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Original Research Article

Predicting the success of intrauterine insemination using a clinically based scoring system

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ABSTRACT

Background: Aim of the study was to predict the success of intrauterine insemination (IUI) using a clinically based scoring system. Retrospective cohort study in the institute of reproductive medicine, the Madras medical mission, Chennai
Methods: The 240 patients meeting the inclusion criteria and exclusion criteria who underwent IUI with husband/ donor sperms were retrospectively assessed. 10 parameters each influencing the success of IUI were taken and a total score was derived for each patient and their predictive cut off for success of IUI was determined. Each factor was also analysed individually for the success of IUI. All the patients were followed up till their serum beta human chorionic gonadotropin (hCG) test done 16 days post insemination.
Results: On evaluating, ROC curve was obtained and it showed that a cut off of 13.5 had a success prediction post IUI with a sensitivity of 82.9 and specificity of 68.2 on individually analyzing the 10 factors, serum anti-Müllerian hormone (AMH) was found to be influence the success of IUI.
Conclusions: The proposed scoring system integrates the parameters to provide an individualized pregnancy probability estimate. This tool can support clinicians in counselling patients more effectively, aiding in decision making and setting realistic expectations.

Keywords: Intrauterine insemination, Factors affecting IUI, Predictive score, IUI success

INTRODUCTION

Intrauterine insemination (IUI), with or without ovarian stimulation, has been considered one of the first-line approach for treating subfertility. Given that IUI is a less complex, lower-risk, and more cost-effective procedure than IVF, identifying patients who are most likely to benefit from it would be clinically valuable. Several predictive models for pregnancy success following IUI have been developed in the past, yet they are not commonly used in clinical practice.[1] Most existing models are based on semen analysis criteria established by the WHO in 1999 and ovarian hyperstimulation protocols aimed at producing two to three dominant follicles before insemination. However, with the updated WHO semen analysis guidelines introduced in 2010 and evidence supporting strict cancellation protocols to minimize multiple pregnancies, these older models may no longer be fully applicable. While a more recent predictive model by Souter et al focuses on ovarian stimulation and ovulation induction, it primarily addresses infertility due to polycystic ovary syndrome (PCOS) and unexplained infertility rather than specifically predicting IUI success. With these considerations in mind, our study sought to determine the per-cycle pregnancy rate and cumulative pregnancy rate across multiple IUI cycles.[1-4] We aimed to identify the main predictive factors, including demographic details, clinical history, infertility causes,

and semen parameters. Using this information, we aimed to develop a straightforward clinical scoring system based on commonly collected patient data to help provide evidence-based, personalized counselling for couples considering IUI as a treatment option.

METHODS

Our study is a retrospective type of study conducted from 2021 to 2024 at the institute of reproductive medicine, Madras medical mission, Chennai, Tamil Nadu, India on a sample of 240 women who underwent IUI at our institute.

Inclusion criteria

Women aged 18-45 years, who underwent any number of IUI cycles, donor IUI, patient with unilateral patent tubes and also those with mild uterine pathology were included.

Exclusion criteria

Patients who discontinued treatment and those who lost follow-up were excluded. Couples with severe male infertility were not offered insemination and were therefore not included in the study.

All patients underwent a standardized routine assessment, which included hormonal analysis, sonographic and/or, in rare cases, laparoscopic evaluation, and semen analysis. IUI was performed following ovarian stimulation with letrozole and/or low-dose gonadotropins, or during a natural cycle, depending on the woman's clinical findings and preference.[5-8] Letrozole was administered starting on or before the fifth day of the menstrual cycle. Low-dose gonadotropins were added for patients with hypothalamic anovulation or endometriosis, starting on day 5 or day 7 (on alternate days), if deemed necessary.[5,7,8]

Ovulation was triggered with subcutaneous hCG at a dose of 5,000-10,000 IU when the leading follicle reached ≥18 mm in diameter.[6] Semen was collected on the day of insemination following 2-7 days of sexual abstinence. IUI was then performed 24-36 hours after the trigger, following confirmation of follicular rupture via ultrasound.[9] All patients received progesterone supplementation to support corpus luteal function.

