

Original Article

Prognostic Value of Different Sperm Parameters on the Success of Intrauterine Insemination

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Abstract

Objective: To identify the sperm parameters which influence the success of an Intra uterine insemination (IUI) cycle.
Design: A retrospective study conducted at the Dept. of Reproductive Medicine, Chettinad Super Specialty hospital, Chennai.

Patients: Study includes 518 IUI cycles from April 2011 to December 2013.

Methodology: Ovarian stimulation was done with clomiphene citrate alone or in combination with gonadotrophins, depending on the patient's response. In majority of the patients HCG was administered as a trigger. Semen samples were analyzed according to WHO 2010 standards and processed by either direct swim up, pellet with swim up or density gradient methods, according to the nature of the sample.

Results: The overall pregnancy rate was 13.5%. When all the 3 sperm parameters (concentration, motility, morphology) were taken into consideration, variable sperm concentrations did not have a significant impact on the pregnancy rate when it was above 1mil/ml. There was no statistically significant difference in the pregnancy rates among the two motility groups (<32% and ≥32% pre-wash progressive motility) but normal sperm morphology (≥4%, WHO 2010 criteria) showed high prognostic value (p 0.024).

Key Words: Sperm parameters, IUI, Prognostic value, Success rate

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Introduction

Artificial insemination dates back to early 1900's when neat semen was injected into the reproductive tract of a female in order to achieve a pregnancy¹. Now with advancements in the field of reproductive medicine, artificial insemination has taken a more refined name of intra uterine insemination (IUI) involving preparation of semen sample and ovarian stimulation.

IUI is a simple, relatively less-invasive and less-expensive mode of Assisted Reproduction technology (ART) treatment given before advancing towards more complex and expensive procedures like In vitro fertilization (IVF) or Intra cytoplasmic sperm injection (ICSI). It is widely used to treat couples with different etiologies including coital problems, anovulation, idiopathic and also mild to moderate male factor issues². However, the pregnancy rates, across the world differ with each variable in an IUI cycle. This could be because most studies while not only being retrospective, also have different study groups, varied stimulation protocols, the number of inseminations, method of semen processing etc³.

There are multiple factors which influence the outcome of an IUI viz., age of the patient, duration and type of infertility and stimulation protocols² and patients' follicular response and of course, the sperm

parameters. There have been multiple studies stating sperm morphology, motility and total motile sperm count (TMSC) are of predictive value in an IUI cycle²⁻⁵. However, it still remains unproven as to which among all the sperm parameters is the most essential for pregnancy, making it difficult to define the "ideal sperm quality". Therefore, to restrict patients for IUI treatment based on their semen quality seems unjustified.

This retrospective study aims to evaluate the different sperm parameters and their prognostic value in an IUI cycle.

Materials and methods

This retrospective study was conducted at the Dept. of Reproductive Medicine, Chettinad Hospital & Research Institute, Chennai. The study included 518 infertile couples posted for IUI treatment from April 2011 to December 2013. The general characteristics of the patients are described in Table 1 and the prewash sperm parameters in Table 2.

Ovarian stimulation was done with clomiphene citrate alone or along with FSH or HMG, the duration and dosage depending on the patients' response. For clomiphene citrate-stimulated cycles, 50-100 mg clomiphene citrate was given on days 2-6 and when

combined with FSH/HMG the gonadotrophins were administered at 75-150 IU either on alternate days or daily. Transvaginal ultrasound scan was done to determine the number of follicles, mean follicular diameter and thickness of the endometrium. When at least one or two follicles measured 17 mm or more and endometrial thickness of >8mm, 5000 IU hCG injection was administered as trigger 40h after which IUI was done. For patients with multiple follicles GnRH analogue was given as trigger.

