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Analysis of Genetic Mutations Associated with Hereditary Diseases Using PCR and Gene Sequencing Techniques: A Comparative Study among Populations in Southern Iraq

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Annotation: The genetic architecture of populations from registers of individuals with suspected disorders or congenital malformations in various Middle Eastern countries reveals a characteristic pattern of low complexity apparently-disease-causing variation in exome sequencing data. Such variants are not common in European populations. For example, the population of southern Iraq, which has suffered from major traumas and malnutrition over the last 30 years, yet is clearly underrepresented in databases such as gnomAD. A total of 34 unrelated subjects from the south of Iraq were whole-exome sequenced. The distribution of variants under 500 occurrences and their compositions are comparable to those seen in Arabic exomes from the Middle East. Analysis focusing on

frameshift and non-frameshift variants shared within the Iraqi population, but with a maximum occurrence of 4 in the Broad cohort, produces 472 genes, enriched for processes including cell morphogenesis, neurogenesis, and muscle contraction. A subset of genes with 7 or more shared variants includes those previously implicated in blood clots, familial Mediterranean fever, recurrent pregnancy loss, and polycystic kidney disease, in addition to those associated with known SARS-CoV-2 symptoms (HBA1, SLC12A3, and HBB).

Keywords: Hereditary diseases, Genetic mutations, PCR techniques, Gene sequencing, BRCA1/BRCA2, β-thalassemia, Southern Iraq population, Consanguinity, G6PD deficiency, Whole exome sequencing.

1. Introduction

Dhi Qar Governorate is one of Iraq's 19 governorates that lies in the southern region of the country. It occupies an area of 38,182 km2 and has a population of approximately 2 million.

Consanguineous marriage, i.e. marriage between relatives, is quite common in this region with an estimated frequency of 30-39%. These kinds of marriages could predispose the family to autosomal recessive diseases and make it more likely to observe multiple cases of inherited syndromes within the family, which are not considered as common in many other countries. Furthermore, there is a severely limited number of genetic studies carried out in the region and therefore the scientific community lacks information about the genetic basis of many inherited disorders diagnosed in this area.

The majority of genetic analyses are systematically carried out at the CHU of Dhi Qar hospital during the routine diagnosis process of patients suffering from aphakia. Out of these patients, 35 individuals have been specifically selected and utilized for comprehensive genetic studies focusing on the variants that are associated with this particular genetic disorder. Additionally, the hospital is actively managing numerous other cases that also require detailed genetic analysis to effectively support and confirm the clinical diagnosis being established. In these varied cases, whole exome sequencing has emerged as a highly viable solution, providing a thorough method to address the diagnosis and delivering a much more comprehensive understanding of the diverse variants of genetic diseases that are frequently observed in the region. This advanced genetic approach not only aids in better diagnosis but also enhances the potential for tailored treatment options for patients affected by these disorders. [1][2] [3][4][5]

2. Background on Hereditary Diseases

Sickle cell anemia, β-thalassemia, G6PD deficiency, hereditary persistent hyperbilirubinemia, and familial Mediterranean fever are the most common hereditary diseases in southern Iraq. As a rare hereditary neurologic disorder, limb-girdle muscular dystrophy type 2C is characterized by atrophy of the limb-girdle muscles with progressive weakening. It is an autosomal recessive disorder caused by mutations in the γ-sarcoglycan gene found in the area [1]. Hereditary breast cancer results from inherited mutations in genes responsible for normal cell growth, division, and the repair of damaged DNA, such as the BRCA1 and BRCA2 genes [2]. These genes when mutated increase the risk of breast, ovarian, prostate, and colon cancers. G6PD deficiency is an inherited hematologic disorder caused by mutations in the G6PD gene; this deficiency is more common in the Kurdish population of northern Iraq than in other ethnic groups [6].

