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Original Research Article

An Observational Study of Role of Spontaneous Cycle Follicular Monitoring in Unexplained Infertility

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Abstract:

Background: Due to the significant prevalence of unexplained infertility, it is necessary to evaluate the utility of underutilized techniques, such as ultrasonographic follicular monitoring, endometrial alterations, and their association with hormone levels in spontaneous menstruation. Our research sought to identify the minute flaws that were to blame.

Methods: It was an observational study conducted in the Department of Obstetrics and Gynaecology, SKMCH, Muzaffarpur, Bihar from February 2022 to April 2023. The study comprised 50 infertile women with unknown causes. On days 2-3 after the start of menstruation, the subjects were contacted for a baseline transvaginal ultrasound to measure the endometrial thickness, antral follicular count, and hormonal profile. Up until ovulation was confirmed, follow-up ultrasonographic monitoring was performed. On the day the dominant follicle measured 18 to 20 mm, a hormonal profile was performed, and on day 21 serum progesterone levels were measured.

Results: The study group average age was 26.48±3.3 years. In 66% of cases, infertility was primary, and in 34%, it was secondary. At least one, or a combination of modest abnormalities, were present in the tracked cycles of 78% of the women. The average number of antral follicles was 13.8±5.17. Only one woman had fewer than five antral follicles, and 30% of women had FSH levels over 10 IU/L and serum estradiol levels over 80 pg/ml. In 34% of the women, luteal phase defects and early LH surges were seen.

Conclusion: Spontaneous cycle follicular monitoring is a helpful tool to shed light on the subtle defects that contribute to unexplained infertility, such as premature ovarian reserve depletion, defective folliculogenesis, poor oocyte quality, premature luteinization, and luteinized unruptured follicular syndrome. Thus, it appeared to be a valuable supplement to the investigative work-up of women with unexplained infertility to perform transvaginal sonographic examination of a spontaneous cycle.

Keywords: Unexplained Infertility, Transvaginal Ultrasound, Follicular Monitoring, Endometrial Changes, Hormonal Assessment.

Introduction

When routine infertility testing, such as husband's semen analysis, ovulation tests, and tubal patency tests, are unable to find any obvious problem, the condition is referred to as unexplained infertility.[1] According to several research, the prevalence of unexplained infertility varies between 10 and 20%.[2] In the evaluation of infertile couples with unexplained infertility, many diagnostic techniques have been suggested in a number of investigations. In order to identify the subtle defects causing unexplained infertility, this study aims to evaluate the usefulness of unproven techniques like sonographic monitoring of follicular growth and endometrial changes and its correlation with hormonal levels in spontaneous menstrual cycle in women with infertility.

Material and Methods

From February 2022 to April 2023, this observational study was carried out in the Department of Obstetrics and Gynecology, Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar. After

receiving signed and informed consent, 50 women under 35 with unexplained infertility were enrolled in the study.

Routine tests for infertility, such as a thorough history and physical examination, chest X-ray, husband semen analysis, premenstrual endometrial biopsy, and postmenstrual hysterosalpingography, were then performed.

On days 2-3 after the start of menstruation, the subjects were contacted for a baseline transvaginal ultrasound to measure the endometrial thickness, antral follicular count, and hormonal profile. From days 8 through 10 of the menstrual cycle, serial ultrasounds were performed on alternate days until ovulation was confirmed.

Serum FSH, LH, estradiol, and progesterone levels were measured on days 2-3 of the menstrual cycle; LH, estradiol, and progesterone levels were measured at a follicular size of 18–20 mm; and serum progesterone levels were measured on day 21.

The outcome variables were proportion of subjects with poor ovarian reserve (antral follicle count (AFC) <5, day 2 FSH> 10 IU/l), poor quality oocyte (serum estradiol levels <180 pg/ml at a follicle size of 18-20 mm), premature LH surge (serum progesterone >1.5 ng/ml, at a follicle size of 18-20 mm), size of follicle at the time of ovulation, unruptured luteinized follicle and luteal phase defect (day 21 progesterone levels <10 ng/ml and or duration of luteal phase <10 days). The results were compiled and analysed using latest version of SPSS software and results were expressed as mean ± SD.

