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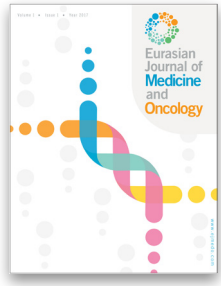

Research Article

Prevalence of Pericentric Inversion of Chromosome 9 in Eastern Anatolia Region and Relationship to Reproductive Efficiency

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Abstract

Objectives: One of the most common, structurally balanced chromosome rearrangements is the pericentric inversion of chromosome (inv[9]). It is considered to be a variant of the normal karyotype, and has been found in both normal populations and patients with various abnormal phenotypes. The aim of this study was to determine the frequency of chromosome 9 rearrangement in the Malatya Province and check whether it is correlated with certain diseases.

Methods: In this study, we investigated the karyotype analysis of 4168 patients admitted in the Turgut Özal Medical Center and Research Hospital, Genetic Disease Diagnosis Center Laboratory, between 2014 and 2016 and retrospectively reviewed their clinical data. Chromosomes from cultured peripheral blood lymphocytes were analyzed using Giemsa Trypsin-Giemsa (GTG) banding.

Results: Pericentric inversion was detected in 71 (1.7 %) of 4168 cases, including 32 (45.1%) cases with inv(9) causing infertilty, 21 (29.6%) causing growth retardation, four (5.6%) causing multiple spontaneous abortion, and 14 (19.7%) causing other abnormalities, all of which were referred to our laboratory.

Conclusion: In this study, the distribution of inv (9) in the Malatya Province was shown, and it is believed that these results would contribute to the knowledge regarding the incidence of inv (9) in the Eastern Anatolia Region and Turkey.

Keywords: Inversion 9, karyotyping, Malatya, polymorphism

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The frequency of human chromosome anomalies (numerical or structural) is reported to be 7.5% in the general population.[1] In humans, chromosomal anomaly, such as pericentric inversion, is observed in all chromosomes, except chromosome 20. In many cases, phenotypic anomaly is not observed as a result of inversions in heterochromatin areas, such as 1qh, 9qh, 16qh, and this condition is called polymorphism.[2] Pericentric inversion of chromosome 9 is considered as one of the most prevalent variations of the human karyotype.[3] Inversion of chromosome 9 is frequently found in normal individuals, and its frequency in the general population is expected to be approximately 1%–3%.[1] Since the clinical significance of inv (9) was defined in 1972, it has become a matter of debate. For instance, the last version of International System for Cytogenetic Nomenclature (ISCN) mentioned inv (9) (p12q13) as a chromosome polymorphism without clinical significance. However, several authors supported possible correlation between inv (9) and certain clinical diagnoses similar to congenital anomalies, such as schizophrenia, increased

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risk of Down syndrome in children, infertility and habitual abortus, facial dimorphism, abnormal phenotypes, and delayed developmental phases.[3, 4] Furthermore, certain studies stressed that paternal or maternal inv (9) carriers could cause unequal crossing over in meiosis and could sometimes produce inconsistent gametes.[5] Thus, whether this chromosomal anomaly, which generally is not reflected in the phenotype, is a normal variant or an abnormal karyotype remains unclear.[6] The aim of the present study was to demonstrate the distribution of inv (9) incidences in the Malatya Province. It was considered that the findings of this study would contribute in collecting inv (9) prevalence information in the Eastern Anatolian region and Turkey and in determining whether it is related to reproductive health.

Methods

In the present study, retrospective analysis of the cytogenetic scanning of 4168 cases aged 0 and 48 years and who visited Inonu University-Turgut Ozal Medical Center Research Hospital due to growth deficiency, infertility, and habitual abortus was performed. Conventional cytogenetic method was used for karyotype analysis. In this method, chromosomes cultured from peripheral blood lymphocytes were analyzed with Giemsa Trypsin-Giemsa (GTG) banding technique. Briefly, 5 ml of peripheral blood samples obtained from each patient were taken to the adequate media and cultured at 37°C for 72 h. One hour before removal, 4 µg/ml colchicine was added to the culture cartridges. Slides were prepared after hypotonic (KCl; 0.075 M) and fixative (3 methanol/1 acetic acid) applications. Cell suspensions were dropped on slides and aged in a hot plate at 90°C for 2 h, and the chromosomes were stained with G banding technique. At least 20 metaphase fields were examined in the prepared slides.

Results

In the present study, karyotypes of 4168 patients were examined and karyotype results, which included inv (9), were identified in 41 females and 30 males [n=71 (1.7%)] (Table 1). There was no correlation between the female and male patients based on inv (9). Furthermore, 45.1% (n=32) of patients with inv (9) were infertile couples who were infertile for at least 1.5 years and at most 18 years, 29.6% (n=21) were child patients with growth deficiency and short stature, 5.6% (n=4) were female patients who had at least three or more habitual abortus, and 19.7% (n=14) were patients referred to our laboratory for other reasons (obesity, gynecomastia, speech disorder). Clinical characteristics of patients diagnosed with inv (9) are summarized in Table 2. 46, XX, inv (9) (p11q13)x2 homozygote karyotype was observed in only two of 71 cases.

