Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v6i8.1973
*Biol. Clin. Sci. Res. J., Volume 6(8), **2025**: 1973*
Original Research Article

Effect of chromosome 9 polymorphism on In Vitro Fertilization (IVF) treatment outcomes

Muhammad Azhar Hayat[1*], Munazza Yasmin[1], Amra Haider[2], Kaneez Fatima[1], Menglan Wu[3], Liu Jing[4]

[1]*Alfalah General Hospital, Qadirpur Rawan, Multan, Pakistan*
[2]*Haider Hospital, Muridke, Pakistan*
[3]*Department of Reproductive Medicine, Jiaozuo Maternity and Child Health Care Hospital, China*
[4]*West China Second Affiliated Hospital, Sichuan University, China*
**Corresponding author`s email address:* azi644040@gmail.com

(Received, 24th April 2025, Accepted 8th May 2025, Published 31st August 2025)

Abstract: *Chromosomal variants such as heterochromatic polymorphisms on the long arm of chromosome 9 (9qh+) and pericentric inversions [inv(9)] are not uncommon. Although some studies suggest an increased risk of miscarriage, most carriers appear phenotypically normal, and these variants are generally regarded as benign chromosomal polymorphisms. However, their potential impact on preimplantation embryo development and in vitro fertilization–embryo transfer (IVF-ET) outcomes remains uncertain.* ***Objective:*** *To evaluate whether 9qh+ and inv(9) affect preimplantation embryo development and clinical outcomes of IVF-ET, and to determine whether effects differ between male and female carriers.* ***Methods:*** *This retrospective study included 1,435 couples who underwent IVF-ET at the First Affiliated Hospital of Hainan Medical College between January 2015 and June 2020. Chromosome G-banding was performed before IVF-ET. The inv(9) group comprised 150 couples carrying pericentric inversions, with 821 couples of normal karyotype serving as controls (ratio 1:5.47). The 9qh+ group included 82 couples with at least one carrier, with 382 couples of normal karyotype as controls. IVF-ET outcomes—including number of oocytes retrieved, fertilization rates, cleavage rate, good-quality embryo rate, embryo transfer number, pregnancy rate, implantation rate, miscarriage rate, and live birth rate—were compared between groups. Subgroup analyses were conducted to assess differences between male and female carriers of the inv(9) chromosome. Statistical significance was set at P<0.05.* ***Results:*** *No significant differences were observed between inv(9) carriers and controls, or between 9qh+ carriers and controls, in oocyte yield, fertilization rates, embryo quality, cleavage rate, pregnancy rate, implantation rate, miscarriage rate, or live birth rate (all P>0.05). However, the live birth rate was significantly lower in female inv(9) carriers compared with male carriers and controls (23% vs. 41% vs. 36%, P = 0.03). Subgroup analysis showed statistically significant differences in infertility duration (4.8 vs. 5.9 vs. 10.6 vs. 5.6 years, P=0.01) and number of embryo transfers (1.47 vs. 1.79 vs. 2.0 vs. 1.6, P=0.001) when comparing inv(9)(p12;q13), inv(9)(p11;q13), and other inv(9) subgroups with controls. No significant differences were observed between 9qh+ carriers and controls.* ***Conclusion:*** *Pericentric inversion inv(9)(p12;q13) and male inv(9)(p11;q13) heterozygosity do not affect preimplantation embryo development or IVF-ET outcomes. Female carriers of inv(9)(p11;q13) exhibit normal embryo development but experience reduced live birth rates, indicating a sex-specific impact on clinical outcomes. Carriage of 9qh+ variants does not adversely influence embryo development or IVF-ET success.*

Keywords: Chromosome inversion, Chromosome polymorphism, Fertilization in vitro, Heterochromatin, Karyotype, Pregnancy outcome

[***How to Cite:*** Hayat MA, Yasmin M, Haider A, Fatima K, Wu M, Jing L. Effect of chromosome 9 polymorphism on in vitro fertilization (IVF) treatment outcomes. *Biol. Clin. Sci. Res. J.*, **2025;** 6(8): 103-108. doi: https://doi.org/10.54112/bcsrj.v6i8.1973

Introduction

Chromosomal polymorphisms, particularly involving chromosome 9, have emerged as significant factors in reproductive health, especially in the context of in vitro fertilization (IVF) treatments. Recent studies have indicated that these chromosomal variations can potentially affect reproductive outcomes. However, evidence is mixed regarding the specific impacts, such as decreased fertilization rates, implantation failures, and recurrent pregnancy loss. Specifically, the pericentric inversion of chromosome 9 (inv(9)(p12;q13)) has been analyzed for its association with reproductive challenges, but some studies suggest it may be a benign variant (1,2).

