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Can spermatozoa be retrieved in non-obstructive azoospermic patients with high FSH level?: A retrospective cohort study

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Abstract

We aimed in this retrospective study to evaluate non-surgical preoperative parameters and testicular histopathology in determining the sperm retrieval rate (SRR) in non-obstructive azoospermic (NOA) patients. We evaluated the data of 1,395 consecutive patients who underwent 1st time micro-dissection testicular sperm extraction (micro-TESE) that was done by fifteen different senior andrologists and a consequent undefined number of biologists assisting them in the operative rooms from January 2010 to May 2013 in a specialised IVF centre. Our study did not demonstrate any statistical significance between the mean age, the mean duration of infertility and finally, the mean of FSH levels of the patients with positive and negative micro-TESE outcomes (*p*-value 0.391, 0.543, 0.767 respectively). Moreover, our study did not demonstrate any association between different types of hormonal therapy prior to micro-TESE and patients with positive micro-TESE outcome (*p*-value 0.219). Interestingly, our study showed positive associations between the testicular histopathology SCO (sertoli cell only syndrome) and high FSH and sperm retrieval rate ($p < 0.001$, 0.02 respectively). Logistic regression analysis revealed high statistical significance between sperm retrieval rate and high FSH level and testicular histopathology (OR 1.6, 0.21, 95% CI lower 1.2, 0.008 and upper 2.1, 0.06 and finally *p* 0.003, <0.001 respectively). This study reveals that preoperative testicular biopsy is unnecessary to predict the sperm retrieval rate in NOA patients.

KEYWORDS
high FSH level, micro-TESE, non-obstructive azoospermia

1 | INTRODUCTION

The active component of each testis consists of several hundred seminiferous tubules measuring up to 70 cm in length. The process of spermatogenesis occurs within these tubules, and in normal testis, all stages of differentiation are present simultaneously (Wistuba, Stukenborg, & Luetjens, 2007). Because all stages of spermatogenesis do occur simultaneously, normal spermatogenesis does not yield mature spermatids in every tubular cross section in a testicular biopsy (Cerilli, Kuang, & Rogers, 2010). Various more immature stages are normally appreciated and should not be misinterpreted as a maturation abnormality (Cerilli et al., 2010). Azoospermia is defined as the complete absence of spermatozoa in the ejaculate, it represents 15% of infertile men and can be due to inadequate hormonal stimulation (pre-testicular), impaired spermatogenesis (testicular) or an obstruction (post-testicular) (Cocuzza, Alvarenga, & Pagani, 2013). Non-obstructive azoospermia (NOA) is the most severe form of male infertility (Cocuzza et al., 2013; Wosnitzer, Goldstein, & Hardy, 2014). The clinical management of men with NOA seeking fertility has been a challenge for andrologists and reproductive medicine specialists

(Esteves & Agarwal, 2013). A coordinated multidisciplinary effort is necessary to offer the best possible chance of achieving a biological offspring to men with NOA (Esteves, 2015). An ideal surgical technique would achieve efficient retrieval of spermatozoon while causing minimal trauma to the testes (Donoso, Tournaye, & Devroey, 2007; Tiseo, Hayden, & Tanrikut, 2015). Micro-dissection testicular sperm extraction (micro-TESE) is a microsurgical method originally described by Schlegel and Li (1998), which has been proposed as a better alternative to TESE in cases of NOA (Shin & Turek, 2013). Schlegel (1999) observed qualitative differences in seminiferous tubules while performing conventional TESE under optical magnification.

We aimed in this retrospective cross-sectional study to detect the association between the sperm retrieval hope and preoperative factors such as age of the patients, duration of infertility, testicular volume, hormonal profile and whether there was a preoperative medical treatment and finally with the histopathology that was detected intraoperative in 1,395 patients who underwent micro-TESE.

