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RESEARCH ARTICLE

Chromosomal Abnormalities as a Cause of Recurrent Abortions in Iraq

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Abstract

To evaluate the incidence of chromosomal abnormalities in Iraqi couples who experience recurrent abortion and identify additional factors that may be predictive of abortion, such as parental age and unfavorable obstetric or abnormal semen analysis. The present study examined 70 couples with at least two pregnancy losses were referred to the Iraqi Center for Cancer and Medical Genetics Research. All subjects provided a detailed personal medical history and ancestral history and underwent a physical examination. Among the 70 couples tested, Chromosomal abnormalities were detected in 16 (11.42%) of 70 couples, seven males (4.99%) and nine females (6.42%). Fifteen of chromosomal abnormalities were structural and one of them was numerical. These abnormalities included four balanced reciprocal translocations, one Robertsonian translocation, one case of trisomy X-chromosome and the other cases have a different chromosomal aberration inversion, deletion and derivative. Our results showed that 11.42% of couples with recurrent abortion had chromosomal abnormalities, with no other abnormalities. Couples who experience ≥2 pregnancy losses of unknown origin should undergo a cytogenetic analysis, and findings showing a chromosomal abnormality in either parent must be followed by genetic counseling.

Keywords: *Recurrent abortion, Chromosomal abnormality, Balanced carrier.*

Introduction

Abortion is the most common complication of pregnancy and affects ~15% of all clinically recognized pregnancies [1]. Abortion is defined as the spontaneous loss of pregnancy before the fetus reaches viability, and therefore includes all pregnancy losses from the time of conception until 24 weeks of gestation [2]. Among all factors causing abortion, the only undisputed causes of recurrent pregnancy loss are genetic, anatomic, and immunologic factors [3].

Although alloimmune pathologies, inherited thrombophilias, endocrinopathies, infections, and environmental exposure have been implicated in pregnancy loss, they do not represent a major cause of recurrent abortion [3]. Most women with a history of recurrent abortion receive care from a gynecologist, who may have detected gynecological causes and excluded most serious maternal disorders [4]. At 50%-70% of miscarriages, a chromosomal abnormality is identified in the products of conception (POC).

This abnormality may derive from a balanced carrier parent or may result from a recurrent numerical abnormality, which is usually not inherited, but may cause recurrent abortion [5, 6]. Although many structural rearrangements occur de novo, the majority appears to be familial; thus, a cytogenetic analysis of the couple is important to exclude the possibility of structural rearrangements. Additionally, genetic counseling is indicated for couples who have experienced ≥2 losses.

Because most balanced rearrangement carriers produce both balanced and unbalanced gametes, a combination of normal and abnormal conceptions is frequently seen in such couples. Rearrangements are more likely to be found in couples who have experienced both miscarriages and live births rather than in those who have only experienced a miscarriage [7].

Chromosomal rearrangements may not only be lethal to the developing embryo or fetus, but may also cause significant congenital anomalies and mental retardation in an infant, if the pregnancy continues to term [8].

Materials and Methods

Subjects

Cytogenetic study was done for 70 Iraqi couples who presented with recurrent abortion at Iraqi cancer Center. Patients either visited the clinic on their own accord or were referred by an obstetrician or family practitioner for diagnosis, management, and counseling.

Methods

After excluding immunologic effects, uterine malformations and other causes of recurrent abortion, 70 couples with at least two pregnancy losses were referred to Iraqi center for cancer and medical genetics research. The mean age of the females was 29 years, while it was 36 years for the males. Chromosomes were obtained from peripheral blood cultures according to Rooney and Czepulkowski [8]. Three to five milliliter of sodium-heparinized whole blood was collected from each patient and control individual.

An amount of 0.5 cc of each patient and control individual's blood sample was added to 5 cc of a complete media containing RPMI 1640, fetal calf serum (10%), PHA (10 µg/ml), L-glutamate (2 mM), Penicillin (200 unit/ml), and Gentamycin (50 µg/ml). After 70 hours of incubation in 37°C, colcemide was added (0.2 µg/ml). After 90 min, the cells were harvested by centrifugation (150 × g for 10 min). Then, 5 ml of 0.075 M KCl solution was added and mixed and incubated at 37°C for 15 min.

After centrifugation (150 × *g* for 10 min), hypotonic supernatant was removed. Then, 5cc cold, fresh fixative solution (3:1 methanol-acetic acid) was added drop-wise to the cell pellet. Centrifugation was done afterwards, and the supernatant removed. These two latter steps were repeated until a clear pellet was obtained. Finally, cells obtained were dropped on distinct slides. Staining with Giemsa was performed for some of the slides prepared for each patient and analyzed by cytovision system. Twenty metaphases were analyzed in all cases except for mosaicism, which was analyzed up to 50 metaphases.

