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A COMPARATIVE ANALYSIS OF TREATMENT ACCESS, OUTCOMES, AND COSTS FOR MONOGENIC DISORDERS IN SAUDI ARABIA: HIGHLIGHTING DISPARITIES AND THE GENE THERAPY LANDSCAPE

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ABSTRACT
Genetic disorders impose a substantial health burden in Saudi Arabia, driven by high consanguinity rates (56–60%) and a high prevalence of autosomal recessive diseases. This study conducted a detailed, disease-specific analysis of 205 patient records from 2024–2025 to compare treatment access, outcomes, and costs across different genetic disorders and regions. We compared cohorts with thalassemia, sickle cell anemia, G6PD deficiency, Tay-Sachs disease, and cystic fibrosis. Our findings reveal critical disparities: patients with hemoglobinopathies (sickle cell anemia and thalassemia) who received gene therapy demonstrated significantly superior clinical outcomes compared to those on conventional regimens (e.g., blood transfusions), despite the high initial cost of advanced therapies (average ~SAR 931,561). Furthermore, access to these transformative treatments was heavily concentrated in urban centers like Riyadh and Jeddah, creating significant regional inequities. For disorders like Tay-Sachs, where no disease-modifying therapy exists, outcomes were uniformly poor, highlighting an unmet therapeutic need. These results underscore the urgent necessity for a multi-pronged national strategy: standardizing treatment eligibility criteria, decentralizing specialized care to bridge regional gaps, and robustly expanding clinical trial infrastructure to ensure equitable access to cutting-edge therapies for all Saudi patients.

Index Terms- Genetic disorders, Consanguinity, Saudi Arabia, Healthcare disparities, Clinical trials.

INTRODUCTION

Genetic Disorders Across the World and in Saudi Arabia

Genetic disorders are a significant and rising global health concern. These disorders arise from alterations in an individual's DNA, ranging from single-gene mutations to complex chromosomal anomalies. Worldwide, millions of people are affected by various genetic conditions, with prevalence rates differing across regions due to genetic diversity, environmental factors, cultural practices, and healthcare access.[1] While advances in genomic technologies have greatly improved early detection and diagnosis, treatments often remain limited to symptom management rather than curative approaches.[2]

A substantial proportion of genetic disorders are inherited in an autosomal recessive manner—the inheritance of two defective gene copies, one from each parent. This pattern of inheritance becomes particularly concerning in populations where consanguineous marriages (*i.e.*, marriages between close relatives) are common, increasing the likelihood of passing on recessive genetic disorders. Consanguinity is especially prevalent in the Middle East, North Africa, and South Asia.[3]

In Saudi Arabia, the rate of consanguineous marriage is among the highest in the world, with estimates ranging from 56–60%.[4,5] This sociocultural practice has led to a disproportionately high prevalence of inherited genetic disorders within the population, including thalassemia, sickle cell anemia, glucose-6-phosphate dehydrogenase (G6PD) deficiency, Tay-Sachs disease, and cystic fibrosis. These disorders contribute significantly to morbidity and mortality and place a heavy financial burden on the Saudi healthcare system.[6]

In response, the Saudi government has implemented nationwide genetic screening programs, particularly premarital screening and genetic counseling initiatives, aimed at reducing the incidence of inherited disorders.[7,8] Despite these efforts, the rates of genetic disease remain high, underscoring the urgent need for more effective and potentially curative interventions such as gene therapy.[9]

The Promise and Importance of Gene Therapy

Gene therapy is an emerging medical treatment that targets the root genetic cause of a disease rather than merely alleviating symptoms. It involves the insertion, removal, or modification of genetic material within a patient's cells to correct defective genes. Since its inception in the late 20th century, gene therapy has evolved from experimental applications to approved treatments for several serious and previously untreatable genetic disorders.[10]

Globally, gene therapy has demonstrated remarkable clinical success in treating monogenic diseases such as spinal muscular atrophy (SMA), certain forms of inherited blindness, hemophilia, and primary immunodeficiency disorders. Countries such as the United States, Germany, China, and the United Kingdom have pioneered large-scale gene therapy programs, establishing regulatory frameworks and gene therapy centers that provide global benchmarks for development and access. For Saudi Arabia, the implications of gene therapy are profound; with a population burdened by genetic illness, gene therapy offers the possibility of improved survival, better quality of life, and even curative outcomes for many patients. However, several challenges must be addressed, including high treatment costs, a need for improved infrastructure and regulatory guidelines, and unequal access across regions.

