INITIAL ANALYSIS OF SEVERAL CLINICAL FEATURES AND SPERM CONCENTRATION IN MEN WITH PERICENTRIC INVERSION OF CHROMOSOME 9 FINDING ASSISTED REPRODUCTIVE TREATMENTS

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Abstract

Objectives: To evaluate some clinical features and sperm concentration among men with pericentric inversion of chromosome 9, and to find assisted reproductive treatments. ***Methods:*** A retrospective, descriptive study was conducted on 36 men with pericentric inversion of chromosome 9 at the Military Institute of Clinical Embryology and Histology, Vietnam Military Medical University, from January 2020 to December 2023. Age, height, weight, and body mass index (BMI) were recorded. Semen analysis was conducted according to World Health Organization (WHO) 2021 guidelines. ***Results:*** 36 male patients with pericentric inversion of chromosome 9 were observed, of which the majority had variant 46,XY,inv(9)(p11q13) with a rate of 72.22%. Evaluation of clinical characteristics showed that height, weight, and BMI were all within the normal ranges for men. Semen analysis: 24/36 patients (66.67%) had normal sperm concentration; only 12/36 patients (33.33%) were observed to have a slight decrease in sperm concentration; no cases of severe oligozoospermia or azoospermia were recorded. A case of pericentric inversion of chromosome 9 was recorded as inherited in the family after natural reproduction. ***Conclusion:*** In men who found assisted reproductive treatments in our assisted reproductive center and were recorded pericentric inversion of chromosome 9 in the karyotype, age, height, weight, and BMI were all within the normal ranges of Vietnamese people and manifested mild oligozoospermia or normal sperm concentration.

Keywords: Pericentric inversion of chromosome 9; Oligozoospermia; Assisted reproduction.

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INTRODUCTION

Infertility is a common medical problem that affects many couples of reproductive age worldwide, in which genetic factors are important causes. Chromosomal abnormalities, especially structural variations such as inversions, have been noted to contribute to reproductive disorders. In fact, the most common inversion observed in humans is the pericentric inversion of chromosome 9, which is highly susceptible to rearrangements, especially pericentric inversions, in which the p (short) and q (long) arms of chromosome 9 are rotated 180° around the centromere. The pericentric inversions of chromosome 9: inv(9)(p11q13) and inv(9)(p12q13) are common cases, accounting for 1 - 3.57% of the general population [1].

The pericentric inversion of chromosome 9 is generally considered by cytogeneticists to be benign and does not cause serious clinical features [1]. The clinical features associated with this variant in humans vary between developmental stages, and there is no clinical feature specific to a specific developmental stage. However, some studies have shown that the chromosome 9 inversion may be associated with various conditions such as congenital anomalies, growth retardation, idiopathic reproductive failure [2], infertility [3], and recurrent miscarriage [4]. In men, in particular, this inversion may affect spermatogenesis, leading to reduced sperm concentration, motility, and morphological abnormalities. Therefore, we conducted this study: *To evaluate some clinical features and sperm concentration in men who found assisted reproductive treatments in our assisted reproductive center and recorded pericentric inversion of chromosome 9 in the karyotype.*

MATERIALS AND METHODS

1. Subjects

Including 36 men with pericentric inversion of chromosome 9 at the Military Institute of Clinical Embryology and Histology, Vietnam Military Medical University, from January 2020 to December 2023.

* *Inclusion criteria:* Men finding assisted reproductive treatments; patients had karyotype results confirming the pericentric inversion of chromosome 9 (inv(9)).

* *Exclusion criteria:* Obstruction of the vas deferens, varicocele, hypothalamic-pituitary axis disorders, history of scrotal or testicular surgery; other genetic causes of infertility; patients with acute or chronic infectious diseases affecting the reproductive system; did not agree to participate in the study.

* *Time and location:* From January 2020 to December 2023, at the Military Institute of Clinical Embryology and Histology, Vietnam Military Medical University.

2. Methods

* *Study design:* A retrospective, descriptive study.

* *Sample size:* Total sampling: All male patients with chromosome 9 inversion were examined and treated for infertility at the Military Institute of Clinical Embryology and Histology. During the study period, we collected 36 patients who met the criteria to participate in the study.

* *Research process:*

Male patients examined and treated for infertility at the Military Clinical Embryology Institute were recruited and underwent karyotype testing. Chromosomal analysis and karyotype were established using bioinformatics software. More than 20 G-banded metaphase chromosomes were detected for each patient. Chromosomal disorders were described in accordance with the International System for Human Cytogenetic Nomenclature, 2020.

Male patients with pericentric inversion of chromosome 9 were clinically examined to record personal information, including age, medical history, reproductive history, and clinical symptoms.

