

## Case Report

### Successful Pregnancy Outcome in a Couple with Long-Standing Infertility: Overcoming Severe Male Factor Azoospermia, Polycystic Ovarian Syndrome, and Intrahepatic Cholestasis of Pregnancy

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## Abstract

<b>Keyword:</b>  Azoospermia; PCOS; Intrahepatic cholestasis of pregnancy; Testicular sperm extraction; IVF.  <b>Corresponding author:</b>  Dr. Hanan Jawad Kadhim. Consultant of Obstetrics & Gynecology. Arbil, Iraq.  <b>Phone:</b> + 9647511631774  <b>Mail:</b> hananjawad0750@gmail.com	<b>ABSTRACT</b>  This report describes the successful management of a couple with 15 years of primary infertility due to severe male factor azoospermia and female polycystic ovarian syndrome (PCOS). Following surgical sperm retrieval and in vitro fertilization (IVF), the patient conceived on the first attempt. The pregnancy was complicated by severe intrahepatic cholestasis of pregnancy (ICP) at 22 weeks, with markedly elevated liver enzymes and bile acids. Despite the indication for termination at this gestational age, multidisciplinary management with close maternal–fetal monitoring enabled continuation of pregnancy until 34 weeks, when an elective cesarean section resulted in the delivery of a healthy female infant. Both mother and baby were discharged in good condition. This case highlights the value of collaborative reproductive and hepatological management in optimizing outcomes in complex infertility and pregnancy scenarios.
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## Introduction

Infertility is a challenging condition that affects couples both medically and psychologically. Male factor azoospermia and female polycystic ovarian syndrome (PCOS) represent two of the most common causes. The advent of microsurgical sperm retrieval and IVF has revolutionized treatment, even in severe cases. Intrahepatic cholestasis of pregnancy (ICP) is a rare but serious complication associated with adverse fetal outcomes, particularly when bile acids are markedly elevated. Management often requires balancing maternal risks with fetal maturity. Intrahepatic cholestasis of pregnancy, commonly known as cholestasis of pregnancy, is a liver condition that can occur in late pregnancy. The condition triggers intense itching, but without a rash. Itching is usually on the hands and feet but also can occur on other parts of the body<sup>1</sup>.

Cholestasis of pregnancy is a liver condition that causes severe itching late in pregnancy. It's also known as intrahepatic cholestasis of pregnancy (ICP) or obstetric cholestasis affects about 1 to 2 in 1,000 people during pregnancy. More people are diagnosed with ICP during the winter than other times of the year, but researchers aren't sure why. Data suggests it's more common in people of Hispanic and Swedish backgrounds<sup>2</sup>.

Intrahepatic cholestasis of pregnancy is manifested by pruritus and elevated bile acids. The etiology of cholestasis is poorly understood and management is difficult due to the paucity of data regarding its diagnosis, treatment, and related adverse outcomes<sup>3</sup>.

Intrahepatic cholestasis of pregnancy (ICP) poses significant risks to maternal and neonatal health. The increasing incidence of ICP and its association with elevated levels of total bile acids, transaminases, and bilirubin. It associated with a marked

increase in the risk of preterm birth, cesarean delivery, and neonatal asphyxia as the severity of ICP escalates<sup>4</sup>.

We report a rare case of a couple with dual infertility factors, in which successful pregnancy was achieved after microsurgical sperm retrieval and IVF. The pregnancy was complicated by severe ICP at 22 weeks but was managed expectantly until a safe delivery at 34 weeks.

## Case Presentation

A 36-year-old woman presented with 15 years of primary infertility. The etiology was male factor azoospermia and female PCOS. The male partner had undergone four prior surgical interventions and multiple medical treatments without benefit. Two years prior to presentation, the couple visited our center.

The female partner underwent ovulation induction and metabolic optimization for PCOS, while my colleague Dr. Nawfal performed a microsurgical open testicular sperm extraction (TESE) on the male partner. Only four viable spermatozoa were retrieved. ICSI/IVF was performed, and fertilization succeeded. On November 9, 2024, the patient achieved a clinical pregnancy. Serum  $\beta$ -hCG was 2345 mIU/mL, and viability was confirmed. At 22 weeks of gestation, the patient developed generalized pruritus and laboratory findings consistent with severe intrahepatic cholestasis of pregnancy:

ALT: 650 U/L

AST: 578 U/L

Bile acids: 198  $\mu$ mol/L.

Bilirubin: 2.6 mg/dL

**After sequence of closed management:**

ALT 300.9 U/L

AST 134.1 U/L

BILE ACID 81.9 umol/L

Bilirubin 1.40 MG/DL

**At day of operation:**

ALT 407.0 U/L

AST 163.2 U/L

BILE ACID 5.8 umol/l

Bilirubin 1.8 mg/dl

Given the severity, termination of pregnancy was considered. However, after multidisciplinary discussion with hepatology, the decision was made for conservative management under strict monitoring.

