	69 (95.83)	37 (94.87)	32 (96.96)	0.6608
	Heavy	3 (4.17)	2 (5.13)	1 (3.04)	
	Total	72	39	33	
Dysmenorrhea	Absent	57 (79.16)	31 (79.48)	26 (78.78)	0.9423
	Present	15 (20.84)	8 (20.52)	7 (21.22)	
	Total	72	39	33	
Dyspareunia	Absent	67 (93.05)	35 (89.74)	32 (96.96)	0.2333
	Present	5 (6.95)	4 (10.26)	1 (3.04)	
	Total	72	39	33	

**Table 4: Number of letrozole cycles and letrozole dose distribution in the study population.**

Number of Letrozole cycles	Overall	LH Surge kit group	TVS group	P value
One	41 (56.94)	24 (61.53)	17 (51.51)	0.3956
Two	13 (18.05)	8 (20.51)	5 (15.15)	0.5585
Three	13 (18.05)	5 (12.82)	8 (24.24)	0.2126
Four	5 (6.94)	2 (5.12)	3 (9.09)	0.5119
Total	72	39	33	-
Mean	1.75	1.62	1.91	0.2642
SD	0.99	0.91	1.07	-
Median	1.00	1.00	1.00	-
Quartile 1	1.00	1.00	1.00	-
Quartile 3	2.25	2.00	3.00	-
<b>Letrozole dose (mg)</b>				
2.5	51 (70.83)	31 (79.48)	20 (60.60)	0.0812
5	21 (29.17)	8 (20.51)	13 (39.40)	
Total	72	39	33	

The average day at which ovulation was diagnosed was lower for the LH Surge kit women (15.21 days, median=15 days) compared to the TVS group (16.24 days, median=16 days) (Table 5). This implied that the LH surge kit helped diagnose induced ovulation almost a day earlier compared to the transvaginal sonography. This difference was statistically significant ( $p=0.0124$ ). The mean endometrial thickness on TVS was 8.32 mm. Total 10 patients (13.89%) reported pregnancy in the follow up period of the study (Table 6). We have followed women for 4 cycles to see pregnancy outcome after we detected ovulation. The rate of pregnancy was

higher in the TVS group of patients (6, 18.19%) compared to the LH surge kit patients (4, 10.26%). Among those who conceived, max conceived in first cycle with 2.5 mg letrozole (40%), followed by second cycle with 2.5 mg letrozole (30%), followed by third cycle with 5 mg letrozole (20%), followed by fourth cycle with 5 mg letrozole (10%). However, this difference was not statistically significant ( $p=0.3358$ ). The mean and median follicle size on rupture as assessed by the TVS was seen to be 22x22 mm. minimum size was 16x18 mm (3% cases), maximum size was 24x26

mm (12% cases) and majority ovulate at follicle size of 2x24 mm (33%).

**Table 5: Day of ovulation as per method of diagnosis.**

Ovulation day	LH Surge kit group	TVS group	P value
Mean	15.21	16.24	0.0124
SD	1.15	2.02	
Median	15.00	16.00	
Quartile 1	14.00	15.00	
Quartile 3	16.00	17.00	

## DISCUSSION

Ovulatory disorder can be identified in 18-25% of women presenting with infertility requiring ovulation induction.

**Table 6: Pregnancy based on method of diagnosis and type of infertility.**

Pregnancy status	LH surge kits	TVS group	Grand total	P value
<b>Primary infertility</b>	28	24	52	0.3181
<b>No Pregnancy</b>	25 (89.28)	19 (79.16)	44	
<b>Pregnancy</b>	3 (11.72)	5 (20.83)	8	
<b>Secondary infertility</b>	11	9	20	0.8840
<b>No Pregnancy</b>	10 (90.90)	8 (88.88)	18	
<b>Pregnancy</b>	1 (9.09)	1 (11.12)	2	
<b>Grand total</b>	39	33	72	

