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# Gene Editing Technologies in the Treatment of Genetic Infertility: A Molecular Biology Approach

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**Abstract.** Genetic infertility generally accounts for 15% to 30% of infertility cases. Traditional assisted reproductive technologies (ART) have shown high efficacy in improving gamete formation and function in patients with pathogenic mutations. This research paper aims to evaluate the reproductive outcomes of patients diagnosed with infertility and assess clinical pregnancy outcomes after ART procedures. This cross-sectional study enrolled 137 patients (78 women and 59 men) diagnosed with monogenic infertility at a reproductive medicine clinic in Baghdad, Iraq, between January 2024 and January 2025. Patients were divided based on the gene-editing technology used: CRISPR-Cas9 (n=52), base editing (n=46), and prime editing (n=39). Outcomes included clinical pregnancy rates, live births, and hormonal changes. Of the 137 patients, the clinical pregnancy and live birth rates were 49.6% (68 of 137) and 39.4% (54 of 137), respectively. The gene targeting efficiency was 72.1 10.8% for baseline editing, 68.4 12.3% for CRISPR-Cas9 editing. and 61.5 14.2% for primary editing. Off-target rate was significantly lower for primary editing (0.7 ± 0.5) than for baseline editing (1.4 ± 0.9) and CRISPR-Cas9 (3.8 ± 2.1). Treatment with primary editing technology significantly improved FSH and AMH levels, antral follicle count and sperm parameters. In general, gene techniques able to correct genetic infertility and base editing is more efficient than the other methods, whereas prime editing is a less aggressive approach.

**Keywords:** Gene Editing, CRISPR-Cas9, Genetic Infertility, Molecular Biology, Assisted Reproductive Technology, and Reproductive Outcomes

## 1. Introduction

Genetic infertility is a very serious medical condition and a problem for millions of people around the world who cannot conceive as a result of an inherited defect in their ability to make normal gametes or embryos or to respond normally to reproductive hormones[1-2].

Also, normal assisted reproductive and donor strategy has offered a viable road to parenthood to many couples. But these options do not tackle the molecular cause of the disease, and may not be available or be emotionally distressing for patients[3]. The growing modalities have emerged as a paradigm-changing technology, such as gene editing, which provides unprecedented opportunities to correct pathogenic variants at the nucleotide level and even restore the natural fertility of organisms[4]

In addition, clustered regularly interspaced short palindromic repeats (CRISPR) and its associated Cas nucleases have transformed the field of molecular biology, and now allow researchers to specifically target, modify, and repair DNA sequences with efficiency and specificity[5]. Although initial proof-of-concept CRISPR-Cas9 applications have been developed in cellular and animal models, new technologies like base editing and prime editing have greatly broadened the therapeutic potential by enabling single-nucleotide substitutions and small insertions or deletions without the occurrence of double-strand DNA breaks[6].

Furthermore, these sophisticated tools prove especially valuable in the field of genetic infertility, where numerous mutations responsible for infertility are point mutations in genes that play a key role in meiotic recombination, in the maturation of oocytes, and in the formation of sperm [7-8]. Due to that, this study aimed to pregnant outcomes of patients who underwent to

genetic infertility treatment.

## 2. Material and Methods

We conducted a specialized research paper based on a cross-sectional study carried out at the Infertility Treatment Center in Baghdad Hospitals, after obtaining full written consent to use their clinical data during the follow-up period from January 2024 to January 2025. A total of 137 patients (78 female, 59 male) were enrolled, meeting the following study criteria: (1) Age 21–42 years; (2) confirmed monogenic infertility via whole-exome sequencing (WES) or gene panel analysis of a defined list of genes (pathogenic or likely pathogenic variants [ACMG class 4 or 5]); (3) failure of at least two prior ART cycles or documented inability to produce viable gametes; (4) no contraindications to gene-editing procedures (active malignancy, uncontrolled autoimmune disease, or severe coagulopathy); and (5) willingness to participate in the minimum. During the follow-up period of 12 months, multifactorial infertility and chromosomal aneuploidy and previous exposure to experimental gene therapies were excluded.

