

## Case Report

# Healthy live birth following ICSI with retrograde ejaculated cryopreserved sperm

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## Abstract

**Background:** Retrograde ejaculation is a medical condition that occurs when semen enters the urinary bladder (retrograde) during orgasm instead of passing through the penis (antegrade). Complete retrograde semen flow causes male infertility. An advanced technique intracytoplasmic sperm injection (ICSI) can be used to achieve fertilization in the case of male sub-fertility e.g. Oligo-Astheno-Teratozoospermia.

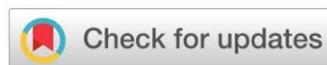
**Case Presentation:** A couple with primary infertility visited the concept fertility centre, where male was diagnosed with retrograde ejaculation for which ICSI was offered with back-up semen freezing after an initial semen analysis.

**Management & Results:** Female was stimulated with long stimulation protocol and thirteen matured eggs were injected by cryopreserved sperms extracted from urine sediment. Fertilization occurred in twelve eggs out of which two good quality embryos were transferred after day five in vitro culturing and rest were vitrified. The patient conceived triplets and gave birth at 33 weeks, but two babies had neonatal death within four days and the patient has one healthy baby girl.

**Conclusion:** Applying assisted reproductive techniques to aid pregnancy in cases of retrograde ejaculation has paucity of knowledge in Pakistan and this case report is the first in Pakistan to describe the diagnosis and successful treatment of infertile couples, with advanced reproductive technology, where the male partner suffered from retrograde ejaculation.

## Keywords

Oligo-Astheno-Teratozoospermia, Retrograde ejaculation, Infertility, Intracytoplasmic sperm injection (ICSI)



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## Introduction

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Retrograde ejaculation is a medical condition in which patient has all sensations of ejaculation with no or reduced antegrade ejaculate<sup>1</sup>. Indications of retrograde ejaculation can be; deficiency or irregularity in the production of ejaculate, the capability to drain the bladder during erection, the presence of orgasm without ejaculation and fructose and spermatozoa in urine specimen after coitus<sup>2</sup>. Multiple factors can be involved in retrograde ejaculation such as congenital abnormality, spinal trauma, retroperitoneal lymph node dissection, diabetes mellitus, bladder neck surgery or an idiopathic reason<sup>3</sup>. Retrograde ejaculation is an uncommon cause of male infertility and in most cases, the treatment comprises of recovery of spermatozoa from the urine or seminal tract followed by assisted reproductive techniques like intrauterine insemination (IUI) or Intracytoplasmic sperm injection (ICSI)<sup>4</sup>. The treatment of retrograde ejaculation has seldom been practiced or published locally. Therefore, our case report is first to publish the case study describing the treatment of infertility due to retrograde ejaculation, followed by ICSI with successful pregnancy outcome in Pakistan.

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## Case Presentation

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A couple presented with the diagnosis of primary infertility. The female was 20 years and the male was 33 years old. The female had a normal hormone profile except raised prolactin and vitamin D deficiency. The male previously diagnosed with diabetes, for which he was taking continuous medication.

For male; a detailed semen analysis was requested and for this patient instructed to produce a semen sample for analysis in a sterile labelled specimen container. Retrograde ejaculation was suspected when no antegrade ejaculate was produced into the container after experiencing orgasm. The later week with the

four days of abstinence, the post ejaculatory alkalinized urine sample was asked to produce by him, so that presence of sperm can be examined. The doubt of retrograde ejaculation was confirmed with the presence of 38 million/ml sperm count where 3 million/ml of them being progressively motile in the urine sediment. Given the deprived morphology and motility of spermatozoa retrieved from the urine, the option of back-up freezing of retrieved alive sperms was considered to avoid surgical sperm retrieval (SSR) on the day of oocyte pick-up.

For this procedure the sample was prepared by advising patient to empty his bladder by passing urine. The male was instructed to get alkaline urine by drinking one tablespoon of baking soda in a large glass of water the evening before the appointment and one more time the morning of the appointment and then advised to drink an additional 300ml of water before producing the sample. He was then given 80ml sterile labelled specimen container to collect any antegrade ejaculate and a further two other labelled containers to collect urine immediately after orgasm. An antegrade sample of 0.2ml was produced upon analysis, but no spermatozoa were found in it, therefore, the whole urine sample was centrifuged at 2100g for 5 minutes in sterile 14ml conical tubes. Using sterile technique, the supernatant in each tube was discarded following the initial centrifugation, and the sediment in all tubes aspirated and collected into a single 14ml conical tube containing 1ml of sperm wash medium (Sperm washing medium, Vitrolife Sweden) and centrifuged at 2100g for 5 minutes. Following removal of supernatant, the pellet of urine sediment was examined microscopically in which 31% active motile spermatozoa were observed. To eliminate puss cells along with other contamination the urine pellet was then gently layered onto a 0.5ml

each of 90% and 45% density gradient (Puresperm, Vitrolife Sweden) and centrifuged for 15 minutes at 1600g. The supernatant was again separated and the pellet aspirated into a 1ml sperm washing medium (Sperm washing medium, Vitrolife Sweden) and centrifuged for 5 minutes at 2100g. Further, all the retrieved sperms into the sperm wash then placed in straws and frozen with slow freezing method.

