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Original Research Article

Chromosomal Abnormalities and Primary Infertility

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ABSTRACT

Background: Primary infertility refers to the couples who are not able to achieve parenthood after one year of unprotected intercourse without using birth control measures. Chromosomal abnormalities are one of the important causes for primary infertility which requires proper diagnosis and genetic counseling.
Aim: To estimate numerical and structural chromosomal abnormalities in patients with primary infertility who were referred for karyotyping to Division of Human genetics, Department of Anatomy, St. John's Medical College, Bangalore.
Materials and methods: A total of 203 patients with primary infertility were referred for karyotyping and counseling to Division of Human genetics, Department of Anatomy, St. Johns Medical College, Bangalore from January 2010 to June 2016. There were 117 male and 86 female patients and their age ranged from 20 to 40 years.
Chromosomal preparations were done using the peripheral lymphocyte culture method followed by GTG banding technique, automated photography and karyotyping.
Results: Out of 203 patients (117 males & 86 females) referred with history of primary infertility 36 showed chromosomal abnormalities out of which 17 had numerical abnormalities, 15 had structural abnormalities and 4 had both structural and numerical abnormalities.
Conclusion: We conclude that chromosomal analysis and possible genetic influences are important parameter in the assessment of cases with Primary infertility. The results influence the ultimate decision which needs to be considered before any procedure can be taken for preimplantation genetic diagnosis and assisted reproductive techniques.

Key words: Primary infertility, numerical abnormalities, structural abnormalities, pre implantation genetic diagnosis

INTRODUCTION

Primary infertility refers to the couples who are not able to achieve parenthood after one year of unprotected intercourse without using birth control measures. It is considered to be a multifactorial condition as it involves various causes. The most common causes of female infertility are ovulation disorders, blocked fallopian tubes, polycystic ovary syndrome (PCOS) and endometriosis. The main causes involved in male infertility include abnormal sperm production, problems with delivery of sperm, testicular cancer and exposure of reproductive parts to excessive heat or radiation. Chromosomal abnormalities form one of the important causes for primary infertility which requires proper diagnosis and genetic counseling. In a population of infertile or sterile probands, chromosomal aberrations are found at a frequency of 10-20%. [1]

Many recent studies describe the involvement of inversions, translocations,

deletions, gene mutations, polymorphisms, and heterochromatin in primary infertility. Embryonic chromosomal abnormalities due to abnormal segregation can result in recurrent implantation failure which needs timely intervention .With the introduction of preimplantation genetic diagnosis it is possible to screen embryos with chromosomal abnormalities and improve the reproductive outcome of pregnancy.

Objectives

To estimate numerical and structural chromosomal abnormalities in patients with primary infertility who are referred for karyotyping to Division of Human Genetics, Department of Anatomy, St. Johns Medical College, Bangalore.

MATERIALS AND METHODS

A retrospective study was conducted on 203 patients with primary infertility who were referred for karyotyping and counseling to Division of Human Genetics, Department of Anatomy, St. John's Medical College, Bangalore from January 2010 to June 2016. There were 117 male and 86 female patients and their age ranged from 20 to 40 yrs.

Chromosomal preparations were done using the peripheral lymphocyte culture method followed by GTG banding technique, automated photography and karyotyping.

Statistical methods: The percentage of abnormality was calculated.

RESULTS

In this study, the cytogenetic analysis (karyotyping) of 203 samples including males and females revealed that a total of 167 were found to have a normal karyotype while about 36 cases showed chromosomal abnormalities contributing to 17.73%.

Table1: Structural and Numerical chromosomal abnormalities in patients with primary infertility.

