

Etiological Profile of Azoospermic Patients attending Male Biological Reproductive Unit of Mahatma Gandhi Institute of Medical Sciences, Sewagram (Maharashtra), India

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Abstract

Introduction- The term “Azoospermia” is defined as the complete absence of sperm in the ejaculate, is identified in approximately 1% of all men and in 10 to 15% of infertile males. The semen analysis should be performed according to the 2010 WHO guidelines, and at least two semen samples obtained more than two weeks apart should be examined.

Material and Method- The present cross sectional hospital based study was conducted in reproductive biology unit of department of physiology, MGIMS, Sewagram (M.S.) India, during study period September 2011 to August 2013. Subjects belonged to age group of 21 to 45 year. The semen samples were obtained from male partner (referred from gynecology department) of infertile couples attending the reproductive biology unit. 90 freshly diagnosed patients were selected for study. The patients were interviewed about their case histories, their reproductive problems, and their family background. All WHO Guidelines was strictly followed so that identity of subject should not be revealed. In subject with absence of spermatozoa in semen three consecutive semen analysis were performed at an interval of one month each.

Observations- The prevalence rate of Azoospermic patient was found to be 19.90%. We observed that out of 90 azoospermic patients, 40 % of patient was of Obstructive Azoospermia and remaining 60 % was of Non- Obstructive Azoospermia. We found that the most common aetiology of obstruction was Epididymal cyst (23 patients), contributing 63.89 % to its aetiology. Most common aetiology of Non-obstruction was Varicocele (23 patients) contributing 42.59%.

Conclusions- The current study highlighted the etiological spectrum of azoospermia cases.

Keywords- Infertility, Azoospermia, Obstructive, Non obstructive, Varicocele.

Introduction

From the time of the earliest records in every culture there has been reference to infertility & in every culture there are prayers or ceremonies to try to ensure fertility. Fertility denotes the ability of a men & woman to reproduce. Conversely infertility denotes

lack of fertility, an involuntary reduction in the ability to reproduce children. Infertility is relative; sterility is total inability to produce.

According to World Health Organization, “Infertility is the inability of a sexually active non contracepting couple to achieve pregnancy in one year”. Infertility is a common condition with important psychologic, economic, demographic and medical implications. Demand for infertility services has grown substantially even though the prevalence of infertility has been stable.

The misconception that infertility is typically associated with the female is commonly faced in the

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management of infertile men. It is uncommon for a patient to present for an infertility evaluation with an abnormal semen analysis report before an extensive female partner workup has been performed. Usually, even men with potentially treatable causes of infertility are treated with assisted reproductive techniques (ARTs) instead of specific therapy.

However, once the diagnosis of azoospermia is established, no sperm can be found in the ejaculate; as a consequence, assisted reproduction cannot be applied due to the absence of sperm. Therefore, an understanding of azoospermia is very important for us. Infertility varies across regions of the world and is estimated to affect 8 to 12 per cent of couple worldwide (**Sciarrà J. et.al., 1994**)¹. Underlying these numbers exists a core group of couples, estimated to be 3 to 5 per cent, who are infertile due to unknown or unpreventable conditions. A prevalence of infertility above this level suggests preventable or treatable causes (**Fathalla MF et.al., 1991**)². Infertility tends to be highest in countries with high fertility rates, an occurrence termed “**barrenness amid plenty**” (**van Balen F et.al., 2001**)³.

Definitions of Primary infertility vary between studies, but the operational definition, put forth by the WHO, defines Primary infertility as the “Inability to conceive within two years of exposure to pregnancy (*i.e.*-sexually active, non-contracepting, and non-lactating) among women 15 to 49 yr old” (**Reproductive health indicators Report Geneva: WHO; 2001**)⁴. Secondary infertility refers to the inability to conceive following a previous pregnancy. Globally, most infertile couples suffer from Primary infertility (**Inhorn MC. Global et.al.,2003**)⁵.

