Study on demographic variables of controlled ovarian Hyperstimulation and Intrauterine Insemination (husband) in a tertiary medical college and hospital in Kolkata

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ABSTRACT

Background: Intrauterine Insemination (IUI) is anage old reliable and safe procedure for couples having infertility. Success rate of IUI with ovulation induction ranges from 8-20% depending on many factors. **Aims and Objectives:** The current study was to assess the factors which are responsible for favourable outcome of IUI after ovulation induction. **Materials and Methods:** Total 67 couples were included fulfilling inclusion and exclusion criteria. They underwent 90 cycles of IUI with each couple having maximum of 3 cycles. Ovulation induction was done byeitherclomiphene citrate or letrozole or gonadotrophins. Semen preparation was done by density gradient method. The participant's demographic parameters were analyzed. **Results:** Out of 90 IUI, 8 were successful resulting in a success rate of 8.8% per cycle and 11.9% per couple. Factors which had positive impact were age less than 35 years, less than 10 years of infertility, normal and overweight BMI. Anovulation and unexplained infertility had better outcome. Type of infertility did not have any impact on the outcome. **Conclusion:** The study concluded that IUI after ovulation induction is more useful in cases like unexplained infertility and anovulation in a patient aged less than 35 years with less than 10 years of infertility and normal or overweight BMI.

Key words: BMI; Anovulation; Age; Demographic factors; Success rate

INTRODUCTION

Infertility is the inability to contribute to conception within 12 months of regular unprotected vaginal intercourse. Epidemiological data shows the prevalence to be 8-32%.[1,2] Causes can be divided into female, male, unexplained infertility. Female factors include ovulation disorder, tubal disease, endometriosis and all together accounts for 40 percent of total infertility. Male factors account for 30% and unexplained infertility 10%.[3] Rest of them includes both male and female factors. A combination of controlled ovarian hyperstimulation or COH and intrauterine insemination or IUI remains an important option available to an infertility specialist and it is a widely used treatment modality for a broad range of indications. Common indications are cervical factor, anovulation, mild male factor, mild endometriosis, and unexplained infertility. These common conditions are well prevalent in the society and bear the bulk of the infertility cases both primary and secondary, especially with the changing socioeconomic characteristics in the society; the cases like anovulation due to PCOS and male factor infertility are on rise. In this regard IUI is a very simple, cost effective procedure but with limited success rate compared to IVF.

The reported pregnancy rates per cycle ranges from 8-22%.[3] Commonly clomiphene is used as the drug of choice for ovulation induction, but recently letrozol is

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gaining more prominence and is on the verge of replacing clomiphene as the first line drug of choice for ovulation induction. Gonadotrophin is usually used in resistant cases and requires more vigilant monitoring of follicular growth. After ovulation induction the processed semen from either husband or donor is put into the uterine cavity through cervix via an insemination cannula. Several prognostic factors with regard to IUI outcome have been identified. It includes factors like patient profile, duration of infertility, type of infertility, stimulation protocol, follicular response, endometrial thickness, timing of IUI, semen parameters like post wash count. IUI is a simple low cost procedure without any significant side effects. Also in unexplained infertility it is a first line cost effective approach in developing countries rather than going for ART.

AIMS AND OBJECTIVE

To assess the demographic factors responsible for favourable outcome after ovulation induction and IUI.

MATERIALS AND METHODS

It is a prospective cross-sectional study done between a period of March 2018 to July 2019 in ESIC, Joka, Department of Gynecology and Department of Pathology. A total of 67 couples was identified through OPD andtotal 90 cycles of IUI were done in a period aforementioned. The study was pre-approved by the ethical committee of ESIC, Joka.

The inclusion criteria included females with unexplained infertility, endometriosis with at least one patent tube and only peritoneal spots <5 mm depth found in laparoscopy (Mild endometriosis) and anovulation diagnosed by ultrasonography and mild male factor infertility (sperm count 5-15 million/ml).

Exclusion criteria were women with bilateral tubal block as seen by HSG followed by Diagnostic laparoscopy and Hysteroscopy, severe endometriosis (Endometriosis with bilateral tubal block or bilateral ovarian involvement), unexplained genital bleeding and pregnancy contraindicated due to various medical comorbidities like severe cardiac diseases. Also males with Severe male factor infertility (sperm count <5 million/ml) andPostwash sperm count <5 million/ml were not included in the study.

