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Prevalence and patterns of chromosomal abnormalities among Egyptian patients with infertility: a single institution's 5-year experience

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Abstract

Background: Chromosomal abnormalities represent an important cause of human infertility. Little is known about the prevalence of chromosomal abnormalities among Egyptian couples with infertility. We estimated the cytogenetic profiles and semen analysis patterns among infertile couples. We analyzed data from medical archives of 2150 patients with infertility in Mansoura University Children's Hospital, Egypt from 2015 to 2019. The data included karyotypes and semen analysis reports.

Results: Chromosomal abnormalities were reported in 13.5% of infertile patients (290/2150); 150 out of 1290 (11.62%) males and 140 out of 860 (16.28%) females. Within the infertile males, the numerical chromosomal abnormalities were detected in 134/1290 (10.38%) males, and structural abnormalities were found in 16/1290 (1.24%) males. Within the infertile females, numerical sex chromosome abnormalities were detected in 75/860 (8.72%) females, structural sex chromosome abnormalities were found in 31/860 (3.6%) females, mosaicism of the sex chromosome was found in 22/860 (2.56%) females, and male pseudohermaphrodites were detected in 12/860 (1.39%) females.

Conclusions: Numerical chromosomal aberrations are the most frequent patterns among infertile couples. Attention should be paid to the traditional chromosomal analysis as an important diagnostic step in the infertility work-up.

Keywords: Chromosomes, Genetics, Infertile couples, Karyotype

Background

Genetic causes account for half the cases of human infertility [1]. Among genetic causes, chromosomal abnormalities are frequently described [2]. With regard to the prevalence of chromosomal abnormalities among the infertile couples, a marked variability was observed [3, 4]. The incidence of autosomal chromosomal abnormalities ranges from 1.1 to 7.2% among the infertile males [5–9], and represents 10% among the infertile females [10]. Within males, chromosomal abnormalities are reported with oligospermia and azoospermia [11–17]. Within females, chromosomal abnormalities contribute in the development of repeated abortions, primary ovarian failure, and XX gonadal dysgenesis [18].

In Arab region, several studies were conducted to describe the frequency of chromosomal abnormalities among infertile couples, but with variable results [19]. There is a trend to integrate genetics into the daily practice of the artificial reproductive techniques [20].

In the current study, we described the cytogenetic profile and semen analysis of the infertile couples referred for genetic counseling in Delta region of Egypt.

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Methods

A retrospective descriptive study was carried out from January 2015 to December 2019 in the Genetics Unit of Mansoura University Children's Hospital, Egypt. This unit provides genetic counseling for Delta region of Egypt that includes ten governorates with 41% of the total Egyptian population [21]. A total of 2150 Egyptian infertile cases {1290 (60%) males and 860 (40%) females} were investigated for chromosomal abnormalities. We retrieved data from patients' medical archives, under data manager supervision, during the working hours. The data included the age, gender, associated oligo/azoospermia, type of infertility, duration of marriage, and the cytogenetic analysis of chromosomes.

In our genetics unit, the cytogenetic analysis was performed on peripheral blood lymphocytes according to G-banding technique [22]. About 1 ml blood was mixed with 5 ml Roswell Park Memorial Institute (RPMI) growth medium for the cell culture, 1 ml fetal bovine serum and 0.1 mg/ml phytohemagglutinin. Then, the mixture was incubated at 37 °C. After 72 h, 10 µg/ml N-desacetyl-N-methylocolchicine (Colcemid™) was added, and incubated for 90 min. The cells were then harvested by a hypotonic solution (90 min with 0.075 M KCl at 37 °C), fixed and washed thrice with a fixative solution (acetic acid and methanol in a ratio of 1:3). Then, the metaphases were spread and stained using the standard G-banding technique. For each case, a cytovision system was used to analyze the metaphases.

Fluorescence in situ hybridization (FISH) technique was done for some cases according to a previously published technique [22]. About 10 µl probe was added to the target area. The cover slip was applied to the slide immediately, and sealed with a rubber cement. The slide was placed in a hot plate at 72 °C for 2 min, and then placed in an incubator at 37 °C overnight. The cover slip was removed from the slide, and immersed in 70 ml 0.4 × standard saline citrate (SSC)/0.3% NP-40 solution in a coplin jar at a warm water bath (73 ± 1°C) for 2 min. Then, the slide was immersed in 70 ml 2 × SSC/0.1% NP-40 in a coplin jar at 25 °C for 2 min. The slide was dried in the dark, and 10 µl 4, 6-diamidino-2-phenyl-indole II counter stain was added to the target area of the slide. The cover slip was applied to each slide. The slide was examined by a fluorescence microscope using a suitable filter set.

