J Assist Reprod Genet (2009) 26:119–122
DOI 10.1007/s10815-009-9296-8

GENETICS

Cytogenetic abnormalities in 179 cases with male infertility in Western Region of Turkey: Report and review

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Received: 20 November 2008 / Accepted: 16 January 2009 / Published online: 30 January 2009

Abstract

Purpose In this study we aimed to evaluate the postnatally screened karyotype results in couples who were referred because of primary infertility between 2000 and 2006 in Izmir.

Methods The records of a total of 179 cases were evaluated retrospectively.

Results A total of 21 cases (11.74%) showed chromosomal alteration. Thirteen (7.26%) were 47,XXY; three (1.68%) were pericentric inversion of chromosome 9; one (0.56%) 46,XY/45,XO; one (0.56%) 46,XY/47,XXY/48,XXXY; one (0.56%) 46,XY,t(X;1); one (0.56%) 46,XY/46,XY,del (Y)(q11.2) and one (0.56%) 46,XX.

Conclusions The rate of gonosomal chromosomal abnormalities was nearly three times higher in our region than the rate in the literature. Chromosomal analysis is strongly suggested particularly in those who suffer fertility problems.

Keywords Male infertility · Chromosomal abnormality

Capsule The first report from west region of Turkey with a table showing a review of the literature and summarizing overall incidences.

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Introduction

Infertility is a failure to conceive after at least one year of unprotected intercourse. It affects approximately 15% of couples in reproductive age who, in attempting their first pregnancy, meet with failure [1]. In half of the couples, causes are male-related, associated with impaired spermatogenesis. Concensus is that an understanding of the fundamentals of male infertility is an important part of providing complete urologic care to male infertility cases [2]. Among the variety of reasons for male infertility, genetic factors in about of 30% of infertile males should be taken into account, including chromosome abnormalities and gene mutations.

Chromosomal abnormalities are one of the most important causes of male infertility. It could be approximated that the overall incidence of a chromosomal factor in infertile males ranges between 2% to 8%, with a mean value of 5% [3]. This value increases to about 15% in azoospermic males, largely due to cases with 47,XXY aneuploidy.

The most common type of karyotype abnormality observed in infertility is represented by Klinefelter's syndrome (KS) and also Y chromosome long arm microdeletions which is described as the most frequent non-chromosomal alteration [4].

In our study we aimed to evaluate the postnatally screened karyotype results in couples who were referred to genetics department due to primary infertility, infertility and azoospermia.

Material and methods

The study was conducted retrospectively based on the records of the patients both in the Departments of Urology and Medical Genetics. The records of a total of 179 infertile cases who were referred to Medical Genetic Department for cytogenetic analyses were evaluated between 2000 to 2006. The mean age was 35.00±6.06 and cases were between 22 and 47 years old.

Cases that underwent a detailed physical examination and hormonal tests were included into the study. Cases were classified into groups using sperm count. Azoospermia was defined as the total absence of sperm cells and oligozoospermia was defined as the sperm cell count less than 5×10^6 cells/ml in seminal liquid. Each diagnosis of oligozoospermia and azoospermia was confirmed by at least two consecutive spermiograms performed in ejaculated semen collected at least 3 days apart.

Azoospermia group involved 86 cases and oligozoospermia group involved 73 cases. The sperm counts of 20 cases were unavailable because of the retrospective nature of the study.

Cytogenetic analyses were performed from peripheral blood lymphocyte culture. In brief, the cultures of peripheral blood lymphocytes were treated with colcemid after 72-h incubation period and chromosomes were analyzed by GTG banding at approximately 400–450 band resolution. At least 50 metaphases were analyzed for each patient and up 100 metaphases were analyzed in case of mosaicism.

Results

A total of 179 cases with infertility were evaluated retrospectively. Twenty-one out of 179 (11.74%) cases showed chromosomal alteration. Three cases (1.68%) showed 46,XY,inv(9)(p11;q13) which is accepted to be a variant in the population. Thirteen (7.26%) were 47,XXY; one (0.56%) 46,XY/45,XO; one (0.56%) 46,XY/47,XXY/48,XXXY; one (0.56%) 46,XY,t(X;1); one (0.56%) 46,XY/46,XY,del(Y)(q11.2) and one (0.56%) 46,XX (Table 1).