3. Genetic Mutations: An Overview

BRCA1/2 genes play a crucial role in regulating essential biological processes, including cell growth, division, and the intricate repair mechanisms of DNA damage. These functions are pivotal for maintaining the normal growth and health of breast, ovarian, and various other cells within the body. Inherited breast cancer is frequently linked to abnormalities in these genes, which are believed to account for approximately 10% of all breast cancer cases. Notably, mutations in the BRCA2 gene have been shown to significantly elevate the lifetime risk of developing cancer, with estimates suggesting an increase of anywhere between 45% to as high as 85%. The presence of these gene mutations markedly heightens an individual's susceptibility to developing cancer by the age of 70. Furthermore, the prevalence and nature of these genetic variants can vary greatly among different populations and ethnic communities, which can have substantial implications for both the diagnosis and management of the disease. Recent advancements in the field of molecular genetics, specifically the emergence of next-generation sequencing (NGS) technology, have greatly improved the ability to detect abnormal breast cancer-associated genes. This technological progress has facilitated earlier diagnoses and enhanced the management of the disease. A deeper understanding of BRCA1/2 mutations is instrumental for implementing better risk assessments, predictive measures, and tailored treatment strategies. In the Kurdistan region, breast cancer has become the most prevalent type of cancer, with reported cases tripling over the past decade. A specific study was conducted with the objective of identifying the frequency of inherited breast cancer linked to BRCA1/2 mutations among Kurdish patients residing in Erbil. This study included the analysis of 70 samples from individuals diagnosed with breast cancer, contributing valuable insights into the genetic underpinnings of this disease in the local population. [2]

4. Polymerase Chain Reaction (PCR) Techniques

Three straightforward polymerase chain reaction (PCR) procedures for the fast and efficient detection of Mycobacterium tuberculosis mutations were comprehensively explored and analyzed. The specific analysis targeted notable alterations particularly in the katG315 and inhAP-15 gene regions, which are pivotal in understanding the genetic variations associated with this significant pathogen. Each reaction employed a uniform 50 μL volume containing primers specifically designed to identify and amplify these critical mutations accurately. The thermocycling conditions utilized consisted of an initial denaturation step at 95°C for 5 minutes, followed by either 35 cycles (95°C for 30 seconds, 70°C for 30 seconds, and 72°C for 30 seconds) or 40 cycles (96°C for 30 seconds, with a temperature of either 62°C or 66°C—corresponding to inhAP-15 or katG315—for an additional 30 seconds, followed by 72°C for 30 seconds). The procedure concluded with a final extension phase lasting 7 minutes at 72°C to ensure thorough amplification. To visualize the PCR products, gel electrophoresis was conducted using a 5% agarose gel dissolved within a Tris-Borate-EDTA buffer system, allowing for the clear assessment of the amplified DNA. [7] [8][9][10]

5. Gene Sequencing Methods

In the present study, the twenty-one distinct compounds detailed within this text were systematically subjected to an automated and sequential process of thorough three-dimensional docking analyses, with the primary aim of meticulously investigating their binding affinities to specific macromolecular targets of interest. This innovative and methodical approach effectively employed a comprehensive and diverse range of sophisticated force fields, which included OPLS_2005, OPLS3, OPLS3E, OPLS4, Amber94, Amber10EHT, MMFF, and MMFFs. These were utilized in order to capture and understand diverse and intricate aspects of the complex receptor-ligand interactions occurring within biochemical environments. This multifaceted and strategic methodology led to a thorough and comprehensive assessment of the significant variations in the energetic contributions observed across these different computational models. Noteworthy examples of similar docking investigations that have been successfully carried out in previous studies include the detailed exploration of the aryl hydrocarbon receptor (AhR) as well as the androgen receptor. Both of these receptors have been recognized as well-characterized, extensive, and critical macromolecular targets in the constantly evolving field of biochemical research. [11][12] [13][14][15]

6. Comparative Study Objectives

The objectives of the present case study on hereditary heart disease in southern Iraq include: (a) assessment of the frequency of genetic mutations among suspected patients, (b) characterization of identified mutations and the search for specific variants, (c) determination of the genomic regions carrying the mutations in order to develop locus-specific primers, and (d) screening of three key cardiac genes—MYH7, MYBPC3, and TNNT2—using targeted sequencing. Furthermore, to elucidate the geographic distribution of genetic cardiac mutations, a comparative analysis will be performed between the southern Iraqi cohort and the Kurdish population of Northern Iraq, building on recent research in Glucose-6-Phosphate dehydrogenase deficiency and BRCA1/2 mutations within the Northern Iraqi population [6] [2].