Results

A total of 70 Iraqi couples with a history of recurrent abortion were examined. Their ages ranged from 20 to 48 years, with a mean of 30 years. The number of recurrent abortions varied from 2 to 7 abortions/couple. In our revealed data, chromosomal abnormalities were found in (2 out of 18 subjects) =11.11% of the couples with a history of two abortions. In addition, other abnormalities were allocated in (3 out of 22 subjects) =13.63% with three abortions, and in (4 out of 30 subjects) =13.33% with four or more abortions.

Among these 70 couples, 16 (11.42%) were found to be carriers of different chromosomal abnormalities, seven males (4.99%) and nine females (6.42%). Importantly, fifteen of chromosomal abnormalities were structural and one of them was numerical. The microscopic investigation revealed four balanced reciprocal translocations; one Robertsonian translocation, one case of trisomy X-chromosome and the other cases have a different chromosomal aberration inversion, deletion and derivative Table 1.

Table 1: Cytogenetic findings, number of abortions and age in cases with abnormal karyotype

Karyotype	No. of abortions	Age
1-46, XY-12,+der (12),-21,+der(21)	3	33
2-46,XY,der(2)del (2p)	5	36
3-46,XY,inv(3) (q24-27)+q21	2	27
4-46,XY,-16+(inv16p)	4	38
5-46,XX,-8,+8delq	2	20
6-46,XX,t(3;22)(q11;p11	4	33
7-46,XY,t(7;21)(p24;q11)	5	29
8-46,XXX	3	24
9-45,XX,t(13;14)(q10;q10)	4	30
10-46,XX,t(4;6)(p24;q25)	6	26
11-46,XY,t(11;22)(q23;q13)	3	42
12-46,XX,-3,+3 invq,-6,+6 del q,-x,+x del	7	29
13-46,XY,-1,+1 del q,-3,+3 inv q,-6,+6 del q,-x,+x del q	7	34

14-46,XX,der(9;15)(p24;q25)	3	25
15-46,XX,-3,+3 del q,-9,+9 inv q	2	31
16-46,XX,-5,+5 del q	4	33

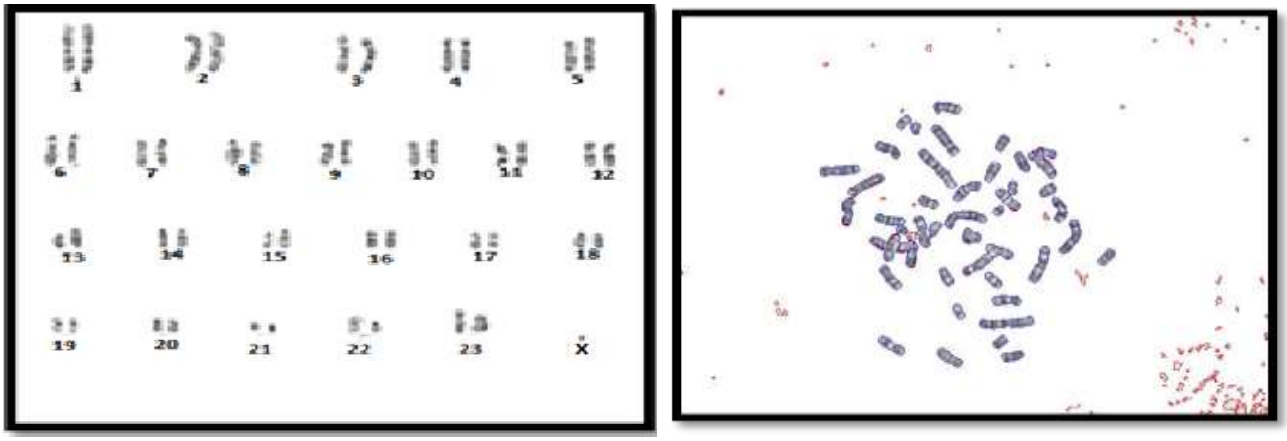

Figure 1: Karyotype of human female 46, XX,-3, +3 invq,-6, +6 del q,-x,+x del q using Giemsa staining