Results

Table 1 shows the demographic breakdown of the participants who were recruited for the study. The subjects average age was 26.48±3.3 years. Infertility lasted an average of 4.39±2.86 years. As may be seen in the paragraphs that follow, 78% of the women had one or more minor faults in their monitored cycles.

According to Table 2, on Day 2/3, mean serum levels of FSH were 8.25±3.36 IU/L (4.02–21.58), LH was 6.97±4.07 IU/L (3.1–26.29), estradiol was 72.74±29.64 pg/ml (30.3–181.5), and progesterone was 0.69±0.39 ng/ml (0.2–2.46). The average number of antral follicles was 13.8±5.17. AFC of 5 or less was observed in 2% of participants, 5–10%, 10%–15%, and 15%–20% of subjects, respectively. On the day that the dominant follicle size reached 18–20 mm, the mean blood levels of progesterone, estradiol, and LH were 1.93±1.47ng/ml (range: 0.28–6.40ng/ml), 264.25±109.6pg/ml (range: 65–598pg/ml), and 32.35±21.1IU/L (range: 8–96IU/L), respectively.

Table 1: Demographic Profile

Parameters	No. of patient (n=50)	Percentage (%)
Age (in years)		
• <30	45	90%
• >30	5	10%
Body Mass Index (kg/m^2)		
• <23	33	66%
• 23-24.9	12	24%
• >25	5	10%
Type of infertility		
• Primary	33	66%
• Secondary	17	34%
Duration of infertility (years)		
• <5	34	68%
• >5	16	32%

Serial ultrasound scan revealed that one woman's follicle failed to grow over 11 mm, hence she was left out of the study. The follicle's mean diameter at its maximum size was 19.53±2.07 mm. In 24% of the subjects on cycle day 14, in 46% on cycle day 16, in 14% on cycle day 18, in 2% on cycle day 20, and in 2% on cycle day 22, the dominant follicle burst. In six women, the follicle either did not break or developed insufficiently.

Table 2: Hormone levels on day 2/3 of menstrual cycle (n=50)

Hormones	Day 2/3 (Mean±SD)	Day of follicle size (18-20 mm) (Mean±SD)	Day 21
LH (IU/L)	6.97±4.07	32.35±21.10	NA
FSH (IU/L)	8.25±3.36	NA	NA
Estradiol (pg/ml)	72.74±29.64	264.25±109.62	NA
Progesterone (ng/ml)	0.69±0.39	1.93±1.47	16.89±12.36

In our study, the luteal phase lasted a minimum of 6 days and a maximum of 15 days. One lasted six days, while four women endured 15 days. 40.5% of the women, or the majority, had luteal phases that

lasted 13 days. On day 21, the mean blood progesterone levels were 16.89±12.36 ng/ml (the range was 0.28 51.15 ng/ml).

Discussion

An efficient, user-friendly, secure, and trustworthy non-invasive method of assessing reproductive potential is ultrasound imaging.

Day 3 FSH, LH, estradiol, antimullerian hormone (AMH), and AFC levels are the ovarian reserve tests. An important indicator of ovulation is the level of serum progesterone on day 21 of the menstrual cycle or one week before menstruation is anticipated in an irregular cycle. If the value is greater than 3ng/ml, ovulation may be in progress.

In the study, 50 participants were recruited, and 22% of them had cycles that were typical in terms of follicular growth, endometrial growth and differentiation, ovulation, and hormone levels. 78% of the remaining cycles exhibited a minimum of one subtle flaw or a combination of them. Upon follow-up, it was discovered that two women had spontaneous pregnancies during the monitored cycle, and one had a spontaneous pregnancy but had an abortion. Ovulation inducement was used on one woman, and she responded by getting pregnant.

