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Cytogenetic Study in Couples with Primary Infertility

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Abstract

Fertility denotes the ability of a man and woman to reproduce. Conversely, infertility denotes lack of fertility, an involuntary reduction in the ability to produce children. A total of thirty three couples were studied in an attempt to find out the cytogenetic causes in primary infertility. The couples were assessed for other contributory factors like age, consanguinity, anatomical abnormalities, hormonal causes or any other medical causes. Cytogenetic analysis of the infertile couples revealed that chromosomal abnormalities were present in one of the partner in 36.36% of couples. Chromosomal abnormalities were found in 24.24% females and 12.12% males. Among the chromosomal abnormalities, numerical abnormalities were present in 18.18% couples and structural abnormalities were present in 12.12% couples. Most common among the numerical abnormalities was 47, XXY i.e 3 cases, mosaicism was seen in 3 cases (2 females and 1 male). 46, XY karyotype was found in two phenotypic females with primary infertility. Structural abnormalities were present in 12.12% of female patients.

Keywords- *Primary infertility, chromosomal aberrations, karyotyping, numerical abnormalities, structural abnormalities.*

Introduction

Infertility is seldom, if ever, a physically debilitating disease. It may however, severely affect the couple's psychological harmony, sexual life and social function[1] In some cultures childlessness may cast a heavy shadow on the psychological and social adequacy of the female and diminish the social standing of the male partner. Most cultures regard children as an extension of self as bearers and perpetuators of the family name and tradition as well as an expansion of one's hopes, aims and strivings.

Infertility may be further classified as primary infertility, in which no previous pregnancies have

occurred, and secondary infertility, in which a prior pregnancy, although not necessarily a live birth, has occurred[2].The definition proposed by WHO states that 'Infertility can be primary, if the couple has never conceived despite cohabitation and exposure to pregnancy (without contraception) for a period of two years[3]. 60-80 million couples experience infertility worldwide[4].The important role of genetic factors in pathogenesis of infertility is now increasingly recognized [5]. Chromosome aberrations may cause infertility in both men and women[6,7].The main cause of female infertility is amenorrhoea not due to pregnancy, lactation or menopause is around 3-4 % [8,9].The contribution of male factors to infertility is 30-50%. Environmental as well as genetic factors are involved in the decrease of the reproductive potential in male[10]. The main genetic factors involved in male infertility are chromosomal abnormalities and Y-chromosomal microdeletions within the Yq11 region [11].

Material and Methods

The study was conducted over a period of 21 months, thirty three couples with history of primary infertility referred to the Genetic Division of Anatomy Department Grant Medical College Mumbai were selected for this study. The patients were referred from this Institute itself, other Government Hospitals, and Municipal & Private Hospitals in and around Mumbai.

All couples having a history of primary infertility attending the genetic clinic were initially screened with a detailed gynaecological and clinical history. All these patients were screened for chromosomal abnormalities, after due consent. Patients were evaluated for detailed family history and occupational history. Clinical examination of the patients, ultrasonography, Barr body examination of patient was done wherever necessary. Cytogenetic analysis was carried out in all these couples.

Karyotyping:-

1-2 ml of peripheral blood of the patient was collected in sterilized, heparinized 5ml syringe by venipuncture. Planting of the culture was done on the same day. The contents of each culture vial were mixed gently and incubated for 3 days at 37°C. For each patient two vials were planted with PHA-M. The planted cultures were shaked well after every 24 hours. This enhances better growth. Harvesting of the culture was done using colchicines (Gibco BRL). After harvesting, Giemsa banding was done. Metaphases were screened under microscope.

Observations and Results

Table no1- Gender wise comparison of age in years

Age in years	Primary infertility				Total	
	Male		Female			
	No	%	No	%	No	%
<=20	0	0.00	4	12.12	4	6.06
21 to 25	6	18.18	15	45.45	21	31.82
26 to 30	14	42.42	11	33.33	25	37.88
31 to 35	10	30.30	3	9.09	13	19.70
36 to 40	2	6.06	0	0.00	2	3.03
>=40	1	3.03	0	0.00	1	1.52
Total	33	100	33	100	66	100

Table no 2- Other associated parameters studied

Sr No	Parameter studied	No of patients	%
1	Anatomical Abnormalities in both sexes	17	25.76
2	Hormonal imbalance in females	4	12.12
3	Hormonal imbalance in males	2	6.06
4	Associated medical illness in both sexes	5	7.58
5	Menstrual Disorders in females	9	27.27
6	Oligospermia and Azoospermia in males	9	27.27
7	Consanguinity in couples	3	9.09

