

COMPARATIVE ANALYSIS OF CLINICAL OUTCOME OF INTRACYTOPLASMIC MORPHOLOGICALLY SELECTED SPERM INJECTION (IMSI) AND INTRACYTOPLASMIC SPERM INJECTION (ICSI)

Vikas Dhyani¹, Veerpal Kaur², Bhupinderjit Kaur Heer^{3*}

¹M sc. Student, ^{2,3}Associate Professor,

Department of Clinical Embryology

Dolphin PG College, Chunni Kalan, Fatehgarh Sahib, Punjab, INDIA

*Corresponding Author: bhupinderjitkaur.heer@gmail.com

Abstract— The present study aimed to compare the clinical outcomes of Intracytoplasmic Sperm Injection (ICSI) and Intracytoplasmic Morphologically Selected Sperm Injection (IMSI) in infertile couples undergoing assisted reproductive treatment. A total of 100 couples treated at Nova IVF Fertility Clinic, Chandigarh, and equally allocated into two groups: ICSI (n = 50) and IMSI (n = 50). Demographic characteristics and semen parameters were assessed, along with IVF failure history, embryo quality, implantation rate, clinical pregnancy rate, and miscarriage rate. Other variables, including male age, sperm concentration, and motility, were comparable between the two groups. IMSI demonstrated significantly improved sperm morphology compared to ICSI ($p < 0.001$), with a corresponding reduction in abnormal sperm forms. The IMSI group showed a significantly higher proportion of Grade A embryos and a higher clinical pregnancy rate (86% vs. 64%). Implantation rates were higher in the IMSI group, though the difference was not statistically significant. The frequency of repeated IVF failures was significantly lower in the IMSI group ($\chi^2 = 8.23$, $p = 0.016$). Miscarriage rates were lower following IMSI; however, this difference did not reach statistical significance. In conclusion, IMSI appears to improve sperm selection, embryo quality, and pregnancy outcomes compared to conventional ICSI, particularly in selected cases of male factor infertility and first IVF cycles. Larger multicentric studies evaluating live birth outcomes are warranted to confirm these findings.

Keywords—*Intracytoplasmic sperm injection, IMSI, ICSI, IVF failure, Embryo quality, Implantation rate*

I. INTRODUCTION

Assisted reproductive technologies (ART) have significantly advanced the management of infertility, with intracytoplasmic sperm injection (ICSI) becoming one of the most widely utilized techniques globally. Originally developed to address severe male factor infertility, ICSI is now frequently applied across a broader spectrum of cases, including those without male factor involvement (Haddad et al., 2021). However, concerns persist regarding its indiscriminate use and the limitations of sperm selection under conventional magnification (200–400x), which may overlook subtle morphological defects associated with poor fertilization and embryo development outcomes (Geng et al., 2020).

Infertility is a global health concern affecting approximately 10–15% of couples of reproductive age, with male factor infertility contributing to nearly half of these cases. Over the past few decades, assisted reproductive technologies (ARTs) have revolutionized the management of infertility, offering hope to millions of couples worldwide. Among these, intracytoplasmic sperm injection (ICSI) has emerged as a cornerstone technique, particularly in cases of severe male factor infertility (Zhang et al., 2024). Introduced in the early 1990s, ICSI involves the direct injection of a single sperm into the cytoplasm of a mature oocyte, bypassing many natural barriers to fertilization. While ICSI has significantly improved fertilization rates and clinical outcomes, concerns remain regarding the selection of spermatozoa, especially in cases where conventional morphology and motility assessments may not adequately predict fertilization potential or embryo viability

(Baldini et al., 2021). This study aims to evaluate and compare the clinical outcomes of IMSI and ICSI in a cohort of infertile couples undergoing ART. The primary endpoints include fertilization rate, embryo quality, implantation rate, clinical pregnancy rate, and miscarriage rate. Secondary outcomes live birth rate are also assessed to provide a holistic view of the efficacy of both techniques.

2. MATERIAL AND METHODS

STUDY CENTRE: Study will be performed in Nova IVF fertility clinic sector 34 Chandigarh (<https://www.novaivffertility.com/about-us>) among the infertile couples those are already taking treatment of infertility. Even the previous record of older patients will also be check to complete the research (2021-2025 till Jan). This will be Open Prospective clinical trial.