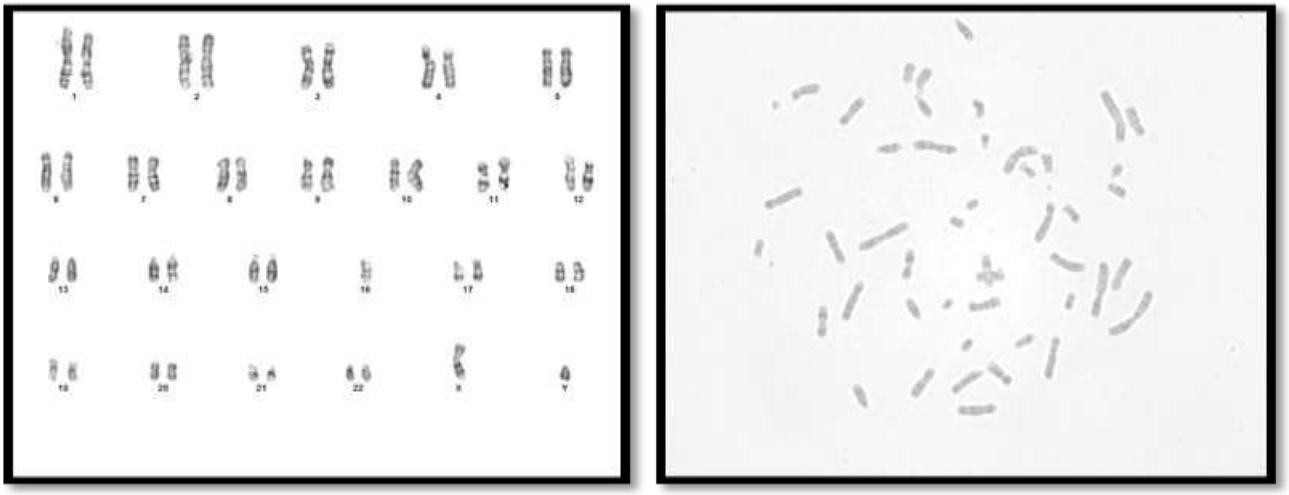

Figure 2: Karyotype of human male 46,XY,-1,+1 del q,-3,+3 inv q,-6,+6 del q,-x,+x del q using Giemsa staining

Discussion

The current study indicated that in 4% - 8% of couples with recurrent abortion in which at least one of the partners has a chromosomal abnormality. It has been noted that more spontaneous miscarriages which happened in the first and second trimesters are caused by chromosomal abnormalities.

These chromosomal abnormalities may be either numerical or structural. Frankly, the incidence of chromosomal abnormalities among the participating couples was 11.42% (5.71% of individuals) which was higher compared to the incidence reported in other studies conducted in the Middle East. For instance, in Saudi Arabia and Oman the incidence of chromosomal abnormalities in miscarriage cases was 6.7% and 5.5%, respectively [9, 10]. In addition, multiple studies have drawn a detailed survey showing worth-noted differences in the frequency of chromosomal aberrations [9, 11]. Other data from Japan and Netherland (Leiden) depicted that the range of chromosomal abnormalities incidence among abortion cases vary between 4.5% and 13.4%, respectively. Moreover, data from Italy and Netherlands (Rotterdam) have shown similar and worth-considering figures with a percentage of 9.6%.

This indicates the relativity of these data across the world which in turn underlines the importance of chromosomal abnormalities as a rather crucial cause of abortion [9, 10, 11].More importantly, the mentioned studies have given a quite different percentage of incidences as there are variations in sample size, the criteria for couples' evaluation, and techniques used in cytogenetic analysis [12].

Frankly, it is believed that the incidence of chromosomal aberrations in abortion cases may vary across different populations [10]. In our study, we found that the incidence of chromosomal abnormalities among couples with recurrent abortions was 11.42%, which is not significantly different from the global incidence. In general, the incidence of chromosomal abnormalities is higher in women than in men, which was the same in the current study [9, 12].

This is possibly because abnormalities are compatible with fertility in females and associated with sterility in males [12, 13]. Kiss *et al*. (2009) found that chromosome abnormalities exist in 5% of the couples with a history of two abortions, in 10.3% with three abortions, and in 14.3% with four or more abortions [14]. In another study conducted in Egypt by Eldahtory who indicated that (2 out of 27 subjects) = 7.4% of the couples with a history of two abortions, and (3 out of 23 subjects) = 13% with three abortions and (4 out of 23 subjects) = 17.39% with four or more abortions [15].

Comparing to the current study, chromosomal abnormalities were noticed in (2 out of 18 subjects) =11.11% of the couples with a history of two abortions, in (3 out of 22 subjects) =13.63% with three abortions, and in (4 out of 30 subjects) =13.33% with four or more abortions. The structural chromosomal abnormalities that we encountered were divided into balanced reciprocal chromosomal translocations (4 out of 16 subjects), Robertsonian translocation (1 out of 16 subjects), whereas other cases have a different chromosomal aberration; such as inversion, deletion and derivative. The distribution of structural chromosomal rearrangements in our study is similar to that reported worldwide by El-Dahtory and Boue [16, 17].

More importantly, reciprocal translocations were the most common abnormalities (4 out of 16 subjects) in our studies which have been also reported in the literature. Additionally, numerical chromosomal aberrations are less frequently encountered among couples with repeated abortions. These aberrations are usually in the form of sex chromosomal aneuploidy and they occur in a low frequency (<0.15% of cases [18]. We encountered one case with trisomy X. In conclusion, our results showed that, 11.4% of the couples with recurrent abortion had chromosomal abnormalities, with no other abnormalities.

Exposure of males to certain lifestyle, environmental and/or occupational hazards may increase the risk of aneuploid spermatozoa. In particular, a risk of aneuploidy is increased by tobacco smoking, and occupational exposure to benzene, insecticides, and perfluorinated compounds. Increased aneuploidy is often associated with increased DNA damage in spermatozoa [19]. We suggest that it is necessary to perform cytogenetic investigation for couples who have recurrent abortion. By performing other advanced techniques such as FISH and *in-situ* hybridization, chromosomal abnormalities can be detected much easier in even larger population.

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