

**ICSI-A RAY OF HOPE IN DIFFERENT CAUSES OF INFERTILITY**

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ABSTRACT

Background- Different success rate of Intracytoplasmic Sperm injection (ICSI) are seen in different causes of infertility. In present study, we evaluated ICSI outcome in different causes of infertility.

Materials and Methods- This is a retrospective study of ICSI cycles performed on 120 subjects at ART unit of Omega hospital Pvt Ltd, Nagpur between Jan 2020 and December 2021 to see ICSI outcomes in different causes of infertility. **Results-** In present study, out of 120 subjects, majority 52(43%) subjects were in the age group of 31-35 years followed by 49(41%) subjects in 25-30 years age group. Majority 55(46%) subjects were having infertility of 5-10 years, 52(43%) subjects were having infertility of <5 years. Majority 83(69%) subjects were having primary infertility, 45(37%) subjects had male infertility, 41(34%) subjects had ovulatory factor, 15(13%) subjects had unexplained infertility. 77(64%) subjects had biochemical pregnancies. 64(53%) subjects had clinical pregnancy by Ultrasound. 59(49%) subjects had live birth. 17(14%) subjects had abortion, 13 (11%) subjects had preterm labour. 3(2%) babies had to be admitted in NICU. Most important 74% mothers & 96% babies reported no complications. **Conclusion-** We found that ICSI is an effective option in couples with different causes of infertility. Therefore, physicians should have adequate training and required information regarding ICSI to improve the pregnancy outcomes reducing burden of infertility in the community.

KEYWORDS : ICSI, Pregnancy Rate, causes of infertility**INTRODUCTION-**

Infertility is a significant global health problem. It affects 15% of couples world-wide. 56% of these couples need treatment to conceive.¹

Unexplained infertility is seen in approximately 20% of sub-fertility.²

In unexplained infertility, no abnormalities are found during the fertility work-up including semen analysis, tests of ovulation, tubal patency, and pelvic cavity.³

Whether ICSI should be preferred to IVF for unexplained infertility is not clear. Oocyte damage is one of the potential problems with ICSI & it is unpredictable.⁴

Intracytoplasmic Sperm injection (ICSI) is an operative technology in the fields of ART.⁵

ICSI has become a gold standard technique for the treatment of male infertility.⁶

ICSI use has increased from 15.4 to 66.9% during 1996–2012 in non-male factor.⁷

General use of ICSI for infertility is not recommended in ART.⁸ ICSI may be useful to overcome tubal factor and endometriosis.⁹

Studies have shown a higher risk of congenital abnormalities, cardiovascular, musculoskeletal defect, low birth weight,

preterm delivery and increase perinatal mortality in IVF/ ICSI children.¹⁰

AIMS & OBJECTIVES-

To evaluate ICSI outcomes in different causes of infertility.

MATERIALS AND METHODS

This is a retrospective study of ICSI cycles performed on 120 patients at the Assisted Reproductive Technology (ART) unit of Omega hospital Pvt Ltd, Nagpur between Jan 2020 and Dec 2021. Sample size of 120 was considered sufficient for this study assuming the 15% prevalence of infertility in India, 7% precision and 95% Confidence Interval. Informed consent was sought from the study subjects to participate and to use their data from previous clinical records. Medical record of patients who underwent full assessment of infertility were identified. The patients' data including history, female age, and laboratory results, such as the assessment of follicle-stimulating hormone (FSH), Blood Hormones Assay and the details of the husband's semen analysis were collected from their files.

Male factor infertility was determined according to WHO criteria. Female was investigated for various factors of infertility.