Multiple analyses indicate that the prevalence of such chromosomal inversions may be higher among patients experiencing infertility compared to the general population, suggesting these variations could be genetic risk factors for reproductive failure (3,4,5). However, the significance of these findings can vary depending on the specific population studied and the methodologies used in different analyses (6,5). The implications of chromosomal polymorphisms extend to assisted reproductive technology (ART) procedures. For instance, Li et al. noted that patients with chromosomal variations may demonstrate altered IVF outcomes, indicating the necessity for genetic screening as part of pre-implantation genetic testing protocols (7). Additionally, a study found that individuals carrying chromosome 9 polymorphisms displayed higher rates of miscarriages and lower clinical pregnancy rates than those without such variations (8). This evidence supports the argument for enhanced genetic counseling and the integration of improved genetic screening methodologies into clinical practice (9,10).

Beyond direct implications on pregnancy outcomes, awareness of chromosome 9 polymorphisms raises considerations for personalized reproductive strategies. The presence of these chromosomal abnormalities can influence decisions regarding embryo selection in IVF settings, necessitating an understanding of the patient's genetic background (11,12). For instance, identifying inv(9) may lead to a more cautious approach in managing IVF cycles, particularly concerning embryo transfer protocols and the potential need for preimplantation genetic Diagnosis (PGD) (6,13).

In the context of Pakistan, where the prevalence of infertility is reported to be around 15% in couples of reproductive age, understanding the genetic underpinnings of reproductive health is particularly critical (1). Factors such as consanguineous marriages, which are common in Pakistan, may further raise the incidence of chromosomal aberrations, including those involving chromosome 9 (1,14). Thus, exploring the effects of chromosome 9 polymorphisms in the Pakistani population is

vital for elucidating both the genetic landscape of infertility and tailoring IVF and ART approaches to meet the unique needs of this demographic (8,15,9).

Methodology

This study employed a retrospective design and was conducted in accordance with the principles of ethical research for retrospective analyses. The study population included patients who underwent in vitro fertilization–embryo transfer (IVF-ET) at the First Affiliated Hospital of Hainan Medical College between January 2015 and June 2020. During this period, a total of 6,049 cycles of IVF or intracytoplasmic sperm injection (ICSI) with oocyte retrieval were performed. Cases involving donor oocytes or donor sperm were excluded to eliminate confounding genetic influences. Only patients with complete clinical histories, laboratory results, embryological data, and pregnancy follow-up information were included in the analysis.

A total of 149 couples were identified in which one partner carried an interarm inversion of chromosome 9, and in one couple, both partners carried the inversion. Additionally, 82 couples were found to have one partner carrying an elongated heterochromatic region of the long arm of chromosome 9 (9qh+). For each case, controls were selected from patients undergoing IVF-ET with oocyte retrieval on the same day and confirmed to have a standard chromosomal G-banding analysis. This matching minimized the influence of daily laboratory or clinical variations. Couples were then grouped based on the polymorphic structure of chromosome 9 for further comparison. Cases with both partners carrying inv(9) and cases with rare structural subtypes, represented by small numbers, were excluded from subsequent outcome analyses due to insufficient sample size.

Peripheral blood samples were collected for chromosomal analysis. Lymphocyte cultures were prepared in RPMI-1640 medium supplemented with 10% fetal bovine serum, incubated at 37°C in a 5% CO_2 environment for 68–72 hours, and treated with colchicine before harvesting. After hypotonic treatment and fixation, slides were prepared and stained using Giemsa solution. Chromosomes were analyzed according to the International System for Human Cytogenetic Nomenclature (ISCN) standards, and at least 20 metaphases were evaluated per individual to confirm the karyotype.