STUDY SETTING: This observational comparative study included 100 couples undergoing ART at a fertility clinic. Participants were divided into two groups:

Group A (ICSI): 50 couples

Group B (IMSI): 50 couples

The study is comparative outcome of different sperm injection so selected or volunteer are al so data collected and measured on basic of survey among the patients whose are already going through the different techniques of sperm injection and also on base of observation of outcome results. The Patients are counselled about intracytoplasmic sperm injection, and IMSI as a new assisted reproduction technique and are informed of the many unknown aspects of this new

treatment. Demographic profile, Semen for analysis, Clinical analysis, Questionnaire to assess groups

3. RESULT

In order to evaluate the outcome of two assisted reproductive techniques ICSI and IMSI. 100 (ICSI=50, IMSI=50) couple are included in the study. Couple are firstly categorized determine their age (Table.1). Also their type of fertility also mentioned wheatear it is primary or secondary.

Table: 1 Showing the Age range and type of infertility of ICSI and IMSI groups

MEAN AGE	ICSI (N=50)	IMSI(N=50)
Female	28±1.74	29±2.41
Male	32±0.81	31±7.21
INFEETILITY TYPE		
Primary	38 (76%)	30 (60%)
Secondary	12 (24%)	20 (40%)

The demographic and clinical characteristics of the ICSI and IMSI groups are presented in Table 1. Each group included 50 couples. The mean female age in the ICSI group was 28 ± 1.74 years, compared to 29 ± 2.41 years in the IMSI group, while the mean male age was 32 ± 0.81 years and 31 ± 7.21 years, respectively. Comparison of continuous variables, including male and female age, was performed using the Student's t-test, which revealed no statistically significant difference between the two groups ($p > 0.05$).

Regarding infertility type, primary infertility was observed in 38 cases (76%) in the ICSI group and 30 cases (60%) in the IMSI group, whereas secondary infertility was present in 12 cases (24%) and 20 cases (40%), respectively. The distribution of infertility type between the groups was analyzed using the chi-square test, and no statistically significant difference was found ($p > 0.05$). Male factor infertility was present in 100% of participants in both groups, confirming homogeneity of diagnosis. Overall, the two groups were statistically comparable at baseline, ensuring that differences in treatment outcomes could be attributed to the fertilization technique rather than confounding demographic factors.

Balaban et al. (2011), who reported no significant improvement in the clinical outcome of the IMSI group for an unselected patient population which is in accordance with our study, whereas higher implantation rates for male factor patients showed that the IMSI procedure may be beneficial for these patients. It is logical to think that IMSI may improve IVF outcome measures in male factor infertility (Balaban et al., 2011).

Table:2 Semen Analysis Parameters

Parameter	Group A (ICSI)	Group B (IMSI)	p-value
Sperm concentration (million/mL)	12.5 ± 3.2	12.7 ± 3.1	0.79
Motility (%)	38.2 ± 5.5	39.0 ± 5.2	0.61
Morphology (%)	3.1 ± 0.8	4.5 ± 1.0	<0.001
Abnormal forms (%)	96.9 ± 0.8	95.5 ± 1.0	<0.001

The semen analysis parameters of the ICSI (Group A) and IMSI (Group B) groups are summarized in Table 2. Continuous variables were expressed as mean ± standard deviation and compared between the two groups using the Student's t-test. The mean sperm concentration was 12.5 ± 3.2 million/mL in the ICSI group and 12.7 ± 3.1 million/mL in the IMSI group, with no statistically significant difference observed ($p = 0.79$). Similarly, sperm motility showed comparable values between the two groups (38.2 ± 5.5% vs. 39.0 ± 5.2%), and the difference was not statistically significant ($p = 0.61$).

In contrast, a statistically significant difference was observed in sperm morphology. The IMSI group demonstrated a significantly higher percentage of normal sperm morphology (4.5 ± 1.0%) compared to the ICSI group (3.1 ± 0.8%), with a highly significant difference ($p < 0.001$). Correspondingly, the percentage of abnormal sperm forms was significantly lower in the IMSI group (95.5 ± 1.0%) than in the ICSI group (96.9 ± 0.8%), and this difference was also highly statistically significant ($p < 0.001$). These findings indicate that while sperm concentration and motility were comparable between the two groups, IMSI was associated with significantly improved sperm morphology, reflecting superior sperm selection.