Eligibility of study subjects was determined on the basis of following criteria

Inclusion criteria-

- Male infertility
- Ovarian infertility

- Tubal infertility
- Unexplained infertility
- Endometriosis

Exclusion criteria-

- Testicular atrophy
- Anatomical abnormalities
- Infection
- Uterine fibroids
- Systemic disease
- History of ICSI/IVF failure more than three times

Stimulation protocol and embryology procedures

Ovarian stimulation was started on menstrual day 3. The dose of gonadotropin was determined based on the subject age, her day 3 FSH level, and Antral Follicle Count (AFC). Response of stimulation was monitored by follicular growth and oestradiol (E2) level. hCG was given when three or more follicles reach the size of 17mm. Ovum pick up was done 34–36h post hCG. For ICSI cycles, cumulus was removed 2h after oocyte retrieval to examine oocyte maturation. Metaphase II (MII) oocytes were injected by husband's spermatozoa, at least 1h after removing the cumulus cells. Oocytes that did not complete maturation were discarded. Fertilization was assessed 16–18h after insemination.

Operational definitions-

Biochemical pregnancy was determined by a positive human chorionic gonadotropin (hCG) 14 days after the embryo transfer.

Clinical pregnancy was defined by gestational sac and fetal heart using ultrasound scan after 6–7 weeks of pregnancy.

Live birth was defined as delivery of a live child 24 – 40weeks after conception.

Table 1-Questionnaire

Parameters studied
Age in years
Type of Infertility
Duration of Infertility in years
No. of previous cycles
Total dose of gonadotropin in international units (IU)
No. of Biochemical & pregnancies
Live Birth Rate
Complications in mother & baby

Statistical analysis

Statistical analysis was performed by SPSS Version 10.1, 2011. Data were expressed as means, S.D., median, percentages and 95% confidence interval (95% CI).

RESULTS

Table 2- Demographic characteristics of study subjects

Age distribution	No. of subjects n=121	% of subjects n=121
25-30 years	49	41%
31-35 years	52	43%
36-40 years	18	15%
Duration of Infertility		
<5 years	52	43%
5-10 years	55	46%
11-15 years	13	11%
Type of Infertility		
Primary	83	69%
Secondary	37	31%

In present study, out of 121 subjects, majority 52(43%) subjects were in the age group of 31-35 years followed by 49(41%) subjects in 25-30 years age group & 18(15%) subjects in 36-40 years age group.

Mean age was 31.6 years ±3.95 S.D & Median age was 32 years Majority 55(46%) subjects were having infertility of 5-10 years, 52(43%) subjects were having infertility of <5 years while 13(11%) subjects were having infertility of 11-15 years. 83(69%) subjects were having primary infertility while 37(31%) subjects were having secondary infertility. (Table 2)

Table 3-Infertility factor & Total dose of Gonadotropin required

Infertility factor	No. & % of subjects n=121	95% Confidence Interval
Male factor	45(37%)	29-47%
Ovulatory factor	41(34%)	26-44%
Unexplained infertility	15(13%)	7-20%
Tubal factor	8 (7%)	3-13%
Endometriosis	5(4%)	1-9%
Fibroid	2(2%)	0-6%
Cervical factor	2(2%)	0-6%
Other factors	1(1%)	0-5%
Total dose of Gonadotropins required		
2100-2500 IU	27(23%)	15-31%
2600-3000 IU	16(13%)	8-21%
3100-3500 IU	41 (33%)	31-48%
3600-4000 IU	10(8%)	4-15%
>4000 IU	27(23%)	22-39%

In present study, out of 120 subjects, majority 45(37%, 95% CI 29-47%) subjects had male factor for infertility, 41(34%, 95% CI 26-44%) subjects had ovulatory factor, 15(13%, 95% CI 7-20%) subjects had unexplained infertility, 8 (7%, 95% CI 3-13%) subjects had tubal factor for infertility, 5(4%, 95% CI 1-9%) subjects had endometriosis, 2(2%, 95% CI 0-6%) subjects each fibroid & cervical factor while 1(1%, 95% CI 0-5%) subject had other factors for infertility.