2 | MATERIALS AND METHODS

2.1 | Study design and settings

We evaluated retrospectively 1,395 consecutive patients who underwent 1st time micro-TESE from January 2010 to May 2013. Data of these patients were gathered from the Andrology Clinic of a specialised IVF centre (Adam International Hospital, Giza, Egypt). The Research Ethical Committee of Beni-Suef Faculty of medicine approved the study protocol which conforms to Helsinki declaration 1964. Prior to enrolment into the micro-TESE procedure, eligible participants signed an informed consent including permission to use their data for analysis with their confidentiality guaranteed.

2.2 | Evaluation of the Study participants

Men with clinical and laboratory data indicating non-obstructive azoospermia (NOA) who underwent surgical retrieval of sperm cells by means of micro-TESE were evaluated for the sperm retrieval rates and their respective testicular histopathology, in addition to any potential postoperative complications in the form of weekly visits for 1 month.

2.3 | All the patients were subjected to the following

All the participants were evaluated for full fertility history and genital examination. The testis was measured using Prader's orchidometer (Prader, 1966) which was then correlated by scrotal ultrasound (SONOLINE G40, Diagnostic Ultrasound Systems, Manufactured by Siemens AG, Eriangen, Germany) (1–2 ml atrophied, 2–8 ml small volume, 8–12 ml moderate, >12 ml normal). We used Lambert formula to determine the testicular volumes = Length (L) × width (W) × height (H) × 0.71 (Lambert, 1951; Paltiel et al., 2002; Sakamoto et al., 2007). All the patients had their serum hormone levels measured using chemiluminescence immunoassay (CLIA) technique, with values in the range: 1.5–14 mIU/ml for FSH, 1.5–8 mIU/ml for LH, 2.5–17 ng/ml for prolactin, 2.4–8.3 ng/ml for total testosterone and 20–47 pg/ml for estradiol were taken as normal. A fasting morning serum sample for basal hormones determination was obtained prior to the micro-TESE attempt. All assays were performed using Cobas E411 immunoassay analyzer (Roche Diagnostics GmbH, Mannheim, Germany). Moreover, Giemsa Karyotype was used for standard cytogenetic procedure in all cases by analysis of at least 20 G-banded metaphases from a peripheral blood lymphocyte culture, and in all cytogenetically normal cases, molecular screening for Yq microdeletions was carried out on DNA extracted from peripheral blood using PCR (Simoni et al., 1999). Micro-TESE was performed under general anaesthesia with the patient in a supine position. A floor-standing operating microscope (Leica M500; Leica microsystems Pty Ltd, Gladesville, NSW, Australia) was used throughout the procedures. A senior andrologist with expertise in microsurgery was responsible to setup and implement the technique of micro-TESE as reported in the literature (Amer, Ateyah, Hany, & Zohdy, 2000; Schlegel, 1999).

2.4 | Testicular tissues were observed under optical magnification

X24 (dual-headed binocular tube and eyepieces 200, 300, 350-mm objective lens, motorised foot-operated zoom system). If no morphologically dilated tubules were observed, the incision was extended and blunt dissection performed between the septa of the testicular parenchyma to expose multiple areas. Copious irrigation of the field with Ringer's lactate solution was carried out to prevent blood from obscuring the field, and multiple samples were taken from the most dilated tubules. If there was no morphological difference in the appearance of testicular tissue, the samples were taken randomly, and a testicular fragment was excised and sent for histopathological evaluation (a sample representative of the predominant tissue at microscopic examination during surgery). If spermatozoa were not found, the contralateral testis was exposed via the same technique. Testicular tissues were taken in a Petri dish 1 ml HEPES-buffered sperm medium (Ham's F10 medium, Gibco BRL, Grand Island, NY, USA), and testicular biopsies were minced using sterile glass slides and shredded with 2 Jeweller forceps's under an Olympus stereo microscope (SZ-PT, Tokyo, Japan) to separate individual tubules and then examined immediately under an inverted microscope (Olympus IMT2) with Hoffman optics modulation (X400) for the presence of testicular spermatozoa in the entire Petri dish.

