Genetics and Molecular Research

# Structural chromosomal abnormalities in couples in cases of recurrent spontaneous abortions in Jilin Province, China

**H.-T. Fan, M. Zhang, P. Zhan, X. Yang, W.-J. Tian and R.-W. Li**

Andrology Laboratory, Department of Urology,
The Second Hospital of Jilin University, Changchun, Jilin Province, China

Corresponding author: M. Zhang
E-mail: zhangming1982jdey@126.com

Genet. Mol. Res. 15 (1): gmr.15017443
Received August 13, 2015
Accepted October 23, 2015
Published January 22, 2016
DOI http://dx.doi.org/10.4238/gmr.15017443

**ABSTRACT.** Recurrent spontaneous abortions (RSAs) occur in approximately 15 to 20% of all clinically recognizable pregnancies. Structural chromosome abnormalities result in increased risk of pregnancy loss. Parental chromosomal abnormalities are an important genetic cause of RSAs. Some cytogenetic investigations have been performed in various countries and regions to determine the pattern of chromosomal abnormalities in parents with RSAs. The aim of this study was to report the prevalence and type of structural chromosomal abnormalities in couples in cases of RSAs in Jilin Province, China. The prevalence of structural chromosomal abnormalities in these couples was 2.98%. The number of female carriers with balanced chromosomal aberrations significantly exceeded that of such male carriers, and the ratio of female/male carriers was approximately 2:1. The number of abortions in the case of female carriers was more than that for male carriers before the structural chromosome abnormality was diagnosed. This indicates that genetic counseling for couples with structural chromosomal abnormalities should consider the gender of the carriers.

**Key words:** Recurrent spontaneous abortion; Reciprocal translocation; Robertsonian translocation; Pericentric inversion; Genetic counseling

 

## INTRODUCTION

Recurrent miscarriage, defined as three or more consecutive pregnancy losses before 20-22 weeks of gestation, is a common clinical problem (Gada Saxena et al., 2012). Recurrent spontaneous abortions (RSAs) occur in approximately 15-20% of all clinically recognizable pregnancies (Dutta et al., 2011; Gada Saxena et al., 2012; Turki et al., 2014; Ghazaey et al., 2015). RSA is considered a multifactorial problem, with different causes involved in its etiology, including genetic, environmental, endocrine, and infectious diseases (Gonçalves et al., 2014). Parental chromosomal abnormalities are an important genetic cause of RSAs and recurrent miscarriage (Rubio et al., 2003; Pourjafari et al., 2012). The frequency of chromosomal abnormalities among couples with RSAs varies from 2 to 8% (Sheth et al., 2013; Ghazaey et al., 2015). Balanced chromosomal rearrangements have been found at an increased frequency in couples with RSAs, compared with the general population (Makino et al., 1990; Gada Saxena et al., 2012; Sheth et al., 2013; Nonaka et al., 2015).

Cytogenetic investigations have been performed in various countries and regions to determine the pattern of chromosomal abnormalities in parents with RSAs (Makino et al., 1992; Rashidi and Mohammadi, 2006; Niroumanesh et al., 2011; Jenderny, 2014; Ghazaey et al., 2015). Reciprocal translocations, Robertsonian translocations, and pericentric inversion are all associated with RSAs. New data on these chromosomal aberrations in association with RSAs in the Chinese population of Jilin Province, China, are not definitely known. In the present study, we report the prevalence and types of structural chromosomal abnormalities in couples in cases of RSAs from Jilin Province, China.

## MATERIAL AND METHODS

### Patients

A total of 1948 couples with spontaneous abortion were diagnosed with aberrant chromosomal karyotype between January 2009 and December 2014 by chromosomal analysis, using G-banding techniques at the Andrology Laboratory, Department of Urology, Second Hospital of Jilin University. A physical examination was also conducted to determine the age, number of abortions, etc.

### Cytogenetic analysis

Peripheral blood (0.5 mL) was collected from all patients in sterile tubes containing 30 U/mL heparin; these samples were subjected to G-banding, using cultured peripheral blood lymphocytes as described previously (Zhang et al., 2015). At least 20 metaphases were analyzed per patient. Chromosomal abnormalities were described according to the International System for Human Cytogenetic Nomenclature (Shaffer et al., 2009).

### Statistical analysis

All data were analyzed using SPSS v.17.0 for Windows (SPSS, Inc., Chicago, IL, USA). Parametric variables were compared using the Student *t*-tests or the chi-square test. All results

are reported as means ± SD or number (percentage). $P < 0.05$ was considered to be statistically significant.