Outcome

The primary outcome of the study was pregnancy, determined by a positive serum β-hCG test 16 days following IUI. The success of IUI was assessed based on both the pregnancy rate per cycle and the cumulative likelihood of achieving pregnancy over the multiple cycles.[10-12]

Scoring system

The scoring model was developed using 10 clinical and laboratory factors (Table 1), which included the woman's age, body mass index (BMI), AMH level, total progressive sperm motility count (TPSMC), endometrial thickness, number of follicles, number of IUI attempts, presence of any coexisting uterine pathology, tubal patency, and the number of inseminations per cycle.[13-17]

Fallopian tube patency was confirmed through hysterosalpingography (HSG) or chromopertubation. The number of IUIs per cycle (single or double insemination) was documented.

Each of the 10 factors was assigned a score from 0 to 2. Based on a maximum score of 20, an IUI success prediction score was calculated for each couple. Further statistical analysis was conducted to determine the significance of this scoring system.

Post-IUI, patients were started on luteal phase support, and serum β-hCG levels were measured on day 16 to assess pregnancy outcomes.[18-20]

Table 1: Factors and various score assigned based on patient's characteristics.

Factor	Score 0	Score 1	Score 2
Patient's age (in years)	More than 40	35 to 40	Less than 35
BMI (kg/m^2)	More than 30	25 to 30	19 to 25
Tubal patency		Unilateral spill	Bilateral spill
TPMSC	Less than 20%	20 to 30 %	More than 30%
AMH less than 30 years	Less than 1.6	More than 4.6	1.6 to 4.6
AMH 30 to 35 years	Less than 1.2	More than 3.8	1.2 To 3.8
AMH more than 35 years	Less than 1	More than 2.6	1 to 2.6
Number of cycles	3rd or more	2nd	1st
Endometrial thickness	Less than 7 or more than 14	7 to 9 mm	10 to 14 mm
Number of inseminations per cycle		Single insemination	Double insemination
Number of ruptured follicles		1 dominant or ruptured follicle	More than 1
Other factors like fibroid, polyp, adenomyosis	Presence		Absence

Statistical analysis

The collected data were entered in the Microsoft excel 2016 and analysed with IBM SPSS statistics for Windows, version 29.0. (Armonk, NY: IBM Corp). To describe about the data descriptive statistics frequency analysis and percentages analysis were used for categorical variables and the mean and SD were used for continuous variables. To find the significant difference between the bivariate samples in independent groups the independent sample t test was used. To find the significance in categorical data Chi-square test was used similarly if the expected cell frequency is less than 5 in 2×2 tables then the Fisher's exact was used. To find the efficacy of the total score to predict the pregnancy the receiver operating characteristics curve (ROC) was used with sensitivity, specificity and cut-off. The logistic regression analysis was used to find the influencing factors for pregnancy. In all the above statistical tools the probability value 0.05 is considered as significant level

RESULTS

Among the total 233 patients analysed, the total pregnancy was 41 (17.6%) and those non pregnant was 192 (82.4%) post IUI (Table 2).

Table 2: Demographical data of total patients.

Post IUI	N (%)
Pregnancy	41 (17.6)
Non pregnant	192 (82.4)

Using chi square test, the following 4 parameters were evaluated and results were noted. On analysing the number of attempts of pregnancy (Figure 1), 1st attempt (144 patients) yielded a pregnancy of 70.7%, 2nd attempt (60 patients) yielded 17.1%, 3rd attempt (25 patients) 12.2% of positive pregnancy test. When the number of inseminations were analysed (Figure 2), single insemination gave 29 positive pregnancy (70.7%) and double insemination gave 12 positive (29.3%) test result where a total of 173 patients had undergone single insemination and 60 had underwent double insemination.

