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A Study on Evaluation in Male Infertility of Genetic Factors Role

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Abstract – Male infertility is most obvious examples of a complex disease. Genetic factors of spermatogenic dysfunction, like as chromosomal aberrations, account for 10–15 percent of extreme male infertility, according to many male mouse models, mutation screening, and correlation studies conducted in the last few years. The standard GTG (G-banding Trypsin Giemsa) banding technique was used to determine the chromosomal abnormalities. A total of 68 percent of study participants had azoospermia, 18 percent had oligospermia, 6 percent had severe oligospermia, and 8 percent had oligoasthenoteratospermia (OAT) xvi.

Keywords – Evolution, Infertility, Male Infertility, Genetic Factor, Chomosome

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INTRODUCTION

Metals that are toxic Dioxins, anti-metabolites, dyes, herbicides, fungicides, and even household dust are all part of a toxic cocktail to which people are continuously subjected. As a result, the human body's essential systems are constantly at risk of being damaged. The reproductive system, particularly spermatogenesis, appears to be impacted as well. Long-term toxic exposure may result in workplace infections, permanent improvements in the reproductive system (poor sperm production, spermatogenesis disorders), and even infertility (1-6). One of the causes of oxidative stress is the decrease of antioxidant enzymes (superoxide dismutase SOD, catalase CAT or glutathione peroxidase GPx) which erodes the protection against reactive O2 forms (9, 10). Male reproductive health can be better by supplementing beneficial elements like zinc or selenium, which induce favorable improvements in sperm count and motility. Melatonin, beta-carotene, and luteine are all nutrients that tend to maintain sperm production (11-16).

Infertility affects about 15 percent of pairs and inherited variants are thought to induce male infertility to 15 percent – 30 percent. Genetics plays a role in infertility through influencing a number of physiological mechanisms like spermatogenesis, hormonal homeostasis, and sperm content. Understanding the hereditary reason of reproductive failure is important for successfully managing an infertile pair. Male factor infertility is most perplexing reproductive diseases, and its frequency is rising notwithstanding the fact that its cause is unclear.

- **Epidemiology and prevalence of male infertility**

The percentage of infertile men ranged from 25 percent to 12 percent, and the percentage of infertility due to male factor ranged from 20 percent to 70 percent. The difficulty of diagnosing male reproductive disorder adds to the complication of determines the epidemiology and incidence of male infertility. Prospective epidemiologic studies can help doctors better understand male infertility.

- **Male infertility Genetic causes**

Men that are infertile have a higher prevalence of chromosome mutations, which is inversely proportional to their sperm count. The average prevalence of a chromosomal element in infertile males is calculated to vary between 2 and 8 percent, with a mean value of 5 percent. Sex chromosome abnormalities are the most common, but there are also a variety of structural autosomal anomalies. Klinefelter's syndrome is the most common type of karyotype abnormality found in infertile individuals (KS). In a study of 750 severe oligozoospermic men (sperm count 5 (106 /ml) (15), chromosomal aberrations were found in 42 (5.6%) of them, with 29 (69.0%) of them being of the Klinefelter's type.

Four of the more prominent sex chromosome aneuploidies observed in infertile males are 47, XYY, 46, XX, and Y chromosome aneuploidies (inversions, Yq deletions, etc.). X-autosomal and Y-autosomal translocations involving the chromosomes of the sexes are also normal (15).

METHODOLOGY:

- **Study design**

This cross-sectional study included 100 infertile men ranging from 22 to 45 age of year. Committee on Institutional Ethics (IEC) IEC granted ethical approval to conduct this research.

- **Study Population:**

This study involved 100 infertile men ranging from 22 to 45 age of years who had abnormal semen parameters.

- **Inclusion Criteria:**

Oligozoospermia, Teratospermia, Asthenozoospermia, and Azoospermia were found in infertile men with abnormal semen analysis findings.