Table 1. Incidence of inv9 in patients

Sex	Inv(9) carriers	Frequency (%)
Female	41	0.98
Male	30	0.72
Total	71	1.7

Table 2. Karyotype and diagnoses of patients with inv(9)

Case (%)	Diagnose
32 (45.1)	Infertility
21 (29.6)	Growth retardation
4 (5.6)	Recurrent miscarriage
14 (19.7)	Other
71 (100)	Total

Discussion

Pericentric inversion of the heterochromatin region of chromosome 9-[inv (9), inv (9) (p11q13) or inv (9) (p12q13)] is the most prevalent pericentric inversion in the human karyotype. In a study conducted in prenatal cases that belonged to four major ethnic groups, it was found that inv (9) prevalence was the highest among the African American population (3.57%), whereas it was reported in 2.42% of Hispanic, 0.73% of white, and 0.26% of Asian populations. In another study conducted in the Asian population, inv (9) incidence in prenatal group was predicted as 1.2% in Singapore and 1.95% in normal and patient population in Japan as.[7] In a study conducted by Mierla and Stoian with infertile patients, inv (9)-containing karyotype was found in 2.27% of individuals in the patient group and 3.76% in the control group. Although inv (9) was accepted as a minor chromosomal inversion that is not associated with an abnormal phenotype, several studies in the literature have reported contradictory views on its correlation with sterility and subfertility.[8] In a study conducted by Yüce et al., inv (9) anomalies were identified in 41 of 2876 cases (1.42%) of which 18 were males and 23 were females.[5] In a study conducted by Elbistan et al.,[9] inv (9) was identified in 62 of 4131 cases (1.5%). It was determined that 30 of 62 inv (9) cases were males (48.4%) and 32 were females (51.6%). Lee et al.[10] investigated the correlation between inv (9) and hematological disorders and found that 1.46% of individuals in the healthy group (n=3223) had inv (9) anomaly. In the present study, inv (9) was identified in 71 of 4168 cases (1.7%), of which 57.7% were females and 42.3% were males. Furthermore, it was found that only two of the analyzed cases had homozygotic pericentric inv (9) karyotype. These cases were referred to our laboratory due to infertility. In a study conducted by Rao et al.,[1] 42 of 3392

cases had various inversions, whereas only 27 had inv (9). Based on the results of the study conducted by Sipek et al. in three different laboratories with 26597 female and male Czech patients, inv (9) was identified in 421 cases (1.6%). Gender-specific incidence demonstrated that inv (9) incidence rate was generally higher in females than in male; however, the differences were not statistically significant. [3] In certain studies, inv (9) was associated with various diseases. For instance, Boue et al. reported the effects of inv (9) on different aspects of infertility.[11] Based on the findings of a study conducted by Kumar et al. with 500 infertile couples of Indian origins, 25 couples with infertility had cytogenetic anomaly that contained inv (9). In 18 couples, females had a normal karyotype, but only the males had inv (9). On the other hand, in 7 couples, males had normal karyotypes, whereas females carried inv(9).[12] In a study by Jeong et al., inv (9) (p11q13) karyotype was identified in only 8 of 431 newborns. On the other hand, patients with inv (9)(p11q13) had various dysmorphic characteristics and/or congenital anomalies.[7] Of the 62 cases with inv (9), 43.5% were couples with habitual abortus, 6.45% were individuals with congenital anomaly, 3.22% were patients with growth deficiency and mental retardation, and 4.83% were patients with gender anomalies.[9] In a study conducted by Dana et al.[13] in the Romanian population with 900 infertile couples, inv (9) rate was found to be 3.76%, whereas the same rate was found to be 2.27% in healthy controls. However, this difference between normal and infertile populations was not statistically significant. In our study, most cases identified with inv (9) were referred to our laboratory due to infertility as the provisional diagnosis.

Conclusion

Although inv (9) is considered as a normal karyotype variance, there is limited information about its clinical results in the literature. Thus, more comprehensive studies with a wider study group and more number of cases would be beneficial.

Disclosures

Ethics Committee Approval: The study was approved by the Local Ethics Committee.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship contributions: Concept – S.Y., S.S., C.E.; Design – S.Y., S.S., C.E.; Supervision – E.Y.; Materials – S.Y., S.S., C.E., E.L.K., S.K.; Data collection &/or processing – S.Y., S.S., C.E., E.L.K., S.K.; Analysis and/or interpretation – S.Y., S.S., C.E., E.L.K., S.K.; Literature search – S.Y., C.E.; Writing – S.Y., C.E.; Critical review – S.Y., C.E.

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