Factors Affecting the Success Rate of Intrauterine Insemination in the Treatment of Subfertility Following Controlled Ovarian Hyperstimulation

Rabia Imran, Shehla Baqai*, Asifa Siraj**, Sumaira Khan***, Uzma Urooj****, Sadaf Zohra*****

Department of Obstetrics & Gynecology, Combined Military Hospital, Muzaffarabad/National University of Medical Sciences (NUMS) Pakistan, *Department of Obstetrics & Gynecology, Combined Military Hospital, Lahore/National University of Medical Sciences (NUMS) Pakistan, **Department of Obstetrics & Gynecology, Pak-Emirates Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, ***Department of Obstetrics & Gynecology, Combined Military Hospital, Mardan/National University of Medical Sciences (NUMS) Pakistan, ****Department of Obstetrics & Gynecology, Pakistan Naval Ship, Hafeez Hospital, Islamabad Pakistan, *****Department of Obstetrics & Gynecology, Combined Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

Objectives: To determine the success rate of Intrauterine Insemination following Controlled Ovarian Hyperstimulation in patients with subfertility and to determine the frequency of prognostic factors affecting the success rate of this treatment modality.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Obstetrics & Gynecology, Pak-Emirates Military Hospital, Rawalpindi Pakistan, from Feb to Aug 2019.

Methodology: A total number of 135 sub-fertile patients, aged 18 to 40 years, with a duration of subfertility > 2 years, were included in the study. Couples with bilateral tubal blockade, smoking, combined male and female factor infertility and previous ovarian surgery were excluded. Controlled ovarian hyperstimulation was done with Clomiphene Citrate for five days, followed by ovulation triggered by recombinant human chorionic gonadotropin (HCG) and standard insemination with a prepared sample of the husband's semen after 36 hours.

Results: Success of the procedure was seen in 23(17.04%) patients, while the remaining 112(82.96%) were unsuccessful. The mean age was 29.20±4.90 years. Of 135 patients, 83(61.48%) had primary subfertility, and 52(38.52%) had secondary subfertility. The mean duration of subfertility was 5.60±3.35 years. The mean basal FSH was 5.76±2.54 IU/l. The mean number of IUI cycles was 1.39±0.49.

Conclusion: This study concluded that the success rate of intrauterine insemination following controlled ovarian hyperstimulation in the treatment of subfertility was 17.04%, and the duration and type of subfertility, aetiology of subfertility, basal Follicle-stimulating hormone levels and the number of Intrauterine insemination cycles are the prognostic factors affecting the success of the procedure.

Keywords: Controlled ovarian hyperstimulation, Intrauterine insemination, Subfertility.

INTRODUCTION

Subfertility is the inability of a couple to reproduce. According to Ahmed HM, the prevalence of subfertility in Pakistan is 22%, with 4% categorized as primary subfertility and 18% classified as secondary subfertility.[1] revealing that more than one-fifth of the married population is sub-fertile in Pakistan.[2] Artificial insemination can be used to treat various causes of subfertility. In IUI treatment, the processed semen is directly introduced into the uterus.[3] This procedure can be performed with or without COH. Unexplained subfertility, cervical hostility, mild endometriosis, anti-sperm antibodies and male sexual dysfunctions like impotence, hypospadias, and retrograde ejaculation are some of the indications for IUI.[4,5]

It is natural for the couple to want to know their chances of success in advance. Therefore, identifying the factors which directly affect the outcome of COH/IUI is highly crucial.[6] The patient's age is considered the single most significant factor contributing to the quality and quantity of ovarian reserve. The basal Follicle-Stimulating Hormone (FSH) levels are most frequently tested for ovarian screening.[7,8] One study found that FSH may not predict ovarian response or pregnancy in unexplained subfertile couples treated with IUI. However, PRs did decrease when FSH concentration was more than 7IU/l (p=0.28).[9]

Our study aims to determine the success rate of COH+IUI treatment modality and evaluate the prognostic factors affecting the success of IUI like duration and type of subfertility, aetiology of

Correspondence: Dr Rabia Imran, Department of Obs & Gynecology, Combined Military Hospital, Muzaffarabad, Pakistan

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subfertility, basal FSH levels and the number of IUI cycles. The results of our study enable healthcare providers to counsel subfertile couples regarding their chances of conceiving according to different prognostic factors.

METHODOLOGY

This cross-sectional study was carried out from February to August 2019 at the Department of Gynecology and Obstetrics, Pak Emirates Military Hospital (PEMH) Rawalpindi. Permission had been sought from the Hospital Ethical Committee [A/28/Feb 2019] to conduct the study. The sample size was calculated using the WHO sample size calculator, taking anticipated population proportion 14.28%.[10]

Inclusion Criteria: Were all sub-fertile patients undergoing IUI with a duration of subfertility>2 years and women aged 18-40 years.

Exclusion Criteria: We excluded patients with bilateral Tubal Blockade, Previous Ovarian surgery, Smoking, Combined male & female factor sub-fertility, Sperm count <5x10^6/ml, number of dominant follicles>5, Stage 3-4 endometriosis(moderate & severe), Intracavity lesion in the uterus (unicornuate/septate uterus) and basal FSH >12mIU/l.