- **Exclusion Criteria:**

Patients with Normozoospermia and those who refuse to give informed consent.

- **Sample collection:**

All study participants' peripheral blood (2ml) was collected in a heparin and EDTA vacutainer for chromosomal analysis and Y microdeletion detection, respectively. To study sperm aneuploidy & DNA fragmentation, semen samples were collects through masturbation after 3-5 days of abstinence. For sperm aneuploidy and sperm DNA fragmentation parameters, ten fertile men between the ages of 35 and 45 who have two healthy children were used as controls. All study participants and controls gave their informed consent.

- **Chromosomal Analysis:**

The standard G-banding protocol was used with minor modifications for chromosomal analysis.

- **Molecular diagnosis of microdeletion detection on the Y chromosome:**

Multiplex PCR was used to create microdeletions in the AZFa, AZFb, and AZFc genes. The Y microdeletion of genomic DNA was standardized based on Simoni et al., guidance 1999, with slight modifications.

- **Sperm DNA Fragmentation Analysis:**

The manufacturer's instructions were followed when estimating DNA integrity using a commercially available kit. A part of the sperm from the control and patient groups was washed in 20 mL PBS and spinning at 2000 rpm for 10 minutes. The cells were re-suspended in 4 percent Paraformaldehyde fixation buffer and permeabilized with 0.25 percent after the supernatant was discarded. The supernatant was discarded, and 1 mL of ice-cold 70% ethanol was added, which was then stored at -20°C until further use.

- **Statistical Analysis:**

For qualitative data, frequency/percentage was used, and for quantitative data, mean and standard deviation were used to summarize the data. The mean of sperm aneuploidy and the rate of DNA fragmentation were compared using the student's t-test.

Results

The goal of this study is to perform a genotypic analysis of sperm and peripheral blood in infertile men. The study subjects' ages ranged from 22 to 45 years old, with a mean and standard deviation of 35.55.1, while the control group's ages ranged from 35 to 45 years old, with a mean and standard deviation of 40.53.117. Infertile men with azoospermia accounted for 68 percent of the study's 100 participants, oligospermia for 18 percent, severe oligospermia for 6%, and oligoasthenoteratospermia (OAT) for 8%. Figure 1 explain the distribution of all study participants and their clinical indications.

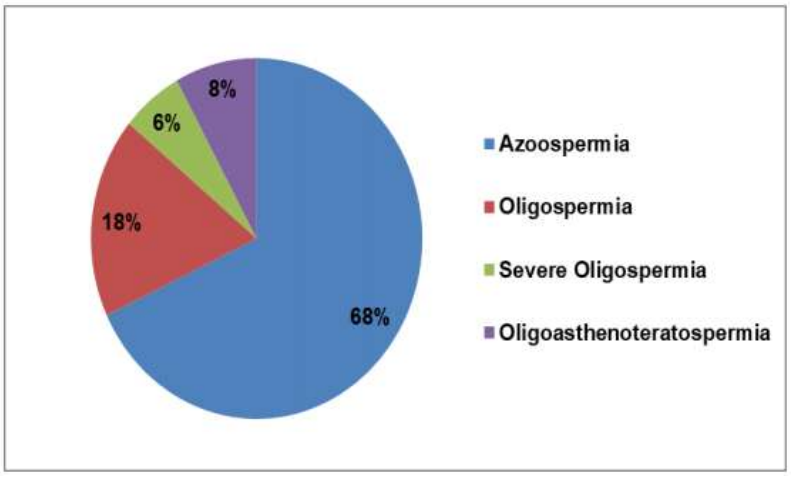

Figure 1: Distribution of clinical indication among subjects (n=100)

- **Pedigree analysis:**

A pedigree is a record of an individual's family that is used to investigate the transmission of a hereditary condition. Human genetics can be studied ethically using pedigree charts. They're useful when there are a lot of people in the family and there's a good family history going back several generations. To rule out inherited infertility issues, we gathered all of the study subjects' family histories and pedigrees. None of the infertile men came from a family with a history of infertility issues (both male and female). Consanguineous marriages were found in 5% of the cases, with the remaining 95% being non-consanguineous marriages. Figure 2 depicts one of the pedigrees obtained from the research subject.

