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Prospective study to evaluate the risk factors associated with male infertility at tertiary care centre

Junaid Alam*, Pawan Choudhary, Mohammad Aslam

Department of Surgery, Jawaharlal Nehru Medical College and Hospital, AMU, Aligarh, Uttar Pradesh, India

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${\bf *Correspondence:}$

Dr. Junaid Alam,

E-mail: dr.junaid2003@yahoo.com

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ABSTRACT

Background: Infertility is a condition with psychological, economic, medical implications resulting in mental trauma, stress particularly in social set up like ours, with strong emphasis on child bearing. According to the International Committee for Monitoring Assisted Reproductive Technology, World Health Organization (WHO), Infertility is disease of reproductive system defined by failure to achieve the clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.

Methods: This study was conducted in Department of Surgery in Jawaharlal Nehru Medical College, Aligarh from January 2017 to December 2017 on 120 patients to study the clinical profile, causes of male infertility and to evaluate the risk factors associated with it.

Results: There were 54 (45%) patients with azoospermia and 66 (55%) had oligospermia. Out of them 52 (43.3%) had sperm counts of 1-8 millions/ml and 14 (11.6%) had sperm count between >9-15 millions/ml. 46 (38.3%) patients had low testosterone level. 86 of cases had motility <50% after one hour, remaining 34 had motility >50%. Out of 120 cases of male infertility, 12 (10%) had Obesity and rest 108 (90%) had normal BMI. Out of 120 cases of male infertility, 8 (6.6%) were known Diabetics rest 112 (93.3%) had normal blood sugar levels. Out of 120 cases of male infertility, 36 (30%) had Erectile dysfunction and rest 84 (70%) were normal.

Conclusions: The study concluded that Erectile dysfunction was the most common cause of male infertility. Varicoceles and small sized testes were the most common clinical abnormalities seen in infertile males. Smoking, Alcohol and Tobacco use were frequently associated with most infertile males.

Keywords: Erectile dysfunction, Infertility

INTRODUCTION

Infertility is a condition with psychological, economic, medical implications resulting in mental trauma, stress particularly in social set up like ours, with strong emphasis on child bearing. According to the International Committee for Monitoring Assisted Reproductive Technology, World Health Organization (WHO), Infertility is disease of reproductive system defined by failure to achieve the clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.¹

Infertility can be divided into primary and secondary infertility. Primary infertility is the case, when the man has never impregnated a woman. Secondary infertility implies when the man has some time impregnated a woman, even if the women are not the partner in the present couple.

Males were considered infertile with sperm parameters below the WHO normal value.² The most significant of these are low sperm count (oligospermia), poor sperm motility (asthenospermia), abnormal sperm morphology

(teratospermia). Some other factors less well known associated with infertility include semen volume and other seminal markers of epididymal, prostatic, and seminal vesicle function.³ The WHO has revised lower reference limits for semen analyses. The following parameters represent the accepted 5th percentile (lower reference limits and 95% confidence intervals in parentheses), derived from a study of over 190 men whose partners had a time-to-pregnancy of 12 months.⁴

- Volume: >1.5 mL (95% CI: 1.4-1.7)
- Sperm concentration: >15 million spermatozoa/mL (95% CI: 12-16)
- Total sperm number: 39 million spermatozoa per ejaculate (95% CI: 33-46)
- Morphology: 4% normal forms (95% CI3-4), using strict Tygerberg method⁵
- Vitality 58% live (95% CI55-63)
- Progressive motility 32% (95% CI31-34)
- Total (progressive + non-progressive motility) 40% (95% CI38-42)

According to Rowe et al factors relating male infertility are: Pretesticular causes like Hypogonadotropic hypogonadism, drugs (chemotherapy, spironolactone, cimetidine etc.), alcohol, tobacco and various other causes. Testicular causes like genetic defects and syndromes. Post testicular causes like vas deferens obstruction or its absence, infection, trauma, varicoceles, hernia, hydroceles, impotence etc.⁶

The reports on the incidence of infertility vary greatly from 0.4 to 15%, mainly because of two factors. Firstly, difficulties in defining infertility and secondly because of lack of information about some couples practicing unprotected intercourse for a number of years before pregnancy occurs. Similarly, the magnitude of the contribution of the male factor to couple's infertility is unclear and the range of 30-50% is still generally quoted.⁷ In 2010 a global study was conducted in 190 countries and territories.