Infertile couples were selected as per inclusion and exclusion criteria from OPD after taking their informed consent.A detailed history of both the partners were taken followed by general physical examination, differenthormonal tests like LH, FSH, Insulin, Thyroid function, Prolactin were carried out. Baseline antral follicle count, Follicular growth were monitored inunstimulated cycles to assess ovulation. BMI of the female patients were noted down and classified according to WHO [Normal= 18.5-24.9, Overweight = 25-29.9, Obesity gr 1= 30-34.9, Underweight= <18.5]. BMI of the males are also categorized in a similar fashion.

Once timed induction or hyperstimulation was decided the womenwere subjected to undergo Controlled ovarian hyperstimulation by eitherclomiphene citrate or purified FSH/HMG or letrozole in titrating doses from day 2 of menstrual cycle.After the hyperstimulation the patients were monitored by transvaginal sonography for follicular development from day 10 of menstrual cycle onwards. If one or more follicle size reaches more than 18 sq mm and endometrial thickness reaches more than 7 mm and if there are no features of ovarian hyperstimulation syndrome (abdominal swelling, pain, vomiting, ascites) then the patient will be triggered with HCG injection 5000 U or 10000 U through intramuscular route for triggering the ovulation. The male partner was asked to attend within 36-42 hours after trigger for supplying the semen sample which was then processed by density gradient method.

The semen sample was obtained by masturbation after 72 hours of abstinence. At first a prewash count was taken with the help of neubers chamber and microscope. The media was preheated to 37ºC in a thermal bath for 2 hours before the procedure starts. Then 1 ml of 90% (v/v) media was taken in a conical tube (Falcon tube) with a sterile pipette. It was gently overlaid with 1 ml of 45% (v/v) gradient media. The whole semen was then placed on top of two layers. It was centrifuged at 1500 rpm for 15 minutes. The supernatant was discarded leaving the pellet with as little of media as possible. In another test tube 5 ml of sperm wash media was taken and the pellet was transferred via pipette. It was then centrifuged at 1500 rpm for 10 minutes. The supernatant was discarded and pellet with 0.5-1 ml solution was prepared. A small amount of (0.2 micro liter) of this sample was put under microscope with Neubers chamber. Under 10X focal length the number of motile sperms were counted in the middle counting chamber of neubers chamber and if the post wash count was more than 5 million/ ml then the sample was taken for further steps. The final processed sample was used for insemination through insemination cannula. Urine pregnancy testwas done after 14 days and a transabdominal ultrasound was done after 6 weeks. Positive urine pregnancy test and ultrasonic evidence of pregnancy were taken as successful outcome. The

participant's demographic parameters were analyzed. All the expenses were carried out by Department of Obstetrics and Gynecology, ESIC Joka. IUI set with insemination cannula supplied by Krischo Medical products Pvt Limited, Bangalore, Karnataka.

The statistical analysis was done by using p value (<0.05) which will be statistically significant with 95% confidence interval. Data were entered in Microsoft Excel Sheet. Descriptive analysis by calculating percentages, confidence interval, mean with SD. Median and range. Appropriate statistical test was applied as per the need of study.

RESULTS

Total 90 IUI were done and out of 90 IUI 8 were successful. Total 67 couples underwent IUI and out of them 29 couple had 1 cycle of IUI, 23 couples had 2 cycles of IUI and 15 couple had 3 cycles. Common demographic factors we studied were age, duration of infertility, type of infertility, BMI of wife and causes of infertility. p value< 0.05 were taken as statistically significant. Success rate were observed to be 20% below 25 years of age and 15.6% between 25-35 years [Table 1]. Similarly it is 13.33% for infertility duration less than 5 years and 13.63% for duration between 5-10 years [Table 2]. The study also indicates that success rate is similar in both primary and secondary infertility [11.53% vs 13.33%] [Table 3]. It also shows in normal BMI [18.5-24.99] that of overweight BMI [25-29.99] successful conception occurs in 12.5% an 15% of cases respectively. [Table 4]. Finally the study also demonstrates that anovulation has highest success rate (16.6%) followed by unexplained infertility (13.3%).[Table 5].

DISCUSSION

In this study above 35 years of age the success rate of IUI falls steeply to 4% which is statistically significant. The success rate is 15.62% between 25-35 years of age and goes up to 20% below 25 years of age (Table 1).