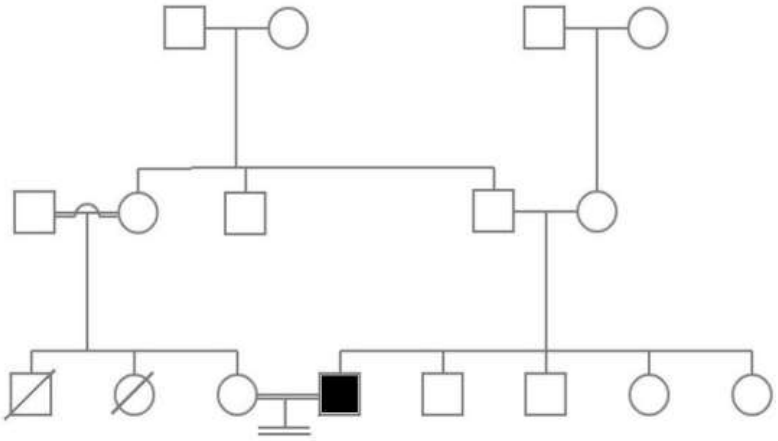

Figure 2: Pedigree of an infertile man

- **Chromosomal analysis:**

Chromosomal analysis using standard GTG banding in 100 subjects revealed a normal karyotype of 46,XY (Figure 15), as well as chromosomal abnormalities (11%) and normal polymorphic variants (8%) in the current study. The most typical sex chromosomal abnormality of Klinefelter syndrome 47,XXY was observed in 7% of the chromosomal abnormalities, and balanced carrier translocation of different chromosomes (autosomal abnormality) was observed in 4%. Table 1 summarizes the results of the detected chromosomal analysis.

Table 1: Chromosomal abnormalities observed in 100 infertile men

	Karyotype	Frequency (%)
No chromosomal abnormalities (Normal)	46,XY	81%
Numerical Abnormalities - Klinefelter Syndrome	47,XXY	7%
Balanced carrier translocation	46,XY,t(13;19)(q12;q13.4)	
	46,XY,t(7;9)(q11.2;p13)	4%
	46,XY,t(2;7)(q21;p12)	
	45,XY,t(13;14)(q10;q10),inv(Y)	
Polymorphic Variant of chromosome 15	46,XY,15ps+	4%
	46,XY,15pstk+ps+	
Polymorphic Variant of chromosome Y	46,XYqh-	2%
Inversion of chromosome 9	46,XY,inv(9)(p11q13)	2%

