

Study of Evaluation of Causes of Male Infertility at a Tertiary Care Hospital

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ABSTRACT

Introduction: Worldwide 580 million males experience infertility at some point of time in their life; of these, 372 million reside in low- and middle-income countries. Male subfertility is one of the most rapidly growing fields in medicine, with dramatic advances and treatment. If a male infertility factor is present, it is almost always defined by the finding of an abnormal semen analysis, although other male factors may play a role even when the semen analysis is normal.

Aims: To classify the causes of male infertility at pre-testicular, testicular, and post-testicular levels.

Materials and methods: This study was conducted at the Department of Obstetrics and Gynecology in collaboration with the Department of Radio Diagnosis, Institute of Postgraduate Medical Education and Research, Kolkata.

Results: Pre-testicular cause was seen in 7% of patients. Erectile dysfunction is the commonest. In testicular causes, varicocele is the most common (29.6%), followed by idiopathic (25.9%) and trauma in 14.8%, and other causes, such as torsion, infective orchitis, and cryptorchism show a common incidence of 7.4%. In post-testicular, varity in 51.8% is due to ejaculatory duct obstruction and accessory gland dysfunction, and acquired hernia surgeries have a common incidence of 14.81%. The least common cause is epididymal asthenozoospermia.

Conclusion: In male infertility evaluation history and clinical examination, semen analysis is the common tool for all groups of patients. Pre-testicular male infertile is mainly due to consequences of primary or secondary dysfunction of endocrine or exocrine glands influencing the male reproductive axis. Testicular group of male infertility are due to variety of genetic, congenital, and acquired insults to the proper testicular function; post-testicular cause of infertility is due to pathology in the pathway of sperm passage; this is influenced by congenital and acquired defects and diseases respectively. The idiopathic group of patients needs further evaluation by use of advanced seminal tests like immunological tests, semen culture, special staining of the spermatozoa, sperm DNA integrity tests, appropriate genetic evaluation and. Evaluation of ultrastructural abnormalities of spermatozoa, for detection of defects in outer dense fibers, microtubules, mitochondria, connecting piece, and acrosome.

Keywords: Male infertility, Post-testicular, Pre-testicular, Testicular.

How to cite this article: Umashankar KM, Mukherjee J, Banerjee SN, Cristy R, Seal BN, Drakshyani CL. Study of Evaluation of Causes of Male Infertility at a Tertiary Care Hospital. J South Asian Feder Obst Gynae 2016;8(2):113-122.

Source of support: Nil

Conflict of interest: None

Date of received: 17 Nov 2015

Date of acceptance: 10 Feb 2016

Date of publication: April 2016

INTRODUCTION

Worldwide 580 million men experience infertility at some point of time in their life; of these, 372 million reside in low- and middle-income countries.¹ Male subfertility is one of the most rapidly growing fields in medicine, with dramatic advances and treatment. If a male infertility factor is present, it is almost always defined by the finding of an abnormal semen analysis, although other male factors may play a role even when the semen analysis is normal. While the patient's semen may seem to be the target for diagnostic and therapeutic interventions and analysis, certain conditions like diabetes mellitus can cause male infertility by more than one mechanism, for example, effect on sperm DNA, increased genital tract infections, coital dysfunction, and retrograde ejaculation. Other factors may cause infertility for a specific period of time; for example, stress and fever hamper spermatogenesis only for a particular period. Common habits of human beings like excess consumption of alcohol leads to increased desire for coitus but decreased performance of the act of coitus. Long-term effects of alcohol decrease the serum concentration of testosterone. Smoking increases carboxyl hemoglobin, which hampers the optimum spermatogenesis.

OBJECTIVES

To classify the causes of male infertility at pre-testicular, testicular, and post-testicular levels. The pre-testicular causes involve mainly hypothalamus and pituitary. Post-testicular causes mainly involve low obstruction.

MATERIALS AND METHODS

This study was conducted at the Department of Obstetrics and Gynecology in collaboration with the Department of Radio Diagnosis, Institute of Postgraduate Medical Education and Research, Kolkata. During the study period of 1 year (from August 1, 2009, to July 31, 2010),

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100 male patients attending infertility clinic and outpatient units for the treatment of infertility, and those who had abnormal semen analysis, were evaluated with detailed history-taking, which includes occupational history and any medical disorders like diabetes mellitus, liver disorders, thyroid disorders, or recurrent upper respiratory infections. Any surgical disorders like hernia, hydrocele repair, renal transplant, or scrotal surgeries were also taken into consideration. Personal history related to habits like smoking, alcohol, excess caffeine, and other recreational drugs and marital history related to the psychological well-being of the couple, coital knowledge, and coital dysfunction were also noted. General physical examination for the assessment of pallor, icterus, cyanosis, clubbing, pedal edema, lymph adenopathy, obesity, patient's habitus, the pattern of virilization, the presence or absence of temporal pattern of balding and fine wrinkles, gynecomastia, and situs inverses were noted. Systemic examination and genital examination for systemic or local disorders were done. All patients were subjected to routine investigations followed by semen analysis and those who had abnormal semen analysis on two occasions were evaluated with hormonal assay, transscrotal ultrasound, transscrotal Doppler, and transrectal ultrasound.

