Genetics of stroke in Qatar: Current situation and future opportunities

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ABSTRACT

Recent studies have shown that genetic factors may play an important role in the pathogenesis of stroke, as known modifiable and non-modifiable risk factors may account for only 50% of the risk of stroke. Evidence for a genetic basis can be elucidated from twin studies, family history studies, and animal models. Qatar is currently leading the stroke initiative in the Gulf region with a view toward joining the genomic revolution. In collaboration with a team of scientists from Royal Holloway College, University of London, and Imperial College London, we took the initial step in this field by establishing the first biorepository of deoxyribonucleic acid in stroke in the Middle East. In this review, we describe our current situation in the field of stroke genetics with an exploration of future opportunities.

Key words: Genetics, Hamad Medical Corporation, Qatar Foundation, Stroke

Stroke is a leading cause of death, accounting for 11.13% of total deaths and the main cause of disability worldwide [1]. Stroke is divided into hemorrhagic and ischemic strokes. Approximately 85% of all strokes are ischemic, mainly caused by acute thromboembolic occlusion of intracranial arteries. Several conditions are known as "risk factors" have been identified that increase a person's risk of primary or recurrent stroke. Established risk factors for stroke include age, history of cerebrovascular events, smoking, alcohol consumption, physical inactivity, hypertension, dyslipidemia, diabetes mellitus, cardiovascular diseases, obesity, metabolic syndrome, diet, and nutrition [1,2]. The frequency of these risk factors varies from country to country, with hypertension and diabetes mellitus being the most common. However, the incidence of such factors also varies among individual patients, which leads to the question as to why do patients without well-established risk factors still suffer from stroke?

Genetic factors may play an important contributing role in the pathogenesis of stroke. Evidence for a genetic basis can be elucidated from twin studies [3,4], family history studies [5,6], and animal models [7,8]. Human genetic association studies in stroke have identified a considerable number of candidate genes that are associated with stroke [9,10]. However, while stroke may be the clinical outcome of a number of single-genes, it is more commonly thought to be a polygenic multifactorial disease [11]. The breakthrough in whole-genome analysis technologies together with the improvement of bioinformatics has improved our understanding of the functioning of genes and their variants. However, such advances in knowledge still require large-scale collaborative studies with rigorous design and phenotyping. In the state of Qatar, we achieved our first step in this field by establishing the first bio-repository of deoxyribonucleic acid (DNA) in stroke in the Middle East by collaborating with a team of experts from the Royal Holloway College University of London and Imperial College London, United Kingdom. In this article, we describe our current situation in the field of stroke genetics with an exploration of future opportunities.

GENETIC RESEARCHES IN QATAR

Qatar is currently leading the stroke initiative in the Gulf region with a view toward joining the genomic revolution. The Qatari government has encouraged genetic research by investing in research infrastructure to provide institutes with advanced facilities for genetic research activities to study, and possibly treat, some of the genetic disorders that affect their society [12].

Qatar Foundation (QF)

The QF is the main scientific body in Qatar that was founded in 1995 to serve the people of Qatar by supporting and operating programs in three core mission areas: education, science and research, and community development. QF Research, Development, and Innovation (QF RDI) is a division of QF that is responsible for supporting and funding different kinds of research activities through the following entities: Qatar Science and Technology Park, Qatar Biobank for Medical Research, Qatar Genome Programme, Qatar Biomedical Research Institute,

Sidra Medicine, Doha International Family Institute, and World Innovation Summit for Health [12,13].

Shafallah Centre for Children with Special Needs

It is one of the early established research bodies in Qatar. It was founded in 1999 for the welfare of people with intellectual disabilities, mainly autism spectrum disorders. The center provides both clinical genetic and molecular diagnostic services in addition to conducting both independent and collaborative research projects [12,13].

Hamad Medical Corporation (HMC)

Since 2002, HMC has also been the main provider of clinical and metabolic genetic services for the population of Qatar [13].

HIGHLY CHARACTERIZED DNA REPOSITORY OF ISCHEMIC STROKE IN QATAR ASTHE FIRST STEP TOWARD JOINING THE GENOMIC REVOLUTION

Our first step toward joining the global genomic revolution was achieved upon successfully obtaining approval from the Qatar National Research Fund for our research grant proposal entitled "Highly characterized DNA repository of ischemic stroke in Qatar." We became part of an international multicentre study called BRAINS (Bio-Repository of DNA in Stroke) which aimed to investigate the influence of genetic factors on stroke risk in European, South Asian, and Qatari populations and to explore the genetic differences between these ethnicities [14]. This project was designed initially to involve patients with ischemic stroke. However, we extended our objectives later to include all stroke victims, ischemic as well as hemorrhagic (intracerebral hemorrhage), through further new grant research entitled "Creating a Qatari Centre of Excellence in Stroke Genetics." Our projects started in May 2014 and were completed in May. 2018. During this period, we have achieved many tasks. Local interested researchers were oriented in stroke genetics as well as being trained on the principles of laboratory of genetics, especially, human blood DNA extraction. We recruited patients of all nationalities who developed strokes during the study period. Blood samples were collected and detailed data such as demographic and socioeconomic data, cardiovascular risk factors, stroke classification, functional stroke status (Barthel index score), and brain images were recorded from stroke patients prospectively. We recruited the targeted 1500 patients, and a blood sample from each subject was stored in a dedicated –80°C freezer. DNA extraction was performed in HMC genetic laboratory and a high-molecular-weight genomic DNA was obtained. All patients were followed for 1 year, and their gene extracts were stored at the genetic laboratory in a –80°C refrigerator until we will start the most important next phase of our project, which will be the analysis of this unique wealth of demographic and genetic data. We are aiming to establish the first biobank for stroke patients in Qatar and the Middle East.

FUTURE OPPORTUNITY

After completion of the first grant, my team has gained excellent experience in this difficult field and is confident to continue the work by applying for our next research grant proposal, "Progressing the Qatari Center of Excellence in Stroke Genetics." This grant will include conducting a genome-wide association study to determine genetic loci among our stroke patients that act as predisposing factors for stroke and ultimately designing drug targets to treat stroke in Qatar. In order to facilitate direct translational research on stroke, this wealth of demographic data and blood samples will be used to establish the first biobank in Qatar. This biorepository is unique in the Middle East; it will place Qatar at the forefront of the genetics revolution and may potentially create population-specific pharmaceutical interventions. It is critical that the hard work and funding that have been spent on the biorepository now allow it to be analyzed.

CONCLUSION

Qatar is currently leading the stroke initiative in the Gulf region with a view toward joining the genomic revolution. Our first step toward joining the global genomic revolution was achieved upon working as a part of an international multicentre study called BRAINS, and a high-molecular-weight genomic DNA was obtained. We will be entering the next most important phase of our project, which will be the analysis of this unique wealth of genetic data once our next grant is approved.

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