

## Original Article

### Predictive value of serum Follicle Stimulating Hormone and testicular volume as markers for the outcome of surgical spermatozoa retrieval in men with azoospermia

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#### Abstract

**Background:** To predict the outcome of surgical retrieval of spermatozoa using serum FSH and testicular volume as markers in men with Azoospermia.

**Method:** It was a cross sectional study from February 2008 to July 2011 done at the Department of Reproductive Medicine at a tertiary care hospital. Forty seven men with Azoospermia who had undergone surgical testicular or epididymal spermatozoa retrieval were included in the study. The data was analyzed in two groups- serum FSH levels: 1-14 and > 14 IU/mL; testicular volumes were analyzed under 2 groups: <8 ml and ≥8 ml.

**Findings:** Spermatozoa were successfully retrieved in 57% of the men with azoospermia. Spermatozoa retrieval rates in the group of men with FSH values 1-14 IU/ml were 64.9% and > 14 IU/ml were 30% and the difference was statistically significant with a p value of 0.0479 and an odds ratio of 4.3. Regarding testicular volume, the spermatozoa retrieval in the group < 8 ml & ≥ 8 ml were 33.3% and 57.8% respectively, with a p value of 0.09 and odds ratio of 4.13

**Conclusion:** The chance of spermatozoa retrieval is 65% in men with normal FSH and it is a better predictor for surgical spermatozoa retrieval.

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**Key Words:** Azoospermia, Follicle stimulating hormone, Spermatozoa retrieval, Testicular volume.

#### Introduction

Azoospermia is defined as absence of spermatozoa in a neat and centrifuged semen sample confirmed by repeat analysis done at 3-4 weeks interval as per WHO guidelines 2010. Azoospermia due to hypogonadotropic hypogonadism is treated by hormonal therapy. Structural chromosomal abnormalities are present in about 1% of azoospermic men. Karyotyping study has shown terminal Y chromosome deletions in azoospermic men who are phenotypically normal<sup>1</sup>. The treatment option for this group of men is surgical testicular spermatozoa retrieval. In group of men where the cause is due to bilateral vasal obstruction, epididymal spermatozoa retrieval can be offered. Success of testicular spermatozoa retrieval varies from 30-70 %<sup>2,3</sup> in azoospermic men with defective spermatogenesis. Surgical spermatozoa retrieval may involve multiple biopsies which is done either prior to oocyte pickup or concurrently. Retrieval of very few live spermatozoa

will be sufficient for treatment with ICSI. If there is no spermatozoa retrieval, then it results in stress and emotional disturbance to the couple. So it is important to predict the success of surgical spermatozoa retrieval preoperatively.

Y chromosome contains AZF region which is responsible for spermatogenesis. It is further divided into 3 subdivisions as AZFa, AZFb, AZFc. Mutations in AZFa and AZFb are not so common, but causes complete absence of spermatozoa in testes. Mutation in AZFc is most common, spermatozoa can be retrieved from testes in this group of men as a copy of it is present in chromosome 3<sup>1</sup>. To predict the presence of spermatozoa in testes by these mutational studies is expensive and the expensive equipment required are not available in most laboratories. It is therefore, necessary to identify markers which are inexpensive and readily available to predict the presence of sperm in testes.

Serum FSH level is an indicator of testicular function and in turn of spermatogenesis. Bulk of the testis is made of seminiferous tubules where spermatogenesis takes place. The objective of the present study is to explore the importance of serum FSH and Testicular volumes in azoospermic men as predictive markers, prior to surgical testicular exploration.

## Materials and Methods

The present study is a cross sectional retrospective study conducted in the Department of Reproductive Medicine at a tertiary care hospital (Chettinad Super Speciality Hospital) from February 2008 to July 2011. All men with azoospermia who have undergone surgical spermatozoa retrieval during the study period were included in the study, no sampling was done. Informed consent of the patients was taken prior to the surgical procedures.

Azoospermia was confirmed by repeat analysis of neat and centrifuged sample of semen done at an interval of 3-4 weeks. Serum FSH was determined by ELISA. Testicular volume was determined by clinical palpation done by a single Andrologist. The average of the testicular volume was taken for analysis. Surgical spermatozoa extraction was done either from testes or epididymis.

### a. Testicular Spermatozoa Extraction

Under general/spinal anaesthesia, multiple testicular biopsies were done and sent to embryology lab in HEPES (Hydroxy Ethyl Piperazine Ethane Sulfonic acid) based medium. The biopsied sample was minced using tuberculin syringe with needle under stereo zoom microscope. Spermatozoa were visualized under 10x inverted microscope. When spermatozoa were seen, they were cryopreserved for use in cases where it was done prior to oocyte pickup. If the procedure was done concurrently along with oocyte pickup, the spermatozoa were prepared and used for ICSI. A randomly selected sample was sent for histopathological examination and graded according to Johnson's scoring system.

### b. Epididymal Sperm Extraction

Three different procedures used for epididymal sperm extraction were Percutaneous Epididymal Sperm Aspiration (PESA), Microscopic Epididymal Sperm Aspiration (MESA) and Macroscopic Epididymal Sperm Aspiration (MAESA), all were done under general or spinal anaesthesia.

## Ethical clearance

No ethical clearance was required, as routine clinical data collected during the patients treatment process was analysed retrospectively. However, informed consent of the patient was taken prior to the surgical procedure. Confidentiality of the participants was strictly maintained during analysing and presenting the results.