Chromosomal abnormalities	Males	Number of Patients	Females	Number of Patients	Total
Numerical	47,XXY	13	47,XXX	1	17
	mos47,XXY/46,XY	1	mos47,XXX/46,XX	2	
Structural	46,XY(short Y) 46,XY(long Y) 46,XY,t(5;16) 45,XY,t(13;14) 45,XY,t(14;14)	7 1 1 1 1	46,XX(11;22) 46,X,del(X)(q25q28) 46,XX,inv(9)	1 2 1	15
Numerical and structural	47,XX,inv(Y) 47,XXY,t(1;4) 47,XXY,inv(9)	1 1 1	mos45,X/46,Xdup(X)(q)	1	4

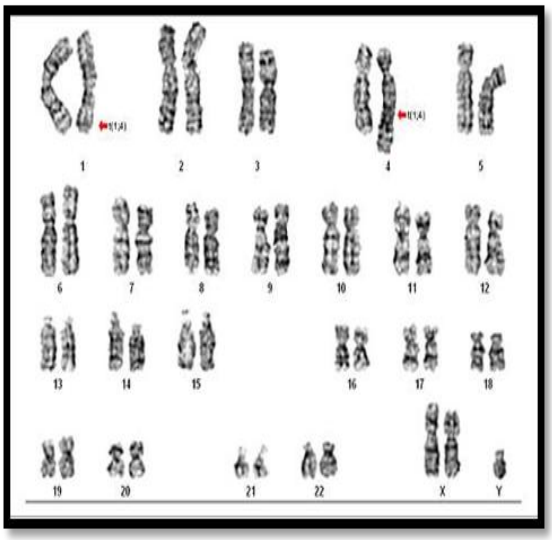

Fig1: Karyotype: 47, XXY, t (1; 4) of male presented with hypogonadism and primary infertility

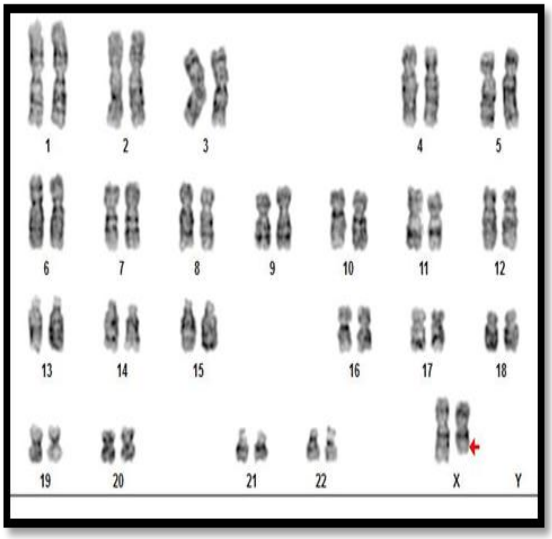

Figure 2: Karyotype: 46, Del(X) (q25q28) of female presented with primary ovarian failure

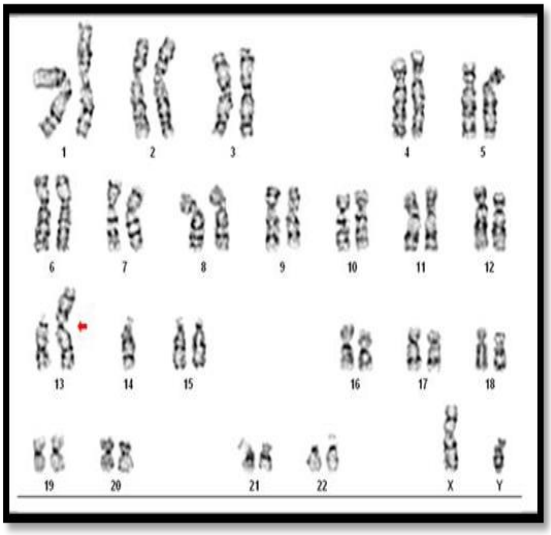

Figure 3: Karyotype: 45, XY, rob (13; 14) (q10; q10) of male presented with primary infertility

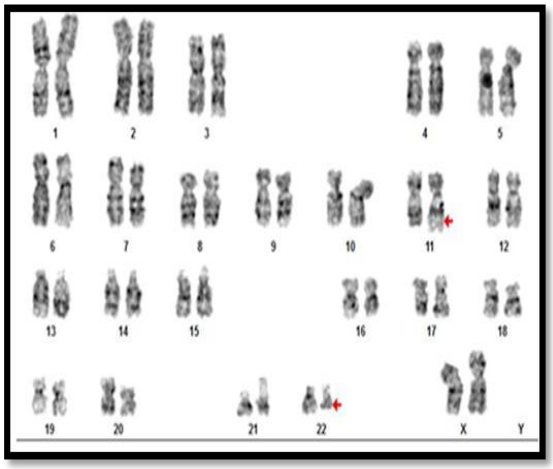

Figure 4: Karyotype: 46, XX, t (11; 22) (q24; q12) of female presented with recurrent implantation failure.