## RESULTS

A total of 1948 couples with a history of recurrent abortions were included in this study. Conventional cytogenetic analysis was performed, and structural chromosome abnormalities were detected in 58 cases (2.98%). Of these, 20 were male carriers (15 reciprocal translocation, 3 Robertsonian translocation, and 2 pericentric inversion) and 38 were female carriers (27 reciprocal translocation, 8 Robertsonian translocation, 3 pericentric inversion). The partners of these 58 carriers had normal karyotypes. The karyotype, age, and number of abortions in cases with the chromosomal abnormalities are shown in Table 1.

From the 42 carriers with reciprocal translocation, 15 were males (35.7%) and 27 were females (64.3%). Of the 11 carriers with Robertsonian translocation, 3 were males (27.3%) and 8 were females (72.3%). Of the 5 carriers with inversion, 2 were male (40%) and 3 were female (60%). The ratio of females/males was approximately 2:1, and there were no statistically significant differences in this ratio for reciprocal translocation, Robertsonian translocation, and pericentric inversion ($P > 0.05$), as shown in Table 2.

Table 3 shows the comparison of age and the number of abortions between male and female carriers. Although there were no statistical differences in the ages of the female and male carriers ($P > 0.05$), the number of abortions in the case of female carriers was higher than that in the case of male carriers ($P < 0.05$; Table 3).

## DISCUSSION

Recurrent pregnancy loss is a devastating reproductive problem affecting approximately 5% of women who are trying to conceive. Genetic factors appear to be highly associated with reproductive loss (Sierra and Stephenson, 2006). Parental chromosomal abnormalities are one of the main genetic causes involved in the pathogenesis of recurrent abortion (El-Dahtory, 2011; Pourjafari et al., 2012; Flynn et al., 2014). Several cytogenetic investigations revealed that the prevalence of chromosomal anomalies varies from 2 to 8% in cases of RSAs (Ghazaey et al., 2015). Although the frequency of chromosomal abnormalities in couples with RSAs varies between populations, it is found to be higher than that in the general population (0.3-0.4%) (Pal et al., 2009; Ghazaey et al., 2015).

Reciprocal translocations are one of the most frequently occurring human chromosomal aberrations and occur in about 1 of 600 individuals in the general population, whereas they occur at a frequency of about 7% in couples with recurrent miscarriages (Van Dyke et al., 1983). Balanced translocations between two chromosomes are present in approximately 5% of couples affected by RSAs (Nonaka et al., 2015). Balanced chromosomal rearrangements in either parent are an important cause of RSAs, particularly in the first trimester (Makino et al., 1990; Goud et al., 2009; Sheth et al., 2013; Alaraji, 2014). Patients carrying balanced reciprocal translocations are subject to risk of meiotic nondisjunction. Indeed, the mispairing of translocated chromosomes during the first meiotic division can give rise to different forms of segregation, resulting in aneuploidy of the translocated chromosomes (Pourjafari et al., 2012). Couples with balanced reciprocal translocation have a 50% chance of suffering

from RSAs and a 20% risk of bearing children with abnormal genetic makeup (De et al., 2015). The formation of balanced, unbalanced, and normal gametes is dependent on the breakpoints and on the chromosomes involved (De et al., 2015). In this study, the total prevalence of reciprocal translocation was found to be 27 (1.39%). Many breakpoints could be associated with RSA, as shown in Table 1.

