

# Liveborn baby by ICSI of micro-TESE derived cryopreserved-thawed sperm of non-mosaic Klinefelter syndrome father

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## ABSTRACT

**Klinefelter syndrome (KS) is the most common sex chromosome abnormality in azoospermic males and its prevalence changes in different countries. Until recently KS patients were accepted as sterile however with the impact of microsurgical testicular sperm extraction (Micro-TESE) and good freezing modalities healthy pregnancies and live born babies achieved. Klinefelter syndrome males have a wide variety of semen findings from severe azoospermia to nearly normal sperm findings but mostly in the range of azoospermia and severe oligoasthenoteratospermia. For some social and economical reasons, patients decide to have Micro-TESE operation first as in this case. The number of publications and case reports has been increasing and implantation rates and clinical outcomes are comparable with the fresh Micro-TESE derived sperm used cases. The use of cryopreserved-thawed sperms of KS patients for intracytoplasmic sperm injection (ICSI) could be**

**a choice in especially socioeconomically deprived couples since the implantation rates and clinical outcomes are similar.**

**Keywords: Cryopreserved-thawed sperms, Klinefelter syndrome, Liveborn baby, micro-TESE**

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## INTRODUCTION

Male factor infertility due to nonobstructive azoospermia (NOA) is not uncommon but among that group Klinefelter syndrome (KS) comprises only a small proportion [1]. Several reports revealed good pregnancy outcomes in cases of KS where fresh sperm derived by microsurgical testicular sperm extraction (Micro-TESE) at the day oocyte pick-up but the number of cryopreserved sperm used cases of KS is quite limited [2]. The advance of vitrification techniques and culture media, the difference between cryo and fresh sperms is minimalized. The important matter is the transmission of genetic abnormalities to the offspring but it was shown that focal spermatogenesis originated from euploid germ cells is present in non-mosaic KS males and therefore majority of babies born from non-mosaic KS patients are chromosomally normal [3]. We present a healthy liveborn

baby following intracytoplasmic sperm injection (ICSI) of cryopreserved sperms from non-mosaic KS father in this case report.

## CASE REPORT

A 34-year-old male previously diagnosed as Klinefelter syndrome (non-mosaic) admitted to our IVF center for having a baby at May 2012. The time of infertility was 6 months and in his history patient gave information about a childhood high fever, a traffic accident and appendectomy. No history of alcohol use, smoking or drug addiction was given. His wife was 28-year-old healthy woman with no medical history apart from rhinoplastic surgery and surgery for thyroid disease. She was not using any medication and had no bad habits. Routine hormonal and serological screening before IVF was done and KS was verified by previous karyotype analysis.

Since the time for infertility was short and the main reason of infertility was nonobstructive azoospermia (NOA) due to KS, two options were given to the couple for their course, first micro-TESE operation and freezing of retrieved sperms and IVF treatment thereafter and second was micro-TESE operation on the day of oocyte pick up (OPU). Social and economical factors pushed the couple to decide on first choice and micro-TESE was performed first and retrieved sperms were frozen and kept in two straws for use.

Following the retrieval of sperms and freezing, his wife was taken into long standard IVF protocol beginning with GnRH analogue on 21th day of previous cycle and on the 3rd menstrual day, she was given 225 IU Gonadotropin (Merck, Serono, Switzerland) until cycle day 11 where in transvaginal ultrasound examination the leading follicles were 18 mm, 17 mm, 16 mm on the right side and 17 mm, 16 mm, 16 mm on the left side and ovitrelle 250 micrograms (Merck Serono, Switzerland) for final oocyte maturation was given and oocyte pick up was done 36 hours later. Eight oocytes were retrieved; seven mature oocytes were observed following denudation and injected with thawed sperms and on the next morning three oocytes were found fertilized. Due to the restrictions of embryo transfer in Turkey only one embryo with eight cell even, grade two morphology was transferred where one other was frozen and another embryo was arrested in development.  $\beta$  hCG value at 12th day was 57.71 mIU/mL and two days after the  $\beta$  hCG value was doubled. Fetal heart beat was observed by transabdominal ultrasound at 21st day after embryo transfer at sixth week of gestation.