Among azoospermic cases, 71 had normal karyotype (82.56%), 15 had abnormal karyotype (17.44%). Sixty-eight oligozoospermic cases had normal karyotype (93.15%) and 5 had abnormal karyotype (6.85%). The remaining 19 patients whose sperm count were unavailable showed normal 46,XY male karyotype; one had 46,XY,t(X;1) (Table 2).

Table 1 Chromosomal abnormalities among 179 infertile men

Karyotype	Number	%
47,XXY	13	7.26
46,XY, inv(9) (p11;q13)	3	1.68
46,XY/45,XO	1	0.56
46,XY/47,XXY/48,XXXY	1	0.56
46,XY,t(X;1)	1	0.56
46,XX	1	0.56
46,XY/46,XY,del(Y)(q11.2)	1	0.56
Total	21	11.74

Discussion

The prevalence of chromosome abnormalities is higher in infertile men and it is well-known that the sperm count is inversely related to the existence of chromosomal anomaly. Evaluation of 15 similar studies from the literature including a total of 9374 cases showed 6.54% chromosomal anomaly rate (Table 3) [5–19]. In our study 11.74% of all cases revealed chromosomal alteration including inv (9). The incidence of those abnormalities in our review ranged between 2.0% and 18.90%. Chromosomal abnormalities are more frequently observed in the population of azoo-and/or oligozoospermic males than in the general population [20]. Lissitsina et al. reported that the incidence of sex chromosome abnormalities in azoospermia group was higher than that in the oligozoospermia group [18]. In the presented study chromosomal abnormalities were detected in 17.44% of 86 azoospermic cases and 6.85% of 73 oligozoospermic cases. The most common type of karyotype abnormality in infertile cases is represented by KS, and Y chromosome long arm micro deletions represent the most frequent chromosomal structural abnormalities [4]. The incidence of KS was 7.26% in our study which is similar to the literature. KS is the most common abnormality of sexual differentiation, and occurs in approximately 1 in 500 live births. KS is a form of primary testicular failure with testicular hypotrophy and elevated gonadotropin plasma levels, and it represents the most common form of male hypogonadism [21]. Ferlin et al. reported that the prevalence of KS among infertile men is very high, up to 5% in severe oligozoospermia and 10% in azoospermia [22]. It has been always assumed that more than 90% of nonmosaic 47,XXY males are azoospermic [22]. In our study we detected that 13 cases had nonmosaic 47,XXY karyotype. Eleven of these cases had azoospermia (84.62%) and two (15.38%) had oligozoospermia. Among azoospermia and oligozoospermia groups they comprised 12.79% and 2.74% respectively.

Table 2 Chromosomal abnormalities in azoospermia and oligozoospermia cases

Sperm count	Karyotype		Number	%
	Gonosomal	Autosomal		
Azoospermia (n=86)	47,XXY		11	12.79
	46,XY/45,XO		1	1.16
	46,XY/47,XXY/48,XXXY		1	1.16
	46,XX		1	1.16
	46,XY/46,XYdel(Y)(q11.2)		1	1.16
Total			**15**	**17.44**
Oligozoospermia (n=73)	47,XXY		2	2.74
		46,XY,inv(9)(p11;q13)	3	4.11
Total			**5**	**6.85**