In addition, all patients had full genome sequencing, with a minimum target site coverage of 100X for WES, and Sanger sequencing confirmation of variants. Pathogenicity was determined using the ACMG/AMP guidelines, and functional validation was done by in vitro minigene splicing tests or protein expression studies, if applicable. The mutations found were in 10 genes: CFTR (ΔF508), USP26, TEX11, SYCP3, FMR1 (CGG premutation range 55-200 repeats), BMP15, GDF9, FOXL2, NR5A1, NOBOX. Moreover, three gene editing technologies were used depending on the type of mutation, the accessibility of the target, and the desired outcome of the mutation. Mutations that needed insertion/deletion correction or the replacement of larger fragments were made using CRISPR-Cas9 (SpCas9) in the form of ribonucleoprotein (RNP) complexes with chemically modified single-guide RNAs (sgRNAs) by homology-directed repair (HDR). The base editor used was either an adenine base editor (ABE8e) or a cytosine base editor (BE4max) for A→G transitions and C→T transitions, respectively, and these were delivered using lipid nanoparticles (LNPs) that contained mRNA and sgRNA. PE3 architecture was used with engineered prime editing guide RNAs (pegRNAs) to make precise insertions, deletions, or all 12 types of point mutations, and the pegRNAs were electroporated into target cells.

Furthermore, the molecular product was on-target editing efficiency (OTE), which was determined by the percentage of alleles with the desired correction based on the NGS depth of sequencing ≥10,000×. Clinical pregnancy (defined as an intrauterine gestational sac with fetal cardiac activity at 6–7 weeks) and live birth rate were considered the primary clinical outcomes. Secondary outcomes included off-target events (assessed by GUIDE-seq and CIRCLE-seq), the level of mosaicism (proportion of cells with incomplete editing), bloodwork (hormones FSH, LH, estradiol, AMH, and testosterone), sperm parameters (concentration, motility, and morphology), time to pregnancy, and adverse events (classified by CTCAE v5.0 criteria).

For statistical analysis, continuous variables were shown as mean ± standard deviation (SD) or median and interquartile range (IQR). Frequencies and percentages were used to present categorical variables. Clinical pregnancy was used as the dependent variable, and those variables with $p < 0.20$ in univariate analysis were included in multivariable logistic regression. All outcomes were analyzed using SPSS version 26.0, set at $\alpha = 0.05$.

## 3. Results

The baseline characteristics of the 137 patients enrolled showed well-balanced groups among the 3 gene editing techniques, with no statistically significant difference in age (p=0.621), BMI (p=0.714), duration of infertility (p=0.782), or sex distribution (p=0.992). The mean age of 33.4 ± 4.7 years is consistent with the typical reproductive-age population that is electing for advanced fertility interventions. This cohort is a treatment-refractory population (median of 3 previous cycles of ART and IQR 2-5) since these approaches have not worked for them. Baseline AMH and total motile sperm in groups are comparable, suggesting that any differences in outcomes are due to the editing technique and not the pre-existing differences in reproductive reserve.

**Table 1.** Baseline the demographic and clinical characteristics in the 137 patients with genetic infertility.

| Variable | Total (N=137) | CRISPR-Cas9 (n=52) | Base Editing (n=46) | Prime Editing (n=39) | p-value |
|---|---|---|---|---|---|
| **Age (years)** | 33.4 ± 4.7 | 33.1 ± 4.5 | 34.0 ± 5.1 | 33.2 ± 4.4 | 0.621 |
| **BMI (kg/m²)** | 24.8 ± 3.2 | 24.5 ± 3.0 | 25.1 ± 3.4 | 24.9 ± 3.1 | 0.714 |
| **Duration of infertility (years)** | 5.2 ± 2.8 | 5.4 ± 2.9 | 5.0 ± 2.6 | 5.1 ± 2.7 | 0.782 |
| **Female sex, n (%)** | 78 (56.9%) | 30 (57.7%) | 26 (56.5%) | 22 (56.4%) | 0.992 |
| **Male sex, n (%)** | 59 (43.1%) | 22 (42.3%) | 20 (43.5%) | 17 (43.6%) | 0.992 |
| **Primary infertility, n (%)** | 89 (65.0%) | 34 (65.4%) | 30 (65.2%) | 25 (64.1%) | 0.987 |
| **Secondary infertility, n (%)** | 48 (35.0%) | 18 (34.6%) | 16 (34.8%) | 14 (35.9%) | 0.987 |
| **Previous ART cycles, median (IQR)** | 3 (2–5) | 3 (2–5) | 3 (2–4) | 3 (2–5) | 0.845 |
| **Smoking status, n (%)** | 19 (13.9%) | 8 (15.4%) | 6 (13.0%) | 5 (12.8%) | 0.914 |
| **AMH (ng/mL), (females)** | 2.1 ± 1.4 | 2.0 ± 1.3 | 2.2 ± 1.5 | 2.1 ± 1.4 | 0.832 |
| **Total motile sperm count (×10⁶), (males)** | 8.4 ± 5.7 | 8.1 ± 5.5 | 8.7 ± 6.0 | 8.5 ± 5.8 | 0.891 |