Saudi Healthcare Context: Regional Distribution and Access Disparities

Saudi Arabia's healthcare system has witnessed transformative growth in recent decades, positioning itself as a leader in the Gulf Cooperation Council (GCC) region. The government has heavily invested in hospital infrastructure, medical research, and public health programs. However, regional disparities persist,

particularly in access to specialized and high-tech services such as gene therapy.

The country is divided into several administrative regions: Riyadh, Makkah, Madinah, Eastern Province, Qassim, Tabuk, Jeddah, Abha, and others. While cutting-edge medical facilities and advanced genetic laboratories have been built in metropolitan areas like Riyadh, Jeddah, and Dammam, rural and remote areas still suffer from under-resourced health centers, shortages of trained professionals, and limited logistical support.

Access to gene therapy is particularly affected by these disparities, as treatments typically require sophisticated infrastructure, highly trained geneticists and molecular biologists, and ongoing follow-up systems. Currently, gene therapy services in Saudi Arabia are concentrated in a few urban centers, leaving patients in peripheral regions underserved.

Additionally, the high cost of gene therapy represents a significant barrier. While Saudi citizens enjoy a highly subsidized healthcare system, the absence of a national policy for gene therapy coverage imposes a burden to most patients and institutions. Moreover, limited patient enrollment in clinical trials or research programs further hampers access, even when such trials are among the few viable treatments for patients.

Given the high burden of inherited disorders in Saudi Arabia, coupled with the emerging promise and current limitations of gene therapy, we conducted an analysis of gene therapy eligibility, accessibility, and utilization across the Saudi Kingdom.

This study seeks to identify demographic, clinical, and healthcare system determinants that influence gene therapy outcomes and access. We used information from patient profiles to analyze factors such as nationality, region, disease type/severity, mutation type, treatment categories, cost, and research participation to determine the factors most associated with therapy eligibility and successful treatment outcomes. These findings provide insights to aid clinicians, policymakers, and researchers in formulating strategies for expanding equitable access to gene therapy, optimizing clinical outcomes, and ultimately reducing the genetic disease burden in Saudi Arabia.

This study conducts a disease-specific, comparative analysis of patient cohorts with thalassemia, sickle cell anemia, G6PD deficiency, Tay-Sachs, and Cystic Fibrosis across Saudi Arabia. We aim to: 1) Compare treatment outcomes and costs between conventional therapy and gene therapy where available; 2) Evaluate regional disparities in access to advanced care for each disorder; and 3) Identify the determinants of successful treatment enrollment and outcomes.

Genetic Counselling and Ethical Issues

Abiib et al. provide an extensive summary of Qatar's genetic counseling services, including its unique demographic reality of high consanguinity and large family sizes. Qatar has expanded genetic counseling into different sectors of health care and invested in developing local capabilities through academic education and professional certification. Initiatives like the Qatar Genome Program have enabled research on precision medicine and established a national vision on culturally adapted genetic health care.[11]

Oncology Early-Phase Clinical Trials in the Middle East and North Africa

The challenges of running Phase I cancer clinical trials in the Middle East and North Africa (MENA) region have been discussed by Alotaibi et al., who note advancements in clinical trials for cancer, but cite infrastructural, regulatory, and education gaps across the region. The authors advise harmonizing regulations, strengthening research infrastructure, and amplifying academia-industry regulatory collaboration to counter challenges and provide for sustainable clinical trial environments.[12]

Advances in SMA Treatments in the GCC

Salama et al. reported the genetic etiology, incidence, and novel treatments of SMA in the GCC, and describe the high disease incidence caused by the high frequency of consanguineous marriages. SMA is caused by mutations in the survival motor neuron genes *SMN1* and *SMN2*, and the disease severity is affected by the number of functional copies of these genes because they have some capacity to compensate for each other's loss of function. Thus, screening for and treating SMA requires a nuanced analysis of molecular genetics. Several gene therapies have received U.S. Food and Drug Administration (FDA) and European Medical Administration (EMA) approval for treating SMA such as Nusinersen and Onasemnogene abeparvovec, and these therapies show promising safety and efficacy in GCC populations. Salama et al. suggest reinforcement of genetic screening programs in parallel with contemporary therapeutics to reduce disease burden.[13]

Genetic Disorders Among Saudi Arabians

One of the most significant published retrospective series of exome sequencing in patients with genetic disorders in Saudi Arabia was reported by Alqahtani et al. This study found potential disease-causing genetic variants in patients with rare diseases and identified consanguineous marriages in family history as a significant risk factor for autosomal recessive diseases. The authors advise increased utilization of exome sequencing as an initial diagnostic test to establish the genetic diagnosis of rare diseases in highly consanguine populations.[14]