2.5 | Inclusion criteria of the patients

Patients who suffer from primary infertility of any duration with testicular volume <15 ml and their ejaculates were repeatedly azoospermic with a normal volume and alkaline pH. Obviously, also

subjects with FSH level >8 mIU/ml, who usually represent the majority of NOA patients, were included in our study.

2.6 | Exclusion criteria of the patients

Patients who suffer from severe systemic illness (end-stage renal disease; liver cell failure; congestive heart failure), cryptozoospermia, complete retrograde ejaculation, obstructive azoospermia (e.g., distended epididymides; impalpable vasa deferentia; vasectomy; findings suggestive of ejaculatory duct obstruction such as palpable seminal vesicles on digital rectal examination, hypospermia <1.5 ml ejaculate or acidic semen pH; and dilated ejaculatory ducts or absent seminal vesicles on TRUS), NOA due to hypogonadotropic hypogonadism, bilateral intra-abdominal cryptorchidism, AZF Yq micro-deletion involving the sub-regions *a* or *b*. Patients receiving anabolic steroids and/or exogenous testosterone therapy within at least 6 months prior to the time of surgery were also excluded. Finally, we excluded all patients with history of epididymorchitis and postpubertal mumps orchitis.

2.7 | Statistical methods

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 25. Data were summarised using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were done using the non-parametric Mann–Whitney test (Chan, 2003a). For comparing categorical data, chi-square (^{2}) test was performed. Fisher exact test was used instead when the expected frequency is less than 5 (Chan, 2003b). Multivariate Logistic regression was done to detect independent predictors of favourable outcome (Chan, 2004). P-values less than 0.05 were considered as statistically significant.

3 | RESULTS

Our study demonstrated that the mean age of the patients with positive micro-TESE outcome was 37.21 ± 9.71 years, whereas the mean age of the patients with negative micro-TESE outcome was 36.38 ± 7.62 years and this difference was of statistical insignificance (*p*-value 0.391) (Table 1). Furthermore, the mean duration of infertility of the patients with positive micro-TESE outcome was 8.01 ± 5.94 years, the mean duration of infertility of the patients with negative micro-TESE outcome was 7.1 ± 6.1 years, and this difference was of statistical insignificance (*p*-value 0.543) (Table 1). In addition, the mean of FSH levels in positive cases and negative cases was 19.52 ± 13.08 mIU/ml and 19.81 ± 14.21 mIU/ml respectively. This difference was of no statistical significance (*p*-value 0.767) (Table 1). A total of 450 patients had positive micro-TESE outcome. A total of 320 patients (71.1%) were working in Non-risky jobs, 130 (28.9%) were working in risky jobs, 400 were Egyptians (88.8%), 50 were non-Egyptians (11.2%), 80 (17.7%) were non-smokers, 30 (6.6%) were ex-smokers, 340 (75.7%) were smokers, none of them (0%) was drug abuser respectively (Table 2). A total of 945 patients had negative micro-TESE outcome. A total of 628 patients (66.5%) were working in Non-risky jobs and 317 (33.5%) were working in risky jobs, 830 (87.8%) were Egyptians and 115 (12.2%) were non-Egyptians, 211 (22.3%) were non-smokers, 50 (5.3%) were ex-smokers, 679 (71.9%) were smokers and 5 (0.5%) were drug abusers respectively (Table 2). These differences were of statistical insignificance (*p*-values 0.724, 0.411, 0.213 respectively) (Table 2). Our study did not reveal any association between positive micro-TESE outcome and testicular volumes (*p*-values 0.051, 0.258 respectively) (Table 3).

