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Prognostic Factors Influencing Pregnancy Rates in Intrauterine Insemination Cycles
İntrauterin İnseminasyon Sikluslarinda Gebelik Oranlarini Etkileyen Prognostik Faktörler

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ÖZ

Amaç: Bu çalışmada kontrollü ovarian stimulasyon (KOH)/ intrauterin inseminasyon (IUI) sonrası gebelik sonuçlarını etkileyen prognostik faktörlerin belirlenmesi amaçlanmıştır.

Gereç ve Yöntemler: Bu retrospektif kohort çalışmasında, Ocak 2017 ve Nisan 2019 tarihleri arasında toplam 202 gonadotropin-IUI siklusu analiz edildi. Gebelik saptanan (n=44) ve saptanmayan (n=158) iki grup, demografik özellikler, siklus sonuçları ve sperm parametreleri açısından karşılaştırıldı. Gebeliği etkileyebilecek faktörleri belirlemek için lojistik regresyon analizi yapıldı.

Bulgular: Klinik gebelik oranı tüm grupta % 21.8 olarak hesaplandı. Lojistik regresyon, IUI başarı oranlarını öngörmede dört önemli faktör tanımladı; infertilite etiyolojisi (OR: 0.208; 95% CI: 0.079-0.547, P: 0.001), artmış total progresif motil sperm sayısı (TPMSS) (OR: 1.027;95% CI: 1.001-1.053; P: 0.047), endometrial kalınlık (OR: 1.346; 95% CI: 1.120-1.617; P: 0.002) ve azalmış infertilite süresi (OR: 0.951; 95% CI: 0.928-0.975, P <0.001), gebelik için en önemli risk faktörleriydi.

Sonuç: Bu çalışmada analiz edilen çeşitli parametrelerden infertilite etiyolojisi, infertilite süresi, endometrial kalınlık ve yıkama sonrası progressif motil sperm sayısı, intrauterin inseminasyonun başarısını etkileyen en önemli prognostik faktörlerdir.

Anahtar Kelimeler: İntrauterin inseminasyon, prognostik faktörler, infertilite, gebelik oranı

ABSTRACT

Aim: The aim of this study was to determine the prognostic factors for pregnancy outcomes after controlled ovarian stimulation (COS)/intrauterine insemination (IUI).

Material and Methods: In this retrospective cohort study, a total of 202 gonadotropin plus IUI cycles were analyzed between January 2017 and April 2019. Demographic features, cycle outcomes and sperm parameters were compared between pregnant (n=44) and non-pregnant groups (n=158). Logistic regression analysis was performed to identify factors that could predict a pregnancy.

Results: : The clinical pregnancy rate was calculated as 21.8% in the whole group. Logistic regression identified four significant factors in predicting the IUI success rates; the etiology of infertility (OR:0.208; 95% CI: 0.079-0.547, P:0.001), increased TPMSC (OR:1.027; 95% CI:1.001-1.053; P:0.047), endometrial thickness (OR:1.346; 95% CI:1.120-1.617; P:0.002) and shorter duration of infertility (OR:0.951; 95% CI: 0.928-0.975, P<0.001) which were the most significant risk factors for pregnancy achievement.

Conclusion: Among various parameters analyzed in this study; infertility etiology, infertility duration, endometrial thickness and post-washed total progressive motile sperm count were found to be the most important prognostic factors in predicting successful outcome of IUI.

Keywords: Intrauterine insemination, prognostic factors, infertility, pregnancy rate

INTRODUCTION

Intrauterine insemination (IUI) is a procedure that processed and concentrated motile sperm are placed directly into the uterine cavity around the time of ovulation. It is a less expensive and less invasive treatment compared with more advanced assisted reproductive technologies (ART) like in vitro fertilization and embryo transfer (IVF-ET) (1). It is widely used around the world as a first line treatment for infertile couples with indications male subfertility, ejaculatory disorders, cervical factor infertility, ovulatory dysfunction and unexplained infertility (2). The minimum requirements for performing the procedure are patency of at least one fallopian tube, ovulation in the IUI cycle and adequate number of motile sperm (3).