Semen analysis was conducted according to WHO 2021 standards to assess sperm concentration, then classified according to levels [5]:

- Normal: Sperm concentration ≥ 15 million/mL;

- Mild oligozoospermia: Sperm concentration 5 - 15 million/mL;

- Severe oligozoospermia: Sperm concentration < 5 million/mL;

- Azoospermia: No sperm in semen after three times on testing.

* *Data processing:* Data were processed and analyzed using STATA 14.0 software. Quantitative variables are described as mean ± standard deviation (SD). Qualitative variables are described as percentages (%).

3. Ethics

All procedures performed in the study involving human participants were approved by the Military Institute of Clinical Embryology and Histology. Patients voluntarily participated in this study. Patients' personal information is guaranteed confidential while conducting the study and when publishing the study and used only for scientific purposes. The Military Institute of Clinical Embryology and Histology granted permission for the use and publication of the research data. The authors declare to have no conflicts of interest in the study.

RESULTS

1. Characteristics of pericentric inversion of chromosome 9

Table 1. Results of karyotype testing (n = 36).

Karyotypes	Frequency (n)	Rate (%)
46,XY,inv(9)(p11q13)	26	72.22
46,XY,inv(9)(p11q13),Yqh+	8	22.22
46,XY,inv(9)(p11q13),Yqh-	1	2.78
46,XY,inv(9)(p12q13)	1	2.78

Of the 36 infertile male patients participating in the study, 26 patients had karyotype testing results of 46,XY,inv(9)(p11q13), accounting for the highest rate (72.22%). Other variants appeared at lower frequencies.

2. Clinical features

Table 2. Clinical features of study patients (n = 36).

Features	Mean ± SD	Min	Max
Age (years)	30.72 ± 3.06	26	40
Height (cm)	169.83 ± 5.76	160	180
Weight (kg)	68.47 ± 6.53	55	80
BMI (kg/m^2)	23.70 ± 1.43	19.49	26.17

Table 2 showed that age, height, weight, and BMI characteristics of men with pericentric inversion of chromosome 9 were all within the normal range of Vietnamese people.

3. Sperm concentration

Table 3. Sperm concentration results (n = 36).

Sperm concentration	Frequency (n)	Rate (%)
Normal	24	66.67
Mild oligozoospermia	12	33.33
Severe oligozoospermia	0	0
Azoospermia	0	0

In enrolled men with pericentric inversion of chromosome 9, a majority of patients (n = 24) manifested normal sperm concentration, accounting for 66.67%.

There were 12 cases of mild oligozoospermia, accounting for 33.33%. We did not record any cases of azoospermia or severe oligozoospermia.

4. Hereditary to offsprings

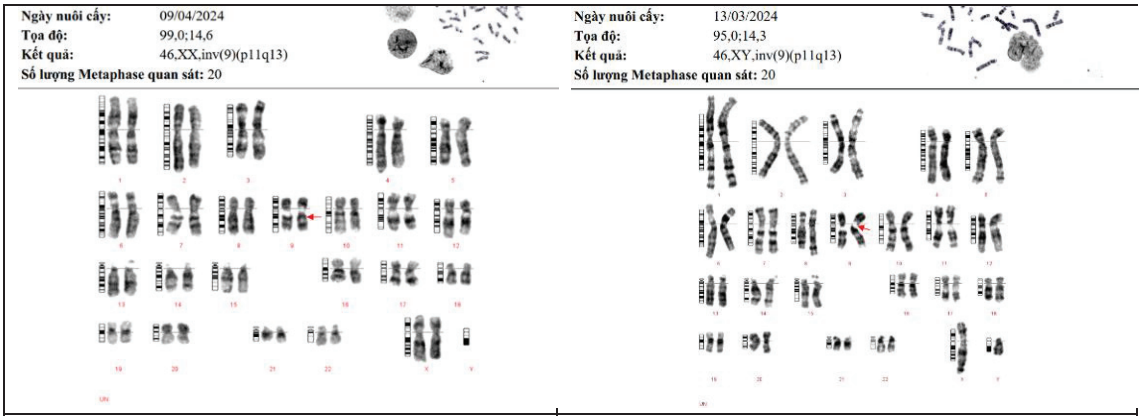

Figure 1. Karyotypes of mother (left) and son (right) both carry the pericentric inversion of chromosome 9.

The results of the karyotype test in figure 1 show that the karyotype of the mother 46,XX,inv(9)(p11q13) (left) and the son 46,XY,inv(9)(p11q13) (right) both carry the pericentric inversion of chromosome 9.

DISCUSSION

Pericentric inversion of chromosome 9 is a frequently observed chromosomal rearrangement in humans. It is relatively common, found in approximately 1 - 3.57% of the general population [1], though rates vary by ethnic group. Its high frequency suggests that it may not have significant deleterious effects on individuals carrying the inversion. Pericentric inversions occur when there are breaks in both p and q arms of a chromosome, and the fragment between the breaks is reinserted in an inverted orientation. For chromosome 9, this often involves breaks at p11 and q13, with re-ligation causing a flip in the orientation of this region. This mechanism involves balanced chromosomal rearrangement without gene loss, generally allowing carriers to have normal phenotypes and natural fertility, while there may be a slight increase in reproductive risks due to potential meiotic missegregation.

