The role of Whole Exome Sequencing (WES) in predicting PGT-M in high-consanguinity populations

V. Ferracuti, I. Elkhatib, R. Gonzales, H. Didar, A. Bayram, A. Abdala, N. Hourani, S. Siqueira, R. Del Gallego, H. Fatemi, D. Nogueira
ART Fertility Clinics, Abu Dhabi, UAE

Objective

To investigate what proportion of couples undergoing Whole Exome Sequencing (WES), stratified by couple characteristics, ultimately require PGT-M.

Materials and Methods

A retrospective cohort study including 2,356 IVF patients with definitive WES results treated at a tertiary referral IVF center between March 2020 and September 2025.

Couples undergoing IVF with WES followed by PGT-A and/or PGT-M were included. Consanguinity was classified as couple, female parental, or male parental (close, far, none). Associations with WES positivity were evaluated using descriptive analyses and multivariable penalized logistic regression.

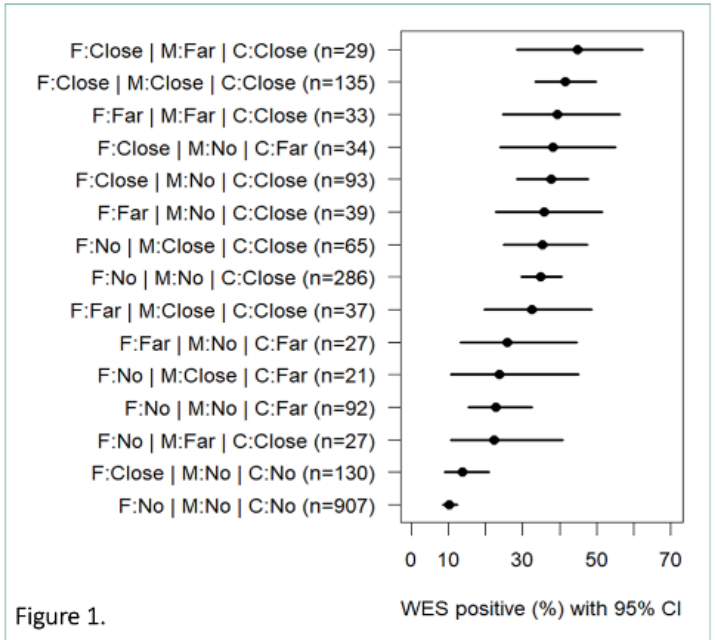

Figure 1.

Predictor	Contrast	Adjusted OR (95% CI)	P-value
Recurrent implantation failure	Yes vs No	0.97 (0.52–1.73)	0.923
Recurrent miscarriage	Yes vs No	1.07 (0.76–1.49)	0.709
Previous affected pregnancy	Yes vs No	17.8 (9.7–34.2)	<0.001
Couple consanguinity	Close vs No	7.26 (5.47–9.70)	<0.001
	Far vs No	4.24 (2.85–6.25)	<0.001
Female parental consanguinity	Close vs No	1.47 (1.09–1.98)	0.012
	Far vs No	0.98 (0.65–1.46)	0.917
Male parental consanguinity	Close vs No	1.02 (0.74–1.39)	0.910
	Far vs No	1.16 (0.76–1.75)	0.486

Table 1. Multivariable associations with WES positivity after adjustment for consanguinity and clinical indications

Results

Overall, 20.4% patients had WES-positive result, showing a strong gradient according to couple consanguinity: 10.0% in non-consanguineous couples, 27.7% in far-related couples, and 36.7% in close-related couples (Figure 1). Close couple consanguinity was the strongest independent predictor of WES positivity (Table 1), followed by far couple consanguinity. Female, but not male, parental consanguinity showed a modest independent association. Previous affected child was also strongly associated with WES positivity, whereas recurrent miscarriage and recurrent implantation failure were not.

Conclusion

Couple consanguinity should be prioritized in pre-WES counseling and IVF planning to optimize the use of PGT-M and more efficient genetic and embryology resource allocation in high-consanguinity regions. Incorporating population structure into reproductive genetic guidelines improves estimation of WES diagnostic yield and supports accurate counselling in regions with high consanguinity, while the 10.0% positivity rate in non-consanguineous couples highlights the broader clinical relevance of WES.

Poster number: L26/P-642

Contact: virginia.ferracuti@artfertilityclinics.com