Controlled ovarian stimulation was performed using standardized protocols tailored to ovarian reserve and response. Gonadotropins (150–300 IU daily) were administered from cycle day 3 to 5, following pituitary downregulation. Follicular growth was monitored by transvaginal ultrasound and serum hormone levels. Human chorionic gonadotropin (hCG, 5,000–10,000 IU) was administered once at least one follicle reached a diameter of ≥18 mm. Oocyte retrieval was performed 36 hours after hCG injection under ultrasound guidance. In cases with premature luteinizing hormone surges or elevated serum progesterone (>1.5 ng/ml), the cycle was cancelled or all embryos were cryopreserved for transfer in subsequent cycles.

Oocytes were fertilized using either conventional IVF or ICSI, depending on semen parameters. Conventional IVF involved co-incubating oocytes with prepared sperm at a concentration of 1:30,000, whereas ICSI was performed using micromanipulation to inject a single sperm into each mature oocyte. Fertilization was assessed approximately 18 hours post-insemination, and normally fertilized oocytes with two pronuclei (2PN) were cultured further. Embryos were cultured in sequential media at 37°C, 6% CO_2, and 95% humidity, and were evaluated at 48 and 72 hours for cleavage-stage development, and at 120 hours for blastocyst formation.

Embryo quality was graded according to established morphological criteria for cleavage-stage embryos and blastocysts. Embryo transfer was performed on day 3 or day 5 after oocyte retrieval, with a maximum of two embryos transferred per cycle. Transfers were performed under ultrasound guidance using soft catheters, following standard laboratory loading procedures. Patients were advised bed rest following transfer, and luteal phase support with vaginal progesterone gel (90 mg daily) was initiated on the day of oocyte retrieval. Progesterone support was continued for up to 60 days post-transfer in pregnant patients. Clinical pregnancy was confirmed by ultrasound examination performed at 30–32 days post-transfer

Outcome measures included baseline patient demographics (age, BMI, infertility duration, baseline FSH), laboratory parameters (number of oocytes retrieved, fertilization rates, cleavage rates, embryo quality, number of embryos transferred), and clinical outcomes (pregnancy rate, implantation rate, miscarriage rate, and live birth rate). Fertilization rate was defined as the proportion of oocytes achieving regular 2PN fertilization out of the total number of inseminated oocytes. Implantation rate was defined as the number of gestational sacs observed by ultrasound divided by the total number of embryos transferred. The miscarriage rate was defined as the proportion of clinical pregnancies that ended before 20 weeks of gestation. All parameters were compared between chromosome 9 polymorphism carriers and matched controls.

Results

A total of 6,049 IVF/ICSI cycles were screened between January 2015 and June 2020. Among them, 150 couples were identified with at least one partner carrying a pericentric inversion of chromosome 9 [inv(9)], representing a prevalence of 1.25%. The distribution of karyotype subtypes by gender is presented in Table 1. The majority were inv(9)(p12q13) (51.7%) and inv(9)(p11q13) (45.0%), with smaller numbers carrying other variants. Overall, female carriers accounted for 55.6% and male carriers for 44.4%. These findings are shown in Table 1.

Table 1. Karyotype Distribution by Gender

Karyotype	Husbands (n)	%	Wives (n)	%	Total (n)	%
inv(9)(p11q13)	29	42.65	39	57.35	68	100.00
inv(9)(p12q13)	36	46.15	42	53.85	78	100.00
inv(9)(p13q21)	1	33.33	2	66.67	3	100.00
inv(9)(q21.2q34.2)	0	0.00	1	100.00	1	100.00
inv(9)(p13q13)	1	100.00	0	0.00	1	100.00
Total	67	44.37	84	55.63	151	100.00

Comparison of baseline characteristics between couples carrying inv(9) and controls revealed no statistically significant differences in female or male age, BMI, basal FSH, or infertility duration. This indicates that the two groups were comparable at baseline, as summarized in Table 2.

Table 2. Baseline Clinical Characteristics of Couples with inv(9) vs. Controls

Parameter	Inv(9) Group (n=150)	Control Group (n=821)	*P* value
Female age (years)	34.2 ± 5.09	33.5 ± 5.07	0.130

Male age (years)	36.7 ± 5.97	35.9 ± 6.23	0.159
Female BMI (kg/m²)	21.9 ± 2.43	21.4 ± 2.64	0.090
Baseline FSH (IU/L)	8.2 ± 3.66	8.5 ± 3.85	0.291
Duration of infertility (years)	5.7 ± 4.45	5.6 ± 3.90	0.849

Analysis of laboratory and clinical outcomes between inv(9) carriers and controls showed no significant differences. The number of oocytes retrieved, fertilization rates, embryo development, implantation rates, miscarriage rates, and live birth rates were all similar between groups. These results are detailed in Table 3.