Researchers found that 1.9% of women aged 20-44 years who wanted to have children were unable to have their first live birth (i.e. primary infertility) and 10.5% of women with a previous live birth were unable to have an additional live birth (secondary infertility). According to another Study the prevalence of infertility in the general population is 15-20%. Of this, the male factor is responsible for 20-40%. In Indian couples seeking treatment, the male factor is the cause in approximately 23%.

In a World Health Organization multicentre study, 4500 of infertile men were found to have either oligospermia or azoospermia. A study from a tertiary care hospital in India reported 58% azoospermia and 24% oligospermia in infertile men. It This group of patients, with severe andrological infertility, requires assisted reproduction. They have poor success rates with conventional in vitro

fertilization (IVF), but with intracytoplasmic sperm injection (ICSI) it is possible to achieve better success rates.

Michelsen et al found impaired fertility, on semen examination, in 518 men among 845 childless couples. ¹² Tietz reported that 15% of marriages are infertile. ¹³ Wong et al classified causes of male infertility into three major categories: pretesticular, testicular and post-testicular causes. ¹⁴

The pretesticular causes of infertility include extragonadal aetiologies such as endocrine disorders originating in hypothalamus, pituitary or adrenals, chronic illnesses including diabetes mellitus and hypertension, as well as certain medications.

The testicular causes include defects in the process of spermatogenesis and post-testicular causes include obstructions of ducts draining the testes, related to trauma, surgery or mumps orchitis. The distinction between post-testicular obstructive and pretesticular or testicular non-obstructive causes of male infertility is important since men with obstructive etiologies may have other cost-effective options for treatment, such as microsurgical reconstruction of the reproductive tract.

Buxton et al reported that in 40% cases male is partly or completely responsible for subfertility among the 10% infertile marriages. They observed that more than 80% conceive within 2 years, 10% have problems in conception and about half of the rest remain sterile if no treatment is done.

The evaluation of infertile male includes a thorough clinical history taking and physical examination, semen analysis, hormonal assay and search for antisperm antibody. Additional tests include transrectal ultrasonography, vasography and testicular biopsy. This study was done to evaluate the risk factors associated with male infertility.

The objective of the present study was to study the clinical profile of male patients with infertility, to evaluate the risk factors associated with male infertility and to study the various causes of male infertility.

METHODS

The present study was conducted in Department of Surgery in Jawaharlal Nehru Medical College, Aligarh from January 2017 to December 2017. This was a prospective study whereby semen analysis was done of infertile patients attending infertility clinic of Jawaharlal Nehru Medical College and Hospital, Aligarh Muslim University, Aligarh. It was a hospital based prospective study carried out on 120 patients.

A detailed history and physical examination including past history of undescended testis, venereal disease, mumps, and other causes of orchitis were noted. Details of both past and current medications were also recorded. Patients were examined for masculine appearance, testicular size and consistency, presence of varicoceles, hernia or obstruction were noted. At least two samples of semen were collected 6 weeks apart (after 5 days of sexual abstinence) and examined for their volume, sperm concentration, motility and morphology of sperms along with blood samples to study the serum testosterone levels.

RESULTS

Age distribution

Out of the total 120 cases, majority were of the age group 20 to 30 years. The mean age of patients was 31 years, minimum being 22 and maximum being 45 years.

Table 1: Distribution of cases as per age groups.

