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"SONOGRAPHIC EVALUATION OF MALE INFERTILITY IN PATIENTS ATTENDING UROLOGY OUTPATIENT DEPARTMENT AT TERTIARY CARE CENTRE – A PROSPECTIVE OBSERVATIONAL STUDY"

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ABSTRACT:

Background:

Infertility is growing at an alarming pace, especially in the urban areas. Regardless of color, ethnicity, or other factors, it affects between 15% and 20% of people worldwide who are of reproductive age. In India, primary infertility prevalence is between 3.9 to 16.8%, according to World Health Organization. According to recent research on the situation of infertility in India, male reproductive abnormalities or illnesses account for almost 50 percent of infertility cases. Etiologies of male infertility are generally underestimated, ignored, under-diagnosed and under-treated. This observational study evaluated male infertility patients by using Trans Rectal Ultrasound (TRUS) and Trans Scrotal Ultrasound (TSU).

Method:

The current prospective observational cross-sectional study was carried out at the Government Tertiary care center over the course of 18 months, from 2018 to 2020. Serum FSH was obtained for all patients (ref. range- 1.4-14.6 mIU/mL). Bilateral testes, epididymides, tunica vaginalis sac, and vas deferens, were examined methodologically. The prostate-vesicular region is assessed at transrectal US (TRUS) in transverse, longitudinal, and oblique scans. The prostate, ejaculatory duct, seminal vesicles, and terminal vas deferens were call thoroughly examined. The findings of the sonograms were tabulated and analyzed.

Outcome of the study:

The study included 40 men (age range, 22–40) attending the urology clinic at the tertiary care center (Osmania General Hospital), Hyderabad, and diagnosed with infertility. Testicular cause was the most common etiology of infertility. Varicocele was the most common etiology among the testicular group followed by testicular atrophy. 10 out of 40 patients had an elevated FSH, and all these patients had

testicular atrophy, with a P value of <0.001 (highly significant). All 8 patients (20%) with post-testicular etiology had dilated upstream ductules.

Conclusion:

A comprehensive evaluation of male infertility is crucial, as surgical interventions may provide a cost-effective solution and preserve the possibility of future pregnancies. Additionally, identifying the causes of male infertility through uro-radiologic assessments and screening for conditions like testicular microlithiasis can help improve the overall health and fertility of men.

Keywords: *Infertility, male infertility, varicocele, trans-scrotal Doppler, Trans Rectal Ultrasound, Trans Scrotal Ultrasound*

INTRODUCTION

When a couple is unable to conceive after a year of unprotected sexual activity, it is considered infertility.[1] Regardless of race, ethnic origin, etc., 15-20% of people of reproductive age have infertility globally.[2] There is evidence of male-factor infertility in 30–40% of infertile couples.[3,4]

WHO reports that between 3.9 and 16.8% of Indian women suffer from primary infertility.[5] According to the statistics, 20% of cases of infertility involved both genders and 40% of cases involved men.[6] In line with a recent report on the situation of infertility in India, men's reproductive abnormalities or illnesses account for close to 50% of infertility cases.[6] The causes of male infertility are typically neglected, underdiagnosed, undertreated, and underestimated.

Physical examination has traditionally been the principal method used in the clinical evaluation of individuals with infertility. For instance, varicocele, the most frequent abnormal finding in infertile males, is normally detected through physical examination; nevertheless, palpation has been shown to have low diagnostic accuracy.

Many abnormalities that are easily discovered by the US, such as testicular tumors and testicular microlithiasis (TM), may remain undetected during a physical examination.[7] Evaluation of male infertility with clinical examination is less sensitive and specific, especially for assessment of the internal reproductive tract; hence, imaging forms an integral part of male infertility evaluation. Imaging plays a significant role in determining the etiology of infertility and classifying it as either obstructive or non-obstructive.

This lacuna in understanding etiopathogenesis has stagnated the growth of treatment strategies. This suggests the need for further studies on male infertility. Hence, this study attempts to evaluate male infertility patients by using TRUS, TSU, and trans-scrotal Doppler.

METHODOLOGY:

This observational cross-sectional study included 40 men (age range, 22–40) attending a Urology clinic at tertiary care Centre (Osmania general hospital), Hyderabad, and diagnosed with infertility. The present study was done over a period of 18 months, from 2018 to 2020. IHEC (Institutional Human Ethical Committee) clearance was obtained. The patients with abnormal semen parameters as per WHO 2010 criteria were included in the study.

