The role of semen parameters in pregnancy of women having intrauterine insemination

Nilgun Turhan[1], Muzeyyen Uyanık[2], Aydin Kosus[3], Nermin Kosus[3], Aslıhan Pekel[4], Ergun Uyanık[5]
[1]Bayındır Hospital, Obs&Gyn, İstanbul, [2]Medicana Hospital, Obs&Gyn, Bursa, [3]Self Employed, Obs&Gyn, Ankara,
[4]Medical Park Hospital, Embriology, Ankara, [5]Bursa Yuksek Ihtisas Training and Research Hospital, Obs&Gyn, Bursa, Turkey

Abstract

Aim: To research the role of semen parameters in the likelihood of pregnancy of the couples with unexplained infertility who underwent intrauterine insemination. Material and Method: 545 cycles of IUI performed in our clinic due to unexplained infertility were included in the study. The IUI cycles were divided into two groups according to whether they achieved pregnancy: Group 1 pregnancy (77 cycles) and Group 2 non-pregnancy (468 cycles). Sperm parameters were statistically evaluated before and after the sperm washing. ROC (Receiver Operating Characteristic) analysis was performed to identify the effective cut-off values to predict pregnancy. P<0.05 was considered significant. Results: Morphology was observed to be statistically higher in the pregnant group than in the non-pregnant group before and after sperm washing (p=0.033 and p=0.028, respectively). No statistically significant difference was observed in any other parameters (p>0.05). As a result of the pre-wash ROC analysis of sperm parameters, only morphology was found to be significant for the pregnancy to be predicted (p=0.029). When different cut-off values were analyzed in terms of morphology, the highest cut-off value in sensitivity and specificity was found to be 4.5. As a result of post-wash ROC analysis, it was detected that morphology, +4 and +3 values of sperm motility had statistically significant effects on the detection of pregnancy (p=0.029, p=0.020, and p=0.043, respectively). Other parameters were not observed to have any significant effects for the prediction of pregnancy (p>0.05). A cut-off value of 2.5 for post-wash morphology was found to have 92.9% sensitivity and 75.5% specificity. Discussion: Pre- and post-wash morphology may affect the result of pregnancy by IUI in unexplained infertility. The cut-off values of morphology may predict the likelihood of pregnancy and this could allow advanced treatments to start sooner.

Keywords

Unexplained Infertility; Semen Parameters; Morphology; Pregnancy

DOI: 10.4328/JCAM.5778 Received: 20.02.2018 Accepted: 27.03.2018 Published Online: 28.03.2018 Printed: 01.09.2018 J Clin Anal Med 2018;9(5): 407-10
Corresponding Author: Muzeyyen Uyanık, Department of Obs&Gyn. Medicana Hospital, Bursa, Turkey.
E-Mail: drmuzeyyenuyanik@gmail.com
ORCID ID: 0000-0002-2032-178X

Introduction

No causal agent can be detected in approximately 10-20% of infertile couples, who are then diagnosed with unexplained infertility. The Intrauterine Insemination method (IUI) is often preferred as it is easier, less expensive, and less invasive than other assisted reproductive techniques (ART) [1]. It is rather difficult to predict the results of pregnancy with sperm parameters. However, it is important for the patients' psychology and finances to accurately predict those who are unlikely to achieve pregnancy with IUI. Sperm count and motility, sperm morphology, and the methods of sperm preparation during IUI are important parameters that can affect the rate of pregnancy with IUI. It is observed in several studies that predictive values of sperm parameters in the course of IUI show differences between various centers. We also aimed to retrospectively examine the cycles of IUI applied in our clinic and to identify the differences between the cases of pregnancy and non-pregnancy in terms of sperm parameters.

