



Assessment of Fertility in Mosaic Klinefelter Syndrome Patients in Baghdad City Using Karyotyping, Sister Chromatid Exchange, and Semen Analysis



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Abstract

Background: Klinefelter's syndrome was discovered in 1942 AD when Dr. Harry Klinefelter, under the supervision of Dr. Fuller Albright at the Massachusetts General Hospital in Boston, published a report explaining the case of nine 6-foot-tall males. **Objective:** The purpose of the present study was to determine the relationship between fertility effectiveness and mosaic Klinefelter syndrome. **Methodology:** In our study, karyotyping was conducted for 20 patients with mosaic Klinefelter syndrome, and the percentage of Klinefelter cells containing 47 chromosomes relative to the total number of cells was calculated. The percentages of mosaicism patients ranged between 7.31% to 20.0%, and semen tests were conducted after abstaining from sexual intercourse for 72 hours and not taking stimulant drugs for a one month), and the characteristics of the semen were examined such as motility, total number, acidity, and liquefaction, In a sister chromatid exchange experiment for patients with mosaic Klinefelter syndrome, the number of exchanges per 50 cells was counted and compared with the count of the control group. **Results:** Sample No. 1 was the most effective study group for semen, for which the percentage of mosaicism was 7.31%, and sample No. 20 was the least effective study group for semen. Sample No. 20, for which the percentage of mosaicism was 20%, indicated that the greater the percentage of mosaicism was small, the greater the effectiveness was, and the greater the percentage was, the lower the effectiveness was, which indicated that the percentage had a significant impact on the sexual activity of the individual. There are significant differences in sister chromatids exchanges between the group of mosaicism patients (67.22 ± 4.17 exchange/50 cells) and the control group (56.11 ± 2.4 exchange/50 cells). **Conclusion:** There was a relationship between the percentage of mosaicism and the frequency of fertilization, as well as between the percentage of male sex hormones and the percentage of An increase in the components of semen, and thus an increase in the rate of fertilization of the ovum, sister chromatids exchanges is increased in patients compared to the control group. [Bangladesh Journal of Infectious Diseases, June 2026;13(1):208-214]

Keywords: Mosaic Klinefelter Syndrome; Mosaicism; Semen; fertilization, karyotyping; SCEs

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Introduction

This disease was discovered in 1942 AD when Dr. Harry Klinefelter, under the supervision of Dr. Fuller Albright at the Massachusetts General Hospital in Boston, published a report explaining

the case of nine 6-foot-tall males who had enlarged breasts and a lack of hair on the face and the rest of the body parts and testicles¹, and they exhibited an increase in the secretion of follicle-stimulating hormone. The sum of those characteristics

possessed by males was called Klinefelter syndrome, after the name of the first researcher in the research, Klinefelter, even though he was under the supervision of Albright, and the reason remained unknown until 1959, when chromosomal examination techniques were introduced². Dr. Patricia Jacobs found that the cells of people who have Klinefelter syndrome contain 47 chromosomes instead of the 46 chromosomes contained in a normal cell, and they found that the extra chromosome is the X chromosome. In general, males with Klinefelter syndrome have a pair of X chromosomes instead of one chromosome; their genotype is 47, XXY, while the normal genotype is 46, XY, and approximately 80.0% of those with Klinefelter syndrome have 47 chromosomes with an extra X chromosome³. There is a percentage that shows the presence of three chromosomes, 48, XXXY, and a percentage that shows four, 49, XXXXY, or five, 50, XXXXY, and so on, and a percentage of them carry two types of cells in their bodies; one type is normal cells, and another type carries the genetic mosaic of Klinefelter syndrome which is called in this case Mosaicism^{4,5}.

The physiological problem that people with Klinefelter syndrome show is the problem of delayed childbearing, as it was found that most of them suffer from a lack or absence of sperm in their semen, and men with this syndrome constitute approximately 15% of those who do not have sperm in the community, which is the reason for the discovery of their infection with this syndrome⁶. For the case of mosaicism, the patient had two cell lines, both of which were from the same zygote; one of these lines contained 47 chromosomes, and the other contained 46 chromosomes. This percentage is very important for determining the patient's health status⁷.

