

EMBRYOLOGICAL AND CLINICAL OUTCOMES OF ICSI-MICROTESE IN NON-OBSTRUCTIVE AZOOSPERMIC PATIENTS WITH A HISTORY OF MUMPS ORCHITIS

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ABSTRACT

Objective: This study aimed to evaluate the effectiveness of micro-TESE combined with ICSI in patients with non-obstructive azoospermia (NOA) who had a history of mumps orchitis, focusing on sperm retrieval rates, embryological development outcomes, and clinical pregnancy results.

Materials and Methods: This retrospective study analyzed 293 patients with NOA who underwent micro-TESE, assessing sperm retrieval rates, hormone profiles, and subsequent embryological and clinical outcomes, with a particular focus on those with a history of mumps orchitis.

Results: The overall sperm retrieval rate (SRR) among NOA patients was 59.4% (174/293). Remarkably, patients with a history of mumps orchitis (n=51) demonstrated a significantly higher SRR of 94.1% (p < 0.05) compared to those with other etiologies. Additionally, SRR-positive patients exhibited significantly elevated levels of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) (p = 0.022 and p = 0.015), suggesting a possible compensatory response of the hypothalamic–pituitary–testicular axis. Among the 48 ICSI cycles performed in the mumps orchitis group, the fertilization rate was 70.4 ± 22.7 %, the Day 5 blastocyst formation rate reached 60.4%, the β-hCG positivity rate was 82.8%, and the ongoing pregnancy rate was 69.0%.

Conclusion: Micro-TESE combined with ICSI proves to be an effective and optimal treatment for NOA patients, especially those with a history of mumps orchitis, achieving high sperm retrieval and promising ongoing pregnancy outcomes. The findings also underscore mumps as an ongoing threat to male fertility in Vietnam, reinforcing the importance of early diagnosis and timely medical intervention.

Keywords: Non-obstructive azoospermia (NOA), microdissection testicular sperm extraction (micro-TESE), mumps orchitis, sperm retrieval.

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1. INTRODUCTION

Azoospermia, defined as the complete absence of spermatozoa in the ejaculate, affects approximately 1% of men in the general population and 10–15% of those with infertility [1, 2]. It is classified into two major types: obstructive azoospermia (OA), characterized by normal spermatogenesis with blockage of the sperm transport pathway, and non-obstructive azoospermia (NOA), resulting from impaired spermatogenic function within the testes [3]. NOA accounts for approximately 60% of all azoospermia cases [4]. While sperm retrieval rates in OA are consistently high (96–100%), they vary widely in NOA, ranging from 30% to 60% depending on the underlying cause [5]. Common etiologies of NOA include Klinefelter syndrome, Y chromosome microdeletions in the azoospermia factor region (YCMDS), cryptorchidism, and mumps orchitis. In Vietnam, mumps is an endemic infection occurring throughout the year, with an incidence of 10–40 cases per 100,000 population. Studies have reported that 30–87% of men with mumps develop bilateral orchitis as a complication [6]. Mumps orchitis is a notable contributor to NOA; for example, Nguyen Cao Thang reported a prevalence of 23.86% (21/88) among NOA patients [7]. Although NOA is typically associated with severely impaired spermatogenesis, residual foci of functional seminiferous tubules may persist in some patients, allowing for potential sperm retrieval. The microdissection testicular sperm extraction (micro-TESE) technique, first described by Schlegel in 1999, has emerged as the most effective method for sperm retrieval in NOA patients [8]. By using an operating microscope to identify dilated seminiferous tubules more likely to contain sperm, micro-TESE increases retrieval rates while minimizing testicular tissue damage [9]. Despite its promise, limited research has focused specifically on NOA secondary to mumps orchitis, particularly in relation to embryological development and clinical pregnancy outcomes following treatment. This study aims to evaluate the efficacy of micro-TESE combined with intracytoplasmic sperm injection (ICSI) in NOA patients with a history of mumps orchitis. Specifically, it focuses on assessing sperm retrieval rates, embryological development outcomes, and clinical pregnancy results in this patient population.

2. MATERIALS AND METHODS

2.1. Study population

In vitro fertilization cycles using sperm obtained via microdissection testicular sperm extraction (micro-TESE) combined with intracytoplasmic sperm injection (ICSI) at the Andrology and Fertility Hospital of Hanoi from January 2022 to June 2024.

- Inclusion criteria:

- + Patients diagnosed with non-obstructive azoospermia (NOA) based on medical history, clinical

examination, semen analysis, hormonal profile, and testicular volume assessment via ultrasound.