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Despite technical developments in controlled ovarian stimulation (COS) and semen preparation, the success rates of IUI are lower than the ART (2). European Society of Human Reproduction and Embryology (ESHRE) data showed a pregnancy rate (PR) per cycle of 12.4% after IUI compared with 28.9% after IVF-ET (4), and this PR has been relatively stable from year to year (5). In some studies, overall pregnancy rates of controlled ovarian stimulation with intrauterine insemination have been reported as high as 30%, although results vary depending on the studied groups of patients and the study parameters (6).

In the literature, several prognostic factors have been reported as influencing pregnancy rates after IUI including woman's age, body mass index (BMI), type and duration of infertility, use of different ovarian stimulation protocols, numbers of sperm inseminated, sperm morphology, progressive motile sperm count, endometrial thickness, number of preovulatory and mature follicles obtained, estradiol (E2) concentration on the day of human chorionic gonadotropin (hCG) administration and the type of catheter used. However, results on the predictive value of these parameters remain highly contradictory. Regardless of the treatment used, couples always desire to know their chances of success. Thus, identifying the factors which are influential in the success rate is highly crucial. The purpose of this study was to identify the parameters which were most influential in the success rate using COS/IUI treatment modality.

MATERIAL AND METHODS

A retrospective study was conducted at the Department of Reproductive Endocrinology, Zekai Tahir Burak Women's Health Education and Research Hospital, University of Health Sciences, Ankara, Turkey, between January 2017 and April 2019 after ethics approval by the Institutional Review Board. The data were collected from the medical records of women with unexplained infertility and polycystic ovary syndrome (PCOS) undergoing their first COS/IUI cycle. The study protocol was conducted in accordance with the principles of the Declaration of Helsinki and the need to obtain informed consent was waived due to the retrospective nature of the study. All the couples had one year duration of infertility. Unexplained infertility was defined as cases where the basic infertility workup [ovulatory cycles, normal uterine cavity with at least one patent fallopian tube on hysterosalpingogram (HSG) or laparoscopy (L/S) and normal semen parameters according to 2010 World Health Organization (WHO) guidelines (7)] was found to be normal. PCOS was diagnosed, after the exclusion of related disorders, as per the revised 2003 Rotterdam criteria (8). The pretreatment evaluation included medical history, cycle day 3 transvaginal sonography and hormone evaluation [follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), thyroid stimulating hormone (TSH) and prolactin], HSG and/or L/S, semen analysis and midluteal serum progesterone level. Body weight and height were measured using an automatic machine and BMI of each woman was calculated by the ratio of weight (kg)/ [height (m)]2 . The husbands of all patients had normal spermiogram results based on at least two semen analyses according to the WHO 2010 criteria. All women had at least one tubal patency, documented by HSG and in some cases also by L/S. The exclusion criteria were as follows: women with basal serum FSH >12 mIU/mL, antral follicle count (AFC) <6, women age >40 years, body mass index (BMI) ≥40 kg/m², systemic diseases, endometriosis, uterine fibroids, male infertility and previous ovarian surgery. Before treatment, patients were evaluated on the second or third day of the cycle using hormone profile and 7.5 MHz endovaginal probe of a General Electric Medical Systems, Logic 200 Pro ultrasound device. Antral follicle assessment was performed and presence of ovarian cysts excluded. COS was initiated with 37.5-150 IU of recombinant FSH (rFSH) or human menopausal gonadotropin (hMG) starting on day 2 or day 3 of the cycle. Ovulation monitoring was performed by transvaginal ultrasound and serum E2 levels starting on day 6 of stimulation and every 2 to 3 days thereafter to evaluate the growth, number and size of ovarian follicles and the endometrial thickness. If follicular development was under 12 mm, gonadotropin dosage was increased. When a follicle reached a mean diameter of 17 to 18 mm, recombinant human chorionic gonadotropin (hCG) (Ovitrelle, Merck Serono, Modugno, Bari, Italy) was administered subcutaneously at a dose of 250 µg for oocyte maturation. Intrauterine insemination was performed 36 hours after hCG administration. We cancelled the IUI cycle when no mature follicles were obtained or when more than two mature follicles were observed.