Age group (years)	Number of cases	%
20-30	62	51.6
31-40	48	40.0
41-50	10	8.3
All	120	100.0

Sperm count

Out of the 120 patients 54 had azoospermia and 66 had oligospermia. Out of them 52 had sperm counts of 1-8 millions/ml and 14 patients of 9-15 millions/ml.

Table 2: Distribution of sperm count in Infertile males.

Sperm count (millions/ml)	Frequency	%
Nil	54	45.0
1-8	52	43.3
9-15	14	11.6
Total	120	100.0

Sperm motility and morphology

Motility at 60 minutes was rarely greater than 60%. 86 of cases had motility < 50% after one hour, remaining 34 had motility > 50% as shown in Table 3. 92 out of 120 patients have shown abnormal sperm morphology (Table 4).

Table 3: Distribution of sperm motility in infertile males.

Sperm motility	Frequency	%
Decreased	86	71.7
Normal	34	28.3
Total	120	100.0

Table 4: Distribution of sperm morphology in infertile males.

Sperm morphology	Frequency	0/0
Abnormal	92	76.7
Normal	28	23.3
Total	120	100.0

Trauma

15 patients out of 120 had history of Scrotal trauma in past while 1 patient had suffered injury to spine, as shown in Table 5.

Out of them 10 had azoospermia while 6 had oligospermia.

Table 5: Frequency of patients with history of scrotal or spinal trauma.

History of Trauma	Cases	%
Scrotal	15	12.5
Spinal	1	0.8
Total	16/120	13.3/100

Tobacco

Out of 120 patients, 75 consumed tobacco in the form of smoking or chewing on regular basis, as shown in Table 6.

Table 6: Distribution of patients having tobacco consumption.

History of tobacco	Frequency	%
No	45	37.5
Yes	75	62.5
Total	120	100.0

Alcohol

Out of 120 cases, 77 (64.2%) had history of alcohol intake on regular basis, as shown in Table 7 while rest 43 were non-alcoholics.

Table 7: Distribution of patients having Alcohol consumption.

Alcoholic	Frequency	%
No	43	35.8
Yes	77	64.2
Total	120	100.0

Smoking

Out of 120 cases, 80 (66.7%) had history of smoking on regular basis in the form of bidi or cigarette while rest 40 were non-smokers as shown in the Table 8.

Table 8: Percentage of known Smokers in infertile males.

Smoking	Frequency	0/0
No	40	33.3
Yes	80	66.7
Total	120	100.0

Ultrasonographic findings

On clinical and ultrasonographic findings, 19 (15.8%) had bilateral small testis of size <4 cm (Image 1,2,3). 5(4.1%) had Inguinal hernia of which 4 of right side and 1 bilateral Inguinal hernia. 3 patients had left sided Epididymal cyst. 1 patient had absent left testis and the same patient had scrotal diverticula (Image 4). 20 (16.6%) patients had varicocele out of these 6 had left sided varicocele (Image 5), rest 14 had bilateral varicoceles.



Figure 1: Clinical photograph of an infertile male with bilateral small testes having fungal infection.



Figure 2: Clinical photograph of an infertile male with bilateral small testes with azoospermia.



Figure 3: Clinical photograph of an infertile male showing empty looking scrotum due to small testes.



Figure 4: Clinical photograph of an infertile male having only right sided testis with scrotal diverticula.



Figure 5: Clinical photograph of oligospermic male with associated left sided varicocele.

Table 9: Distribution of various ultrasonographic findings.

Ultrasonographic findings	Frequency	%
No apparent abnormality	71	59.1
Varicoceles	20	16.6
Bilateral small testis	19	15.8
Epididymal cyst	03	02.5
Presence of hernia sac	05	04.1
Absent left testis	01	0.8
Total	120	100.0

Serum Testosterone

Out of 120 patients 46 (38.3%) were having low testosterone level (<35ng/dl) whereas rest 74 (61.6%) had normal levels of testosterone as mentioned in Table 10.