## Statistical analysis:

Serum FSH levels and testicular volume were taken as the exposure parameters and surgical spermatozoa retrieval was taken as the outcome measure for the purpose of analysis. The men were divided into two groups based on FSH values (1-14 IU/mL and >14 IU/mL). Based on testicular volume men were divided into 2 groups (< 8 mL and ≥ 8 mL). The statistical association between the exposure and outcome parameters was assessed by using chi square test with yate's correction. The p-value and 95% CI were calculated. Statistical package for social sciences (SPSS), version 18 and EPIINFO were used for the analysis. P value < 0.05 was considered statistically significant.

## Results

A total of 47 azoospermic men were recruited, surgical testicular spermatozoa recovery was successful in 27 (57%) men. (Testicular spermatozoa retrieval in 48.6% and epididymal spermatozoa retrieval in 90%.)

Out of 47 men, 37 men were in normal FSH range (1-14 IU/mL) and spermatozoa were retrieved in 24 (64.9%) of them. In the elevated FSH level (>14 IU/mL) group there were 10 men and spermatozoa were retrieved in (30%) 3 of them as shown in Table 1.

**Table 1. Sperm retrieval in different FSH categories**

FSH Level (IU/ml)	Total Number of Men	No. of men with successful Sperm Retrieval (%)
1-14	37	24 (64.9) %
>14	10	3 (30) %

Based on testicular volume, men were divided into 2 groups as < 8 mL and ≥ 8 mL. There were totally 6 & 38 men in each group and spermatozoa were retrieved in 2 (33.3%) & 22(57.8%) men respectively as shown in Table 2.

Out of 47 men, 3 had bilateral hydrocele, so their volume could not be assessed clinically, hence excluded from the study.

Table 2. Sperm retrieval in different testicular volume categories

Testicular Volume (ml)	Total Number of Men	No. of men with successful Sperm Retrieval (%)
<8	6	2 (33.3)
≥8	38	22 (57.8)

On assessing the statistical association between FSH values and spermatozoa retrieval, the odds of retrieving spermatozoa is 4.3 times higher in men with normal FSH when compared to men with elevated FSH levels - Odds Ratio 4.3 with 95 % CI (Chi square with Fisher Exact test) and p-value 0.0479 and found to be significant. The positive predictive value is 65%.

On assessing the statistical association between testicular volume and spermatozoa retrieval, the odds ratio is 4.13 with 95% CI and p value is 0.09, which is not significant.

## Discussion

This analysis was aimed at validating the usefulness of most frequently used parameters like serum FSH concentration and testicular volume for clinical decision making in men with azoospermia.

The present study shows that increase in FSH levels (>14 IU/mL) leads to lower spermatozoa retrieval when compared to men with FSH in the normal range (1-14 IU/mL), which was statistically significant. These observations are consistent with the previous study<sup>4</sup> where increase in FSH levels showed decrease in spermatozoa retrieval rate which was statistically significant. Turunc et.al., (2010) reported a negative correlation between FSH levels and spermatozoa retrieval, but the correlation was not statistically significant. This is contrary to another study<sup>6</sup> reported earlier this year, which showed spermatozoa retrieval is lower in the group with FSH <15 IU/mL. Spermatozoa were retrieved in one man with FSH level as high as 37.1 IU/mL. The predictive value of testicular spermatozoa extraction was 69% for plasma FSH concentration in a study reported by Tournaye et al, (1997). This is comparable to our present study in which the predictive value is 65%.

In our study, testicular volume has been found to be a poor predictor of successful spermatozoa recovery. This is in consistency with the previous studies<sup>7,8</sup> where there is no statistically significant difference in testicular volume between men in whom spermatozoa were retrieved and in those where retrieval was not possible. A positive correlation between spermatozoa retrieval and testicular volume has been found in few studies<sup>4,5,9</sup>. Further, spermatozoa were retrieved in men with testicular size of 5 ml<sup>8</sup>, using micro Testicular Sperm Extraction (TESE) procedure in non-obstructive azoospermic patients. The positive predictive value for testicular volume ≥ 8 ml is 57.8%.

Many prior studies<sup>3,4,10</sup> have taken histopathological examination as predictive factor for successful surgical spermatozoa retrieval. This factor has not been included in this study, as preliminary diagnostic testicular biopsy procedure is not done in our setup. Different areas of testes may have varying histology; single biopsy may not be a representative of whole testes and may miss areas of spermatogenesis.

In conclusion, our evaluation shows that the chance to successfully retrieving spermatozoa by TESE is 65% in men with normal FSH (cut off 14 IU/ml) and that FSH is a better predictor for surgical spermatozoa retrieval than the volume of the testis.

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### Inhale Your Diabetes

Cigarette smoking has been implicated as a causative factor in so many human ailments. Can any new observation make cigarette smoke appear worse than it already is? According to a new study, you need not have to be a smoker to suffer the latest ill-effects attributed to cigarette smoke; you have to be just a passive inhaler. Those effects are Type 2 diabetes mellitus and obesity. For the study, Friedman and colleagues used data from a nationally representative sample of more than 6,300 adults who took part in the US National Health and Nutrition Examination Survey (NHANES) between 2001 and 2006. They used cotinine as biomarker for tobacco exposure. The study included 25% smokers (cotinine > 3 ng/mL), 45% non-smokers (cotinine < 0.05 ng/dL) and 34% secondhand smokers (cotinine > 0.05 ng/dL). After a careful analysis and adjusting for obesity, the investigators found that secondhand smokers had a higher rate of type 2 diabetes (haemoglobin A1c >6.5%), almost the same rate as in smokers. The results were presented on 24/06/12 at the Endocrine Society's 94th Annual Meeting in Houston.

[<http://www.medicalnewstoday.com/articles/247110.php>]

- Dr. K. Ramesh Rao