Serum FSH was obtained for all patients. All patients were further evaluated with TSU and TRUS. Scans were performed in the RS80A model of SAMSUNG with multifrequency (LA4-18B) linear probe and (V5-9) Endo cavity prob. The patient is placed in a supine position for TSU, with the penis lying on the suprapubic area. A gel is then applied to the scrotum, which is supported by a towel placed between the thighs. Bilateral testes, epididymides, tunica vaginalis sac, and vas deferens, were examined methodically. Testicular volume was considered normal when more than 12 cm^3.[15] The formula to calculate testis volume was length*height*width*0.71.[8]

The prostate-vesicular region is assessed at transrectal US (TRUS) in transverse, longitudinal, and oblique scans. The prostate, ejaculatory duct, seminal vesicles, and terminal vas deferens were all thoroughly examined. The seminal tract was considered dilated when the anteroposterior diameter of the Vas deferens is >6mm, the seminal vesicle is >15mm, and the Ejaculatory duct (ED) is >2mm.

The prostate was examined for the presence of any cyst along the course of ED. The findings of the sonograms were tabulated and analyzed.

Statistical analysis:
The data were entered into Microsoft Excel, and SPSS version 20 was used for the analysis. An examination of descriptive statistics was conducted. The mean and standard deviation are used to present the results of continuous measurements. For categorical measurements, the results are shown as percentages. Significance is assessed at a 5 % level of significance. $P < 0.05$ – statistically significant; $P < 0.01$ - statistically highly significant; $P < 0.001$ - statistically highly significant. Fisher's exact test or the Chi-square test was used to determine the significance of research parameters. To determine the significance of study parameters on a continuous scale between two groups, a student t-test (independent, two-tailed) was performed. The significance of research parameters on a continuous scale between the three groups was determined using an ANOVA.

RESULTS:
The age group with the highest number of cases is 26-30, accounting for 45% of the total cases. The age group with the lowest number of cases is 31-35, constituting only 7.5% of the total cases. The age groups 21-25 and 36-40 have 17.5% and 30% of the cases, respectively.
No abnormalities: A total of four cases (10%) experienced infertility without any detected abnormalities. **(Table 1)**

Age distribution (Yrs.)	No. of cases	Percentage
21-25	7	17.50%
26-30	18	45.00%
31-35	3	7.50%
36-40	12	30.00%

Table-1: Age distribution of patients

Combined testicular and post-testicular causes: Similarly, there were four cases (10%) where both testicular and post-testicular factors contributed to infertility.
Post-testicular causes: Four cases (10%) were attributed to infertility resulting from post-testicular factors alone.
Testicular causes: The most prevalent etiology, testicular causes, accounted for 28 cases (70%) of infertility in the population. (Table 2)

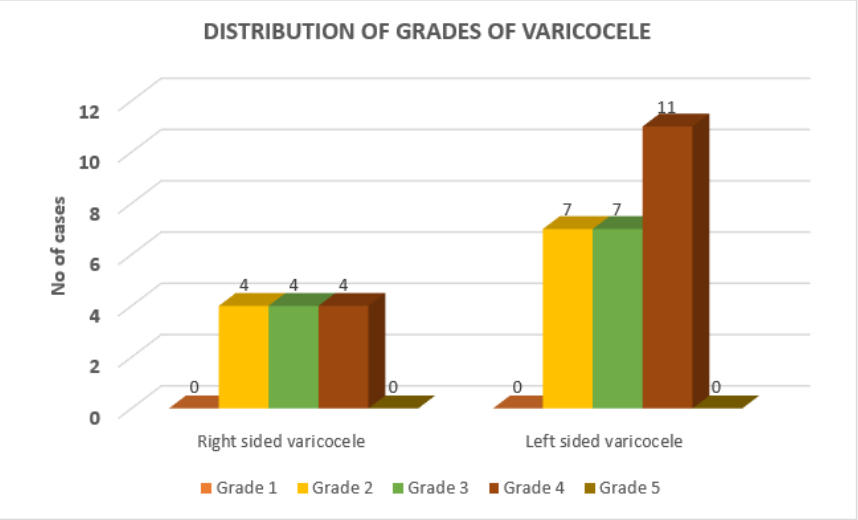
Etiology of infertility	No. of cases	Percentage
No abnormalities	4	10%
Both testicular and post-testicular causes	4	10%
Post testicular causes	4	10%
Testicular causes	28	70%