It was seen that the average age of the patients was 26.88 with a median age of 27 years. The average duration of the marriage in the study was 5.35 years. The average duration of infertility for couple seen our study was higher compared to a similar study conducted in a tertiary care center (42 months or 3.5 years).<sup>5</sup> The average BMI was 25.28 kg/m<sup>2</sup> for the women which is higher than the normal recommended BMI for females in India. Overweight and obese females are at an elevated risk of infertility.<sup>6</sup> The overall average menstrual cycle duration was 31.26 days with a standard deviation of 7.63 days. Letrozole was preferred over clomiphene citrate for induction because it appears to be free of the adverse effects on endometrium and cervical mucus compared to clomiphene citrate.<sup>9</sup> It is also considered as the first line for oligo-ovulatory women and PCOS undergoing ovulation induction, irrespective of the body mass index (BMI). Letrozole in a dose range of 2.5 mg to 7.5 mg was initially considered for ovulation induction. 2.5 mg was the most commonly used dose across both the study groups. The proportion of patients with 2.5 mg letrozole dose was higher in the LH surge kit group (79.48%) compared to only 60.60% in TVS group. This difference was not statistically significant (0.0812) highlighting comparable distribution across both the groups.

The LH surge kit group had a higher proportion of patients receiving only one or two cycles (61.53% for one cycle and 20.51% for two cycles). The TVS group however had a higher proportion of patients receiving

Transvaginal sonography (TVS) is an invasive procedure which needs specific setting and a radiologist to perform the procedure. TVS clearly defines ovulation time and is recognized as the standard reference examination for detecting ovulation. The LH surge kits (LH surge assessment in urine) are a new non-invasive method of assessment of ovulation induction which can be used by the women herself without the need for any such radiologist or specific setting. They are an easily available/easy to use over the counter options compared to TVS. The study comprised of 72 patients with primary and secondary infertility. All the women underwent ovulation induction with tablet letrozole (2.5-7.5 mg from day 2 or 3). Subsequent ovulation was analysed using either of the two methods urinary LH surge testing or TVS for follicular monitoring.

three or more cycles (24.24% for three cycles, 9.09% for four cycles). This difference was not statistically significant. Based on the method of assessment, it was seen that the average date at which the ovulation induction diagnosis was 15.21 days in the LH surge kit group and 16.24 days in the TVS group. This highlighted that ovulation induction was diagnosed a day earlier on an average in the LH surge kit group compared to the transvaginal sonography. This difference was statistically significant ( $p=0.0124$ ). The average follicle size on rupture seen by TVS was 22 mm (median: 22 mm) with 75% of the study population having follicle size of 20 mm or above at time of rupture. It was seen that the rate of pregnancy was similar (10.26% versus 18.19%) across both the groups with an overall pregnancy rate of 13.89%. The above findings showed that the LH surge kit was able to diagnose the ovulation induction a day earlier compared to the transvaginal sonography and the results were statistically significant. It was also seen that the pregnancy rate was comparable across both the groups with no significant difference. The letrozole cycle number and dose requirement across both the groups was also comparable with no significant difference. Both the groups were comparable in terms of demographic and clinical profiles. Similar results have been shown previously by several studies describe methods to detect ovulation by urinary LH surge instead of ultrasonography because it is highly accurate, inexpensive, and less invasive.<sup>12-14</sup> Brand of LH detection kit has an important impact on the final results. Detection of LH in urine using

over the counter urinary LH surge kit is highly accurate, very convenient, feasible, non-invasive and inexpensive.

## CONCLUSION

LH surge kit is a subjective method of assessment and therefore there are more chances of error but it is a very convenient, feasible, non-invasive and inexpensive, and therefore recommended for patients of remote areas who live away from radiologist, females of low socioeconomic status who cannot afford monthly expenses of travelling to hospital, females who are uncomfortable with any invasive procedure and especially in this COVID time where everyone is scared to travel in public transportation. Detection of ovulation by TVS is objective method, more accurate, has less chances of error and therefore recommended standard modality for ovulation detection. But it is expensive, invasive, not feasible for remote areas in this COVID pandemic. So, we suggest LH surge kits to be a good alternative for ovulation detection compared to TVS follicular monitoring.

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