Editorial

Genetic Counselling and Genetic Diseases

Ali Muhammad Waryah

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Pakistan has over 200 million people with rich ethnic diversity, showing significant social and cultural differences from the Kashmir Mountains to the shores of interior Sindh. This variation has divided the population into tribes and isolated clusters of people strongly bonded with their specific customs and trends. The familial obligations in the population have resulted in a well-differentiated cast system, having distinct genetic lineages. The social and economic influences advocate and propagate the custom of inter -family and inter-cast marriages. Consanguineous marriages are more common in Pakistan when compared to other world populations[1]. The global prevalence of consanguineous marriages is around 10%, whereas 73% of marriages in Pakistan are consanguineous and 80% among first cousins[1-3].

Despite the conserved nature of the local Pakistani population, genetically, it is a mixture of various world populations. Diverse ethnic and linguistic based tribes and clans of Pakistan share genetic links with west Asians, East Asians, Europeans and African people, including Turkey, Iran, Azerbaijan, Georgia, Lebanon, Armenia, Syria, Jordan, Iraq, United Arab Emirates, Qatar, Kuwait, Saudi Arabia, Cyprus, Oman, Yemen, China, Hong-Kong, Macau, Taiwan, Mongolia, Japan, North Korea and South Korea[4-7]. This genetic admixture has made it possible to identify multiple alleles and novel genes by recruiting patients from a single population and findings having a global impact. The discovery of novel genes is crucial to understanding the mechanism of the diseases and finding a better treatment and disease management option.

It is well-discussed that genetic variants associated with diseases show ethnic biases[8,9]. Many disease-causing alleles are found explicitly in certain ethnic groups. Such as, IVS 1-5 in *the HBB* gene causing autosomal recessive thalassemia is more common in patients with the Balochi ethnic group, and Del619 is specific to the Memon community of the Karachi[10]. The most frequent *GJB2* gene variant, W24X, causing autosomal recessive deafness, is characteristically found in patients with Indian sub-continent origin[9,11]. Similarly, G61E is a common pathogenic variant of the *CYP1B1* gene, causing primary congenital glaucoma in patients with Arab lineages; alternatively, R390H is commonly found in PCG patients with Pakistani and Indian ethnicities[12-14]. The racial and ethnic biases of disease-causing genetic variants have obligated the need for the categorization of pathogenic mutations based on ethnic groups and different casts of the local population. Identifying disease-causing variants in other clans and isolates of the population is essential as providing genetic counselling to manage and curtail disease propagation in inbred families.

Due to the prominent custom of consanguineous marriages in Pakistan, autosomal recessive disorders are more common than autosomal dominant disorders, whereas fewer x-linked recessive disorders have been reported[15]. Several genetic diseases with variable frequency have been diagnosed in the Pakistani population, but some conditions are more frequent. The highest frequency of Thalassemia, 5.0-7.0%, with over 10 million carriers in the Pakistani people, has been reported [16]. Secondly, recessive hearing loss affects 1.6 in 1000 individuals and shows variable phenotypic presentations due to the involvement of multiple genes and alleles. The treatment options for inherited disorders are minimal; gene therapy and gene editing by crispercas9 are still in the initial stage and may not cater to all the genes of a specific disease in any population. In this scenario, genetic counselling is the only hope for large consanguineous families, which are bound to continue marriages within the same ethnic group or clan due to social compulsions.

A genetic counsellor may attempt to convey scientific facts of inheritance to affected families in layperson's language. If a disease-causing mutation is known, the marriage of two affected with the same mutation may be avoided, and an entire generation may be rescued from permanent disability. On the other hand, two affected with a mutation in different genes may get knotted, and all their offspring may have a normal phenotype. Identification of carriers is also crucial in recessive disorders; the marriage of two carriers may be discouraged, and the chance of being affected might be zero. Arrangement of marriages after genetic counselling among patients; may lead to normal children in the next generation. The families affected with genetic diseases may arrange marriages within the family and prevent disease in the coming generation after successful mutation screening and genetic counselling.

REFERENCES

1. Bhinder MA, Sadia H, Mahmood N, Qasim M, Hussain Z, Rashid MM et al. Consanguinity: A blessing or menace at population level? Review. *Ann Hum Genet*. Jul 2019; 83(4): 214-219. doi:10.1111/ahg.12308. Epub 2019 Mar 19.
2. Sharma SK, Kalam MA, Ghosh S, Roy S.