Table-2: Etiology of infertility based on the site of pathology

Infertility etiology varies, in cases with testicular causes, 25% had testicular atrophy and 75% had varicocele with or without testicular atrophy. Among post-testicular cases 13% had ED calculus, 25% had ED stricture, 37% had ED cyst, and 25% had seminal vesicle agenesis. Understanding these factors provides insights into the diverse causes contributing to infertility in this population. (Table 3, Graph 1))

Etiology in testicular cases	**No. of cases**	**Percentage**
Testicular atrophy	7	25%
Varicocele +/- testicular atrophy	21	75%
Etiology in post-testicular cases	**No. of cases**	**Percentage**
ED calculus	1	13%
ED stricture	2	25%
ED cyst	3	37%
Seminal vesicle agenesis	2	25%

Table-3: Etiology of infertility in testicular and post-testicular cases



Graph-1: Distribution of patients based on the grade of varicocele.

In this graph, we see that grade 1 varicoceles were not reported for either the right or left side. Grade 2 varicoceles were observed in four cases and seven cases, on the right side and the left side respectively. Similarly, grade 3 varicoceles were present in four cases on the right side and seven cases on the left side. Grade 4 varicoceles were found in four cases on the right side and eleven cases on the left side. Notably, there were no reported cases of grade 5 varicoceles for either side.

Varicocele grade	**N**	**Mean Testicular volume**	**Std. Dev.**
2	11	14.82	4.81

3	12	12.08	4.2
4	15	11.07	3.51

Table-4: Statistical significance of varicocele grade and testicular volume

The above table depicts the distribution of varicocele grades with mean testicular volume. The p-value for testicular atrophy between grades 4 and 2 was 0.03 (significant). Therefore, with an increase in the grade of varicocele, there is an increased probability of testicular atrophy. (Table 4)

FSH LEVELS	**No of cases**	**Percentage**
Elevated FSH	10	43%
Normal FSH	13	57

Table-5: Distribution of FSH levels among patients with testicular atrophy (N=23)

Table 5 demonstrates the distribution of FSH levels among patients with testicular atrophy. The analysis reveals that 43% of patients with testicular atrophy had elevated FSH levels, while 57% had normal FSH levels.

Laterality of Testicular Atrophy	**No of cases**	**Percentage**
Bilateral testicular atrophy	6	46%
Unilateral testicular atrophy	7	54%

Table-6: Distribution of patients with elevated FSH in terms of laterality

Table 6 shows that, among those with both testicular atrophy and elevated FSH, 46% were diagnosed with bilateral testicular atrophy, while 54% had unilateral testicular atrophy.

Post testicular cause	**Upstream ductule dilation**		**Total**	**p-value**
	Present	**Absent**		
Present	8	0	8	<0.001
Absent	0	32	32	
Total	8	32	40	

Table-7: Association between Post testicular cause and upstream dilation

Upstream dilated ductules were present in each of the 8 patients with a post-testicular origin, but not in any of the patients with a testicular cause. The p-value associated with this combination is reported as <0.001, indicating a highly significant relationship between the two variables. (Table 7)

Discussion:

Approximately 8% of males of reproductive age seek medical attention for infertility, which is a prevalent issue. Therefore, every examination of an infertile couple must carefully consider the male

partner. A couple shouldn't be labeled as infertile until they've had regular sexual activity without the use of a contraceptive method for a full year, as 80% of couples become pregnant during the first year of trying. The probability of getting pregnant each cycle for young, healthy couples is between 20 and 25 percent.

Risk factors including advanced maternal (>35 years) or paternal (>45 years) age, urogenital surgical history, cryptorchidism, varicocele, orchitis, gonadotropin use and genital infections, etc. necessitate early assessment. 13–15% of couples around the world struggle with infertility, which is a prevalent clinical issue. The frequency is higher in underdeveloped countries with fewer resources for diagnosis and treatment. The prevalence varies among nations. This study aims to study the imaging features of male infertility in this subcontinent, with a special focus on comparing TSU and TRUS findings in obstructive infertility.

Endocrine evaluation:

Male reproductive organs are significantly influenced by androgens. As part of the minimum examination, serum FSH and testosterone levels are measured, which, respectively, represent the germ cell epithelium and the Leydig cell condition. When low-normal or below-normal testosterone levels are present with raised FSH and LH levels it indicates generalized testicular failure, which may be caused by a congenital condition (such as Klinefelter syndrome) or an acquired condition. FSH and LH levels that are simultaneously low may indicate hypogonadotropic hypogonadism.