Furthermore, our study demonstrated significant associations between positive micro-TESE outcome and sertoli cell only syndrome (SCO), 1ry spermatocyte arrest, spermatid arrest and finally hypospermatogenesis (*p*-values <0.001, <0.001, 0.002, <0.001 respectively) (Table 3). Meanwhile, there were insignificant associations between positive micro-TESE outcome and tubular sclerosis and secondary spermatocyte arrest (*p*-values 0.597, 0.870 respectively) (Table 3). Additionally, the majority of the patients who had positive micro-TESE outcome were of high FSH level and this was of statistical significance (*p*-value 0.02) (Table 3). Finally, our study did not demonstrate any association between hormonal therapy and different types of hormonal therapy prior to micro-TESE and patients with positive micro-TESE outcome (*p*-values 0.219, 0.198 respectively) (Table 4). After adjustment of age, duration of infertility

TABLE 1 The association between the age and the infertility duration of the non-obstructive azoospermic patients and micro-TESE outcomes

	Final result										
	+ve					−ve					
	Mean	*SD*	Median	Minimum	Maximum	Mean	*SD*	Median	Minimum	Maximum	*p* value
Age (years)	37.21	9.71	36.00	20.00	77.00	36.38	7.62	35.00	19.00	73.00	0.391
infertility duration (years)	8.01	5.94	5.00	2.00	40.00	7.05	6.11	5.00	1.00	40.00	0.543
FSH level	19.52	13.08	16.40	1.43	111.40	19.81	14.21	17.00	1.20	109.60	0.767

Note. +ve: favourable micro-TESE outcome; −ve: non-favourable micro-TESE outcome.

TABLE 2 The association between the socio-demographic characteristics of the non-obstructive azoospermic patients with positive and negative micro-TESE outcomes

	Final result				
	+ve		−ve		
	Count	%	Count	%	*p* value
Occupation					
Non-risky	320	71.1	628	66.5	0.724
Risky	130	28.9	317	33.5	
Residence					
Egyptian	400	88.8	830	87.8	0.411
Non-Egyptian	50	11.2	115	12.2	
Special habits					
Non smoker	80	17.7	211	22.3	0.213
Ex-smoker	30	6.6	50	5.3	
SMOKER	340	75.7	679	71.9	
Smoker, drug abuse	0	0.0	5	0.5	

Note. +ve: favourable micro-TESE outcome; -ve: non-favourable micro-TESE outcome.

TABLE 3 The association between the testicular volume and the degree of spermatogenesis impairment and the level of FSH and micro-TESE outcomes

	Final result				
	+ve		−ve		
	Count	%	Count	%	*p* value
Right testis volume					
Atrophied	5	1.1	2	0.2	0.051
Normal	60	13.3	220	23.3	
Moderate	245	54.4	466	49.3	
Small	140	31.1	257	27.2	
Left testis volume					
Atrophied	4	0.8	5	0.5	0.258
Normal	62	13.7	224	23.7	
Moderate	234	52	453	47.9	
Small	150	33.3	263	27.8	
Level of FSH					
Normal	63	14	292	30.8	0.02
High	387	86	653	69.2	
Testicular histopathology					
Sertoli cell only (SCO)	224	49.8	534	56.5	<0.001
Tubular sclerosis	69	15.3	135	14.3	0.597
1ry spermatocyte arrest	78	17.3	225	23.8	<0.001
2ry spermatocyte arrest	12	2.7	31	3.3	0.870
Spermatid arrest	31	6.9	20	2.1	0.002
Hypospermatogenesis	36	8	0	–	<0.001

Note. +ve: favourable micro-TESE outcome; -ve: non-favourable micro-TESE outcome.

and hormonal therapy prior to micro-TESE, logistic regression analysis revealed high statistical significance between positive micro-TESE outcome and high FSH level and testicular histopathology, especially SCO as it was representing the majority of the cases, who are mostly associated with high FSH. Thus, high FSH level may be hopefully considered a predictive factor in this group of patients (OR 1.6, 0.21, 95% CI lower 1.2, 0.008 and upper 2.1, 0.06 and finally *p*-values 0.003, <0.001 respectively).