In majority 36(30%, 95% CI 22-39%) subjects, total dose of Gonadotropins required was >4000 IU, in 27(23%, 95% CI 15-31%) subjects, total dose of Gonadotropins required was 2100-2500 IU, in 16(13%, 95% CI 8-21%) subjects, total dose of Gonadotropins required was 2600-3000 IU while in 10(8%, 95% CI 4-15%) subjects, total dose of Gonadotropins required was 3600-4000 IU, ICSI cycle was successful in majority of cases when the dose of gonadotropins exceeded >4000 IU. (Table 3)

Table 4-No. of Biochemical pregnancies, Clinical pregnancies & Live Births

Biochemical pregnancies	No. & % of subjects n=120	95% Confidence Interval
No. of Biochemical pregnancies	77(64%)	55-73%
No. of Clinical pregnancies	64(53%)	44-62%
No. of Live Births	59(49%)	40-58%
Live birth rate in different factors of infertility		
Infertility factor	No. & % of subjects n=120	95% Confidence Interval
Male factor	27 (46%)	33-59%
Ovulatory factor	18 (30%)	4-21%
Unexplained infertility	6(10%)	7-15%
Tubal factor	4 (7%)	3-13%
Endometriosis	1(2%)	0-5%
Fibroid	00 (0%)	00
Cervical factor	2(3%,	0-12%
Other factors	1(2%)	0-5%

In present study, out of 120 subjects, 77(64%, 95% CI 55-73%) subjects had biochemical pregnancies. 64(53%, 95% CI 44-62%) subjects had clinical evidence of pregnancy by

Ultrasound. 59(49%, 95% CI 40-58%) subjects had live birth. In present study, out of 59 subjects with live birth, 27 (46%, 95% CI 33-59%) of subjects of male infertility, (18)30% subjects of ovulatory factor, 6(10%, 95% CI 4-21%) had unexplained infertility followed by 4 (7%) tubal factors, 2(3%, 95% CI 0-12%) had cervical factor & 1(2%) had endometriosis & other factors each after ICSI cycle. (Table 4)

Table 5- Complications in mother & Baby

Complications in mother	No. & % of subjects n=121	95% Confidence Interval
No complications	90 (74%)	64-82%
Abortion	17(14%)	8-22%
Preterm labour	13 (11%)	6-18%
Ectopic pregnancy	1 (1%)	0-5%
Complications in baby	No. & % of subjects n=121	95% Confidence Interval
No complications	116 (96%)	90-99%
Admitted in NICU	3(2%, 95%)	0-7%
Prematurity	2 (2%)	0-6%
Congenital defects	00(0%)	00(0%)
Death	00(0%)	00(0%)

In present study, out of 120 subjects, 17(14%, 95% CI 8-22%) subjects had abortion, 13 (11%, 95% CI 6-18%) subjects had preterm labour, 1 (1%, 95% CI 0-5%) had ectopic pregnancy.

3(2%, 95% CI 0-7%) babies had to be admitted in NICU, 2 (2%, 95% CI 0-6%) had subjects had preterm labour, 0(0%) had congenital defects & death each.

Most important, in 74%, (95% CI 64-82%) mothers & 96%, (95% CI 90-99%) babies, there were no complications. (Fig 8)

DISCUSSION

In present retrospective study, out of 120 subjects, majority 52(43%) subjects were in the age group of 31-35 years followed by 49(41%) subjects in 25-30 years age group & 18(15%) subjects in 36-40 years age group.

Mean age was 31.6 years ± 3.95 years (mean ± S.D.) & Median age was 32 years (Fig 1) Majority 55(46%) subjects were having infertility of 5-10 years, 52(43%) subjects were having infertility of <5 years while 13(11%) subjects were having infertility of 11-15 years.