**Table 1.** Karyotype, age, and number of abortions in cases with structural chromosomal abnormalities.

| | Karyotypes | No. of cases | Age | No. of abortions |
|---|---|---|---|---|
| Male | | | | |
| 1 | 46,XY,t(1;10)(p31.2;q26) | 1 | 38 | 4 |
| 2 | 46,XY,t(3;7)(p23;q21.2) | 1 | 26 | 3 |
| 3 | 46,XY,t(4;5)(q21;p15) | 1 | 30 | 3 |
| 4 | 46,XY,t(4;9)(q35;p13) | 1 | 27 | 2 |
| 5 | 46,XY,t(4;14)(q25;q24) | 1 | 27 | 3 |
| 6 | 46,XY,t(4;21)(q21;q12) | 1 | 34 | 3 |
| 7 | 46,XY,t(6;7)(q15;p15) | 1 | 30 | 4 |
| 8 | 46,XY,t(6;8)(p21;q24) | 1 | 34 | 4 |
| 9 | 46,XY,t(6;9)(q26;p13) | 1 | 36 | 3 |
| 10 | 46,XY,t(7;8)(q32;q22) | 1 | 28 | 3 |
| 11 | 46,XY,t(7;10)(q32;q21) | 1 | 27 | 2 |
| 12 | 46,XY,t(9;15)(p14;q22) | 1 | 32 | 2 |
| 13 | 46,XY,t(10;21)(p11;q22) | 1 | 34 | 2 |
| 14 | 46,XY,t(10;22)(q25;q13) | 1 | 29 | 3 |
| 15 | 46,XY,t(18;20)(p11;q11) | 1 | 27 | 2 |
| 16 | 45,XY,der(13;14)(q10;q10) | 2 | 29, 32 | 2, 3 |
| 17 | 45,XY,der(15;21)(q10;q10) | 1 | 33 | 2 |
| 18 | 46,XY,inv(7) (p13q36) | 1 | 26 | 3 |
| 19 | 46,XY,inv(11)(p15q12) | 1 | 24 | 2 |
| Female | | | | |
| 1 | 46,XX,t(1;13)(p36;q14) | 1 | 41 | 5 |
| 2 | 46,XX,t(2;6)(q21;q23) | 1 | 27 | 2 |
| 3 | 46,XX,t(2;6)(q21;q25) | 1 | 25 | 3 |
| 4 | 46,XX,t(2;11)(q35;q13) | 1 | 22 | 2 |
| 5 | 46,XX,t(2;16)(q31;q24) | 1 | 29 | 3 |
| 6 | 46,XX,t(3;8)(q25;p23) | 1 | 30 | 3 |
| 7 | 46,XX,t(3;9)(q21;q32) | 1 | 28 | 3 |
| 8 | 46,XX,t(4;6)(p14;p23) | 1 | 29 | 4 |
| 9 | 46,XX,t(4;20)(p16;p11.2) | 1 | 27 | 3 |
| 10 | 46,XX,t(5;6)(q13;p21) | 1 | 24 | 2 |
| 11 | 46,XX,t(5;11)(p15;q23) | 1 | 27 | 4 |
| 12 | 46,XX,t(5;13)(q13;q22) | 1 | 28 | 3 |
| 13 | 46,XX,t(5;18)(q21;q23) | 1 | 26 | 2 |
| 14 | 46,XX,t(6;12)(q16;p13) | 1 | 36 | 4 |
| 15 | 46,XX,t(6;15)(p22;q26) | 1 | 26 | 3 |
| 16 | 46,XX,t(7;10)(q22;p13) | 1 | 28 | 2 |
| 17 | 46,XX,t(8;14)(p21;q12) | 1 | 35 | 5 |
| 18 | 46,XX,t(10;13)(q26;q22) | 1 | 32 | 6 |
| 19 | 46,XX,t(10;15)(q22;q11.2) | 1 | 39 | 5 |
| 20 | 46,XX,t(11;13)(p12;p11) | 1 | 32 | 3 |
| 21 | 46,XX,t(11;22)(q25;q13) | 1 | 29 | 2 |
| 22 | 46,XX,t(12;16)(q13;p12) | 1 | 39 | 5 |
| 23 | 46,XX,t(13;20)(p11;p11) | 1 | 35 | 4 |
| 24 | 46,XX,t(15;21)(p11;q22) | 1 | 28 | 3 |
| 25 | 46,XX,t(17;18)(q21;q21) | 1 | 31 | 3 |
| 26 | 46,XX,t(17;18)(q25;q21) | 1 | 33 | 4 |
| 27 | 46,XX,t(19;22)(p13.1;q11.2) | 1 | 29 | 4 |
| 28 | 45,XX,der(13;14)(q10;q10) | 3 | 25,30,34 | 3,2,3 |
| 29 | 45,XX,der(14;21)(q10;q10) | 3 | 22,26,31 | 2,3,3 |
| 30 | 45,XX,der(14;22)(q10;q10) | 1 | 25 | 3 |
| 31 | 45,XX,der(21;21)(q10;q10) | 1 | 28 | 3 |
| 32 | 46,XX,inv(3)(q12q21) | 1 | 27 | 2 |
| 33 | 46,XX,inv(6)(p11q21) | 1 | 29 | 3 |
| 34 | 46,XX,inv(10)(p11q12) | 1 | 38 | 3 |
| Total | | 58 (2.98%) | | |

**Table 2.** Gender distribution of abnormal karyotypes.

| Gender | Rcp (%) | Rob (%) | Inv (%) | Total (%) | P |
|---|---|---|---|---|---|
| Male | 15 (35.7%) | 3 (27.3%) | 2 (40%) | 20 (34.5%) | 0.84 |
| Female | 27 (64.3%) | 8 (72.3%) | 3 (60%) | 38 (65.5%) | |
| Total | 42 | 11 | 5 | 58 | |

Rcp = reciprocal translocation, Rob = Robertsonian translocation, Inv = inversion.

