

DISCRETION VALUES OF FINE NEEDLE ASPIRATION CYTOLOGY (FNAC) IN INFERTILE MALES

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ABSTRACT

Objective: To analyse the spectrum FNAC findings in patients presenting with infertility, and correlate them with occupational and smoking history, thus highlighting the diagnostic importance of FNAC.

Study Design: Cross sectional descriptive study.

Setting: The study was done in Health Care Hospital , University Town, Peshawar.

Study duration : The study was done from October 2016 to September 2017 (one year study period)

Materials & Methods: A total of 144 patients with complaint of infertility were referred from Health Care Hospital for Fine Needle Aspiration Cytology (FNAC) . All patients with complaint of infertility , azoospermia or severe oligospermia with sperm count of less than 5 million/mL on semen analysis for duration of more than 1 year were included in the study. Patients with already known diagnosis, patients with history of orchidectomy or patients with history of radiotherapy and chemotherapy were excluded. Testicular fine needle aspiration for cytological evaluation was done in all patients. Slides were prepared for cytological evaluation and examined by histopathologist. Cytological findings, occupational history and smoking history were noted on the proforma and the results were drawn accordingly.

Results: A total of 144 patients were included in the study. Age of the study sample ranged from 28 -38 years, with mean of 31 years \pm 2.7 SD. Duration of infertility in the study sample ranged from 1 to 3 years, with mean of 2 years \pm 1.1 SD. The testicular FNAC showed the findings of germ cell aplasia in 139 (96%) patients ,and normal spermatogenesis in 5 (4%) cases. About 96 (67%) cases were heavy vehicle drivers with travel history to foreign countries, 35 (24%) cases were office workers requiring long sittings, and remaining 13 (9%) cases were involved in farming profession , suggesting possible pesticide exposure. About 123 (86%) cases had positive smoking history.

Conclusion: This study concluded that germ cell aplasia is on the rise in our setup in patients presenting with azoospermia. FNAC testis is a satisfactory procedure for evaluating the cause of azoospermia. Larger studies are recommended to find the cause of rising incidence of germ cell aplasia in our setup.

Keywords: Infertility, Azoospermia, Testis, Fine-needle aspiration cytology.

INTRODUCTION

Infertility is the inability to conceive a baby after one year duration of coitus with same partner without using any contraception^{1,2,3,4}. In the males , infertility usually presents as azoospermia or severe oligospermia on semen analysis^{5,6}. Azoospermia is the absence of sperms in the semen , while oligospermia is decreased number of sperm cells in the semen, usually less than 5 million/mL of semen¹.

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The worldwide prevalence of infertility in males is about 5%^{7,8}. It is estimated that about 10-15% of men evaluated for infertility have azoospermia on semen analysis^{9,10}. Azoospermia as such is seen in about 1% of general population , and only 15-20% of men seek medical attention^{5,6,9}. In Pakistan, the prevalence of infertility in males is about 10-15%^{11,12,13}.

The azoospermia is identified by semen analysis in males^{1,14}. Semen analysis is done to assess the sperm count, sperm motility , and in some cases presence or absence of antisperm-antibodies^{1,14}. Additional tests are performed in cases who don't respond to medications, and include ultrasound, fine needle aspiration cytology (FNAC) and biopsy of testes^{15,16}. Azoospermia may be pretesticular, testicular or post testicular^{17,18}. The testicular azoospermia is irreversible¹⁸. The pretesticular azoospermia is due to hormonal imbalance, while post-testicular azoospermia is due to male genital duct obstruction¹⁸. Both the pretesticular and post testicular types respond to hormone and surgical treatment^{11,18,19,20}.

A minimally invasive technique is required to find out underlying cause of infertility in males⁹. Usually, testicular biopsy was recommended for investigating the underlying cause of azoospermia in males, but it is highly invasive technique⁹. In recent years, fine needle aspiration cytology (FNAC) has been recommended for diagnosing different lesions of testes because it is minimally invasive^{1,21}. FNAC is being used as an alternative to open testicular biopsy for evaluating testicular cytology⁹. Obrant and Persson were the first to perform testicular FNAC in patients of azoospermia, and the method was popularized since then²². FNAC is a reliable technique for finding the cause of azoospermia^{1,5,23,24}. FNAC has certain advantages over biopsy¹. It is a quick, simple and inexpensive procedure^{1,25}. Its diagnostic accuracy in detecting spermatogenesis is better than that of biopsy because for FNAC, multiple sites of testis can be sampled while biopsy is taken from only one site^{1,9,26}.

This study was done to determine the spectrum of FNAC diagnoses in azoospermic patients in our setup, thus highlighting diagnostic importance of FNAC and to correlate the occupational and smoking history in patients of azoospermia. This study will help in increasing the awareness of clinicians and general population regarding etiologies of azoospermia in our population.