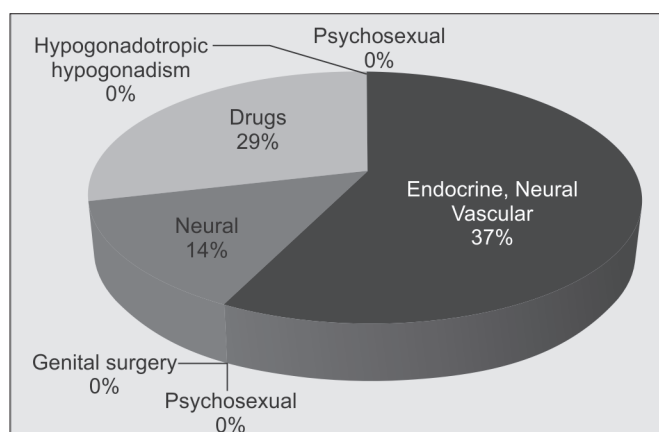
RESULTS

Table 1 in this study, 64% (n=64) patients were between 25 and 35 years, 31% (n=31) between 35 and 45 years, and 4% (n=4) more than 45 years. Only 1% (n=1) patient was less than 25 years.

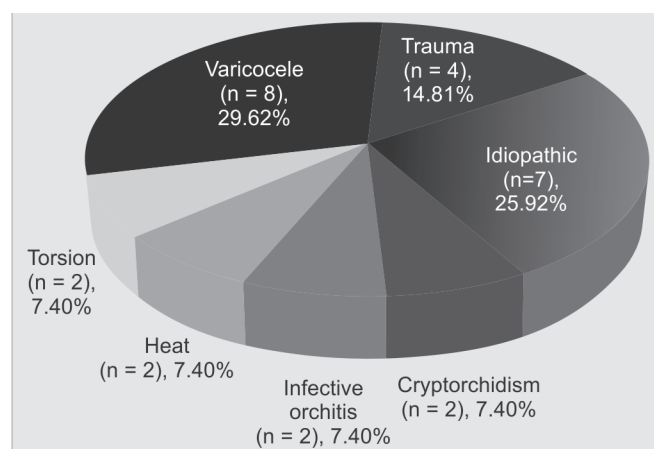
In this study, erectile dysfunction was seen in 57.14% (n=4) of cases, ejaculatory failure due to neural cause in 14.28% (n=1), and due to drugs in 28.57% (n=2).

Table 1: Distribution of patients according to age

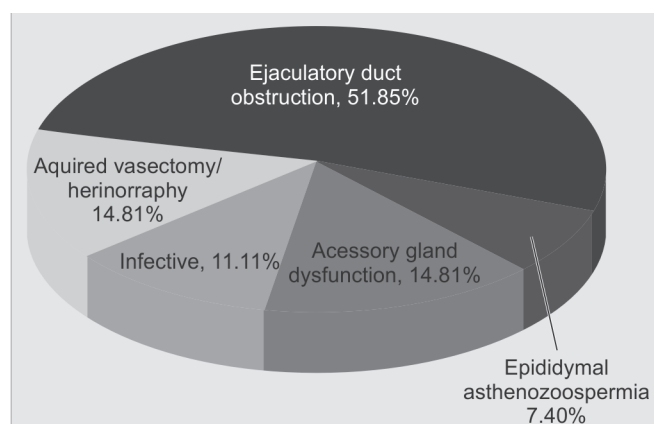
Age in years	n = 100	%
<25	1	1
25–35	64	64
>35–45	31	31
>45–55	4	4



Graph 1: Distribution of pre-testicular causes of male infertility



Graph 2: Distribution of testicular causes of male infertility



Graph 3: Distribution of post-testicular causes of male infertility

Table 2: Significant past surgical history

Sl. no.	Surgery	n = 10	%
1	Herniorrhaphy	3	30
2	Herniotomy	1	10
3	Undescended testis	2	20
4	Torsion	2	20
5	Hydrocele	2	20

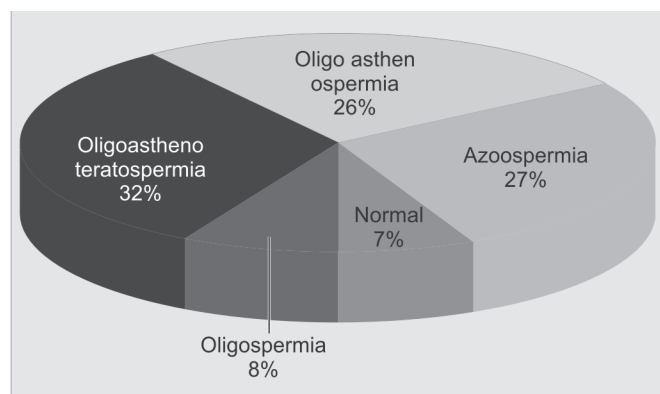
Reports 1–19 describe testicular infertility. In this study, distribution of 27 testicular cases were 25.92% (n = 7) idiopathic, 29.62% (n = 8) varicocele, 14.81 % (n = 4) traumatic, 7.40% (n = 2) torsion, 7.40% (n = 2) antispermatogenic agents heat, 7.4% torsion, 7.4% (n = 2) infective orchitis, and 7.4% (n = 2) cryptorchidism.

