Predictive Factors for Pregnancy after Intrauterine Insemination: A Prospective Study

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Abstract:

Introduction: Intrauterine insemination (IUI) is a widely used first-line treatment for selected cases of subfertility due to its simplicity, cost-effectiveness, and minimal invasiveness. However, its success is influenced by multiple factors related to the couple, ovarian stimulation protocol, and semen parameters. Identifying predictive factors for pregnancy following IUI can help in optimizing patient selection and improving outcomes.

Objectives: To evaluate the clinical, hormonal, and procedural factors associated with successful pregnancy following IUI and to identify significant predictors that influence the likelihood of conception.

Materials and Methods: This prospective interventional open-label study was conducted in the Department of Obstetrics and Gynecology, Eden Hospital, Medical College and Hospital, Kolkata, over one year. Protocol development began in November 2016, and patient recruitment and data collection took place from January to July 2017 after ethics committee approval, followed by data analysis and thesis preparation. Women seeking infertility treatment in the OPD were counselled and enrolled after meeting the inclusion and exclusion criteria. Based on a previous study [xiv] and the formula $n = 4pq/l^2$, the calculated sample size was 257; however, due to time constraints and single-researcher limitations, 50% of this number ($\approx$130 IUI cycle) were included.

Results: In our study, female age, male age, BMI, and type of infertility were not significantly associated with pregnancy outcomes, although no women were older than 35 years and most pregnancies occurred in men over 35 years, contrasting with Mathieu et al., who reported poorer outcomes with increasing male age [93]. The majority of pregnancies (75%) occurred in women with infertility duration less than six years, with the highest conception rates seen in unexplained infertility (75%) followed by endometriosis (25%). Laparoscopic tubal patency assessment were more common in the conception group. Hormonal analysis showed that all who conceived had LH and FSH $\leq$10 mIU/mL, significantly lower prolactin (p = 0.0298), and no significant differences in TSH. Fasting and postprandial blood sugar levels were higher in the conception group but within normal limits. All pregnancies occurred when two preovulatory follicles were present, while endometrial thickness had no significant effect. Semen analysis revealed significantly higher semen volume, pre-wash sperm count, motility, and post-wash count among those who conceived.

Conclusion: Several factors including cause of infertility, infertility duration, FSH, LH and PROLACTIN level, follicular response, semen volume, prewash sperm count, motility and post-wash sperm count are predictive of IUI success. Careful selection of patients and individualized stimulation protocols based on these predictors can enhance pregnancy outcomes in IUI cycles.

Keywords: Intrauterine insemination, infertility, predictive factors, pregnancy rate, ovarian stimulation, sperm motility.

Introduction

Infertility, defined as the failure to achieve clinical pregnancy within one year of regular frequent unprotected sexual intercourse, affects approximately 10–15% of couples worldwide [1]. Intrauterine insemination (IUI) is one of the most commonly used first-line assisted reproductive technologies (ART), particularly in cases of unexplained infertility, mild male factor infertility, ovulatory dysfunction, and cervical factor infertility [2]. The procedure involves the placement of

washed and concentrated motile sperm directly into the uterine cavity around the time of ovulation, thereby increasing the chances of fertilization by bypassing cervical barriers and enhancing sperm delivery to the oocyte [3].

Despite its widespread application, the success rate of IUI remains relatively modest, ranging between 10% and 20% per cycle [4]. This variability is attributed to multiple factors including patient characteristics, type of ovarian stimulation, number of dominant follicles, endometrial receptivity, and semen quality parameters [5]. Consequently, predicting which couples are more likely to benefit from IUI is crucial to avoid unnecessary delays in progressing to more advanced ART techniques such as in vitro fertilization (IVF).

