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**RESEARCH ARTICLE**

# INTERPRETATION OF TESTICULAR BIOPSIES OF THE INFERTILES

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**ABSTRACT**

To identify different histological feature of testis of infertile males and classify the types into well defined groups to use Johnsen Score for grading of the degree of spermatogenesis, to find out age distribution and to compare the results obtained with similar studies. During 12 months period from January 2017 to January 2018,100 consecutive testicular biopsies were collected from infertile males. After being immediately fixed in Bouin's solution, for at least 24 hours, they were embedded in paraffin and 4 micron sections were cut and stained by hematoxylene and eosin. Elastic Van Gieson stain was used when indicated to show the fibrosis. Hundred infertile males were included in this study, (97) had primary infertility and only (3) had secondary infertility,. Eighty six had azoospermia and (14) had severe oligospermia . The youngest male was (18) years old and the oldest was ( 43 ) years old. The mean age of the males with primary infertility was ( 28.19) years and that for the secondary infertility group was (33) years. Out of the total, (33) were between the ages of (30 – 34) years. Primary infertility is more common than secondary infertility amongst those seeking testicular biopsy. Sertoli cell only syndrome was the commonest histologic finding in our community. The majority of infertile males were in the 4th decade. Johnsen score 2 is the most prevalent score found among all patients.



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## INTRODUCTION

During the last decade there has been an explosion of interest in male infertility. The incidence of infertility appears to be increasing. Male infertility is one of the most rapidly growing fields in medicine (Jamal, 2011) Infertility is an inability to produce a pregnancy after one year of regular, unprotected intercourse (AL Rayes, 2010). Primary infertility applies to couples who have never had a child (Renee *et al*., 2012). Secondary infertility applies to those who have had a child but cannot achieve fertility again despite engaging in unprotected sexual intercourse for a reasonable period (Ezeh, 2013; Ishikawa, 2010). Unexplained infertility is a nebulous diagnosis that is justified only after thorough and meticulous investigation of both partners have been done. Its incidence is about (10– 15%) of couples presenting with infertility. The incidence varies with the population studied and the criteria used (Benjamin *et al*., 1997; Ahmed, 2002) Testicular biopsy provides the most direct evidence bearing on the state of spermatogenesis in infertile men. Diagnostic testicular biopsy is performed on azoospermic patients to differentiate between obstructive and non obstructive azoospermia.

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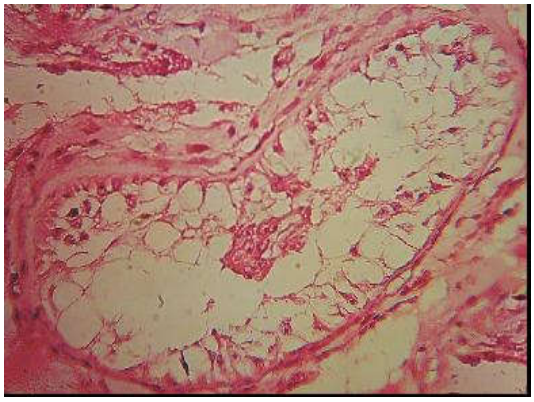
It is also used in severe oligospermic patients. Therapeutic testicular biopsy in the management of patients with nonobstructive azoospermia who decide to undergo intracytoplasmic sperm injection (ICSI) (Yoshikawa *et al*., 2008) .

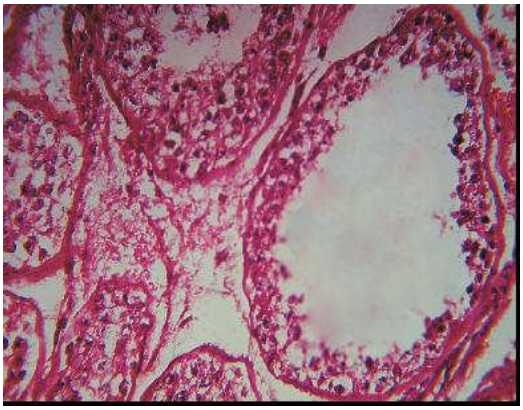
## MATERIALS AND METHODS

One hundred biopsies were received the, after being immediately fixed in Bouin's solution, for at least 24 hours, they were embedded in paraffin and 4 micron sections were cut and stained by hematoxylene and eosin. Elastic Van Gieson stain was used when indicated to show the fibrosis. The histological criteria adopted in the assessment of the biopsies were the size, shape and uniformity of the tubules, the thickness of the basement membrane, spermatogenic activity and maturation, adequacy of Leydig cells and evidence of any inflammation or fibrosis of the interstitial tissue. Johnsen Scoring was used to asses the grading of spermatogenesis. The results were expressed in percentages and frequencies. The differences in the prevalence of histological findings were tested for their significance by the use of Chi square.(2) Probability values < 0.001 were regarded as statistically significant.