In this study, distribution of 27% (n=27) post-testicular cases were 51.85% (n=14) ejaculatory duct obstruction, 14.81% (n=4) accessory gland dysfunction, 14.81% (n=4) acquired hernia surgeries, 11.11% (n=3) infective cases, and 7.4% (n=2) epididymal asthenozoospermia.

Table 2 in this study, significant past history was seen in 10% (n=10) patients. Of them, 30% (n=3) had herniography, 10% (n=1) had herniotomy, 20% (n=2) had surgery for undescended testis, while torsion was seen in 20% (n=2) of cases and hydrocele in 20% (n=2) of cases.

Table 3: Significant past medical history

Sl. no.	Medical	n = 12	%
1	Depression	4	33.33
2	Tuberculosis	3	25
3	Malaria	2	16.66
4	Hypertension	1	8.33
5	Mumps	2	16.66

**Graph 4:** Distributions of seminogram**Table 4:** Distribution of the seminal abnormalities in various groups

	AZO (n=27)		OLI (n=8)		OA (n=26)		OAT (n=32)	
	1	%	1	%	0	%	1	%
Pre-testicular	1	3.7	1	12.5	0	–	1	3.1
Testicular	12	44.4	2	25	8	30.7	5	15.6
Post-testicular	7	25.9	1	12.5	9	34.6	7	21.8
Idiopathic	7	25.9	4	50	9	34.6	19	59.3

Table 3 in this study, 12% (n=12) had significant past history. 33.33% (n=4) had past medical history of depression, 25% (n=3) had tuberculosis, 16.66% (n=2) had malaria, 8.33% (n=1) had hypertension, and 16.66% had mumps.

The chart shows the distribution of the seminogram. In this study OAT was seen in 32% (n=32) of cases, AZO in 27% (n=27), OA in 26% (n=26), and oligospermia in 8% (n=8) of patients and the result was normal in 7% (n=7).

The percentages in the table shown are the column percentages.

Table 4 in this study, 3.7% of the azoospermics (n=1) were in the pre-testicular group, 44.4% (n=12) in the testicular group, 25.9% (n=7) each in the post-testicular and idiopathic groups.

In this study, 50% of oligospermics (n=4) were in the idiopathic group, 25% (n=2) in the testicular group, 12.5% (n=1) each in pre-testicular and post-testicular groups.

In this study, 30.7% of the OA (n=8) cases were in the testicular group, 34.6% (n=9) each in post-testicular and idiopathic groups. No cases of OA were found in the pre-testicular group.

A total of 3.1% (n=1) of the OAT cases were in the pre-testicular group, 21.8% (n=7) in the post-testicular group, 15.6% (n=5) in the testicular group, and 59.3% (n=19) in the idiopathic group.

DISCUSSION

Table 1: In this study, 64% were in the age group 25 to 35 years and 31% between 35 and 45 years. In one study, less than 25 years age group comprised 1.7% patients, 26 to 35 years age group 76%, and above 36 years 22%.¹ A recent meta-analysis of male fertility research published between 1980 and 1999 concluded that increasing age is associated with decreased semen volume, decreased sperm motility, and decreased number of morphologically normal sperm^{2,3} (Kid et al).

Graph 1: In this study, pre-testicular male infertility is 7%, erectile dysfunction attributed for 57.14% (n=4), and ejaculatory dysfunction 28.5%. As per data from Comhaire et al, sexual/ejaculatory inadequacy comprised 3%; the Escher Capri workshop group (1994) accounted for 1.7% sexual factors.⁴

Graph 2: In this study, testicular infertility attributed to 27% of total infertility and 25.92% idiopathic, 29.62% varicocele, 14.81% traumatic, 7.40% anti-spermatogenic agents heat, 7.4% torsion, 7.4% infective orchitis, and 7.4% cryptorchidism. According to data from Comhaire et al (1987); the Escher Capri workshop group (1994); and Burkman LJ, Cardington CC, Franken DR, et al (1988); Western Siberian study; and Sudanese study, varicoceles were seen in 13, 12.3, 37.4, 11.3, and 22% respectively.^{5,6,8-11} In the present study varicocele is seen in 29.62%; the prevalence of varicoceles in men presenting with infertility is 20 to 40% (Dubin and Amelar; Cockett et al; Aafjes and Van Der Vijver; Marks et al).^{10,11} Varicocele is the most common correctable cause of male infertility. Approximately 90% of varicoceles are left sided. Whereas most studies report an approximately 10% prevalence of bilateral varicoceles, detrimental effects of varicoceles have included reflux of renal and adrenal metabolites from the renal vein (Comhaire and Vermeulen),¹² decreased blood flow (Saypol et al),¹³ and hypoxia (Chakraborty et al).¹⁴ The work of Burkman LJ, Cardington CC, Franken DR, et al (1988) shows testicular failure in 9.4%, cryptorchism, in 6.1%,¹⁵ and mumps orchitis in 3.6%. In the present study cryptorchism is seen in 7.4%; cryptorchidism is present in 3 to 4% of fullterm boys.¹⁸ By 1 year of age, 1 to 1.6% of boys demonstrate undescended testes (Scorer and Farrington, cryptorchidism). Sperm concentrations below 12 to 20 million/ml are found in 50% of patients with bilateral cryptorchidism and in approximately 25% of patients with unilateral cryptorchidism. Increasing evidence points to a defect in the hypothalamic-pituitary-gonadal axis in patients with cryptorchidism (Canlorbe et al).⁶