4 | DISCUSSION

Our retrospective study did not reveal any association between positive micro-TESE outcome and non-invasive preoperative parameters (age, duration of infertility and testicular volume). Similarly, Bryson et al (2014) observed that NOA patients with severe testis atrophy, specifically with testicular volumes of 2 ml or less, had the same sperm retrieval rate (SRR) as patients with volumes above 10 ml (55% vs. 55%).

Moreover, Ramasamy, Trivedi, Reifsnyder, Palermo, and Rosenwaks (2014) concluded that age had no predictive value for SRR. Li et al (2017) demonstrated that testicular volume and FSH in men with NOA do not predict sperm retrieval at a primary micro-TESE attempt. In contrast, some factors, such as age, might possess predictive value for successful sperm recovery (Li et al., 2017).

In the testis, testosterone and dihydrotestosterone (DHT) target Sertoli cells through the androgen receptor (AR) (Silva, Leite, & Wassermann, 2002). Sertoli cells secrete testosterone-dependent paracrine stimuli for germ cells, and FSH target Sertoli cells through FSH receptors (FSHR); thus, these two previous steps regulate Sertoli cells to support spermatogenesis (Shiraishi & Matsuyama, 2017). Noteworthy, testosterone is one of the most important factors for initiating and maintaining spermatogenesis (McLachlan, 2002). Furthermore, findings from luteinizing hormone receptor knock out (LuRKO) mice revealed the importance of LH action for spermatogenesis (Griffin et al., 2010). Consequently, LH became the main regulatory gonadotropin for spermatogenesis more than FSH (Huhtaniemi, 2015). There were several trials utilising FSH, classically using human menopausal gonadotropin (hMG) and more recently recombinant human (rhFSH) (Attia, Abou-Setta, & Al-Inany, 2013; Rastrelli, Corona, Mannucci, & Maggi, 2014; Valenti et al., 2013). This is because the stimulation of Sertoli cells has been believed to contribute more directly to restoration of spermatogenesis than hCG alone because of the localisation of Sertoli cells (Attia et al., 2013; Rastrelli et al., 2014; Valenti et al., 2013). Our study did not demonstrate any beneficial role for different modalities of hormonal therapy on the SRR in our patients. Noteworthy, we tried different hormonal programs on empirical basis as we supposed that the majority of these patients were SCO with high FSH level.

On the other hand, Hussein, Ozgok, Ross, Rao, and Niederberger (2013) reported the usefulness of clomiphene citrate as the initial

TABLE 4 The association between the hormonal therapy prior to micro-TESE and micro-TESE outcomes

	Final result				
	–ve		+ve		
	Count	%	Count	%	*p* value
Hormonal therapy					
Yes	308	32.6	118	26.2	0.219
No	637	67.4	332	73.7	
Type of hormonal therapy					
HCG + HMG	98	31.8	33	27.9	0.198
Anti-oestrogen	50	16.2	16	13.6	
Testosterone	58	18.8	21	17.8	
Purified or recombinant FSH	13	4.2	9	7.6	
HCG + HMG + Anti-oestrogen	31	10.1	10	8.4	
HCG + HMG + Testosterone	28	9.1	6	5.1	
Anti-oestrogen +Testosterone	22	7.1	15	12.7	
Aromatase inhibitor	4	1.3	2	0.17	
HCG + HMG + FSH + Anti-oestrogen + Testosterone	4	1.3	6	5.1	

Note. HCG: human chorionic gonadotropin; HMG: human menopausal gonadotropin; +ve: favourable micro-TESE outcome; -ve: non-favourable micro-TESE outcome.

treatment prior to micro-TESE as a result of optimising intratesticular testosterone levels because many men with NOA have low testosterone levels and an abnormal testosterone to estradiol ratio (T/E2 ratio); however, E2 increases inevitably due to elevated testosterone. Similarly, Reifsnyder, Ramasamy, Husseini, and Schlegel (2012) showed a partial effect of testosterone optimisation on micro-TESE outcomes following treatment with clomiphene citrate, hCG or aromatase inhibitors. However, a definitive conclusion regarding sperm production after the enhancement of endogenous testosterone production following medical interventions cannot be drawn due to the lack of well-designed clinical trials (Esteves, 2015).