Majority 83(69%) subjects were having primary infertility while 37(31%) subjects were having secondary infertility. (Table 2) Our findings are consistent with other Song J et al found that average age of 241 women in the ICSI group was 31.2 ± 4.0 years, P = 0.951.¹¹

Mahnaz A et al found that out of 1492 women, mean maternal age was 32.3 ± 5.3 years. They found that the pregnancy rate reduced when the woman's age increased (OR=0.93, 95% CI=0.91-0.95).¹²

Mahnaz A et al found that mean duration of infertility was 7.2 ± 5.07 years.¹² Mahnaz A et al found that 1172 (78.5%) women had primary infertility. 320 (21.5%) women had secondary infertility.¹² Mahnaz A et al found that pregnancy rate was lower in primary infertility than secondary infertility, but there was no significant difference.¹²

In present study, out of 120 subjects, majority 45(37%) subjects had male factor for infertility, 41(34%) subjects had ovulatory factor, 15(13%) subjects had unexplained infertility, 8 (7%) subjects had tubal factor for infertility, 5(4%) subjects had endometriosis, 2(2%) subjects each fibroid & cervical factor while 1(1%) subject had other factors for infertility.

In majority 36(30%) subjects, total dose of Gonadotropins required was >4000 IU, in 27(23%) subjects, it was 2100-2500

IU, in 16(13%) subjects, it was 2600-3000 IU while in 10(8%) subjects, it was 3600-4000 IU, ICSI cycle was successful when the dose of gonadotropins exceeded >4000 IU. (Table 3) Mahnaz A et al found that the occurrence of different causes of infertility was- ovulatory factor (7.4%), tuboperitoneal factor (5.2%), unexplained factor (10%), male factor (59.1%), recurrent abortion (2.1%), uterine factor (0.4%), Mix (14%). Other factors (impotency, vaginismus, genetic disorder, etc) (1.7%). In outcome of ICSI cycles in different causes of infertility, the difference was not statistically significant.¹²

Mahnaz A et al found total dose of gonadotropin of nonpregnant group was significantly higher than pregnant group.¹²

W Alasmari et al found that fertilization rates were higher in the unexplained infertility group than in the severe and mild male infertility groups. There were no significant differences in fertilization rates between the unexplained infertility group and groups with female factor infertility.¹³

In present study, out of 120 subjects, 77(64%) subjects had biochemical pregnancies. 64(53%) subjects had clinical evidence of pregnancy by Ultrasound.

59(49%) subjects had live births.

46% of subjects of male infertility had live birth, 30% subjects of ovulatory factor had live birth followed by tubal factor after ICSI cycle. (Table 4)

W Alasmari et al found that the unexplained infertility group had significantly lower biochemical pregnancy rates than severe and mild male infertility groups.¹³

W Alasmari et al found that the clinical pregnancy rates and live birth rates did not significantly differ between the unexplained and male factor infertility groups. The biochemical pregnancy, clinical pregnancy and live birth rates were significantly lower in female infertility groups than in mild male infertility groups.¹³

In present study, out of 120 subjects, 17(14%) subjects had abortion, 13 (11%) subjects had preterm labour, 1 (1%) had ectopic pregnancy.

3(2%) babies had to be admitted in NICU, 2 (2%) had subjects had prematurity, 0(0%) had congenital defects & death each. Most important, in 74% mothers & 96% babies, there were no complications. (Fig 8)

Wen J et al found in 2008 over 6000 births from ART with an increase in birth defects in patients who underwent ICSI. Combined, IVF and ICSI were associated with an increased risk of birth defects. (αOR of 1.24 (CI 1.09, 1.41). IVF had a reduced risk of birth defects than ICSI in fresh cycles. (OR of 0.68) (CI 0.53, 0.87).¹⁴

Lie RT et al found in 56 studies comparing IVF and ICSI to naturally conceived children, a significantly increased risk of birth defects in both IVF and ICSI children. There was greater increase in those with ICSI than IVF.¹⁵

CONCLUSION-

ICSI is an important treatment option for various indications of infertility. The present study showed that pregnancy rate was affected by the total dose of gonadotropin, endometrial thickness, quality of embryo transferred.

Physicians and embryologists should critically assess the specific needs of each individual patient and utilize ICSI when appropriate indications are present.

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