Journal of **R**eproduction & **I**nfertility
Volume 27, Issue no. 1
https://doi.org/10.18502/jri.v27i1.22124

Case Report

Check for updates

Inter-chromosomal Effect in a Robertsonian Translocation (13;14) Carrier with a Child Affected by Down Syndrome: A Case Report

Sahra Sahraeean [1], Asiyeh Jebelli [2], Saeed Ghadimi Haddadan [3], Kobra Tayyari[3], Leila Emrahi [3*]

1- Dr. F. Nabipour Pathobiology Laboratory, Kerman, Iran
2- Department of Cell and Molecular Biology, Faculty of Biological Sciences, Kharazmi University, Tehran, Iran
3- Legal Medicine Research Center, Iranian Legal Medicine Organization, Tehran, Iran

** Corresponding Author:*
Leila Emrahi, Legal Medicine Research Center, Iranian Legal Medicine Organization, Tehran, Iran
E-mail:
leila.emrahi@gmail.com

Received: 10, Jan. 2026
Accepted: 16, May 2026

Abstract

Background: Although the balanced carriers of Robertsonian translocations (ROBs) typically exhibit normal phenotypes, they may experience recurrent abortions or have offspring with chromosomal disorders. A proposed mechanism is the inter-chromosomal effect (ICE), where disrupted meiotic segregation may increase aneuploid gamete production. This study presents a male case carrier of t(13;14) who had a deceased child with Down syndrome (DS) and investigates t(13;14) as a potential factor contributing to the birth of a child with DS.

Case Presentation: A couple with a history of recurrent abortions and a deceased child with DS was referred to a medical genetics laboratory. Karyotype analysis revealed that the male partner was a carrier of t(13;14) (45,XY,t(13;14)), while the female partner had a normal karyotype. The couple's subsequent pregnancy resulted in a healthy female fetus inheriting t(13;14). The deceased child had a karyotype of 47, XY, +21, consistent with DS. In this study, the role of t(13;14) and ICE as potential contributors to the birth of a child with DS was explored.

Conclusion: Prenatal screening for carriers of ROBs is strongly recommended to assess the risk of unbalanced chromosomal disorders in offspring.

Keywords: Down syndrome, Inter-chromosomal effect, Robertsonian translocation.
To cite this article: Sahraeean S, Jebelli A, Ghadimi Haddadan S, Tayyari K, Emrahi L. Inter-chromosomal Effect in a Robertsonian Translocation (13;14) Carrier with a Child Affected by Down Syndrome: A Case Report. J Reprod Infertil. 2026;27(1):75-79. https://doi.org/10.18502/jri.v27i1.22124.

Introduction

Robertsonian translocations (ROBs), first described by Robertson in 1916, are chromosomal abnormalities resulting from the fusion of two acrocentric chromosomes (1). These translocations are among the most common structural chromosomal abnormalities, with an incidence of 1.23 per 1,000 individuals. The most frequent ROB is t(13;14), accounting for 75% of balanced ROBs and occurring in 0.97 per 1,000 live births (2, 3).

While balanced ROB carriers typically exhibit normal phenotypes, reproductive challenges may arise due to the loss or gain of chromosomal material during meiosis (4). These challenges include infertility, recurrent spontaneous abortions, aneuploid gamete formation, offspring with several congenital anomalies, mental retardation, or uniparental disomy-associated abnormality (5, 6).

Previous studies reported a significant association between advanced maternal age and chromosome 21 nondisjunction in both meiosis I and meiosis II in the egg, increasing the risk of trisomy 21 or Down syndrome (DS) in infants. No such association was found in sperm or post-zygotic mitotic errors (7). However, new evidence revealed ROBs may induce an inter-chromosomal effect (ICE), which disrupts the segregation of non-rearranged chromosomes, increasing the risk of aneuploid gametes. ICE was first described by Lejeune, who reported an increased incidence of

DS in children of parents with reciprocal translocations (8, 9). Also, high disomy frequencies in sperm were reported in even low-level mosaic ROB carriers (10).

This study reports a case of a male carrier of t(13;14) whose child with DS was born to a 24-year-old mother and died at 4 months of age. The potential role of t(13;14) and ICE in the birth of a child with DS, despite the low maternal age, was explored which typically confers a lower risk.