Sister chromatid exchanges (SCEs) refer to the reciprocal exchange of DNA segments between the two sister chromatids of a single replicated chromosome during the cell cycle, most commonly observed after DNA synthesis in the S phase and before or during mitosis. The chromatids involved are genetically identical copies of one another (generated in DNA replication), and the exchange typically occurs at homologous loci, leaving the net genetic content unchanged. The phenomenon can be visualized using cytogenetic techniques such as incorporation of the thymidine analog 5-bromodeoxyuridine (BrdU) and subsequent differential staining, which reveals alternating chromatid staining patterns (e.g., "harlequin" chromatids) indicative of exchanges⁸. Although

SCEs occur at a low basal frequency in normal somatic cells and may represent part of the physiological DNA replication/repair dynamics, an increased frequency of SCEs is widely regarded as a sensitive biomarker of genomic instability, replication stress, and defects in DNA repair pathways. Elevated SCEs rates have been linked to exposure to genotoxic agents (e.g., ionising radiation, cross-linking chemicals, antineoplastic drugs) and to inherited syndromes of chromosomal instability⁹.

In the context of Klinefelter syndrome (typically the 47, XXY karyotype in males), the presence of an extra X chromosome may result in altered cell-cycle kinetics, increased chromosomal mis-segregation, and compromised DNA repair capacity. Thus, SCE can be deployed in KS research as a cytogenetic marker to assess the extent of chromosomal instability inherent to the syndrome¹⁰. In practical terms, the SCEs assay in KS may help elucidate whether the extra X chromosome correlates with increased rates of sister chromatid exchanges, thereby potentially contributing to some of the known clinical sequelae of KS such as germ-cell impairment, increased cancer risk, or neurodevelopmental perturbations. Including SCE measurements in KS research therefore offers a mechanistic window into genome maintenance and stability in aneuploidy contexts¹¹. Our study was aimed to determine the relationship between fertility effectiveness and mosaic Klinefelter syndrome.

Methodology

Study Settings and Population: An experimental study was carried out in the College of Applied Sciences, University of Samarra, Samarra, Iraq, from September 2025 to December 2025. Karyotyping was performed on 20 patients, and semen analyses were performed after the patients had abstained from sexual intercourse for 72 hours or from sexual stimulant drugs for 1 month. Tests were conducted for semen pH, motility, morphology, total sperm count, volume and liquefaction¹².

Study Procedure: Karyotyping was performed on 20 patients, and semen analyses were performed after the patients had abstained from sexual intercourse for 72 hours or from sexual stimulant drugs for 1 month. Tests were conducted for semen pH, motility, morphology, total sperm count, volume and liquefaction¹². Sister chromatid exchanges (SCEs) were assessed using a standard cytogenetic differential staining technique that

distinguishes between sister chromatids following incorporation of a thymidine analogue. Metaphase cells were prepared and differentially stained to visualize SCEs, which were then counted under the microscope. The frequency of SCEs was expressed as the average number of exchanges per 50 cells according to established protocols¹³.

Table 1: Normal values of Semen

Parameter	Normal value
Total Sperm Count (Million)	40×10 or more
Liquefaction	After 30 min
pH	7.2 to 7.8
Morphology	≥70%
Volume	2.0 to 5.0 ml
Motility	50% or more motile

Statistical analysis: The Statistical Package for the Social Sciences (SPSS) application (2019) was utilized to assess the impact of various groups on study parameters. The T-test and Least Significant Difference (LSD) were employed to compare means significantly. The Chi-Square test was employed to compare percentages significantly. Estimation of the correlation coefficient among various factors in patient groups within this study.

Ethics approval: The study was conducted in accordance with the ethical standards of the

institutional research committee. Ethical approval was obtained from the relevant institutional ethics committee (approval code: CSEC/1025/0148 October 27, 2025). Written informed consent was obtained from all participants prior to inclusion in the study.