Statistical analysis

The data were analyzed using the statistical package of the social sciences version 25. Descriptive statistics were calculated and expressed as frequency and proportion.

Results

The mean age of the infertile males was 34.33 ± 3.39 years while that for the infertile females was 28.42 ± 3.13 years. Most of our studied cases had primary infertility (78%), while 22% of our patients had secondary infertility. The average duration of marriage was 57.7 ± 10.1 months. Chromosomal abnormalities were detected in 290/2150 (13.5%) infertile cases. These abnormalities were more frequent in females than males {16.28% (140/860) vs. 11.63% (150/1290)}. Numerical chromosomal abnormalities were the most frequent pattern among infertile males, being 134/1290 (10.38%) males. On the other hand, there were 16/1290 (1.24%) males with structural chromosomal abnormalities. Table 1 shows chromosomal abnormalities and semen analysis reports among the studied infertile men.

Table 2 shows chromosomal abnormalities among the studied infertile females. Numerical sex chromosome abnormalities were found in 75/860 (8.72%) females. Structural sex chromosome abnormalities were found in 31/860 (3.6%) females. Mosaicism of X chromosome was found in 22/860 (2.56%) females. Male pseudo-hermaphrodite (XY) was detected in 12/860 (1.39%) females.

Discussion

Cytogenetic analysis of chromosomes is considered an important tool in the infertility work-up [23]. The current study showed that 13.5% of infertile patients had chromosomal abnormalities. This finding agrees with Radojcić et al. [24] and Butnariu et al. [25] who reported that nearly 13% and 16% of infertile patients had chromosomal abnormalities, respectively. On the other hand, other studies reported lower prevalences of chromosomal abnormalities when compared with the current study [26–30]. In our study, the selection bias might explain this relatively high frequency of chromosomal aberrations [31]. However, differences in the sample size and ethnicity should also be considered.

Chromosomal abnormalities among infertile females and males were 16.28% and 11.63%, respectively. Our finding confirms and supports several studies about the importance of the cytogenetic analysis of chromosomes in the infertility work-up [23, 28, 29].

In the current study, Klinefelter syndrome (KS) (47, XXY) was the most common numerical chromosomal aberration among infertile men that copes with several studies [32, 33]. All classic KS cases had azoospermia similar to previously published reports [34, 35]. In our study, only seven patients (4.6%) of the infertile men had a mosaic form of KS (46, XY/47, XXY) that copes with Samplaski et al. [34] who found six mosaic cases out of 86 KS males. In our mosaic cases, two cases had

Table 1 Chromosomal abnormalities and sperm analysis reports among 150 infertile men

Chromosomal abnormalities	Karyotype	Number of patients (*n*, %)	Semen analysis
Numerical abnormalities	47,XXY	84 (56)	Azoospermia
	46,XX	11 (7.33)	Azoospermia
	47,XYY	10 (6.67)	6 Azo/4 oligospermia
	46,XY/47,XXY	7 (4.66)	5 Azo/2 oligospermia
	45,X	6 (4)	Azoospermia
	48,XXXY	5 (3.33)	Azoospermia
	47,XY+mar	5 (3.33)	Oligospermia
	48,XXYY	4 (2.67)	Azoospermia
	49,XXXXY	2 (1.33)	Azoospermia
Structural abnormalities	45,XY,t(13;14)(q10;q10)	10 (6.67)	Azoospermia
	46,XY,3q,t(3;21)(p10;q10)	2 (1.33)	Oligospermia
	46,XY,t(1;5)(q31;q11)	1 (0.67)	Oligospermia
	46,XY,t(1:15)(p31;q26)	1 (0.67)	Azoospermia
	46,XY,t(3:16)(p21;p13)	1 (0.67)	Azoospermia
	45,XYp,t(10:21)(q26:q11)	1 (0.67)	Azoospermia

Data are expressed as numbers and percentages

Table 2 Chromosomal abnormalities among 140 infertile females

Cytogenetic results	Karyotyping	Number of cases (*n*, %)
Numerical abnormalities		
Turner syndrome	45,X	70 (50)
Trisomy X	47,XXX	5 (3.57)
Structural abnormalities		
Iso-chromosome Xq	46,X,i(Xq)	10 (7.14)
Deletion Xq	46,X,Xq-	11 (7.86)
Deletion Xp	46,X,Xp-	10 (7.14)
Mosaicism of X chromosome	45,X/46,XX	10 (7.14)
	46,XX/46,X,Xp-	4 (2.86)
	46,XX/46,X,Xq-	3 (2.14)
	45,X/46,X,Xp-	5 (3.57)
Male karyotype	46,XY	12 (8.58)

Data are expressed as numbers and percentages

oligospermia denoting better phenotype than their non-mosaic counterparts that copes with several reports [34, 36, 37]. Knowing the exact cytogenetic type of KS could help in the selection of the best assisted reproductive technique. Sperms could be obtained in approximately 50% of azoospermic KS cases from focal areas of spermatogenesis in the testes using the microsurgery sperm retrieval technique [35]. Moreover, it is well-known that specific pre-implantation genetic diagnosis (PIGD) could also be performed to minimize the risk of transmitting genetic defects to offsprings [35].

