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Cytogenetic analysis in couples with recurrent miscarriages- a case-control study

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ABSTRACT

Introduction: Recurrent miscarriage (RM) is defined as two or more pregnancy losses before 20 weeks of gestation. It affects approximately 15-20% of the couples. Chromosomal anomaly is an important cause of recurrent pregnancy loss. The aim of the present study was to evaluate the frequency of chromosomal abnormalities in couples with RM in our region and compare with normal control.
Materials and methods: The present case control study was conducted in a total of 200 couples from January 2023 to December 2024. Among this 100 couples were considered as the patient group (cases) who suffered from RM and the control group consisted of 100 healthy couples with no history of RM. Peripheral blood T-lymphocytes were cultured using RPMI cell culture medium for obtaining metaphase spreads and chromosome analysis.
Results: Among 100 cases, six cases (6%) presented abnormal karyotype. One sex chromosomal trisomy, one Robertsonian translocation, one reciprocal translocation, one inversion, one deletion and one marker chromosome were found. The partners of these six carriers and the control group presented with normal karyotype.
Conclusion: A total of 6% cases of chromosomal abnormalities were found in couples with recurrent pregnancy loss, thus justifying the requirement of cytogenetic testing in these patients.

Keywords: Recurrent miscarriage, Robertsonian translocation, Reciprocal translocation, Inversion.

INTRODUCTION

It affects approximately 15-20% of the couples [1]. It is caused by anatomical, immunological, endocrine, infectious, nutritional, environmental and genetic factors [2]. The chromosomal anomalies can be numerical or structural. The numerical chromosomal abnormalities are caused by nondisjunction during gametogenesis. Common numerical chromosomal abnormalities are trisomy, monosomy and polyploidy [3]. Also, chromosomal rearrangement or translocation with no overall gain or loss causes recurrent pregnancy losses [4]. 3-5% of couples with one partner may have reciprocal translocation or balanced rearrangement [2]. Presence of translocation or inversion may result in spontaneous pregnancy losses as well as offspring with congenital defects [5].

Prenatal cytogenetic analysis is an effective tool for diagnosing chromosomal anomalies in couples with RM. Chromosomal deletion, duplication, inversion, reciprocal and Robertsonian transloacation all may result in RM [6]. Routine cytogenetic analysis is still not common in our country. The aim of the present study was to evaluate the frequency of chromosomal abnormalities in couples with RM in our region as no such study has been carried out earlier here.

MATERIALS AND METHODS

The present case control study was conducted in the Multidisciplinary Research Unit (MRU), Silchar Medical College, Silchar, Assam, India. Approval for the study was taken from the Institutional Ethical Committee. A total of 200 couples were taken for the study from January 2023 to December 2024. Among this 100 couples were considered as the patient

group (cases) who suffered from RM. All the selected couples had no identified causes of RM. The control group consisted of 100 healthy couples with no history of RM.

The inclusion criteria were any paient with first trimesteric RM. Patient with RM due to uterine abnormality, hormonal imbalance, antibodies to cardiolipin, lupus anticoagulant, Rh factor or any recent infection were excluded from the study. Detailed history of the patients were taken in a structured proforma and consent was taken from the couples. Conventional karyotyping was performed using 2 ml of peripheral blood collected in sodium heparin vial. Cell culture was done in RPMI cell culture medium with fetal bovine serum in CO_2 incubator at 37°C for 67.5 hours. Metaphase chromosomes were arrested by addition of colchicine followed by treatment with hypotonic KCL solution. Then fixation was done using 3:1 methanol and glaciel acetic acid solution followed by G banding with Giemsa and trypsin treatment according to standard protocol. Karyotypes were recorded using recommendations of ISCN, 2020.

Data were analysed in Microsoft excel sheet. The reports were described in number and percentage.

RESULTS

Patients were recruited randomly from a single center. All of them belonged to different ethnic background and low socioeconomic status. The consanguinity among recruited subjects (52.1%) were cousins. The ratio of male/females was approximately equal (1:1.12).

Among 100 cases, six cases (6%) presented abnormal karyotype. Among these three were female and three were male carriers; one sex chromosomal trisomy (46,XY/47,XXY), one Robertsonian translocation (45,XX,der,(14:21),(q10;q10)), one reciprocal translocation (46,XX,t(1;11)(q31;q23)), one inversion (46,XY,inv(9)(p11q12)), one deletion (46,XX,del(X_q)) and one marker chromosome (47,XY+marker) were found. The partners of these six carriers presented with normal karyotype. No chromosomal abnormality was found in the control group.

Gender	Karyotype	Age	No of miscarriages	Chromosomal abnormalities
Male	46,XY/47,XXY	41	3	Trisomy
Female	45,XX,der,(14;21),(q10;q10)	37	3	Robertsonian translocation
Female	46,XX,t(1;11)(q31;q23)	40	4	Reciprocal translocation
Male	46,XY,inv(9)(p11q12)	34	3	Inversion
Female	46,XX,del(X_q)	45	3	Deletion
Male	47,XY+marker	43	4	Marker

Table 1: Showing karyotype, age, no of miscarriages and chromosomal abnormalities.