The term “Azoospermia” is defined as the complete absence of sperm in the ejaculate, is identified in approximately 1% of all men and in 10 to 15% of infertile males (**Jarow JP et.al.,1989**)⁶. This diagnosis must be confirmed by centrifugation of a semen specimen for 15 min at room temperature with high-powered microscopic examination of the pellet and a centrifugation speed of at least 3,000 rotation per minute. The semen analysis should be performed according to the 2010 WHO guidelines, and at least two semen samples obtained more than two weeks apart should be examined. (**WHO Lab. Manual. Geneva:WHO Press,2010**)⁷ and **Schlegel PN et.al.,2004**)⁸.

There are scarcity of studies on the current topic in the study area. With the above background, the present study was planned to see the aetiological profile of azoospermic infertile males attending a tertiary care hospital of Central India region.

Material and Method

The present cross sectional hospital based study was conducted in reproductive biology unit of department of physiology, MGIMS, Sewagram (M.S.) India, during study period September 2011 to August 2013. Subjects belonged to age group of 21 to 45 year. The semen samples were obtained from male partner (referred from gynecology department) of infertile couples attending the reproductive biology unit.

We obtained an informed written consent from all study participants. The use of confidential patient data in this study was fully within the recent guidelines.

Selection of Patient :-

During the above mentioned period 603 patients visited the reproductive biology unit, out of which 120 patients were diagnosed as Azoospermic. Out of 120 azoospermics patients 30 were follow up cases. They were excluded and 90 freshly diagnosed patients were selected for study. The patients were interviewed about their case histories, their reproductive problems, and their family background. All WHO Guidelines was strictly followed so that identity of subject should not be revealed.

Samples were analyzed as per WHO guidelines (**WHO laboratory Manual, 2010**)⁷. In subject with absence of spermatozoa in semen three consecutive semen analysis were performed at an interval of one month each. Finding of absence of spermatozoa was confirmed by centrifuging the sample at 3000 rpm for 15 min and examining the sample under compound microscope.

Inclusion criteria :-

Subjects belonged to active Reproductive age group and which demonstrated azoospermia in semen analysis.

Exclusion criteria :-

Unmarried male attended reproductive unit for complaints other than infertility & vasectomized subject.

Semen analysis :-

The semen samples were collected after a sexual abstinence of 3 to 5 days (Preidt.R.,2003)⁹. The most preferred method for collection of sample was Masturbation (Self-Stimulation), another method was Coitus interruptus (withdrawal of penis just prior to ejaculation during sexual intercourse). The semen specimen was collected in a small, clean wide mouthed jar of 10 to 20 ml. Micro & Macroscopic examination of Semen was performed. The following parameters were studied for confirmation of etiology of azoospermia:

Hormonal assay of FSH, LH & free testosterone.

Karyotyping for detecting defect in sex chromosomes.

Testicular size measurement by Electronic Digital Caliper.

Fructose test for estimation of fructose in seminal plasma.

Transrectal ultrasonography.

Scrotal ultrasonography.

All the data was abstracted on a standardized data collection form. We used a spreadsheet to enter the data electronically and used statistical software SPSS.

Observations

Our study was conducted during the period of September 2011 to August 2013 and total 603 patients were visited out the Biological Reproductive Unit. Out of these, 120 patients were Azoospermic. Out of 120 Azoospermic patients, 30 follow-up patients were excluded from the study. Only 90 newly diagnosed Azoospermic Patients along with 10 controls (exhibiting normal seminogram characteristics) were selected for study.

