



Successful Fertility Treatment by a Non-IVF Centre

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Abstract

Objectives: High infertility levels are of great concern in the Indian society and there has been a recent surge in the use of ART and other fertility procedures like IUI. Around 10% of young couples during their reproductive career seek fertility treatment. The etiology can be multi-fold-male factor, female factor, combined and unexplained. Ovulation induction with IUI/Timed intercourse is a therapeutic modality in these patients with varied causes of infertility. IVF is not a necessary and only modality of treating these patients. The main thrust of this study was to highlight that by doing basic procedures like treating RTIs, diagnostic & operative hystero-laparoscopy and ovulation induction with IUI/Timed Intercourse can achieve fertility in 50% of clientele. IVF is not mandatory in all cases of infertility.

Materials and Methods: This is a prospective study of 257 patients who visited the fertility clinic of a tertiary care hospital from Jan 2018 till June 2019. In all cases of Infertility, a detailed history taking followed by clinical examination was done. Investigations including USG for follicular study & HSG for tubal patency for female & Semen analysis for male partner were done. All women were subjected to Ovulation studies with timed intercourse for 3 to 6 cycles if basic male and female investigations were normal. However all cases of bilateral tubal blocks/endometriomas/structural abnormalities of uterus was straightaway subjected to hystero-laparoscopy. Dilatation and curettage were done to rule out tuberculosis in case of bilateral blocks and long standing infertility cases. Depending upon the cause, patients were subjected to further 3 cycles of ovulation induction and IUI. Patients with Male factor in the form of azoospermia/severe OATS and couples who didn't respond to 6 cycles of ovulation induction with IUI were referred to ART centres for further management.

Results: Total patients visiting fertility clinic were 257. Total patients conceived till June 2019 is 120 (48.6%). 74 (61.6%) patients conceived had primary infertility. 46 (38.4%) had secondary infertility. 116 patients had uterine pregnancies and 4 patients had ectopic pregnancies. Forty two patients conceived after OI+IUI & 62 patients conceived after OI+TI.

Conclusion: Basic infertility procedures like HSG, Diagnostic & operative Hystero-Laparoscopy, treating RTIs and ovulation induction with IUI/Timed intercourse can achieve fertility in 50% of the clientele.

Keywords: Infertility; Ovulation induction; Intra-uterine insemination

Introduction

The reproductive potential of humans is inferior compared to animals. Rising infertility levels are of great concern in Indian society and there has been a sharp rise in use of ART and other infertility procedures in recent past. WHO defines Infertility as [1] failure to conceive after 1 year of unprotected vaginal inter-course? Infertility in a couple who have never had a child is called primary infertility. Secondary infertility is defined as infertility in a couple who already had at least one pregnancy between them. The etiology of infertility is manifold in couples but at times couples present with unexplained causes."

According to WHO," Nearly 10% young couples during their reproductive career visit fertility clinics for seeking treatment (WHO, 1991). The issue of infertility has a lot of bearing on mental and social wellbeing of the couple. The mental make-up of infertile couples and seeking fertility treatment at times go well beyond the scope of reproductive impairment [2]. Nearly 10 million couples in India are infertile and the figures are ever increasing by 5% every 2 years [3]. According to WHO estimates the burden of primary infertility ranges from 3.9% and 16.8 % in Indian clientele [4].

Infertility is a social stigma in India. Couples are under lot of stress when not able to conceive and the tag of being labeled infertile further adds to the problem. The anxiety level among these

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infertile couples to conceive is too high. The female partner at times becomes very depressive due to constant family pressure. Seeking fertility treatment is a big issue in certain families and financial status of couples is crucial in deciding mode of treatment. Many couples resort to divorce as a permanent solution to this major crisis in their life.

