Obstetrics

Correlation of Age and Perifollicular Vascularity in Success of Intrauterine Insemination Treatment Using Transvaginal Doppler among Infertile Women

Dr. Asha Verma[1], Dr. Lata Rajoriya[2], Dr. Prerna Soniya[3*], Dr. Kusum Verma[4], Dr. Anil Gurjar[5], Dr. Rekha Meghnani[6]

[1]Professor, Department of Obstetrics and Gynecology, SMS Medical College, Jaipur, Rajasthan, India

[2]Professor, Department of Obstetrics and Gynecology, SMS Medical College, Jaipur, Rajasthan, India

[3]Junior resident, Department of Obstetrics and Gynecology, SMS Medical College, Jaipur, Rajasthan, India

[4]Assistant professor, Department of Obstetrics and Gynecology, SMS Medical College, Jaipur, Rajasthan, India

[5]Assistant professor, Department of Obstetrics and Gynecology, SMS Medical College, Jaipur, Rajasthan, India

[6]Junior Specialist, Department of Obstetrics and Gynecology, SMS Medical College, Jaipur, Rajasthan, India

Abstract: To study the correlation of age and perifollicular vascularity with success of intrauterine insemination. Sample size-112 patients Women were prescribed 50 mg clomiphene citrate orally from second day of menstrual cycle for 5 consecutive days. They underwent serial transvaginal ultrasound scans starting from day 6 and continued every alternate day. The size of the follicles was calculated by using the mean of the two maximum diameters. Perifollicular Doppler blood flows was assessed in dominant follicles >18mm. Human chorionic gonadotrophin 5000IU was given to the patient when the dominant follicle reached 18mm in diameter. IUI was carried out using prepared/washed semen (husbands). Majority (49.11%) of the patients was in the age group of 26-30yrs and only 3% patients were in the age group ≥36 yrs. No patient in age group >30 yrs had grade 3 vascularity. Out of 12 positive cases, 10 (83%) pregnancies occurred in age group<30 yrs. There were no positives in patients in age group >36 yrs. The mean age of patients in positive group was 26.50 and in negative group it was 27.96. Our study found that perifollicular vascularity in young age is a good predictor in success of stimulated intrauterine insemination treatment.
Keywords: Age, Perifollicular Vascularity, Transvaginal Doppler, Infertile Women.

INTRODUCTION

Infertility is generally defined as one year of unprotected intercourse without conception during child bearing age. Intrauterine insemination with husband's semen is a technique widely used as a low cost; first line assisted reproductive therapeutic option for infertile couples.

Female fertility declines with age due to a decrease in oocyte quality [1]. Chromosomal aneuploidy is the major cause of the age-related decline of oocyte quality. An increase in maternal age results in an increased embryonic aneuploidy rate resulting in an increase in pregnancy loss both prior to and after implantation. The increased embryonic aneuploidy rate results predominately from meiotic non-disjunction errors in the oocytes of these older women [2]. As the actual cause of this age-related increase in oocyte chromosomal meiotic non-disjunction errors is unclear at this point in time, a number of hypotheses have been proposed [1]. One such speculative cause is an increasingly compromised microcirculation around the leading follicle causing reduced oxygen levels in the follicular fluid [3, 4].The oocyte has no direct vascular supply as there is no internal circulation in the follicle. The oocyte is dependent on oxygen diffusion from the microvasculature in the thecal layer around the follicle through the basement membrane of the follicle, granulosa cells, follicular fluid, and surrounding zona pellucid [3]. Angiogenesis is the process by which new capillary blood vessels develop from pre-existing mature vessels and leads, therefore, to neovascularization [5]. Doppler ultrasonography is a simple and noninvasive method and has recently been used to assess uterine or ovarian blood flow in normal cycling women. We aimed to study the correlation of age and perifollicular vascularity with success of intrauterine insemination.

MATERIALS AND METHODS

This prospective, descriptive type of observational study was conducted in the Department of Obstetrics and Gynaecology, SMS Medical College,

Jaipur, Rajasthan including infertile couples attending the infertility clinic.

SAMPLE SIZE

Sample size was calculated at 80% study power and alpha error of 0.05 assuming 20% success in high grade and 0% success in low grade in vascular ovaries as found in the seed article (correlation between perifollicular vascularity and outcome in stimulated intrauterine insemination treatment cycles)

112 patients were required following above assumptions as final sample size for present studies. We included infertile women aged 20-38 yr age group with normal ovarian reserves, at least one patent fallopian tube and of unexplained infertility. We excluded women with poor ovarian reserve, severe male factor infertility, polycystic ovarian disease, endometriosis, and any previous surgery on ovary.

Detailed history and clinical examination was done. Women were prescribed 50mg clomiphene citrate administered orally starting second day of the menstrual cycle for 5 consecutive days.

All patients had undergone serial transvaginal ultrasound scans starting from day 6 and continued every alternate day. The size of the follicles was calculated by using the mean of the two maximum diameters. Perifollicular Doppler blood flows was assessed in dominant foliicles >18mm. We placed the power doppler color over each follicle and then took a cross sectional image of the follicle with the maximum color intensity representing the greatest doppler frequency shifts. The follicular circumference was frozen and the perifollicular blood flow (PFBF) was graded based on Chui *et al.* [8].