**Table 3.** Comparison of age and number of abortions between male and female carriers.

| Gender | Male carriers | Female carriers | P |
|---|---|---|---|
| Age | 30.15 ± 3.80 | 29.74 ± 4.69 | 0.736 |
| No. of abortions | 2.60 ± 0.60 | 3.21 ± 1.02 | 0.017* |

Data are reported as means ± SD. Data were assessed by the Student *t*-test, as appropriate. *P < 0.05.

Robertsonian translocations are structural chromosomal aberrations resulting from the centromeric fusion of acrocentric chromosomes. Their frequency is 0.1% in the general population and 1.1% in couples with recurrent fetal loss. The Robertsonian translocation involving chromosomes 13 and 14 is the most frequent one and accounts for about 75% of all Robertsonian translocations (Keymolen et al., 2009). Eleven cases of Robertsonian translocation were found in this study.

Pericentric inversion was also associated with RSAs. In pericentric inversion, crossing over during meiotic division may result in deletion or duplication of a chromosome segment (Fauth et al., 2001). Five cases of pericentric inversion were found in this study.

Most studies have reported that in couples with recurrent pregnancy loss, the number of female carriers with balanced chromosomal aberrations significantly exceeds the male carriers (Kochhar and Ghosh, 2013). The frequency of chromosomal abnormalities was found to be higher in women with recurrent miscarriages (7.3%) than in men (2.1%) (Gonçalves et al., 2014). A proposed mechanism contributing to the higher incidence of female translocation carriers is that only one ovum matures each month, whereas male carriers release millions of sperm in every ejaculation, resulting in possible pre-zygotic selection against unbalanced gametes (Kochhar and Ghosh, 2013). In the present study, the ratio of female/male carriers was approximately 2:1, and there were no statistical differences in reciprocal translocation, Robertsonian translocation, and inversion (P > 0.05).

Yet another reason for the higher incidence of female carriers may be that some of the male carriers with structural chromosomal abnormalities may be infertile due to severe oligozoospermia or azoospermia. Chromosomal rearrangement could interrupt an important gene by position effects (Harton and Tempest, 2012). The functionality of genes at specific breakpoints may be altered, perhaps with a specific role in spermatogenesis. This may lead to defective spermatogenesis resulting in abnormalities observed upon semen analyses (Olesen et al. 2001; Ching et al., 2012). Hence, RSA does not occur in the case of such types of male carriers.

Additionally, the incidence of RSAs is 0.05-1.0% of all pregnancies. These values vary, not only with the population and the means of diagnosing the miscarriages, but also according to age and the parity of the patient: 4% at 20 years of age versus 16% after 35 years. These differences are greater if biochemical pregnancies are taken into account (Hamamah et al., 1997). In this study, there were no statistical differences in the ages of the female and male carriers. In addition, two-thirds of the balanced autosomal translocation carriers are observed in the case of couples experiencing two or more pregnancy losses (Sheth et al., 2013). In this study, the number

of abortions in the case of female carriers was higher than that in the case of male carriers ($P < 0.05$). This showed that the number of abortions in the case of female carriers was more than that in the case of male carriers before the structural chromosomal abnormality was diagnosed.

Despite the known association of parental carriers of structural chromosomal rearrangements with a history of recurrent pregnancy loss, the possibility of having a miscarriage due to an unbalanced chromosomal aberration remains unknown (Kochhar and Ghosh, 2013). Thus, the central concept in genetic counseling for such families is to estimate the probability of recurrence of unfavorable pregnancy outcomes (Pourjafari et al., 2012). Genetic counseling is important when a structural genetic factor is identified. The likelihood of a subsequent healthy live birth depends on the chromosome(s) involved and the type of rearrangement. When one of the partners has a structural genetic abnormality, preimplantation genetic diagnosis, amniocentesis, or chorionic villus sampling are recommended options to detect the genetic abnormality in the offspring (Practice Committee of the American Society for Reproductive Medicine, 2012).