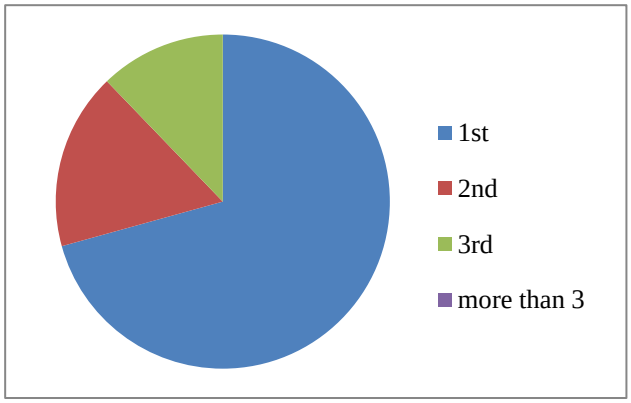

Figure 1: Number of attempts and pregnancy.

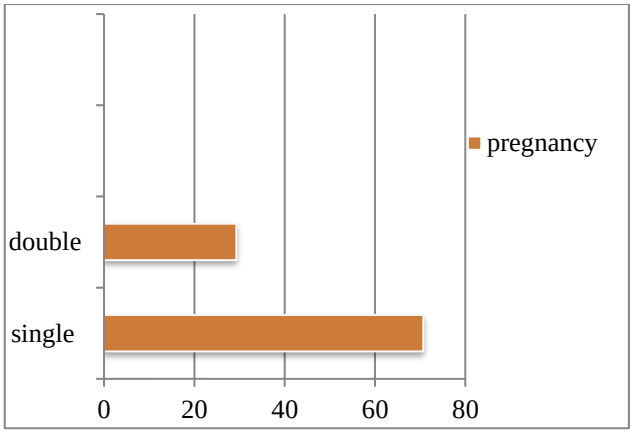

Figure 2: Number of inseminations and pregnancy.

When the spills of the fallopian tubes were analysed (Figure 3), bilateral spill was noted in 184 patients out of which 35 became pregnant post IUI and unilateral spill was seen in 49 patients out of which 6 turned positive. On analysing the other factors like the uterine factors (Figure 4), all 9 cases of adenomyosis lead to negative pregnancy test (0%), 2 cases of arcuate uterus gave 50% pregnancy, 2 cases of bicornuate uterus leads to 50% pregnancy. Among 16 patients with fibroid, 4 (9.8%) became pregnant and 11 patients with polyp, 4 turned positive (9.8%).

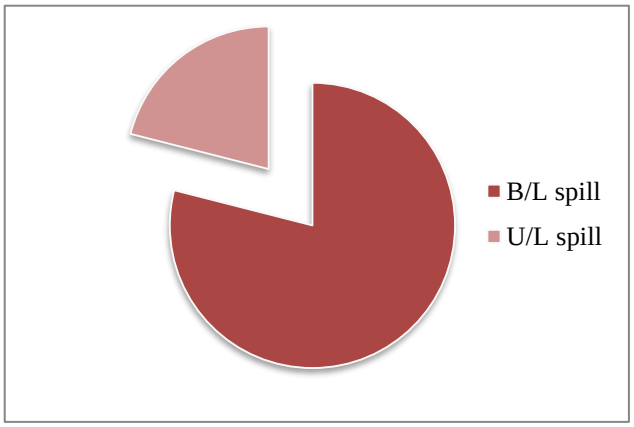

Figure 3: Tubal patency and pregnancy.

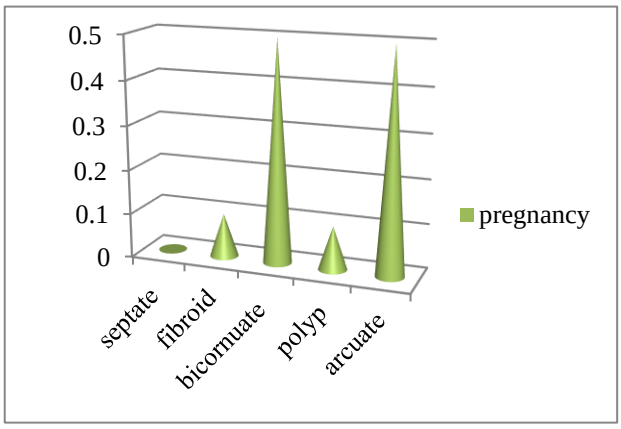

Figure 4: Uterine factor and pregnancy.