DISCUSSION

Numerical abnormalities were more than structural abnormalities. Out of 36 abnormalities 31 were sex chromosomal and 5 were autosomal abnormalities. Most common numerical abnormality in men was 47, XXY-Klinefelter syndrome contributing to 17% of male infertility. Prevalence of chromosomal abnormalities are more among males (23.93%) than females (9.3%).Even though short Y, Inversion 9 and Y are polymorphic variants possibility of these being reason for primary infertility cannot be ignored. Out of 5 patients who had translocation 2 had robertsonian translocation and 3 of them had reciprocal translocation suggesting defective gametogenesis due to abnormal segregation during meiosis as one of reasons for reproductive failure in these patients.

Most of previous studies were done on patients who were undergoing artificial reproductive techniques. In a study done by Turan et al., on 480 patients having recurrent IVF failure abnormal chromosome organization was observed in 39 (15.8%) females and in four (1.7%) males. Moreover, chromosomal polymorphisms were detected in 15 (6%) females and 28 (12%) males and almost all chromosomal abnormalities were associated with sex chromosomes. [2] In study done by Kate et al., from India the frequency of major chromosomal anomalies was 10.2% in infertile males with primary infertility with

an incidence of autosomal chromosome abnormalities were 6.4% and sex chromosome abnormalities were 3.8%. [3] In a study done by Cyrus Azimi et al., out of 896 patients, 710 infertile females (79.24%) had a normal karyotype, and 186 patients (20.76%) showed abnormal karyotype. [4] Two of our patients had inversion of chromosome 9 which is said to be a polymorphic variant but study done by Capkova *et al* investigated chromosomal abnormalities in couples with reproductive disorders, and showed that structural aberrations, including inversion 9, were more frequent among infertile couples. [5] Marozzi et al. described six Primary ovarian failure patients with rearranged Xq chromosomes and confirmed that the second region for Primary ovarian failure extends from Xq26.2 to Xq28 which was deleted in two of our patients who presented with menstrual irregularities and elevated levels of follicular stimulating hormone. [6] According to Ricarde Lange et al., sex chromosome mosaicism is one of the causes of female infertility. [7] Prevalence of Klinefelter syndrome was higher (17%) in present study when compared to previous study conducted in India. Stern et al. studied chromosomal translocations in 514 individuals who had recurrent implantation failure. [8] They found that around 3.2% had chromosome translocations. Percentage of translocations in present study was 2.46% which was comparable with study done by Stern et al., [8] Study done by Choi B H et al., revealed that carriers of Robertsonian translocations are phenotypically normal however, they exhibit reproductive dysfunction, such as oligospermia in males. [9]

Management and genetic counseling: Patients with numerical abnormalities more commonly Klinefelter syndrome who presented with hypogonadism/ azoospermia along with primary infertility was suggested to go for artificial insemination and sperm donation. Male patients who had short Y were subjected for Y microdeletion studies to look for AZF regions which are responsible for the process of defective spermatogenesis. Patients with structural abnormalities especially translocations were counseled to go for preimplantation genetic diagnosis followed by artificial reproductive techniques. If couple chose for normal pregnancy, amniocentesis during 4th month of pregnancy was suggested. Two female patients presented with primary ovarian failure and low ovarian reserves along with primary infertility had terminal Xq deletion were counseled to go for ovum donation.

CONCLUSION

We can conclude that chromosomal analysis and possible genetic influences is an important parameter in the assessment of cases with Primary infertility. Hence cytogenetics helps in ultimate decision before any procedure like preimplantation genetic diagnosis and assisted reproductive techniques.

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