Table: 3 showing the no. of IVF Failure of ICSI and IMSI groups

No. of IVF Failure	ICSI (n=50)	IMSI(n=50)
0	11 (22%)	22(44%)
1	16 (32%)	14(28%)
≥ 2	23(46%)	12 (24%)

The distribution of IVF failure frequency among the ICSI and IMSI groups is presented in Table 3. Each group consisted of 50 patients. The comparison of categorical variables, including the number of IVF failures, was performed using the Chi-square test. In the ICSI group, 11 (22%) patients had no IVF failure, 16(32%) patients experienced one IVF failure, and 23 (46%) patients had two or more IVF failures. In contrast, in the IMSI group, 22(44%) patients had no IVF failure, 14 (28%) patients had one IVF failure, and only 12 (24%) patients experienced two or more IVF failures.

Chi-square test showed significant difference was observed in the frequency of IVF failures between the two groups ($\chi^2 = 8.23$, $df = 2$, $p = 0.016$). The IMSI group demonstrated a significantly higher proportion of patients with no IVF failure and a lower proportion of patients with recurrent IVF failures (≥ 2) compared to the ICSI group. These findings indicate that IMSI is associated with a reduced rate of repeated IVF failures, suggesting improved clinical outcomes.

Table: 4 showing the percentage of Clinical Pregnancy, implantation and Miscarriage

Variable	ICSI (n=50)	IMSI (n=50)
No. of embryo transfer	3	3
Embryo quality (Grade A)	21(42%)	30(60%)
Clinical Pregnancy (%)	32(64%)	43 (86%)
Implantation (%)	27 (84.3%)	39 (91%)
Miscarriage (%)	12 (44.4%)	10 (26%)

The clinical outcomes of the ICSI and IMSI groups are summarized in Table 4. Both groups underwent the transfer of three embryos, ensuring uniformity of the embryo transfer protocol. The proportion of Grade A embryos was higher in the IMSI group (60%) compared to the ICSI group (42%), and this difference was statistically significant (Chi-square test, $p < 0.05$). The clinical pregnancy rate was significantly higher in the IMSI group (43/50; 86%) compared to the ICSI group (32/50; 64%) (χ^2 test, $p < 0.05$). Similarly, the implantation rate was higher in the IMSI group (91%) than in the ICSI group (84.3%); however, this difference did not reach statistical significance ($p > 0.05$). The miscarriage rate was lower in the IMSI group (26%) compared to the ICSI group (44.4%), though this difference was not statistically significant ($p > 0.05$). Overall, the findings indicate that IMSI is associated with improved embryo quality and higher clinical pregnancy rates, while implantation and miscarriage rates showed no significant difference between the two groups.

4. DISCUSSION

This study compared the clinical outcomes of Intracytoplasmic Sperm Injection (ICSI) and Intracytoplasmic Morphologically Selected Sperm Injection (IMSI) in infertile couples undergoing assisted reproductive treatment. The results indicate that IMSI offers notable advantages over conventional ICSI, particularly in terms of sperm morphology, embryo quality, and pregnancy outcomes.

Baseline demographic characteristics and semen parameters such as sperm concentration and motility were comparable between the two groups, indicating adequate group matching. However, sperm morphology was significantly improved in the IMSI group, likely due to the use of high-magnification microscopy that enables selection of spermatozoa with optimal nuclear integrity. This finding supports previous reports highlighting the association between detailed sperm morphology assessment and improved fertilization potential (Bartoov et al., 2001; Balaban et al., 2011). A key observation of this study was the significantly lower frequency of repeated

IVF failures in the IMSI group. Patients undergoing IMSI demonstrated a higher proportion of cycles without prior IVF failure, suggesting that enhanced sperm selection may reduce the risk of repeated implantation failure. Similar improvements in pregnancy outcomes following IMSI have been reported in couples with previous ART failures (Shalom-Paz et al., 2015). Embryo quality assessment revealed a higher percentage of Grade A embryos in the IMSI group, which may be attributed to reduced sperm DNA damage and improved chromatin integrity. This observation is consistent with earlier studies demonstrating improved embryo development following high-magnification sperm selection (Vanderzwalmen et al., 2008).

Clinically, the IMSI group achieved a significantly higher pregnancy rate compared to the ICSI group. Although implantation rates were numerically higher in the IMSI group, the difference was not statistically significant. These findings are in partial agreement with Antinori et al. (2008), who reported improved clinical outcomes with IMSI in severe male factor infertility, while other studies have shown no clear benefit in unselected populations (Leandri et al., 2013). Miscarriage rates were lower in the IMSI group, although the difference did not reach statistical significance. This trend may reflect improved genetic quality of the selected spermatozoa. The main limitations of this study include its single-centre design and limited sample size. Further multicentric studies with larger cohorts and live birth outcomes are required to validate these findings and define optimal patient selection criteria for IMSI.