Prevalence and determinants of consanguineous marriage and its types in India: evidence from the National Family Health Survey, 2015-2016. *J Biosoc Sci*. 2021 Jul; 53(4): 566-576. doi:10.1017/S0021932020000383.
3. Hina S, Malik S. Pattern of Consanguinity and Inbreeding Coefficient in Sargodha District, Punjab, Pakistan. *J Biosoc Sci*. 2015 Nov; 47(6): 803-11. doi:10.1017/S0021932014000431
4. Pigeyre M, Saqlain M, Turcotte M, Raja GK, Meyre D. Obesity genetics: insights from the Pakistani population. Systematic Review. *Obes Rev*. 2018 Mar; 19(3): 364-380. doi:10.1111/obr.12644.
5. Anwar I, Hussain S, Rehman AU, Hussain M. Genetic variation among the major Pakistani populations based on 15 autosomal STR markers. *Int J Legal Med*. 2019 Jul; 133(4): 1037-1038. doi:10.1007/s00414-018-1951-0.
6. Mohyuddin A, Ayub Q, Underhill PA, Tyler-Smith C, Mehdi SQ. Detection of novel Y SNPs provides further insights into Y chromosomal variation in Pakistan. *J Human Genet*. 2006; 51(4): 375-378. doi:10.1007/s10038-005-0357-2.
7. Qamar R, Ayub Q, Mohyuddin A, Helgason A, Mazhar K, Mansoor A, et al. Y-chromosomal DNA variation in Pakistan. *Am J Human Genet*. 2002 May; 70(5): 1107-24. doi:10.1086/339929.
8. Sheikh SA, Waryah AM, Narsani AK, Shaikh H, Gilal IA, Shah K et al. Mutational spectrum of the CYP1B1 gene in Pakistani patients with primary congenital glaucoma: novel variants and genotype -phenotype correlations. *Mol Vis*. 2014; 20: 991-1001.
9. Shaikh H, Waryah AM, Narsani AK, Iqbal M, Shahzad M, Waryah YM et al. Genetic Testing of Non-familial Deaf Patients for CIB2 and GJB2 Mutations: Phenotype and Genetic Counselling. *Biochem Genet*. 2017 Dec; 55(5-6): 410-420. doi:10.1007/s10528-017-9828-3.
10. Ansari SH, Shamsi TS, Ashraf M, Bohray M, Farzana T, Khan MT et al. Molecular epidemiology of beta-thalassemia in Pakistan: far reaching implications. *Int J Mol Epidemiol Genet*. 2011; 2(4): 403-8.
11. RamShankar M, Girirajan S, Dagan O, Ravi Shankar HM, Jalvi R, Rangasayee R et al. Contribution of connexin26 (GJB2) mutations and founder effect to non-syndromic hearing loss in India. *J Med Genet*. 2003 May; 40(5): e68. doi:10.1136/jmg.40.5.e68.
12. Waryah YM, Iqbal M, Sheikh SA, Baig MA, Narsani AK, Atif M et al. Two novel variants in CYP1B1 gene: a major contributor of autosomal recessive primary congenital glaucoma with allelic heterogeneity in Pakistani patients. *Int J Ophthalmol*. 2019; 12(1): 8-15. doi:10.18240/ijo.2019.01.02.
13. Souzeau E, Hayes M, Ruddle JB, Elder JE, Stafferi SE et al. CYP1B1 copy number variation is not a major contributor to primary congenital glaucoma. *Mol Vis*. 2015; 21: 160-4.
14. Badeeb OM, Micheal S, Koenekoop RK, den Hollander AI, Hedrawi MT. CYP1B1 mutations in patients with primary congenital glaucoma from Saudi Arabia. *BMC Med Genet*. 2014; 15: 109. doi:10.1186/s12881-014-0109-2.
15. Waryah AM, Ahmed ZM, Bhinder MA, Choo DI, Sisk RA, Shahzad M et al. Molecular and clinical studies of X-linked deafness among Pakistani families. *J Human Gen*. 2011 Jul; 56(7): 534-40. doi:10.1038/jhg.2011.55.
16. Khaliq S. Thalassemia in Pakistan. *Hemoglobin*. 2022 Jan; 46(1): 12-14. doi:10.1080/03630269.2022.2059670.

AUTHOR AFFILIATION:

Prof. Dr. Ali Muhammad Waryah
Department of Molecular Biology & Genetics
Liaquat University of Medical & Health Sciences
Jamshoro, Sindh-Pakistan.
Email: aliwaryah@lumhs.edu.pk