Pericentric inversion is one type of chromosomal rearrangement, which has been categorized as a minor chromosomal rearrangement not expected to correlate with abnormal phenotype. Most clinicians have considered inv (9) to be a benign chromosomal polymorphism [23–25]. Uehara et al. reported that infertile couples with an inv (9) carrier showed a significantly higher incidence of intrauterine fetal death, compared with infertile couples with a translocation carrier or those in which the etiology was unknown [26]. The inv (9) may often cause clinical problems in offspring of the carrier and infertility with unknown mechanisms related to sex [24]. We detected 3 cases (1.68%) that have 46,XY,inv (9)(p11;q13) karyotype. Sperm count of those three cases suggested oligozoospermia. In the presented study other chromosomal abnormalities were 46,XY/45,XO; 46,XY/47,XXY/48,XXXY;46,XX and 46,XY/46,XY,del(Y)(q11.2) which belonged to azoospermia cases. The review of the literature revelaed a mean of 3.77% autosomal and 3.68% gonosomal chromosomal anomaly rate. In our study those values were 1.68% and 10% respectively. Among gonosomal chromosomal anomalies 1.12% was structural and 2.68% was numerical whereas those values were 1.11% and 8.93% in our study. Comparison of our results with the review of the literature shows a relatively higher incidence of gonosomal, in particular, numerical gonosomal, chromosomal anomalies in our center which is similar to the literature reporting on Turkey [7, 16]. Although our results reflect a regional pattern of those referrals, combined with the previous results from Turkey, further studies focusing on this issue may be suggested to clarify this relatively higher incidence.

In conclusion the results of this study and the review of the literature showed that infertile men had a higher prevalence of chromosomal alterations, even though they did not show a phenotypical feature of a particular genetic disease. Therefore, the authors of this study strongly point out the importance of

Table 3 The review of the literature in male infertility

Author	Total	Gonosomal chromosome (n/%)		Chromosomal anomalies (n/%)		In General (n/%)
		Anomaly		*Gonosomal*	*Autosomal*	*Chromosomal anomalies*
		Structural	*Numerical*			
Mau et al. [5]	150	–	6 (4.0)	6 (4.0)	12 (8.0)	18 (12.0)
Tuerlings et al. [6]	1792	6 (0.3)	24 (1.3)	30 (1.6)	42 (2.3)	72 (4.0)
Gunduz et al.[7]	102	–	13 (12.7)	13 (12.7)	3 (2.9)	16 (15.6)
Meschede et al.[8]	432	–	2 (0.4)	2 (0.4)	7 (1.6)	9 (2.1)
Peschka et al.[9]	781	4 (0.5)	7 (0.8)	11 (1.4)	19 (2.4)	30 (3.8)
Nakamura et al.[10]	1790	19 (1.0)	80 (4.4)	99 (5.5)	126 (7.0)	225 (12.6)
Dohle et al.[11]	150	1 (0.6)	8 (5.3)	9 (6.0)	7 (4.6)	16 (10.6)
Morel et al.[12]	335	–	2 (0.5)	2 (0.5)	–	9 (2.6)
Rao et al.[13]	251	2 (0.7)	8 (3.1)	10 (3.9)	18 (7.1)	28 (11.1)
Clementini et al.[14]	2078	36 (1.7)	6 (0.2)	42 (2.0)	–	42 (2.0)
Nagvenkar et al.[15]	88	3 (3.4)	2 (2.2)	5 (5.6)	5 (5.6)	10 (11.3)
Samli et al.[16]	819	14 (1.7)	36 (4.3)	50 (6.1)	17 (2.0)	67 (8.1)
Meza-Espinoza et al.[17]	227	5 (2.0)	36 (15)	41 (18)	2 (0.8)	43 (18.9)
Lissitsina et al.[18]	90	–	5.6	5.6	7.8	13.4
Mohammed et al.[19]	289	3 (1.0)	19 (6.5)	22 (7.8)	1 (0.3)	23 (8.0)
Total	**9374**	**93/8265 (1.12)**	**249/9284 (2.68)**	**342/9284 (3.68)**	**259/6871 (3.77)**	**608/9284 (6.54)**
Our study	**179**	**2 (1.11)**	**16 (8.93)**	**18 (10.0)**	**3 (1.68)**	**21 (11.74)**

karyotyping in evaluating males who need assisted reproductive technologies for genetic counseling.

Acknowledgement We would like to thank the cytogenetics staff of the Department of Medical Genetics.

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