EDITORIAL

GENETICS AND ISCHEMIC HEART DISEASE: SHOULD WE OPT FOR GENETIC TESTING FOR PRIMARY PREVENTION?

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Cardiovascular diseases (CVD) are a prevalent health concern within the general population of Pakistan, where the average lifespan is notably lower than the global average, with men typically living to 67 years and women to 69 years. According to the 2019 Global Burden of Disease study, Pakistan had an estimated age-standardized incidence rate of CVD at 918.18 per 100,000 (compared to the global rate of 684.33 per 100,000), along with an age-standardized death rate of 357.88 per 100,000 (globally, this rate is 239.85 per 100,000).[1]

Coronary heart disease (CHD), as revealed by the Framingham Heart Study focusing on individuals aged 40 to 94 without prior heart disease, displayed a lifetime risk of 49% for men and 32% for women when reaching the age of 40.[2]

There has been a declining trend in death rates in the United States attributed to CVD, CHD, and stroke since 1975. Data from 2000 to 2008 also indicate a decline in CHD mortality.[3]

Worryingly, the World Health Organization (WHO) reports a concerning rise in CHD-related fatalities in Pakistan. In 2020, 240,720 individuals died due to CHD, accounting for 16.49% of all deaths. This highlights an escalating trend of CHD-related mortality in Pakistan. It's important to note that most individuals presenting with cardiac events have one or more established or borderline risk factors aside from age and gender.[4-6]

While some essential risk factors are discernible, others may remain elusive. The screening of these risk factors and the evidence for targeted therapeutic interventions are still emerging and require further exploration.[7]

The starting point for assessing CVD risk factors is variables used to predict major cardiovascular events. These include age, sex, blood pressure, cholesterol levels, diabetes mellitus, and smoking status. Although risk assessment tools like the Pooled Cohort Equation in 2014 and Astro-CHARM have been developed, they have yet to provide satisfactory assessments for potential new CVD risk factors.[8]

CHD is recognized as a multifactorial disorder resulting from genetic and environmental factors interplay. Environmental risk factors have been identified in approximately 80% of CHD cases.[9] Several risk scores, such as the Framingham Risk Score, PROCAM, Reynolds Risk Score, and QRISK 2, have been proposed to guide the use of statins in high-risk groups.[10-14] Yet, these risk scores often lack precision and may either overestimate or underestimate future CHD events.[15,16]

The variation in disease susceptibility among individuals with similar environmental factors and conventional coronary artery disease risk factors (CRFs) may be attributed to genetic variations.[17] Genetic analysis can potentially enhance risk discrimination beyond the consideration of CRFs alone. Family history of heart disease, accounting for more than 40% of risk estimation, has long been considered a part of CRFs.[18] Candidate gene studies have been conducted to identify common variants in genes associated with disease pathways.[19] Single-nucleotide polymorphisms (SNPs) have been employed as markers of genetic diversity. Among these SNPs, those located on the 9p21 locus have shown the strongest association with CHD risk to date.[20,21] However, despite the clear link between these variants and incident CHD, 9p21 locus SNPs have not definitively improved the prediction or classification of CHD risk compared to traditional risk factors.[22-24]

It is important to note that most genetic studies on CHD have predominantly focused on European/Caucasian populations, and their applicability to the South Asian population, including Pakistan, requires further investigation.[25,26] In this context, the Pakistani population, much like other Asian countries, is underrepresented in genetic research on CHD. Shahid SU et al. did some work in this respect,[27] showing 21 SNPs risk score for genetic risk analysis in the Pakistani population.

In conclusion, while different risk assessment tools have been developed for the Pakistani population aged 40 years and above, there is an urgent need to expand cardiac risk evaluation by identifying genetic markers related to CHD, particularly in the younger population. This will be crucial for advancing our understanding

of CHD risk factors and developing more effective prevention and intervention strategies.

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