Original Article

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Relationship between sperm parameters and clinical outcomes of Intra Uterine Insemination (IUI)

Abstract

Background: Intrauterine insemination (IUI) is a widely utilized method for treating the infertile couples. The aim of the present study was to determine the pregnancy and abortion rates after IUI and to examine the relationship of sperm parameters with these rates.

Methods: This retrospective study was performed on 911 infertile couples undergoing IUI treatment in Shahid Akbarabadi IVF Centre from May 2017 to May 2019. To evaluate the correlation of sperm parameters with the clinical pregnancy and abortion rates, odds ratio (OR) with 95% confidence intervals (CI) was calculated.

Results: In this study, the pregnancy rate following IUI was 15.7% (143/911), and among women who achieved pregnancy, the abortion rate was 42.0% (60/143). According to the multiple logistic regression analysis, none of the sperm parameters was associated with the pregnancy rate. Couples with either male or female factor infertility etiologies were more likely to get pregnant than those with unexplained infertility. Regarding the abortion rate, multiple logistic regression analysis revealed that normal sperm count was related to a lower abortion rate (adjusted OR=0.25, 95% CI=0.07–0.91).

Conclusion: The present study did not reveal a significant relationship between none of the sperm parameters and pregnancy rate after IUI treatment. However, among women who got pregnant, continuation of the pregnancy was associated with the normal sperm count. Furthermore, analysis of all semen parameters together in comparison to one parameter alone might be more accurate to predict pregnancy or abortion. Further prospective cohort studies with a large number of couples are required.

Keywords: Intrauterine Insemination; Pregnancy; Abortion; Sperm Parameters; Infertility

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Infertility is the inability to establish a clinical pregnancy after 12 months of regular intercourse without contraception due to an impairment of male or female's capacity to reproduce (1). Intrauterine insemination (IUI) is one of the most commonly used treatment for infertility, and it is usually suitable for couples with mild male factor infertility, unexplained infertility, psychological sexual dysfunction, cervical factors and mild endometriosis (2, 3). In addition, this procedure is easier to perform and is less expensive as well as less invasive compared to other assisted reproductive techniques (ART) (2, 4, 5). The pregnancy rate after IUI has varied in some previous studies from about 10.0% to 20.0% (3-9). Many factors may influence the effectiveness of IUI outcomes including women's age, duration of infertility, number of follicles, etiology of infertility, ovarian stimulation, endometrial thickness as well as timing and frequency of insemination (4, 5, 10, 11).

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Literature reviews display conflicting results for value of one or two sperm parameters on IUI outcomes (2, 12, 13). There are different reports about the simultaneous predictive value of two parameters of sperm morphology and count on pregnancy outcomes of patients treated with IUI (2, 4, 13, 14). This study examined the value of semen parameters to predict pregnancy and abortion rates in a sample of infertile couples undergoing IUI treatment. The studied sperm parameters were sperm concentration, progressive motility and sperm morphology.

Methods

Ethical issues: All procedures performed in the current study were in accordance with the ethical standards of the Ethics Committee of Iran University of Medical Sciences (IR.IUMS.FMD.REC.1398.163).

Participants and study design: This retrospective study was performed on 911 infertile couples undergoing first IUI treatment at Shahid Akbarabadi Hospital in Tehran, Iran. The data were collected from May 2017 to May 2019. To be eligible for this study, the couples had to meet the following criteria: (a) experiencing male, female and unexplained infertility problem, (b) having female age<35 years, and (c) having mild semen factor defined as total sperm concentration of more than 10 million motile sperm per ejaculate (15). In addition, couples with severe male factor infertility were excluded from the present study.

Semen analysis and preparation: Semen analysis was performed in the andrology laboratory according to World Health Organization (WHO) 2010 criteria. Semen samples with a concentration of ≥ 15 million per milliliter, progressive motility of \geq 32% and normal morphology of \geq 4% were defined as normal parameters. Sperm number of \Box 15 million per milliliter, progressive motility \Box 32% and normal sperm morphology of \Box 4% were categorized as abnormal parameters. After liquefaction of semen sample following a maximum of 30-min incubation, the sample volume, viscosity, PH, sperm concentration, progressive motility and morphology were evaluated by manual analysis. In order to Diff-Quick stain, a thin semen smear was prepared on a clean slid, then the dried smear was stained using the manufacture's protocol (Dianzist Azma, Iran), and at least 200 spermatozoa were marked for each slide.

All samples were prepared by density-gradient centrifugation (DGC) method. Approximately one hour

before IUI, the sperms were prepared using two-layer density gradient technique (40%, 80%) (Sil-Select Plus, Belgium, FP18SIP06U, FP18SIP06L). Two milliliters of semen samples were added up to the two layers, and next were centrifuged at 300g for 15 minutes (min). The pellet was gently transferred into the clean tube and washed twice with fresh medium at 300g for 5 min. Then, 0.5 ml of fresh sperm washing medium (Sil-Select Plus, Belgium, FP18FL08) was added to the pellet and placed into incubator until insemination. The washed sample was injected intrauterine using insemination catheter.