Table 1: Demographic pattern

General Parameters	Median
Age of Husband(yrs)	34
Age of wife(yrs)	29.5
Duration of Infertility(yrs)	4.75
Endometrial thickness(mm)	9.65

Table 2: Pre-wash sperm parameters

Sperm parameters	Median
Sperm concentration (mil/ml)	49.5
Progressive motility(%)	34.5
Morphology(%)	11

Table 3: Indications for infertility

Indications	Distribution (%)	Pregnancy (%)
Anovulation	37.6	16.4
Anovulation+ single patent tube	1.2	0
Single patent tube	5.6	13.8
Endometriosis	1.9	0
Congenital Uterine anomalies	1.4	0
Male factor	8.3	14
Combined causes (male and female)	2.3	0
Unexplained	41.7	13

Semen processing: On the day of IUI, semen samples were subjected to analysis according to the WHO criteria, 2010⁶. The samples were then processed either by swim-up method or pellet with swim up method or discontinuous double density gradient techniques, depending on the nature of the sample. The media used for sperm processing were Quinn's advantage sperm washing media and Quinn's double density gradient media (40% & 80%). The swim up method and double density gradient method are as detailed in the WHO manual, 2010⁶.

Pellet with swim up method : The semen sample was mixed with equal amounts of sperm wash medium and centrifuged at 1500rpm for 10minutes. The supernatant was discarded and 0.5-0.7ml of media was overlaid on the pellet and the tube was inclined at an angle of about 45° and incubated for 30-45mins at 37 °C. The topmost 0.4ml was removed and sperm count and motility were assessed and used for insemination.

Urine pregnancy test was done 3 weeks after the IUI for diagnosis of pregnancy. A clinical pregnancy was defined as presence of foetal heart by ultrasound scan done two weeks after a positive urine test.

Results

A total of 518 cycles were studied retrospectively of which 73 resulted in pregnancies giving an overall pregnancy rate of 13.5%. The median age of the women, duration of infertility and endometrial thickness associated with pregnancy was 29.5, 4.75 and 9.65, respectively (Table 1). The indication for infertility (male and female causes) along with the associated pregnancy rates are as shown in Table 3. There was no statistically significant difference in pregnancy rates among different age groups of women under 40years and type of infertility. The 1st and 2nd IUI cycles yielded pregnancy rates of 13.6% and 14.2%, respectively. A maximum of 5 IUI cycles were performed totally, however, no pregnancies occurred after the 4th cycle.

The median sperm concentration observed on analysis of pre-wash sample was 49.5 with a progressive motility of 34.5 (Table 2). A summary of some of the clinical parameters and sperm parameters along with their associated pregnancy rates are presented in Tables 4 and 5.

The statistical calculations were done with the help of SPSS software. A p value of <0.05 was considered statistically significant(S) and any value greater than that (p >0.05) was considered as not significant(NS).

Discussion

Intra uterine insemination is a relatively simpler and less-expensive treatment for infertile couples (except severe male factor and bilateral tubal block) with the pregnancy rates around the world between 10-20%⁷. This is because of multiple variables involved in an IUI cycle which influence its outcome. In our study we attempted to determine the sperm variables predictive of IUI success.

In this study, it was seen that there were no significant difference in the pregnancy rates among different age groups of women under 40years, type of infertility, duration of infertility (until 12years), number of cycles (1-4cycles) or the endometrial thickness b(7-13mm). This is in concurrence with studies done by Brzechffa et al,1998 and Goverde et al, 2000^{8,9}.

While IVF/ICSI is the preferred mode of treatment for severe male factor infertility, IUI has been proven as a treatment modality for mild to moderate male subfertility² with good female factors. The three main sperm parameters are sperm concentration, motility and morphology, along with it were considered post wash total motile sperm concentration (TMSC – volume of inseminate x sperm concentration x motility) and method of processing.

In the pre-wash parameters, the initial sperm concentration in the native semen sample is not frequently cited in literature as an influential factor in

an IUI cycle³. In a study by Dorjpurev et al, it was seen that the initial sperm concentration of >20 or <20 mil/ml did not make a difference to the pregnancy rates¹⁰. Also, a study by Zadehmodarres in 2009, studied 350 cycles showing no difference among initial sperm concentration and pregnancy rate¹¹. In our study too, there was no statistical difference in the pregnancy rates among different groups of sperm concentration unless the concentration was less than 1mil/ml.