In our study, mumps orchitis is seen in 7.4% cases. Mumps associated with orchitis is seen in 30% of patients, the orchitis is bilateral in 10 to 30% (Beard et al).¹⁶ Permanent testicular atrophy may develop within several months to several years after infection. This may result in atrophy of the seminiferous tubules. Severe bilateral orchitis may result in hypergonadotropic hypogonadism and gynecomastia. Testicular torsion in the present study is seen in 7.4% of cases. The severity of the semen abnormalities appears to be directly related to the duration of testicular torsion. The fertility of adults with prepubertal testicular torsion does not appear to be reduced (Pure et al).^{17,7} In the present study, heat exposure is seen in 7.4% cases. Heat exposure through the use of saunas (Brown-Woodman et al; Sekihan et al) and hot baths (Lue et al)¹⁸ is shown to have a detrimental effect on semen parameters. Occupations with heat exposure and infertility include bakers, drivers (industrial machinery, taxis, trucks), ceramic oven operators, welders, and workers in submarines (Velez De La Called et al).⁵ In addition, a dysfunction of testicular thermoregulation has been suggested to occur in paraplegic men in wheelchairs (Bindley).¹⁹ Impaired semen quality and spermatogenesis have resulted from experimental hyperthermia (Procope).²⁰

Reports 13,14,15,16,17,20,21 describe posttesticular infertility. *Graph 3*: In this study, post-testicular infertility attributed was 27%, 51.85% had ejaculatory duct obstruction, 14.81% had accessory gland dysfunction, 14.81% had acquired hernia surgeries, 11.11% infective cases, 7.4% epididymal asthenozoospermia. No case of immunological, idiopathic, post-vasectomy, or cystic fibrosis was found. In the work of Burk Man LJ, Cobbington CC, Franken DR, et al (1988) ejaculatory duct obstruction was seen in 6.1%²¹ western Siberia the most frequent cause of male infertility was inflammatory disease of male accessory glands (12.9%).²² WHO bulletin has reported an incidence of, accessory gland dysfunction as 4%.²³ In one study accessory gland dysfunction was seen in 13% cases (n=271).²⁴ Data from Comhaire et al estimate accessory gland infection as 8%, obstructive azoospermia 2.5%, iatrogenic causes 1%.¹ In this study obstructive azoospermia was seen in 25.9% (n=7) of cases, iatrogenic causes was seen in 14.81% of cases. Obstruction of the ductal system is found in 7 to 12% of all infertile

men and is much more common in azoospermic men (Dubin and Amelar; Greenberg et al; Jarow et al).^{25,26} In a study in Sudan, hernia repair and surgery on hydrocele was seen in 6.7% of cases of infertility; in our study, hernia repair accounted for 14.81% cases.

Table 2: In this study past surgical history was significant in 10% of patients, 30% had herniography, 10% had herniotomy, 20% had surgery for undescended testis, and torsion was seen in 20% of cases. Hydrocele was seen in 20% of cases. The work of Burkman LJ, Cardington CC, Franken DR, et al showed the incidence of cryptorchism up to 6.1% and a study in Sudan had incidence of cryptorchism up to 6.7%.²⁵ In another study, orchidectomy was seen in 2.6% of cases, herniography in 2.6%, and other surgeries 20.9%.²⁷ *Table 3*: In this study, 12% had significant past medical history attributing to cause of infertility: 33.33% had depression, 25% had tuberculosis, 16.66% had malaria, and 8.33% had hypertension, and mumps was seen in 16.66%. In one study the systemic illness was seen in 0.2% cases.³ In another study, the systemic disease accounted for 44% cases.¹⁵ Antihypertensive medications have frequently been associated with sexual dysfunction. Spironolactone, an aldosterone antagonist that has been associated with sexual dysfunction, also may be detrimental to semen quality through its anti-androgen activity (Tidd et al).³ After a febrile illness, spermatogenesis may be impaired for up to 3 months (Buch and Havlovec).²⁸