Table 3. Pregnancy Outcomes of inv(9) vs. Controls

Parameter	inv(9) Group (n=150)	Control Group (n=821)	*P* value
No. of oocytes retrieved	10.1 ± 5.45	9.7 ± 5.25	0.424
2PN rate (%)	66.82	66.01	0.356
Abnormal fertilization rate (%)	7.18	6.87	0.887
High-quality embryo rate (%)	46.25	48.37	0.912
Cleavage rate (%)	96.25	97.66	0.295
No. of embryos transferred	1.6 ± 0.509	1.6 ± 0.518	0.948
Pregnancy rate (%)	38.67	43.85	0.305
Implantation rate (%)	30.08	33.56	0.768
Miscarriage rate (%)	18.97	14.72	0.731
Live birth rate (%)	31	36	0.239

To further explore the influence of carrier sex, the baseline characteristics of female and male inv(9) carriers were compared with those of controls. As shown in Table 4, no differences were observed in age, BMI, basal FSH, or infertility duration among the three groups

Table 4. Baseline Characteristics of Female and Male inv(9) Carriers vs. Controls

Parameter	Female Carriers (n=84)	Male Carriers (n=67)	Control Group (n=821)	F-value	*P* value
Female age (years)	34.5 ± 4.84	33.8 ± 5.37	33.5 ± 5.07	1.657	0.191
Male age (years)	36.6 ± 6.03	36.7 ± 5.93	35.9 ± 6.23	0.905	0.405
Female BMI (kg/m²)	21.7 ± 2.29	22.1 ± 2.60	21.4 ± 2.64	1.933	0.145
Baseline FSH (IU/L)	7.9 ± 2.92	8.4 ± 4.41	8.5 ± 3.85	0.908	0.404
Duration of infertility (years)	6.1 ± 4.60	5.0 ± 4.20	5.6 ± 3.90	1.371	0.254

When examining pregnancy outcomes stratified by sex, a significant difference emerged in live birth rates. Female carriers had a markedly lower live birth rate (23%) compared to male carriers (41%) and controls (36%), despite similar embryological parameters. These findings are summarized in Table 5.

Table 5. Clinical Characteristics and ART Outcomes of Female and Male inv(9) Carriers

Parameter	Female Carriers (n=84)	Male Carriers (n=67)	Control Group (n=821)	F-value	*P* value
Oocytes retrieved	9.9 ± 5.0	10.5 ± 5.95	9.7 ± 5.25	0.601	0.548
2PN rate (%)	67.5	66.2	66.0	0.564	0.569
Abnormal fertilization rate (%)	6.6	8.0	6.9	0.897	0.408
High-quality embryo rate (%)	43.9	48.4	48.4	0.464	0.629
Cleavage rate (%)	95.9	96.5	97.7	0.860	0.423
No. of embryos transferred	1.6 ± 0.50	1.6 ± 0.51	1.6 ± 0.52	0.007	0.993
Pregnancy rate (%)	33.3	44.8	43.9	0.779	0.459
Implantation rate (%)	25.4	35.5	33.6	0.921	0.398
Miscarriage rate (%)	25.0	13.3	14.7	0.146	0.864
Live birth rate (%)	23.0	41.0	36.0	3.299	0.03*

Subgroup analysis comparing inv(9)(p12q13), inv(9)(p11q13), rare inv(9) variants, and controls revealed no baseline differences, except for infertility duration, which was significantly longer among the rare variants. This is presented in Table 6.

Table 6. Baseline Characteristics of inv(9) Subtypes vs. Controls

Parameter	inv(9)(p12q13) (n=76)	inv(9)(p11q13) (n=68)	Other inv(9) (n=5)	Control Group (n=821)	F-value	*P* value
Female age (years)	33.99 ± 4.47	34.09 ± 5.50	37.00 ± 7.58	33.50 ± 5.07	1.205	0.307
Male age (years)	36.21 ± 5.20	37.03 ± 6.58	38.20 ± 8.28	35.90 ± 6.23	0.883	0.450
Female BMI (kg/m²)	21.90 ± 2.26	21.70 ± 2.63	22.88 ± 2.65	21.50 ± 2.64	1.303	0.272
Baseline FSH (IU/L)	8.60 ± 3.99	7.31 ± 3.03	11.06 ± 3.55	8.50 ± 3.85	2.310	0.075
Duration of infertility (years)	4.80 ± 3.52	5.93 ± 4.50	10.60 ± 5.03	5.60 ± 3.90	3.752	0.010*

Clinical and embryological outcomes of inv(9) subtypes are summarized in Table 7. While the number of embryos transferred per cycle differed significantly (P = 0.001), no other outcomes showed significant differences.

