Original article

Follicle-Stimulating Hormone and Age as Predictors Forpositive Sperm Retrieval in Patients with Azoospermia

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Abstract

Azoospermia is the complete absence of sperm in the semen, one of the causes of infertility, affecting around 1% of the male population and 10-12% of the male with infertility. Follicle-stimulating Hormone [FSH] and age are commonly used predictors to estimate the outcome of sperm retrieval. However, the precision of the FSH level and age of patients as predictors for positive sperm retrieval is variable between studies. The purpose of this research was to investigate the effect of the patient's age and FSH level on successful sperm retrieval. A pilot retrospective medical records review study was conducted. Sixty-eight infertile patients with azoospermia who underwent sperm retrieval procedures were included. Trans-epididymal sperm aspiration [TESA] was conducted on 35 azoospermic patients, and 33 patients underwent trans-epididymal sperm extraction [TESE] at Albayda Fertility Teaching Centre/Libya. Data was collected from the 1st of October 2017 to the 15th of October 2022. SPSS software version 26 was used for data analysis. All the included subjects were with primary subfertility. The total number of cases with successful sperm extraction were 34 [50%] and it was 17 [48.6%] and 17 [51.5%] for TESA and TESE respectively and the difference was non-significant between the two procedures [$\chi^2 = 0.059$, p = 0.81]. Patients with successful sperm retrieval rates had significantly lower mean FSH levels [9.82 mIU/mL, SD ± 7.43] than patients with high FSH levels [16.26 mIU/mL, SD ± 11.56, p = 0.008]. The mean age of successful sperm retrieval was 41 years [SD ± 7 years]. Patients who were aged 40 years and above also had the highest extraction rate [71.0%] compared with patients between 20-29 years and 30-39 years [27.3% and 34.6%, respectively], and. Low FSH levels and older age were associated with a higher success rate of sperm retrieval. Further studies are warranted to investigate the cause of low sperm retrieval rates among younger azoospermic patients.

Keywords: *Follicle-stimulating Hormone [FSH], Age, Sperm Retrieval, Azoospermia.*

Introduction

The 5th edition of the World Health Organisation [WHO] manual [1] defines azoospermia as no spermatozoa are found in the sediment of a centrifuged semen sample [1]. The American Urological Association has adopted a more detailed definition for azospermia: no sperm found after centrifugation of semen sample at 3000 × g for 15 minutes and examination of the pellet [2,3]. One percent of males in the general population and 10%–12% of infertile males have azoospermia [2,3]. 60% of cases of azoospermia are non-obstructive azoospermia [NOA], which is brought on by testicular failure [3].

Pre-testicular, testicular, and post-testicular are the three broad groups into which the aetiologies of azoospermia can be divided [4]. Endocrine abnormalities that have a negative impact on spermatogenesis are the primary causes of non-obstructive azoospermia [5]. Intrinsic spermatogenic disorders within the testes are the established causes of testicular aetiologies [5]. Non-obstructive azoospermia includes both endocrine and spermatogenic disorders [pre-testicular and testicular disorders] [2,3,5].

Obstructive azoospermia [OA] refers to the post-testicular causes of azoospermia, which include ductal system obstruction at any point in the male reproductive tract [2,3].

Every azoospermia etiology has a unique prognosis, ranging from sperm discovery in the reproductive tract to production returns [5]. Treatment for the pre- and post-testicular abnormalities that lead to azoospermia is frequently possible, which might make it easier to

restore fertility potential. In contrast, testicular disorders are typically irreversible, and interventions linked to intrinsic testicular abnormalities have much lower success rates [4,5]. Trans-epidermal sperm extraction [TESE] is one of several sperm extraction techniques, and it is carried out through an open scrotal incision. A surgical microscope may or may not be used during the procedure. A small transverse incision is made in the anterior aspect of the tunica albuginea, exposing the testis. More than half of men may not have spermatozoa when using standard open testicular sperm extraction techniques. Although it is believed that when using a microscope, vessels are easier to identify so there is a lower risk of vascular damage to the tunica albuginea [6,7]. However, it was found that, the risks of the procedure, such as hematoma, scarring, or testicular atrophy, are the same whether or not the microscope was used [6,7]. In microsurgical TESE there was a success rate of around 38% [8], which means that there is no difference in the sperm success rate whether microscope used or no during TESE.

Men with obstructive azoospermia are frequently subjected to trans-epidermal sperm aspiration [TESA] because it is the least invasive procedure, does not call for specialized surgical tools or an andrologist or urological surgeon to perform, and is frequently carried out by a gynecologist [9]. In men without dilated efferent epididymal tubules, as in cases of non-obstructive azospermia, trans-epidermal sperm aspiration frequently fails to produce enough sperm for cryopreservation, but it occasionally provides enough spermatozoa for a fresh-cycle IVF-ICSI [6, 9].