Among the patient parameters female age is important as oocyte quality declines with increasing age. Success rate improves if the age is < 35 years which is statistically significant. Age > 35 years has a negative impact on success of IUI. It is probably due to a combination of progressive follicular depletion, decline in granulosa cell function, poor oocyte quality, reduced endometrial receptivity and higher rate of chromosomal abnormality. The rate is comparable to the result of study conducted elsewhere.[4] Another study also observed that IUI success rate steeply reduces as age increases specially after 40 years. Similarly, one study reported 15.3% success rate for age < 25 years which corroborates with our finding of 20% and gradually deteriorating with age.[5]

Duration of infertility is directly related to the success of IUI. In this study success rate is 13.46% for couples having infertility for less than 10 years whereas success rate downs by half to 6.67% in couples having infertility for more than 10 years (Table 2).Moreover, the success rate is similar between 5-10 years and less than 5 years. Though the results are in accordance with the fact that success rate reduces as the duration of infertility increases but the two other similar studies suggested that success rate reduces if duration is more than 5 years and further reduces after 10 years of infertility.[6] Also the success rate in other studies found out to be 15.1% in duration less than 5 years which corroborates with our findings of 13.33% but it slightly increases in 5-10 years as 13.63%.[7]

Table 1: Age wise success rate (pregnancy)

Age (years)	Success rate	Percentage (%)	P value
<25	2/10	20	0.005
25-35	5/32	15.62	0.005
>35	1/25	4.00	0.006

Table 2: Infertility duration wise success rate

Duration of infertility (years)	Success rate	Percentage (%)	p value
> 5 years	4/30	13.33	0.01
5-10 years	3/22	13.63	0.01
>10 years	1/15	6.67	0.5

*IUI success rate doubles if duration of infertility is less than 10 years which is statistically significant

Table 3: Infertility type wise success rate

Type of infertility	Success rate	Percentage (%)	P value
Primary	6/52	11.53	0.18
Secondary	2/15	13.33	0.2

Table 4: Success rate by BMI of wife

BMI of wife	Success rate	Percentage (%)	P value
Normal	5/40	12.5	0.4
Overweight	3/20	15	0.6
Obesity gr1	0/3	0	0.00
Underweight	0/4	0	0.00

Table 5: Success rate of IUI by causes of infertility (n=67 patients)

Causes	Success rate	Percentage (%)	P value
Anovulation	4/24	16.66	0.02
Mild male factor	2/23	8.7	0.1
Unexplained	2/15	13.33	0.03
Mild endometriosis	0/5	00	0.00

*Among the causes anovulation has highest success rate (16.6%) followed by unexplained infertility (13.3%). Both of these findings are statistically significant.

This study demonstrates that success rate is similar in both primary and secondary infertility [11.53% vs 13.33%] (Table 3). The difference is not statistically significant. The result corresponds to findings of previous other studies.[6,8] They did not find any statistically significant difference in the success rate by type of infertility in their study.

The study shows that success rate in normal BMI [18.5-24.99] is 12.5% and that of overweight BMI [25-29.99] is 15% but obesity grade 1 and underweight patients have poor success rate (Table 4). The findings are statistically not significant. However in another study it was also demonstrated that success rate in overweight female increases possibly because obesity is associated with PCOS, one of the commonest cause of anovulation leading to poor oocyte quality and oocyte depletion but also the findings suggest that anovulation is more commonly detected and treated and therefore success rate improves.[7] Similar study conducted in 2018 found the success rate in normal BMI to be 15.1 % which is similar to our finding of 12.5% but rate falls with increase in BMI in that study.[7,9,10]

Common causes which are included in this study are anovulation, mild male factor infertility, unexplained infertility, mild endometriosis. The success rate for anovulation is 16.66% and for unexplained infertility is 13.33% but the success rate drops down to 8.7% in mild male factor (Table 5). Therefore, IUI is more successful when the cause in anovulation and unexplained infertility and this result is statistically significant.It also corroborates with a previous study which showed success rate for unexplained infertility to be 15%.[11,12]

Limitations

Sample size was small due to limited resources and limited time. Also due to the timeframe of one year all the 67 couples could not complete the entire 3 cycles of IUI. Furthermore 6 cycles of IUI would have given more success rate.

CONCLUSION

Success rate of IUI improves in the demographic scenario of female age less than 35 years, less than 10 years of infertility, normal and overweight BMI and in cases of anovulation and unexplained infertility. There is no relationship between success rate of IUI and types of infertility such as primary or secondary infertility. However further studies are required with larger sample size to validate the findings of this study.

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Author's Contribution:
AS- Design of the study, Preparation of first draft, Manuscript preparation; **RR-** Concept of the study, Review of literature, Critical revision of manuscript; **JRC-** Concept and contribution of overall study; **BSD-** Statistical analysis and interpretation, review of literature.

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