Results

The karyotype of the study sample was shown (Table 2).

Figure I shows the karyotyping of cells from patients with Klinefelter syndrome.



Figure I: Klinefelter's cell 47, XXY

Table 2: Karyotype of Patients

Sample	Karyotype	Age	Abnormal cell	Normal cell	Percentage
1	mos47,XXY,+X[3]/46,XY[38]	22	3	38	7.31
2	mos47,XXY,+X[4]/46,XY[38]	36	4	38	9.52
3	mos47,XXY,+X[5]/46,XY[45]	33	5	45	10
4	mos47,XXY,+X[6]/46,XY[50]	41	6	50	10.71
5	mos47,XXY,+X[6]/46,XY[47]	38	6	47	11.32
6	mos47,XXY,+X[5]/46,XY[38]	29	5	38	11.62
7	mos47,XXY,+X[7]/46,XY[51]	43	7	51	12.06
8	mos47,XXY,+X[5]/46,XY[35]	27	5	35	12.5
9	mos47,XXY,+X[6]/46,XY[40]	30	6	40	13.04
10	mos47,XXY,+X[7]/46,XY[45]	28	7	45	13.46
11	mos47,XXY,+X[5]/46,XY[31]	24	5	31	13.88
12	mos47,XXY,+X[8]/46,XY[49]	28	8	49	14.03
13	mos47,XXY,+X[6]/46,XY[36]	37	6	36	14.28
14	mos47,XXY,+X[9]/46,XY[52]	25	9	52	14.75
15	mos47,XXY,+X[5]/46,XY[28]	38	5	28	15.15
16	mos47,XXY,+X[8]/46,XY[44]	32	8	44	15.38
17	mos47,XXY,+X[6]/46,XY[31]	42	6	31	16.21
18	mos47,XXY,+X[7]/46,XY[35]	36	7	35	16.66
19	mos47,XXY,+X[9]/46,XY[40]	20	9	40	18.36
20	mos47,XXY,+X[10]/46,XY[40]	24	10	40	20

Figure II shows the karyotyping of normal cells for the same patient.

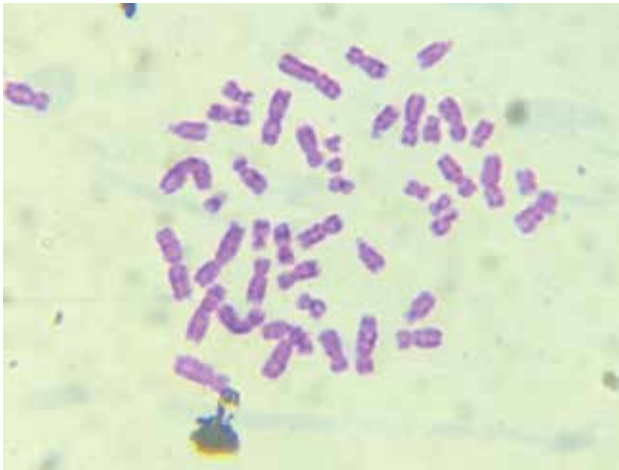


Figure II: Normal cell 46, XY

The semen analysis results obtained from the study participants are presented in Table 3, following the same participant group and sequence as those reported in Table 2. This arrangement allows for direct comparison of the measured semen parameters with the corresponding data presented previousn.

Table 3 compares the mean sister chromatid exchange (SCE) frequency between patients and healthy controls. The mean SCE frequency was

Table 4: Sister Chromatid Exchanges In Patients with Klinefelter syndrome as a Comparison with the control

Mean sister chromatid exchange (exchange/50 cells) ± standard error for patients	Mean sister chromatid exchange (exchange/50 cells) ± standard error for control
67.22±4.17	56.11±2.4