Semen samples were collected at the laboratory using the swim-up technique after 2 to 5 days of abstinence and 2 hours before insemination. Intrauterine insemination was performed using a soft catheter (Gynemed Medical Products, Lommel, Belgium). Following the transfer, all patients received 400 mg/day vaginal progesterone supplementation for luteal phase support starting on the day of IUI until 12 weeks of gestational age if the patient conceived. A serum hCG assay was performed 12 days after IUI if menstruation had not started. A clinical pregnancy was defined as the presence of a gestational sac with fetal cardiac activity on ultrasound at least 4 weeks after insemination.

The primary outcome measures were demographic features, infertility duration and etiology, days of stimulation, the number of intermediate-sized (12-15 mm) and dominant (≥ 16 mm) follicles, total gonadotropin dose used, endometrial thickness and serum E2 levels on the day of hCG injection. All the patients who had a positive pregnancy test on day 12 were considered in the "positive" group while patients who had a negative pregnancy test on day 12 were considered in the "negative" group and these two groups were compared.

Statistical analysis

Statistical Package for the Social Sciences version 22.0 (SPSS Inc., Chicago, IL, USA) was used for data analyses. Normal distribution of each variable was assessed by using Shapiro-Wilk test. Continuous variables were presented as mean (standard deviation), and intergroup differences were investigated using Student t test or Mann–Whitney U test where appropriate. Categorical variables were expressed as n (%). Differences between categorical data were evaluated using the Chi-square test. Receiver operator characteristics curve analysis was used to find the predictive factors for pregnancy. Logistic regression method was used to evaluate the risk factors affecting IUI outcomes. A p value < 0.05 was considered statistically significant.

RESULTS

A total of 202 infertile patients who met the study criteria were included in this study. The clinical pregnancy rate was calculated as 44 (21.8%) in the whole group. The age of the patients ranged from 19-40 years and BMI values were between 18-39 kg/m2. There were no statistically significant differences between pregnant and non-pregnant patients in terms of age and BMI (p>0.05). The duration of infertility was significantly shorter in the pregnant group than in the nonpregnant group (34.6±11.7 vs. 50.9±27.8 months; p<0.001). Demographic characteristics, basal hormone values and cycle characteristics are shown in Table 1. No statistically significant differences were observed between the groups regarding those parameters (p>0.05) with the exception of endometrial thickness (10.3±1.8 vs. 9.1±2.3; p<0.001) on hCG triggering day. Pregnancy rates were higher in patients diagnosed with PCOS

(p:0.029). There were no statistically significant differences between the 2 groups in terms of type of infertility, developing intermediate and dominant follicle numbers (Table 2).

ROC analyses demonstrated that the AUCs indicative of infertility duration, endometrial thickness and total progressive sperm count (TPMSC) values for predicting pregnancy were 0.320 (95% CI: 0.242-0.397, p<0.001), 0.673 (95% CI: 0.588-0.759, p<0.001), and 0.604 (95% CI: 0.489-0.678, p: 0.042), respectively. The cut-off values according to the highest Youden index were calculated to be 45 months (sensitivity: 70.5%, specificity: 53.9%), 9.3 mm (sensitivity: 77.3%, specificity: 53.2%), 29.2 million (sensitivity: 43.2%, specificity: 44.3%) (Figure 1). The logistic regression analysis model, which included significant clinical findings, showed that the etiology of infertility (OR:0.208; 95% CI: 0.079-0.547, p:0.001), increased TPMSC (OR:1.027, 95% CI;1.001-1.053; P:0.047) and endometrial thickness (OR:1.346, 955 CI:1.120-1.617; P:0.002), decreased duration of infertility (OR:0.951; 95% CI: 0.928-0.975, P<0.001) were significant risk factors for pregnancy (Table 3).

Table 1. Demographic characteristics, baseline hormone values and cycle characteristics of the patients

Parameter	Pregnant (n:44)	Non-pregnant (n:158)	P value
Age (years)	28.2±5.4	28.5±5.0	0.738
BMI (kg/m2)	24.8±3.6	25.0±4.3	0.788
Infertility duration (months)	34.6±11.7	50.9±27.8	<0.001
TPMSC (milllion)	32.5±14.6	28.6±13.2	0.042
E2 (pg/ml)	40.5±14.7	41.4±14.6	0.723
FSH (mIU/ml)	6.3±1.5	6.6±1.9	0.252
LH(U/L)	7.6±5.0	6.0±4.1	0.435
E2 on hCG day (pg/ml)	537.7±499.3	443.4±349.0	0.429
Total gonadotropin dose used (IU)	730.7±347.6	733.9±351.8	0.899
Stimulation duration (days)	12.9±3.5	13.0±4.0	0.629
Endometrial thickness (mm)	10.3±1.8	9.1±2.3	<0.001