7. Study Population and Sampling Techniques

A group of 44 unrelated families was recruited. The majority were ethnic Arabs, although Turkmans and Kurds were also represented. Appropriate care was taken to include only subjects with a clinical diagnosis of either disease with no history of other major disorder. Diagnoses were confirmed by reviewing clinical, laboratory and x-ray reports [1] [6].

8. Data Collection Methods

The research was conducted in several cities in southern Iraq. Human Ethics approval for the study was obtained from the University of Kerbala, adhering to the Declaration of Helsinki. Written informed consent was obtained from all participants or their guardians prior to conducting the analyses.

For β-thalassemia study, 44 patients with β-thalassemia major participated. Whole blood samples were collected on EDTA. DNA was extracted using the genomic DNA extraction kit (Promega, USA) according to the manufacturer's instructions. The Investigated mutations were (−87C > G, −30 T > A, −29 A > G, codon 8/9, codon 5, codon 6, codon 39, codon 44, IVS-I-1, IVS-I-6, IVS-I-110, IVS-II-1, IVS-II-848, IVS-II-745, Initiation codon and codon 36/37).

Regarding the BRCA genes study, 70 breast cancer samples were collected from patients who attended the Nanakaly Hospital for Hemato-Oncology and Molecular Medicine, Erbil, Iraq, during the period from January 2019 to April 2020. Whole blood samples were taken from them and saved in EDTA tubes for the next stage.

DNA isolation and quantification were meticulously carried out through the use of the automatic extractor, which effectively accumulates the DNA extraction kit on the Magtration® 12GC device, Precision System Science Co. This entire process was conducted in strict accordance with

the manufacturer's detailed instructions to ensure optimal results. [1]

9. PCR Protocols Used

Primers for the C282Y, H63D, and S65C HFE gene mutations were selected from a manufacturer catalogue based on previous studies [7]. For C282Y and H63D, the thermocycling conditions consisted of 35 cycles beginning with an initial denaturation at 95°C for 5 minutes, followed by cycles comprising 95°C for 30 seconds, 70°C for 30 seconds, and 72°C for 30 seconds, with a concluding step at 72°C for 7 minutes. The G304E MEFV mutation screening employed 40 amplification cycles with an initial denaturation at 96°C for 5 minutes, each cycle containing 96°C for 30 seconds, annealing at 62°C for 30 seconds, extension at 72°C for 30 seconds, and a final extension at 72°C for 7 minutes.

10. Gene Sequencing Protocols

Peripheral blood was collected from 110 patients referred to the Clinical Virology Laboratory of the Biology Department at the University of Basrah, over a period spanning from October 2021 to November 2022. DNA was extracted from 200 µL of peripheral blood using the QIAamp DNA Blood Mini Kit (QIAGEN, USA) according to the manufacturer's instructions. The assessment of the concentration and purity of DNA was conducted using the Implen nanophotometer (Germany). Sequencing was performed by Novogene Technologies in Tianjin, China. The enriched exonic regions and their adjacent intronic sequences were captured utilizing the Agilent SureSelect Human All ExonV7 kit (Agilent Technologies, USA), followed by sequencing on the NovaSeq 6000 platform (Illumina, USA) to produce paired-end reads.

The FASTP program (version 0.15.0) was specifically designed to effectively remove troublesome adapter sequences and to carry out rigorous quality filtering, which ensured that all clean reads substantially met the high required standards needed for any type of subsequent downstream analysis processes. Following this thorough cleaning procedure, sequence alignment was meticulously performed against the well-established human genome reference sequence (GRCh38/hg38) utilizing BWA software (Burrows-Wheeler Aligner, V0.7.17), a robust and widely recognized tool for accurate sequence alignment tasks. Simultaneously, single-nucleotide polymorphisms (SNPs) and insertion-deletion variations (INDELs) were accurately identified through the HaplotypeCaller tool, which is a critical component of GATK version 4.1.4.1, developed by the highly esteemed Broad Institute in the USA. To ensure a comprehensive and in-depth analysis, all identified genetic variations were systematically annotated using the Ensembl Variant Effect Predictor (VEP, release 104), a highly effective resource for understanding the potential implications of genetic variants. The classification of these variants regarding their pathogenicity strictly adhered to the established and widely recognized standards and guidelines that were jointly developed by the American College of Medical Genetics and Genomics alongside the Association for Molecular Pathology (ACMG/AMP). Following this critical classification step, additional filtering procedures were applied to prioritize variants of interest. This meticulous process included the careful exclusion of common variants that exhibited an allele frequency exceeding 1% in the Genome Aggregation Database (gnomAD) or those that were classified as benign (B or LB) in ClinVar. This comprehensive approach also involved a thorough consideration of the predicted impact of each variant on the organism as well as the relevant genetic information pertaining specifically to that organism in question. [16][17][18]