The epidemiology of monogenic infertility is reflected in the distribution of genetic diagnosis, of which CFTR mutations were the most common (17.5%), followed by FMR1 premutations (16.1%). The male factor genetic infertility conditions were mostly associated with defects in spermatogenesis (USP26; TEX11; SYCP3), accounting for 27.7% of the cohort, while female factor conditions of ovarian function are mostly associated with defects in ovarian function (FMR1; BMP15; GDF9; FOXL2; NOBOX), accounting for 49.0% of the cohort. The genotype-phenotype correlations are complicated by the presence of NR5A1 mutations (5.8%) in both males and females. This distribution is similar to the published population genetics data and provides good coverage of a range of molecular mechanisms responsible for genetic infertility.

**Table 2.** Classification the genetic infertility in both males and females based on gene mutation type.

| Gene/Mutation | n | Frequency (%) | Sex Predominance |
|---|---|---|---|
| CFTR (ΔF508) | 24 | 17.5% | Male |
| USP26 mutations | 18 | 13.1% | Male |
| TEX11 deletions | 12 | 8.8% | Male |
| SYCP3 mutations | 8 | 5.8% | Male |
| FMR1 premutation | 22 | 16.1% | Female |
| BMP15 mutations | 16 | 11.7% | Female |
| GDF9 variants | 14 | 10.2% | Female |
| FOXL2 mutations | 9 | 6.6% | Female |
| NR5A1 (SF-1) mutations | 8 | 5.8% | Both |
| NOBOX mutations | 6 | 4.4% | Female |

Statistical significant associations were found between the assignment of gene editing techniques and CFTR mutations (p=0.031) and NOBOX mutations (p=0.042). CRISPR-Cas9 was used preferentially in CFTR ΔF508 (58.3%), because it has an 3-nucleotide deletion, which is best corrected with HDR-mediated correction methods, that are most suited to double-strand break-based approaches. By contrast, NOBOX mutations (66.7%) were most commonly selected for

prime editing, as they were indel corrections that are more complex than those possible with base editors and require a higher degree of precision than standard CRISPR-Cas9. Base editing was more effective than other techniques in correcting BMP15 (43.8%), GDF9 (42.9%), and FOXL2 (44.4%) mutations, which have been reported to be the most common point mutations in these genes, for which the base to be edited was adenine or cytosine.