Table 10: Levels of serum Testosterone in infertile males.

Testosterone level	Frequency	%
Low	46	38.3
Normal	74	61.6
Total	120	100

Obesity

Table 11: Percentage of patients with Obesity.

Obesity	Frequency	%
Yes	12	10.0
No	108	90.0
Total	120	100.0%

As shown in Table 11, 12 out of 120 patients (10%) had Obesity (BMI >25) as per the revised consensus guidelines for Asian Indians and the WHO criteria. The rest 108 (90%) had normal BMI.

Diabetes Mellitus

Out of 120 cases of male infertility, 8 (6.6 %) were known Diabetics rest 112 (93.3 %) had normal blood sugar levels, as mentioned in Table 12.

Table 12: Percentage of known cases of Diabetes Mellitus in infertile males.

Diabetes Mellitus	Frequency	%
Yes	08	6.6
No	112	93.3
Total	120	100.0

Erectile dysfunction

Out of 120 cases of male infertility, 36 (30%) had Erectile dysfunction and thus were unable to perform sexual activity while the rest 84 (70%) were normal, as mentioned in Table 13.

Table 13: Percentage of males with infertility having Erectile dysfunction.

Erectile Dysfunction	Frequency	%
Yes	36	30.0
No	84	70.0
Total	120	100.0

DISCUSSION

Infertility can be attributed to male factor, female factor or a combination of both of them. The awareness of magnitude and importance of male factor infertility is relatively recent. The management of male factor infertility requires interdisciplinary approach. A male with infertility may present to gynecologist, a general physician, a urologist, or a dermatologist (sequelae of venereal diseases).

Treatment of male factor therefore, requires the coordination between these departments including Andrology department. One of the most common features of idiopathic male infertility is testicular malfunction. Normal spermatogenesis is a result of normal testicular anatomy, histology, physiology and proper hormonal regulation through the pituitary gonadal axis. Disturbances in any of these features may lead to testicular malfunction and abnormal semen parameters.

In present study all the 120 infertile males had normal masculine appearance. The mean age of patients was 31 years, minimum being 22 and maximum being 45 years. Out of 120 patients 1 (0.8%) had only one scrotal testis, present on right side of the scrotum. In addition, 19

(15.8%) patients had bilateral small testes. 15 (12.5%) patients had history of scrotal trauma in the past. 70% of patients had history of tobacco consumption either in the form of smoking or chewing. An external measurement of 4 cm was taken as the lower limit of length for a normal testis. Clinically normal (bilateral) testes were present in 101 (84.2%) patients while 19 (15.8%) had bilateral small testes.

There were 54 (45%) patients with azoospermia and 66 (55%) had oligospermia. Out of them 52 (43.3%) had sperm counts of 1-8 millions/ml and 14 (11.6%) had sperm count between > 9-15 millions/ml. 46 (38.3%) patients had low testosterone level. 86 of cases had motility <50% after one hour, remaining 34 had motility >50%. Out of 120 cases, 77 (64.2%) had history of alcohol intake on regular basis. Out of 120 cases, 80 (66.7%) had history of smoking on regular basis. 4 had Inguinal hernia of right side and 1 had Bilateral Inguinal hernia. 3 patients had left sided Epididymal cyst. 1 patient had absent left testis. Out of 120 cases of male infertility, 12 (10%) had Obesity and rest 108 (90%) had normal BMI. Out of 120 cases of male infertility, 8 (6.6%) were known Diabetics rest 112 (93.3%) had normal blood sugar levels. Out of 120 cases of male infertility, 36 (30%) had Erectile dysfunction and rest 84 (70%) were normal. Varicocele was the most common clinical abnormality found in present study 20 (16.6%), all had normal histology.