- + Patients who consented to undergo micro-TESE for sperm retrieval.

- + Couples who agreed to proceed with ICSI for embryo creation.

- Exclusion Criteria:

- + Patients with azoospermia resulting from obstructive causes such as vasectomy, epididymal obstruction, or ejaculatory duct obstruction.

- + Patients with azoospermia secondary to testicular trauma.

- + Couples in which donor oocytes were used or the female partner had uterine abnormalities.

- NOA patients attributed to mumps orchitis were included based on the following criteria:

- + Medical history: documented mumps infection occurring during or after puberty.

- + Complication: clinical history of orchitis following mumps infection, characterized by symptoms such as testicular swelling and pain.

2.2. Study design

- Study design: Retrospective descriptive study.

Sample size and sampling method: we used a convenience sampling approach, enrolling all cycles that met the established inclusion and exclusion criteria within the study period.

- Study Procedures:

Patient selection and baseline data collection: Eligible participants were selected based on predefined inclusion and exclusion criteria. Baseline clinical data were collected, including age, body mass index (BMI), hormonal profiles of both partners, semen analysis results, and medical history, including cryptorchidism, mumps orchitis, radiotherapy, chemotherapy, and any prior surgical interventions.

Ovarian stimulation and oocyte retrieval: Female partners underwent controlled ovarian stimulation for 8–14 days. Oocyte retrieval was performed 34–36 hours following the administration of human chorionic gonadotropin. Retrieved oocytes were incubated, and cumulus–corona cells were removed in preparation for ICSI.

Micro-TESE and sperm preparation: Under general anesthesia, micro-TESE was performed to identify and extract seminiferous tubules with the highest likelihood of containing sperm. The excised testicular tissue was finely minced and examined under a microscope. Sperm-containing samples were isolated, washed, and prepared in petri dishes for use in ICSI.

ICSI and embryo culture: Mature oocytes were injected



with sperm retrieved via micro-TESE. Fertilization was assessed 16–18 hours post-injection. Embryo quality was evaluated on day 3 (cleavage stage) according to the 2011 Istanbul consensus and on day 5 (blastocyst stage) using the Gardner grading system (1999) [10, 11]. Embryo transfer (fresh or frozen) on day 3 or day 5 was determined based on embryo quality and endometrial conditions, following consultation with the couple.

- Data collection on embryos and clinical pregnancy:

+ Sperm retrieval success rate from the micro-TESE procedure.

+ Number of mature oocytes.

+ Fertilization rate, embryo quality on day 3, and day 5.

+ Positive serum β -hCG rate represents the percentage of embryo transfer cycles that yield a positive serum (blood) test for human chorionic gonadotropin (β -hCG), usually performed 10 to 14 days following the embryo transfer.

+ Ongoing pregnancy rate is defined as pregnancy with detectable heart rate at 12 weeks' gestation or beyond.

2.3. Statistical analysis

Data were analyzed using SPSS version 28.0. Descriptive statistics were used to summarize baseline characteristics. Continuous variables were presented as mean \pm standard deviation (SD). Normality of quantitative variables was assessed, and comparisons were conducted using Student's t-test for normally distributed data or the Mann-Whitney U test for non-normal distributions. A p-value less than 0.05 was considered statistically significant.

2.4. Ethical considerations

The study was approved by the Scientific Committee of the Andrology and Fertility Hospital of Hanoi with Decision No.04/QĐ-ĐC-BVNH/2025. All patient information was kept strictly confidential and was used solely for scientific research purposes.

3. RESULTS

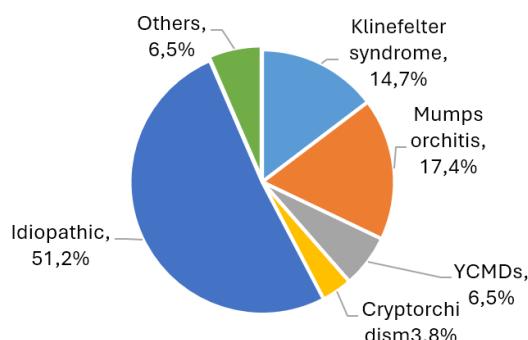


Figure 1. Distribution of the causes of non-obstructive azoospermia (n=293)

A total of 293 non-obstructive azoospermia (NOA) patients underwent microdissection testicular sperm extraction (MicroTESE) in this study. Among them, 150 patients (51.2%) were classified as idiopathic, 43 (14.7%) had Klinefelter syndrome, 19 (6.5%) had Y chromosome microdeletions (YCMDS), 11 (3.8%) had a history of cryptorchidism, 51 (17.4%) had a history of mumps orchitis, and 19 (6.5%) had other identified causative factors (Figure 1).