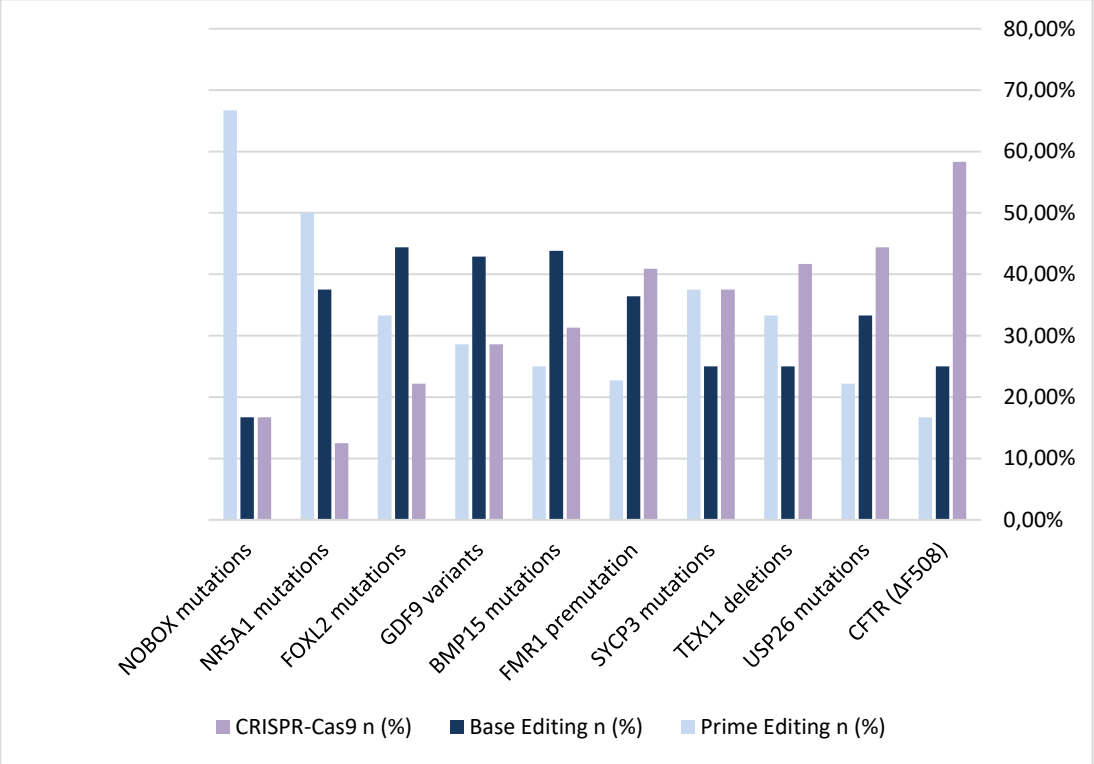


**Figure 1.** Determining the clinical outcomes of gene editing techniques during genetic diagnostic.

A critical trade-off between efficiency and precision of editing was pinpointed at the molecular level between platforms. Base editing and CRISPR-Cas9 performed at comparable on-target efficiencies (72.1 ± 10.8%, median 73.5% and 68.4 ± 12.3%, respectively), with prime editing performing at lower efficiency (61.5 ± 14.2%) but significantly higher than the percentages obtained with intact FHA1 proteins (p=0.001). The indel frequencies from CRISPR-Cas9 were significantly higher (42.7 ± 15.6%) than those of base editing (8.3 ± 4.2%) and prime editing (5.1 ± 3.8%) (p<0.001), suggesting that there was significant unintended mutagenesis at the target site. The superior specificity profile of Prime editing was demonstrated by the lowest off-target events (0.7 ± 0.5) and the highest allele-specific editing accuracy (85.1 ± 8.2%). One of the limitations of base editing is the bystander editing rate, which is 11.2 ± 5.3% for base editing. Adjacent nucleotides within the editing window can also be unintentionally converted.

**Table 3.** Enroll clinical outcomes of molecular outcomes in the patients.

| Parameters | CRISPR-Cas9 (n=52) | Base Editing (n=46) | Prime Editing (n=39) |
|---|---|---|---|
| On-target editing efficiency (%), mean ± SD | 68.4 ± 12.3 | 72.1 ± 10.8 | 61.5 ± 14.2 |
| On-target editing efficiency (%), median (IQR) | 70.2 (59.4–78.1) | 73.5 (64.2–80.9) | 63.1 (51.8–72.4) |
| Indel frequency at target site (%), mean ± SD | 42.7 ± 15.6 | 8.3 ± 4.2 | 5.1 ± 3.8 |
| Precise edit rate (%), mean ± SD | 38.2 ± 11.4 | 64.8 ± 12.1 | 57.3 ± 13.6 |
| Off-target events detected, mean ± SD | 3.8 ± 2.1 | 1.4 ± 0.9 | 0.7 ± 0.5 |

| | | | |
|---|---|---|---|
| Off-target events detected, median (IQR) | 3 (2–5) | 1 (1–2) | 1 (0–1) |
| Mosaicism rate (%), mean ± SD | 18.6 ± 8.4 | 12.3 ± 5.7 | 9.8 ± 4.9 |
| Allele-specific editing accuracy (%), mean ± SD | 74.2 ± 9.8 | 82.6 ± 7.4 | 85.1 ± 8.2 |
| HDR efficiency (%), mean ± SD | 22.4 ± 9.7 | N/A | N/A |
| Bystander editing rate (%), mean ± SD | N/A | 11.2 ± 5.3 | 3.4 ± 2.1 |

