EDITORIAL

Premarital genetic screening for healthy couples: advantages and challenging

³ Majid Alfadhel¹

4 Premarital genetic screening (PGS) refers to the procedure
5 whereby couples are tested for genetic abnormalities
6 before marriage in order to determine the likelihood
7 that their future children may inherit certain genetic
8 conditions. This screening can lower the prevalence of
9 genetic illnesses and assist potential parents in making
10 educated reproductive decisions (1).

Some countries started adopting premarital genetic 11 screening; however, most of the PGS is done in private 12 clinics and laboratories. The method of PGS varies 13 according to the genetic laboratory. Some genetic 14 laboratories offer gene panels for certain genetic disorders, 15 others offer whole exome sequencing (WES) or whole 16 genome sequencing (WGS) for couples and detect the 17 18 shared pathogenic, likely pathogenic, and even variant of 19 uncertain significance (VOUS) in some laboratories. The American College of Medical Genetics recommends 20 adopting a more precise gene panel system based on 21

carrier frequency as the appropriate approach, in addition 22 23 to recommending not testing variants and instead testing 24 the entire gene (2). Interestingly, they do not recommend 25 doing WES or WGS for the couple most likely to avoid VOUS. Additionally, they endorse that Carrier screening 26 paradigms should be ethnic and population-neutral and 27 more inclusive of diverse populations to promote equity 28 and inclusion. Furthermore, they recommend that all XX 29 individuals should be offered carrier screening for the 30 following X-linked genes: ABCD1, AFF2, ARX, DMD, 31 F8, F9, FMR1, GLA, L1CAM, MID1, NROB1, OTC, 32 PLP1, RPGR, RS1, and SLC6A8 (2). 33

Among PGS's benefits are: couples can make well-informed 34 decisions for their marriage, evaluate the likelihood of 35 having a child with specific genetic abnormalities, and 36 take preventive actions like prenatal genetic testing or 37 preimplantation genetic diagnosis. Nevertheless, the PGS 38 39 has certain drawbacks, such as psychological impact, stigmatization, false positive and negative results, and a rise 40 in the number of spinsters (3). The PGS should, in all cases, 41 be optional rather than mandatory, and the couple should 42 be informed of the test's advantages and disadvantages. It 43 is possible that not all of the genes that cause a condition 44 are known or examined, that the causative variants are in 45 a region that isn't included in the test, that the technology 46 can't detect the causative variants, that the analysis of the 47 gene sequence and its structural variants is technically 48 challenging, and that the variants are misclassified in 49

terms of pathogenicity (e.g., laboratory's algorithm for 50 classification of variants) (2). Both before and after PGS, 51 education and counseling are essential. 52

As a result of improved molecular genetic testing and 53 public knowledge, PGS usage has grown over the past 54 10 years. Although it has many benefits, it could also be 55 harmful. As a result, education and counseling are essential 56 both before and after PGS, and PGS ought to be optional 57 rather than required. A global collaboration approach 58 between clinical geneticists and molecular geneticists will 59 help to make PGS more useful in the coming decade. 60

Author details

Majid Alfadhel¹

 1. Genetics and Precision Medicine Department (GPM)
 63

 and Medical Genomic Research Lab, King Abdullah
 64

 International Medical Research Centre(KAIMRC), King
 65

 Saud Bin Abdulaziz University for Health Sciences, Ministry
 66

 of National Guard Health Affairs (MNGHA), King Abdulaziz
 67

 Medical City, Riyadh, Saudi Arabia
 68

References

- Bener A, Hussain R. Consanguineous unions and child 70 health in the State of Qatar. Paediatr Perinat Epidemiol. 71 2006;20(5):372–8. https://doi.org/10.1111/j.1365-72 3016.2006.00750.x 73
- Gregg AR, Aarabi M, Klugman S, Leach NT, Bashford MT, 74 Goldwaser T, et al. Screening for autosomal recessive and 75 X-linked conditions during pregnancy and preconception: 76 a practice resource of the American College of 77 Medical Genetics and Genomics (ACMG). Genet Med. 78 2021;23(10):1793–806. https://doi.org/10.1038/s41436-021-01203-z 80
- YuFei Q. Genetic testing in premarital screening: 81 assessing hereditary risks. Midway Medical [cited 2025 82 May 20]. Available from: https://mediwaymedical.com/ 83 genetic-testing-in-premarital-screening 84

Correspondence to: Majid Alfadhel

*Genetics and Precision Medicine Department (GPM) and Medical Genomic Research Lab, King Abdullah International Medical Research Centre(KAIMRC), King Saud Bin Abdulaziz University for Health Sciences, Ministry of National Guard Health Affairs (MNGHA), King Abdulaziz Medical City, Riyadh, Saudi Arabia **Email:** dralfadhelm@gmail.com

OPEN ACCESS This is an open access article distributed in accordance with the Creative Commons Attribution (CC BY 4.0) license: https://creativecommons.org/licenses/by/4.0/) which permits any use, Share — copy and redistribute the material in any medium or format, Adapt — remix, transform, and build upon the material for any purpose, as long as the authors and the original source are properly cited. © The Author(s).

61

62

69