MATERIALS AND METHODS

It was a Cross Sectional Descriptive study done from October 2016 to September 2017. A total of 144 male patients with complaint of infertility, referred from Health Care Hospital Peshawar for Fine Needle Aspiration Cytology (FNAC) were included in the study. All the patients had azoospermia or severe oligospermia with sperm count of less than 5 million/mL on basis of semen analysis. Testicular fine needle aspiration was done.

Inclusion criteria

All patients with complaint of infertility, azoospermia or severe oligospermia with sperm count of less than 5 million/mL on semen analysis for duration of more than 1 year were included in the study.

Exclusion criteria

Patients with already known diagnosis, patients with history of orchidectomy or patients with history of radiotherapy and chemotherapy were the exclusion criteria .

The patients were informed about the procedure. Scrotal skin was cleaned. Scrotal skin was stretched over the testis. FNAC was done and slides were prepared for examination .The slides were examined by histopathologist. Cytological findings, occupational history and smoking history were noted on the proforma and the results were drawn accordingly.

DATA ANALYSIS

Data was analyzed using SPSS version 16. The quantitative variables i.e. age and duration of azoospermia were presented by mean and standard deviation. The qualitative variables i.e. the FNAC findings were presented by calculating frequency and percentages.

RESULTS

Age and duration of infertility are shown in table 1. The FNAC diagnoses of 144 patients is shown in table 2. Possible etiological factors for infertility are shown in table 3.

Table 1: Age and duration of infertility in 144 cases of azoospermia

| Variables | Range | Mean \pm sd |
|---------------------------------|---------|---------------|
| Age (years) | 28 - 38 | 31 \pm 2.7 |
| Duration of infertility (years) | 1 - 3 | 2.5 \pm 1.1 |

Table 2: Pattern of morphological diagnosis on FNAC in 144 patients of azoospermia

| Morphological diagnosis on FNAC | n (%) |
|---|-----------|
| Germ cell aplasia | 139 (96%) |
| Normal cytology (obstructive azoospermia) | 5 (4%) |

Table 3: Possible etiological or risk factors of azoospermia in study sample

| Etiological/Risk factors | n (%) |
|--------------------------|-----------|
| Smoking | |
| Yes | 123 (86%) |
| No | 21 (14%) |
| Occupation | |
| Heavy vehicles driver | 96 (67%) |
| Office workers | 35 (24%) |
| Farmers | 13(9%) |

DISCUSSION

Infertility causes immense social and psychological problems in males²⁷. Semen analysis reveal azoospermia or severe oligospermia in such patients²⁷. If the sperm count does not improve on medications, patients are subjected to FNAC of the testes to know the underlying cause of azoospermia^{1,28}. The different cytomorphological patterns detected in infertile patients on FNAC include normal spermatogenesis, hypospermatogenesis and germ cell aplasia^{1,11}. In case of normal spermatogenesis, the smear is cellular⁹. The smear show spermatogenic cells admixed with Sertoli cells⁹. The spermatogenic cells show transitional forms from

spermatogonia to spermatozoa, which is characterized by decrease in size of nucleus and condensation of chromatin material in nucleus. In case of germ cell aplasia, the smear is cellular with total absence of germ cells⁹. The smear shows only Sertoli cells⁹.

In the present study, age of the study sample ranged from 28 years to 38 years, with mean age of 31 years \pm 2.1 SD (Table 1). Duration of infertility ranged from 1 year to 3 years, with mean duration of 2.5 years \pm 1.1 SD (Table 1). In one study done by Dabbagh, the mean age of the study sample was 28 years and the mean duration of infertility was 6 years⁹. In another study done by Khan M, mean age of patients was 31 years, while mean duration of infertility was 2.7 years¹. These findings are same as in the present study. In another study done Uma in 2015, mean age of study sample was 28 years²⁸. Mean age of infertile male patients in study done by Ahmed in Bangladesh in 2014 was 32 years²⁴. The age distribution in these studies is same as in our study. Battella from Italy showed the mean age of 37 years in his study sample²⁹. The higher mean age in his study is due to the culture of late marriage in Western countries, thus resulting in late identification of infertility. Another such study conducted in Iraq by Ali SA in 2012 reported the mean age of 42 years which is higher than our study, because their sample had 6 patients over the age of 50 and 3 patients over the age of 60, which resulted in higher mean age³⁰.