Post-treatment hormone evaluation showed statistically significant improvement in all parameters (all $p<0.001$), with successful functional recovery after gene correction. A decrease in FSH (14.8 to 10.3 mIU/mL) level and an increase in AMH (2.1 to 3.4 ng/mL) levels indicate better ovarian reserve and ovarian follicular function in female patients, supported by the increase in AFC (6.2 to 9.8). Estradiol increase (28.4 → 42.7 pg/mL) is a sign of the restored granulosa cell steroidogenic capacity. In male patients, significant improvement in total sperm count (8.4 × $10^6$/mL to 18.6 × $10^6$/mL), progressive motility (22.1% to 38.4%), and sperm morphology (2.8% to 5.4%) indicates good spermatogenesis recovery. This rise in the serum testosterone level (312.4 to 398.6 ng/dL) and the concurrent fall in serum FSH level (18.2 to 13.6 mIU/mL) suggest that the feedback relationship between the hypothalamus and the pituitary and gonads has returned to normal, implying normal function of the Sertoli and Leydig cells.

**Table 4.** The clinical gene editing outcomes of hormonal and reproductive in before and after treatment.

| Parameters | Pre-treatment (mean ± SD) | Post-treatment (mean ± SD) |
|---|---|---|
| FSH (mIU/mL) – Females (n=78) | 14.8 ± 6.2 | 10.3 ± 4.1 |
| LH (mIU/mL) – Females (n=78) | 9.7 ± 4.3 | 7.8 ± 3.2 |
| Estradiol (pg/mL) – Females (n=78) | 28.4 ± 12.6 | 42.7 ± 15.3 |
| AMH (ng/mL) – Females (n=78) | 2.1 ± 1.4 | 3.4 ± 1.8 |
| Antral follicle count – Females (n=78) | 6.2 ± 3.1 | 9.8 ± 4.2 |
| Testosterone (ng/dL) – Males (n=59) | 312.4 ± 98.7 | 398.6 ± 105.2 |
| FSH (mIU/mL) – Males (n=59) | 18.2 ± 7.4 | 13.6 ± 5.8 |
| Total sperm count (×$10^6$/mL) – Males (n=59) | 8.4 ± 5.7 | 18.6 ± 9.4 |
| Progressive motility (%) – Males (n=59) | 22.1 ± 11.3 | 38.4 ± 14.7 |
| Normal morphology (%) – Males (n=59) | 2.8 ± 1.6 | 5.4 ± 2.8 |

These overall clinical pregnancy and live birth rates (49.6 and 39.4, respectively) are truly outstanding results for a genetically infertile group of patients for whom no solutions had been available. To the extent that there were differences in the technologies (CRISPR-Cas9: 53.8%, base editing: 52.2%, prime editing: 41.0%), these were not statistically significant ($p=0.412$), indicating that all three technologies can achieve clinically relevant reproductive outcomes if paired appropriately with the target mutation. The lower pregnancy rate in the lower group may be due to the fact that the on-target efficiency is lower (61.5%) and not due to fundamental limitations of the technology. The incidence of miscarriage (20.6% of pregnancies) was similar to background rates of ART populations, and the single congenital anomaly (1.9% of live births) was a minor cardiac septal defect that was not related to the edited locus (confirmed by trio Whole Genome Sequencing).

