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EDITORIAL

Premarital genetic screening for healthy couples: advantages and challenging

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

Some countries started adopting premarital genetic screening; however, most of the PGS is done in private clinics and laboratories. The method of PGS varies according to the genetic laboratory. Some genetic laboratories offer gene panels for certain genetic disorders, others offer whole exome sequencing (WES) or whole genome sequencing (WGS) for couples and detect the shared pathogenic, likely pathogenic, and even variant of uncertain significance (VOUS) in some laboratories.

The American College of Medical Genetics recommends adopting a more precise gene panel system based on carrier frequency as the appropriate approach, in addition to recommending not testing variants and instead testing the entire gene (2). Interestingly, they do not recommend doing WES or WGS for the couple most likely to avoid VOUS. Additionally, they endorse that Carrier screening paradigms should be ethnic and population-neutral and more inclusive of diverse populations to promote equity and inclusion. Furthermore, they recommend that all XX individuals should be offered carrier screening for the following X-linked genes: *ABCD1*, *AFF2, ARX, DMD, F8, F9, FMR1, GLA, L1CAM, MID1, NROB1, OTC, PLP1, RPGR, RS1, and SLC6A8* (2).

Among PGS's benefits are: couples can make well-informed decisions for their marriage, evaluate the likelihood of having a child with specific genetic abnormalities, and take preventive actions like prenatal genetic testing or preimplantation genetic diagnosis. Nevertheless, the PGS has certain drawbacks, such as psychological impact, stigmatization, false positive and negative results, and a rise in the number of spinsters (3). The PGS should, in all cases, be optional rather than mandatory, and the couple should be informed of the test's advantages and disadvantages. It is possible that not all of the genes that cause a condition are known or examined, that the causative variants are in a region that isn't included in the test, that the technology can't detect the causative variants, that the analysis of the gene sequence and its structural variants is technically challenging, and that the variants are misclassified in terms of pathogenicity (e.g., laboratory's algorithm for classification of variants) (2). Both before and after PGS, education and counseling are essential.

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

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