



Implantation Failure

causes and treatment options



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Failed IVF is a frustrating situation for couples and their fertility doctors. Some infertile couples undergo many IVF cycles and produce good quality embryos but the embryos consistently fail to implant. This is called **Implantation Failure (IF)**. The process of implantation involves two main components, a healthy embryo that should have the potential to implant and a receptive endometrium that should enable implantation.

Experts have found that the endometrium offers a non-receptive environment for an embryo for most of the menstrual cycle except during the short frame of time known as 'window of implantation'. Implantation window is a period during which the endometrium is optimally receptive to implanting blastocyst. This receptive stage of endometrium (implantation window) lasts for the period of 4 days spanning between the days 20 and 24 of a regular menstrual cycle (day LH + 7 to LH + 11).



Causes:

Maternal: Inadequate endometrial receptivity (65% of IF): IF might be due to undiagnosed uterine pathology mainly hyperplasia, polyps, endometritis, synechiae or fibroids. The impact of fibroids without cavity distortion or <4 cm size on implantation remain controversial. Decreased endometrial receptivity could be because of thin lining, altered expression of adhesive molecules, immunological factors or thrombophilias.

Embryonic: Genetic & chromosomal cause (30% of IF): High rate of chromosomal abnormalities in human embryos is responsible for IVF failure in majority of cases. The incidence of chromosomal abnormalities increase significantly with advancing maternal age starting from as early as 30s. By mid-40s, over 75% of human embryos from such women are chromosomally abnormal. The % of implanting embryos is greatly dependent on the maternal age. Around 45% of embryos implant under maternal age of 35 years which falls to 15% at 40-42 years.

Failure of the zona to rupture has been suggested as a possible cause of implantation failure.

Several quality control methods have been suggested for identifying suboptimal components of a culture system which affects embryo growth and hinder implantation.

Multifactorial: (5% of IF): Patients with endometriosis have decreased ovarian response, embryo quality, implantation & pregnancy rates which may cause implantation failure.

Hydrosalpinx lower implantation and pregnancy rates by direct embryo toxicity or adverse effect on endometrium. Reflux of hydrosalpinx fluid into the uterine cavity may result in diminishing embryonic endometrial apposition.

Investigation & Treatment for Implantation Failure

1 Improving endometrial receptivity: Studies have shown that hysteroscopic treatment of intrauterine pathologies improves the pregnancy outcome. Many clinicians recommend hysteroscopic removal of sub mucous fibroids which distort the uterine cavity.

Improvement of uterine blood flow by medications has shown to increase the endometrial thickness in patients with thin endometrium. Endometrial scratching has also increased the chances of implantation.

Many immunological factors are involved in implantation failure, but effectiveness of treatment with immunomodulators remains unresolved. Some authors have reported that prolonged heparin treatment increased the pregnancy rates.

With the advent of **Endometrial Receptivity Array (ERA)** test, it is possible to screen the human endometrium for its receptivity status in natural and stimulated cycles. It is a molecular diagnostic tool that can identify whether the endometrium is receptive or not by analysing the expression of a group of 238 genes

related to endometrial receptivity. It is an OPD procedure done on LH surge + 7 in natural cycle or LH +5 in HRT cycle. The ERA test has shown that some patients have a delayed **window of implantation (WOI)**, others have an advanced WOI and others can unusually have short windows of receptivity. This identification and characterisation of the WOI allows the personalisation of the embryo transfer.

2 Selection of Good quality Embryos: By using pre-implantation genetic screening (PGS) and selecting chromosomally normal embryos for replacement significantly increased the implantation rates. **Assisted hatching** improve pregnancy rates by creating an opening in the zona pellucida either mechanically, chemically or by laser before ET.

Since the introduction of IVF, embryos have been routinely transferred into the uterus around the 4 – 8 cell Stage (day 2-3), at the time when they would naturally be in the fallopian tube. Transfer of embryo at the blastocyst stage is a more physiological approach because the human embryos enter the endometrial cavity only 5 days after fertilisation.

Improved embryo transfer technique is

essential in each cycle and must be done very carefully and gently in cases of implantation failure.

3 Multifactorial Treatment Options: Literature has shown that suppressing endometriosis before planning ART significantly increases the clinical pregnancy and ongoing pregnancy rates. Surgical removal of endometriomas might be deleterious for ovarian reserve.

As explained above hydrosalpinx lowers the pregnancy rate, therefore laparoscopic salpingectomy is recommended in all women with hydrosalpinx before IVF treatment, definitely in cases of implantation failure.

Stress interferes with infertility treatment. Psychotherapy reduces anxiety and depression and possibly enhances conception rates.

At Akanksha IVF center we have many patients of implantation failure referred from other centres. Our team comprising experienced specialists and embryologists is well equipped to handle such cases with good and convincing results.

In few selected cases we advise these couples the option of having **Donor Oocytes or Surrogacy** after intensive counselling.