Case Presentation

A couple with a history of a deceased DS child was referred to the Hayat medical genetics laboratory in Tabriz, Iran, in November 2023. A detailed family pedigree was constructed and revealed a history of stillbirth of unknown cause, suggesting a possible inheritance of the chromosomal rearrangement. Karyotype analysis was performed on peripheral blood lymphocytes using standard G-banding techniques at a 550-band resolution. Karyotype analysis revealed that the male partner was a carrier of a Robertsonian translocation t(13;14) (45,XY,der(13;14)(q10;q10)) (Figure 1A), while the female partner had a normal karyotype (Figure 1B). At the time of referral, the female partner was pregnant. Amniotic fluid sampling and whole-genome oligo-array analysis confirmed that the fetus was a female carrier of the paternal t(13;14). The child was born healthy and remains unaffected. Her karyogram is also provided in figure 2.

Cytogenetic analysis of the deceased child, whose karyogram was included for confirmation, revealed a karyotype of 47,XY,+21, consistent with DS in figure 1A. Given the potential role of ICE in Robertsonian translocation carriers, and the familial history of reproductive issues, this case highlights the possibility of the paternal t(13;14) contributing to meiotic non-disjunction and the subsequent birth of a child with DS.

Discussion

Previous research indicated the relationship between maternal age and nondisjunction errors (meiosis I, meiosis II, or post-zygotic). Mothers aged 40 and older have a greatly increased risk for both meiosis-I errors and meiosis-II errors compared with women under age 25, increasing the risk of trisomy 21 in offspring (11). However, in parents of younger age, especially young mothers, the occurrence of DS may be associated with other factors. Chromosome rearrangements, includ-

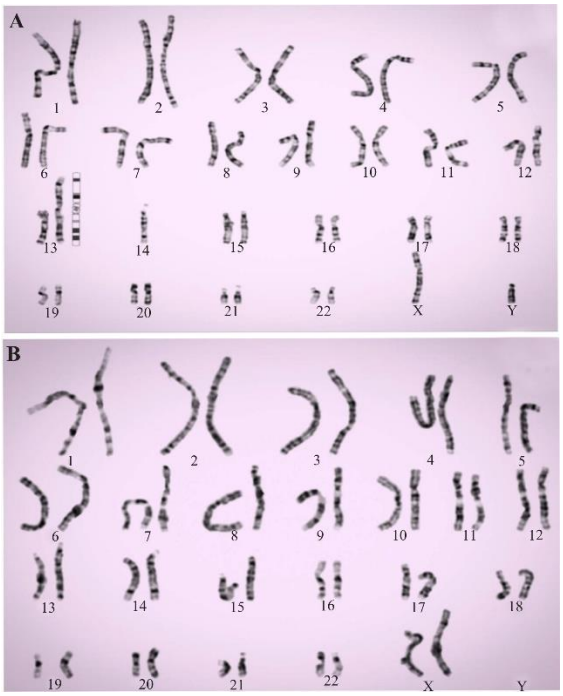

Figure 1. Parental karyograms: (A) karyogram showing the Robertsonian translocation t(13;14) in the male partner (carrier) and **(B)** normal female karyogram