Table 7. Clinical Characteristics and ART Outcomes of inv(9) Subtypes vs. Controls

Parameter	inv(9)(p12q13) (n=76)	inv(9)(p11q13) (n=68)	Other inv(9) (n=5)	Control Group (n=821)	F-value	*P* value
Retrieved oocytes (Mean ± SD)	10.2 ± 5.10	10.28 ± 5.80	7.80 ± 6.14	9.8 ± 5.25	0.602	0.602
2PN fertilization rate (%)	64.45	68.66	76.92	66.01	0.549	0.649
Abnormal fertilization rate (%)	4.11	4.86	7.69	6.87	0.184	0.907
High-quality embryo rate (%)	50.49	41.44	36.36	48.37	0.650	0.583
Cleavage rate (%)	95.15	97.75	89.74	97.66	0.476	0.699
Embryo transfer per cycle	1.47 ± 0.503	1.79 ± 0.442	2.0 ± 0.707	1.6 ± 0.518	5.535	0.001*
Clinical pregnancy rate (%)	46.05	30.88	20.0	43.85	1.584	0.192
Implantation rate (%)	37.5	25.4	10.0	33.56	0.846	0.469
Miscarriage rate (%)	17.14	23.80	0.0	14.72	0.138	0.937
Live birth rate (%)	34.0	25.0	33.0	36.0	0.947	0.417

Baseline characteristics of couples with 9qh+ polymorphism compared to controls are presented in Table 8. No significant differences were found in age, BMI, basal FSH, or duration of infertility.

Table 8. Baseline Characteristics of 9qh+ Carriers vs. Controls

Parameter	9qh+ Female Carriers (n=30)	9qh+ Male Carriers (n=53)	Control Group (n=382)	F-value	*P* value
Female age (years)	31.9 ± 4.49	32.6 ± 4.46	33.0 ± 5.05	0.883	0.414
Male age (years)	34.8 ± 5.12	35.2 ± 5.08	35.3 ± 5.93	0.126	0.882
Female BMI (kg/m²)	21.4 ± 2.51	22.1 ± 2.44	21.5 ± 2.68	1.347	0.261
Baseline FSH (IU/L)	9.01 ± 3.06	7.8 ± 2.69	8.6 ± 4.46	0.858	0.425
Duration of infertility (years)	5.1 ± 3.26	5.2 ± 2.80	5.9 ± 3.97	1.259	0.285

Finally, the embryology and ART outcomes of 9qh+ carriers are compared with those of controls in Table 9. Across all laboratory and clinical parameters, including the number of oocytes retrieved, fertilization rates, embryo quality, implantation rates, and live birth rates, no significant differences were detected (all P > 0.05).

Table 9. Embryology and Clinical Outcomes of 9qh+ Carriers vs. Controls

Parameter	9qh+ Female Carriers (n=30)	9qh+ Male Carriers (n=53)	Control Group (n=382)	F-value	*P* value
Oocytes retrieved	10.5 ± 5.1	10.9 ± 5.0	10.6 ± 5.2	0.126	0.882
2PN rate (%)	63.75	63.84	66.30	0.154	0.857
Abnormal fertilization rate (%)	7.77	7.23	6.25	0.848	0.429
High-quality embryo rate (%)	36.84	50.14	49.92	1.949	0.144
Cleavage rate (%)	93.59	95.89	96.73	0.117	0.889
Embryos transferred	1.70	1.77	1.69	0.542	0.582
Pregnancy rate (%)	50.0	41.5	44.5	0.280	

Discussion

The discussion below synthesizes our study's findings on the impact of chromosome 9 polymorphisms, particularly the pericentric inversion (inv(9)), on IVF outcomes, in comparison to existing literature from the past five years.

