

The impact of BRCA pathogenic variants on reproductive outcomes in PGT cycles

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Introduction

BRCA1 and BRCA2 are tumor suppressor genes, and pathogenic variants (PV) in these genes impair double-strand DNA repair. Given that oocytes are especially susceptible to DNA damage, this impairment may reduce ovarian reserve, increasing the risk of early oocyte depletion and premature ovarian insufficiency. Previous studies have explored the reproductive outcomes in BRCA PV carriers with inconclusive results.

Methods

A retrospective case-control study of women who underwent PGT treatments with controlled ovarian stimulation followed by ovum pick-up at a tertiary IVF unit between 2012-2025.

Results

The study included 251 women who underwent a total of 529 IVF cycles. Among them, 120 were carriers of BRCA PV - 70 women with BRCA1 who underwent 190 cycles, and 50 with BRCA2 who underwent 141 cycles. The control group comprised 131 women who underwent 198 IVF cycles with PGT-M for monogenic diseases unrelated to ovarian reserve.

There were no significant differences between the study groups in women's and men's ages, BMI, protocol type, gonadotropin (GT) ingredient, or ovarian reserve parameters (AMH, AFC and FSH). Women with BRCA PV received a lower total median GT dose - 2425 IU [1666 - 3537] compared to the control group, who received 3000 IU [1906 - 4500] ($p < 0.01$).

The median number of retrieved oocytes was 13 [8 - 18] in BRCA PV carriers and 11 [7 - 19] in controls ($p = 0.5$). A Poisson mixed-effects regression adjusting for BRCA status, age, BMI, and infertility diagnosis found no significant association between BRCA status and the number of retrieved oocytes. Fertilization rate was significantly higher in the BRCA PV groups - 78.2% in BRCA1 carriers and 77.1% in BRCA2 carriers - compared to 67.2% in the control group ($p < 0.01$).

70 women of similar age underwent both PGTM and PGT-A; ten carried BRCA1 PV, seven carried BRCA2 PV, and the remaining 53 had other mutations. Aneuploidy rates were 46.4% for BRCA1, 29.1% for BRCA2, and 50.0% for the control group, with no significant difference.

Conclusion

This is the largest study on women carriers of BRCA PV, which found no evidence that carrying these mutations negatively affects ovarian reserve and IVF outcomes. The study confirmed that age significantly influences both oocyte retrieval and aneuploidy rates. Further studies are needed to support the results of this study due to its important clinical implications.