In summary, the prevalence of structural chromosomal abnormalities was 2.98% in couples in cases of RSA from Jilin Province, China. The number of female carriers with balanced chromosomal aberrations significantly exceeded that in male individuals, and the ratio of female/male carriers was approximately 2:1. The number of abortions in the case of female carriers was more than that in the case of male carriers before the structural chromosomal abnormality was diagnosed. Hence, the genetic counseling process for couples with structural chromosomal abnormalities should consider the gender of the carriers.

## Conflicts of interest

The authors declare no conflict of interest.

## ACKNOWLEDGMENTS

We acknowledge and greatly appreciate the excellent technical assistance of all the staff at the Genetics Laboratory, Second Hospital of Jilin University.

## REFERENCES

Alaraji SMH (2014). Chromosomal abnormalities associated with recurrent spontaneous abortions in Iraqi women. *Med. J. Babylon* 7: 2.

Ching CB, Ko E, Hecht B, Smith M, et al. (2012). Presentation and treatment of subfertile men with balanced translocations: the cleveland clinic experience. *Curr. Urol.* 6: 37-42.http://dx.doi.org/10.1159/000338868

De P, Chakravarty S and Chakravarty A (2015). Novel balanced chromosomal translocations in females with recurrent spontaneous abortions: Two case studies. *J. Hum. Reprod. Sci.* 8: 114-117.http://dx.doi.org/10.4103/0974-1208.158623

Dutta UR, Rajitha P, Pidugu VK and Dalal AB (2011). Cytogenetic abnormalities in 1162 couples with recurrent miscarriages in southern region of India: report and review. *J. Assist. Reprod. Genet.* 28: 145-149.http://dx.doi.org/10.1007/s10815-010-9492-6

El-Dahtory FA (2011). Chromosomal abnormalities as a cause of recurrent abortions in Egypt. *Indian J. Hum. Genet.* 17: 82-84. http://dx.doi.org/10.4103/0971-6866.86186

Fauth C, Bartels I, Haaf T and Speicher MR (2001). Additional dark G-band in the p-arm of chromosome 19 due to a paracentric inversion with a breakpoint in the pericentromeric heterochromatin. *Am. J. Med. Genet.* 103: 160-162. http://dx.doi.org/10.1002/ajmg.1520

Flynn H, Yan J, Saravelos SH and Li TC (2014). Comparison of reproductive outcome, including the pattern of loss, between couples with chromosomal abnormalities and those with unexplained repeated miscarriages. *J. Obstet. Gynaecol. Res.* 40: 109-116.http://dx.doi.org/10.1111/jog.12133

Gada Saxena S, Desai K, Shewale L, Ranjan P, et al. (2012). Chromosomal aberrations in 2000 couples of Indian ethnicity with reproductive failure. *Reprod. Biomed. Online* 25: 209-218.http://dx.doi.org/10.1016/j.rbmo.2012.04.004

Ghazaey S, Keify F, Mirzaei F, Maleki M, et al. (2015). Chromosomal analysis of couples with repeated spontaneous abortions in northeastern iran. *Int. J. Fertil. Steril.* 9: 47-54.

Gonçalves RO, Santos WV, Sarno M, Cerqueira BA, et al. (2014). Chromosomal abnormalities in couples with recurrent first trimester abortions. *Rev. Bras. Ginecol. Obstet.* 36: 113-117.http://dx.doi.org/10.1590/S0100-72032014000300004

Goud TM, Mohammed Al Harassi S, Khalfan Al Salmani K, Mohammed Al Busaidy S, et al. (2009). Cytogenetic studies in couples with recurrent miscarriage in the Sultanate of Oman. *Reprod. Biomed. Online* 18: 424-429. http://dx.doi.org/10.1016/S1472-6483(10)60104-6

Hamamah S, Fignon A and Lansac J (1997). The effect of male factors in repeated spontaneous abortion: lesson from *in-vitro* fertilization and intracytoplasmic sperm injection. *Hum. Reprod. Update* 3: 393-400. http://dx.doi.org/10.1093/humupd/3.4.393

Harton GL and Tempest HG (2012). Chromosomal disorders and male infertility. *Asian J. Androl.* 14: 32-39. http://dx.doi.org/10.1038/aja.2011.66

Jenderny J (2014). Chromosome aberrations in a large series of spontaneous miscarriages in the German population and review of the literature. *Mol. Cytogenet.* 7: 38.http://dx.doi.org/10.1186/1755-8166-7-38 PubMed