In our study, a total of 150 couples with at least one partner carrying the inv(9) karyotype were identified out of 6,049 IVF/ICSI cycles, indicating a prevalence of approximately 2.48%. This prevalence aligns closely with findings by Dutta et al., who reported that the pericentric inversion of chromosome 9 is notably common, comprising a significant portion of chromosomal anomalies in infertility cases. (16). Similarly, Azonbakin et al. noted that inv(9) is a prevalent structural rearrangement associated with infertility and recurrent pregnancy loss (17). The distribution of specific inv(9) variants presented in our study, primarily inv(9)(p12q13) and inv(9)(p11q13), is consistent with reports of prevalent subtypes in various populations, indicating a potential biological commonality across diverse demographics (18).

Regarding baseline characteristics, couples with inv(9) displayed no significant differences compared to control groups in terms of age, BMI, basal FSH, and infertility duration. This finding echoes the research by Li et al., which also reported similar baseline parameters between couples with chromosomal aberrations and those without, suggesting that chromosomal variations might not inherently affect these metrics but are coincidental findings in the context of infertility (19). Other studies that examined couples with chromosomal inversions have noted comparable baseline clinical characteristics, reinforcing the notion that these genetic factors do not contribute overtly to differences in demographic or hormonal profiles (20).

Our analysis of clinical outcomes revealed no significant differences in oocyte retrieval, fertilization rates, embryo development, miscarriage rates, or live birth rates between individuals with inv(9) and controls. This observation is supplemented by findings from Gkeka et al., who noted that chromosomal inversions, including inv(9), did not contribute to significant differences in ART outcomes, including pregnancy and live birth rates (21). Additionally, Xie et al. highlighted that while reproductive failures often occur in inv(9) carriers, the outcomes of IVF

treatments remain largely unaffected when analyzed collectively, suggesting that the presence of these inversions may not significantly impact fertility treatments in a direct manner (22).

Examining the delineation of outcomes by sex illustrated that female carriers experienced a markedly lower live birth rate (23%) compared to male carriers (41%) and controls (36%). Such gender disparity in outcomes aligns with findings from Shao et al., who posited that male carriers might possess better reproductive outcomes despite chromosomal abnormalities due to underlying biological factors that might favor spermatogenesis (23). Conversely, female carriers have often been reported to demonstrate reduced reproductive success, potentially due to factors beyond simple chromosomal presence, such as advanced maternal age or other reproductive health markers prevalent in this demographic (24,25). This trend highlights the importance of individualized patient assessment beyond chromosomal screening in managing IVF outcomes.

Subgroup comparisons within inv(9) variants did not yield significant baseline differences, although substantial findings arose concerning infertility duration among rare variants. This observation suggests that rarer polymorphisms may be correlated with prolonged infertility challenges. The finding is in concordance with other studies that noted the complex interplay between specific inversions and their clinical implications regarding reproductive history, as observed by Alhalabi et al. (26).

Lastly, while echoes of our findings in patients carrying the 9qh+ polymorphism were comparable to those in controls across all established metrics, the literature emphasizes that chromosomal anomalies, including inversions, still warrant attention in genetic counseling areas within infertility evaluations. Concerns regarding gamete integrity and potential offspring anomalies in inversion carriers remain relevant topics in genetic discussions surrounding ART procedures (27,28).

Thus, while our findings suggest that carriers of pericentric inversions of chromosome 9 do not exhibit statistically significant differences in common IVF parameters compared to controls, the emerging distinctions related to gender-specific outcomes and variant-specific infertility durations emphasize the need for ongoing genetic investigation. The multifaceted nature of infertility related to chromosome 9 inversions necessitates personalized fertility strategies and potentially expanded preimplantation genetic testing efforts (20,29).

Conclusion

Pericentric inversion inv(9)(p12;q13) and male inv(9)(p11;q13) heterozygosity do not affect preimplantation embryo development or IVF-ET outcomes. Female carriers of inv(9)(p11;q13) exhibit normal embryo development but experience reduced live birth rates, indicating a sex-specific impact on clinical outcomes. Carriage of 9qh+ variants does not adversely influence embryo development or IVF-ET success.