Table 3 – Frequency of chromosomal abnormalities in study population

Chromosomal abnormality	(Male)		(Female)	
	n	%	n	%
Numerical	04	12.12	02	6.06
Structural	00	00	04	12.12
Sex reversal	00	00	02	6.06

Table 4- Karyotype of study population with Structural Chromosomal abnormalities

Sr No	Karyotype (Females)
1	45,XX,-13t(13q/14q)
2	46,X,i(Xq)
3	46,XX,15p+
4	46,XX, 15s+

Table 5- Karyotype of study population with Numerical Chromosomal abnormalities

Sr No	Karyotype (Females)	Sex of patients
1	46,XX / 45X 90% 10%	Female
2	46,XX /45X 50% 50%	Female
3	46,XY /47,XXY 40% 60%	Male
4	47,XXY	Male
5	47,XXY	Male
6	47,XXY	Male

Discussion

Infertility ranks high among the causes of deep unhappiness in marriage. The inability to procreate is thus always perceived as a denial of basic rights, san injustice and a disappointment, sometimes bordering on grief.

Age impacts on fertility; aging of the reproductive system plays an important role in it. In our present study we found that out of the 33 women referred for primary infertility 15 (45.45%) were in the age group 21-25.A paternal age greater than 40 is associated with a 20% greater chance of birth defects in the offspring [12]. The male patients referred for primary infertility was maximum in the age group 26-30 i.e 14 (42.42%).

Consanguineous marriages have an above-average risk of producing offspring homozygous for some deleterious recessive gene [13]. In the present study, 3 couples i.e 9.09% had a history of consanguinity.

Disorders of ovulation account for about 30% to 40% of all cases of female infertility[2]. Out of the 33 females studied 9 patients, (27.27%) with primary infertility showed menstrual disorders. Of these 9 patients 2 had primary amenorrhoea, and chromosome constituent of both these patients was 46, XY.

Spontaneous pregnancy losses occurring before 10 weeks of gestation may result from a number of alterations in normal progesterone production or use[2]. In our present study 4 out of 33 (12.12%) women with primary infertility had hormonal problems In males 2 out of 33 (6.06%) males with primary infertility had hormonal problems.

Any severe systemic illness such as tuberculosis, diabetes mellitus, renal and liver failure, metastatic cancer etc can lead to disruption of hypothalamic – pituitary- ovarian axis and cause infertility[2] .In present study, 5 patients i.e 7.58% had associated medical illness.

Several disorders of spermatogenesis lead to permanent and irreversible infertility. In the present study 9 male patients i.e 27.27% had oligospermia and azoospermia.

Chromosomal abnormalities

The rate of Chromosomal aberrations in the general population is less than 1%, while it is higher in patients with poor reproductive history. Worldwide, 2-7% of couples are infertile[14] .

In the present study of 33 couples, in none of the couple, both partners showed chromosomal abnormality. Chromosomal abnormalities were found in 12 couples i.e 36.36%. Out of these abnormalities 6 i.e 18.18% were numerical abnormalities. Structural abnormalities were found in 4 couples i.e 12.12%. Among the numerical abnormalities 2 were found in the females and 4 in males. Quilter et al [15], suggested that routine cytogenetic analysis of infertile male patients is required. The numerical abnormalities in present study included mosaicism in (2 females and 1 male), 4 males with Klinefelter syndrome. Duzcan et al[14] found mosaicism as a cause of infertility in 1.97% patients. Duzcan et al[14] also reported 6.15% phenotypic females with XY karyotype.Two phenotypic females with a karyotype 46, XY were found in the present study. Both these women had

been referred for primary infertility. In the present study, structural abnormalities were found in 4 couples they were 45,XX,-13t(13q/14q), 46, X,I (Xq), 46XX,15S^{+}, 46,XX,15p$^{+.}$ Female: male ratio, reason for this ratio is explained by by Kjessler et al [16] , as in males chromosomal translocations may lead to spermatogenic arrest rendering them sterile. In the present study, the female to male ratio of chromosomal abnormality is 2:1.

Conclusion

Chromosomal disorders play a significant role in primary infertility. The identification of chromosomal aberrations facilitates the genetic counselling for further management and for providing options for assisted reproductive technology and finally for adoption.

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