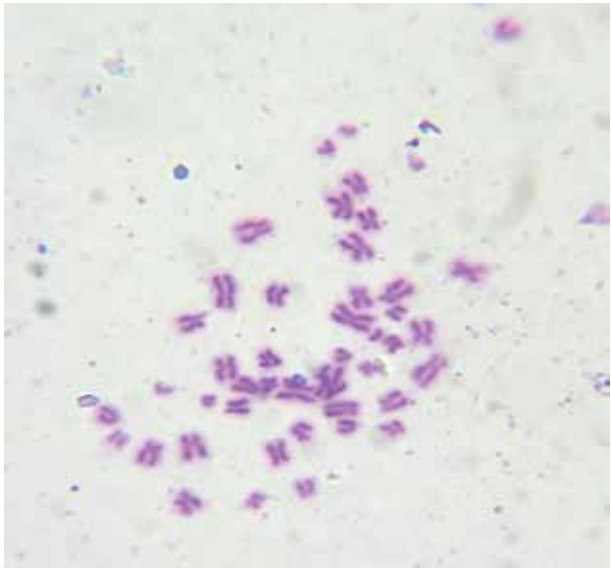


Figure III: Showing the Sister Chromatid Exchanges For Patients

Table 3: Biological Activity in Semen

Sample	percentage	T. Sperm Count (Million)	Liquefaction 40	pH	Morphology	Volume	Motility
1	7.31	55	38	7.8	80	4.7	68
2	9.52	53	37	7.7	78	4.5	65
3	10	50	36	7.7	77	4.3	62
4	10.71	48	35	7.6	76	4.1	59
5	11.32	46	34	7.6	76	4	57
6	11.62	42	31	7.5	75	3.8	55
7	12.06	41	30	7.4	71	3.7	54
8	12.5	41	28	7.4	70	3.6	53
9	13.04	38	27	7.4	70	3.3	51
10	13.46	35	26	7.2	68	3.3	49
11	13.88	35	24	7.2	67	3.2	46
12	14.03	34	23	7.1	64	3.1	44
13	14.28	33	23	7	61	3	41
14	14.75	31	22	7	60	2.9	40
15	15.15	30	21	7	55	2.9	39
16	15.38	30	21	6.9	54	2.7	37
17	16.21	28	20	6.8	51	2.6	36
18	16.66	27	19	6.7	46	2	35
19	18. 36	26	15	6.4	35	1.6	34
20	20	22		6.1	29	0.8	33

significantly higher in patients (67.22 ± 4.17 exchanges per 50 cells) than in healthy controls (56.11 ± 2.40 exchanges per 50 cells) ($P < 0.05$), suggesting increased chromosomal instability in the patient group.

Figure III shows the Sister Chromatids Exchanges of patients with Klinefelter syndrome cells.

Figure IV shows the Sister Chromatids Exchanges of normal cells for the same patient.