Declarations

Data Availability statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (IRBEC-MMS-0412-24)

Consent for publication

Approved

Funding

Not applicable

Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

MAH (PhD, Reproductive Medicine)
Manuscript drafting, Study Design,
MY (Gynecologist)
Review of Literature, Data entry, Data analysis, and drafting articles.
AH (Gynecologist)
Conception of Study, Development of Research Methodology Design,
KF (Aesthetic Physician)
Study Design, manuscript review, critical input.
MW
Manuscript drafting, Study Design,
LJ (Gynecologist)
Conception of Study, Development of Research Methodology Design,

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

References

1. Mešanović S., Perić M., & Vareškić A. Prevalence and possible effects of pericentric inversion of chromosome 9 on reproductive failure in a human population of northeast Bosnia and Herzegovina: a 10-year retrospective study. European Journal of Medical and Health Sciences 2023;5(2):1-4. https://doi.org/10.24018/ejmed.2023.5.2.1662

2. Nonaka T., Takahashi M., Nonaka C., Enomoto T., & Takakuwa K.. The analysis of chromosomal abnormalities in patients with recurrent pregnancy loss, focusing on the prognosis of patients with inversion of chromosome 9. Reproductive Medicine and Biology 2019;18(3):296-301. https://doi.org/10.1002/rmb2.12281

3. Trieutien S., Pham D., Lê H., Van H., Nguyen P., Van T.et al.. Survey of structural autosomal abnormalities and autosomal variants in infertile patients treated at some IVF centers in Vietnam. The Application of Clinical Genetics 2025; Volume 18:29-40. https://doi.org/10.2147/tacg.s510933

4. Angelova L., Tsvetkova M., & Levkova M. Chromosomal polymorphism in Bulgarian patients with reproductive problems – one genetic centre experience. Journal of Imab - Annual Proceeding (Scientific Papers) 2021;27(4):4133-4138. https://doi.org/10.5272/jimab.2021274.4133

5. Liu Q., Zhou W., Huang Z., Huang X., Wu J., Ji X.et al.. Exploring the impact of pericentric inversion of chromosome 9 on fertility in sperm donors. Asian Journal of Andrology 2024;26(3):302-307. https://doi.org/10.4103/aja202369

6. Liang L., Zhang X., Zhang Z., Xu S., Wu Y., Zhang X.et al.. Effect of chromosomal polymorphisms on the outcome of in vitro fertilization and embryo transfer. Journal of Obstetrics and Gynaecology Research 2023;49(9):2351-2360. https://doi.org/10.1111/jog.15732

7. Li S., Cheng Y., Zhou D., Zhang Y., Yin T., & Yang J. Chromosomal polymorphisms associated with reproductive outcomes after IVF-ET. Journal of Assisted Reproduction and Genetics 2020;37(7):1703-1710. https://doi.org/10.1007/s10815-020-01793-8

8. Jesus A., Silva-Soares S., Silva J., Severo M., Barros A., & Dória S. Reproductive success of assisted reproductive technology in couples with chromosomal abnormalities. Journal of Assisted Reproduction and Genetics 2019;36(7):1471-1479. https://doi.org/10.1007/s10815-019-01486-x

9. Obukohwo O., Oreoluwa O., Comfort O., & Olanike A. Investigating the genetic basis of unexplained infertility and potential chromosomal abnormalities. Obm Genetics 2024;08(02):1-28. https://doi.org/10.21926/obm.genet.2402246

10. Viotti M. Preimplantation genetic testing for chromosomal abnormalities: aneuploidy, mosaicism, and structural rearrangements. Genes 2020;11(6):602. https://doi.org/10.3390/genes11060602

11. Dufton M. and Bouzayen R. Complex reciprocal translocations, more complex than initially thought: a case report. F&S Reports 2021;2(4):487-492. https://doi.org/10.1016/j.xfre.2021.08.003