The present study showed that the spermatozoa were retrieved in 32.25% of patients undergoing their first extraction attempt (450/1,395). A comparable extraction rate was reported by the study published by Friedler et al (2002) who noted that first TESE yielded mature spermatozoa in 39% (32/83) of men with NOA. However, prior studies (Enatsu, Miyake, Chiba, & Fujisawa, 2016; Ramasamy & Schlegel, 2007) reported a SRR by micro-TESE ranging between 40% and 65% in NOA patients. Therefore, the SRR reported here is under the lower end of most published results. Our finding might be attributed partly to different expertise levels between the fifteen senior andrologists of our team in retrieving spermatozoa from these patients and a consequent undefined number of biologists assisting them in the operative rooms. Similarly, Ishikawa, Nose, Yamaguchi, Chiba, and Fujisawa (2009) reported a very long learning curve, which may negatively interfere with positive sperm retrieval rate. Furthermore, our study included (NOA) patients with poor clinical diagnosis and prognosis.

Our current study demonstrated that the commonest histopathological patterns of the included patients with no prior biopsies were SCO (54.3%), primary spermatocyte arrest (21.7%), tubular sclerosis (14.6%), hypospermatogenesis (2.6%), spermatid arrest (3.7%), 2ry spermatocyte arrest (3.1%) respectively. Furthermore, there was an association between SRRs and the respective testicular histopathology which was of high statistical significance except tubular sclerosis and secondary spermatocyte arrest. The incidence of SCO was nearly similar to that reported by previous studies (Caroppo et al., 2016; Enatsu et al., 2016; Ramasamy & Schlegel, 2007), but significantly higher than that of Talas, Yaman, and Aydos (2007) who reported that SCO was evident in only 16.2% of histological patterns. The proportion of all maturation arrest patterns in the present study (28.5%) was higher than that reported by Tsujimura et al (2002) (7.1%), Ramasamy and Schlegel (2007) (8.9%), Enatsu et al (2016) (12.2%) and Caroppo et al (2016) (15.4%), but nearly equal to the incidence mentioned by Talas et al (2007). Moreover, distribution of hypospermatogenesis pattern in this study was lower than that found by Ramasamy and Schlegel (2007) (7.4%), Enatsu et al (2016) (13.1%), and significantly lower than that reported by Tsujimura et al (2002) (21.4%), Talas et al (2007) (20.6%) and Caroppo et al (2016) (23.8%). Recently, a study conducted by Abdel Raheem et al. (2013) has suggested that preoperative histopathology is the most important factor in predicting SRRs in men who undergo repetitive biopsy. In contrast, it is well noted that an isolated testicular biopsy is an invasive procedure that can cause inflammatory changes, haematoma, fibrosis or atrophy (Schlegel & Su, 1997). Thus, an isolated diagnostic biopsy should not be performed and testicular biopsy should be performed concurrently with TESE (Kalsi et al., 2015).

Our current study demonstrated that SSRs were 100% in cases with hypospermatogenesis, 60.8% with spermatid arrest, 33.8% with tubular sclerosis, 29.6% with SCO, 27.9% with secondary