BMI: Body mass index, TPMSC: Total progressive sperm count, E2: Estradiol, FSH: Follicle stimulating hormone, LH: Luteinizing hormone

p value 20,05 is considered statisti cally signifecent

Table 2. Comparison of characteristics of infertility and follicle size during treatment between the groups

Parameter	Pregnant (n:44)	Non-pregnant (n:158)	P
Infertility type number (n) (%)			
Primary	36(21.1)	135(78.9)	0.555
Secondary	8(25.8)	23(74.2)	
Infertility etiology n (%)			
PCOS	32(27.1)	86(72.9)	**0.029**
Unexplained	12(14.3)	72(85.7)	
Obesity n(%)			
BMI≥30 kg/m2	3(13)	20(87)	0.421
BMI<30 kg/m2	41(22.9)	138(77.1)	
Intermediate follicle count (12-15 mm) n (%)			
<2	35(21.7)	126(78.3)	0.977
≥2	9(22.0)	32(78.0)	
Dominant follicle count (≥16 mm) n (%)			
Monofollicular	34(20.0)	136(80.0)	0.157
Bifollicular	10(31.3)	22(68.8)	

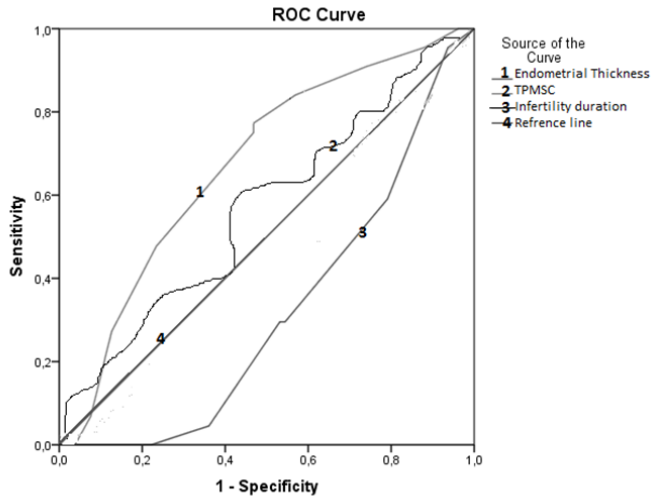
PCOS: Polycystic ovary syndrome, BMI: Body mass index,p value 20,05 is considered statisti cally signifecent

Table 3. Logistic regression method of predictive factors for IUI outcomes

Parameter	Wald	P	OR	95% CI
Age (years)	1.088	0.297	1.043	0.963-1.130
BMI (kg/m2)	0.532	0.466	0.964	0.873-1.064
Infertility etiology	10.127	0.001	0.208	0.079-0.547
TPMSC (mil)	3.951	0.027	1.170	1.006-1.059
Endometrial thickness (mm)	10.053	0.002	1.346	1.120-1.617
Infertility duration (months)	15.687	<0.001	0.951	0.928-0.975

BMI: Body mass index, TPMSC: Total progressive motile sperm count, OR: Odds ratio, CI: Confidence interval, p value<0.05 is considered statistically significant.

Figure 1. ROC curve analysis of predictive factors for pregnancy



DISCUSSION

The aim of this retrospective study was to elucidate the factors influencing IUI outcome in order to strive for a better patient selection and prediction of success rates following IUI treatment. Among the various parameters that were studied infertility etiology, infertility duration, endometrial thickness and total progressive motile sperm count significantly affected treatment success.

Causes of infertility appeared to be a predictive factor influencing pregnancy rates. In our study, the clinical pregnancy rate was calculated as 21.8% in the whole group. Pregnancy rates were significantly higher in PCOS group than unexplained group. Other causes influencing negatively IUI success rate, such as endometriosis, tubal factor, low ovarian reserve, male factor, were excluded in terms of homogeneity of the study. Overall pregnancy rates as high as 30% have been reported for patients undergoing COH/IUI as mentioned before. The great variation in pregnancy rates may be due to multiple factors including the small size of the study population, variability in characteristics of patients, ovarian stimulation protocol and insemination techniques. Comparable results have been given in the literature (2,9).