Mitochondrial Diseases: Molecular Insights and Therapies

Aldossary et al. summarize the molecular mechanisms of mitochondrial disorders and recent therapeutic developments. The authors outline the role of mitochondria as pivotal in cellular energy generation and discuss defects in oxidative phosphorylation leading to heterogeneous clinical syndromes. The paper briefly discusses recent developments in molecular diagnosis and on tailoring treatment to enhance mitochondrial function, and how there is a pressing need for more translational research.[15]

Precision Medicine and Genetic Screening in the GCC

The increasing role of genetic screening across the GCC is presented through a new special issue for 2024 in *Genetics in Medicine Open*. The authors describe how biobanking and population-specific genetic knowledge are contributing to tailored strategies for disease prevention and treatment and are hastening genomics' adoption in routine clinical care.[16]

Epidemiology and Management of Rare Diseases in Saudi Arabia

In an extensive epidemiological study, Fasseeh et al. cite Saudi Arabia's high prevalence of rare diseases fueled by socio-cultural determinants such as consanguinity. The authors highlight the economic and social burden of rare diseases and suggest policy-initiated interventions to promote genetic counseling, early diagnosis, and treatment.[17]

Barriers to Clinical Trial Participation in MENA

A systematic review by Alshammari et al. evaluated patient and institutional problems in clinical trial participation in the MENA region. The authors identify inadequate public awareness, regulatory problems, and infrastructural deficits as the primary issues and propose more comprehensive patient education programs and more effective regulatory processes to improve recruitment and retention in clinical trials.[18]

Genetic Counselling and Ethical Issues

Al-Shafai et al. discuss how issues of genetic counseling ethics are tackled from the Arab perspective and stressing the significance of sensitive communication styles that are culturally adapted. The authors affirm that treating stigma at the community level and confidentiality are vital in making counseling and uptake of genetic services effective. The authors add the significance of continuous training to equip counselors with skills aligned with the sociocultural context.[19]

Research Gap Analysis and Comparison with Our Study

Despite the comprehensive scope of these, several research gaps remain.

- Longitudinal and Outcome-Based Data: Studies have[11,14] reported descriptive and cross-sectional data with respect to genetic counseling and diagnosis; however, these lack adequate long-term follow-up to assess patient outcomes and the real impact of interventions in the field.
- Unified Regional Frameworks: Previous reviews[12,18] have reported the disintegration of clinical trial regulations and infrastructure across MENA and GCC, with no regional unified strategy put forth as of yet. Our study therefore advances a framework that integrates regulatory, infrastructural, and educational elements pertinent to genetic disorders and clinical trials.
- Population-Wide Genetic Screening: While prevalence studies[13,14,17] have revealed high frequencies of genetic disorders associated with consanguinity, there has been little research on population-wide screening programs and the challenges of their implementation. Our work begins to establish a basis for the design and pilot implementation of such programs on a scale that respects socio-cultural values.
- Translation to Clinical Practice: There are many obstacles in the translation of molecular and therapeutic advances in mitochondrial and neurogenetic diseases into routine clinical management. Understanding the current patient demographics and accessibility to treatments will help to overcome barriers and facilitate the progression of genetic diagnostics and novel treatments into clinical practice.
- Ethical and Sociocultural Considerations: While counseling ethics have been addressed[19], there is a need for the inculcation of cultural competence training within genetic services. There is a need to develop and test culturally appropriate counseling protocols within the context of clinical genetics.
- Integration of Genomic Data into Precision Medicine: Whilst programmatic provision of genetic screening is ever-expanding (16), screening results are rarely integrated into personalized treatment and health policy. This study proposes the integration of data systems with electronic health records and clinical decision support.
- Patient and Provider Education: Barriers to research participation and genetic literacy[12,18] have been identified yet little in terms of interventions with demonstrated efficacy. Our studies include educational initiatives targeting both patients and providers to bolster participation levels and outcomes.

Bridging this gap requires research to integrate genetic epidemiology, health systems analysis, ethical frameworks, and implementation science for the refinement of both genetic healthcare delivery and genetic research in the GCC and MENA regions.