Statistical analysis: In the current study, continuous variables were presented as mean \pm standard deviation (SD) and categorical variables as number (percentage). To evaluate the effect of demographic and clinical characteristics on the clinical pregnancy and abortion rates, logistic regression analyses were used to estimate crude odds ratios (OR) and adjusted odds ratios (OR Adj) with a 95% confidence interval (CI). Data analysis was carried out using IBM SPSS Statistics for Windows, Version 24.0 (IBM Corp., Armonk, NY, USA). All statistical tests were two-sided and level of significance was set at 0.05.

Results

Couples' characteristics: The demographic and clinical characteristics of the couples are outlined in table 1. The mean age of males and females was 34.37 ± 5.29 and 30.46 ± 4.77 years, respectively. The infertility reasons were as follows: male factor (44.8%), female factor (34.1%) and unexplained (21.1%). In total, 819 (89.9%), 202 (22.2%) and 350 (38.4) of 911 specimens had normal count, normal progressive motility and normal morphology, respectively. The distribution of specimens based on these indices is presented in table 2.

Pregnancy and abortion rates: The pregnancy rate was 15.7% (143/911) in the present study. Among women with clinical pregnancy, the abortion rate was 42.0% (60/143). These rates were also calculated in different categories of independent variables (see Tables 1 and 2).

Factors affecting pregnancy rate: As presented in table 3, the couples with either male factor or female factor infertility etiologies are more likely to get pregnant than those with unexplained infertility (OR=1.85, 95% CI=1.08–3.18, and OR=1.96; 95% CI=1.12–3.41, respectively). According to simple analysis, there was no relationship between the clinical pregnancy rate with total sperm count (OR=1.04; 95%

CI=0.57-1.90), progressive motility (OR=1.22; 95% CI=0.81-1.85) and sperm morphology (OR=1.15; 95% CI=0.80-1.66). The same results were also obtained in the multiple logistic regression analysis (i.e. adjusted analysis). Factors affecting abortion rate in women who get

pregnant: Both simple and multiple logistic regression

analyses revealed that among independent variables, only normal sperm count was associated with a lower abortion rate (OR=0.25, 95% CI=0.08–0.85 and OR_{Adj}=0.25, 95% CI=0.07–0.91, respectively). Other variables were not associated with the abortion rate in both simple and multiple logistic regression analyses (Table 4).

Table 1. Demographic/infertility	characteristics,	pregnancy	and	abortion	rates i	in the	infertile	couples	undergoing	g IUI
treatment										

	Total	Pregnancy rate	Abortion rate among pregnant women
	(n=911)	(n=143)	(n=60)
Female's age (years)			
<35	719 (78.9)	115 (16.0)	46 (40.0)
>35	192 (21.1)	28 (14.6)	14 (50.0)
Male's age (years)			
<35	532 (58.4)	91 (17.1)	34 (37.4)
>35	379 (41.6)	52 (13.7)	26 (50.0)
Cause of infertility			
Male factor	408 (44.8)	69 (16.9)	27 (39.1)
Female factor	311 (34.1)	55 (17.7)	25 (45.5)
Unexplained	192 (21.1)	19 (9.9)	8 (42.1)
Count			
Normal	819 (89.9)	129 (15.8)	50 (38.8)
Abnormal	92 (10.1)	14 (15.2)	10 (71.4)
Progressive motility			
Normal	202 (22.2)	36 (17.8)	15 (41.7)
Abnormal	709 (77.8)	107 (15.1)	45 (42.1)
Morphology			
Normal	350 (38.4)	59 (16.9)	21 (35.6)
Abnormal	561 (61.6)	84 (15.0)	39 (46.4)
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Values are presented as "n (%)"

Table 2. Pregnancy and	abortion rates in di	lifferent categories	of semen analysis in t	he infertile couples u	ndergoing IUI
treatment					

Count	Progressive motility	Morphology	Total (n=911)	Pregnancy rate (n=143)	Abortion rate among pregnant women (n=60)
Abnormal	Abnormal	Abnormal	84 (9.2)	14 (16.7)	10 (71.4)
Abnormal	Abnormal	Normal	4 (0.4)	0 (0)	0 (0)
Abnormal	Normal	Abnormal	3 (0.3)	0 (0)	0 (0)
Abnormal	Normal	Normal	1 (0.1)	0 (0)	0 (0)
Normal	Abnormal	Abnormal	381(41.8)	50 (13.1)	19 (38.0)
Normal	Abnormal	Normal	240(26.3)	43 (17.9)	16 (37.2)
Normal	Normal	Abnormal	93 (10.2)	20 (21.5)	10 (50.0)
Normal	Normal	Normal	105(11.5)	16 (15.2)	5 (31.2)