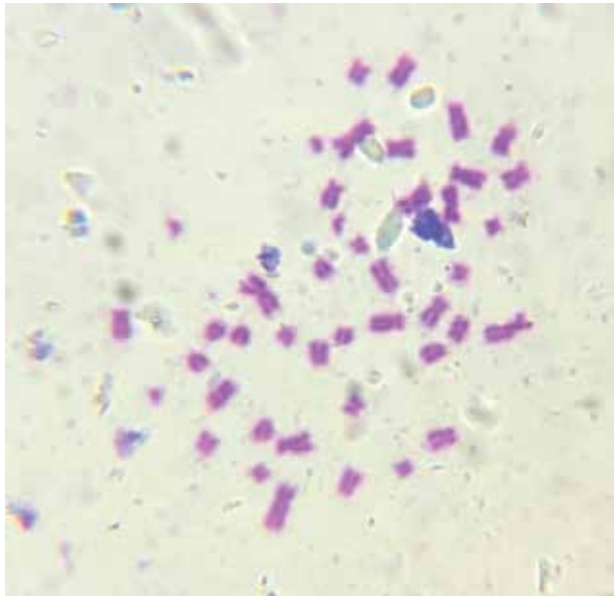


Figure IV: Showing the Sister Chromatid Exchanges for Normal Cells

Discussion

The lower the percentage of mosaicism is, the greater the percentage of effective semen (the sexual activity of the sample); however, if the percentage of mosaicism increases, all the percentages of the semen decrease, and there are significant differences at the level of probability $p \leq 0.1$. This reason may be attributed to the fact that the natural ratios depend on the ratios of the natural cells in the body, which affects the production of sperm and sexual potency¹⁴. This ratio has a significant impact on male sex hormones, which are involved in male phenotypic characteristics such as voice and hair growth¹⁵. The most important of these effects of the ratio is the maturation of the testes and the production of sperm that are able to fertilize the ovum¹⁶. There are also significant differences in the percentages of sperm and motility, numbers, and the pH value, and all of these differences are related to the percentage of mosaicism, as the lower the percentage is, the greater the effectiveness of the patient's sperm¹⁷.

The results obtained were consistent with what was agreed upon¹⁸ when they compared patients who were completely infected with this syndrome with those

with mosaic syndrome. The pregnancy of those with the syndrome did not succeed completely except through external fertilization, while those with mosaicism were pregnant by internal fertilization by Easier¹⁹. But it relied heavily on the percentage of mosaicism, as the less the pregnancy happened, the easier it was, and they noticed that the psychological impact and stimulating drugs have a great and effective role, as well as marriage to people who do not have any inheritance for this syndrome, which is consistent with what happened²⁰. When they monitored several patients, and their number was 137 with this mosaic syndrome and samples were taken from the patients' semen, then the number of sperm that have a normal chromosomal number 23 and the other with 24 chromosomes, and the number in the sperm is close to what is found in the cells of the body, was released²¹. They returned the semen to the testicles, and after the sperm was fertilized with the ovum, many of them had repeated miscarriages; except in some samples, they were pregnant, but they did not find the reason; they attributed this to the presence of a genetic predisposition to infection with this syndrome, which is not identical to what he obtained²². When they conducted their study on two generations while observing who is the origin of this anomaly, the sufferers of this mosaic syndrome had bloody urine and sperm abnormalities²³.

There were significant differences between the sister chromatid exchanges for the group of patients and the control group, as the average percentage of sister chromatid exchange for patients reached 67.22 ± 4.17 exchanges per cell, while for the control group the percentage was 56.11 ± 2.4 exchanges per cell, and this is a large difference. The results were identical to what was obtained in a study²⁴, as the higher the percentage of abnormal cells containing 47 chromosomes, the higher the percentage of sister chromatid exchange. This is evidence that normal cells containing 46 chromosomes have less sister chromatid exchange. This result was identical to what was stated in a study²⁵. When they conducted their research on patients with Klinefelter syndrome, the differences were clear between the group of patients and the control group.

Conclusion

There was a relationship between the percentage of mosaicism and the frequency of fertilization, as well as between the percentage of male sex hormones and the increase in an in the components of semen, and thus an increase in the rate of fertilization of the ovum. A lower percentage of mosaicism is associated with an increase in the rate of fertilization. Also, the

higher the percentage of mosaicism, the higher the percentage of sister chromatid exchanges in abnormal cells.

Acknowledgements

None

Conflict of interest:

No competing interests exist by the authors.

Financial Disclosure

The author(s) received no specific funding for this work.

Authors' contributions

Conceptualization, methods and literature review, Preparation of the draft manuscript, Finalization of manuscript: Qutaiba Hommadi Al-Samarraie.

Data Availability

Any questions regarding the availability of the study's supporting data should be addressed to the corresponding author, who can provide it upon justifiable request.

Ethics Approval and Consent to Participate

All the participants involved in this study were informed, and an agreement was obtained verbally from each participant before sample collection. This study was approved by a local committee of publication ethics in the medical city, Baghdad, Iraq, under reference number 0214 on July 11, 2024.

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How to cite this article: Al-Samarraie QH. Assessment of Fertility in Mosaic Klinefelter Syndrome Patients in Baghdad City Using Karyotyping, Sister Chromatid Exchange, and Semen Analysis. Bangladesh J Infect Dis 2026;13(1): 208-214

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Article Info

Received on: 1 June 2025

Accepted on: 12 October 2025

Published on: 1 June 2026

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