METHODS

Study Design

This study employed a retrospective cross-sectional design to analyze real-world data from patients with genetic disorders who were seen at various specialized hospitals and genetic clinics across Saudi Arabia. By using historical data collected from 2018–2023, we aimed to identify clinical patterns, treatment outcomes, and access issues related to gene therapy and related interventions. The retrospective nature of the study enabled a timely and resource-efficient exploration of patient profiles and healthcare disparities without the need for follow-up.

Patient Population and Inclusion Criteria

The dataset includes a total of 205 patients with confirmed diagnosis of a genetic disorder. These patients were identified through molecular genetic testing or clinical geneticist evaluations at selected hospitals and specialty clinics across Saudi Arabia. All patients were assessed for eligibility to receive gene therapy, received either gene therapy or conventional treatment, and were part of observational follow-up programs. Eligibility assessment included evaluating clinical severity, genetic mutation type, and availability of gene therapy for the specific condition.

Inclusion criteria

- Confirmed genetic diagnosis through molecular testing or clinical geneticist evaluation.
- Complete patient records with demographic, clinical, and genetic information.

Exclusion criteria

- Patients with incomplete or inconclusive diagnoses
- Missing essential data on key variables (*e.g.*, treatment type, severity, or outcome)

Data were sourced from Electronic Health Records (EHRs), genetic test reports, or specialty clinic patient databases. All records were verified by hospital data custodians for accuracy and completeness. De-identified patient data were securely transferred to the research team for analysis in accordance with institutional and national regulations.

Missing Data Handling

The dataset was assessed for missing or incomplete entries, particularly for cost and outcome variables. The approach to missing data included.

- Exclusion of cases with major missing variables that would compromise the validity of statistical tests (*e.g.*, outcome or treatment type).
- Listwise deletion was used for cost analysis to ensure robustness of financial comparisons.
- No imputation was performed for clinical or economic variables to maintain data integrity and avoid introducing bias.

Variables Collected

A STROBE-style flow diagram is shown in **Figure 1** with the following information.

- Total number of patients screened
- Numbers of patients excluded and reasons.
- Subgroups receiving gene therapy or conventional treatments
- Final analytic sample used for hypothesis testing

Data were categorized into four main domains.

1) Demographic Variables
- Nationality: Saudi / Non-Saudi
- Region: Central, Eastern, Western, Northern, Southern Saudi Arabia
- Age at diagnosis

2) Clinical Variables
- Type of genetic disorder (based on ICD-10 or disorder category)
- Severity level: Mild, Moderate, Severe (based on physician assessment or disease-specific severity scales)
- Treatment received: Gene therapy, pharmacologic treatment, supportive care, or no treatment
- Clinical outcome: Improvement, Stabilization, Progression, or Death
- Survival indicator: Alive / Deceased during the 5-year observation period

3) Genetic Variables
- Type of mutation: Missense, Nonsense, Frameshift, Deletion
- Causative gene

4) Economic Variables
- Estimated total cost of therapy (in Saudi Riyals), including drug cost, hospitalization, genetic counseling, and diagnostics

Statistical Analysis

All statistical analyses were conducted using IBM SPSS Statistics (Version 27). Descriptive statistics were computed for demographic and clinical variables, presented as frequencies (percentages) for categorical data and means (± standard deviations) or medians (interquartile ranges) for continuous data, based on their distribution.

To address the study's hypotheses, inferential analyses were performed as follows.

- **Chi-square tests of independence** were used to examine:
  - The association between disease severity (mild, moderate, severe) and eligibility for gene therapy (H1).
  - The relationship between consanguinity/family history and disorder severity (H2).
  - Regional variation in access to gene therapy (H3).

- The relationship between clinical trial participation and receipt of gene therapy (H4).
- Subgroup and Comparative Analyses: For disease-specific comparisons, patients were stratified by diagnosis. Within the sickle cell anemia and thalassemia cohorts, Chi-square tests compared clinical outcomes (improved, stable, worsened) between those receiving gene therapy and those receiving conventional treatment. Independent samples t-tests (or Mann-Whitney U tests for non-parametric data) were used to compare the mean cost of therapy between these two treatment groups. One-way ANOVA (or Kruskal-Wallis tests) was employed to compare average treatment costs and age across different geographic regions for each disease cohort.

A p-value of < 0.05 was considered statistically significant for all tests. Where applicable, 95% confidence intervals (CIs) were calculated to support inferences about effect sizes and precision.

Ethical Considerations

This study adhered to international ethical guidelines and Saudi national data protection laws. Specifically, Institutional Review Board (IRB) approval was obtained from all participating hospitals, all identifiable data were removed to protect patient privacy, files were encrypted and access was limited for data security, and patients were not contacted. Due to the retrospective nature of the study and use of de-identified data, our institutional guidelines did not require obtaining patient consent for the use of data. This study was conducted in compliance with the Declaration of Helsinki and relevant Ministry Of Health research policies.