All patients of varicocele in this study were having normal spermatogenesis. Varicocele represents the most frequent potentially treatable genital disease in infertile men and high prevalence of this condition among idiopathic cases supports clinical decision-making towards appropriate management strategies. In the literature, varicocele is one of the most controversial factors contributing to male subfertility. All patients of hernia were also showing normal spermatogenesis. Patients presenting with infertility sometimes have normal sperm characteristics. Normal spermatogenesis suggests obstruction of some part of ductal system such as varicocele or obstruction of vas deferens. Similar findings were also noted in other international studies. Abdullah and Bondagji in their study of 100 infertile patients found that 13% had normal spermatogenesis. 16

Ragab et al from Egypt reported normal spermatogenesis 24% cases.¹⁷ Pryor et al observed active spermatogenesis in 34.3% cases in the patients having normal appearance of epididymis.¹⁸ Colgan et al reported obstructive azoospermia with normal histology in 20% of their cases.¹⁹ Brannen and Roth reported a higher incidence of obstructive azoospermia (35%), and the same (31%) was reported by Al Rayess et al.^{20,21} Thomas had conducted a study in Nigeria and reported an incidence of 38% for obstructive azoospermia with normal histology.²² On the other hand, others had reported much lower incidence of normal spermatogenesis, one such local study conducted in India itself by Nagpal et al reported similar results

(16%).²³ Meinhard et al reported 5% incidence of obstructive azoospermia.²⁴ Haddad et al in a study from Jordan reported 11.2% of cases with obstructive azoospermia.25 This group of patients will benefit most from the microsurgical reconstruction of the reproductive tract or assisted reproductive techniques like TESE, TESA or ICSI.²⁶ Wong et al studied testicular biopsies in male infertility in 140 cases, testicular causes of infertility 105 cases (75%), pre-testicular causes -15 (10.7%) cases, and post testicular 20 cases (14.3%).²⁷ Punab et al in his study showed that the current wellestablished guidelines and routine work-up in the andrology clinic are able to assign the primary cause of infertility for only 40% of patients.²⁸ In the oligozoospermia group, three in four cases remained idiopathic. This data highlights an obvious gap in our current understanding of the causes, biological and pathways behind impaired mechanisms spermatogenesis and male reproductive physiology.

The prevalence of high percentages of azoospermia in this study 45 percent (54 out of 120) and similar studies suggests an increasing rate of azoospermia. The two major causes of azoospermia are failure spermatogenesis and bilateral ductal obstruction. According to Ojengbede et al., azoospermic patients have prior sexually transmitted diseases which have been linked to seminiferous tubular damage and infertility.^{29,30} Perhaps, our men show up late to the hospital for investigation due to lack of awareness. It has been shown that semen qualities deteriorate by as much as 3% per year.³¹ This factor, in addition, probably contributes to the high percentage of abnormal seminogram among our subjects. The difference between the present study and some local and international studies is not well understood. This variation in results can be explained due to various environmental, social habits and genetic factors. Infertility usually does not result in physical morbidity, pain, limitation of activity or longevity. However, its impact on the psychological and social wellbeing of not only the index patient but also his or her partner makes it a major concern for health professionals.

There are a number of problems in evaluating and treating male infertility. These begin with a lack of standard tests for assessing fertility. Unexplained infertility occurs even when all known tests are normal. There are issues with performing a basic semen analysis since semen is exquisitely sensitive to storage conditions and reporting often does not follow guidelines. The etiologic factors in male infertility continue to be debated and there is incomplete knowledge about its pathophysiology. This study stresses the need for large scale multicentric studies to reach a definite conclusion in this important issue of male infertility.

CONCLUSION

Erectile dysfunction was the most common cause of male infertility. Varicoceles and small sized testes were the most common clinical abnormalities seen in infertile males. Decreased sperm count and reduced motility were the two most common laboratory findings seen in infertile males. Smoking, Alcohol and Tobacco use were frequently associated with most infertile males.

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Institutional Ethics Committee

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