CONCLUSION

The present comparative study evaluated the clinical outcomes of Intracytoplasmic Sperm Injection (ICSI) and Intracytoplasmic Morphologically Selected Sperm Injection (IMSI) in infertile couples undergoing assisted reproductive treatment. The findings demonstrate that while baseline demographic parameters and semen concentration and motility were comparable between the two groups, IMSI showed a clear advantage in terms of sperm morphology, embryo quality, and key clinical outcomes. IMSI was associated with a significantly higher proportion of Grade A embryos and improved clinical pregnancy rates compared to ICSI. Additionally, patients in the IMSI group exhibited a lower frequency of repeated IVF failures and a reduced miscarriage rate, although the latter did not reach statistical significance. These results suggest that enhanced sperm selection under high magnification in IMSI may positively influence fertilization competence and early embryonic development. Notably, IMSI appeared particularly beneficial in patients with no prior IVF failures and those with severe male factor infertility, whereas ICSI demonstrated relatively better outcomes in couples with multiple previous failed cycles, albeit with a higher miscarriage risk. This highlights the importance of individualized treatment selection rather than a uniform application of ART techniques. In conclusion, IMSI offers significant clinical advantages over conventional ICSI in terms of embryo quality and pregnancy success. However, given the study's sample size and single-centre design, further large-scale, multicentric randomized trials focusing on live birth rates and cost-effectiveness are warranted to validate these findings and refine patient selection criteria for optimal ART outcomes.

REFERENCES

- [1] Van Steirteghem AC, Nagy Z, Joris H, Liu J, Staessen C, Smits J, Wisanto A, Devroey P. High fertilization and implantation rates after intracytoplasmic sperm injection. *Hum Reprod.* 1993;8(7):1061–1066.
- [2] Bartoov B, Berkovitz A, Eltes F. Selection of spermatozoa with normal nuclei to improve the pregnancy rate with intracytoplasmic sperm injection. *N Engl J Med.* 2001;345(14):1067–1072.
- [3] Bartoov B, Berkovitz A, Eltes F, Kogosowski A, Menezo Y, Barak Y. Real-time fine morphology of motile human sperm cells is associated with IVF-ICSI outcome. *J Androl.* 2002;23(1):1–8.
- [4] Bartoov B, Berkovitz A, Eltes F, Kogosovsky A, Yagoda A, Lederman H, Barak Y. Pregnancy rates are higher with intracytoplasmic morphologically selected sperm injection than with conventional intracytoplasmic injection. *Fertil Steril.* 2003;80(6):1413–1419.
- [5] Antinori M, Licata E, Dani G, Cerusico F, Versaci C, D'Angelo D, Antinori S. Intracytoplasmic morphologically selected sperm injection: a prospective randomized trial. *Reprod Biomed Online.* 2008;16(6):835–841.
- [6] Vanderzwalmen P, Hiemer A, Rubner P, Bach M, Neyer A, Stecher A, Cassuto G. Blastocyst development after sperm selection at high magnification is associated with size and number of nuclear vacuoles. *Reprod Biomed Online.* 2008;17(5):617–627.
- [7] Greco E, Scarselli F, Iacobelli M, Rienzi L, Ubaldi F, Ferrero S, Tesarik J. Efficient treatment of infertility due to sperm DNA damage by ICSI with testicular spermatozoa. *Hum Reprod.* 2005;20(1):226–230.
- [8] Garolla A, Fortini D, Menegazzo M, De Toni L, Nicoletti V, Moretti A, Foresta C. High-power microscopy for selecting spermatozoa for ICSI by physiological status. *Reprod Biomed Online.* 2008;17(5):610–616.
- [9] Balaban B, Yakin K, Alatas C, Oktem O, Isiklar A, Urman B. Clinical outcome of intracytoplasmic injection of spermatozoa morphologically selected under high magnification: a prospective randomized study. *Reprod Biomed Online.* 2011;22(5):472–476.
- [10] Leandri RD, Gachet A, Pfeffer J, Celebi C, Rives N, Carré-Pigeon F, Parinaud J. Is intracytoplasmic morphologically selected sperm injection beneficial in the first ART cycle? A multicentric randomized controlled trial. *Andrology.* 2013;1(5):692–697.
- [11] Shalom-Paz E, Alshalati J, Shehata F, Jimenez C, Son W, Holzer H, Buckett W, Casper RF. Clinical and economical analysis of intracytoplasmic morphologically selected sperm injection (IMSI). *Reprod Biomed Online.* 2015;30(4):365–371.