

Original Article

## Prevalence of chromosomal aberrations in couples with recurrent miscarriages in the city of Mashhad, Iran: a cross-sectional study

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### Abstract

**Background:** Recurrent miscarriage is defined as two or more recurrent spontaneous miscarriages. Several causes have been suggested, among which, chromosomal abnormalities in couples is considered to have a role in this regard. However, its significance varies among different populations. The present study was carried out to evaluate the prevalence of chromosomal aberrations in couples with recurrent miscarriages in the city of Mashhad.

**Materials and Methods:** A retrospective study was performed on patient records at Medical Genetics Clinic of Imam Reza hospital in Mashhad (north-east of Iran) between 2003 and 2006.

**Results:** Of 151 records of recurrent miscarriages, 59 couples had undergone Karyotyping testing. Among those who had Karyotyping results, only one (1.7%) had chromosomal abnormality. The observed abnormality was associated with chromosome 9 inversion. The prevalence of consanguineous marriage among these couples was 59.0%.

**Conclusion:** In our study, unlike similar studies in other countries, the prevalence of chromosomal abnormalities was much lower. This could be interpreted either due to laboratory errors in our clinic or the real reduction in the association of chromosomal abnormalities with recurrent miscarriages in our population. Regarding our data, it seems that, at least among our population, costly Karyotyping testing is not necessary to predict further miscarriages or it could be limited to fewer cases having other associated factors.

**Keywords:** Recurrent miscarriages, Karyotyping disorders, Chromosomal abnormalities, Iran

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### Introduction

Miscarriage is a common outcome of pregnancy. If this phenomenon is repeated for a couple, it could lead to great emotional (1) and financial outcomes. Abortion is referred to termination of pregnancy, whether spontaneous or deliberate, before the period, in which, the embryo is developed enough to continue life. Generally, abortion is considered to be the termination of

pregnancy before 20 weeks or a fetal weight less than 500g. While the same phenomenon after 20 weeks is called stillbirth, in which, the causes differ from that of earlier weeks (2, 3). Spontaneous miscarriage means abortion without any mechanical or medical means in order to evacuate uterus (4). Recurrent miscarriage, in its most accepted definition, is three or more recurrent spontaneous miscarriages. However, many experts believe that the treatment should start for

couples experiencing two or more recurrent miscarriages due to the fact that the risk for further abortions is equal to the risk for the fourth pregnancy abortion (about 30%) (5, 6).

Several causes such as anatomical and structural problems of the uterus, endocrine aspects, autoimmune disorders and chromosomal aberrations have been proposed for recurrent miscarriage. Chromosomal aberrations cause production of abnormal or unbalanced spermatozoa and oogonium which in turn may lead to miscarriages. As a result, to reject this possibility, couples diagnosed with recurrent miscarriages undergo Karyotyping testing (7). On the other hand, some studies did not show any correlation between Karyotype disorders and recurrent miscarriage, and consider other factors more crucial (8, 9). In addition to lack of information on the prevalence of chromosomal aberrations in couples with recurrent miscarriages in Iran, the fact that Karyotyping testing is rather costly, highlights the significance of a study to assess the prevalence, as well as providing an evaluation of its association with family history of miscarriages, the role of age and the history of miscarriages in first-degree relatives.

The aim of this study was to evaluate the prevalence of Karyotype disorders in couples with recurrent miscarriages referred to the Genetics Clinic of Imam Reza hospital in Mashhad, Iran. The high cost of Karyotyping testing and limited access to laboratory testing in Mashhad, as well as its little effect on prognosis encouraged us to carry out this study to find factors involved in recurrent miscarriages.

## Methods

Our study was a cross-sectional descriptive study with simple non-random sampling method on medical records of individuals with recurrent miscarriages at the Genetics clinic of one Imam Reza hospital in Mashhad, North-east of Iran. All medical records available between 2003 and 2006 were retrieved and analyzed for maternal age, consanguineous marriage, Karyotyping testing, family history of miscarriages in first and second degree relatives, stillbirth and the number of alive children.

Of 2000 records available, 151 were diagnosed with recurrent miscarriage. Totally, 59 had Karyotyping testing result. Subsequently, the prevalence of chromosomal aberrations was determined. Due to low prevalence of chromosomal aberrations, we were not able to assess it on the basis of age and family history in first-degree relatives. Approval was received from the Research Ethics Committee of Mashhad University of Medical Sciences. Informed written consent was obtained from all participants.

Statistical analysis was performed with Pearson's Chi-square and the data was analyzed by SPSS (SPSS Inc., Chicago, IL, USA).

## Results

Of 151 medical records, 59 couples had Karyotyping testing results, of whom, only one (1.7%) had chromosomal aberrations. The aberration observed was inversion in chromosome 9 in a male partner.

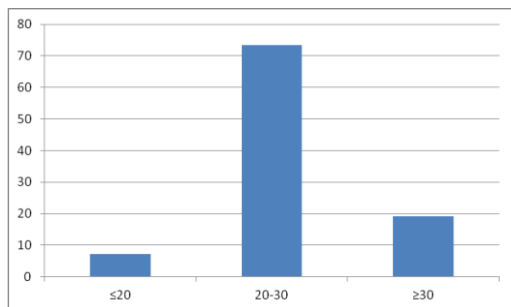
Among couples diagnosed with recurrent miscarriages, couples with two spontaneous miscarriages constitute the highest percentage (Table 1).