Low antral follicular count is described by the American Society of Reproductive Medicine (ASRM), 2012, as having between 3 and 10 antral follicles in both ovaries. This is regarded as the single best indicator of ovarian response and consequently the success of conception.[4] In our study, subjects who had less than five antral follicles had day 2 FSH levels greater than 10 IU/L, day 2 estradiol levels greater than 80 pg/ml, and less than 180 pg/ml at follicle sizes of 18 to 20 mm.

On day 14, the dominant follicle began to form, and on day 18, it burst. This woman's luteal phase was only six days long. She was referred for in-vitro fertilization after a follow-up visit.

In this study, a negative association between day 2/3 serum FSH levels and antral follicular count was observed, with a correlation coefficient of -0.33 and a p value of 0.18. In their investigation, R Fanchin et al. found a correlation between antral follicular count and blood FSH levels on day 3 of the menstrual cycle ($r=-0.29$, $p<0.001$). According to ASRM, serum FSH levels between 10 and 20 IU/L were considered a sign of a poor ovarian response, with a sensitivity and specificity of 80% and 100%, respectively.[6] 30% of the participants in our study had serum FSH levels greater than 10 IU/L, whereas 70% had levels less than 10 IU/L.

The quality of maturing oocytes, their capacity for fertilization, and the post-fertilization development are reflected in serum estradiol levels at follicle sizes of 18–20 mm.[8] In our investigation, 9 patients had prominent 18–20 mm follicles with blood estradiol levels less than 180 pg/ml. Seven of them had one or more indicators of inadequate folliculogenesis and early ovarian reserve depletion. Four people had day two FSH levels > 10IU/L, four others had day two estradiol levels > 80 pg/ml, and one had AFC <5 and three others had AFC <10. When day 21 blood progesterone levels are less than 10 IU/L, luteal phase deficit, a condition related to insufficient progesterone production by the corpus luteum and failure to maintain normal secretory endometrium necessary for embryo implantation, occurs.[9] 17 women participated in our study with serum progesterone levels under 10 pg/ml.

One woman alone had a luteal phase that lasted less than 10 days. Four of the 17 women with luteal phase defects had inadequate follicle growth and an intact follicle, two had premature ovarian reserve depletion, premature luteinization, and delayed ovulation, and three had no cause identified. Even more studies have shown that luteal phase defect cycles had a higher incidence of tiny follicles.[10,11] Our work also shows that luteal phase deficiency is linked to luteinized unruptured follicular syndrome. Compared to a study by Ying Y K et al., where it was observed in 15% of instances, it was seen in 23.5% of participants in our study.[12]

Premature luteinization was discovered in women with early endometrial conversion as detected by ultrasonography and blood progesterone levels greater than 1.5 ng/ml at prominent follicles measuring 18–20 mm. Clinical pregnancy rates are negatively impacted by premature luteinization, which is likely caused by embryoendometrial asynchrony. Premature luteinization affected 34% of the patients in our study, compared to 10% of the subjects in a study by Check JH et al.[13]

Conclusion

Spontaneous cycle follicular monitoring is a helpful tool to shed light on the subtle defects that contribute to unexplained infertility, such as premature ovarian reserve depletion, defective folliculogenesis, poor oocyte quality, premature luteinization, and luteinized unruptured follicular syndrome.

Thus, it appeared to be a valuable supplement to the investigative work-up of women with unexplained infertility to perform transvaginal sonographic examination of a spontaneous cycle.

The absence of anti-mullerian hormone levels as an indicator of ovarian reserve was one of our study's weaknesses. Additionally, we only monitored one cycle. Serum progesterone levels at dominant follicle sizes of 18–20 mm may be arbitrarily raised in situations of premature luteinization, and this procedure should have been repeated in the subsequent cycle. Only up to day 22 was ultrasound used for follicular monitoring; if a rupture was not seen by

that time, no additional follow-up scans were performed.

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