The patient was co-managed by hepatologists, with regular blood tests, ultrasound, and fetal surveillance. Her symptoms were managed symptomatically, and fetal growth remained appropriate.

At 34 weeks (June 20,2025), due to worsening maternal condition and to minimize fetal risks, an elective cesarean section was performed. A healthy female infant was delivered with good Apgar scores. Both mother and baby recovered well and were discharged in stable condition.

## Discussion

This case highlights several important points:

**1. Severe Male Factor Infertility:** Even in non-obstructive azoospermia with limited sperm yield, IVF/ICSI offers hope for conception.

Meiosis is an essential stage in the life cycle of sexually reproducing species, underlying formation of haploid gametes and serving as the basis of genetic diversity. Aberrant meiotic recombination often leads to gametogenic failure or produces aneuploid gametes resulting in subfertility or infertility, miscarriage or birth defects<sup>5</sup>.

The initial autologous cycles with a diagnosis of male factor with surgically obtained sperm, that diagnosed as azoospermia, the outcomes for ICSI cycles using surgically acquired sperm. The reported outcomes reported per initial cycle included clinical pregnancy, live birth, biochemical pregnancy, and miscarriage.

After frozen embryo transfers in patients with NOA had 7% higher odds of live birth compared to MF due to obstructive azoospermia. After fresh ET, patients with NOA had 5% higher chance of live birth than those with OA<sup>6</sup>.

**2. PCOS as a Female Factor:** Metabolic and reproductive optimization is crucial to maximize IVF outcomes.

In females with polycystic ovarian syndrome (PCOS), the most prevalent endocrine condition is chronic anovulation and hyperandrogenism. This illness influences females from conception to death, posing several risks to the health of a female, thus reducing the quality of life. It also increases the rates of mortality and morbidity. There are many various phenotypes that fall under the same illness. In females with PCOS,

anovulation is linked to low follicle-stimulating hormone (FSH) levels and a halt in antral follicle growth during the last stages of maturation<sup>7</sup>.

Phenotype-D PCOS women undergoing ICSI in one retrospective study, the primary outcome in PCOS patients with Phenotype-D a higher fertilization per inseminated oocytes and higher blastulation per zygotes. This resulted into a higher EBR per inseminated oocytes and more euploid blastocysts available for transfer. The live birth rate per first euploid transfers was comparable, so were all other outcomes considered<sup>8</sup>.

**3. Intrahepatic Cholestasis of Pregnancy:** Markedly elevated bile acids ( $>100$   $\mu\text{mol/L}$ ) are associated with high risk of stillbirth. Most guidelines suggest delivery between 34–36 weeks. Our patient developed severe ICP at 22 weeks, where termination would usually be considered. With careful monitoring, continuation of pregnancy until 34 weeks was possible, leading to a favorable neonatal outcome.

Intrahepatic cholestasis of pregnancy is associated with adverse perinatal outcomes, but the association with the concentration of specific biochemical markers is unclear.

The risk of stillbirth is increased in women with intrahepatic cholestasis of pregnancy and singleton pregnancies when serum bile acids concentrations are of 100  $\mu\text{mol/L}$  or more. Because most women with intrahepatic cholestasis of pregnancy have bile acids below this concentration, they can probably be reassured that the risk of stillbirth is similar to that of pregnant women in the general population, provided repeat bile acid testing is done until delivery<sup>9</sup>.

Individuals with intrahepatic cholestasis of pregnancy are at increased risk of adverse perinatal outcomes including preterm birth, neonatal respiratory distress and admission to a neonatal intensive care unit, with an increased risk of stillbirth when bile acid

levels are  $\geq 100 \mu\text{mol/L}$ . There is inequity in bile acid testing availability and timely access to results, along with uncertainty of how to treat, monitor, and ultimately deliver these pregnancies. Optimization of diagnostic and management protocols can improve maternal and fetal postnatal outcomes<sup>10</sup>.

**4. Multidisciplinary Management:** Collaboration between reproductive specialists, hepatologists, and obstetricians was essential to balance maternal safety with fetal maturity.

## Conclusion

This case demonstrates that even couples with longstanding dual infertility factors can achieve successful outcomes with advanced assisted reproductive technologies. Moreover, with vigilant multidisciplinary care, severe pregnancy complications such as intrahepatic cholestasis can be managed safely, allowing continuation of pregnancy to viability and resulting in the delivery of a healthy infant.

## Figures







Fig 1: Photo for the baby in NICU

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