Regarding the clinical characteristics of the patients, our study results showed that some clinical characteristics were within normal limits, which is consistent with previous studies that pericentric inversion of chromosome 9 is often considered benign and does not cause

serious clinical features in most cases [1]. This benign nature is a primary reason why the inversion of chromosome 9 is often considered a chromosomal polymorphism rather than a pathogenic mutation. A study by Dana et al. (2012) on 1,800 infertile patients noted that the rate of pericentric inversion of chromosome 9 in both infertile men and women was not significantly higher than that of the normal population [6].

The reduction in sperm concentration in several patients with pericentric inversion of chromosome 9 in our study is also consistent with some previous studies. The study by Xie et al. (2020) noted that in 31 male patients with pericentric inversion of chromosome 9, there were 3 cases of oligospermia and 3 cases of azoospermia [7]. Maeda et al. (1991) pointed out that pericentric inversion of chromosome 9 can be linked to the disruption of specific genes on chromosome 9 associated with spermatogenesis during meiosis, leading to reduced sperm production or production of morphologically abnormal sperm [8]. However, all patients in our study had slightly reduced or normal sperm concentrations, suggesting that the pericentric inversion of chromosome 9 has little effect on sperm concentration. Numerous cases have demonstrated that individuals with pericentric inversion of chromosome 9 are capable of achieving natural conception, and there is a possibility that their child may inherit this inversion as well [9]. This occurs because, despite the structural rearrangement, the genetic content remains balanced, meaning that there is no significant gain or loss of critical genetic material.

The results of this study also highlight the important role of genetic testing, such as karyotype, in the diagnosis of unexplained infertility. The detection of the pericentric inversion of chromosome 9 in infertile patients without obvious clinical symptoms suggests that genetic testing could provide insights into the potential genetic causes of infertility that are not diagnosed by conventional clinical methods and, therefore, assist in family planning, including assisted reproductive technologies if necessary. Although this study has provided important information for men with pericentric inversion of chromosome 9, there are some limitations that need to be considered. First, the small sample size may limit the ability to generalize the results. Second, this is only a descriptive study, has not evaluated the relationship, and has only considered one genetic factor, which is the pericentric inversion of chromosome 9, while other factors such as environment and other genetics that may also contribute to the cause of infertility have not been fully investigated. Therefore, further research with a larger

sample size and more information is needed to clarify the relationship between the pericentric inversion of chromosome 9 and infertility.

CONCLUSION

In men who found assisted reproductive treatments in our assisted reproductive center and were recorded pericentric inversion of chromosome 9 in the karyotype, age, height, weight, and BMI were all within the normal ranges of Vietnamese people and manifested mild oligozoospermia or normal sperm concentration.

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REFERENCES

1. Kosyakova N, Grigorian A, Liehr T, et al. Heteromorphic variants of chromosome 9. *Molecular Cytogenetics*. 2013; 6:14.

2. Collodel G, Moretti E, Capitani S, et al. TEM, FISH and molecular studies in infertile men with pericentric inversion of chromosome 9. *Andrologia*. 2006; 38(4):122-127.

3. Minocherhomji S, Athalye AS, Madon PF, et al. A case-control study identifying chromosomal polymorphic variations as forms of epigenetic alterations associated with the infertility phenotype. *Fertil Steril*. 2009; 92(1):88-95.

4. Elkarhat Z, Kindil Z, Zarouf L, et al. Chromosomal abnormalities in couples with recurrent spontaneous miscarriage: A 21-year retrospective study, a report of a novel insertion, and a literature review. *Journal of Assisted Reproduction and Genetics*. 2018; 36(3):499.

5. WHO. WHO laboratory manual for the examination and processing of human semen. <https://www.who.int/publications/i/item/9789240030787>, accessed: 10/27/2024. 2021.

6. Dana M and Stoian V. Association of pericentric inversion of chromosome 9 and infertility in Romanian population. *Maedica (Bucur)*. 2012; 7(1):25-29.

7. Xie X, Li F, Tan W, et al. Analysis of the clinical features of pericentric inversion of chromosome 9. *J Int Med Res*. 2020; 48(9):300060520957820.

8. Maeda T, Ohno M, Matsunobu A, et al. A cytogenetic survey of 14,835 consecutive liveborns. *Jinrui Idengaku Zasshi*. 1991; 36(1):117-129.

9. Liu Q, Zhou WJ, Huang ZH, et al. Exploring the impact of pericentric inversion of chromosome 9 on fertility in sperm donors. *Asian J Androl*. 2024; 26(3):302-307.