Table 5 and *Graph 4*: In this study majority of patients had OAT (32%), followed by azoospermia (27%), OA (26%), and oligospermia (8%). Majority of azoospermics are in the testicular group (44.4%), 3.7% in the pre-testicular group, and equal number in post-testicular and testicular groups. 50% of oligospermics are in idiopathic groups. Majority of OAT are in the pre-testicular group (59.3% cases), and the least OAT is in the idiopathic group. Post-testicular group had 21.8% OAT; in testicular group it is 15.6%. In one study, idiopathic azoospermia was seen in 0.5% cases.^{3,15} In a study at Duhok, Iraq, idiopathic azoospermia was seen in 13%,²⁷ oligoasthenospermia in 20.7%.²⁸ In a study in Kuwait, idiopathic oligospermia was seen in 30% of cases and 50% of the cases were due to testicular causes.¹ Testicular oligoasthenospermia is seen in 30.7% cases in the present study, whereas in Kuwait study it was seen in 50% cases.¹

Table 5: Oligoasthenoteratospermia is the most common seminal abnormality (32% of cases), AZO in 27% of cases, OA in 26% of patients, and oligospermia in 8% of patients. Only 7% of patients had normal sperms

Study	Oligoasthenoteratospermia	Azoospermia	Astheniospermia	Oligospermia
Mongolia 29	1.2	20.5	7.4	11.6
Duhok, Iraq 1	20	13	20	—
Another study 2	4	—	6	6
Kuwait 35	—	38	—	62
Nigeria 30	4	3	—	15
Present study	32	27	26	8



Fig. 1: Transscrotal USG probe



Fig. 2: Transscrotal Doppler probe



Fig. 3: Transrectal ultrasound probe

SUMMARY

In this study, majority of the patients are between 25 and 35 years (58%), had infertility for 5 to 10 years, past surgical history of herniography in 30%, herinotomy in 10%, and hydrocele excision and torsion cryptorchism contributed for 20%.

The most common past medical disorder is depression 33.33%, tuberculosis in 25%, mumps and malaria both 16.6%, and least common disorder is hypertension in 8.33%.

Pre-testicular cause, is seen in 7% of patients. Erectile dysfunction is the commonest and the next commonest is ejaculatory failure.

In testicular causes varicocele is the commonest with 29.6%, trauma in 14.8%, and the other causes are torsion, infective orchitis, and cryptorchism shows a common incidence of 7.4%. idiopathic in 25.9%.

In post-testicular varity, 51.8% cases are due to ejaculatory duct obstruction, accessory gland dysfunction, and acquired hernia surgeries has a common incidence

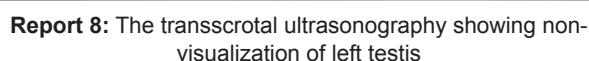
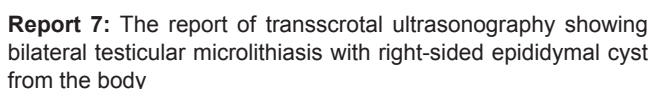
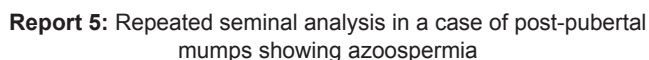
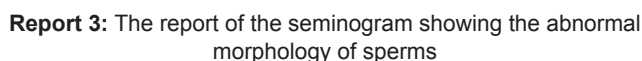
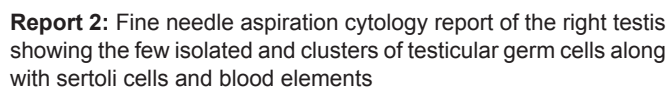
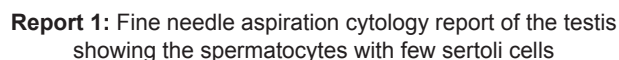
of 14.81%. Least common cause is the epididymal asthenozoospermia.

Majority of the azoospermics are in the testicular group, azoospermics are equally distributed in post-testicular and idiopathic groups. A total of 50% oligospermics are in the idiopathic group, 25% are in the testicular group, whereas oligospermics are equally distributed in post-testicular and pre-testicular groups. Highest incidence of seminal abnormalities is seen among 25- to 35-year-olds, azoospermia in 51.8%, oligospermia in 65.35%, and OAT in 71%.

Oligoasthenoteratospermia is the most common seminal abnormality in this study; the second most common is azoospermia. Least common is oligospermia.

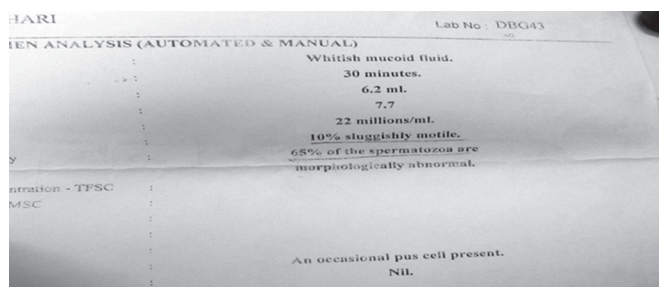
CONCLUSION

- In male infertility evaluation history and clinical examination, semen analysis is the most common tool for all groups of patients.
- Pre-testicular male infertile is mainly due to consequences of primary or secondary dysfunction of endocrine or exocrine glands influencing the male reproductive axis. But this group can also be influenced by many iatrogenic medical and surgical interventions.
- In testicular group, male infertility is due to variety of genetic, congenital, and acquired insults to the proper testicular function. This group of patients are evaluated by serum FSH, serum testosterone, transscrotal ultrasound, and transscrotal Doppler Figs 1 and 2. This group is influenced by the occupational and personal habits of patients.
- Post-testicular cause of infertility are due to pathology in the pathway of sperm passage. This is influenced by congenital and acquired defects and diseases respectively. Further, there are conditions that are