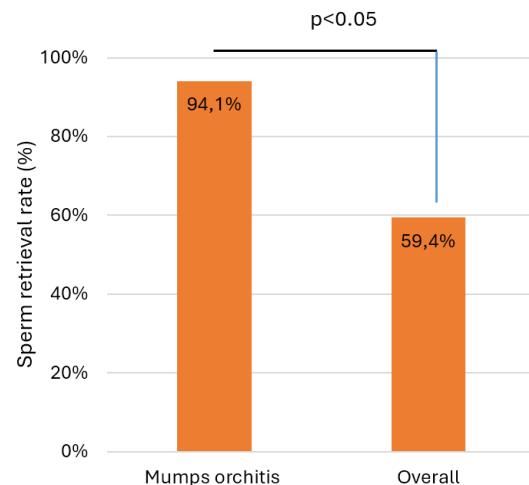


Figure 2. Comparison of sperm retrieval rates between all NOA patients and those with a history of mumps orchitis

The overall sperm retrieval rate among NOA patients was 59.4% (174/293), whereas those with a history of mumps orchitis had a significantly higher retrieval rate of 94.1% (48/51) ($p < 0.05$). (Figure 2)

Table 1. Comparison of baseline characteristics in NOA patients with and without successful sperm retrieval

Characteristic	SRR (+)	SRR (-)	p value
Number of aspiration cycles, n (%)	174 (59.4%)	119 (40.6%)	-
Paternal age (years)	32.0 ± 4.6	31.9 ± 4.3	0.759
FSH (mIU/mL)	30.1 ± 16.2	26.3 ± 15.1	0.022*
LH (mIU/mL)	16.0 ± 8.5	13.6 ± 7.9	0.015*
Testosterone (nmol/L)	11.7 ± 7.7	12.6 ± 10.4	0.631
Left testicular volume (mL)	5.8 ± 4.2	5.9 ± 3.8	0.400
Right testicular volume (mL)	5.6 ± 4.0	6.0 ± 3.7	0.166

Data are expressed as Mean \pm Standard deviation. FSH, follicle-stimulating hormone; LH, luteinizing hormone; all tests were performed using the Mann-Whitney U test.

*Significant at $p < 0.05$

The results showed no statistically significant differences between groups in the mean age of the husband ($p = 0.759$), testosterone concentration ($p = 0.631$), or testicular volume (left: $p = 0.400$; right: $p = 0.166$). However, follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels were significantly higher in the positive sperm retrieval group (FSH: 30.1 ± 16.2 mIU/mL; LH: 16.0 ± 8.5 mIU/mL) compared to the negative group (FSH: 26.3 ± 15.1 mIU/mL; LH: 13.6 ± 7.9 mIU/mL), with p -values of 0.022 and 0.015, respectively.

Table 2. Patient characteristics, embryological, and clinical outcomes of ICSI–MicroTESE cycles in NOA patients with a history of mumps orchitis

Characteristics	$\bar{X} \pm SD$ or n/N	Min- max/ %
No. of ICSI cycles (n)	48	-
Maternal age (years)	28.2 ± 4.0	20 - 37
Paternal age (years)	31.8 ± 4.1	24 - 41
Maternal AMH (ng/mL)	4.2 ± 2.1	1.0 - 7.7
Maternal BMI (kg/m ²)	21.2 ± 7.9	16.6 - 26.8
No. of mature oocyte (n)	14.7 ± 7.9	3 - 43
Fertilization rate (%)	70.4 ± 22.7	8.3% - 100%
Good embryo rate on day 3	385/504	76.3%
Blastocyst rate on day 5	246/407	60.4%
Positive serum β -hCG rate (n=58 ET cycles)	48/58	82.8%
Ongoing pregnancy rate (≥ 12 weeks) (n=58 ET cycles)	40/58	69.0%

Data are presented as mean \pm standard deviation or percentage. ET, embryo transfer.

Subsequently, we analyzed the outcomes of 48 ICSI cycles performed in patients with mumps orchitis-related NOA who had successful sperm retrieval. As shown in Table 2, the mean age of the female partners was 28.2 ± 4.0 years (range: 20–37), while the mean age of the male partners was 31.8 ± 4.1 years (range: 24–41). The mean anti-Müllerian hormone (AMH) level in female partners was 4.2 ± 2.1 ng/mL (range: 1.0–7.7), and their mean body mass index (BMI) was 21.2 ± 7.9 kg/m² (range: 16.6–26.8).