In TESA The epididymis is punctured with a tiny 30-gauge needle, and its contents are aspirated. If sperm are not found by the microsurgical epididymal sperm aspiration procedure, the surgeon may proceed with testicular sperm extraction [6, 7, 9]. Sperms provided by any of the above extraction procedures followed by Artificial Reproductive Technology [ART], such as intracytoplasmic sperm injection [ICSI], which is the definite treatment for many azoospermic patients [9].

Identifying patients with a high likelihood of achieving effective spermatozoa recovery is essential in infertile couple counselling. Serum FSH is a factor reflecting testicular spermatogenic function, and studies have shown that FSH is a major predictor of sperm retrieval [10,11]. This cheap indicator [FSH level], as well as age, can help in identifying which azoospermic patients can benefit more from sperm retrieval procedures and determining those who are more likely to have positive results to lower the cost and not to give high expectations to those patients [11]. The purpose of this study was to assess age and FSH levels as predictors of successful spermatozoa retrieval rates in azoospermic infertile men.

Methods

The present study was a prospective comparative study conducted after obtaining the ethical approval from the Al-Mukhtar committee for Bio-safety and Bioethics (MCBB) reference number (NBC: 007. H. 23. 6). Study was conducted based on the data collected from Albayda National Fertility Centre records over a period of five years. Written consent was obtained from the participants before the commencement of the procedure. The scope of this study was to investigate the role of variables such as FSH, which is a cheap, established, readily available test, and age in successful sperm recovery. The study involved a retrospective analysis of the medical records of non-obstructive azoospermia [NOA] patients who underwent sperm retrieval surgery, and statistical analysis was performed to assess the effect of FSH levels, age on the success rate of sperm retrieval. The findings of this study could potentially aid in improving the success rate of sperm extraction surgery in azoospermic patients. Males included were from all over the country and they were aged between 20 and 52 years.

A history was taken from patients to assess for risk factors that may have led to azoospermia, such as cryptorchidism, bilateral inguinal hernia, mumps in
childhood, or a family history of cystic fibrosis. A thorough physical examination was carried out, with special attention paid to the volume of the testes, the presence of epididymal dilatation, and the existence of vas deferens or tumors. For patients with azoospermia, semen samples obtained by masturbation between 3 to 5 days of abstinence were analyzed twice and azoospermia was diagnosed based on the 5th edition of the WHO manual [1]. FSH levels were measured before the procedure, and the age at the time of the procedure was documented.

Sixty-eight infertile men were patients with azoospermia who underwent either testicular sperm aspiration [TESA] or testicular sperm extraction [TESE] sperm retrieval procedures at the Albayda Fertility Teaching Centre in Libya. Both procedures were performed according to the urologist's preference, with no specific criteria for who would have a TESE or

TESA procedure. All sperm extraction procedures were performed by a urologist, with TESE under spinal anaesthesia and TESA under local anesthesia. There was no postoperative complication in all cases included. Data were collected from October 1st, 2017 to October 15th, 2022.

Statistical analyses were performed using SPSS [version 26]. The continuous data were expressed by mean and standard deviation, and the student t-test was used to compare the data. Categorical data were represented as numbers and proportions. and the Chi-square statistic test was used to compare the categorical data. A P- value of <0.05 was considered significant.

Results

Table 1 summarizes the characteristics of the patients. All 68 included in the study had primary infertility, and most of the patients were between 30 and 49 years old. Half of the patients had successful sperm extraction [50]). There were no differences in the success rate between the TESA and TESE sperm retrieval methods [48.6% and 51.5%, respectively [$\chi2$ = 0.059, p = 0.81]].

Table 1. Characteristics of the study subjects [n = 68]

Parameter	Number	Percentage
Age (years)		
20-29	11	16.2%
30-39	26	38.2%
40-49	28	41.2%
50 and above	3	4.4%
Infertility type		
Primary	68	100.0%
Secondary	0	0.0%
Sperm retrieval method		
TESA	35	51.5%
TESE	33	48.5%
Sperm retrieval result		
Positive	34	50.0%
Negative	34	50.0%
Title 1	Title 2	Title 3

While comparing FSH levels with the outcome of the sperm retrieval procedure [Figure 1], it was evident that patients with positive sperm retrieval rates had significantly lower mean FSH levels [9.82 mIU/mL, SD ± 7.43] than cases with high levels of FSH [16.26 mIU/mL, SD ± 11.56, t [66] = 2.7, p = 0.008].
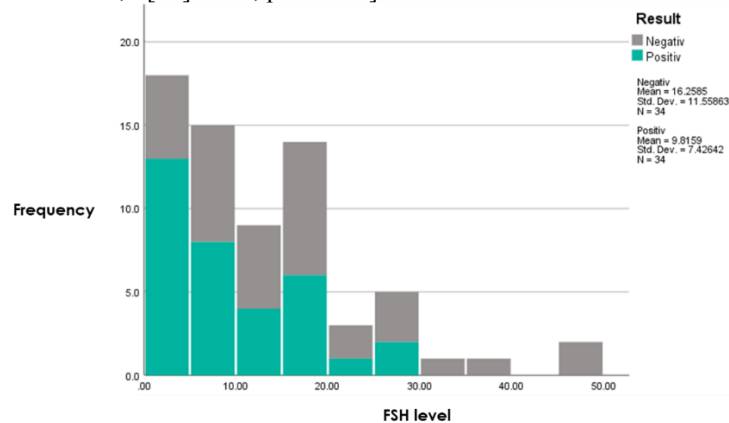

Figure 1: FSH levels and sperm extraction result in patients with primary subfertility.