In the present study, about 139 (96%) cases had the diagnosis of germ cell aplasia on FNAC, while about 5 (4%) cases had normal cytology (Table 2). So germ cell aplasia was the predominant diagnosis followed by normal spermatogenesis. Similar data is reported by two different studies done by Qublan and Ali S, in which germ cell aplasia is the commonest diagnoses followed by normal spermatogenesis^{23,30}. In one study done by Khan M, the commonest diagnoses was hypospermatogenesis, (seen in about 32% cases), followed by germ cell aplasia (seen in 26% cases), and maturation arrest (seen in 19.6% of the patients)¹. In another study done by Kurien A, the most frequent diagnosis on cytological evaluation was normal spermatogenesis seen in 50.5% cases, followed by hypospermatogenesis, which was seen in 15.3% cases, maturation arrest in 13% cases, and testicular atrophy, which was seen in 12% cases, germ cell aplasia was least common being found in 3.6%⁷. The germ cell aplasia was least common in their study, in contrast to the present study where germ cell aplasia was the commonest diagnoses. In another study done by Uma P in 2015, the commonest pattern observed on cytology was normal spermatogenesis (seen in 28% cases), followed by duct obstruction (seen in 16% cases), maturation arrest (in 14% cases) and germ cell aplasia being the least common (seen in 14% cases)²⁸. In another study done by Khan M, the commonest cytological pattern seen on FNAC was hypospermatogenesis (seen in 32.1% of cases), followed by germ cell aplasia (seen in 26.8% of the cases), normal

spermatogenesis (seen in 18.8% of cases), maturation arrest (seen in 19.6% of the cases)¹. So, germ cell aplasia was second common cytological diagnosis followed by normal spermatogenesis¹. In another study done by Dabbagh, a total of 67 infertile males were studied and the FNAC findings showed maturation arrest in 58.2% cases, normal spermatogenesis in 17.9% cases, germ cell aplasia in 10.4% cases, hypospermatogenesis or germ cell hypoplasia in 5.9%, and complete tubular hyalinization in 7.4% cases⁹. So, germ cell aplasia was third commonest cytological pattern in infertile males in that study⁹. The comparison with all these studies showed that the incidence of germ cell hypoplasia is alarmingly high in our population. Further studies are warranted to find out the cause of rising incidence of germ cell aplasia in our setup.

When etiological factors were studied, it was found that about 123 (86%) cases were chronic smokers (Table 3). When job description was considered in the study sample, it was found that about 96 (67%) cases were heavy vehicle drivers (Table 3). Most of them were in foreign countries, thus having positive history of travel. About 13 (9%) cases were involved in farming profession, thus having positive history of exposure to pesticides. Smoking and exposure to pesticides have been linked to infertility in males³¹. In a study done by Gaur, it was found that patients who smoked had higher risk of oligospermia and hence infertility³¹.

The study showed that the incidence of germ cell aplasia in azoospermic patients is alarmingly high in our setup. It is highly recommended that larger studies should be done to find the cause of germ cell aplasia. Association of germ cell aplasia with smoking and farming profession is already established in literature³¹. But the association of infertility and with heavy vehicle driving need further studies.

CONCLUSION

Incidence of Germ cell aplasia is alarmingly high in patients of azoospermia in our setup. Further studies are warranted to find out the cause of higher incidence of germ cell aplasia. FNAC testis is a reliable, cost effective, and non invasive procedure to detect cause of azoospermia.

REFERENCES

1. Khan M, Khadim MT, Ali SS, Zubair M. Cytomorphological spectrum of testicular fine needle aspiration cytology in cases of azoospermia. Pak J Pathol. 2017; 28(3): 128-34.
2. Strayer DS. Rubin's Pathology: Clinicopathologic Foundations of Medicine, 7th ed. Philadelphia: Lippincott Williams & Wilkins, 2015; 2015. p. 979.
3. Legro RS, Strauss JF. Molecular progress in infertility: polycystic ovary syndrome. Fertil Steril. 2002; 78: 569-76.