Duration of infertility was found to be significantly associated with IUI success rates. We observed a significant decrease in pregnancy rate with increased duration of infertility. Similar to our study, Hansen et al. and Ashrafi et al. observed a significant decrease in pregnancy rate with prolonged duration of infertility (10,11). However Merviel et al., Ganguly et al., and Tay et al. did not find any significance associated with duration of infertility (9,12,13). Wiser et al. reported significantly higher pregnancy rates with length of infertility below 6 years when compared with above 6 years (14.2% vs. 6.1%) (14).

We also found that endometrial thickness on hCG triggering day had an impact on IUI outcome. Endometrial thickness was found to be higher in patients who conceived. Esmailzadeh and Faramarzi showed that the mean endometrial thickness on the day of ovulation triggering was significantly higher in IUI cycles where pregnancy achieved (10.1 mm vs. 7.7 mm) (15). However, Merviel et al. stated the contrary (9).

Total progressive motile sperm count has been studied in our study and found to be a potential predictive factor for a successful COS/IUI. There are conflicting findings in different studies. Most of the studies did not describe when and how sperm motility was calculated. Some studies reported total motile sperm count (TMSC) values pre-wash (9, 16), while others reports post-wash TMSC (13,17). Also, some studies counted TMSC using the percentage of progressively motile spermatozoa (16), while others use total motile spermatozoa (13). This paradox makes it very difficult to compare results for TMSC amongst different studies. In our study, post-wash TPMSC was used as variable, which is the product of the sperm volume collected based on sperm concentration and the percentage of sperm with progressive motility in the ejaculate after preparation and are subsequently available for insemination in IUI. In a systematic review by Ombelet et al. (18) a TPMSC of more than 10 million was most frequently indicated as a threshold above which pregnancy rates after IUI increased significantly. According to our study, TPMSC was significantly associated with IUI success rates and 29.2 million was found as a cut off value. In a meta-analysis of 16 trials (19), the predictive value of post-wash TMSC on the IUI outcome was studied and the researchers concluded that an optimal cut-off value for the post-wash TMSC at insemination could not be identified for patient counseling. The authors agreed that although there is not enough data on this subject, the cut-off value for a post-wash TMSC during the fertility workup should be based on the clinic's own population and sperm preparation technique.

Another parameter influencing IUI success rates is the female age. Several studies have shown that an increase in the woman's age leads to a decrease in the pregnancy rate and also increase in the spontaneous abortion rates (1,9,10). Based on these studies, it was believed that advancing age adversely affects oocyte quality and number, endometrium and corpus luteal function and thus decreases the pregnancy rate. In line with our findings, Ejzenberg et al. and Erdem et al. found no association between female age and pregnancy rate (20,21). The possible explanation could be that the patients were under 40 years and that ovarian stimulation improves the follicle and endometrial development and the resultant good quality corpus luteum prevents luteal phase defect. Therefore, IUI can be a good option prior to more expensive IVF-ET in patients aged 40 and younger who present with a good ovarian reserve.

Body mass index has also been studied as a prognostic factor. Obesity has been found to be associated with anovulatory infertility due to hyperinsulinemia, insulin resistance and hyperandrogenemia which affects the hormonal environment (12). Ganguly et al. and Thijssen et al. reported no significant differences in pregnancy rates between different BMI groups which is similar to our study (p=0.78) (12,22). The possible reason could be that in our study BMI values were <40 kg/m2 and ovarian stimulation protocol was adjusted to overcome the weight effect.

In the current study, there were no statistically significant differences between the 2 groups (primary or secondary) in terms of type of infertility which has been also shown in some studies (2,9,21). Our results disagree with some studies (3,22). This could be explained by the fact that seconder infertile women had already proven their fertility before so they had a greater chance of achieving pregnancy after IUI than those primary infertility.

