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EDITORIAL

Geomapping genetic diseases in KSA, the opportunity and challenges

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Editorial

The Kingdom of Saudi Arabia (KSA) is the focal point of the Arab and the source of its tribes. With a population of twenty million, it is among the Arab countries which are most affected by various devastating inherited diseases. Those diseases undoubtedly affect the future health plan for families and society in addition to forceful consequence on national health expenditure. As a result, a major KSA 2030 vision pronounce clear statement in preventing those widely spread diseases and invest in providing the best medical services in protection and prevention. Seventeen years back, the Ministry of Health (MOH) initiated a very prosperous national program that provides premarital screening and genetic counseling to control the high prevalence of hemoglobinopathies that constitutes significant burden in health system. However, it only includes sickle cell anemia and thalassemia. It is now obvious that the high rate of intra-tribal consanguineous marriages significantly causes those two diseases but also majority of other genetic disorders that exemplified in numerous inherited metabolic disorders (IMD) (1). The IMD was the second successful target for MOH that is now detected partly by the National Newborn Screening Program.

According to March of Dimes (www.marchofdimes.org), KSA ranked second in terms of the prevalence of birth defects, with hundreds of genetic disorders reported in the last 20 years' research papers. In addition to IMD, it also has high frequencies of naive neuro-degenerative, ciliopathies, and numerous skeletal dysplasias. Furthermore, unrecognized rare congenital renal, immune and hepatic disorders have been recognized as widely spread in many regions.

National research studied the cohort at large specialized hospitals in KSA (Riyadh), and documented more than 150 neurodegenerative diseases; majority of them are recessive disorders attributed to consanguinity and primarily follow the same clinical features indeed it caused by the same gene mutation "founder mutation". This genetic alteration is observed with high frequency in a specific geographically or culturally isolate society where one or more of the ancestors were a carrier of the altered gene. KSA is considered as a top country in this phenomenon and some of these founder mutations are tribal-specific. For example, G187X mutation in *SLC26A3* "non-else" appears to be an Arab founder mutation causing very common hereditary diarrheal disease called familial chloride diarrhea. Other recent examples include an ancestral founder mutation in *ADAT3* (Val144Met), *CYP2U1* (Asp316Val), and *ISCA2* (Gly77Ser) gene mutations.

Many observational genetic cohort studies confirmed this phenomenon even in very orphan and newly published diseases and dysplasias, hence endorsing the practice for doing diagnostic target gene testing for quick and cheaper screening instead of more expensive genetic and genomic analysis like whole exome sequence.

National research studies on the diversities of genetic diseases and its demography have been performed in a very limited number. Alowain et al. [2] plotted the first published founder mutations geomap from KSA and came up with mutation and their geographical distribution. Indeed, he provided very useful preliminary mutational landscape of autosomal recessive disorders in KSA population. More recent article by Monies et al. [3] confirmed the notion of disease caused by recessive mutations being the major finding in all diagnostically 2200 patient cohort. They were able to unravel more than 75% of cases, in whom 40% are recurrent "founder" mutation in different independent families.

Having the leading and robust science capability, King Abdulaziz City for Science and Technology has the largest stored genome data for Saudi population. However, it so far utilized for research only and it lacks the clinical correlation and individual disease/health detailed characteristics. On the other side, tertiary referral hospitals start to attain the genomic technologies and build patient's genomic database, but with limited volume and feeble bioinformatics capacity and capability. Hospitals with capacity of doing clinical next generation sequencing like King Abdulaziz Medical City (at National Guard), King Faisal Specialist Hospital and King Fahad Medical City are regress with many logistics and ethical limitation that halt potential collaborative clinical works.

Ideally, national effort for molecular characteristics of severe "common" inherited disorders should be set up

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through collaborations between research centers located in hospitals with close clinical connection and from various regions to create a well-documented molecular data bank. This mutual effort should aim to establish data bank that can be utilized to develop a carrier screening tests like newborn screening as well as premarital screening. This definitely is going to prime for the best treatment and prevention health strategies. All patient's data should be well-defined clinically, radiologically, biochemically, or enzymatically for better annotating those variants that puzzle any genomic profiling. Once complete, the initial draft of the emerging and comprehensive databank should work as a source for guanine clinical and diagnostic purposes. Hence, it will work as cost-effective tool to reduce expenditure and minimize outsourcing expensive genetic/genomic investigation. By establishing and implementing this Clinical Genomic DataBank, we hope to serve as a model for customizing diagnostic genetic testing and work as expandable national bank for institutions and diagnostic laboratories.

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