Simple logistic regi	ession	Multiple logistic regression		
OR Crude (95% CI)	Р	OR Adj (95% CI)	Р	
0.97 (0.94 - 1.01)	0.160	0.98 (0.94 - 1.04)	0.549	
0.98 (0.94 - 1.01)	0.168	0.99 (0.94 - 1.03)	0.599	
1.85 (1.08 - 3.18)	0.025	1.94 (1.12 - 3.36)	0.018	
1.96 (1.12 - 3.41)	0.018	1.98 (1.13 - 3.47)	0.017	
1 (Ref)		1 (Ref)		
1.04 (0.57 - 1.90)	0.894	1.04 (0.55 - 1.94)	0.912	
1 (Ref)		1 (Ref)		
1.22 (0.81 - 1.85)	0.347	1.27 (0.83-1.95)	0.275	
1 (Ref)		1 (Ref)		
1.15 (0.80 - 1.66)	0.447	1.16 (0.79 - 1.69)	0.449	
1 (Ref)		1 (Ref)		
	OR Crude (95% CI) 0.97 (0.94 - 1.01) 0.98 (0.94 - 1.01) 1.85 (1.08 - 3.18) 1.96 (1.12 - 3.41) 1 (Ref) 1.04 (0.57 - 1.90) 1 (Ref) 1.22 (0.81 - 1.85) 1 (Ref) 1.15 (0.80 - 1.66)	$\begin{array}{c} 0.97\ (0.94\ -\ 1.01) \\ 0.98\ (0.94\ -\ 1.01) \\ 0.160 \\ 0.168 \\ \end{array}$ $\begin{array}{c} 1.85\ (1.08\ -\ 3.18) \\ 1.96\ (1.12\ -\ 3.41) \\ 1\ (Ref) \\ \end{array}$ $\begin{array}{c} 0.025 \\ 0.018 \\ 0.018 \\ 1\ (Ref) \\ \end{array}$ $\begin{array}{c} 1.04\ (0.57\ -\ 1.90) \\ 1\ (Ref) \\ \end{array}$ $\begin{array}{c} 0.894 \\ 1\ (Ref) \\ \end{array}$ $\begin{array}{c} 0.347 \\ 1\ (Ref) \\ \end{array}$ $\begin{array}{c} 0.347 \\ 1\ (Ref) \\ \end{array}$	OR crude (95% CI)POR Adj (95% CI) $0.97 (0.94 - 1.01)$ 0.160 $0.98 (0.94 - 1.04)$ $0.98 (0.94 - 1.01)$ 0.168 $0.99 (0.94 - 1.03)$ $1.85 (1.08 - 3.18)$ 0.025 $1.94 (1.12 - 3.36)$ $1.96 (1.12 - 3.41)$ 0.018 $1.98 (1.13 - 3.47)$ $1 (Ref)$ $1.04 (0.57 - 1.90)$ 0.894 $1.04 (0.57 - 1.90)$ 0.894 $1.04 (0.55 - 1.94)$ $1 (Ref)$ $1.22 (0.81 - 1.85)$ 0.347 $1.22 (0.81 - 1.85)$ 0.347 $1.27 (0.83 - 1.95)$ $1 (Ref)$ $1.15 (0.80 - 1.66)$ 0.447	

Table 3. Simple and multiple logistic regression analyses of demographic and clinical factors predicting IUI pregnancy rate (n=911)

OR: Odds Ratio, CI: Confidence Interval, Ref: Reference Group.

Table 4. Simple and multiple logistic regression analyses of demographic and clinical factors predicting IUI abortion rate among women with clinical pregnancy (n=143).

	Simple logistic reg	ression	Multiple logistic regression			
	OR Crude (95% CI)	Р	OR Adj (95% CI)	Р		
Female's age (years)	1.01 (0.95-1.09)	0.714	0.99 (0.90-1.09)	0.785		
Male's age (years)	1.02 (0.95-1.09)	0.609	1.03 (0.94-1.13)	0.563		
Cause of infertility						
Male factor	0.88 (0.32-2.48)	0.815	0.67 (0.23-1.97)	0.465		
Female factor	1.15 (0.40-3.29)	0.800	0.98 (0.33-2.93)	0.975		
Unexplained	1 (Ref)		1 (Ref)			
Count						
Normal	0.25 (0.08-0.85)	0.026	0.25 (0.07-0.91)	0.036		
Abnormal	1 (Ref)		1 (Ref)			
Progressive motility						
Normal	0.98 (0.46-2.12)	0.967	1.20 (0.55-2.66)	0.645		
Abnormal	1 (Ref)		1 (Ref)			
Morphology						
Normal	0.64 (0.32-1.26)	0.197	0.78 (0.38-1.62)	0.509		
Abnormal	1 (Ref)		1 (Ref)			

OR: Odds Ratio, CI: Confidence Interval, Ref: Reference Group.