Ovarian reserve is another prognostic factor influencing IUI success rate. The performance of hormone assays (E2 and FSH) on the second or third day of the cycle is one way of evaluating ovarian reserve. The generally admitted thresholds are 9.4 IU/L and 80 pg/mL respectively (9). In the present study, there were no statistically significant differences in pregnancy rates according to the basal FSH and E2 concentrations (p=0.25 and p=0.72). The possible explanation could be that in our study patients with poor ovarian reserve status such as, basal serum FSH levels >12 mIU/mL, antral follicle count (AFC) <6, age >40 years, endometriosis and previous ovarian surgery, were excluded. Similarly, Merviel et al. and Mullin et al. reported the same results (9,23). However, Dinelli et al. observed a significant decrease of pregnancy rate with the basal FSH levels >7 mIU/mL (3). The same conclusion was reported by Soria et al. where women with basal FSH levels <9 IU/L had 3.1 times more chances to become pregnant after IUI in comparison with basal FSH levels >9 IU/L (24).

Cycle characteristics including length of stimulation, the total dose of gonadotropin used, E2 concentration and number of follicles on hCG injection day have been also studied. We found no association between these parameters and clinical pregnancy. In our clinical practice, we aim to obtain one or two mature follicles and cancel cycles with three or more. Merviel et al. and Michau et al. and reported that pregnancy rates were significantly higher in cycles with two mature follicles compared to one (9,25). In the present study, the pregnancy rates with two follicles were higher than one (31.3% vs 20%, p=0.15) but this was not was not statistically significant. In our study, monofollicular development was higher (84%) than bifollicular. This was possibly due to the low doses of gonadotropin used in our protocols to avoid multiple pregnancy which is associated with multifollicular growth. In agreement with our study, Scchieri et al. and Wu et al. also did not find significant differences

between the results of IUI and the number of mature follicles (1, 26).

The main drawback of this study is its retrospective nature. Sample size is not large enough to detect the differences in some subgroup analysis. Further prospective randomized studies with larger sample sizes are needed to confirm the results of this study.

CONCLUSION

Our study aimed to identify the prognostic factors that influence the pregnancy outcome following COS/IUI treatment. The clinical pregnancy rate was calculated as 21.8%. Among various parameters infertility etiology, infertility duration, endometrial thickness and post-washed total progressive motile sperm count found to be the most important prognostic factors in predicting successful outcome of IUI. A better formulated prediction model with larger study population would be helpful in counseling both clinicians and subfertile couples to arrive at a decision with regards to their treatment options based on the factors present.

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REFERENCES

1. Sicchieri F, Silva AB, Silva ACJSRE, Navarro PAAS, Ferriani RA, Reis RMD. Prognostic factors in intrauterine insemination cycles. JBRA Assist Reprod. 2018 Mar 1;22(1):2-7.

2. Ghaffari F, Sadatmahalleh SJ, Akhoond MR, Eftekhari Yazdi P, Zolfaghari Z. Evaluating The Effective Factors in Pregnancy after Intrauterine Insemination: A Retrospective Study. Int J Fertil Steril. 2015 Oct-Dec;9(3):300-8.

3. Dinelli L, Courbière B, Achard V, Jouve E, Deveze C, Gnisci A, et al. Prognosis factors of pregnancy after intrauterine insemination with the husband's sperm: conclusions of an analysis of 2,019 cycles. Fertil Steril. 2014;101(4):994-1000.

4. Ferraretti AP, Goossens V, de Mouzon J, Bhattacharya S, Castilla JA, Korsak V, et al. Assisted reproductive technology in Europe, 2008: results generated from European registers by ESHRE. Hum Reprod. 2012 Sep;27(9):2571-84.

5. Ferraretti AP, Goossens V, Kupka M, Bhattacharya S, de Mouzon J, Castilla JA, et al. Assisted reproductive technology in Europe, 2009: results generated from European registers by ESHRE. Hum Reprod. 2013 Sep;28(9):2318-31.

6. European IVF-Monitoring Consortium (EIM); European Society of Human Reproduction and Embryology (ESHRE), Kupka MS, D'Hooghe T, Ferraretti AP, de Mouzon J et al. Assisted reproductive technology in Europe, 2011: results generated from European registers by ESHRE. Hum Reprod. 2016 Feb;31(2):233-48.

7. WHO. World Health Organization: WHO Laboratory manual for the examination and processing of human semen - 5th ed. Geneva: WHO Press 2010.

8. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril. 2004 Jan;81(1):19-25.

9. 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. Fertil Steril. 2010 Jan;93(1):79-88.