The etiological factors responsible for infertility are manifold and vary from couple to couple. The magnitude of infertility ranges from 10% to 30% of total patients visiting for gynecological consultation [5]. Etiology is multi-factorial with Male factors contributing 25% to 30% of cases, female factors 30% to 35%, 30% due to combined factors and no obvious reasons in 15% of the clientele [6]. In the recent past marked changes in lifestyle and dietary habits with subsequent increase in obesity has lead to a dramatic increase in number of couples seeking fertility treatment.

“Intrauterine Insemination (IUI) is a commonly employed procedure in fertility clinics in couples and has proven beneficial in unexplained infertility, male factor infertility, and those with cervical factors. Compared to a natural cycle results have been better with ovulation induction combined with IUI in recent past” [7,8]. Performing IUIs regularly in subsequent cycles in a patient increases the success rate per cycle. The main use of IUI in our centre has been in cases with unexplained infertility and male factor infertility besides patients not responding to ovulation induction with timed intercourse for 3 cycles” [9]. Though IUI is the most common and routinely practiced insemination technique [10] but couples age, the infertility factor involved and protocol used for ovarian induction have a lot of bearing on the final outcome. Infections especially RTIs must be checked and treated in all couples prior to commencing with IUIs. RTIs are an important factor especially in cases of secondary infertility. These patients need to be adequately treated for infections especially Chlamydiae before starting any other infertility procedure. However, damaged and distorted fallopian tubes and moderate and severe endometriosis on laparoscopy are straightaway indications for IVF. The tag of being labeled infertile is psychologically traumatic to the couple. So, it is upto the gynecologist to steer the course of these patients smoothly across the traumatizing influence of this condition. It is a situation where one has to decide when to treat conservatively and when to treat aggressively.

Material and methods: This is a prospective study conducted in the Department of Obstetrics and Gynecology in a tertiary hospital of Armed Forces of India.

Inclusion criteria: All cases of Primary infertility & secondary infertility with no or 1 live issue who visited the gynecological out-patient department were randomly selected. A detailed history taking followed by examination and a particular set of investigations were done.

Exclusion criteria: All cases with absolute indications for IVF/ICSI like azoospermia, Grade IV Endometriosis, B/L Hydro-salpinges etc.

Method of Study

The couples attending the out-patient department of fertility clinic at our hospital were examined clinically after detailed history taking including examination of male partners. Couples whose examination was suggestive of RTIs/PID were given a course of antibiotics for both partners for 2 weeks as per the CDC guidelines

prior to starting infertility treatment. Hormonal profile including Thyroid along-with sugars and HSG for tubal patency was done for female partner and a Semen Analysis was done for the Male partner. If the baseline investigation were normal for both partners they were subjected to 3 to 6 cycles of Ovulation induction on Day 2 of cycle with IUI/Timed Intercourse depending upon case to case basis. Any patient with bilateral blocks on HSG, endometriomas or any structural uterine anomalies were subjected to Diagnostic hystero-laparoscopies and treated accordingly. Patients who didn't conceive after 6 cycles of ovulation induction with IUI/TI were also subjected to Diagnostic Hystero- laparoscopies to further delineate the cause of infertility. Patients with confirmed bilateral tubal blocks on laparoscopy with thickened tubes with segmental blocks suggestive of tuberculosis were given six months course of ATT as per standard regimen. Patients with mild to moderate oligo-asthenospermia were treated with antibiotics as per culture sensitivity, anti-oxidants and clomiphene for 3 months duration. Patients with azoospermia or severe OATS or unexplained infertility not responding to OI+IUI (6cycles) were referred to ART centres for further management. Proper counseling of the couples regarding the case and mode of treatment was done. Written and informed consent of couple was taken prior to performing IUI at our centre Total 100 IUI cycles were carried out between January 2018 to June 2019 at our hospital. In an IUI cycle, the female partner is advised to report on day 2/3 of her cycle for under-going a base line Trans-Vaginal Ultrasound Scan (TVS) to note the antral follicle count. Oral ovulation induction agents in the form of Tab. Clomiphene Citrate 50/100 mg per day or Tab. Letrozole 5 mg/day for 5 days is started from day 2 to 6 and/or Injectable gonadotrophins on day 3, 5 and 7 and then as per requirement of the particular patient. From Day 9 onwards patient is called on alternate day basis to note the serial follicular growth and endometrial thickness. Injection Human Chorionic Gonadotropin (HCG) 10000 IU IM/SC was used as a trigger agent for ovulation when dominant follicle diameter reaches the size of 18 mm to 20 mm depending on the method of stimulation and endometrial thickness is nearly 8 mm. After 36 h of HCG administration, USG was done to look for ovulation and if confirmed sonologically IUI was done. If USG does not reveal signs of ovulation repeat injection HCG 5000 IU was given and ovulation rechecked after 36 h prior to performing IUI. Male partner gives his semen sample in a sterile container 2 h prior to IUI. A pre-wash semen analysis was performed after semen liquefaction had taken place. Density gradient method is commonly employed in our lab to prepare the semen sample. Once the sample is ready and post-wash sample seen on microscope, female partner was made to lie in lithotomy position. After proper focusing of the external os & removing all cervical and vaginal secretions, IUI was done under proper aseptic precautions. Post IUI patient is made to lie for 15 min supine and later on started with Tablet Duphaston 10 mg BD daily as progesterone support in luteal phase. Total IUI cycles performed at our centre during the entire duration of study were 100. In case a patient misses her periods, urine for gravindex test was done. If positive, all conceptions were confirmed with ultra-sonography for intra- uterine gestation.