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## Management & Results

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The first ICSI of this patient was negative due to poor oocyte and sperm quality, but they returned again to clinic after three months for 2nd ICSI cycle after few modifications of life style such as inclusion of healthy diet and physical activity, mainly in male to control his blood sugar levels.

The female was prepared for oocyte collection by using a long protocol with decapeptyl (Ferring Pharmaceuticals, Switzerland) which she continued for three weeks after starting from Day 21 of her menses. A suppression check was done at day 2 of next cycle after which Gonal F of 75 IU (Merck-Serono, Germany) alongside 75 IU Menogone (Ferring Pharmaceuticals, Switzerland) were administered for eight days. A transvaginal scan done on the 5<sup>th</sup> day of stimulation showed the development of tiny antral follicles on each side with serum estradiol of 400pmol/L, while the final trans-vaginal scan performed on the 11<sup>th</sup> day of the cycle showed fifteen good follicles. On that day at 10:00 pm, 5000 IU of HCG (Pregnyl, Organon, Netherland) was administered and twenty oocytes were retrieved after 36<sup>th</sup> hours.

The male patient was then requested to give fresh alkaline urine sample on the day of oocyte retrieval but failed to do so because of anxiety

issue. Therefore, frozen sperms straws were used by warming them at room temperature. Thawed sample was then suspended into 1 ml of sperm wash medium and centrifuged for 5 minutes at 2100g. The supernatant was removed and 1.0 ul of the processed sample was added to a pre-warmed 5ul sperm-slow droplet and ICSI was performed as per the protocol<sup>4</sup>.

Healthy sperms were injected in 13 metaphase II oocytes using the Integra TI micromanipulator (Research Instruments Limited) and fertilization was checked 17 hours after. Twelve fertilized oocytes were placed in culture medium (G- series, Vitrolife Sweden) in 6% CO<sub>2</sub> incubator. Two good quality embryos were transferred into the woman's womb on Day 5 after the fertilization and for future embryo transfers, additional viable embryos were cryopreserved.

Three gestational sacs were found in ultrasonography after six weeks of embryo transfer. The patient returned to her own city for further antenatal care in a tertiary hospital. The patient gave birth prematurely at 33 weeks to triplets, one boy and two girls. Two babies had neonatal death within four days and patient has one healthy baby girl.

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## Discussion

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Retrograde ejaculation is the most prevalent cause for ejaculatory dysfunction and contributes 0.3-2% in male infertility but is reported to be high as 18% in the case of azoospermia<sup>5</sup>. Retrograde ejaculation has numerous causes like congenital or acquired abnormalities of urethra, interference with normal neurological control of ejaculation as occurs in diabetes and use of adrenergic blocking agents. It can be treated surgically or with drugs but not always do we achieve antegrade ejaculation<sup>3</sup>. It usually diagnosed in men who have been evaluated for infertility or

reported retrograde ejaculation as a consequence of surgical treatment. Therefore, examination of the post-ejaculatory urine sediment is always recommended in these cases particularly when no clear cause of the condition can be found. It is thought to be due to the passage of spermatozoa into the bladder in the result of the progressive widening of the bladder neck, following the route of least resistance especially when the bladder is empty<sup>6</sup>. For this, usually urine collected after orgasm for analysis, and with pre-treatment any spermatozoa found in the pellet after urinary centrifugation is suitable to yield fertilization when used in assisted conception procedures as this will almost reduce the combined effects of low pH, urea toxicity and osmotic stress of urine<sup>7</sup>.

This case presentation highlights the significance of advanced reproductive techniques for infertile couple where males are suffering from retrograde ejaculation and assisted them towards successful conception.

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## Conclusion

The usage of centrifuged urine in cases of retrograde ejaculation for ICSI has the scarcity of knowledge on such methods in Pakistan. The aim of this case report was to sensitize our colleagues in the field of fertility to consider retrograde ejaculation as a cause of infertility and to offer ICSI as a valid treatment option in such cases.

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## Conflicts of Interest

None.

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