Material and Method

The retrospective study included a total of 545 cycles of IUI (500 couples with the diagnosis of unexplained infertility) in the ART center of the Faculty of Medicine, Turgut Ozal University. Ethics committee approval was received for this study. The 545 cycles of IUI were divided into two groups: Group 1 pregnancy (77 cycles) and Group 2 non-pregnancy (468 cycles). All the couples involved in the study had failed to get pregnant for a minimum of one year. Males were evaluated by physical examination, at least two sperm analyses [2], and a detailed history. All the couples were screened for hepatitis B and C, syphilis, and HIV. Patients who had pelvic infection, untreated endometriosis, or who did have bilateral tubal ligation, hepatititis B and C, syphilis, HIV were not included in the study. Starting on the third day of the cycle, ovulation induction in the IUI cycles hMG (human menopausal gonadotropin)/ recombinant Follicule Stimulating Hormone (FSH) was used. Ovarian response was monitored with TVUSG. Ovulation was triggered with 5000–10000 IU urinary or 0.25μg recombinant Human Chorionic Gonadotropin (hCG) when at least one follicle reached 18mm. The IUI was performed with a catheter (Gynetics 4219 Emtrac Plus, Gynetic Medical Products N.V., Hamont-Achel, Belgium) 36 hours after hCG injection. Serum BhCG levels were tested to confirm pregnancy two weeks after the hCG injection. Sperm samples were analyzed for concentration and motility with a Makler counting chamber using World Health Organization (WHO) guidelines. Morphology was assessed by Kruger strict criteria. Two layer density gradient technique [3] (45%-90%) was used for sperm preparation. 1 ml of 90% gradient was placed at the bottom of the tube and 1 ml of 45% gradient was placed upon this. This was incubated at 37 C for 30 minutes before adding the semen. It was centrifuged at 300 g for ten minutes. The upper part was discarded. The pellet at the bottom was placed into a falcon tube and 3 ml of sperm washing solution was added and centrifuged at 300 g for ten minutes. After the upper portion was removed, the remaining part was resuspended with 0.5 ml fresh HTF sperm washing solution. The concentration and motility were evaluated after preparation. The Statistical Package Program for the Social Sciences (SPSS 16.0; SPSS Inc., Chicago, IL, USA) was used for statistical analysis. To check whether the data was normally distributed, Shapiro-Wilk test was performed. Median (minimum-maximum) was used to show continuous data. Mann-Whitney test was used to compare independent groups. Logistic regression analysis was used to examine the effects of sperm parameters on the prediction of pregnancy. ROC analysis was performed to find the most effective cut-off values to detect pregnancy. P<0.05 was considered significant.

Results

Not a single difference was identified between pregnant and non-pregnant groups in terms of the parameters (p>0.05) in the Table-1. Morphology was observed to be significantly higher in the pregnant group than the non-pregnant group before and after the washing (p=0.033 and p=0.028, respectively).

Table 1. Distribution of the parameters of patients undergoing IUI according to groups

	Pregnant	Non pregnant	P
Women age	29(21- 43)	29(18- 44)	0.358
Men age	32(23- 49)	31(21- 55)	0.940
Duration of infertility	2(1-15)	2(0.5- 16)	0.077
Dose of Gonadotropin	50(50- 475)	75(25- 500)	0.513
Total dose	250(250- 5550)	450(125- 4500)	0.381
Duration of induction	5(5- 15)	5(3- 22)	0.345
Dominant follicle count	1(1- 4)	1(1- 6)	0.917
Endometrial thickness	8(3.3- 14.7)	8.4(3- 21.5)	0.338

The distribution of pre- and post-wash values of spermiogram parameters according to groups is summarized in Table-2. After the ROC analysis was performed with pre-wash sperm parameters, morphology was observed to be the only significant measure to predict pregnancy (p= 0.029). While morphology itself could predict 58.6% of the pregnant patients, other parameters were reported to have no significant value (p>0.05) [Table-3]. When various cut-off values were examined in terms of morphology, the cut-off value with the highest sensitiv-

Table 2. The division of semen parameters into groups according to pregnancy and non pregnancy