Table- 1: Distribution of Infertile male with different Seminogram characteristics

Seminogram characteristics	No. of Patient	Prevalence (%)
Normozoospermia	46	7.63
Oligo-astheno-teratozoospermia	252	41.79
Astheno-teratozoospermia	185	30.68
Azoospermia	120	19.90
Total	603	100.00

The prevalence rate of Azoospermic patient was found to be 19.90. The prevalence rate of Astheno-teratozoospermia was 30.68, of Oligo-astheno-teratozoospermia were 41.79, and of Normozoospermia were 7.63 respectively. 90 newly diagnosed Azoospermic patients were distributed depending upon their Aetiological factor. The incidence rate of each Aetiological factor causing Azoospermia was calculated separately.[Table-1]

Table 2: Distribution of patients according to Pathophysiology of Azoospermia

Type of Azoospermia	No. of patient	Percentage (%)
Obstructive Azoospermia	36	40
Non-Obstructive Azoospermia	54	60
Total	90	100.00

In this study, 90 Azoospermic patients were classified on the basis of Pathophysiology diagnosed in Sonological findings as Obstructive and Non-Obstructive Azoospermic patient.

We found 36 cases had obstruction and were classified into Obstructive Azoospermia while in 54 cases obstruction was not seen and were classified into Non- Obstructive Azoospermia.

We observed that out of 90 azoospermic patients, 40 % of patient was of Obstructive Azoospermia and remaining 60 % was of Non- Obstructive Azoospermia. [Table-2]

Table-3: Aetiological factors of Obstructive Azoospermia in the Study Population

Aetiological factors of Obstructive Azoospermia	No. of patient	Percentage (%)
Seminal vesicle cyst	3	8.33
Epididymal cyst	23	63.89
Epididymal nodules	5	13.89
Calcification in Seminal vesicle	5	13.89
Total	36	100.00

36 Obstructive patients diagnosed by Sonological study were distributed on the basis of their Aetiology. We found that the most common aetiology of obstruction was Epididymal cyst (23 patients), contributing 63.89 % to its aetiology. Epididymal nodules and Calcification in Seminal vesicle were the second most common aetiology seen which account for 13.89 % each. It is followed by Seminal vesicle cyst obstruction with 8.33 %.[Table-3]

Table-4: Aetiological factors of Non-obstructive Azoospermia in the Study Population

Aetiological factors of Non-Obstructive Azoospermia	No.	(%)
Klinefelter's syndrome	4	7.40
Microdeletion	5	9.25
Hypergonadotrophic hypogonadism (Primary testicular failure)	19	35.20
Varicocele	23	42.59
No detectable aetiology	3	5.56
Total	54	100.00

54 Non-Obstructive patients were distributed on the basis of their Aetiology. We found that the most common aetiology of Non-obstruction was Varicocele (23 patients) contributing 42.59%. Hypergonadotrophic hypogonadism (Primary testicular failure), was the second most common aetiology (19 patient) seen in with 35.20 %. It is followed by next aetiology Microdeletion contributing 9.25%. Next to it, Klinefelter's syndrome was observed which account for 7.40%. Lastly, No detectable aetiology were observed in 3 cases with the Incidence rate of 3 % . [Table-4]

Discussion

In the present study in population of central India region, we observed that the prevalence rate of Azoospermic patient was 19.58 % which is similar to those reported by American society for Reproductive Medicine.

Azoospermia have various etiologies. The most common Aetiological factor causing Azoospermia observed in this study was Epididymal Cyst and

Varicocele with the Incidence rate of 25.56 % each. It is followed by Hypergonadotrophic hypogonadism (Primary testicular failure) with the Incidence rate of 21.10%. Next to this, the Incidence rate of Y-Chromosome Microdeletion, Epididymal Nodule and Seminal Vesicle calcification was observed at the rate of 5.56 % each. It is then accompanied by Klinefelter's syndrome with the Incidence rate of 4.44 %. The Incidence of seminal vesicle cyst and idiopathic azoospermia ranked last with the least contribution of 3.33% each. We did not find any case of Hypogonadotrophic hypogonadism.

Moon M H et.al.,2006¹⁰ studied on "Scrotal US for Evaluation of Infertile Men with Azoospermia" and found that Epididymal Obstruction was the major cause in obstructive azoospermia. Our observation of higher incidence of epididymal cyst in obstructive azoospermia is supported by this study.

T. XA et.al,2010¹¹ studied 56 cases of obstructive azoospermia and found 23.21% (13 cases) of them had epididymal obstruction.