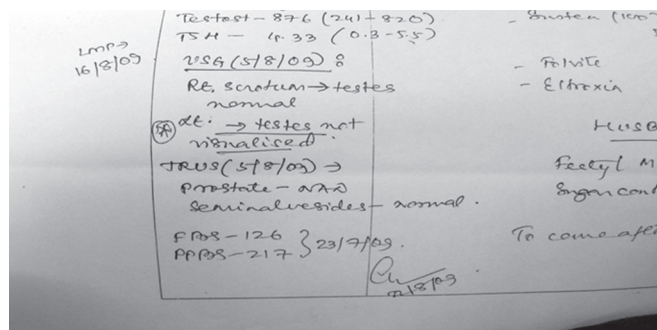


hostile for sperm motility and maturation. The main tool in this group is the TRUS (Fig. 3).

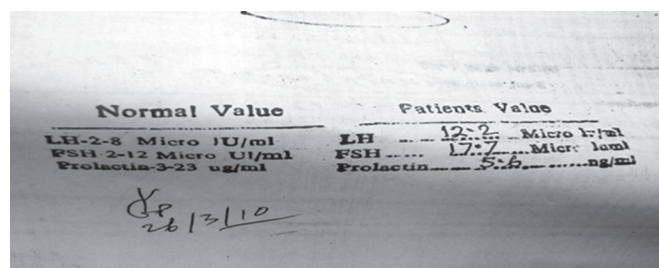
- The idiopathic group of patients need further evaluation by use of advanced seminal tests like



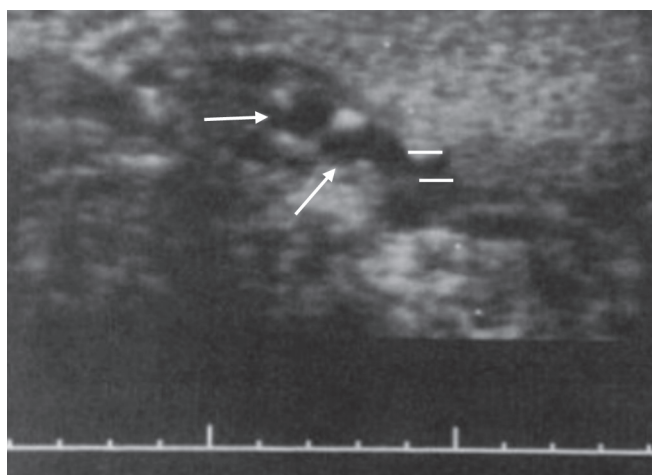
Report 9: Seminogram showing asthenospermia due to 65% abnormal sperms



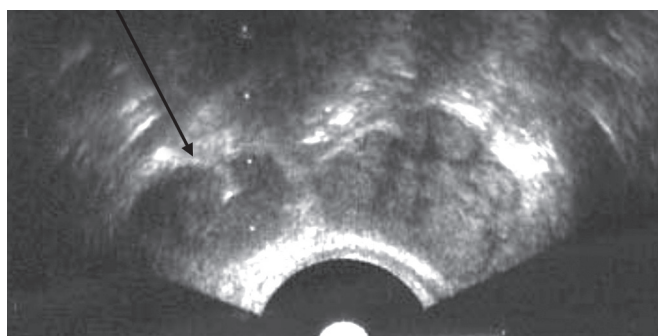
Report 10: History showing the report of nonvisualization of left testis on ultrasound



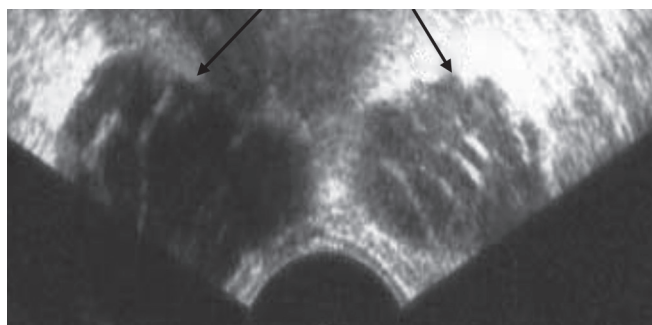
Report 11: Report showing the elevated FSH and LH in case of bilateral testicular microlithiasis with azoospermia