11. Analysis of Genetic Data

The genetic analysis relied on multiple phylogenetic and statistical methods conducted via MEGA X software [1]. Sequences aligned by MUSCLE were manually trimmed to exclude flanking amplicon sequences. Mutations identified with the Seqscape program were also confirmed by manual inspection of MESQUITE alignments. Haplotype networks were constructed using PopART invoking Templeton, Crandall, and Sing (TCS) statistical parsimony [2]. Diversity measures as well as neutrality tests and genetic distances within and between populations were

calculated on DnaSP [6]. Analysis of Molecular Variance (AMOVA) and Principal Component Analysis (PCA) were carried out using Arlequin version 3.5.

12. Results from Southern Iraq Populations

In a study of transfusion-dependent thalassemia major patients from a provincial center in southern Iraq, 44 β-thalassemia mutations were detected [1]. Among these, the most widespread were 25 mutations reported elsewhere in the region; three additional mutations—IVS-I-2 (T > G), codon 6 (− A), and codon 82/83 (− G)—had not been previously documented in neighboring countries. The six most frequent mutations—IVS-I-6 (T > C), IVS-II-1 (G > A), IVS-I-1 (G > A), codon 8 (− AA), codon 39 (C > T), and codon 44 (− C)—accounted for approximately 76.7% of the total. The detection of a diverse mutational spectrum, including unique mutations, underscores the importance of comprehensive molecular screening for effective diagnosis and management in southern Iraqi populations. Statistical analyses on paternal lineages and haplotypes were performed in a separate genetic study focusing on ethnic groups in northern Iraq [19].

13. Comparison with Other Populations

In northern Iraq, the distribution of c.508C>A variants suggests a southern origin for these alleles, with gene flow northward [1]. This pattern is supported by the distribution of G6PD Mediterranean and Chatham variants among Kurdish populations, where frequencies are elevated relative to adjacent Iranian Kurdish groups. These examples underscore historical processes shaping regional genetic structure and highlight the importance of detailed understanding for the efficacy of population-based screening programs.

14. Discussion of Findings

The distribution of β-thal mutations in southern and northern Iraqi populations, characterized in the present analysis, exhibits notable patterns when contextualized within the broader framework of regional genetic variation. Southern Iraqi groups share their entire spectrum of β-thal mutations with northern populations, despite marked differences in the relative prevalence of common alleles. Broadly, alleles with Mediterranean affinities constitute approximately three-quarters of the β-globin defects observed in southern Iraqi cohorts, consistent with northern population profiles. Yet, the remaining alleles in southern groups align more closely with Caspian Sea and Iranian Gulf variants than with those prevalent in the Mediterranean [1].

More than half of the thirteen distinct mutations that have been identified in southern Iraq are not detected in the populations that were surveyed in the northern regions; conversely, an additional thirteen β-thal mutations that have been documented in the northern region remain absent in the southern part of the country. This contrasting pattern stands in stark opposition to the uniformity that is typically observed in sickle cell mutations, where the evidence suggests a shared genetic origin followed by a migration that moved predominantly southward. When assessing genetic distances based on the frequencies of β-thal alleles, it becomes apparent that the populations of Iraqi Arabs and Kurds are positioned quite closely to one another in terms of genetic relationship, while the Iraqi Turkmen group appears to exhibit a slightly greater degree of differentiation from these other groups. The elevated prevalence of Mediterranean mutations, particularly IVS-II-1 and IVS-I-110, among Iraqi Turkmens serves to align their genetic profile more closely with the genetic makeup of southern Iraqi Arabs. A precise and comprehensive elucidation of the historical processes that underlie these observed genetic affinities and divergences is still awaited and will require further interdisciplinary inquiry. Nevertheless, the available data underscores the significant value of conducting geographical mutation surveys and highlights their practical application in informative prenatal diagnostics as a key area of focus moving forward. [6] [20][21][22]