The age of the patients was also a major predictor for a successful sperm retrieval as demonstrated on Figure 2. Patients who were aged 40 years and above had the highest extraction rate (71.0%) compared with patients between 20-29 years and 30-39 years (27.3% and 34.6%, respectively). The mean age of patients with a successful sperm retrieval rate was 41 years (SD ± 7 years).
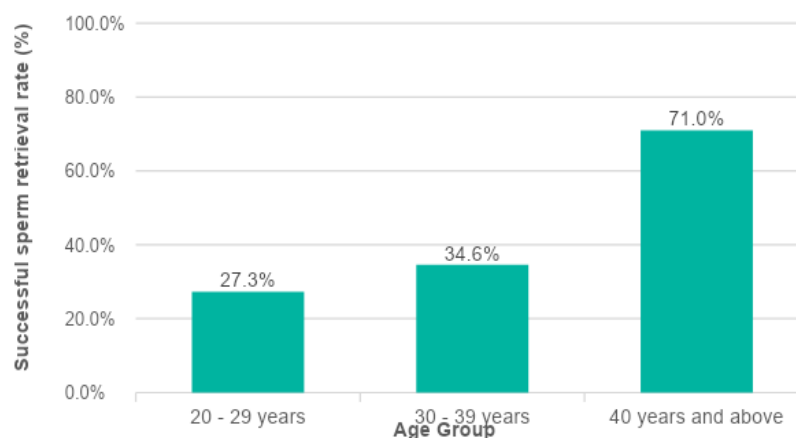

Figure 2: Age and percentage of patients with successful sperm retrieval rates.

Discussion
About ten percent of men who experience infertility have a diagnosis of azoospermia [3]. Various factors can lead to non-obstructive azoospermia [NOA], an untreatable testicular failure that is characterized by impaired testicular endocrine [producing testosterone] and/or exocrine [producing sperm] function [6, 10]. Serum hormone levels, histopathological and genetic studies, and age are factors that can predict the outcome of retrieval procedures [6, 11]. To predict the likelihood of sperm extraction being successful and to minimize the psychological and physical burden on patients, pre-operative counseling should be given to those with azoospermia. To give them an estimate of the expected success rate of surgical sperm retrieval and for a better understanding of the spermatogenic predictors in NOA patients [12].

In the present study, the rate of surgical retrieval of viable spermatozoa was 50%. A similar retrieval rate of 50% was previously reported in the literature [6,7]. In comparison, our rate was considerably lower than the 65.5% successful retrieval rate reported by Eken and Gulec [2018] [13].

Ramasamy and colleges [2008] mentioned that by their neural computational system and nomogram to predict the probability of successful sperm retrieval that the older age and higher FSH predict better chances of sperm retrieval with internal validation; the nomogram accuracy was 59.6% [7]. The current study agrees with that nomogram in one point that older patients have a better chance for positive sperm retrieval as males over 40 years old in this study had a 71% positive extraction rate. The results of the current study also agree with Aljubran and Safar [2022] [15], whose study reported that sperm retrieval rates [SRRs] were higher in men ≥50 years old than men <50, [73% in men ≥50 years and 56% in men <50 years]. Of the 44 men ≥50 years old [7, 14], while a higher FSH has a low probability of positive sperm extraction [15].

The current study demonstrated that men with FSH levels lower than 9.82 IU/mL had a higher sperm retrieval than men with FSH levels higher than 16.26 IU/mL. Additionally, however, sperm retrieval was possible even when FSH levels rose noticeably above 50 IU/mL which agrees with Ramasamy [2013] and CHEN [2011] [7, 11]. Males aged over 40 had a 71% positive extraction rate, while men in the 30-39 age range had a rate of 34.65%, and men in the 20-29 age range had the lowest rate of 27.3%.

This may offer the possibility of developing guidelines for sperm retrieval in azoospermic patients that could help the physician to make a better clinical decision for the patient's selection, who is more likely to benefit from the procedure. In addition, these findings can help in couple counseling.

Conclusion

Azoospermic infertile men with a lower FSH levels and an older age had a higher success rate of sperm retrieval. Further studies are warranted to investigate the cause of low retrieval rates among younger adults.

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