Female age is consistently reported as a major determinant of IUI success, with conception rates declining significantly after the age of 35 years due to diminished ovarian reserve and oocyte quality [6]. Additionally, the duration of infertility has been shown to inversely correlate with pregnancy rates, with couples experiencing infertility for more than five years exhibiting poorer outcomes with IUI [7]. Hormonal factors such as baseline serum FSH, LH, estradiol, and anti-Müllerian hormone (AMH) levels also play a predictive role in assessing ovarian responsiveness and subsequent fecundability [8].

Endometrial thickness and pattern, as visualized on transvaginal ultrasound during the peri-ovulatory phase, serve as surrogate markers of endometrial receptivity. An endometrial thickness of ≥7–8 mm with a triple-line pattern is considered optimal for implantation, although thresholds may vary across studies [9]. Similarly, the number and size of dominant follicles at the time of ovulation trigger are important predictors, with multifollicular development generally associated with higher pregnancy rates, albeit with an increased risk of multiple gestations. Semen parameters, particularly total motile sperm count (TMSC) post-wash, play a pivotal role in determining IUI outcomes. While a minimum TMSC threshold of 5–10 million is commonly suggested, there is no universally accepted cutoff, and pregnancy can still occur at lower counts under favorable conditions [10]. Other sperm characteristics such as morphology and progressive motility also contribute to the fertilizing potential but are subject to significant inter-laboratory variability.

The type of ovarian stimulation protocol used—whether with clomiphene citrate, letrozole, gonadotropins, or a combination—can significantly influence follicular recruitment and endometrial development. Letrozole, an aromatase inhibitor, has emerged as a favorable alternative due to its lower anti-estrogenic effect on the endometrium compared to clomiphene citrate and its comparable

or better pregnancy outcomes in many studies. Given these multifactorial influences, the present prospective study aims to evaluate and quantify the predictive value of various clinical, biochemical, sonographic, and semen-related parameters in determining pregnancy outcomes following IUI. Identifying such factors is critical for optimizing patient selection, individualizing stimulation protocols, counseling couples effectively, and enhancing the overall cost-effectiveness and efficiency of infertility management.

Materials and Methods

Study Design: Prospective interventional open label study.

Study Setting and timelines: Protocol writing started from November 2016. Patient recruitment and data captured started from January 2017 after obtaining ethics committee approval and continued till July 2017. This was followed by data analysis and thesis writing.

Place of study: Eden hospital, Department of obstetrics and gynecology, Medical College and Hospital Kolkata.

Period of study: One year.

Study Population: Women seeking treatment for infertility from the OPD were counselled and recruited for the study after satisfying the inclusion criteria and exclusion criteria.

Sample Size: Taking reference from earlier study[xiv] and applying the pregnancy rate into the formula of (n=4pq/l2), sample size was calculated as 257. However, as there was time constraint and limited time available for follow up and being single handed researcher, I have taken 50% of the above sample size. Therefore, approximately 130 intrauterine insemination (IUI) cycles were enrolled in the study.

Study Variables

- Husband's Age
- Wife's Age
- Duration of infertility
- Type of Infertility
- Cause of infertility
- BMI
- Diameter of largest follicle (DOLF)
- Endometrial thickness
- LH
- FSH
- FBS
- PPBS
- TSH
- PRL
- Semen characteristics

Inclusion Criteria

➢ **Couples with**

- non severe male factor infertility(semen concentration 5-20 million sperms/ml, normal morphology <30% (WHO criteria) and progressive motility <50% before sperm preparation as per the WHO (1992) guidelines) ,
- Unexplained infertility (couples for whom the results of a standard infertility evaluation are normal (standard tests includes a normal semen analysis [WHO 1992], ovulatory cycles and a HSG or laparoscopy showing patent tubes).
- Minimal endometriosis: score 1–5; mild endometriosis: score 6–15 by the revised AFS criteria.
- Ovulatory dysfunction
➢ Patency of at least one tube, confirmed by diagnostic laparoscopy or hysterosalpingography (HSG)

Exclusion Criteria

- bilateral tubal blockage
- moderate to severe endometriosis
- severe male factor infertility, with TMF postwash of <1 million
- refusing to come for regular follicular study

