

## Chromosomal abnormality in couple with repeated abortion

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### Abstract

**Objective:** A proportion of cases with repeated abortion are caused by chromosomal abnormality in one or both parents. Several studies have been done to determine the role of chromosomal abnormalities in couples with repeated fetal loss in various countries. The aim of this study was detection of chromosomal abnormalities in couple with repeated abortion .

**Subjects and Methods:** Cytogenetic study was done for 50 Iraqi couples who presented with repeated abortion at the Medical Center In Mosul Medical College .It was done in a private lab.Cells were studied using lymphocyte culture technique arrested at G- metaphase.

**Results:** We found that the percentage of chromosomal abnormalities was (6%). It was not significantly different from that reported worldwide. The nature of these abnormalities were : first case 46, XX,t(5;X)(q35;q23-q25), second case 46XY,add(15)(p12) and the third one 46,XY,del (16)( q21).

**Conclusion:** This study should help physicians working in the region to realize the contribution of chromosomal abnormalities as one of the causes of repeated fetal loss. It should also help in setting priorities of cytogenetic screening individual cases.

### Introduction

Pregnancy loss is defined as the unexpected and unplanned spontaneous loss of pregnancy before the fetus becomes capable of extra uterine survival<sup>1</sup>. Numerous different factors have been suggested to contribute to this. These factors can be grouped under specific classes, such as chromosomal, genetic, maternal (anatomic features and maternal diseases), endocrinological, immunological, disorders of coagulation and exogenous. Chromosomal aberrations leads to reduced fertility in both men and women<sup>2</sup>. Approximately 15%-20% of clinically recognizable pregnancies end in spontaneous abortion<sup>3</sup>. The

incidence of chromosomal abnormalities in these abortions is as high as 50%. A modest but clinically important proportion of spontaneous abortions is caused by a balanced chromosomal aberration in one of the parents<sup>4,5</sup>. This results from the production of gametes and embryos with unbalanced chromosome sets<sup>6</sup>. The clinical consequences of such abnormal gametes include sterility, repeated abortions, and giving birth to malformed children. Several studies have been done in various countries to determine the contribution of chromosome abnormalities in parents with fetal wastage<sup>7</sup>. To our knowledge, no such studies have been done in Mosul city. The aim of this study was to assess the frequency and nature of

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chromosomal aberrations that contribute to the occurrence of repeated abortions in Mosul. This should assist physicians in Mosul by increasing their awareness of the frequency of cytogenetic abnormalities in cases with repeated abortions. It also provides figures for comparison with other countries and research centers.

### Subjects and Method

This study include 50 couples (100 cases both partner) with repeated abortion who were referred for cytogenetic studies from the Medical Center In Mosul Medical College to private laboratory, between March 2009 and May 2010. All cases were ascertained to have had two or more abortions. Couples who were referred because of having previous children with congenital anomalies and abortions were not included in the study. The obstetric history of couples was either recorded on the request form or retrieved from the files of patients. Chromosomal study was done after exclusion of all causes of abortion. For routine

cytogenetic analysis, 0.3 ml of peripheral blood was incubated in complete lymphocyte culture medium (in RPMI 1640, with 0.15% phytohemagglutinin and incubator at 37°C for three days). Metaphases were harvested by adding colcemid for 20 minutes, followed by hypotonic KCl treatment and fixation, using standard 3:1 methanol-acetic acid fixative.

Microscopic examination of 15-30 cells were done after standard trypsin G-banding (GFG)8,9. Chromosomes were visually analysed using software cytovision and microscopic photography and karyotyping were done for documentation of abnormal cases.

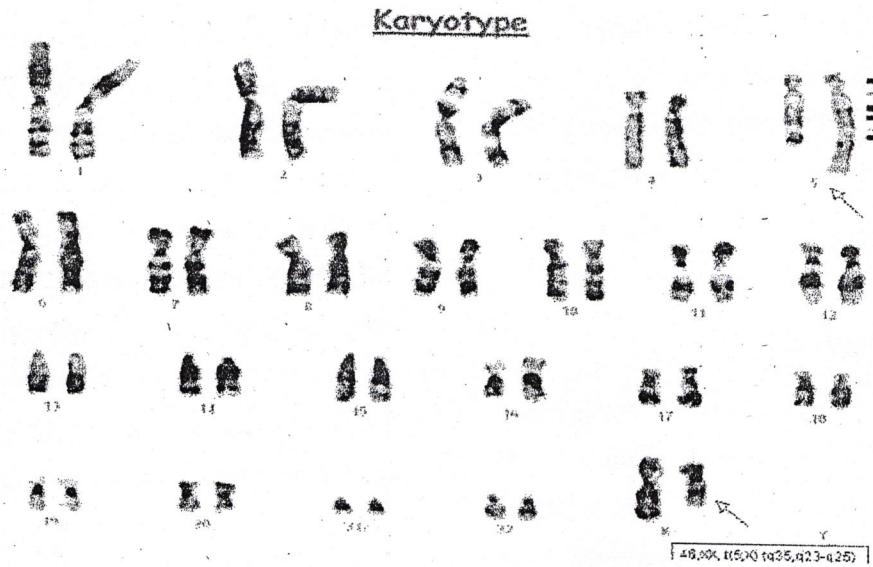
### Results

Of the 50 couples(100 cases), three cases (2 males and 1 female) showed the major chromosomal abnormalities, with an incidence of 6%. The major chromosomal abnormalities consisted of One reciprocal translocation, 2 de novo translocation such as in (table 1 & fig.1,2,3 ).