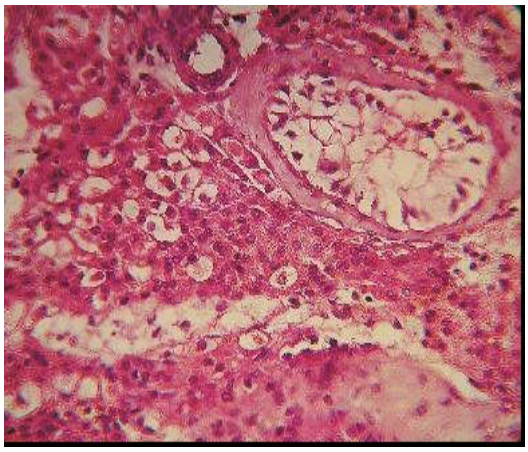


**Sertoli cell only syndrome (H&E X400)**

**Sertoli cell only syndrome (Elastic Van Gieson X400)**

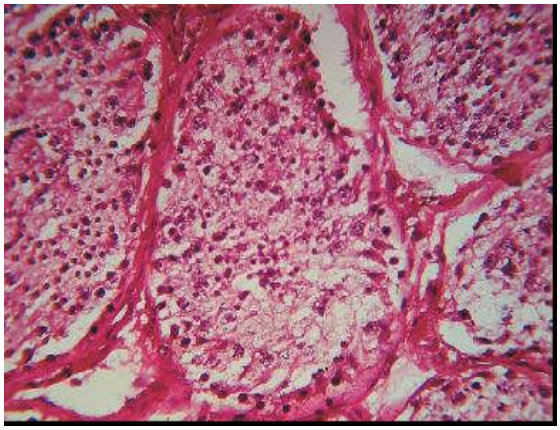


**Maturation arrest (H&E X400)**

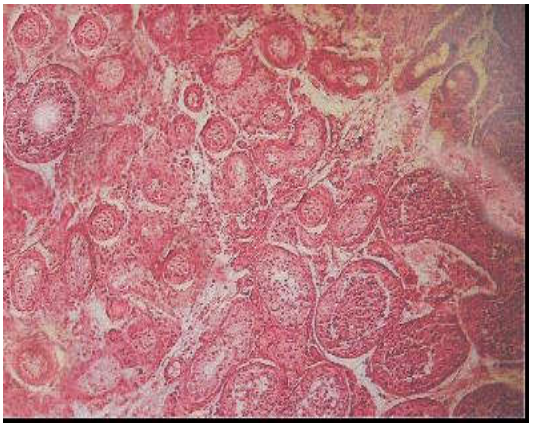


**Klinefelter syndrome (H&E X400)**

**Klinefelter syndrome (Elastic Van Gieson)**



**Extratesticular outflow obstruction (H&E X400)**



**Patchy failure of spermatogenesis (H&E X100)**

**Atrophic testis (Elastic Van Gieson X400)**

## RESULTS

Hundred infertile males were included in this study, (97) had primary infertility and only (3) had secondary infertility,. Eighty six had azoospermia and (14) had severe oligospermia . The youngest male was (18) years old and the oldest was ( 43 ) years old. The mean age of the males with primary infertility was ( 28.19) years and that for the secondary infertility group was (33) years. Out of the total, (33) were between the ages of (30 – 34) years. The majority of those with primary infertility were in their thirties. The secondary infertility group included (3) males, (2) of them were in their thirties. (42%) of them had Del Castillo syndrome, and (23%) had maturation arrest, (13%) had Klinefelter syndrome. (9%)males had outflow obstruction, (7%) had patchy failure of spermatogenesis and another (6%) had atrophic testes.