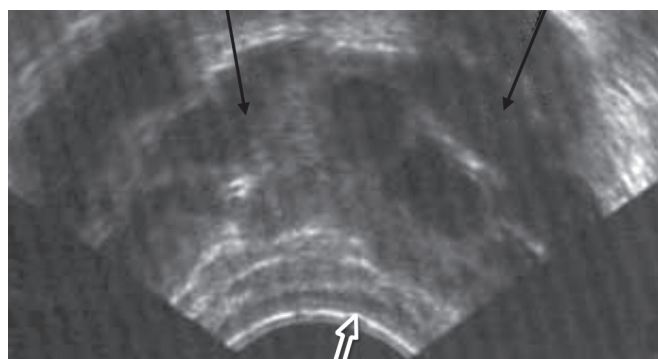
Report 12: Report of scrotal ultrasonogram showing varicocele



Report 13: Transscrotal ultrasonogram report showing seminal vesical cyst

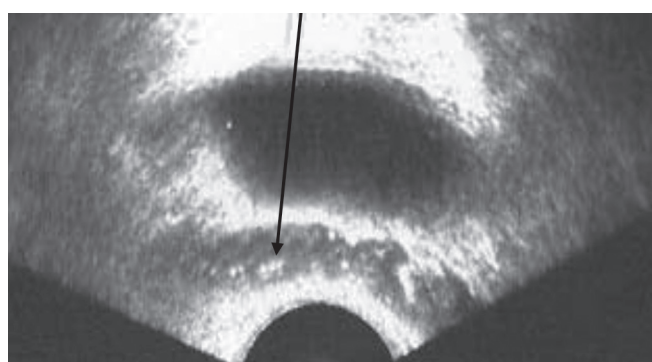


Report 14: Transscrotal ultrasonogram showing bilateral seminal vesical enlargement

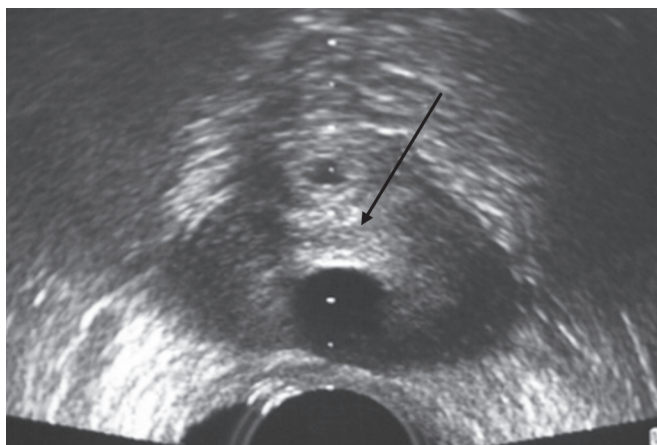


Report 15: Transscrotal ultrasonogram showing the enlargement of seminal vesicals and ejaculatory duct enlargement

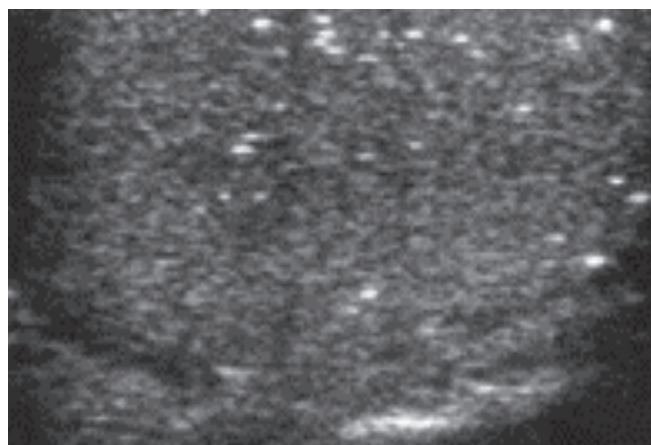
immunological tests, semen culture, special staining of the spermatozoa, sperm DNA integrity tests, and appropriate genetic evaluation. Evaluation of ultra-structural abnormalities of spermatozoa. For detection of defects in outer dense fibers, microtubules, mitochondria, connecting piece, and acrosome.



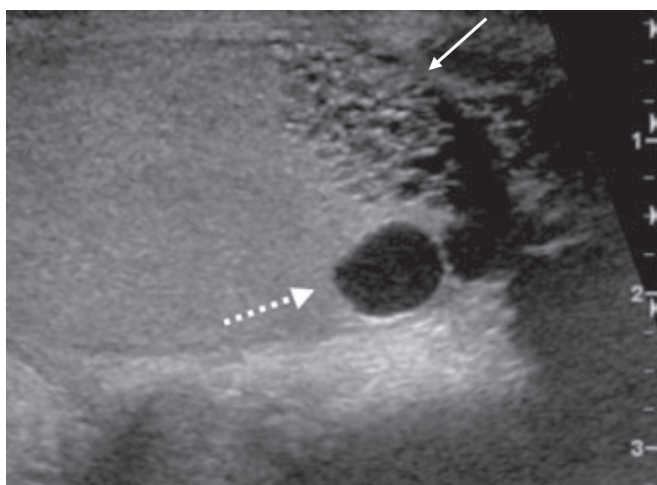
Report 16: Transscrotal ultrasonogram showing seminal vesical calcification