Observations and Results

In the present study, total 257 patients reported for infertility treatment at our centre. 155 cases were of primary infertility and 102 patients had secondary infertility. Total 120 patients had conceived out of 257 at our centre with various treatment modalities from January 2018 to June 2019. 27 patients have been referred to ART

Table 1: Infertility workload of our centre from Jan 2018 to June 2019.

Total patients reported	257
Primary infertility	155
Secondary infertility	102
Successfully conceived till date	120
Referred to ART Centre for IVF/ICSI	27
Lost to follow up	18
On-going treatment	92

Table 2: Age-wise distribution of cases for Number of patients (N=120).

Age group of patients with successful outcome	Number of patients with successful outcome
21-25 years	23(19.1%)
26-30 years	66(55%)
31-35 years	27(22.5%)
36-40 years	04(3.33%)

Table 3: Type of Infertility for Number of patients (N=120).

Type of Infertility with Successful Outcome	Number of Patients
Primary Infertility	74
Secondary Infertility	46

Table 4: Duration of Infertility for Number of patients (N=120).

Duration of Infertility	Number of patients
<2 years	29 (24.1%)
2-5 years	39 (32.5%)
5-10 years	48 (36.6%)
>10 years	04 (3.33%)

Table 5: Factors for Infertility.

Male factor	Female factor	Combined factor	Unexplained
27	43	30	20

centre for further treatment with IVF/ICSI. 18 patients were lost to follow-up likely due to change in work place. Out of 120 successfully conceived infertility cases 74 had primary infertility and 46 had secondary infertility. Remaining 92 patients are still undergoing infertility treatment at our centre at different stages of treatment as shown in Table 1. 75% of patients with successful outcome were below 30 years of age as shown in Table 2. A few patients (4) had conceived after 35 years of age.

Two-third of cases with successful outcome had primary infertility and rest secondary infertility as depicted in Table 3.

Most of the conceptions had history of infertility ranging from 2 to 10 years as depicted in Table 4. Few conceptions did occur in long standing infertility of more than 10 years.

Female factor was responsible for 35% of cases. Male factor contributed 22.5%, combined factors were there in 25% cases and no obvious reason was seen in 17.5% cases as shown in Table 5.

There were 10 couples who conceived only after 2 weeks of antibiotic treatment for RTIs/PID as shown in Table 5. Three patients had conception in the immediate next cycle following HSG as part of evaluation. Eight patients conceived following a 6 months course of ATT in view of bilateral tubal block and tubal morphology suggestive of tuberculosis on laparoscopy. Twenty two patients had male factor

Table 6: Infertility procedures Modality for Number of patients with positive outcome (N=78).