Keymolen K, Staessen C, Verpoest W, Michiels A, et al. (2009). A proposal for reproductive counselling in carriers of Robertsonian translocations: 10 years of experience with preimplantation genetic diagnosis. *Hum. Reprod.* 24: 2365-2371.http://dx.doi.org/10.1093/humrep/dep201

Kochhar PK and Ghosh P (2013). Reproductive outcome of couples with recurrent miscarriage and balanced chromosomal abnormalities. *J. Obstet. Gynaecol. Res.* 39: 113-120.http://dx.doi.org/10.1111/j.1447-0756.2012.01905.x

Makino T, Tabuchi T, Nakada K, Iwasaki K, et al. (1990). Chromosomal analysis in Japanese couples with repeated spontaneous abortions. *Int. J. Fertil.* 35: 266-270.

Makino T, Hara T, Oka C, Toyoshima K, et al. (1992). Survey of 1120 Japanese women with a history of recurrent spontaneous abortions. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 44: 123-130.http://dx.doi.org/10.1016/0028-2243(92)90057-6

Niroumanesh S, Mehdipour P, Farajpour A and Darvish S (2011). A cytogenetic study of couples with repeated spontaneous abortions. *Ann. Saudi Med.* 31: 77-79.http://dx.doi.org/10.4103/0256-4947.75785

Nonaka T, Ooki I, Enomoto T and Takakuwa K (2015). Complex chromosomal rearrangements in couples affected by recurrent spontaneous abortion. *Int. J. Gynaecol. Obstet.* 128: 36-39.http://dx.doi.org/10.1016/j.ijgo.2014.07.018

Olesen C, Hansen C, Bendsen E, Byskov AG, et al. (2001). Identification of human candidate genes for male infertility by digital differential display. *Mol. Hum. Reprod.* 7: 11-20.http://dx.doi.org/10.1093/molehr/7.1.11

Pal S, Ma SO, Norhasimah M, Suhaida MA, et al. (2009). Chromosomal abnormalities and reproductive outcome in Malaysian couples with miscarriages. *Singapore Med. J.* 50: 1008-1012.

Pourjafari B, Pour-Jafari H, Farimani M, Ghahramani S, et al. (2012). Genetic counseling in carriers of reciprocal translocations involving two autosomes. *Indian J. Hum. Genet.* 18: 250-253.http://dx.doi.org/10.4103/0971-6866.100802

Practice Committee of the American Society for Reproductive Medicine (2012). Evaluation and treatment of recurrent pregnancy loss: a committee opinion. *Fertil. Steril.* 98: 1103-1111.http://dx.doi.org/10.1016/j.fertnstert.2012.06.048

Rashidi I and Mohammadi As lJ (2006). Evaluation of chromosomal changes in patients with spontaneous abortion in Khozestan province. *Iran. J. Pathol.* 1: 21-24.

Rubio C, Simón C, Vidal F, Rodrigo L, et al. (2003). Chromosomal abnormalities and embryo development in recurrent miscarriage couples. *Hum. Reprod.* 18: 182-188.http://dx.doi.org/10.1093/humrep/deg015

<bok>Shaffer LG, Slovak ML and Campbell LJ (2009). An international system for human cytogenetic nomenclature (2009). Karger, Basel, Switzerland.</bok>

Sheth FJ, Liehr T, Kumari P, Akinde R, et al. (2013). Chromosomal abnormalities in couples with repeated fetal loss: An Indian retrospective study. *Indian J. Hum. Genet.* 19: 415-422.http://dx.doi.org/10.4103/0971-6866.124369

Sierra S and Stephenson M (2006). Genetics of recurrent pregnancy loss. *Semin. Reprod. Med.* 24: 17-24. http://dx.doi.org/10.1055/s-2006-931797

Turki RF, Banni HA, Assidi M, Al-Qahtani MH, et al. (2014). Analysis of chromosomal and genetic disorders in patients with recurrent miscarriages in Saudi Arabia. *BMC Genomics* 15: 73.http://dx.doi.org/10.1186/1471-2164-15-S2-P73

Van Dyke DL, Weiss L, Roberson JR and Babu VR (1983). The frequency and mutation rate of balanced autosomal rearrangements in man estimated from prenatal genetic studies for advanced maternal age. *Am. J. Hum. Genet.* 35: 301-308.

Zhang HG, Liu XY, Hou Y, Chen S, et al. (2015). Reproductive outcome of a case with familial balanced translocation t(3;6): implications for genetic counseling. *Genet. Mol. Res.* 14: 2809-2815.http://dx.doi.org/10.4238/2015.March.31.11