RESULTS

Cohort Overview and Demographics

The study analyzed data from 205 patients diagnosed with various genetic disorders across eight major regions of Saudi Arabia. The majority of patients were Saudi nationals (90.2%), with the highest representation from Madinah (16.6%), Riyadh (13.7%), and Tabuk (13.7%). Thalassemia was the most frequent disorder, accounting for 24.9% of cases, followed by Sickle Cell Anemia and G6PD deficiency. Disease severity was relatively evenly distributed; however, moderate to severe cases collectively made up 75.1% of the cohort. Treatment approaches were mainly supportive care and blood transfusions, with a smaller proportion of patients receiving bone marrow transplants or gene therapy. Genetic testing identified causative mutations, most commonly in the HBB gene, confirming diagnoses and informing treatment decisions. Nearly half of the patients exhibited clinical improvement, while the overall mortality rate was 5.9%. Therapy costs showed substantial variation, and missing data suggested either gaps in treatment delivery or reporting. This overview provides the foundation for a disease-specific examination of treatment outcomes, costs, and regional access disparities.

Analysis of Treatable Disorders: Thalassemia and Sickle Cell Anemia

Thalassemia and Sickle Cell Anemia are disorders with established curative therapies, including gene therapy, which was compared against conventional approaches such as blood transfusions and supportive care. Patients receiving gene therapy consistently showed higher rates of clinical improvement compared to those receiving only conventional care, while patients on transfusions alone often remained stable, and some experienced disease progression. This contrast highlights the potential of gene therapy to positively alter disease trajectories. Gene therapy, however, was associated with substantially higher treatment costs than conventional approaches, reflecting the complexity of the therapy and the specialized care it requires. Additionally, patients who received gene therapy were predominantly located in urban centers such as Riyadh and Jeddah, whereas conventional therapy recipients were more widely distributed across regions, underscoring geographic inequities in access to advanced treatments.

Analysis of Disorders with Supportive Care Only: Tay-Sachs and Cystic Fibrosis

For disorders without curative options, such as Tay-Sachs and Cystic Fibrosis, the analysis focused on access to specialized supportive care, cost burdens, and regional disparities. Tay-Sachs patients were primarily concentrated in urban centers, where palliative care services were more accessible, although overall access remained limited. In contrast, Cystic Fibrosis patients experienced more variable access, with rural patients receiving less frequent specialized care. Costs for lifelong supportive management were highly variable across regions, reflecting differences in healthcare infrastructure and service availability. Clinical outcomes also differed between these disorders: Tay-Sachs patients universally experienced poor outcomes consistent with the disease's progression, while Cystic Fibrosis outcomes ranged from stable to gradual worsening, highlighting the impact of care quality and accessibility on patient health trajectories.

The Role of Clinical Trial Participation

Across treatable disorders, participation in clinical trials emerged as a key facilitator for accessing gene therapy. All Sickle Cell Anemia patients who received gene therapy were enrolled in clinical trials, emphasizing that research participation is the primary route to these advanced therapies. Similarly, Thalassemia patients undergoing gene therapy were also enrolled in trials, highlighting structural barriers for patients residing outside urban centers or those without trial access. These findings underscore the critical role of clinical trial inclusion in reducing inequities and improving outcomes for patients with rare genetic disorders.

DISCUSSION

Superior Outcomes and Economic Implications of Gene Therapy for Hemoglobinopathies

This study highlights the substantial benefits of gene therapy for treatable hemoglobinopathies, specifically Thalassemia and Sickle Cell Anemia. Patients who received gene therapy consistently demonstrated higher rates of clinical improvement compared to those receiving conventional care such as blood transfusions or supportive management. These findings align with global evidence showing that gene therapy can alter disease trajectories in patients with severe beta-thalassemia or sickle cell disease, particularly when conventional approaches are insufficient. Notably, younger patients were more likely to receive advanced therapies, reflecting clinical preferences for early intervention and the higher tolerance of pediatric populations to intensive treatments. However, the economic burden remains significant. Gene therapy costs were markedly higher than conventional care, illustrating the financial challenges of implementing such cutting-edge interventions. While expensive, these therapies offer the potential for long-term cost-effectiveness by reducing the need for lifelong transfusions or supportive treatments. This underscores the importance of strategic health planning and cost assessment protocols to guide equitable allocation of high-cost therapies within the Saudi healthcare system.

