ORIGINAL ARTICLE

Predictive Factors Affecting Success of Intrauterine Insemination

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ABSTRACT

Aim: To determine the predictive factors for pregnancy after intrauterine insemination.
Design: Prospective observational study.
Setting: Shalamar Hospital, Lahore
Methods: 55 patients undergoing 70 cycles of stimulated IUI between June 2010 and Dec 2016.The primary outcome measures were clinical pregnancy and live birth rate. Predictive factors which were evaluated included, female age, duration of infertility, BMI, number of days of stimulation as well as etiology of infertility.
Results: Over all clinical pregnancy and live birth rate were 11.43% and 8.5% respectively. Among the factors evaluated female age, duration of infertility and days of stimulation significantly influenced the pregnancy rates.
Conclusion: Our result indicate that COH/IUI is not affective treatment at female age of 35 or above and when duration of infertility is >5 years. Gonadotropin use with CC improves pregnancy rate.
Keywords: Intrauterine insemination, preovulatory follicles, stimulation

INTRODUCTION

Intrauterine insemination is frequently used in the treatment of infertile couples with various causes of infertility including cervical factor, ovulatory dysfunction, endometriosis, immunological causes, male factor and unexplained infertility. It is also a mode of treatment for various ejaculatory and coital problems. IUI is generally considered to be an intermediate step of low to moderate complexity before application of more sophisticated assisted reproductive technologies (ART) such as IVF with or without ICSI[1].

The pregnancy rate reported in literature is quite variable ranging from 8-22%. The cumulative Pregnancy rate varies according to indications, use of ovarian stimulation, drugs, age of female patient, and duration of infertility[2].

A recent retrospective report of 2473 cycles identified unexplained infertility and an ovulation as favorable factors to predict the likelihood of pregnancy as compared with other etiological factors[3].

Predictive sperm parameters for successful IUI have been controversial. Several semen parameters have been shown to correlate with IUI such as post wash motility, morphology and total motile fraction. (TMF)[4].

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The objective of present study was to asses significance of prognostic factors including woman`s age, gravidity, duration of infertility, diagnosis, use of ovulation induction and sperm parameters for predicting the outcome of clinical pregnancy.

MATERIAL AND METHODS

This study was carried out and at Shalamar hospital Lahore from 1st June 2015 till 31st Dec 2016.It is a prospective observation study of those couples attending Shalamar hospital outdoor for therapeutic IUI. Indications were unexplained infertility after 3 years of marriage, mild sperm dysfunction, and anovulation, husband abroad and visiting for shorter period of time. Inclusion criteria also included age between 18-40 years,BMI< 30kg/m^2,normal uterine cavity and patent tubes proven by HSG or laparoscopy. Blocked tubes, stage II-IV endometriosis and severe male with TMF post wash of <1 millionwere excluded. Mild male factor was assigned according to WHO criteria 2010, where sperm count <15 million/ml and motility (G_1+G_2)< 40% and morphology 4% is taken as mild male factor, post processed motile sperms for insemination should be between 5 to 10 million/ml and morphology ≥4% according to Kruger's criteria[5] If motile sperm count >20 million and sample not viscous swim up technique can be used, in all other cases of

oligospermia, presence of pus-cells, immature cells, round cells, the density gradient method is used.

Unexplained infertility is defined as when all standard fertility tests of couple including semen analysis, tubal status and ovulatory cycles are normal.

Minimal Endometriosis: score 1-5; mild endometriosis: score 6-15 by revised AFS criteria.For ovulation induction clomiphene citrate or Aromataseinhibitor were used in dosage of 50mg-100mg and 2.5mg-5mgrespectively for 5 days, depending upon response and on cycle day 10 of stimulation ultrasonography was performed, If required, injectable gonadotropin HMG was added until 1-2 follicles of 18-19mm achieved and endometrium of >6mm was present. If follicles were ≥3 of 16mm IUI was cancelled. Triggering of ovulation was done with 5000 iu of human chronic gonadotropin when follicles was of 18-19mm and couple was instructed to refrain from intercourse and was called in hospital for semen preparation and insemination carried out 36 hours after trigger was given.