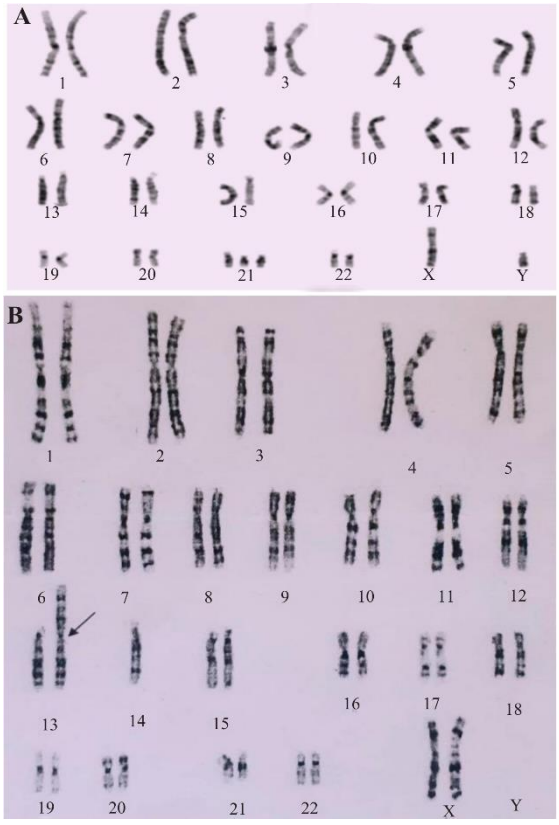

Figure 2. Fetal and sibling karyograms: (A) karyogram of the deceased sibling with trisomy 21 (Down syndrome) and (B) prenatal karyogram of the fetus with the inherited Robertsonian translocation t(13;14)

ing ROBs, are known to increase the risk of chromosomally unbalanced offspring for carrier parents (12). This may occur because such rearrangements interfere with proper chromosome alignment on the meiotic spindle or disrupt other mechanisms required for accurate chromosome segregation. However, the existence of such a phenomenon (known as ICE) is still debated (4).

ICE, a phenomenon recently investigated in translocation carriers, has been reported in male carriers based on spermatozoa analysis (13). A study of six couples with chromosomal rearrangements found that male carriers of ROBs or reciprocal translocations exhibited an increased risk of aneuploidy in sperm, particularly in cases of oligoasthenoteratozoospermia. In carriers of t(13;14), meiotic segregation analysis has reported aneuploidy in gametes, including disomy of sex chromosomes (XX, YY, XY) and autosomes (chromosomes 7, 9, 13, 18, and 21) (14). This study emphasized the need for assessing aneuploidy risk in sperm of men undergoing intracytoplasmic sperm injection (ICSI) to provide personalized risk assessments for offspring (15). Shi and Martin (2001) concluded that ICE is possible in men with ROBs or reciprocal translocations, leading to an increased risk of disomic or diploid gametes (16).

While some findings have suggested a possible association between reciprocal translocations and an ICE (17-19), other studies have reported contradictory findings (20-25). It seems that some reciprocal translocations are presumably not associated with an ICE, but it does not exclude the possibility that translocations affecting particular breakpoints/chromosomal regions could display this phenomenon. Overall, several possibilities may account for these apparent contradictions. Earlier studies used low resolution sperm-FISH or cleavage-stage FISH with a few probes, while more recent preimplantation genetic testing (PGT) studies employ array-CGH or NGS with genome-wide detection. Differences in specificity/sensitivity and the chromosomes assayed alter obvious ICE rates. Technical limitations may cause both false-negative and false-positive aneuploidy detection (26). Segregation patterns and potential ICE differ depending on the gender of carrier parent, indicating a gender effect (27).

A small sample size can overestimate an effect. Differences in cohort ascertainment, statistical power, patient age, IVF protocols, and inclusion criteria likely influence the observed outcomes (9).

Robertsonian, reciprocal or complex rearrangements behave differently. An ICE may occur with some rearrangements (or particular breakpoints) but not others. Embryos may exhibit true biological mosaicism or show apparent mosaicism from whole-genome amplification or assay-related noise. Besides, cleavage-stage biopsies versus blastocyst biopsies yield different results due to mosaicism and selection during development. Some ICE signals at cleavage stage disappear by blastocyst stage (4). The aneuploidy rate observed in gametes was similar in controls and rearrangement carriers, probably due to the well-recognized increase in meiotic error rate associated with women's age. However, the degree of ICE remained unchanged with maternal age, at a similar level across all ages (4).

Although ICE was absent from oocytes in Alfarawati et al.'s (4) research, it was obviously recognized in the cleavage stage embryos of both female and male carriers, providing strong evidence for an effect of the rearrangement during mitosis processes after fertilization. The possibility that particular translocations interfere with the segregation of structurally normal chromosomes early in mitosis may explain some of the discordant observations of interchromosomal effects described in the literature. The previous assumption was that all ICE events originate from meiosis. Mitotic recombination involving rearranged chromosomes can disrupt the normal spatial organization of chromosomes on the spindle, affecting the correct separation of chromosomes. This parallels the main hypothesis for a meiotic ICE, in which pairing between rearranged and normal homologous chromosomes alters the positioning, pairing, and segregation of other chromosomes during meiosis (4, 28).