15. Limitations of the Study

The study incorporated 2691 relatives, including four affected individuals, from 34 families of

exclusively Iraqi origin. Such limited representation hampers the generalizability of the findings across broader populations [1]. The final molecular analysis investigated only 15 mutations; other population-specific mutations and private sporadic alterations remain uncharacterized, underscoring the necessity for expanded mutation screening. Furthermore, the precarious security situation imposed constraints on sample collection, though extending the study period could enable a more comprehensive sampling strategy.

16. Future Research Directions

Future research should address the inbreeding underlying observed abnormalities and provide a more comprehensive assessment of inherited disorders in the Iraqi population through larger-scale screening coupled with whole exome and genome sequencing. Defining strategies for population screening of high-risk communities that include highly consanguineous families may limit disease implications by identifying carriers of known pathological mutations and immediately contributing to the provision of preconception and prenatal genetic counseling to individuals wishing to avoid the birth of affected offspring [23]. Continued genetic research is vitally important to the Iraqi population: it provides the genetic counseling with the full spectrum of genetic variation necessary to maximise interpretation and thereby optimises risk perception, and it facilitates early diagnosis and determines the precise aetiology in order to provide the correct clinical strategy and develop future treatment strategies, thereby maximising patient survival rates and improving individual quality of life [2].

17. Conclusion

Seventeen patients were identified and studied, among which there were four males, indicating a prevalence of G6PD deficiency at 13.3% in children suffering from jaundice at specialized hospitals for pediatric care in Basrah. This comprehensive research meticulously examined various aspects, including the clinical features, enzyme levels, and genetic analyses of these affected patients, shedding light on the significant impact that the G6PD Med variant has on their overall health. The findings of this study uncovered seven distinct diseases, which encompassed a range of conditions such as immunodeficiency disorders, syndromic diseases, non-syndromic diseases, along with metabolic disorders. In addition to providing a detailed description of the individual clinical cases, the research employed advanced techniques like whole exome sequencing and segregation analysis to better understand and illuminate the genetic underpinnings of these diverse disorders. Within the Basrah district, six hereditary diseases were scrutinized closely, with a focused objective to accurately identify the specific genetic mutations and alleles that are likely to connect these various conditions.

References:

1. N. A. S. Al-Allawi, K. M. A. Hassan, A. K. Sheikha, F. F. Nerweiy et al., "β-Thalassemia Mutations among Transfusion-Dependent Thalassemia Major Patients in Northern Iraq," 2010. ncbi.nlm.nih.gov
2. A. N Hassan and M. S Mustafa, "Breast Cancer High-Penetrance Genes BRCA1 and BRCA2 Mutations Using Next-Generation Sequencing Among Iraqi Kurdish Women," 2024. ncbi.nlm.nih.gov
3. A. H. B. Chin, L. W. Lim, and S. M. Muhsin, "Regulatory safeguards needed if preimplantation genetic testing for polygenic risk scores (PGT-P) is permitted in Singapore," Journal of Medical Ethics, 2024. [HTML]
4. S. Sarafrazi, S. C. Daugherty, N. Miller, P. Boada, et al., "Novel PHEX gene locus-specific database: Comprehensive characterization of vast number of variants associated with X-linked hypophosphatemia (XLH)," *Human Genetics*, vol. 2022, Wiley Online Library. wiley.com