Discussion

In this retrospective study, the relationship between the sperm parameters with pregnancy and abortion rates was evaluated in the infertile couples undergoing IUI treatment. In the present study, the pregnancy rate was 15.7%, which is in

consistent with the reported results of most previous studies (e.g., 15.8% (7), 15.7% (16), 15.1% (17) and 14.5% (8)) and inconsistent with (slightly higher) the results of some other studies (e.g., 9.4% (18), 9.9% (19), 11.0% (20), 12.0% (21), 12.6% (22)). These differences may be due to the different population characteristics and study design. Women's age has

been found to be negatively correlated to the pregnancy rate in most previous studies (6, 22-27), whereas not in all ones (19, 28-30). In the ongoing study, the age of women was also correlated with a depletion in pregnancy rate, which was not statistically significant. Couples with unexplained infertility were less likely to get pregnant than other couples. Therefore, it seems that unexplained couples are not suitable cases for IUI treatment and another treatment option should be considered.

As shown in table 1, among normal sperm parameters of semen samples used for IUI in the current study, the couples with the normal sperm concentration are the most and couples with the normal progressive motility are the least. Moreover, in accordance with the results of table 2, the number of samples in the categories with abnormal sperm count is very low; it may be assumed that progressive motility and sperm morphology are the function of sperm concentration.

Both simple and multiple analyses introduced that sperm count alone had no effect on the pregnancy rate of IUI. A similar result was also obtained for progressive motility. According to our results, there was no statistically significant difference in the pregnancy rate after IUI between the couples with normal and abnormal morphology. This finding is the same as the results of the studies performed by Deveneau et al. (4) and Karabinus et al. (31) who have suggested that sperm morphology is not a strict predictor of IUI success. However, several studies have found a strong association between sperm morphology and IUI outcomes (19, 27, 32). These conflicting results might be due to the small sample sizes, study design, population characteristics, different criteria for grading of sperm parameters and inherent fluctuations in the semen parameters.

Regarding abortion rate, among study variables, only normal sperm count was associated with a significant lower abortion rate, which might indicate the importance of sperm concentration in the selection of appropriate cases for IUI treatment. Additionally, as illustrated in table 2, no much difference in the pregnancy rate is found among the groups with all normal sperm parameters and all abnormal sperm parameters (15.2 % vs. 16.7 %), however; the abortion rate is higher in group with all abnormal sperm parameters than in that with all normal sperm parameters (71.4 % vs. 31.2 %). The current study revealed that couples with normal sperm morphology and concentration had a higher pregnancy rate and lower abortion rate than other couples after IUI. Importantly, according to the abortion rate in the categorized groups, it was found that IUI was inappropriate to be performed for couples with normal sperm concentration and abnormal morphology, whether with normal progressive motility or not, because of high abortion rate in such categories. In this manner, Lemmens and also Butcher in their studies showed that normal sperm morphology and normal inseminated progressively motile sperm count had the highest IUI outcome (27, 32).

It is worth noting that a better selection of couples who benefit most from IUI should be based on all three sperm parameters (count, morphology and motility). None of the sperm parameters alone was a sufficient predictive factor for pregnancy and abortion after IUI (4, 27, 31, 33, 34).

The present study had various limitations that should be considered while expanding the results. First, this study was performed only in one center in Tehran; thus, the generalizability of the findings may be limited. Second, for analysis on pregnancy and abortion rate, the sample size (143 couples) was relatively small. Further studies, particularly large-scale population-based prospective cohort studies, are required to demonstrate the complex associations between sperm quality and IUI outcomes. On the other hand, data mining analysis is also suggested to determine the predictors of IUI results.

In summary, the ongoing study did not reveal any significant impact of sperm parameters on the pregnancy rate after IUI. However, in women who were pregnant, normal sperm count was correlated to depletion in the abortion rate. In addition, it seems that in IUI patients, analysis of all semen parameters together than one parameter alone may be more predictive and accurate to achieve pregnancy or abortion. More multi-center prospective cohort studies with large number of couples are needed to provide a more precise assessment of the relationship between sperm parameters and IUI outcomes.

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Conflict of interest: The authors declare that they have no conflict of interest.

Authors' contribution

Z Zandieh: project development and management, manuscript editing. F Mohammadi: data collection and management, manuscript editing. Z Zolfaghari: data analysis. S Ghasemi: data collection. Z Mehdinia: manuscript writing and data analysis. FS Amjadi: manuscript editing and project development. M Ashrafi: project development.

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