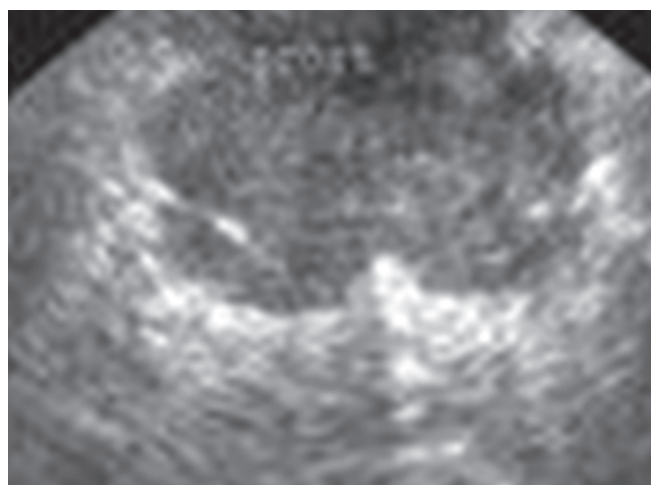
Report 17: Transscrotal ultrasonogram showing large midline cyst



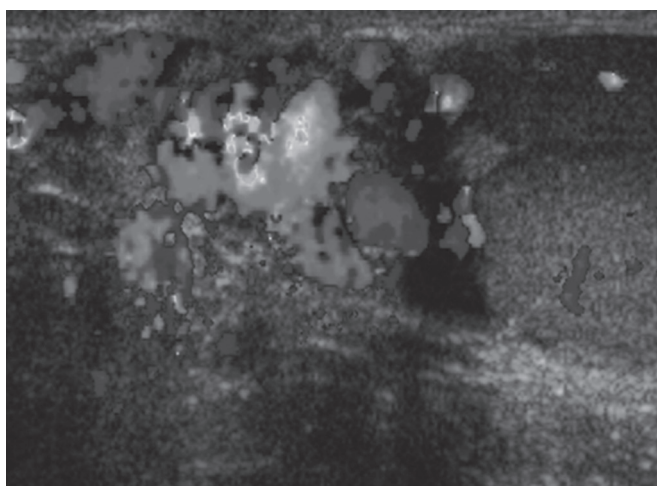
Report 18: Transscrotal ultrasonogram showing testicular microlithiasis



Report 19: Transscrotal ultrasound showing intratesticular cyst in a patient with azoospermia



Report 20: Transscrotal ultrasonogram showing enlarged seminal vesicals



Report 21: Transscrotal Doppler of left hemiscrotum shows multiple dilated peri-testicular veins on color Doppler imaging

- REGISTRATION NO:
- SERIAL NO:
- NAME:
- AGE:
- SOCIOECONOMIC STATUS:
- DURATION OF INFERTILITY:
- OCCUPATIONAL HISTORY:
- CHILDHOOD HISTORY:
- MEDICAL HISTORY:
- SURGICAL HISTORY:
- PERSONAL HISTORY: HABITS – SMOKING, ALCOHOL, TOBACOO CHEWING.
- MARITAL HISTORY:
- DRUG HISTORY:

B. General physical examination

- PALLOR:
- ICTERUS:
- CYANOSIS:
- CLUBBING:
- PEDAL EDEMA:

PROFORMA

A. History

- DATE:

- LYMPH ADENOPATHY:
- OBESITY:
- BLOOD PRESSURE:
- GYNECOMASTIA:
- PATIENT'S HABITUS, THE PATTERN OF VIRILIZATION, PRESENCE OR ABSENCE OF TEMPORAL PATTERN BALDING AND FINE WRINKLES, GYNECOMASTIA, SITUS INVERSES ARE NOTED.

C. Systemic examination

- CARDIOVASCULAR SYSTEM:
- RESPIRATORY SYSTEM:
- ABDOMINAL EXAMINATION:
- CENTRAL NERVOUS SYSTEM EXAMINATION:

D. Genital examination

- PENIS
- SCROTUM
 - TESTIS:
 - TRAN-ILLUMINATION DONE FOR ALL SCROTAL MASSES:
 - EPIDIDYMIS:
 - SPERMATIC CORD AND VAS DEFERENS:
 - TESTICULAR TUNICS AND ADNEXA HYDROCELES:

Rectal examination

- ESTIMATION OF SPHINCTER TONE IS.
- DIGITAL PROSTATIC EXAMINATION OF SIZE, CONSISTENCY, TENDERNESS, MOBILITY.

TESTING PER ANAL SENSATION

E. Investigations

- SEMEN ANALYSIS:
- BL.HB%: TC: DC: ESR: AT 1 HR
- FBS:
- PPBS:
- SERUM CREATININE:
- UREA:
- VDRL:
- HBSAG:
- VCTC:
- LFT:
- URINE RE/ME:
- S.TSH:
- S.TESTOSTERONE:
- LH:
- FSH:
- PROLACTIN:

- Transrectal USG:
- Transscrotal USG:
- Transscrotal DOPPLER:

Additional investigations (as applicable)

- KARYOTYPING:
- VASOGAPHY:

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