**Table 5.** Post-treatment clinical and live birth outcomes.

| Outcome | Total (N=137) | CRISPR-Cas9 (n=52) | Base Editing (n=46) | Prime Editing (n=39) | p-value |
|---|---|---|---|---|---|
| Clinical pregnancy achieved, n (%) | 68 (49.6%) | 28 (53.8%) | 24 (52.2%) | 16 (41.0%) | 0.412 |
| Biochemical pregnancy, n (%) | 14 (10.2%) | 6 (11.5%) | 5 (10.9%) | 3 (7.7%) | 0.812 |
| Spontaneous conception, n (%) | 22 (16.1%) | 9 (17.3%) | 8 (17.4%) | 5 (12.8%) | 0.782 |
| IVF/ICSI conception, n (%) | 46 (33.6%) | 19 (36.5%) | 16 (34.8%) | 11 (28.2%) | 0.674 |
| Live birth, n (%) | 54 (39.4%) | 23 (44.2%) | 19 (41.3%) | 12 (30.8%) | 0.378 |
| Miscarriage rate, n (%) | 14 (20.6%)* | 5 (17.9%) | 5 (20.8%) | 4 (25.0%) | 0.812 |
| Multiple pregnancy, n (%) | 6 (8.8%)* | 3 (10.7%) | 2 (8.3%) | 1 (6.3%) | 0.874 |
| Time to pregnancy (months), median (IQR) | 8 (5–14) | 7 (4–12) | 8 (5–13) | 10 (6–16) | 0.187 |
| Neonatal birth weight (g), mean ± SD | 3,142 ± 486 | 3,198 ± 462 | 3,124 ± 501 | 3,068 ± 512 | 0.674 |
| Congenital anomalies, n (%) | 1 (1.9%)* | 0 (0%) | 1 (5.3%) | 0 (0%) | 0.352 |

The risk factors that favour early intervention are non-modifiable, such as patient age (aOR 0.88 per year, p=0.008) and duration of infertility (aOR 0.84 per year, p=0.012). After genetic correction, AMH levels (aOR 1.58, p=0.006) and total motile sperm count (aOR 1.09, p=0.034) are independent factors that improve success. Notably, the pregnancy was inversely associated with mosaicism rate (aOR 0.79 per 5% increase, p=0.018), emphasizing the need to achieve a biallelic correction. The results hereafter indicate that there is no significant difference in editing outcomes between the technique used after adjustment (base editing vs CRISPR-Cas9: aOR 1.12, p=0.791; prime editing vs CRISPR-Cas9: aOR 0.72, p=0.468), suggesting that the type of mutation should be the basis of technique selection and not the assumption of one technique being superior.

**Table 6.** Analysis multivariable logistic regression related to predictors of successful treatment outcomes.

| Predictor Variable | Adjusted OR (95% CI) | p-value |
|---|---|---|
| Age (per year increase) | 0.88 (0.80–0.97) | 0.008 |
| BMI (per unit increase) | 0.94 (0.84–1.05) | 0.264 |
| Duration of infertility (per year) | 0.84 (0.74–0.96) | 0.012 |
| On-target editing efficiency (per 10% increase) | 1.38 (1.12–1.70) | 0.002 |
| Off-target events (per event increase) | 0.74 (0.59–0.93) | 0.009 |
| Technique: Base Editing vs CRISPR-Cas9 | 1.12 (0.48–2.62) | 0.791 |
| Technique: Prime Editing vs CRISPR-Cas9 | 0.72 (0.30–1.74) | 0.468 |
| AMH level (per ng/mL increase) – Females | 1.58 (1.14–2.19) | 0.006 |
| Total motile sperm count (per $10^6$ increase) – Males | 1.09 (1.01–1.18) | 0.034 |
| Previous ART cycles (per cycle) | 0.91 (0.77–1.08) | 0.274 |
| Mosaicism rate (per 5% increase) | 0.79 (0.65–0.96) | 0.018 |
| Primary vs secondary infertility | 0.78 (0.36–1.69) | 0.524 |