Statistical Analysis

The data were entered into Microsoft Excel and analyzed using SPSS version 24.0 and GraphPad Prism version 5. Numerical variables were summarized as mean ± standard deviation, while categorical variables were presented as counts and percentages. Statistical analysis included independent (unpaired) t-tests for comparing means between two groups and paired t-tests for within-group comparisons. One-way ANOVA was used for comparing means across more than two groups. Chi-square or Fisher's exact test was applied to compare categorical variables, depending on data suitability. A p-value ≤ 0.05 was considered statistically significant.

Result

Table 1: Association of Husband's and Wife's Age with Conception Outcome

Association of Husband's and Wife's Age		No	Yes	Total
Hus Age	<30	16 (13.6%)	3 (25%)	19 (14.6%)
	30-35	48 (40.7%)	3 (25%)	51 (39.2%)
	>35	54 (45.8%)	6 (50%)	60 (46.2v)
	Total	118 (100%)	12 (100%)	130 (100%)
Wife's Age	<30	89 (75.4%)	6 (50%)	95 (73.1%)
	30-35	29 (24.6%)	6 (50%)	35 (26.9%)
	Total	118 (100%)	12 (100%)	130 (100%)

Table 2: Distribution of Clinical and Demographic Variables According to Pregnancy Outcome Following Intrauterine Insemination (IUI)

Distribution of Clinical and Demographic Variables		No	Yes	Total
Duration	<6 years	53 (44.9%)	9 (75%)	62 (47.7%)
	≥6 years	65 (55.1%)	3 (25%)	68 (52.3%)
	Total	118 (100%)	12 (100%)	130 (100%)
Type of Infertility	Primary	92 (78%)	9 (75%)	101 (77.7%)
	Secondary	26 (22%)	3 (25%)	29 (22.3%)
	Total	118 (100%)	12 (100%)	130 (100%)
C/O/I	ANOVULTN	16 (13.6%)	0 (0.0%)	16 (12.3%)
	ENDOMET	6 (5.1%)	3 (25%)	9 (6.9%)
	PCOS	18 (15.3%)	0 (0.0%)	18 (13.8%)
	UNEXPLND	78 (66.1%)	9 (75%)	87 (66.9%)
	Total	118 (100%)	12 (100%)	130 (100%)
Assessment Of Tubel Patency	HSG	50 (42.4%)	4 (33.3%)	54 (41.5%)
	LAP Dye Test	68 (57.6%)	8 (66.7%)	76 (58.5%)
	Total	118 (100%)	12 (100%)	130 (100%)
BMI	<25	55 (46.6%)	7 (58.3%)	62 (47.7%)
	≥25	63 (53.4%)	5 (41.7%)	68 (52.3%)
	Total	118 (100%)	12 (100%)	130 (100%)
DOLF	<20	56 (47.5%)	9 (75%)	65 (50%)
	21-25	54 (45.8%)	3 (25%)	57 (43.8%)
	>25	8 (6.8%)	0 (0.0%)	8 (6.2%)

	Total	118 (100%)	12 (100%)	130 (100%)
ET	≤8	67 (56.8%)	6 (50%)	73 (56.2%)
	>8	51 (43.2%)	6 (50%)	57 (43.8%)
	Total	118 (100%)	12 (100%)	130 (100%)
Post Wash Count	≤20	30 (25.4%)	0 (0.0%)	30 (23.1%)
	21-40	51 (43.2%)	6 (50%)	57 (43.8%)
	>40	37 (31.4%)	6 (50%)	43 (33.1%)
	Total	118 (100%)	12 (100%)	130 (100%)
Post Wash Motility %	≤40	87 (73.7%)	3 (25%)	90 (69.2%)
	>40	31 (26.3%)	9 (75%)	40 (30.8%)
	Total	118 (100%)	12 (100%)	130 (100%)