## DISCUSSION

Infertility is a medico-social problem, because of the majority of the males are young, healthy, presenting with infertility only. Male infertility represents an important factor as the cause of infertility amongst infertile couples (Jamal, 2011). Testicular biopsy is an important diagnostic tool for the evaluation of infertility (AL Rayes, 2010). The most common cause of male infertility is failure of spermatogenesis and hence, biopsy is of no prognostic value The majority of the patients in this study were in the fourth decade with a mean age of (28.34) years. In other studies from Portugal, U.K, Canada and Japan the mean ages were (35), (34), (33.8) and (32.1) years respectively (Renee *et al*., 2012; Ezeh, 2013; Ishikawa, 2010; Sousa, 2011). In this study, males with primary infertility (97%) predominated over those with secondary infertility (3%). The results were comparable to two other studies performed in Nigeria and the United States Both studies reported a ( 89% and 79.5%) respectively of males with primary infertility (Mistal *et al*., 2001). Comparing the histologic findings of this study with others, faces two problems; first is the lack of agreeable histologic classification and second is the presence of certain conditions that do not fall in any readily defined category.

However, and in spite of these problems, we tried as clearly as feasible to categorize the findings into well defined widely accepted groups and to compare the results with others. Testis with Sertoli-cell-only tubules is found in a variety of pathologic entities. These include Klinefelter syndrome, cryptorchidism, following estrogen treatment, gonadotrophin deficiency, irradiation therapy and Del Castillo's syndrome. The latter is the commonest of these entities, which could be separated from the other conditions, if hormonal assessment and ultra-structural morphological studies of Sertoli cells were done (Mistal *et al*., 2000). Unfortunately, and because of lack of facilities these were not done, and we only had the light microscopic appearance to rely on. Thus all cases with Sertoli cell only tubules and showing no other microscopic abnormality were considered as examples of Del Castillo's syndrome. Forty two cases were encountered, of which 37 showed full expression of the disease with complete lack of germ cells. In 5 cases, some of the tubules contained multiplying germ cells and hence, they were considered as partial Del Castillo's syndrome (Sousa *et al*., 2011) With 42 cases, Sertoli cell only syndrome was the most frequently encountered histologic finding (42%). This is comparable to studies from Texas (42%) (Yoshikawa *et al*., 2000). Mosul (41%) (Shuaib, 1993), Portugal (38.5%) (Benjamin, 1997) New York (33%) (Benjamin, 1997) and U.K (30%) (Ezeh *et al*., 2013). While it formed (21.3%) and (7.5%) in India and Pakistan respectively (Ahmed, 2002; Madhu, 2009). Maturation arrest was the second most frequent histologic finding (23%) in this study, of which (17%) showed incomplete arrest, while the rest showed complete arrest. In Portugal, maturation arrest was the second most frequent histologic finding (31.8%), (21.6%) of which showed incomplete arrest, while the rest showed complete arrest (Sousa, 2011). While in Canada, maturation arrest was the most common histologic diagnosis (50%), (33.3%) of which showed incomplete arrest, while the rest showed complete arrest (Renee, 2012).

In other studies from Texas, India, Pakistan and Saudi Arabia, the percentages were (12%), (11.6%), (7.5%) and (7%) respectively (Yoshikawa *et al*., 2000; Ahmed, 2002; Madhu *et al*., 2009) Klinefelter syndrome ranked third among cases in this survey (13%). Histologically, there were variable changes depending on the stage of the disease. However, a common feature among all cases was marked Leydig cell hyperplasia. The figure of this study is comparable to those of the studies from Canada, Japan and Mosul, the percentages were (12%) (7.4%) and (6.5%) respectively (De Braekeleer, 2008; Okada *et al*., 2005). This study had demonstrated the histologic patterns seen in testicular biopsies of infertile males. The observed differences from other studies may be multifactorial; due to environmental influences , differences in the criteria used in the patient selection, reflection of variable interhistologic interpretation, and may be due to some unknown genetic abnormalities that affect different ethnic groups, or different people at different geographical areas.

### Conclusions

Primary infertility is more common than secondary infertility amongst those seeking testicular biopsy. Sertoli cell only syndrome was the commonest histologic finding in our community. The majority of infertile males were in the 4th decade. Johnsen score 2 is the most prevalent score found among all patients.

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