Patient was advised bed rest for 10 minutes and to have intercourse on the same day. Luteal support was provided by natural micronized pessary (cyclogest 400mg)at bedtime for 14^{th} days and to have serum Bhcg carried out 15^{th} days after. Clinical pregnancy was defined as presence of intrauterine gestational sac confirmed by ultrasound.

Statistical Methods: Continuous variables are expressed as mean and standard deviation and categorical variables are presented as percentages. SPSS version 16 was applied. P value <0.05 was taken as significant.

RESULTS

In this study 63 patients who fulfilled the inclusion criteria for IUI were enrolled. Among them 3 patients were cancelled due to failure to achieve desired follicular induction and 3 had ≥3 preovulatory follicles. In 2 couples, procedure was not carried out as male partner failed to produce semen on the day, one had sperm count of <1 million/ml in post wash sample. So total 55 patients were inducted and they underwent 70 cycles during the period of June 2010 till Dec 2016.

Table 1 depicts the various parameters affecting of pregnancy rates in IUI, relating etiology and ovulation induction. As regards etiological factors, anovulation was more frequent 41% followed by unexplained infertility and male factor 28.4% and 21.3% each respectively. While endometriosis was present in 14.2% of cycles.

Pregnancy rates were 14% after ovulation induction and 10% in unexplained infertility. Only 3.6% male conceived with post wash semen fraction between <10million and while 12% and 13.3% conceived if post wash semen fraction was < 20 and <50 million/ml respectively.11.1% (5/45) patients conceived when preovulatory follicles were one and 12% (3/25) conceived when 2 follicles were inducted.

Endometrial thickness of >6mm is conducive to pregnancy, There were 11.8% pregnancies as compared to 2.9% when endometrium was >6mm.Primary infertility was identified in 45 patients and secondary infertility in 10 patients.

Table 1: Factors related to ovulation Induction an Etiology

Parameters	Pregnancy/ Cycle	%age pregnancy
Infertility etiology		
Annovulation	5/35	14%
Male factor	1/15	6.7%
Endometriosis	0/10	0%
Unexplained	2/20	10%
Total motile fraction million/m		
5-10	1/15	3.6%
10-20	3/25	12%
720-50	4/30	13.3%
Number of preovulatory follicles		
1	5/45	11.1%
2	3/25	8%
Enometril thickness		
<6mm	2/70	2.9%
>6mm	8/68	11.8%
Type of infertility		
Primary	7/45	15.6%
Secondary	1/10	10%

Table 2 depicts basic characteristics of study population affecting the success of IUI. The patients who achieved pregnancy had 29.5±4.7 mean age as compared to unsuccessful one`s with mean age of 34± 5.4. P value (0.03) which is significantly higher.

Mean BMI was 28.5± 1.6 and 29.2±1.2 in each group respectively which is not significantly different. Successful group had duration of infertility <5 yrs. as compared to unsuccessful group of 6.9±2.5 which was significant. P value (0.01). Number of days of stimulation had significantly higher impact on

success. P value (.000) when stimulation was done for 7.5± 1.2.

Table 3 overall pregnancy rate per cycle was 11.43% (8/70) of these 8.5% (6/70) were live births while one resulted in miscarriage and one ended as ectopic pregnancy. There was no multiple pregnancy.

Table 2: Factors related to basic characteristic in Study populate

Parameters	Pregnancy		P value
	Yes	No	
Age (yrs)	29.5±4.7	34±5.4	0.03
BMI Kg/m^2	28.5±1.6	29.2±1.2	0.14
Duration of infertility (yrs)	4.4±1.9	6.9±2.5	0.01
Days of stimulation	7.5±1,2	5.1±1.2	0.000

P<.05 Significant

Table 3: Pregnancy outcome of intrauterine insemination

Parameters	Outcome/ cycle	%age Pregnancy
Pregnancy/Cycle	8/70	11.43%
Line birth rate	6/70	8.5%
Miscarriage	1/8	0.13%
Ectopic pregnancy	1/8	0.13%
Multiple pregnancy	Nil	Nil

DISCUSSION

In our study, we tried to determine the predictive factors that would affect the success of IUI. The variables that affected were patient's parameters such as age, duration of infertility, weight of patient and cause of infertility and parameters which were related to ovulation induction included number of dominant follicles, endometrial thickness, number of days of stimulation. It also recorded the influence of total motile fraction (TMF).