In our study, we found 10/1290 (0.77%) patients with XYY syndrome (six cases with azoospermia and four cases with oligospermia). Despite most reported men with this syndrome were fertile, others reported an association with infertility [38]. There were also 11/1290 (0.85%) cases of (XX) male syndrome, and 6/1290 (0.46%) cases of (45, X) male syndrome. The mechanism explaining the male phenotype was the translocation of sex-determining region Y (*SRY)* gene on the X chromosome [6].

Sex chromosome tetrasomy and pentasomy are reported in 1:18000–1:100000 male births. The (48, XXYY, 48, XXXY and 49, XXXXY) syndromes are associated with tall stature, hypergonadotropic hypogonadism, congenital malformations, and psychological problems [39]. In the current study, 5/1290 (0.38%) cases were (48, XXXY) syndrome, 2/1290 (0.15%) cases were (49, XXXXY) syndrome, and 4/1290 (0.31%) cases were (48, XXYY) syndrome.

In the current study, 5/1290 cases (0.38%) had a marker chromosome. The presence of a marker chromosome may be associated with malformations and developmental abnormalities, although it is always found in phenotypically normal individuals [40].

In our study, there were 16/1290 (0.01%) males with structural autosomal abnormalities; ten males were 45,XY,t(13;14) (q10;q10), one male was 46,XY,t(1;5) (q31;q11), one male was 46,XY,t(1;15)(p31;q26), two males were 46,XY,3q,t(3;21)(p10;q10), one male was 46,XY,t(3;16)(p21;p13), and one case was 45,XYp,t(10;21) (q26;q11). This frequency agrees with Kayed et al. [41] and is lower than Yatsenko et al. [7]. Translocations were

observed in 16/1290 (1.24%) infertile men; six cases (0.46%) of reciprocal type and 10 cases (0.77%) of Robertsonian type. The frequency of both translocation types was 1.24% that agrees with other studies [32, 41].

Among infertile women, 70/860 (8.13%) cases were classic Turner syndrome (45, X), 10/860 (1.16 %) cases were mosaic Turner syndrome (45, X/46, XX), and 5/860 (0.58%) patients were triple X syndrome or trisomy X (47,XXX). Women with 47, XXX karyotype have an increased risk of premature ovarian failure [42]. These types of numerical chromosomal abnormalities were nearly similar to previous studies [32, 41].

Structural abnormalities of X chromosome were detected in 55/860 (6.39%) infertile females. Our frequency was higher than that reported in several studies [26, 32, 41] and lower than Kalavathi et al. [43]. Differences in results may be attributed to the variability in the sample size and ethnicity.

From the findings of the study, despite the recent advances in the field of genetics, we confirm the importance of the traditional cytogenetic study of chromosomes during the infertility work-up. Understanding the pattern of chromosomal aberrations could add much in the decision-making while planning for the assisted reproduction.

The strength of this study includes its adequately powered sample size. However, this study has some limitations; mainly inability to generalize the findings to other infertile patients outside the Delta region of Egypt. It is also a retrospective study, and we need a prospective study to examine a fixed number of couples and to investigate both male and female partners in the same couple.

Conclusions

Chromosomal abnormalities are common among Egyptian infertile patients especially women. Klinefelter and Turner syndromes were the most frequent chromosomal abnormalities among Egyptian infertile males and females in the Delta region, respectively. Increasing attention should be paid to the chromosomal analysis as an important diagnostic tool in the infertility work-up.

Abbreviations

FISH: Fluorescence in situ hybridization; KS: Klinefelter syndrome; PIGD: Preimplantation genetic diagnosis; RPMI: Roswell Park Memorial Institute; SRY: Sex-determining region Y; SSC: Standard saline citrate.

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Not applicable.

Authors' contributions

All authors contributed to the study conception and design. FE collected the clinical and laboratory data of the cases. SY shared in data collection, analysis, and shared in writing the manuscript. RAR contributed to interpretation of laboratory data. YW submitted the protocol for the Institutional Research Board, shared in data collection and analysis, interpretation of results, and drafted the article. All authors revised, approved the final manuscript, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Our study was accepted by Institutional Research Board of Mansoura University, Faculty of Medicine, Egypt (Code number: R.19.10.650), and in accordance to principles of 1964 Helsinki Declaration and its later amendment.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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