Conclusion

The co-occurrence of ICE and ROBs underscores the importance of genetic counseling for carriers of t(13;14), particularly in familial cases. In this study, the male carrier of t(13;14), aged 27, and his partner, aged 24, lost a child with DS, while their subsequent child was a healthy carrier of t(13;14). This case highlights the potential role of ICE in the birth of a child with DS. Totally, evidence for ICE depends strongly on the chromosome(s) involved, the translocation type, the

detection method, embryo stage sampled, and cohort size/selection. High-quality, recent datasets of the PGT for structural rearrangements (PGT-SR) tend to argue against a large, general ICE across all carriers, but targeted studies still find ICE in particular subgroups or using certain assays.

Prenatal screening and PGT are recommended for carriers of ROBs to reduce the risk of unbalanced chromosomal disorders in offspring.

Acknowledgement

We sincerely thank the family members for providing the biological samples and clinical information used in this study.

Conflict of Interest

The authors declare that they have no competing interests.

References

1. Li PK, Lai FM, Lee JC, Lai KN. Glomemlonephritis associated with robertsonian translocation t (13; 14). Nephron. 1992;62(2):220-3.
2. Anton E, Blanco J, Egozcue J, Vidal F. Sperm FISH studies in seven male carriers of Robertsonian translocation t (13; 14)(q10; q10). Hum Reprod. 2004;19 (6):1345-51.
3. Malekpour N, Kormi SMA, Azadbakht M, Yousefi M, Hasanzadeh-Nazar Abadi M. The survey of double Robertsonian translocation 13q; 14q in the pedigree of 44; XX woman: a case report. Int J Mol Cell Med. 2017;6(4):243-8.
4. Alfarawati S, Fragouli E, Colls P, Wells D. Embryos of robertsonian translocation carriers exhibit a mitotic interchromosomal effect that enhances genetic instability during early development. PLoS Genet. 2012;8(10):e1003025.
5. Jaiswal S, Upadhyay A, Ali A, Upadhyay S, Kumar A, Rai A. Two familial cases of robertsonian translocations 13; 14 and its clinical consequences. J Genet Syndr Gene Ther. 2016;7(1):1-4.
6. Sahraeean S, Jebelli A, Shahbazi Z, Piryaei F. Homozygosity for robertsonian translocation (14q; 15q) in a newborn with a familial history of recurrent abortion and newborns affected by hepatosplenomegaly: a case report. J Reprod Infertil. 2023;24(4):301-5.
7. Allen EG, Freeman SB, Druschel C, Hobbs CA, O'Leary LA, Romitti PA, et al. Maternal age and risk for trisomy 21 assessed by the origin of chromosome nondisjunction: a report from the Atlanta and National Down Syndrome Projects. Hum Genet. 2009;125(1):41-52.
8. Lejeune J. Autosomal disorders. Pediatrics. 1963; 32:326-37.
9. Mateu-Brull E, Rodrigo L, Peinado V, Mercader A, Campos-Galindo I, Bronet F, et al. Interchromosomal effect in carriers of translocations and inversions assessed by preimplantation genetic testing for structural rearrangements (PGT-SR). J Assist Reprod Genet. 2019;36(12):2547-55.
10. Rogenhofer N, Dürl S, Ochsenkühn R, Neusser M, Aichinger E, Thaler C, et al. Case report: elevated sperm aneuploidy levels in an infertile Robertsonian translocation t (21; 21) carrier with possible interchromosomal effect. J Assist Reprod Genet. 2012;29(4):343-6.
11. Yoon PW, Freeman SB, Sherman SL, Taft LF, Gu Y, Pettay D, et al. Advanced maternal age and the risk of Down syndrome characterized by the meiotic stage of chromosomal error: a population-based study. Am J Hum Genet. 1996;58(3):628-33.
12. Miryounesi M, Diantpour M, Motevaseli E, Ghafouri-Fard S. Homozygosity for a Robertsonian translocation (13q; 14q) in a phenotypically normal 44, xx female with a history of recurrent abortion and a normal pregnancy outcome. J Reprod Infertil. 2016;17(3):184-7.
13. Xu S, Tang D, Fang K, Xia Y, Song J, Wang W, et al. Analysis of meiotic segregation patterns and interchromosomal effects in sperm from a Robertsonian translocation family. Biomed Res. 2014;25 (2):233-9.
14. Douet-Guilbert N, Bris MJ, Amice V, Marchetti C, Delobel B, Amice J, Braekeleer MD, Morel F. Interchromosomal effect in sperm of males with translocations: report of 6 cases and review of the literature. Int J Androl. 2005;28(6):372-9.
15. Comazzetto S, Di Giacomo M, Rasmussen KD, Much C, Azzi C, Perlas E, et al. Oligoasthenoteratozoospermia and infertility in mice deficient for miR-34b/c and miR-449 loci. PLoS Genet. 2014;10(10):e1004597.
16. Shi Q, Martin RH. Aneuploidy in human spermatozoa: FISH analysis in men with constitutional chromosomal abnormalities, and in infertile men. Reproduction. 2001;121(5):655-66.
17. Vozdova M, Oracova E, Musilova P, Kasikova K, Prinosilova P, Gaillyova R, et al. Sperm and embryo analysis of similar t (7;10) translocations transmitted in two families. Fertil Steril. 2011;96 (1):e66-70.
18. Anton E, Vidal F, Blanco J. Reciprocal translocations: tracing their meiotic behavior. Genet Med. 2008;10(10):730-8.
19. Fan J, Zhang X, Chen Y, Zhang J, Zhang L, Bi X, et al. Exploration of the interchromosomal effects