According to the modified grading system, ovarian PFBF was represented as, Grade 1: 1% -25%, Grade 2 : 26%-50%, Grade 3 : 51% -75%, Grade 4 : 76% - 100%.A recording was considered satisfactory for measurement when there were three intense waveforms in a row and an average of each index in both ovaries was calculated. Human chorionic gonadotrophin 5000IU was given to the patient when the dominant follicle reached 18mm in diameter. At that time, the endometrium was evaluated as regards endometrial thickness. IUI was carried out using prepared/washed semen (husbands). All patients received luteal support in the form of progesterone from day of IUI for 14 days.

Patient were called after 2 weeks for urine pregnancy test (UPT) which if positive was considered as clinical pregnancy and thereafter at 6 weeks by the last menstrual period to confirm pregnancy by TVS.

Table-1: Distribution of cases according to age

Age	Grade1		Grade2		Grade3		Total	
	No	%	no	%	no	%	No	%
≤25	10	27.78	22	37.93	5	27.77	37	33.04
26-30	17	47.22	25	43.10	13	72.23	55	49.11
31-35	8	22.22	9	15.52	0	0.00	17	15.18
≥36	1	2.78	2	3.45	0	0.00	3	2.68
Total	36	100.0	58	100.0	18	100.0	112	100.0

Chi square= 7.808 with 6 degrees of freedom; P= 0.253

Table-2: Outcome according to patient's age

Age	Positive		Negative		Total	
	No	%	No	%	No	%
≤25	3	25.00	34	34	37	33.04
26-30	7	58.33	48	48	55	49.11
31-35	2	16.67	15	15	17	15.18
≥36	0	0.00	3	3	3	2.68
total	12	100.00	100	100	112	100.00

Chi square = 0.875 with 3 degrees of freedom; P = 1.000

Table-3: Patients mean age and outcome

	Positives (n=12)		Negative(n=100)		P value=0.21
	Mean	SD	Mean	SD	
Patient's age	26.50	3.371	27.96	3.824	

Table-4: Distribution of patients means age according to grading

	Mean	SD	Minimum	Maximum
Grade 1	28.64	3.79	23	38
Grade2	27.81	3.64	22	35
Grade3	25.88	3.31	20	30

P= 0.035

RESULTS

Out of 112 cases in our study majority 55 (49%) of the patients were in the age group 26-30 years. There were only 3 (3%) patients in the age group ≥36 years. Interstingly none of the patients in age >30 yr had grade 3 vascularity. There was no statistically significant difference between the three groups as regarding age of the patients. 83% of the total positive cases belonged to age group <30 years. There were no positive case in the patients with age group >36 years.

Mean age of patients in positive group was 26.71 and in negative group it was 27.76.Thus we can see that younger age was associated with a better pregnancy outcome. Though the difference was not statistically significant.(P= 0.21).Mean age of patients in grade 1 was 28.64, in grade2 was 27.81 and in grade 3 was 25.88. Grade 3 has maximum perifollicular vascularity was present in patients with mean age of 25.88 i.e in young age. This shows that as age advances, the perifollicular vascularity of dominant follicle becoming less. There was statistically significant difference between the three groups as regarding mean age (P Value- 0.035).

DISCUSSION

Fertility is known to decline in women after the age of 30 yrs of age and strikingly decrease is observed after 35 yrs of age. This age related decline in fertility results from several factors that contribute to overall reproductive failure including progressive follicular depletion and diminished oocyte quality.

There have been many studies which show an association between increasing maternal age and poor pregnancy rates. Horbay *et al.* [6] showed a significant decline in pregnancy rate after IUI in women≥36 yrs. Pregnancy rate in ≤36 yrs age group was 38.10% compared to 18.75% in age group ≥36 yrs.

Compana *et al.* [7] studied 332 infertile couples who underwent 1115 cycles of intrauterine insemination. They reported a pregnancy rate to be 16.1% in age group <30 yrs whereas in 10.6% in age group >39 yrs. Thus he suggested that the outcome of the therapy was adversely affected if the woman's age was >39 yrs.

Brzechffa *et al.* [8] analysed the influence of female and male patient age on clinical pregnancy rate with ovulation stimulation using HMG in combination with intrauterine insemination. This study found that increased female partner age (≥35 yrs) negatively influenced pregnancy rates with IUI therapy.

Stone *et al.* [9] did a retrospective study and found that patient's age was the main determinant of pregnancy outcome. In his study, a total of 18.9%of patients of age group ≤26 yrs were conceived as compared to only 4.7% of age group 41-45 yrs and 0.5% of patients >45 yrs old.

Sanja Kupesic *et al.* [10] showed that younger women had greater ovarian volume, more total antral follicles, and higher intraovarian vascularity as measured by the ovarian flow index. In contrast, value of these three variables decreases as age increased. Out of the total 56 patients, pregnancy rate was 65% in age group ≤30 yrs and only 20% pregnancy rate in 36-40 age groups.

CONCLUSION

Increasing patient age is associated with poor stromal vascularity seen with the help of transvaginal Doppler. Our study found that perifollicular vascularity is a good predictor in success of stimulated intrauterine insemination treatment.

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