A total of 135 sub-fertile couples were recruited in the study by non-Probability Consecutive Sampling. All infertile couples reporting to Out-Patient Department (OPD) Obstetrics and Gynecology, PEMH Rawalpindi undergoing IUI and meeting the inclusion criteria were recruited in the study.

Participants were counselled and explained the procedure in detail, and written informed consent was taken. All possible measures were taken to keep the identity of the participants confidential. Demographic data was collected as per the questionnaire. All the selected patients underwent a thorough workup including patient history, examination and investigations, including baseline investigations (Full Blood Count, Screening for Hepatitis B/C, Ultrasonography of Pelvis), Serum Hormonal Profile (Basal FSH=Day 3 FSH, LH, TSH, Prolactin and Day 21 serum progesterone), hysterosalpingography, and Husband Semen Analysis. Laparoscopy was done for pelvic adhesions /endometriosis.

COH was carried out by Clomiphene Citrate (CC) 50-100 mg orally for five days, starting from the third day of the menstrual cycle. Follicular tracking was done by Transvaginal ultrasound (TVS) on alternate days from the 9th to the 13th day of the menstrual cycle. When one Follicle size ≥16mm in diameter was seen, Ovulation Trigger was given 250µg of recombinant HCG Intramuscular. Standard IUI using the husband's semen was done 36 hours after injecting intramuscular HCG. The husband's semen was prepared by standard Swim-up technique in the hospital laboratory. The procedure was carried out using a nasogastric tube. The tube was gently inserted into the uterine lumen, and one ml sperm suspension was infused near the fundus. The woman was placed in the supine position for 10-15 minutes after IUI. The patient was asked to avoid intercourse for the rest of the cycle to rule out any positive effects on the results. Oral Progesterone was prescribed daily to support pregnancy for 6-12 weeks. A maximum of 2 cycles of IUI were done. The outcome was monitored by serum β-HCG levels (two weeks after insemination) and Trans-Abdominal Ultrasonography (observation of intrauterine gestational sac and fetal cardiac activity at seven-plus weeks of gestation).

Statistical Package for Social Sciences (SPSS) version 23.0 was used for the data analysis. Frequency and percentages were calculated for categorical (qualitative) variables. Mean and Standard Deviation (SD) were calculated for numerical (Quantitative) variables like age. Chi-Square test was applied, and statistical significance was considered at $p \leq 0.05$.

RESULTS

A total of 135 subfertile patients underwent Intrauterine Insemination following controlled ovarian hyperstimulation (COH+IUI), and a successful outcome was seen in 23(17.04%) patients, while the remaining 112(82.96%) showed no success. The range of age in our study was from 18-40 years, with a mean age of 29.20±4.90 years. Therefore, most of the patients, 81 (60.0%), were between 18-30 years of age, as shown in Table-I. Out of 135 patients, 83(61.48%) had primary infertility, and 52(38.52%) had secondary infertility. The mean duration of subfertility was 5.60±3.35 years, Mean basal FSH level was 5.76±2.54 IU/l. Distribution of patients according to Age(years), Duration of subfertility(years), Basal FSH (IU/l), Number of IUI cycles, Socioeconomic status, Type of infertility, Etiology of infertility, Education level, Occupation is shown in Table-I. Success rate with respect to age groups, type of infertility, aetiology of infertility, duration of subfertility Basal FSH, number of IUI cycles, socioeconomic status, education standard, and occupation is shown in Table-II.

Table-I: Clinico-demographic Distribution of Patients (n=135)

Variables	n(%)	Mean±SD
Age (years)		
18-30 years	81(60)	29.20±4.90 years
31–40 years	54(40)	
Duration of Subfertility (years)		
2-5 years	76(56.30)	5.60±3.35 years
6-10 years	37(27.41)	
>10years	22(16.30)	
Basal FSH (IU/l)		
<4	38(28.15)	5.76±2.54 IU/l
4.1-8	66(48.89)	
8.1-12	31(22.96)	
Number of Intrauterine Insemination Cycles		
1	82(60.74)	
2	53(39.26)	
Socioeconomic Status		
Poor	33(24.44)	
Middle	45(33.33)	
Upper	57(42.22)	
Type of Infertility		
Primary	83(61.48)	
Secondary	52(38.52)	
Etiology of Infertility		
Unexplained	37(27.41%)	
Male factor	21(15.56%)	
Cervical Mucosal defect	23(17.04%)	
Polycystic ovarian syndrome	31(22.96%)	
Mild Endometriosis	13(9.63%)	
Hormonal defect	10(7.41%)	
Education Level		
Illiterate	18(13.33%)	
Primary	24(17.78%)	
Middle	21(15.56%)	
Matric	29(21.48%)	
Graduate	43(31.85%)	
Occupation		
House wife	55(40.74%)	
Office work	24(17.78%)	
Field work	37(27.41%)	
Other	19(14.07%)	