	Pregnant	Not pregnant	P
Pre wash(1)			
volume1	2(0.5- 6)	2(0.4- 7)	0.615
count1	50(13- 290)	43(10- 320)	0.091
totalmotility1	51(21- 96)	55(11- 92)	0.371
+4 motility1	8(0- 46)	9(0- 45)	0.788
+3 motility1	31(10–57)	33(1–71)	0.221
+2 motility1	10(4–30)	10(2–37)	0.428
+1motility1	49(4–80)	45(1–89)	0.356
Morphology1	5(1–15)	4(0–18)	0.033
Post wash(2)			
volume2	0.3(0.2–0.3)	0.3(0.2–0.3)	0.074
count2	44.5(10–80)	32(3.5–100)	0.565
+4 motility2	60(30–80)	46(0–80)	0.286
+3 motility2	40(20–70)	47(20–100)	0.592
morphology2	6.5(2–14)	4(1–11)	0.028

P< 0.05 was considered significant.

Table 3. The results of ROC analysis of semen parameters before washing(1)

				95% CI	
	Area	SE	P	Upper	Lower
Volume 1	0.450	0.043	0.206	0.367	0.533
Count 1	0.564	0.042	0.106	0.482	0.645
Total motility1	0.447	0.041	0.177	0.366	0.527
+4 motility 1	0.471	0.039	0.461	0.394	0.547
+3 motility 1	0.456	0.039	0.270	0.380	0.532
+2 motility 1	0.505	0.041	0.891	0.425	0.586
+1 motility 1	0.561	0.041	0.123	0.480	0.642
Morphology1	0.586	0.040	0.029	0.508	0.665

P< 0.05 was considered significant. AUC: Area under the curve. SE: Standart error CI: Confidence interval

ity and specificity was 4.5. It had a sensitivity of 55.6% and specificity of 63.1%. ROC analysis of post-wash morphology showed that morphology, +4 and +3 rates of sperm motility had statistically significant effects on the occurrence of pregnancy (p=0.029, p=0.020, and p=0.043, respectively). It was observed that morphology itself could detect 68.4%, +4 sperm rate 69.6% and +3 sperm rate 33.0% of pregnant cases. Other parameters were not observed to have any significant impacts on pregnancy (p>0.05) [Table-4]. A cut-off value of 2.5 for post-wash morphology had sensitivity of 92.9% and specificity of 78.5%. As for +4 motile sperm rate, cut-off value at the highest sensitivity and specificity was identified to be 49.5 (sensitivity 85.7%, specificity 53.2%). Pre- and post-wash morphology was identified to be the most effective sperm parameter for the detection of pregnancy. It was observed that each unit increase in pre-wash morphology increases the likelihood of pregnancy by a factor of 1.086 and in post-wash morphology by a factor of 1.313. It was also detected that each unit decrease in post-wash volume decreases the likelihood of pregnancy by 100.0%. Other factors were not observed to have any significant impact on the occurrence of pregnancy (p=0.05).

Table 4. sensitivity and specificity values in various cut-off values of prewash(1) sperm morphology

	Cut off	Sensitivity	Specificity
Morphology 1	0.5000	1.000	0.011
	1.5000	0.905	0.134
	2.5000	0.746	0.341
	3.5000	0.603	0.463
	4.5000	0.556	0.631
	5.5000	0.365	0.781
	6.5000	0.317	0.821
	7.5000	0.238	0.864
	8.5000	0.190	0.901
	9.5000	0.111	0.912
	10.5000	0.095	0.926
	11.5000	0.048	0.940
	12.5000	0.016	0.957
	13.5000	0.016	0.963
	14.5000	0.016	0.977
	16.0000	0.000	0.991
	17.5000	0.000	0.994
	19.0000	0.000	1.000