12. Stegemiller M., Murdoch G., Rowan T., Davenport K., Becker G., Hall J.et al.. Genome-wide association analyses of fertility traits in beef heifers. Genes 2021;12(2):217. https://doi.org/10.3390/genes12020217
13. Young D., Klepacka D., McGarvey M., Schoolcraft W., & Katz-Jaffe M. Infertility patients with chromosome inversions are not susceptible to an inter-chromosomal effect. Journal of Assisted Reproduction and Genetics 2018;36(3):509-516. https://doi.org/10.1007/s10815-018-1376-1
14. Ceschin I., Ali T., Carvalho C., Martins C., Bos-Mikich A., Andrade G.et al.. Balanced chromosomal rearrangement in a partner revealed after preimplantation genetic testing for aneuploidies (PGT-A). Jbra Assisted Reproduction 2022. https://doi.org/10.5935/1518-0557.20220058
15. Lee S., Lee T., Song S., Kim D., Choi K., Lee J.et al.. Update on genetic screening and treatment for infertile men with genetic disorders in the era of assisted reproductive technology. Clinical and Experimental Reproductive Medicine 2021;48(4):283-294. https://doi.org/10.5653/cerm.2021.04476
16. Dutta M., Mahanta P., Basumatary B., & Konwar R. A case-control study on chromosomal anomalies in parents experiencing repeated spontaneous abortions from northern India. Cureus 2021. https://doi.org/10.7759/cureus.19819
17. Azonbakin S., Agbanlinsou A., Gouton C., Goussanou Y., Adjagba M., Dangbemey P.et al. Role of Chromosome Abnormalities in Couple Infertility in Cotonou. Global Reproductive Health 2025;10(1). https://doi.org/10.1097/grh.0000000000000103
18. Andó S., Koczok K., Bessenyei B., Balogh I., & Újfalusi A. Cytogenetic investigation of infertile patients in Hungary: a 10-year retrospective study. Genes 2022;13(11):2086. https://doi.org/10.3390/genes13112086
19. Li S., Cheng Y., Zhou D., Zhang Y., Yin T., & Yang J. Chromosomal polymorphisms associated with reproductive outcomes after IVF-ET. Journal of Assisted Reproduction and Genetics 2020;37(7):1703-1710. https://doi.org/10.1007/s10815-020-01793-8
20. Liang S., Yang J., Wu H., Teng X., & Duan T. Effects of chromosome 9 inversion on IVF/ICSI: a 7-year retrospective cohort study. Molecular Genetics & Genomic Medicine 2019;7(9). https://doi.org/10.1002/mgg3.856
21. Gkeka K., Symeonidis E., Tsampoukas G., Moussa M., Issa H., Kontogianni E.et al.. Recurrent miscarriage and male factor infertility: diagnostic and therapeutic implications. A narrative review.. Central European Journal of Urology 2023. https://doi.org/10.5173/ceju.2023.74
22. Xie X., Li F., Tan W., & Tang J. Analysis of the clinical features of pericentric inversion of chromosome 9. Journal of International Medical Research 2020;48(9). https://doi.org/10.1177/0300060520957820
23. Shao Y., Li J., Lu J., Li H., Zhu Y., Jiang W.et al.. Clinical outcomes of preimplantation genetic testing (PGT) application in couples with chromosomal inversion, a study in the Chinese Han population. Reproductive Biology and Endocrinology 2020;18(1). https://doi.org/10.1186/s12958-020-00635-7
24. Li R., Fan H., Zhang Q., Yang X., Zhan P., & Feng S.. Pericentric inversion in chromosome 1 and maleInfertility. Open Medicine 2020;15(1):343-348. https://doi.org/10.1515/med-2020-0404
25. Trieutien S., Pham D., Lê H., Van H., Nguyen P., Van T.et al.. Survey of structural autosomal abnormalities and autosomal variants in infertile patients treated at some IVF centers in Vietnam. The Application of Clinical Genetics 2025; Volume 18:29-40. https://doi.org/10.2147/tacg.s510933
26. Alhalabi M., Kakaje A., & Alhalabi M. Hereditary chromosomal nine inversion (p22q13) 9 as a cause for recurrent pregnancy loss: a case report. Journal of Medical Case Reports 2023;17(1). https://doi.org/10.1186/s13256-023-04137-z
27. Han N. and Liu X.. Azf microdeletion affects semen parameters, sex hormone levels, and chromosome karyotypes in infertile men in Xinjiang. Cellular and Molecular Biology 2023;69(13):106-111. https://doi.org/10.14715/cmb/2023.69.13.17
28. Zhang S., Liang F., Lei C., Wu J., Fu J., Yang Q.et al.. Long-read sequencing and haplotype linkage analysis enabled preimplantation genetic testing for patients carrying pathogenic inversions. Journal of Medical Genetics 2019;56(11):741-749. https://doi.org/10.1136/jmedgenet-2018-105976
29. Kouvidi E., Zachaki S., Tsarouha H., Pantou A., Manola K., Kanavakis E.et al.. Female reproductive ageing and chromosomal abnormalities in a large series of women undergoing IVF. Cytogenetic and Genome Research 2021;161(12):551-555. https://doi.org/10.1159/000521655