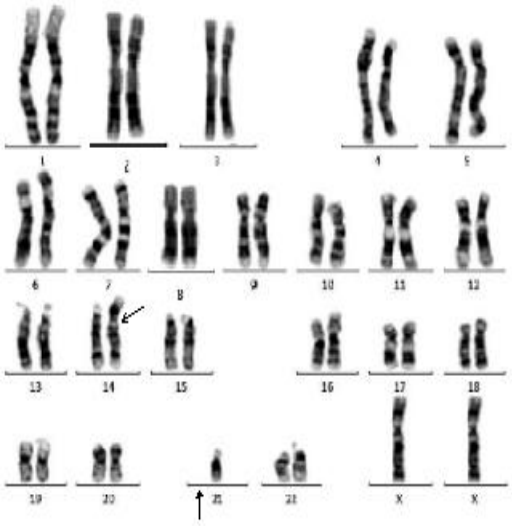

Fig 1: Karyotype of female showing Robertsonian translocation [45,XX,der,(14:21),(q10;q10)]

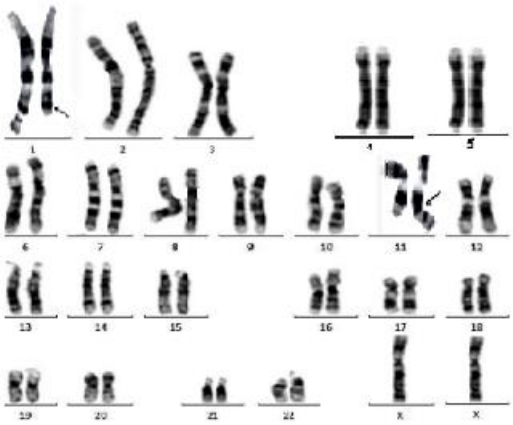

Fig 2: Karyotype of female showing Reciprocal translocation [46,XX,t(1;11)(q31;q23)]

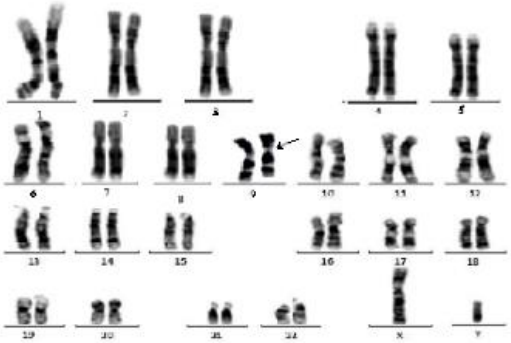

Fig 3: Karyotype of male showing inversion [46,XY,inv(9)(p11q12)]

DISCUSSION

Change in number or structure of chromosome is an well known cause of RM. The underlying mechanism behind RM is multifactorial [7]. Cytogenetic studies provide enough information about the genetic makeup causing RM [8]. The genetic etiology for multiple spontaneous miscarriages includes an unbalanced chromosomal rearrangement which may be the result of one parent being carrier for balanced reciprocal translocation (BRT) [9]. Usually one in 500 people carries a BRT. When one member of a couple carries a BRT; the risk of having a miscarriage is approximately doubled [10].

According to the literature review the prevalence of chromosomal aberrations among the couples with repeated spontaneous miscarriages varied in different studies from none [11] to as high as 21.4% [12]. These differences may be related to sample size and to different criteria. The overall chromosomal anomalies found in our study were 6%. Similar to other studies [13] translocations were the common abnormalities in our study too. In the first case, 46,XY/47,XXY mosaicism were found in the male partner. This couple had three RM. Several studies reported involvement of sex chromosome trisomy in RM [14-16].

A female carrier of Robertsonian translocation (chromosome 14;21) was reported, this couple had three RM. Many researchers suggested female carrier of Robertsonian translocation are more prone to have RM. Our study also reported Robertsonian translocation in female carrier. Involvement of Robertsonian translocation of 14;21 in RM was stated by Hasanzadeh-Nazar Abadi M et al [17].

In the present study, a female carrier of reciprocal translocation between 1;11 was reported with four miscarriages. Similar translocation have been reported by Jobanputra V et al. [18] and Correll-Tash S et al [19]. In many studies, it was stated that reciprocal translocation is one of the leading cause of RM among apparently healthy individual [14,20,21].

In the present study, one case of chromosome 9 inversion have been reported in a male partner. This couple had suffered with three miscarriages. Several studies have reported chromosome 9 inversion in RM. Carriers of chromosome 9 inversion may produce unbalanced gamete thereby giving birth to offspring with unbalanced karyotype [3,7,14,21].
In the present study, one case of X_q deletion have been reported in a female partner who had suffered with three spontaneous miacarriages. One study conducted by Dutta UR et al [22] have reported chromosome X_q deletion in RM.
Also, in the present study, one marker chromosome have been reported in a male partner. This couple had suffered with four spontaneous miacarriages. Dutta UR et al [22] and Hanif MI et al [23] have also reported marker chromosome in RM.

CONCLUSION

We observed a total of 6% cases of chromosomal abnormalities in couples with recurrent pregnancy loss. Accordingly, it is highly recommended to order cytogenetic evaluation in couples with a history of recurrent pregnancy loss in the early stages of clinical evaluation.

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