The pregnancy was followed carefully until 38 weeks 3 days of gestation and 3500 grams healthy male baby with good APGAR score was delivered by cesarean section following amniotic membrane rupture. The only visible problem of baby was 6 digits of hands and all other findings were normal. However, baby lived severe respiratory distress and stayed in the neonatal intensive care unit (NICU) for one month and discharged healthily.

## DISCUSSION

Klinefelter syndrome (karyotype 47,XXY) is the most frequent sex-chromosomal disorder in men [4].

The most prominent features of KS are disturbed endocrinology and a dramatically altered testicular architecture (i.e. Sertoli cell-only syndrome and Leydig cell hyperplasia) [5]. Although the density and number of testicular tubules and mesenchymal structures appeared to be normal, Coerdts et al. showed that reported reduced germ cell numbers in testicular biopsies from 47, XXY fetuses at gestational age of 18–22 weeks [5].

Nonobstructive azoospermia is one of the important reasons of male factor infertility and KS is the most commonly seen sex chromosomal abnormality among NOA patients [1]. The fertilization rates, cleavage of embryos, embryo transfer rates and implantation rates of fresh versus frozen sperms derived by micro-TESE in non-mosaic KS were compared and concluded that the outcomes were similar [6–7].

In another study conducted by Kyono et al., the outcomes of ICSI using fresh or frozen-thawed testicular sperm in patients with non-mosaic KS was found identical. They recommend the use of micro-TESE on the day of OPU in cases of high chance of sperm retrieval. Among the seven pregnancies, five pregnancies achieved by fresh sperms of KS patients while two pregnancies achieved by frozen sperms of KS patients [2].

Micro-TESE described by Schlegel et al. improved sperm retrieval rate to 60% or more [8] but the retrieval of sperm from KS patients ranges between 21% and 45% [9].

In a recent study conducted by Madureira et al., the outcomes of treatment with testicular sperm extraction and ICSI of 65 azoospermic patients with non-mosaic KS were reported with the birth of 17 healthy children. They found the sperm retrieval rate of 38.5%. The first group choose fresh micro-TESE derived sperms on OPU day and in 40% (19/48 patients) of the cases sperm was recovered with the birth of 12 newborn. Of the 17 patients who choose to have micro-TESE and freezing first, in six patients (35%) sperm was recovered and only one baby was born. In failed cases repeated cycles resulted in the birth of four healthy children [3].

In the study of Greco et al., 38 non-mosaic KS patients were operated by TESE and micro-TESE and in 15 cases (39.5%) sperm was retrieved. A total of 26 ICSI cycles were performed; 10 with fresh sperms and 16 with cryopreserved sperms and fertilization rates were similar. Clinical outcomes were found insignificant and sixteen babies were born, eight from fresh sperm group and eight from frozen-thawed sperm group [10]. Sabbaghian et al. showed that KS does not reduce the chance of sperm recovery and ICSI outcome [11]. They also concluded that micro-TESE/ICSI is a successful intervention for the majority of men with KS [11].

Greco et al. reported a case of a healthy boy after fertilization of cryopreserved oocytes with cryopreserved

testicular spermatozoa from a man with non-mosaic Klinefelter syndrome and that was the first case of frozen oocyte injected with frozen sperm of KS patient [10].

New born has polydactyl which is the most frequently observed congenital limb anomaly. For the etiology of polydactyl genetic predisposition factor plays some roles except of KS [12]. So we thought that this finding was incidental.

## CONCLUSION

In conclusion, although clinical outcomes were not significantly different, micro-TESE is recommended to be performed on the day of OPU under 35 years of age since main aim of the treatment is to have a baby not to obtain testicular sperm. However social, psychological and economical reasons may lead the couples decide to have sperms retrieved by micro-TESE first following sperm finding and freezing then they decide to have IVF cycle as in this case. Micro-TESE is the best method for succeeding a pregnancy in couples having male factor infertility due to non-mosaic Klinefelter syndrome.

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## Author Contributions

Şafak Hatirnaz – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Ebru Hatirnaz – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

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## Guarantor

The corresponding author is the guarantor of submission.

## Conflict of Interest

Authors declare no conflict of interest.

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