Infertility procedures Modality	No. of patients with positive outcome
Treatment for RTIs/PID	10
Post HSG	3
ATT	8
T/T for oligo-asthenospermia	22
LOD	5
Laparoscopic drainage of endometrioma	6
Myomectomy	1
Tubal Recanalisation	1
Hystero-laparoscopy	22

Table 7: Conception with different modalities of ovarian stimulation with IUI/TI.

Method	Number of patients
OI+IUI	42
OI+ Timed intercourse	78

Table 8: Fate of conceptions (N=120).

Type of pregnancy	No. of patients
Intra-uterine gestation	116
Ectopic gestation	4
Abortions	4
Successfully delivered till date	52
On-going uterine pregnancies	60

in form of mild to moderate oligo-asthenospermia. They were treated with antibiotics as per culture sensitivity along-with anti-oxidants and clomiphene for 3 months. Hystero-laparoscopy was performed in 22 patients for varied indications. 5 cases of severe PCOS with thickened ovaries were treated with LOD to change the hormonal milieu and improve ovulation along-with use of insulin-sensitizers like metformin and myo & chiro-inositols. Four cases of ovarian endometriomas were managed with Laparoscopic ovarian cystectomy followed by OI+IUI. Tubal re-canalization was performed in 1 case of secondary infertility following death of second child of the patient due to some illness. Myomectomy was performed in a nulligravida with large fundal fibroid as shown in Table 6. Forty two patients had conceived post OI+IUI and 78 patients had conceived following ovulation induction with timed intercourse as shown in Table 7.

Out of total 120 conceptions till date 116 were intra-uterine gestations. 4 patients had ectopic gestations which were managed laparoscopically and 4 had missed abortions managed by medical methods. 52 uterine pregnancies have been successfully delivered till date. Sixty patients with uterine pregnancies are sailing smoothly in the ante-natal period (Table 8).

Discussion

Conrad and Schneider (1980) have used the term medicalisation to denote the process by which a certain behavior comes to be understood as a question of health and illness, subject to the authority of medical institutions. One phenomenon which has become increasingly defined as a medical condition is infertility. Because infertility involves an inability to achieve a desired social role of becoming a parent, it is often associated with psychological distress. In U.S.A, around 10% of young couples seek fertility treatment at