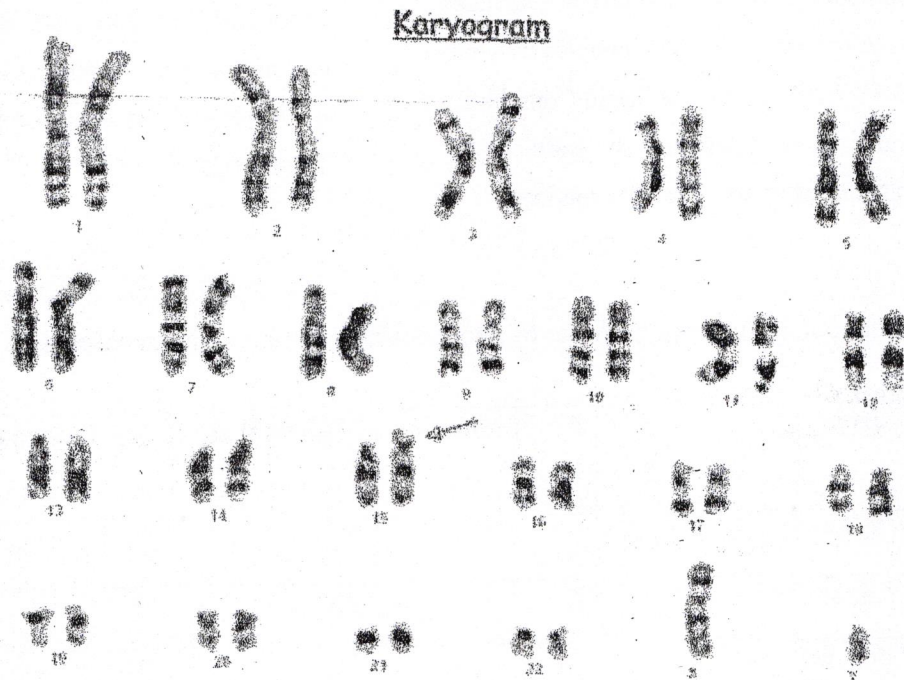
**Table( 1):** Cytogenetic findings, number of abortions and maternal age in cases with translocation.

No.	Karyotype	No.of abortion	Maternal age	Age Paternal
1	XX,t(5;X)(q35;q23-q25) 46	2	21	23
2	46XY,add(15)(p12)	6	26	35
3	46XY,del(16)(q21)	3	32	34

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Figure( 1): metaphase and karyotype showing translocation between chromosome 5 & X : 46 XX,t(5;X)(q35;q23-q25)



Figure(2):Metaphase and karyotype showing de novo translocation chromosome 46,XY,add(15)(p12):

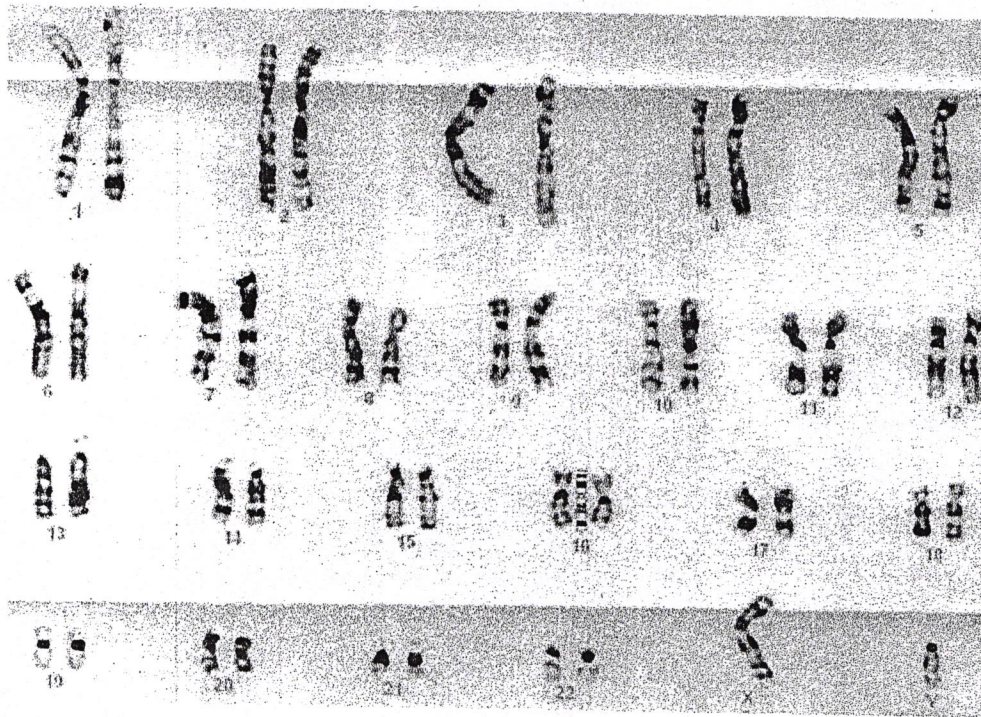


Figure (3):Metaphase and karyotype showing

46, XY, del(16)(q21)