Discussion

IUI is a non-invasive method that should be preferred first for the couples who have been diagnosed with unexplained infertility because it is a less expensive way of treatment [1]. Ovarian stimulation, along with IUI, was reported to be an effective way of treatment for the couples with unexplained infertility by the Royal College of Obstetricians and Gynecologists (RCOG) in 1998 [4]. There are some other factors that effect the likelihood of success in pregnancy with this method of treatment. Especially, various semen parameters have been shown to correlate with IUI outcome, such as count of motile sperm and normal morphology. The evaluation of post-wash semen parameters can give helpful prognostic information [5]. Most of the studies that report the success rate of pregnancy in IUI cases where sperm morphology is evaluated have been performed retrospectively. The effects of semen parameters on the success rate of pregnancy of infertile couples were also retrospectively analyzed in our study, and morphology was observed to be the most effective semen parameter to predict pregnancy. In a meta-analysis performed by Waart et al. [6], 18 original articles that studied the effects of sperm morphology in IUI cycles on pregnancy rates were analyzed and 6 of them were stastistically evaluated. In these 6 studies the Tygerberg, WHO criteria were used and it was concluded that better pregnancy rates could be achieved with sperm morphology that is 4% or higher in IUI cycles. French et al. [7] argued that sperm morphology had a prognostic value for the patients undergoing ICSI, however low it was. Guzick et al. [8] compared the impact of sperm morphology and sperm count and motility on the success rates of pregnancy in their study.They detected that those with 4% and higher sperm morphology had better success rates in pregnancy. Hauser et al. [9] and Lee et al. [10] pointed out that sperm morphology monitored by using strict criteria in IUI cycles had a prognostic value to determine the success rate of pregnancy. By revealing the fact that pregnancy rate decreases from 40.7% to 24% if the teratospermia rate is higher than 70%, Merviel et al. [11] detected in their study of 1038 (IUI) cycles that morphology has a prognostic value. They pointed out that they preferred ICSI method for the cases with teratospermia due to this fact. Similarly, Burr et al. [12] also found that the rate of pregnancy falls from 18.2% to 4.3% when teratospermia is 90%. By detecting the fact that the success rate of pregnancy decreases when normal sperm morphology is <30% or motile sperm count is < 5x106 and the patient is a woman over 35, Badawy et al. [5] pointed out in their study, which involved 714 IUI cycles and analyzed the effects of sperm count and morphology on the success of IUI, that morphology and motility are important. While these studies support our findings, Deveneau et al. [13] argued in their retrospective study comprising 856 IUI cycles that sperm morphology lower than 4% was not related to low pregnancy rates of the patients undergoing IUI, and morphology could not be the only parameter to determine use of IVF method. Similarly, Krabinus and Gelety [14] did not identify any difference in the pregnancy rates even when the samples of morphology that were 4% or 30% worse than 4% were evaluated in their study of 538 IUI cycles. Sun et al. [15] examined the correlation of sperm morphology and IUI cycle in 908 IUI cycles, and divided the patients into 4 groups accord-

ing to their sperm morphology (<5%, 5-19%, 10-14%, >14%) for cut-off value. They found out that the group of <5% had the lowest pregnancy rate, yet they did not find it statistically significant compared to the other groups. Wainer et al. [16] also reported in their study of 2564 IUI cycles that sperm morphology does not affect pregnancy rates. We observed in our study that +4 and +3 motile sperm rates along with morphology have statistically significant impacts on the occurrence of pregnancy according to the results of ROC analysis of pre- and post-wash sperm parameters. We found out that morphology itself could predict 68.4% of pregnant cases, +4 volatile sperm rate 69.6% and +3 volatile sperm rate 33.0%. Aligned with our study, Zhao et al. [17] also reported in their study that sperm motility in the initial sperm sample was an independent factor that could affect pregnancy with IUI. They emphasized the importance of the existence of +3 and +4 motile sperm in the washed semen for the success of IUI.

Limitation

The important limitations of our study are single center experience and relatively small sample size. Some of the couples had been infertile for more than 10 years. For these couples IVF is more appropriate but IUI was preferred as the first treatment option for the couples with unexplained infertility.