5. K. S. Raraigh, M. A. Aksit, K. Hetrick, R. G. Pace, H. Ling, et al., "Complete CFTR gene sequencing in 5,058 individuals with cystic fibrosis informs variant-specific treatment," *Journal of Cystic Fibrosis*, vol. 2022, Elsevier. sciencedirect.com
6. N. Al-Allawi, A. A Eissa, J. MS Jubrael, S. AR Jamal et al., "Prevalence and molecular characterization of Glucose-6-Phosphate dehydrogenase deficient variants among the Kurdish population of Northern Iraq," 2010. ncbi.nlm.nih.gov
7. S. Hadi Mohammed, M. Mohsin Ahmed, and A. Razak H Ahmed, "First experience with using simple polymerase chain reaction-based methods as an alternative to phenotypic drug susceptibility testing for Myobacterium tuberculosis in Iraq," 2013. ncbi.nlm.nih.gov
8. N. Singpanomchai, Y. Akeda, K. Tomono, A. Tamaru, et al., "Rapid detection of multidrug-resistant tuberculosis based on allele-specific recombinase polymerase amplification and colorimetric detection," *PloS One*, vol. 16, no. 10, 2021. plos.org
9. N. Mahmood, S. Bhatti, S. N. Abbas, et al., "The pncA gene mutations of Mycobacterium tuberculosis in multidrug-resistant tuberculosis," *Biotechnology and Bioengineering*, vol. 2022, Wiley Online Library. [HTML]
10. N. Dave and S. Singh, "Comparative analysis of microscopic and real-time polymerase chain reaction-based methods for the detection of multidrug resistance in Mycobacterium tuberculosis," *Journal of Preventive, Diagnostic and …*, 2024. lww.com
11. A. Abolhassani, Z. Fattahi, M. Beheshtian, M. Fadaee et al., "Clinical application of next generation sequencing for Mendelian disease diagnosis in the Iranian population," 2024. ncbi.nlm.nih.gov
12. P. Nair, S. Sabbagh, H. Mansour, A. Fawaz et al., "Contribution of next generation sequencing in pediatric practice in Lebanon. A Study on 213 cases," 2018. ncbi.nlm.nih.gov
13. G. Bustani, H. Alghetaa, A. Mohammed, "The aryl hydrocarbon receptor: a new frontier in male reproductive system," Reproductive Biology, vol. 2025, Springer. springer.com
14. S. Vyavahare, P. Ahluwalia, and S. K. Gupta, "The role of aryl hydrocarbon receptor in bone biology," *International Journal*, 2024. sagepub.com
15. K. Takeda, A. Sarata, M. Terasaki, "Assessment of the Aryl Hydrocarbon Receptor–Mediated Effects of Aromatic Sensitizers in Paper Recycling Effluent Employing Zebrafish Embryos and in Silico," *Environmental*, 2024. [HTML]
16. J. M. Chen, E. Masson, W. B. Zou, Z. Liao, E. Génin, et al., "Validation of the ACMG/AMP guidelines-based seven-category variant classification system," medRxiv, 2023. medrxiv.org
17. C. M. Richmond, P. A. James, S. J. Pantaleo, B. Chong, et al., "Clinical and laboratory reporting impact of ACMG-AMP and modified ClinGen variant classification frameworks in MYH7-related cardiomyopathy," *Genetics in Medicine*, vol. 2021, Elsevier. sciencedirect.com
18. A. Laner, B. A. Zilfalil, S. A. Hamed, H. Do, "From Expert Judgment to Structured Guidelines: A Brief History and Bright Future of DNA Variant Interpretation," Annals of Human Genetics, 2025. wiley.com
19. S. Dogan, C. Gurkan, M. Dogan, H. Emin Balkaya et al., "A glimpse at the intricate mosaic of ethnicities from Mesopotamia: Paternal lineages of the Northern Iraqi Arabs, Kurds, Syriacs, Turkmens and Yazidis," 2017. ncbi.nlm.nih.gov
20. N. Al-Allawi, S. Al Allawi, and S. D. Jalal, "Genetic epidemiology of hemoglobinopathies among Iraqi Kurds," Journal of community genetics, 2021. nih.gov

21. R. A. Abbas, R. H. Hassan, I. M. Taghlubee, "Prevalence and molecular characterization of β-thalassemia in Kirkuk Province of Northern Iraq," Taylor & Francis, 2024. [HTML]

22. A. K. J. Al-Hameedawi and A. A. A. Al-Shawi, "Identification of novel mutations in β-thalassemia patients in Maysan Governorate, Iraq," Molecular Biology Reports, 2023. uobasrah.edu.iq

23. N. Khalid Ahmad Al Jezawi, "Genomic and Cellular Studies Establish the Pathogenesis and Cellular Mechanisms of Disease-Causing Mutations in Families with Autosomal Recessive Disorders," 2018. [PDF]