one time or the other in their reproductive career. Worldwide the magnitude of infertility is to the tune of 8 to 12%. WHO estimates of 2002 indicate that 186 million couples are infertile. Infertility is such a distressing issue in certain societies and cultures that couples seek divorce as final and permanent end to their problem. The age of women has a lot of bearing on the prevalence of infertility. The impact of this factor on infertility is along-with physiological changes that occur in ovaries with ageing. The success rate of ART procedures goes down with increasing age. In our study also 75% of the successfully conceived clientele was below 30 years of age which further strengthens the above fact. The chances of successful conception markedly decrease after 35 years of age in women. Firstly delaying marriage because of career issues and subsequently delaying pregnancy due to professional requirements are leading contributors to this problem of infertility. A Twenty five percent (31) patient above age of 30 years who had conceived after infertility treatment in our study which is a significant fraction further supports the above statement. Out of 120 successful conceptions, 74 patients had primary infertility and 46 patients had secondary infertility. Nearly 60% patients had conceived with infertility of two to five years of duration. Forty percent successfully conceived patients had duration of infertility ranging from 6 to 10 years. Four patients with long standing infertility of more than 10 years duration had also conceived successfully in our study. Financial status of couples and orthodox beliefs in certain societies and lower educational status of couples may be responsible for delay in seeking proper medical help for the problem. Out of 120 successful conceptions, 43 had female factor infertility, 27 had male factor infertility, 30 had combined and 20 couples had unexplained infertility in our study. In case of male factor most patients had mild to moderate oligo-asthenospermia which was treated with antibiotics according to culture sensitivity along-with anti-oxidants and clomiphene for 3 months. So far as female factor is concerned, there were 5 cases of severe PCOS managed with LOD along-with insulin sensitizers like metformin & myo-chiro inositol. Four patients with endometriomas underwent laparoscopic cystectomy followed by OI+IUI. Eight patients were treated with ATT in view of long standing infertility and tubal morphology suggestive of tuberculosis on laparoscopy. The recent surge in incidence of both male and female infertility is mainly attributed to changes in life style and food habits. Increasing incidence of obesity and subsequently PCOS in females is one major factor contributing to an ovulation and subsequent infertility. More indulgence in addictions like smoking and alcohol in modern era have led to increasing incidence of OATS in males and subsequent infertility. In our study, out of 120 patients 78 had conceived after OI+TI. 42 couples had conceived post OI+IUI against total 100 cycles of IUI performed. Out of total 120 successful conceptions, 4 patients had ectopic pregnancies which were managed laparoscopically. Four patients had missed abortions in early pregnancy managed by medical methods. Fifty two patients have been delivered successfully till now and 60 on-going uterine pregnancies are progressing smoothly towards term at various periods of gestation. Thirty two (26.6%) patients were induced with Clomiphene Citrate, 41 (34.16%) with Letrozole and 47 (39.16%) patients were induced by oral Clomiphene/Letrozole combined with gonadotrophin. Success rates were better with combined Clomiphene/Letrozole+Gonadotrophins along-with IUI in our study. Out of 120 conceptions, 89 patients had age less than 30 years which justifies higher pregnancy rates in younger age group patients. Sixty percent conceptions were seen in couples with less than 5 years of infertility and remaining forty percent had long standing infertility

varying from 6 to 15 years of infertility. Pregnancy rates were better in male factor involvement and unexplained cases of infertility with IUI. If we offer combination methods (i.e. ovarian stimulation with IUI) in couples with unexplained infertility 11 compared to a natural cycle IUI or expectant management, success rate and live births are more. Some institutes recommend double IUI in cases of male factor infertility 24 h apart. However, no added advantage has been seen with it but it adds to the cost for the couple. A number of factors are instrumental in deciding the success rate of IUI like age of couple, ovulation induction agent used, duration & cause of infertility and husband's semen analysis. The sperm motility and their viability after 24-h are important predictors of IUI success. IUIs avoid the cervical and immunological factors by by-passing the cervix. Our study had a pregnancy rate of 30% per patient and 15% per cycle which is in comparison with study by Rojanasakul et al. [10]. With pregnancy rate 28% per patient and 8% per cycle [8] and better than study by a Campana et al. [11,12]. Where pregnancy rate per patient were 18.7%, and 5.6% per cycle. The cumulative pregnancy rates vary from 16% to 30% with 3 to 6 cycles of IUI. The above data justifies the use of IUI in treating infertility couples on case to case basis in our study.

The rising trend of infertility in the society needs to be viewed seriously as it affects social, mental or psychological well-being of a couple. The affected couple needs to be evaluated thoroughly and the etiological factor can be treated accordingly. However the literature stresses this point beyond doubt that success rates are better when we combine ovulation induction with IUI in cases of male factor & unexplained infertility.

Conclusion

The present study consists of successful fertility outcome in infertile couples without IVF facilities by a tertiary care centre. 120 couples out of total 257 patients which mount to nearly 50% of patients visiting fertility clinic had a successful outcome. It has been proved time and again that ovarian stimulation in controlled manner with intra-uterine insemination is more successful compared to other methods. The cost factor involved in setting up an IUI lab is far less compared to an IVF centre. More so, IUI being less invasive and with a shorter learning curve is advantageous over IVF. This study emphasizes the fact that every infertility patient does not warrant an IVF. By doing systematic work-up of infertility couples visiting our clinics and doing basic procedures like treating RTIs, diagnostic and operative hysteron-laparoscopies along-with COH+IUI/TI we can achieve fertility in 50% of the clientele.

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