Regarding age, individuals were categorized into three groups; below 20, 20-30, and over 30. Cases within the age group 20-30 were accounted for the highest proportion (Figure 1).

Of 151 couples, 134 (88.7%) had moderate socioeconomic status. Totally, 90 (59%) had consanguineous marriage to their blood relatives, including 71 (47%) to their first-degree relatives and 19 (12.6%) to their second-degree relatives. To investigate family history of miscarriages, mother, sister and brother of each spouse were categorized as first-degree relatives and other distant relatives as second-degree relatives. Totally, 37.7% had family history of miscarriages, 47 (31.1%) in their first-degree relatives and 10 couples (6.6%) in their second degree relatives. Of 151 couples with recurrent miscarriages, 28 (18.5%) had a history of stillbirth and 128 (84.8%) had no alive children. A comparison was made between couples with no consanguineous marriages, first-degree consanguineous marriages and second-degree consanguineous marriages (Figure 2).

**Table 1.** Proportion of couples based on the number of miscarriages.

Number of miscarriages	Proportion of couples	Percentage
2	88	58.3
3	39	25.8
5	20	13.3
6	4	2.6

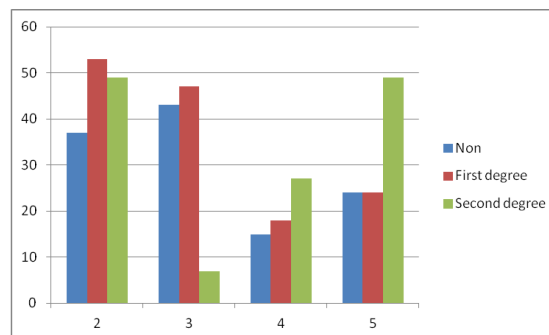


**Figure 1.** Age range of couples with recurrent miscarriages

Results for the number of miscarriages and family history in first and second degree relatives are given (Table 2).

## Discussion

Inversion of chromosome 9 was the only chromosomal aberration observed in our study. Other studies (10, 11) showed that translocations and inversions are the most prevalent chromosomal aberrations among couples with recurrent miscarriages. Chromosome 9 inversion is a structural recombination which may occur spontaneously. Some geneticists regard this as a natural variation. Its prevalence has been estimated to be between 1-1.65% in the general population and 1.52% in patients with Down syndrome (12, 13). A study by Uehara (14) concluded that chromosome 9 inversion is more prevalent in infertile couples, although other studies did not find any correlation between chromosome 9 inversion and recurrent miscarriages (15). Since we observed only one patient with chromosome 9 inversion, no conclusion could be drawn with respect to an increase or decrease of the risk. Although our results confirmed the 1-1.65% prevalence of chromosome 9 inversions, more accurate explanations requires further studies and Karyotyping testing among the total population of Mashhad. Chromosomal aberrations in couples with two or more spontaneous miscarriages have been



**Figure 2.** Association of consanguineous marriage with the number of miscarriages.

explained in several studies. In a study conducted on results from 79 similar studies, the prevalence was estimated to be 2.9% (16). However, several other ones, such as one by Braekeleer found a higher percentage (4.7%) (11). Similar studies in various countries such as Tunisia (6.93%) (10), Japan (4.91%) (13), Mexico (7.6%) (17) and Oman (3.42%) (18) displayed regional pattern of its prevalence. The current study, although conducted on a limited number of patients, showed a lower percentage. This trend may have been caused by laboratory errors in our clinics or by the real low prevalence of its association in Iranian population. Karyotyping testing as a prognosis factor in further abortions seems to be not applicable, not only observed in our study but also in other studies such as one by Carp (19). In a cohort study, Carp employed 916 patients, including 73 patients with Karyotype disorders and 588 with normal Karyotype. They were followed up and eventually 33 out of 73 patients (45.2%) and 325 out of 588 patients (55.3%) gave birth to a live child. The results were not statistically significant and showed that Karyotyping would probably not be a prognosis factor in further pregnancies (8). Four factors appeared to be the risk factors for chromosomal aberrations: high maternal age at second abortion, history of more than three recurrent miscarriages, family history of more than two miscarriages in brother or sister of each partner and history of more than two abortions in parents of each partner. As a result, Karyotyping testing can be limited to a fewer patients (9). Our data displayed a significant correlation between the number of miscarriages and consanguineous marriage which is consistent with that of Sayadi. No direct association was found between the number of miscarriages and history of miscarriages in first and second degree

**Table 2.** Number of miscarriages on the basis of family history

Number of miscarriages	Miscarriages in first-degree relatives		Miscarriages in second-degree relatives	
	Have	Do not have	Have	Do not have
2	24	64	5	83
3	12	27	4	35
4	8	12	1	19
5	3	1	0	4
	P=0.176		P=0.723	

relatives (20).

This study suffers from having limited sample size. Thus, more promising results require a huge sample size. To eliminate the probability of laboratory errors, Karyotyping is suggested to be carried out in at least two separate laboratories so that the results could be compared.

## Conclusion

Regarding our data, it seems that, at least among our population, costly Karyotyping testing is not necessary to predict further miscarriages or it could be limited to fewer cases having other associated factors. Since chromosomal aberrations does not seem to be prognosis factor for further miscarriages, use of this method does not seem to be needed among our population or it can be limited for couples who have other risk factors as well.

## Conflicts of Interest

There is no conflict of interest to declare.

## Acknowledgment

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