### Discussion

In the present study, incidence of chromosomal abnormalities among studied couples with repeated abortions was 6% which is near to the prevalence among couples with repeated abortions found by Pescia et al. (5%)<sup>10</sup>, Farcas et al. (5.76%)<sup>11</sup>, Palanduz et al. (6.5%)<sup>12</sup>, Al Hussain et al. (7.7%)<sup>13</sup>, and Mohammed (7.8%)<sup>14</sup>, but lowest than that reported by Mozdarani et al.(13.92)<sup>15</sup>, Butler and Hamill (17.8%)<sup>16</sup>. Several studies have been carried out to determine the prevalence of chromosomal aberrations among couples with repeated fetal loss. In this study, we found that the incidence of chromosomal

abnormalities among couples with repeated abortions was 6% which is not significantly different from the global incidence.

We found that one woman and two men had chromosomal abnormalities, in a ratio of 2:1. A similar male to female ratio has been found in most of the reported previous studies. The structural chromosomal abnormalities that we encountered were divided into balanced chromosomal translocations (2/3), and inversions (1/3). Table below shows that the distribution of structural chromosomal rearrangements in our study is similar to that reported worldwide.

**Table.** Structural chromosome rearrangements found in couples with recurrent abortions compared to similar studies.<sup>13,15,17,18,19,20,21</sup>

	No. of couples studied	Robertsonian	Reciprocal	Inversion	Others	Number	%
Iraq(Mosul)2010	50	-	1		2	3	6
Netherlands (Leiden)2005 <sup>17</sup>	67	3	5	1	-	9	13.4
Iran(Tehran)2008 <sup>15</sup>	142	4	4	4	7	19	13.9
Netherlands (Rotterdam)2005 <sup>17</sup>	148	3	6	3	2	14	9.6
Saudi Arabia (Riyadh)2000 <sup>13</sup>	193	1	10	2	-	13	7.7
Japan2004 <sup>18</sup>	639	9	19	1	-	29	4.2
France (Strasbourg)2004 <sup>19</sup>	217	4	-	2	-	6	2.8
China(Ruijin)2001 <sup>20</sup>	61	5	1	1	-	7	11.5

This study revealed that the incidence and distribution of chromosomal abnormalities among the investigated couples with repeated fetal loss is comparable to that reported worldwide. Those cases have to be detected as early as possible to allow parents to make an informed reproductive decision regarding subsequent pregnancies. Prenatal diagnosis should be offered to these couples in the case of future pregnancies by doing cell culture from amniotic fluid.

Cytogenetic analysis should be performed in all couples with more than two spontaneous abortions as it is an important part of the investigation. In some cases combined use of classical and molecular cytogenetic is necessary for delineating the chromosome regions involved in specific rearrangements.

Chromosomal abnormalities may play an important role in fetal wastage. Approximately 15%-20% of recognized pregnancies end in a first-trimester spontaneous abortion. In general, such reproductive wastage is a random event for most women.

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#### الخلاصة

هدف البحث: دراسة التغيرات الكروموسومية للأزواج ذوي حالات الإجهاض المتكرر ، التي لها علاقة في حصول تغيرات كروموسومية في الجنين وبالتالي فقدان الجنين في المراحل الأولى من الحمل وهي تعتبر الدراسة الأولى في الموصل .

طريقة إجراء البحث: جمعت عينات دم من الأزواج. وزرعت الخلايا للمقاوية للحصول على الطور الاستوائي للخلية وبعد إن علقنت وصبغت الخلايا على سلايد درست الهيئة الكروموسومية.

النتائج: أظهرت النتائج أن نسبة التغيرات الكروموسومية في هذه الحالات كانت 6% وكانت كالاتي: انتقال كروموسومي في حالة واحدة و انتقال كروموسومي جديد في حالة اخرى و فقدان كروموسومي في حالة ثلاثة من اصل 50 زوج وهذه النتيجة لا تختلف عن دول العالم .

الاستنتاج: يجب على الأزواج ذوي حالات الاجهاض المتكرر إجراء التحليل الكروموسومي من ضمن الاسباب الاخرى لأنها تساعد في معرفة التغيرات في العوامل الوراثية وبالتالي تزودهم بالمعلومات الجينية للحمل المستقبلي.