Among patients parameters female age emerged as significant factor. It is a well-documented factor that affects the oocyte quality, even more effective methods of treatment such as IVF cannot overcome this negative impact of age[6]. In our study patients younger than 30 years were able to achieve significantly higher P (<0.03) pregnancy rate as compared to those of 35 years or above. Other studies have also quoted low pregnancy rate when age is 35 or above.[7] So woman over 35 should consider other options instead of IUI and in women 40 or above, it is a poor treatment choice.

Another important parameter that emerged as predictor of success is duration of infertility. Pregnancy rates were significantly high P (<0.01) when duration of infertility was less than 5 years as compared to 7-8 years. An earlier study also reached the same conclusion that with shorter history of infertility the conception rate is significantly higher[8].

BMI in both groups did not reach statistical difference. Success rate were significantly higher (P <0.000) when clomiphene citrate for five day was combined with gonadotropins for 2-3 days so increasing the days of stimulation to >7 days compared to 5 days stimulation with CC only. Especially in male subfertility,fecundity is only raised when gonadotropins are used for COH[9].

Another study by (Guzick et al)[10] reported pregnancy rate close to 12% in gonadotropin stimulated area of study.All the clinical pregnancies recorded in our study were single and no case of hyper stimulation was recorded. In 68.28% of cycle's monofolliculararesponse was observed and 35.7% of cycles there were two preovulatory follicles.

Although clinical pregnancy rate with monofollicular stimulation is low as the studies have suggested, an enhancement of results if mean number of follicles is 2.1±1.1[10]. But risk of premature LH surge increases when two or more follicles are recruited and this result indesynchronization in endometrial receptivity. This has resulted in use of GnRH antagonist in controlled ovarian hyperstimulation for IUI when more than on follicle is present with improved results in Clinical pregnancy rate[12].

Among the parameters as factors affecting the cycles, success rate was higher in anovulatory and unexplained infertility patient 14% and 10% in each respectively as compared to endometriosis and male factor infertility. In our study 14.2% of cycles there was minimal to mild endometriosis and none of patient was able to conceive. The same result have documented in ametaanalysis where pregnancy rate was reduced to half in endometriosis[13].

Total motile fraction (TMF) is important factor affecting the success. Pregnancy rate was higher 12.0% and 13.30% when TMF was above 10 million/ml. But results were disappointing when count was less than 10 million 3.6%. In our study none of patients had TMF <5 million/ml. Authors have tried to reach a lower limit of TMF at which IUI can be considered as a treatment choice in male factor. A TMF < 1 million is associated with poor pregnancy rates[14]. In couples with TMF <5 million, counselling regarding the option of

IVF/ICSI should be discussed. There was trend toward higher pregnancy rate 11.8% compared to 2.9% when endometrial thickness was >6mm.

No difference was noted in achieving clinical pregnancy with type of infertility 15.6% couples in primary and 10% in secondary infertility were successful.

We obtained pregnancy rate of 11.43% (8/70) and live birth rate/cycle of 8.5%. There were no multiple pregnancies;one of theneonate hadcongenital adrenal hyperplasia. The cumulative pregnancy rate are quite variable for COH/IUI, it varies with indication 10-20% cycle is an acceptable range for all etiologies[15].

CONCLUSION

The purpose if our study was to determine the predictive factors affecting the success of IUI. In this study 3 parameters age, duration of infertility <5 years and addition of gonadotropins to CC or aromatase inhibitors thus increasing days of stimulation to >7 days emerged as significant factors. A large study would help to identify more prognostic factors. Although IUI is simple and relatively noninvasive method, knowledge about prognostic factors affecting the success will help couple to decide whether to opt for IUI with not very encouraging results or directly go for IVF to save time and effort.

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