4. Rosi J, Ackerman LV. Male Reproductive System. Rosai and Ackerman's Surgical Pathology, 10th ed. Elsevier - Health Science Division, 2011; 2011. p. 1336-7
5. Srivastava A, Raghavendran M, Jain M, Gupta S, Chaudhary H. Fine-needle aspiration cytology of the testis: can it be a single diagnostic modality in azoospermia?. *Urol Int.* 2004;73(1):23-7.
6. Schlegel PN. Evaluation of male infertility. *Minerva Ginecol.* 2009; 61: s261-83.
7. Kurien A, Mammen K, Jacob S. Role of fine needle aspiration cytology (FNAC) of testes in male infertility. *Indian J Urol* 2003;19:140-4
8. World Health Organization. The epidemiology of infertility. WHO Tech. Rep. Ser. No 582 p5 1975.
9. Al-Dabbagh AA, Ahmed BS. Testicular Fine Needle Aspiration Cytology versus Open Biopsy in the Evaluation of Azoospermic Men. *Open J Urol.* 2015; 5: 133-41.
10. Yildiz-Aktas, I.Z., Monaco, S.E., Khalbuss, W.E.. Testicular Touch Preparation Cytology in the Evaluation of Male Infertility. *Cyto Journal,* 2011;8, 24.
11. Cocuzza M, Alvarenga C, Pagani R. The epidemiology and etiology of azoospermia. *Clinics.* 2013; 68:15-26.
12. Khan MS, Deepa F, Ahmed Z, Tahir F, Khan MA. Assessment of male reproductive health by conventional method of semen analysis. *J Ayub Med Coll* . 2011;23(1):84-8.
13. Adhikari RC. Testicular fine needle aspiration cytology in azoospermic males. *Nepal Med Coll J.* 2009;11(2):88-91.
14. Sigman M, Jarow JP. Male infertility. In: Walsh PC, Retik AB, Vaughan ED, Weij AJ, Kavoussi LR, Novick AC, et al, editors. *Campbell's urology.* 8th ed. Philadelphia, WB Saunders, 2003: p.1476.
15. Federman DD: The assessment of organ function - the testis. *N Engl J Med.* 1971; 285: 901-4.
16. Cerilli LA, Kuang W, Rogers D. A practical approach to testicular biopsy interpretation for male infertility. *Arch Pathol Lab Med.* 2010; 134: 1197-204.
17. Alam MA, Islam MS. Fine needle aspiration cytology of testis in male infertility-a review. *Dinajpur Med Col J.* 2015;8(2):226-31.
18. Palermo GD, Kocent J, Monahan D, Neri QV, Rosenvaks Z. Treatment of male infertility. *Methods Mol Biol.* 2014; 1154: 385-405.
19. De Muynck A, Siddiqi S, Ghaffar A, Sadiq H. Tuberculosis control in Pakistan: critical analysis of its implementation. *J Pak Med Assoc.* 2001; 51(1):41-7.
20. Hussain T, Tauseef A, Bari A, Rasheed U, Hassan JA. Awareness among general population attending Civil Hospital Karachi about risk factors associated with infertility. *J Pak Med Assoc.* 2014;64(6):725-30.
21. Jhala D, Wee A, Tse G, Baloch Z. Fine-needle aspiration cytology: an advancing horizon. *Patholog Res Int.* 2011; 2011.
22. Persson PS, Ahron C, Obrant KO. Biopsy of testis in azoospermia. *Scan J Urol Nephrol* 1971; 5: 22-6
23. Qublan HS, Al-Jader KM, Al-Kaisi NS, Alghoweli AS, AbuKhait SA, AbuQamar AA et al. Fine needle aspiration cytology compared with open biopsy histology for the diagnosis of azoospermia. *J Obstet Gynaecol.* 2002; 22(5):527-31.
24. Ahmad M, Islam S, Chowdhury M, Khanam SA, Ahmed AM. Testicular FNAC in azoospermia. *Chattogram Maa-O-Shishu Hosp Med Coll J.* 2014; 13: 46-8.
25. Orell SR, Sterrett GF. Introduction. Orell and Sterrett's fine needle aspiration cytology. 5th ed. Edinburgh: Churchill Livingstone. 2012. pp. 1-9.
26. Turek PJ, Cha I, Ljung BM. Systematic fine-needle aspiration of the testis: correlation to biopsy and results of organ "mapping" for mature sperm in azoospermic men. *Urology.* 1997;49(5):743-8.
27. Niederberger CS. Fertility Outcomes After Extended Searches for Ejaculated Spermatozoa in Men with Virtual Azoospermia. *Eur Urol.* 2017 Nov 18. pii: S0302-2838(17)30984-3. doi: 10.1016/j.euro.2017.11.008.
28. 28, Uma P, Usha P. Role of fine needle aspiration cytology in the evaluation of male infertility. *JEMDS* .2015: 4(22):3804-14.
29. Bettella A, Ferlin A, Menegazzo M, Ferigo M, Tavolini IM, Bassi PF, et al. Testicular fine needle aspiration as a diagnostic tool in non-obstructive azoospermia. *Asian J Androl.* 2005;7(3):289-94.
30. Ali SA, Alnajjar SM, Hasan ZB. The role of FNA cytology of the testis in management of male infertility (In Iraq). *Zanco J Med Sci.* 2012;16(3): 233-40.
31. Gaur DS, Talekar MS, Pathak V. Alcohol intake and cigarette smoking : Impact of two major lifestyle factors on male fertility. *Indian J Pathol Microbiol* .2010;53:35-40