In our study, we found that the incidence rate of Epididymal obstruction was 25.56 %

Varicocele is an abnormally dilated pampiniform plexus, which is the venous network that drains blood from the testicles. The impaired venous drainage leads to disruption of the counter-current exchange of heat mechanism from the spermatic cord, which elevates scrotal temperature and impairs spermatogenesis. Other postulated mechanisms include impaired drainage of gonadotoxins from the testes and hypoxia (**Goldstein M.,1989**)¹².

The detrimental effects of varicoceles on fertility and the benefit gained by their repair have been debated for so many year. One of the primary benefits of varicocelectomy in NOA patients is that it has the potential to produce motile sperm; however, the value of varicocelectomy in patients with NOA remains unclear. Nonetheless, cumulative data reveal that varicocelectomy can improve spermogram results (**Cakan M et.al.,2004**)¹³.

Gorelick JI et al.,1993¹⁴ studied , the role of varicocelectomy in patients with NOA-related infertility. He found that among the patient with primary infertility, Varicocele was observed with the incidence of 35%

A study conducted by the **Marcello Cocuzza et.al.,2007**¹⁵ reported that varicocele presence in 25.4% of infertile men.

Kubilay Inci.,2013¹⁶ from Turkey provides a critical appraisal on the role of varicocele repair for men with NOA.

In our study, we found that the incidence rate of varicocele was 25.56 %. So from the above discussion we can conclude that Varicocele should be taken under consideration while evaluating Azoospermic subject.

In this study, We classified 90 Azoospermic patients were on the basis of Pathophysiology diagnosed in Sonological findings as Obstructive and Non-Obstructive Azoospermic patient.

Kim ED et.al.,1999¹⁷ suggested that in azoospermic patients, it is important to distinguish nonobstructive azoospermia from obstructive azoospermia because not all men with azoospermia are ideal candidates for intracytoplasmic sperm injection.

Jing Du et.al.,2010¹⁸ China did study in on Evaluations of male infertility and found in his study that, out of 100 infertile men with azoospermia, 64 were found to have obstructive azoospermia, and the remaining 36 had nonobstructive azoospermia.

M. Moon et.al.,2006¹⁰ evaluated prospectively the accuracy of scrotal ultrasonography in distinguishing obstructive azoospermia from nonobstructive azoospermia in infertile men and found 61 % were found to have non-obstructive azoospermia, and the remaining 39 % had obstructive azoospermia.

In our study, we found 36 cases had obstructions and were classified into Obstructive Azoospermics. While in 54 cases obstructions was not seen and were classified into Non- Obstructive Azoospermics. We conclude that from the study population, the Incidence rate of Obstructive Azoospermia was 40 % and that of Non-Obstructive Azoospermia was 60%.

Our study also observed similar incidence of Obstructive and Non-obstructive azoospermia as seen in the study of M. Moon et al.¹⁰

We distributed 36 Obstructive cases On the basis of their Aetiology, diagnosed by Sonological study. We noticed that the most common aetiology of obstruction

was Epididymal cyst with the incidence of 63.89%. Epididymal nodules and Calcification in Seminal vesicle were the second most common aetiology seen with the Incidence of 13.89 % each. It is followed by Seminal vesicle cyst obstruction with the incidence rate of 8.33 %.

Similarly, on aetiological basis we distributed 54 Non- Obstructive cases diagnosed by Sonological study. We found that the most common aetiology of Non-obstruction was Varicocele contributing 42.59% (23 patients). Hypergonadotrophic hypogonadism (Primary testicular failure), was the second most common aetiology (19 patient) with 35.20 % incidence. It was followed next by Microdeletion contributing 9.25%. Klinefelter's syndrome as a cause of azoospermia had a incidence of 7.40%. Lastly, Idiopathic azoospermia was observed in 3 cases with a incidence of 5.56 %.

Conclusions

The current study highlighted the etiological spectrum of azoospermia cases. Finding of the present study will be useful for early diagnosis & appropriate management of these types of cases.

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