Table-II: Success Rate with Respect to Different Variables (n=135)

Variables	Success rate n(%)		p-value
	Yes	No	
Age (in years)			
18-30	19(23.46%)	62(76.54%)	0.015
31-40	04(7.41%)	50(92.59%)	
Type			
Primary	14(16.87%)	69(83.13%)	0.947
Secondary	09(17.31%)	43(82.69%)	
Etiology			
Unexplained	07(18.92%)	30(81.08%)	0.297
Male factor	02(6.45%)	29(93.55%)	
Cervical mucosal defect	05(21.74%)	18(78.26%)	
Polycystic ovarian syndrome	03(9.68%)	28(90.32%)	
Mild endometriosis	04(30.77%)	09(69.23%)	
Hormonal dysfunction	02(20.0%)	08(80.0%)	
Duration of Subfertility (years)			
2-5	16(21.05%)	60(78.95%)	0.357
6-10	04(10.81%)	33(89.19%)	
>10	03(13.64%)	19(86.36%)	
Basal FSH			
<4	06(15.79%)	32(84.21%)	0.333
4.1-8	14(21.21%)	52(78.79%)	
8.1-12	03(9.38%)	29(90.62%)	
Number of Intrauterine Insemination Cycles			
1	15(18.29%)	67(81.71%)	0.629
2	08(15.09%)	45(84.91%)	
Socioeconomic Status			
Poor	11(33.33%)	22(66.67%)	0.013
Middle	04(8.89%)	41(91.11%)	
Upper	08(14.04%)	49(85.96%)	
Education level			
Illiterate	02(11.11%)	16(88.89%)	0.563
Primary	02(8.33%)	22(91.67%)	
Middle	04(19.05%)	17(80.95%)	
Matric	05(17.24%)	24(82.76%)	
Graduate	10(23.26%)	33(76.74%)	
Occupation			
House wife	11(20.0%)	44(80.0%)	0.745
Office work	03(12.50%)	21(87.50%)	
Field work	05(13.51%)	32(86.49%)	
Other	04(21.05%)	15(78.95%)	

DISCUSSION

Intrauterine insemination is a frequently used and effective treatment modality for subfertility, but the outcome depends on patient and cycle-specific factors.[11] It is most effective for women with ovulatory dysfunction and unexplained infertility and least effective for women with tubal factor and stage III-IV endometriosis.[12,13] Therefore, patients with young age having anovulatory subfertility are ideal candidates, with a 39% success rate.[14]

The success rate of IUI in our patiebnts in treating subfertility with COH was seen in 23(17.04%) patients, while the remaining 112(82.96%) had shown no success, in contrast to a study done in Oman, where the success rate was reported to be 21.58%. Primary subfertility was observed in 58.149%, and secondary subfertility in 41.851%. Rate of succ-essful IUI in

primary subfertility was about 18.93%, while in secondary subfertility was 26%.[15]

A mean clinical PR of 7.23% in natural cycles compared to 10.32% was observed after treatment with gonadotropin stimulation and IUI. The cyclewise success rate was analyzed and found to be highest in the first cycle (14.6%), followed by the second cycle (14.0%) and third cycle (3.5%).[16] Many significant determinants of pregnancy after COH/IUI have been identified, including maternal age, aetiology, infertility duration, endometrial thickness and preovulatory follicle count.[17] In another study, 200 women underwent 541 IUI cycles, resulting in 65 pregnancies. The average rate of successful pregnancies was 12% per cycle and 33% per couple. Multiple pregnancies were seen in 7.6% of the patients. The significant prognostic factors for successful IUI were endometrial thickness >1mm, COH with clomiphene citrate plus recombinant FSH, day of insemination after 16th day, subfertility duration of <5 years and treatment with <5 cycles.[18]

In a retrospective analysis done to assess the prognostic factors of IUI success, 353 patients underwent 1038 cycles of IUI. Gonadotropin ovarian stimulation was applied, and vaginal Progesterone was given to support the luteal phase. IUI was done following ovulation induction with HCG, and a luteinizing hormone (LH) surge occurred in about 10% of the cycles. 14.7% of the cycles resulted in pregnancy, and 80% were ongoing pregnancies. Age strongly predicted success (38.5% in women under age 30 vs 12.5% in those over age 40).[19]

The limitation of our study was the use of soft catheters. The outcome is expected to improve with the use of IUI catheters. If used on properly selected candidates, IUI can be a successful, easy, and safe tool for treating subfertility. Many factors need to be considered when deciding about the choice of treatment, like the age of the patient, subfertility duration, ovarian function, aetiology of subfertility, semen characteristics, tubal status and other gynecologic or medical problems.

CONCLUSION

This study concluded that the success rate of IUI in the treatment of subfertility following COH is 17.04%, and duration and type of subfertility, aetiology of subfertility, basal FSH levels and the number of IUI cycles are the prognostic factors affecting the success of IUI. Therefore, we recommend that these particular factors be considered before IUI in the treatment of subfertility following COH to achieve the maximum number of pregnancies in infertile women.

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