Group statistical analysis was used to determine the results of the other 6 parameters. The mean age giving positive pregnancy is 32.83 and negative results was 33.24.[21] TPSMC mean value of 45.76 yielded positive and 36.66 gave negative results.[22] Mean Endometrial thickness of 8.63 showed positive results while value of 8.81 yielded negative results post IUI. BMI at a mean of 28.07 with SD 4.91 gave positive pregnancy test whereas mean of 28.75 gave negative results. Similarly, mean AMH value of 4.03 was associated with positive pregnancy and mean at 3.40 was found to give negative results. Lastly, on analysing the average number of follicles on the day of IUI, if it was 1.78 it gave good results post insemination. In toto, the total score at a mean value of 15.08 was associated with pregnancy and mean at 12.68 was negatively associated with pregnancy. These values where then put to test for equality of variance and t test for equality of means. The results showed that TPMSC (p=0.047) and total score (p=0.005) were statistically significant in predicting the pregnancy chances post IUI.

Thus, by comparing the positive and negative pregnancy rates (Table 3) using the independent samples test, there is found to be a significant association between TPMSC and total score with pregnancy post Intra uterine insemination.

Table 3: Assessing the positive and negative pregnancy rates and their significance.

Factor	Pregnant	Not pregnant	P value
TPMSC	45.76±26.67	36.66±22.31	0.047
Total score	15.08±1.58	12.68±2.07	0.0005

Clinical score

The clinical score developed from the multivariable analysis assigns between 0 and 2 points for the ten factors: female age, AMH level, BMI, number of attempts, number of inseminations, number of follicles, endometrial thickness, tubal spill, TPMSC and other co-existing factors like uterine factors. The total score ranges from 0 to 20, referred to as the "IUI success score." As the score increases, the likelihood of achieving pregnancy per cycle and cumulatively also increases. For example, if there is a 24-year-old patient whose BMI is 27, AMH 3.4, bilateral spill on HSG, undergoing 3rd cycle of insemination, whose partner's TPMSC is 28%. On day of IUI, 1 ruptured follicle, endometrial thickness measuring 9 mm with no other uterine abnormality gets a score of 14 out of 20. She will be followed up with beta hCG value 16 days post IUI.

ROC curve

The ROC curve (Figure 5) shows that a cut off of 13.5 on an average gives a positive pregnancy post IUI. The cut off 13.5 has a sensitivity of 82.9 and specificity of 68.2 in predicting the pregnancy chances post insemination. When the value was plotted in a ROC curve, it yielded an area of 0.818 (p=0.0005) which was highly significant (Table 4).

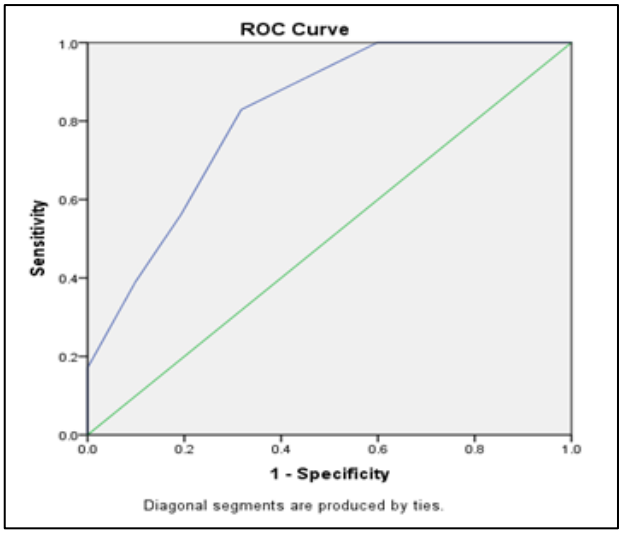

Figure 5: ROC curve for a total score cut off of 13.5.

Table 4: Area according to ROC curve and its significance.