Conclusion

Considering all relevant studies, while various sperm parameters are known to be used for the prediction of pregnancy with IUI, there is not a complete consensus over this issue. We argue with this study that, with respective to unexplained infertility, using morphology cut-off values of 4.5 for pre-wash and 2.5 for post-wash may predict the success of pregnancy by IUI. We emphasize the importance of this finding as it may enable couples to turn to advanced treatments at an earlier stage.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Funding: None

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

References

1. Guzick DS, Sullivan MW, Adamson GD, et al, Efficacy of treatment for unexplained infertility. Fertility and Sterility,1998;70:207-13.
2. Nikbakht R, Saharkhiz N. The influence of sperm morphology, total motile sperm count of semen and the number of motile sperm inseminated in sperm samples on the success of intrauterine insemination. UFS. 2011;5:168-73.
3. Ok EK, Dogan E, Okyay EO, Gulekli B. The effect of post-wash total progressive motile sperm count and semen volume on pregnancy outcomes in intrauterine insemination cycles: a retrospective study, J Turkish-German Gynecol Assoc. 2013;14:142-5
4. Arpita R, Amit S, Anil G, et al, Unexplained infertility: an update and review of practice. Reproductive BioMedicine Online. 2012;24:591– 602.
5. Badawy A, Elnashar A, Eltotongy M. Effect of sperm morphology and number on success of intrauterine insemination, Fertility and Sterility. 2009;91:777-81.
6. Van Waart J, Kruger TF, Lobard CJ, Ombelet W. Predictive value of normal sperm morphology in intrauterine insemination (IUI): a structures literature review. Hum Reprod Update. 2001;7:495-500.
7. French DB, Sabanegh ES Jr, Goldfarb J, Desai N. Does severe teratozoospermia affect blastocyst formation, live birth rate, and other clinical outcome parameters in ICSI cycles? Fertility and Sterility. 2010; 93:1097-103.
8. Guzick DS, Overstreet JW, Factor-Litvak P, et al, Sperm morphology, motility, and concentration in fertile and infertile men.N Eng J Med. 2001;345: 1388-93.
9. Hauser R, Yogev l, Botchan A, Lessing JB, Paz G, Yavetz H. Intrauterine insemination in male factor subfertility: significance of sperm motility and morphology assessed by strict criteria.Andrologia. 2001;33: 13-7.
10. Lee RK, Hou JW, Ho HY, et al, Sperm morphology analysis using strict criteria as a prognostic factor in intrauterine insemination. Int J Androl. 2002;25:277-80.
11. Merviel P, Heraud MH, Grenier N, Lourdel E, Sanguinet P, Copin H. Predictive factors for pregnancy after intrauterine insemination (IUI): An analysis of 1038 cycles and a review of the literature. Fertility and Sterility. 2010;93: 79-88.
12. Burr R, Siegberg R, Matthews C, Flaherty S. The influence of sperm morphology and the number of motile sperm inseminated on the outcome of intrauterine insemination combined with mild ovarian stimulation. Fertility and Sterility. 1996;65: 127-32.
13. Deveneau NE, Sinno O, Krause M, et al, Impact of sperm morphology on the likelihood of pregnancy after intrauterine insemination. Fertility and Sterility. 2014;102: 1584-90.
14. Karabinus DS, Gelety TJ. The impact of sperm morphology evaluated by strict criteria on intrauterine insemination success. Fertility and Sterility. 1997;67:536-41.
15. Sun Y, Li B, Fan LQ, et al, Does sperm morphology affect the outcome of intrauterine insemination in patients with normal sperm concentration and motility? Andrologia. 2012;44: 299-304.
16. Wainer R, Albert M, Dorion A, et al, Influence of the number of motile spermatozoa inseminated and of their morphology on the success of intrauterine insemination. Hum Reprod. 2004;19: 2060-5.
17. Zhao Y, Vlahos N, Wyncott D, et al, Impact of semen characteristics on the success of intrauterine insemination. J Assist Reprod Genet. 2004;21:143-8.

How to cite this article:
Turhan N, Uyanık M, Kosus A, Kosus N, Pekel A, Uyanık E. The role of semen parameters in pregnancy of women having intrauterine insemination. J Clin Anal Med 2018;9(5): 407-10.