10. Hansen KR, He AL, Styer AK, Wild RA, Butts S, Engmann L et al. Predictors of pregnancy and live-birth in couples with unexplained infertility after ovarian stimulation-intrauterine insemination. Fertil Steril. 2016 Jun;105(6):1575-1583

11. Ashrafi M, Rashidi M, Ghasemi A, Arabipoor A, Daghighi S, Pourasghari P,et al. The role of infertility etiology in success rate of intrauterine insemination cycles:an evaluation of predictive factors for pregnancy rate. Int J Fertil Steril. 2013 Jul;7(2):100-7.

12. Ganguly I, Singh A, Bhandari S, Agrawal P, Gupta N. Pregnancy Predictors after Intrauterine Insemination in Cases of Unexplained Infertility: A Prospective Study. Int J Reprod Med. 2016;2016:5817823.

13. Tay PY, Raj VR, Kulenthran A, Sitizawiah O. Prognostic factors influencing pregnancy rate after stimulated intrauterine insemination. Med J Malaysia. 2007;62(4):286-9.

14. Wiser A, Shalom-Paz E, Reinblatt SL, Son WY, Das M, Tulandi T, et al. Ovarian stimulation and intrauterine insemination in women aged 40 years or more. Reprod Biomed Online. 2012; 24(2): 170-173.

15. Esmailzadeh S, Faramarzi M. Endometrial thickness and pregnancy outcome after intrauterine insemination. Fertil Steril. 2007 Aug;88(2):432-7

16. 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. Int J Fertil Steril. 2011 Oct;5(3):168-73.

17. Kleppe M, van Hooff MH, Rhemrev JP. Effect of total motile sperm count in intra-uterine insemination on ongoing pregnancy rate. Andrologia. 2014 Dec;46(10):1183-8.

18. Ombelet W, Dhont N, Thijssen A, Bosmans E, Kruger T. Semen quality and prediction of IUI success in male subfertility: a systematic review. Reprod Biomed Online. 2014 Mar;28(3):300-9.

19. van Weert JM, Repping S, Van Voorhis BJ, van der Veen F, Bossuyt PM, Mol BW. Performance of the postwash total motile sperm count as a predictor of pregnancy at the time of intrauterine insemination: a meta analysis. Fertil Steril. 2004 Sep;82(3):612-20.

20. Ejzenberg D, Gomes TJO, Monteleone PAA, Serafini PC, Soares-Jr JM, Baracat EC. Prognostic factors for pregnancy after intrauterine insemination. Int J Gynaecol Obstet. 2019 Jun 26.

21. Erdem A, Erdem M, Atmaca S, Korucuoglu U, Karabacak O. Factors affecting live birth rate in intrauterine insemination cycles with recombinant gonadotrophin stimulation. Reprod Biomed Online. 2008;17:199-206.

22. Thijssen A, Creemers A, Van der Elst W, Creemers E, Vandormael E, Dhont N, Ombelet W.Predictive value of different covariates influencing pregnancyrate following intrauterine insemination with homologous semen: a prospective cohort study. Reprod Biomed Online. 2017 May;34(5):463-472.

23. Mullin C, Virji N, Saketos M. San Roman G. Day 2 follicles stimulating hormone (FSH) and estradiol (E2): could these values be used as markers to predict pregnancy outcomes in women undergoing ovulation induction (OI) therapy with intrauterine insemination (IUI) cycles? Fertil Steril 2005; 84(Suppl):S162.

24. Soria M, Pradillo G, García J, Ram_on P, Castillo A, Jordana C, et al. Pregnancy predictors after intrauterine insemination: analysis of 3012 cycles in 1201 couples. J Reprod Infertil. 2012 Jul;13(3):158-66.

25. Michau A, El Hachem H, Galey J, Le Parco S, Perdigao S, Guthauser B. Predictive factors for pregnancy after controlled ovarian stimulation and intrauterine insemination: A retrospective analysis of 4146 cycles. J Gynecol Obstet Hum Reprod. 2019 May 3.

26. Wu HM, Tzeng CR, Chen CH, Chen PH. Pelvic endometriosis with peritoneal fluid reduces pregnancy rates in women undergoing intrauterine insemination. Taiwan J Obstet Gynecol. 2013 Dec;52(4):512-5.