Table 3: Association of LH and FSH Levels with Conception Outcome Following Intrauterine Insemination (IUI)

Association of LH and FSH Levels		No	Yes	Total
LH	≤10	99 (83.9%)	12 (100%)	111 (85.4%)
	>10	19 (16.1%)	0 (0.0%)	19 (14.6%)
	Total	118 (100%)	12 (100%)	130 (100%)
FSH	≤10	97 (82.2%)	12 (100%)	109 (83.8%)
	>10	21 (17.8%)	0 (0.0%)	21 (16.2%)
	Total	118 (100%)	12 (100%)	130 (100%)

Table 4: Comparison of Hormonal and Glycemic Parameters with Pregnancy Outcome Following IUI

Pregnancy Outcome Following IUI		Number	Mean	SD	p-value
PRL	No	118	19.2097	6.5211	0.0298
	Yes	12	14.9925	3.8325	
TSH	No	118	2.184	1.6606	0.8799
	Yes	12	2.1075	1.7293	
FBS	No	118	86.4576	6.6995	0.004
	Yes	12	93	12.4023	
PPBS	No	118	108.1695	8.5817	0.0001
	Yes	12	118.5	5.1962	

Table 5: Comparison of Semen Parameters with Pregnancy Outcome Following IUI

Comparison of Semen Parameters		Number	Mean	SD	p-value
S. Vol. (ML)	No	118	2.1991	0.7041	0.0423
	Yes	12	2.625	0.433	
Total sperm count	No	118	105.703	14.2381	0.3215
	Yes	12	110.5	28.0794	
Initial Sperm morphology	No	118	69.9322	21.749	0.1549
	Yes	12	79	7.6038	
Initial sperm Motility	No	118	62.5424	17.6769	0.2525
	Yes	12	68.5	9.0303	
Change in count	No	118	24.2542	10.7363	0.4286
	Yes	12	21.6667	10.9406	
Change in motility %	No	118	23.3436	10.8201	0.651
	Yes	12	21.8135	14.0622	

Table 6: Comparison of Pre-Wash Semen Parameters with Pregnancy Outcome

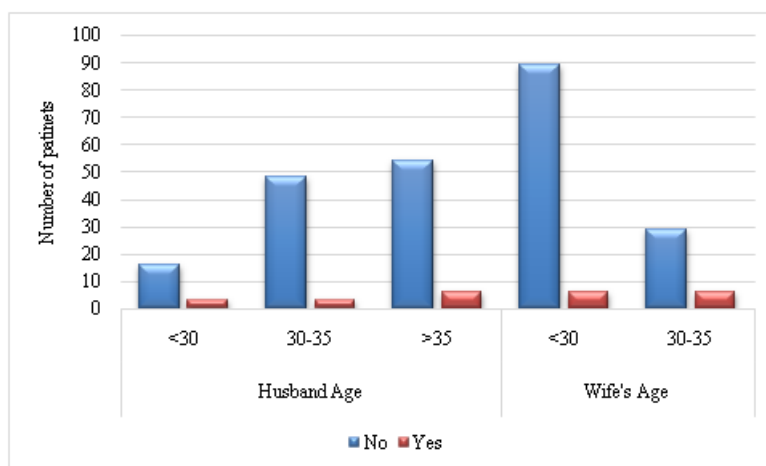| Comparison of Pre-Wash Semen Parameters		Number	Mean	SD	p-value
Pre wash count	No	118	62.0339	19.5269	0.0036
	Yes	12	79.1667	13.6237	
Pre wash motility %	No	118	58.946	17.382	0.0033
	Yes	12	74.6371	16.6284	