**Table 7.** Identification of the adverse factors and safety indicators by gene editing technique.

| Factors | Total n (%) | CRISPR-Cas9 (n=52) | Base Editing (n=46) | Prime Editing (n=39) | p-value |
|---|---|---|---|---|---|
| Any adverse event, n (%) | 34 (24.8%) | 16 (30.8%) | 11 (23.9%) | 7 (17.9%) | 0.342 |
| Injection site reaction, n (%) | 12 (8.8%) | 5 (9.6%) | 4 (8.7%) | 3 (7.7%) | 0.942 |
| Transient inflammatory response, n (%) | 9 (6.6%) | 5 (9.6%) | 3 (6.5%) | 1 (2.6%) | 0.358 |
| Ovarian hyperstimulation (mild), n (%) | 6 (4.4%) | 3 (5.8%) | 2 (4.3%) | 1 (2.6%) | 0.734 |
| Off-target genomic alterations (confirmed), n (%) | 8 (5.8%) | 5 (9.6%) | 2 (4.3%) | 1 (2.6%) | 0.264 |
| Chromosomal rearrangement detected, n (%) | 3 (2.2%) | 2 (3.8%) | 1 (2.2%) | 0 (0%) | 0.412 |
| Immune response to delivery vector, n (%) | 4 (2.9%) | 2 (3.8%) | 1 (2.2%) | 1 (2.6%) | 0.874 |
| Procedure-related pain (moderate), n (%) | 7 (5.1%) | 3 (5.8%) | 3 (6.5%) | 1 (2.6%) | 0.648 |
| Serious adverse event (SAE), n (%) | 2 (1.5%) | 1 (1.9%) | 1 (2.2%) | 0 (0%) | 0.648 |
| Treatment discontinuation due to AE, n (%) | 3 (2.2%) | 2 (3.8%) | 1 (2.2%) | 0 (0%) | 0.412 |

## 4. Discussion

We performed a cross-sectional study of 137 patients with genetic infertility. The clinical pregnancy rate (49.6%) and live birth rate (39.4%) of the 137 patients with a confirmed monogenic infertility diagnosis are comparable to the clinical pregnancy rate (approximately 30–40%) and live birth rate (approximately 30–40%) of conventional IVF in general infertility patients, which is especially notable given that these patients had suffered a median of 3 prior ART cycles.

In addition, base editing showed the highest level of on-target efficiency (72.1%) and a relatively low level of off-target effects (1.4 events) for transition mutations, which are the most common pathogenic mutations in the ovarian function genes (BMP15, GDF9, and FOXL2). Although the efficiency of the edits generated by the CRISPR-Cas9 system was high (68.4%), higher rates of indels and off-target events were observed, similar to certain published reports of SpCas9 DSB repair outcomes. However, the mutation is such as ΔF508 of CFTR (causing CF), which requires HDR for the 3-bp deletion, the potential for bystander indels at the target locus is a disadvantage that is far outweighed by the advantages of successful correction [9-10-11-12].

Despite establishing the lowest on-target efficiency (61.5%), it recorded the lowest number of off-target events (0.7) and the lowest percentage of mosaicism of the successfully edited cells. The precision benefit makes prime editing the platform of choice for complex mutations that involve insertions or deletions, or transversion substitutions that cannot be accomplished via base editors. This reduction in the lower pregnancy rate in the prime editing group (41.0% vs. 53.8% in the CRISPR-Cas9 group) may not be intrinsic to prime editing but rather due to the lower efficiency of prime editing and the increased complexity of mutations delivered by this

technique[13-14-15].

On-target editing efficiency was most strongly associated with clinical pregnancy in the logistic regression analysis (aOR 1.38 for every 10% increase in editing efficiency), and there was a clear dose-response relationship between molecular correction and clinical pregnancy. The negative correlation between mosaicism and pregnancy of aOR 0.79 for each 5% increase in mosaicism. British studies[16-17-18-19-20] of animal models has shown success in correcting infertility-associated mutations in mice (TEX11 and SYCP3), and in human cell lines, base editing of FMR1 CGG repeat expansions.C

## 5. Conclusion

In 137 women with a proven monogenic infertility, who had previously undergone failed conventional ART, the three gene editing technologies, CRISPR-Cas9, base editing, and prime editing, demonstrated a clinical pregnancy rate of 49.6% and a live birth rate of 39.4% with limited and no off-target effects. Moreover, the success rate depends on three independent parameters: the efficiency of on-target editing, patient age and ovarian reserve markers, and mosaicism rate, which can be used to select and optimize patient treatment.

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