in preimplantation genetic testing for structural rearrangements based on next-generation sequencing. Mol Genet Genom Med. 2022;10(9): e2017.

20. Gianaroli L, Magli M, Ferraretti A, Munne S, Balicchia B, Escudero T, et al. Possible interchromosomal effect in embryos generated by gametes from translocation carriers. Hum Reprod. 2002;17 (12):3201-7.
21. Van Hummelen P, Manchester D, Lowe X, Wyrobek AJ. Meiotic segregation, recombination, and gamete aneuploidy assessed in at (1;10) (p22.1;q22.3) reciprocal translocation carrier by three-and four-probe multicolor FISH in sperm. Am J Hum Genet. 1997;61(3):651-9.
22. Blanco J, Egozcue J, Clusellas N, Vidal F. FISH on sperm heads allows the analysis of chromosome segregation and interchromosomal effects in carriers of structural rearrangements: results in a translocation carrier, t (5;8)(q33;q13). Cytogenet Cell Genet. 1998;83(3-4):275-80.
23. Acar H, Yildirim MS, Çora T, Ceylaner S. Evaluation of segregation patterns of 21; 21 Robertsonian translocation along with sex chromosomes and interchromosomal effects in sperm nuclei of carrier by FISH technique. Mol Reprod Dev. 2002;63(2):232-6.
24. Hatakeyama C, Gao H, Harmer K, Ma S. Meiotic segregation patterns and ICSI pregnancy outcome of a rare (13;21) Robertsonian translocation carrier: a case report. Hum Reprod. 2006;21(4):976-9.
25. Syme RM, Martin RH. Meiotic segregation of a 21;22 robertsonian translocation. Hum Reprod. 1992;7(6):825-9.
26. Anton E, Vidal F, Blanco J. Interchromosomal effect analyses by sperm FISH: incidence and distribution among reorganization carriers. Syst Biol Reprod Med. 2011;57(6):268-78.
27. Zhang S, Lei C, Wu J, Zhou J, Xiao M, Zhu S, et al. Meiotic heterogeneity of trivalent structure and interchromosomal effect in blastocysts with robertsonian translocations. Front Genet. 2021;12: 609563.
28. Guichaoua MR, Quack B, Speed RM, Noel B, Chandley AC, Luciani JM. Infertility in human males with autosomal translocations: meiotic study of a 14;22 robertsonian translocation. Hum Genet. 1990;86(2):162-6.