On average, 14.7 ± 7.9 mature oocytes were retrieved per cycle (range: 3 - 43). The mean fertilization rate was $70.4 \pm 22.7\%$ (range: 8.3–100%). A total of 504 embryos were obtained, of which 385 (76.3%) were classified as good or fair quality on day 3. By day 5, 246 out of 407 embryos developed to the blastocyst stage, resulting in a blastocyst formation rate of 60.4%. Among a total of 58 embryo transfer cycles derived from 48 ICSI cycles, seven patients underwent two embryo transfer cycles, and two patients underwent three cycles. The results showed a positive serum β -hCG rate of 82.8% and an

ongoing pregnancy rate of 69.0%.

4. DISCUSSION

In Vietnam, mumps is recognized as a major infectious cause of non-obstructive azoospermia (NOA). In our study, the proportion of NOA patients with a history of mumps orchitis was 17.4% (51/293). This rate is relatively high compared to the study by Guangmin Liu et al (2024) in China, which reported a rate of 8% (50/627) [12]. However, this is comparable to the 23.86% (21 out of 88 cases) reported by Nguyen Cao Thang in a 2022 study [7]. The variation in prevalence rates may reflect differences in geographic, demographic, or healthcare factors affecting exposure and diagnosis.

In our study, the overall sperm retrieval rate (SRR) among patients with non-obstructive azoospermia (NOA) was 59.4%, aligning with previously reported global rates ranging from 30% to 60%. Notably, the SRR among NOA patients with a history of mumps orchitis was exceptionally high at 94.1% (48/51), significantly surpassing the rate observed in patients with other etiologies ($p < 0.05$). This finding also exceeds rates reported in similar studies, where SRRs ranged from 75% to 84.6% in this group [13, 14]. The higher SRR in this study may be attributed to differences in patient selection criteria across studies. Variations in clinical characteristics, underlying causes, or degrees of testicular damage among participants can significantly affect the results. The high SRR supports the hypothesis that testicular damage caused by mumps is often patchy rather than diffuse, allowing microdissection testicular sperm extraction (micro-TESE) to effectively identify and retrieve sperm from focal areas of preserved spermatogenesis.

Our results further revealed that serum follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels were significantly higher in the SRR-positive group. In contrast, testosterone concentrations did not differ significantly between groups. Although elevated FSH and LH are traditionally viewed as markers of severe testicular dysfunction, these findings suggest a more detailed interpretation. In cases of focal testicular damage, such as mumps orchitis, the hypothalamic-pituitary-testicular axis may respond with increased gonadotropin release as a compensatory mechanism to stimulate the remaining functional seminiferous tubules. Additionally, previous studies have shown that Leydig cells, even when partially damaged, can maintain adequate testosterone production under high LH stimulation [15]. Therefore, elevated FSH and LH may, counterintuitively, serve as positive prognostic markers for successful sperm retrieval in selected NOA patients.

Regarding embryological outcomes, the NOA patient group with a history of mumps orchitis demonstrated promising results. The fertilization rate was $70.4 \pm 22.7\%$,



the good-quality embryo rate on Day 3 reached 76.3%, and the Day 5 blastocyst formation rate was 60.4%. These findings suggest that sperm retrieved from this group have superior functional capacity, supporting not only fertilization but also embryo development to the blastocyst stage. Clinical outcomes were equally encouraging, with an 82.8% β -hCG positivity rate and a 69.0% ongoing pregnancy rate, indicating strong potential for successful pregnancies using the ICSI technique in this patient population.

This study confirms that micro-TESE combined with ICSI is an optimal approach for sperm retrieval and treatment in NOA patients, particularly those with a history of mumps orchitis. However, several limitations should be acknowledged. The retrospective, single-center design and incomplete data, especially the lack of live birth outcome information, reduce the overall comprehensiveness and generalizability of our findings. Future prospective, multi-center studies with longer follow-up are warranted to validate and extend these results.

5. CONCLUSION

Micro-TESE combined with ICSI was an effective approach for sperm retrieval and clinical outcomes in NOA patients, especially those with a history of mumps orchitis, achieving a 94.1% sperm retrieval rate and 69.0% ongoing pregnancy rate. Since no curative treatment currently exists, increasing public awareness and promoting early medical intervention were considered essential to reducing infertility from mumps orchitis.

DECLARATION OF INTERESTS

The authors declare that there are no conflicts of interest related to this work.

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