Area	Error	P value
0.818	0.031	0.0005

After analysing all the factors analysed in this particular study, we can conclude that the total score and serum AMH are found to be statistically significant in predicting the IUI outcome. Nagelkerke R Square for this model is 0.403 which shows that it can be applied for 40% of the population.

DISCUSSION

In this study, we were able to show that while the pregnancy rate per IUI cycle was relatively low (17.6 %), repeated cycles led to an average overall success rate of approximately 19%. Per cycle and cumulative pregnancy rates varied considerably by couples' characteristics. Among female factors, younger age, normal BMI and higher AMH were positively associated with pregnancy. Additionally, we found that women with unknown female factor for infertility had higher pregnancy rates compared to women with, unilateral tubal patency, or anatomical alterations or adenomyotic changes or myoma. TPMSC at insemination also correlated with IUI success. More than one follicle, endometrial thickness between 7 to 9 mm, double inseminations, less attempts gave slightly better results. Based on these findings, we propose a clinical scoring system to predict a couple's probability of achieving pregnancy. Couples are assigned 0, 1 or 2 points for each prognostic factor, adding up to a total score ranging from 0 to 20. The probability of predicting pregnancy using this score was 82.8%. Our per cycle pregnancy rate agreed with previous studies, which reported rates between 7 and 20%.

In our cohort, only a few couples underwent four or more IUI cycles, and we observed just a small number of

pregnancies after the fourth cycle. This appeared to be due to the low number of patients continuing beyond three cycles rather than a true decline in per-cycle success rates. This finding aligns with a recent study by Muthigi et al which reported stable pregnancy rates across up to six IUI cycles.[22]

Conversely, Aboulghar et al found a sharp decline in pregnancy rates from cycles 4-6 (5.6%) compared to the first three cycles (16.4%).[23] While their analysis accounted for the drop in patient numbers, their reported success rates were notably higher in the early cycles and significantly lower in the later ones compared to other studies.[10-12] Although it is possible that couples with a higher likelihood of success conceive earlier and discontinue treatment, our data suggest that this selection effect may be less significant than previously believed. Furthermore, careful selection of couples for IUI treatment may help mitigate this effect to some extent

Ten key predictive factors have been identified for counselling patients on infertility treatment with IUI. It has been well-established that female fertility declines as age increases, primarily due to a reduction in both the number and quality of oocytes.[21] As a result, numerous studies have shown lower success rates for IUI as a woman's age increases.[10-17]

The relationship between IUI success rates and AMH levels remains unclear. AMH has been established as a reliable indicator of ovarian reserve and generally decreases with age. However, it is challenging to determine the extent to which the effects of AMH are influenced by age alone. AMH appears to be more reflective of the declining number of oocytes rather than their quality. Morin et al demonstrated that women with diminished ovarian reserve undergoing IVF had similar live birth rates per euploid embryo transfer compared to age-matched controls, suggesting that the mechanisms responsible for reduced oocyte quantity may differ from those responsible for poor oocyte quality.

In the context of IUI, the evidence remains inconclusive. Some studies have identified AMH as a good predictor of pregnancy success, while others found no significant impact on IUI success based on AMH levels. A recent retrospective cohort study, for example, showed no statistically significant difference in live birth rates for women under 35 with AMH levels below 1.0 ng/ml undergoing IUI compared to those with higher AMH levels. However, this study did suggest a trend toward lower conception rates in women with lower AMH. In our cohort, which focused on the first IUI cycle per couple, we observed lower pregnancy rates in women under 35 with AMH below 1.0 ng/ml compared to those with higher AMH levels. For women aged 35 and older, this difference was less pronounced but still present.

Consistent with earlier studies, we also observed higher pregnancy rates per cycle and per patient in women with unexplained infertility compared to those with adenomyosis, fibroids, unilateral tubal factors, or anatomical abnormalities. This finding is clinically reasonable, as endocrine issues causing anovulation or suboptimal follicular development can be addressed through ovarian stimulation combined with IUI. In contrast, anatomical, tubal, and immunological factors cannot be effectively managed by IUI alone.