Table 4: Few clinical parameters and associated pregnancy rates

Clinical Parameters	Pregnancy in percentage (%)	p value
Type of infertility: Primary infertility Secondary infertility	12.7 16.4	0.35
No. of cycles : I II III IV V	13.6 14.2 8.5 21.4 0	0.86 0.33 0.41 1.00
Endometrial Thickness (mm): <7 7.1-9.0 9.1-11.0 11.1-13.0 >13	3.7 14.6 14.5 9.8 18.2	0.14 0.15 0.34 0.17

Significant $p < 0.05$; Not significant $p > 0.05$

Table 5: Sperm parameters and associated pregnancy rates

Sperm Parameters	Pregnancy in percentage (%)	p value
Pre-wash Sperm concentration (mil/ml): $\leq 1-5$ 6-10 11-15 >15	5 2.9 5.3 15.6	0.22 0.07 0.10
Pre-wash Progressive motility (%): <32 >32	11 14.6	0.26
Morphology (%): ≤ 3 >3	3.5 14.2	0.02
Post wash count(mil/ml): <5 >5	15.2 13.1	0.59
Method of processing: Density gradient Direct swim-up Pellet & swim-up	12.5 14.7 11	0.55 0.61

Significant $p < 0.05$; Not significant $p > 0.05$

Studies by Lee et al, 2002, Yalti et al, 2004 and Dorjpurev et al 2011, have observed better pregnancy rates when total motility was $>30\%$,^{10,12,13}. In the study by Dorjpurev, 1773 cycles were studied in which it was observed that the pregnancy rate per cycle (9.3%) improved significantly when the motility was $>30\%$ ($p = 0.001$)¹⁰. This was contrary to our findings wherein motility as an independent factor had no positive influence on the treatment outcome.

A number of studies have shown that of all the sperm parameters, sperm morphology is the positive predictor in an IUI cycle^{3,4,5,10}. The study by Nikhbakht et al, took a sperm morphology threshold value as 5% above which they observed higher pregnancy rates⁵. A systematic review by Ombelet in 2013 cited sufficient evidence stating that sperm morphology of $>4\%$ is a significant predictor of an IUI outcome³. Similar findings were noticed in our study wherein morphology as an independent variable had a statistically significant prognostic value ($p=0.024$) in an IUI cycle, in comparison to sperm concentration and motility. Significantly higher pregnancy rates were observed with morphology of $>3\%$.

In the post-wash sperm parameters, total motile sperm count (TMSC) is the most commonly cited predictor of an IUI outcome. In a study by Khalil et al., in 2001, that involved 2473 cycles, a TMSC of >5 mil/ml or <5 mil/ml gave pregnancy rates of 12.8% and 5.3%, respectively; it was stated that TMSC was one the best predictors for pregnancy in an IUI cycle¹⁴. Even a study conducted by Wainer et al, 2004 stated TMSC of >5 mil/ml being a predictor of pregnancy⁴. But in our study the pregnancy rates among both the groups were similar and therefore did not seem to have a significant positive influence as long as the total insemination count was >1 mil/ml; there were no pregnancies with post-wash concentration of <1 mil/ml.

So far, there have been no studies establishing the effectiveness of any one method of processing for an IUI treatment and therefore no consensus has been reached⁷. Boomsma et al in 2007 conducted a Cochrane database systematic review of the effectiveness of gradient, swim up and wash and centrifugation method. It was concluded that no specific technique could be recommended as sufficient evidence on clinical outcome was lacking¹⁵.

Conclusion

On evaluation of the sperm parameters, the pre-wash sperm concentration, progressive motility, the post-wash total motile sperm count and the method of processing the semen sample did not seem to influence the pregnancy rate significantly. However, the sperm morphology as an independent variable has shown to be a positive predictor of IUI success. It can be inferred that in cases of teratozoospermia ($\leq 3\%$), patients can be counseled for IVF/ICSI as IUI may not be an effective mode of treatment.

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