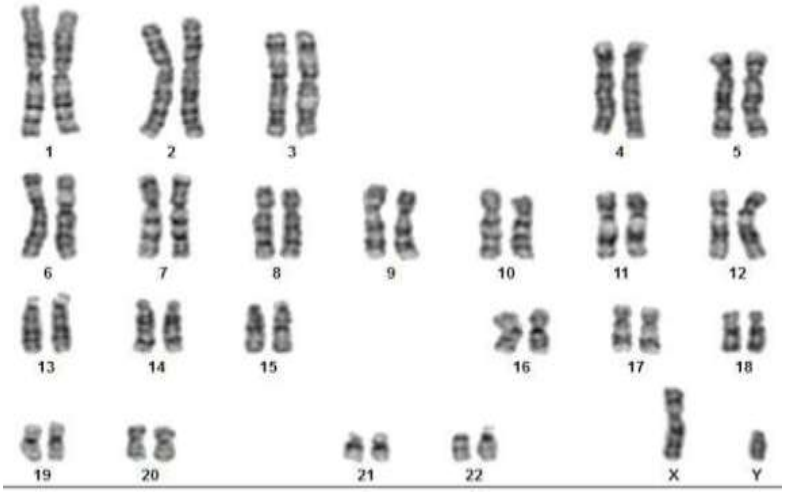

Figure 2: Karyotype showing – 46, XY karyotype

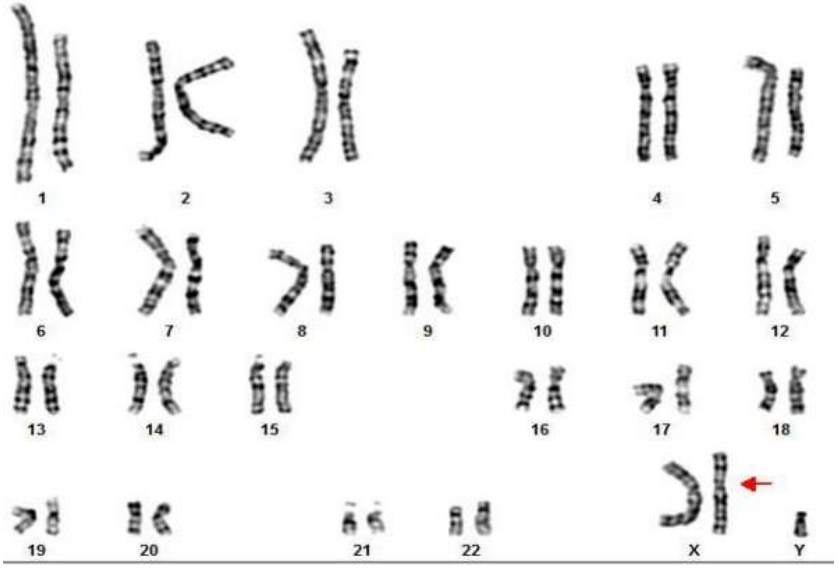

Figure 3: Karyotype showing 47,XXY – Klinefelter syndrome

- **Sperm aneuploidy:**

FISH for sperm aneuploidy and TUNEL assay for sperm DNA fragmentation were performed on a semen sample from patients with oligospermia, severe oligospermia, and OAT (32%) cases. Ten normozoospermic men with two healthy children were used as a control group for these two parameters. 14 percent of infertile men (32%) were ready to give their sperm samples (Figure 33), with oligospermia accounting for 8%, severe oligospermia for 1%, and OAT accounting for 5%. Figure 4 shows sperm FISH with disomy and diploidy on sperms.

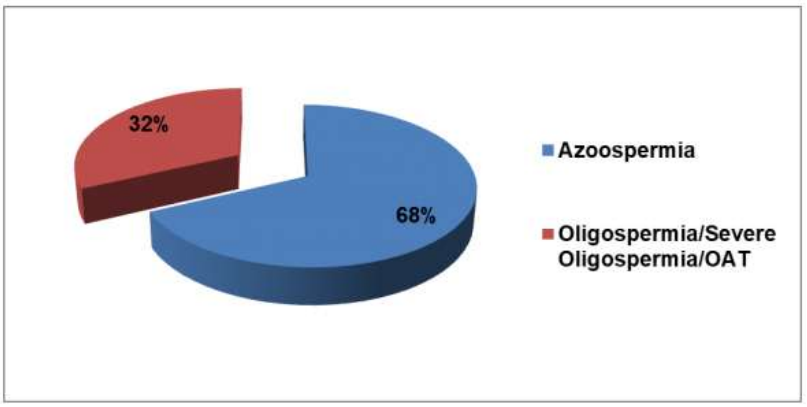

Figure 4: Distribution of case according to seminogram status and willingness

CONCLUSION:

Infertile men had a high sperm aneuploidy than fertile men. Disomy frequency of chromosome 13 and XY has increased. Autosomal aneuploidy was more common than chromosomal aneuploidy in both sexes. The total aneuploidy found was higher than the frequency of diploidy.

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