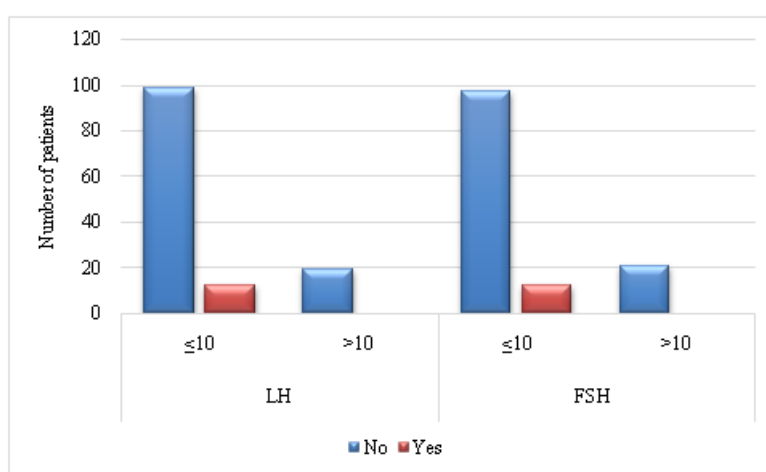**Figure 1: Association of Parental Age with Pregnancy Outcome**

Figure 2: Relationship Between LH/FSH Levels and IUI Outcomes

Among the study participants, a higher proportion of couples with the husband's age over 35 years had conception (50%) compared to those aged 30–35 years (25%) and below 30 years (25%). However, the majority of the husbands in both conception and non-conception groups were aged above 30 years. Regarding the wife's age, 50% of those who conceived were aged 30–35 years, while the remaining 50% were below 30 years. In contrast, among those who did not conceive, a larger proportion (75.4%) of wives were aged below 30 years. Overall, most couples in the study had wives aged below 30 years and husbands aged between 30–35 years.

In this study of 51 infertile couples undergoing 130 IUI cycles, pregnancy occurred in 12 cases (9.2%). Among husbands, the majority were aged >35 years in both pregnant (50%) and non-pregnant (45.8%) groups. Most wives were <30 years old, with 75.4% in the non-pregnant and 50% in the pregnant group. Infertility duration <6 years was associated with a higher pregnancy rate (75% vs. 44.9%). Primary infertility was more common in both groups (78% and 75% respectively). Unexplained infertility was the leading cause in

both groups (66.1% non-pregnant vs. 75% pregnant), followed by PCOS and endometriosis. Tubal patency was assessed mainly by laparoscopy in the pregnant group (66.7%) and HSG in the non-pregnant group (42.4%). A BMI <25 was more frequent among pregnant women (58.3%). Association of the diameter of the largest follicle (DOLF) vs outcome was not statistically significant. Endometrial thickness >8 mm was seen in 50% of pregnant cases. Higher post-wash sperm count (>40 million) and motility >40% were significantly associated with conception (50% and 75% respectively).

Among the 130 IUI cycles, it was observed that all 12 patients who achieved conception had luteinizing hormone (LH) levels ≤10 mIU/mL, whereas 16.1% of the non-conceived group had LH levels >10 mIU/mL. This indicates a favorable association between lower LH levels and conception. Similarly, all patients who conceived had follicle-stimulating hormone (FSH) levels ≤10 mIU/mL, while 17.8% of those who did not conceive had FSH levels >10 mIU/mL. Overall, 85.4% of the total patients had LH ≤10, and 83.8% had FSH ≤10. The analysis revealed that the mean

serum prolactin (PRL) level was significantly lower in patients who conceived (14.99 ± 3.83 ng/mL) compared to those who did not (19.21 ± 6.52 ng/mL), with a p-value of 0.0298. Thyroid-stimulating hormone (TSH) levels showed no significant difference between the conceived (2.11 ± 1.73 µIU/mL) and non-conceived groups (2.18 ± 1.66 µIU/mL; p = 0.8799). However, both fasting blood sugar (FBS) and postprandial blood sugar (PPBS) levels were significantly higher in the conceived group (FBS: 93 ± 12.40 mg/dL, PPBS: 118.5 ± 5.20 mg/dL) compared to the non-conceived group (FBS: 86.46 ± 6.70 mg/dL, PPBS: 108.17 ± 8.58 mg/dL), with p-values of 0.004 and 0.0001 respectively.