spermatocyte arrest, 25.5% with primary spermatocyte arrest respectively. SRR reported for patients with SCO pattern (29.6%) in the present study was higher than that mentioned in the study that was conducted by Modarresi et al (2015) (23.6%) and lower than that reported by Amer et al (2000) (33.3%), Okada et al (2002) (33.9%), Tsujimura et al (2006) (39.1%), Kalsi et al (2015) (40%) and Ramasamy, Yagan, and Schlegel (2005) (41%) and Tsujimura et al, 2002 (42.9%). Meanwhile, SRR in regard to every kind of maturation arrest pattern was lower (32.25%) to the most published results (Kalsi et al., 2015; Ramasamy et al., 2005; Tsujimura et al., 2006) as they reported SRRs of 41.7%, 36%, and 44% respectively. Interestingly, the SRR reported in the current study was lower than that demonstrated by Amer et al (2000). However, it should be noted that the study conducted by Amer et al (2000) demonstrated favourable histopathological patterns as follow: 8 cases were normal histopathology and 7 cases were hypospermatogenesis and 10 cases were early spermatid arrest and 30 cases were mixed pathology respectively. Thus, the histopathological patterns with favourable prognosis represented 55 cases out of the 100 patients who were recruited in this study which is totally different than the histopathological patterns of the current study which are mainly SCO. Furthermore, the SRR in cases with SCO in the study conducted by Amer et al (2000) was 33.3% which is nearly comparable to the current rate that is demonstrated by our study (29.6%). In 2008, the same author with different team performed a study to demonstrate the cut-off value of single tubule diameter as a predictor for sperm retrieval in NOA patients.

Unfortunately, they did not evaluate the association between different histopathological patterns and the respective single tubule diameters (Amer et al., 2008). Thus, we cannot determine the SRR in cases with SCO in the above-mentioned study to compare with the SRR delivered out by the current study as these cases were the main target group in our study. Remarkably, we retrieved spermatozoa in all cases with hypospermatogenesis. Similarly, Tsujimura et al (2006), Colpi et al (2009), Ramasamy et al (2005) and finally Kalsi et al (2015) reported high SRR in cases with hypospermatogenesis. Although the SRR in cases with tubular sclerosis was 33.8%, however, it was lower than reported by Bryson et al (2014) who demonstrated SRR (55%) in cases with testicular atrophy of 2 ml or less and higher than that reported by Amer et al (2000) who demonstrated SRR (12.5%) in cases with tubular hyalinisation. Our current study did not reveal a positive association between SRR and FSH level which was of statistical insignificance. Interestingly, we did further analysis between positive micro-TESE outcome and FSH level assuming that any FSH level above 8 mIU/l to be high and any level below this cut-off value to be normal, this revealed a positive association which was further confirmed by a logistic regression analysis. This can be explained by two facts. Firstly, the majority of the patients were SCO who are mostly associated with high FSH. Secondly, patients with elevated FSH level may have heterogeneous areas of histopathology within their testis (Ramasamy et al., 2009). Consistently, Berookhim, Palermo, Zaninovic, Rosenwaks, and Schlegel (2014) concluded that a combination of testicular volume and serum FSH levels among patients with known SCO pathology may help in patient counselling. In the same vein, Ishikawa (2012) reported that the serum FSH could predict the existence of spermatozoon that could be retrieved by conventional TESE. Quite the reverse, Li et al (2017) showed that FSH and testicular volume possessed low predictive values.

A major limitation of this study was the presence of difference in the expertise levels among the fifteen senior andrologists who performed micro-TESE for the patients and a consequent undefined number of biologists assisting them in the operative rooms which can be one of the confounding factors that resulted in the low SRR.

Another obvious limitation of this study was that results were analysed retrospectively.

Furthermore, we did not register pregnancy and live birth rates. Finally, we did not follow-up the patients for longer periods to detect any potential late postoperative complications.

5 | CONCLUSION

This study reveals that preoperative testicular biopsy is unnecessary to predict the sperm retrieval rate in patients with non-obstructive azoospermia. Finally, our study highlights the probability of retrieving spermatozoon from these patients, despite high FSH level.

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CONFLICT OF INTEREST

All authors declare no conflict of interest.

AUTHORS' CONTRIBUTIONS

Medhat Amer conceived and designed the study. Ahmed Ragab and Asmaa Ahmed collected and analysed the data. Sameh Fayek GamalEl Din interpreted the data and intellectually drafted the manuscript. All authors approved the final version of the draft.

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