BMI is well known to be a predictor of success of any type of ART. Though extremes of BMI may be a negative predictor of success of IUI, the normal range of BMI in our study proved to be a fairly significant marker in predicting the IUI success. Previous studies showed that BMI depicting overweight or obesity provided pregnancy rates equal to normal BMI.

The partner's sperm characteristics and more precisely TPMSC were found to be predictive of IUI success. In this study we observed a significant influence of pre-wash TPMSC on pregnancy rates after IUI. Future studies should further investigate this correlation, as pre-wash semen parameters are much more widely available in routine care.[22]

Though previous studies do show that single and double inseminations give nearly the same positive rates post IUI, higher number of inseminations per cycle and lower attempts of insemination have been found to be associated with better pregnancy rate though not very significant as a separate marker.

Previous studies have identified the number of dominant follicles as a strong predictor of IUI success. Several researchers have reported higher pregnancy rates when at least two preovulatory follicles are present.[10,12,18] Consequently, all previously established models for predicting IUI outcomes have incorporated the number of preovulatory follicles as a key factor.[2-5] In our study, there was not a significant difference between 1 and 2 dominant follicles whether ruptured or unruptured on the day of IUI.

Endometrial thickness on the day of IUI was used as a marker. As a endometrial fit for an implantation influenced by hormones post rupture of follicle will have a role in maintaining a pregnancy.

However, in recent years, the risk of multiple pregnancies has become a growing concern.[6] Studies have demonstrated that implementing strict cycle cancellation policies in cases of multi-follicular development effectively reduces the likelihood of multiple gestations following IUI.[10-12] As a result, the applicability of earlier predictive models is somewhat limited.

In accordance with our national guidelines, our institute cancels any cycle where more than two follicles larger than 16 mm develop.[18] Given this, we included the number of follicles-whether ruptured or impending rupture on the day of IUI as a parameter in our study. However, our findings

indicated that the number of follicles did not play a highly significant role in influencing pregnancy outcomes.

As a whole, when all these 10 factors were put together to obtain a IUI predicative score for the couple, the value was found to be highly significant in detecting pregnancy. A Cut off of 14 out of 20 was derived from analysing the data collected, while had a very high sensitivity in predicting the pregnancy outcome.

Limitations

Our study has several notable strengths. Firstly, it is based on a large clinical population receiving routine care, making our findings highly representative of patients commonly seen in infertility centers. Secondly, our analysis spans multiple years, ensuring the stability and reliability of our results.

Our study has certain limitations. One key limitation is the retrospective nature of data collection, which introduces the possibility of unknown confounders inherent to this study design. Although treatment recommendations were guided by internal protocols, the final decision to undergo IUI and the number of cycles pursued were made by the couples themselves. This introduces the potential for selection bias, as treatment choice and continuation may have influenced outcomes. If couples with a lower likelihood of conception discontinued treatment earlier than those with a higher probability, our results might be skewed towards success. Additionally, factors influencing a couple's choice of treatment such as financial considerations can vary between infertility centres and across different countries, potentially limiting the generalizability of our results. The clinical variables included in our scoring model were assessed only once per couple, either at the first successful cycle or the final unsuccessful attempt. While parameters like age, AMH, TPMSC, BMI, endometrial thickness, number of attempts, and number of follicles may fluctuate over time, their short-term stability suggests minimal influence on our findings. Notably, in 95% of our cohort, all IUI cycles were completed within 12 months, with 50% occurring in consecutive menstrual cycles over a span of three to four months. Lastly, because our data were extracted retrospectively from routine patient records, some variables had missing values. However, as the missing data appeared to be randomly distributed, we applied multiple imputation techniques to minimize their impact on our analysis.

CONCLUSION

Thus, we conclude that IUI success is influenced by multiple clinical factors like female age, ovarian reserve markers, sperm parameters. The proposed scoring system integrates these parameters to provide an individualized pregnancy probability estimate. This tool can support clinicians in counselling patients more effectively, aiding in decision making and setting realistic expectations. Its ease of use makes it suitable for routine clinical practice, with potential to optimize patient selection and improve resource allocation. Further validation in larger diverse population is recommended to confirm its utility and generalizability of this scoring model.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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