FSH and LH levels within the normal range may suggest an extraductal obstruction in azoospermic subjects. However, azoospermic patients with testicular failure and testis histology exhibiting sperm maturation arrest and 10% of those diagnosed with Sertoli-cell-only syndrome may present with non-elevated FSH levels.

In our study, 10 out of 40 patients had an elevated FSH, and the mean testicular volume in these patients was 7.2 mL, with a P value of <0.001(highly significant). A similar observation was noted in a study by **Tong et al,**[9] where the mean testicular volume in patients with elevated FSH was 7.1 mL. Out of the 23 patients with testicular atrophy, 10 (43%) patients had elevated FSH. All patients with normal testicular volume had normal FSH levels.

Testicular volume:

Testicular volume is positively correlated with the seminogram and predicts the possibility of sperm retrieval.[10] In our study 28 patients (71%) had testicular pathology and 4 patients with both testicular and post testicular pathology.

Varicocele:

The pampiniform plexus of the spermatic cord and internal spermatic veins abnormally dilating and extending are known as varicocele. Even though most adult varicoceles (>80%) do not affect male infertility.[7] Numerous studies have shown that, regardless of a normal semen analysis or previous signs of fertility, a man with a varicocele is at risk of later loss of testicular function and fertility.[11]

Varicocele is the most frequently curable cause of male infertility. In contrast to men with normal semen values, 1 in 4 men with abnormal semen parameters has a varicocele, according to the WHO (WHO, 1992). Following varicocele surgery, semen values significantly improved in more than 50% of the affected men.[12,13]

In our study, 21 (65%) out of 32 patients with testicular cause had varicocele. A varicocele was present in 38% of the patients in the testicular group in a study by **Uma Shankar et al**.[12] In a study by **Sakamoto al.,** involving 545 infertile patients, 57.5% of testicular cases had varicocele.

Secondary TSU finding in obstructive azoospermia:

Obstructive azoospermia and nonobstructive azoospermia (primary testicular failure) must be distinguished from one another, even though the use of modern ART for the treatment of azoospermia can circumvent most pathology. This is due to the possibility of surgical or interventional treatment for obstructive azoospermia. On the other hand, it can make sense to start with an advanced assisted reproductive method like ICSI for men who have primary testicular failure. Compared to blockage, primary testicular failure is a more frequent cause of azoospermia, and its origin is frequently

unknown. Contrarily, obstructive azoospermia has a more apparent cause that may be inherited or acquired. So, it is essential to differentiate between obstructive and non-obstructive etiology.
Our study attempts to find the relationship between TSU findings and obstructive infertility. In our study, all 8 patients with post-testicular causes had dilated ductules in the epididymis, with a P value of <0.001. According to the study by **Jing et al.,**[14] the diagnostic effectiveness of imaging evaluation of the seminal tract in distinguishing between obstructive and nonobstructive azoospermia was substantial (P =.02) in the study. So, the finding of dilated ductules should be considered an indication for TRUS examination.

TRUS abnormalities:
The first diagnostic procedure for men who have clinical signs and laboratory tests suggesting a possible seminal tract obstruction should be scrotal sonography. If they display non-obstructive azoospermia signs such as varicocele or testicular pathology, they will be treated by the standard approach for treating these medical conditions. Patients who have proximal obstructive azoospermia can have vasoepididymostomy surgery for management. They should be assessed by TRUS if the scrotal US is normal or if there are signs of distal obstructive azoospermia.
In our study, 8(20%) out of 40 patients had post-testicular etiologies. The etiologies in these cases were ED cyst (37%), ED calculus (13%), ED stricture (25%), and U/L seminal vesicle agenesis (25%).

CONCLUSION:
The value of assessing male infertility has often been underestimated, given the widespread use and ongoing advancements in assisted reproductive technology. While IVF/ICSI (In Vitro Fertilization/Intracytoplasmic Sperm Injection) offers a higher success rate, especially in cases where there is coexisting female infertility or when the female partner is of advanced age, it's important to consider surgical options on a case-by-case basis. This is not only a more cost-effective choice but can also potentially facilitate future pregnancies.
Particular remedial surgeries, such as vasoepididymostomy or transurethral resection of the ejaculatory duct, may be necessary, but the opportunity for these procedures could be missed if the root cause of a man's infertility is not identified through a thorough uro-radiologic assessment.
Furthermore, testicular microlithiasis, which can be a potential predictor of testicular tumors, has been linked to infertility. In addition, infertility itself may increase the incidence of testicular tumors. Therefore, it is advisable for infertile men to be routinely evaluated with ultrasound examinations.

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