In this analysis, the mean semen volume was significantly higher in patients who conceived (2.63 ± 0.43 mL) compared to those who did not (2.20 ± 0.70 mL), with a statistically significant p-value of 0.0423. However, total sperm count was slightly higher in the conceived group (110.5 ± 28.08 million/mL) compared to the non-conceived group (105.70 ± 14.24 million/mL), though this difference was not statistically significant (p = 0.3215). Similarly, initial sperm morphology and motility were better among those who conceived ($79 \pm 7.60\%$ and $68.5 \pm 9.03\%$, respectively), but the differences did not reach statistical significance (p = 0.1549 and 0.2525, respectively). Changes in sperm count and motility post-processing were also not significantly different between the two groups.

Pre-wash semen parameters showed significant differences between patients who conceived and those who did not. The mean pre-wash sperm count was significantly higher in the conceived group (79.17 ± 13.62 million/mL) compared to the non-conceived group (62.03 ± 19.53 million/mL), with a p-value of 0.0036. Similarly, pre-wash motility was significantly better among those who conceived ($74.64 \pm 16.63\%$) than those who did not ($58.95 \pm 17.38\%$), which was also statistically significant (p = 0.0033).

Discussion

The present study of 130 IUI cycles demonstrates compelling associations between several clinical, hormonal, and semen parameters with successful conception. Notably, couples with a shorter duration of infertility (<6 years) and those with husbands and wives aged between 30–35 years exhibited higher pregnancy rates, echoing earlier research that highlights the detrimental impact of prolonged infertility and advancing age on fertility outcomes [11][12].Endocrine evaluation revealed that lower prolactin levels were significantly associated with conception, whereas TSH did not differ significantly between groups. This aligns with previous studies showing that mild hyperprolactinemia can impair follicular development and implantation, while euthyroid status is permissive for conception [13][14]. Elevated fasting and postprandial blood glucose among those who conceived may appear counterintuitive; however, this finding resonates with observations in certain populations where mild hyperglycemia correlates with optimal endometrial receptivity—though the exact mechanism remains debatable and requires caution [15][16]. Semen analysis yielded several interesting findings. Semen volume was significantly greater in those who conceived, aligning with literature that links higher ejaculate volume to improved sperm transport and fertilization potential [17]. Pre-wash sperm count and motility were also significantly better among conceiving couples, consistent with IUI success predictors reported by multiple studies that emphasize the importance of pre-preparation parameters in determining success [18][19]. While post-wash changes in count and motility were not significant, this may reflect the variability introduced during processing and the relatively small number of successful outcome cases in this study. Both male and female factors significantly influence IUI success. For female partners, optimal endocrine status, shorter infertility duration, and ideal age seem to be critical; for male partners, semen quality—particularly baseline concentration and motility—remains a key determinant. These results underscore the importance of comprehensive pre-IUI evaluation, as advocated in recent fertility protocols, including endocrine profiling, metabolic screening, and detailed semen assessment to personalize treatment and enhance success rates [20].

Conclusion

The study shows that successful pregnancy following intrauterine insemination (IUI) is significantly associated with several clinical and laboratory parameters. A shorter duration of infertility and unexplained infertlity were favorable prognostic indicators. Hormonal profiling revealed that Day3 FSH and LH < 10IU/L, lower serum prolactin levels had a statistically significant correlation with positive pregnancy outcomes, while TSH did not show significant differences. Additionally, better semen characteristics—particularly higher semen volume, pre-wash sperm count, and motility—were significantly linked with improved pregnancy rates. Although the changes in sperm parameters post-wash and during follow-up did not reach statistical significance, the overall trend suggested better semen quality contributes positively to IUI outcomes, the importance of comprehensive evaluation and optimization of both female and male factors in enhancing the success rates of IUI procedures.

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