

¹P. Kandavel, ¹A. Al Awadhi, ¹A. El-Khani, ¹A. Attia, ¹F. Al Marzooqi, ¹F. Aldhuhoori, ¹H. Wu, ¹H. Al Mabrazi, ¹H. Sajad, ¹I. Christy, ¹J. Quilez, ¹J. Mafofo, ¹K. Thangarajan, ¹O. Soliman, ¹S. Zhang, ¹S. Pejathaya, ¹T. Magalhaes, ¹V. Kusuma, ¹V. Kumar, ¹Y. Jahangir, ¹M. Ibrahim, ¹I. Eltantawy, ²W. M. Abdulrahman, ²H. H. Mohamed, ²S. M. Al Hosani, ²A. I. Al Mannaei, ²M. S. Al Ameri, ¹V. Zvereff

Affiliations:
1. M42, Abu Dhabi
2. Department of Health, Abu Dhabi

INTRODUCTION

- Premarital screening and genetic counseling (PMSGC) programs aim to identify carriers of genetic disorders to reduce the risk of transmitting disease-causing variants to offspring.
- Many programs across world focus on a limited set of genetic conditions.
- The United Arab Emirates (UAE) has expanded its PMSGC efforts through the Emirati Genome Program (EGP), utilizing whole-genome sequencing (WGS) to screen for over 840 genetic disorders.

METHODS

- We developed an analysis pipeline that processes variant call sets from 30X WGS data of couples, focusing on SNPs, Indels and CNVs in 570 genes linked to autosomal recessive disorders.
- We combined the genotypes of each couple to identify variants of concern associated with pathogenic or likely pathogenic genetic variants, based on ClinVar primarily with help of HGMD annotations.

The Emirati Genome Program has upgraded premarital screening in the United Arab Emirates to cover over **840 genetic disorders**.

More than **1,000 couples** have been screened and **11% couples at risk** of passing one of those genetic disorders to their offspring have been counseled.

Premarital screening Workflow



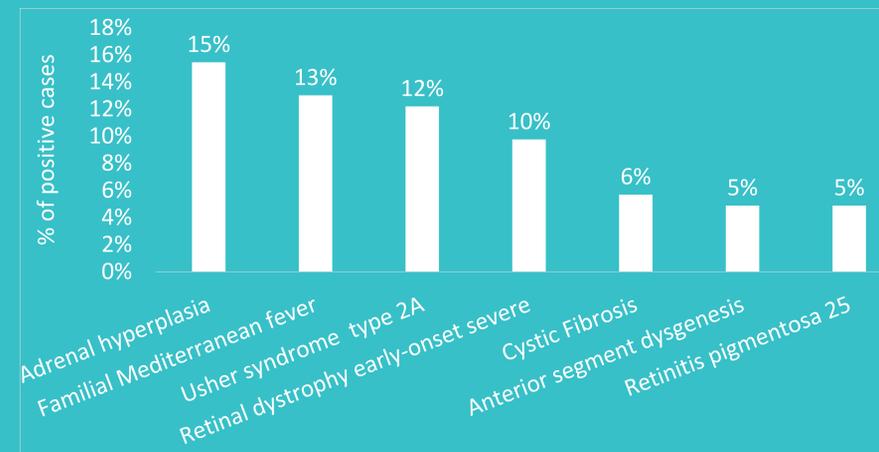
Significances of premarital screening in UAE:

- The automated bioinformatics framework reduces 88.2% of manual review effort
- The screening provides the insight on top diseases cause and respective genes due to consanguinity in UAE
- 400 couples are expected to benefit per month – in total, there are approximately 10,000 marriages per year in Abu Dhabi
- Premarital genetic screening helps to pave the way for healthier future generations by allowing couples to make informed decisions regarding their marriage and future family planning

Automated reporting status



Most prevalent diseases in positive couples



Most prevalent genes in positive couples



RESULTS

- We found ~11% of couples carrying pathogenic variants and reported as positive.
- >88% of couples were reported directly as negative (i.e. no risk), greatly reducing the manual review effort.
- We estimated the positive rate under random mating to be 8.5% from simulations based on 1,000 permutations of sex-matched random pairings.

BENEFIT AND APPLICATIONS

- PMSGC in the UAE identifies at-risk couples and expands as genomic research progresses.
- The EGP program empowers couples to make informed decisions regarding their marriage and family planning.
- It aims to reduce the burden of genetic disorders in future generations.
- This approach improves public health and lowers healthcare costs related to genetic diseases.

Acknowledgements

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