The Inescapable Burden of Untreatable Neurodegenerative Disorders

In contrast, neurodegenerative disorders such as Tay-Sachs and Cystic Fibrosis, which currently lack curative treatments, impose a persistent clinical and economic burden. Tay-Sachs patients universally experienced poor outcomes, consistent with disease pathology, whereas Cystic Fibrosis outcomes varied depending on the quality and accessibility of supportive care. Access to specialized palliative or chronic care was often limited in rural regions, emphasizing the role of infrastructure and healthcare resource availability in patient prognosis. The high variability in the cost of lifelong supportive care further demonstrates the inequities faced by patients with untreatable genetic disorders, highlighting the need for policy-driven interventions to expand access and standardize care services for these vulnerable populations.

Regional Disparities in Access to Both Conventional and Advanced Care

Geographic location emerged as a key determinant of treatment access across all disorders. Gene therapy and other advanced interventions were concentrated in major urban centers such as Riyadh and Jeddah, while patients in less-resourced regions often relied solely on conventional or supportive care. These regional disparities contribute to delayed diagnoses, limited treatment options, and poorer clinical outcomes for patients residing outside metropolitan areas. Addressing these inequities requires targeted investments in regional genetic medicine hubs, the deployment of telemedicine services for remote consultations, and mobile diagnostic units to bridge the urban-rural divide. Even for conventional therapies, differences in access and cost between regions underscore the importance of decentralizing care to ensure equitable healthcare delivery.

Clinical Trials as the Gateway to Cutting-Edge Treatment

Participation in clinical trials was a critical factor enabling access to gene therapy. All patients with Sickle Cell Anemia and a majority of Thalassemia patients receiving gene therapy were enrolled in clinical research, highlighting that trial participation remains the primary avenue for accessing advanced therapies. Factors driving this include funding from research grants, the concentration of specialized facilities in tertiary hospitals, and physician referral patterns favoring trial-eligible patients. These findings emphasize the need to strengthen the clinical trial ecosystem in Saudi Arabia, expand patient registries, and facilitate enrollment to improve access to novel therapies. Encouraging broader participation in research not only provides individual patients with treatment opportunities but also generates locally relevant genomic data to guide national healthcare strategies.

Integrating Genetic, Clinical, and Economic Insights

Overall, this study demonstrates that disease severity, genetic background, geographic location, and research involvement collectively shape patient outcomes and access to advanced therapies. Approximately half of the cohort showed clinical improvement, yet mortality remained notable, particularly for severe or untreatable disorders, highlighting the ongoing need for effective interventions. The average treatment cost, though incompletely documented, reflects a heavy economic burden, reinforcing the importance of transparent data collection and health economic evaluation to inform policy. These findings collectively advocate for expanded genetic counseling, early severity stratification, and age-adjusted treatment protocols to optimize outcomes, reduce inequities, and ensure that both conventional and novel therapies are accessible to all patients across Saudi Arabia.

Comparison to Other Research

Genetic Counseling and Consanguinity

The impact of consanguinity on the incidence and severity of genetic diseases has been well-established, and the use of genetic counseling has grown. Abiib et al. discussed Qatar's extensive genetic counseling infrastructure designed to address high consanguinity rates.[11] Similarly, Alqahtani et al. examined how exome sequencing and counseling are critical first-tier diagnostics in highly consanguineous populations in Saudi Arabia.[14] Our study underscores the importance of culturally tailored counseling programs, including educational and ethical considerations.[27]

Clinical Trial Ecosystem and Access to Innovative Therapies.

Alotaibi et al. identify regulatory and infrastructural gaps limiting early-phase oncology trials in MENA, emphasizing the need for harmonized standards and capacity building.[12] Our findings support the premise that clinical trial participation enhances patient access to gene therapies, reflecting global trends . Saudi Arabia's growing clinical trial capabilities offer promise for expanding therapeutic options, but further investments are needed to overcome barriers documented in.[28] Including patient awareness and streamlined regulations.

Rare Disease Burden and Treatment Challenges

The epidemiological profile in our study is consistent with Fasseeh et al.'s report on the high burden of rare diseases in Saudi Arabia, which is driven by socio-cultural factors such as consanguinity.[17] The economic and social implications call for integrated policy responses to improve early diagnosis and treatment access. Our data contribute additional evidence that expanding newborn screening and precision medicine programs, as recommended in Genetics in Medicine Open (2024), is vital for addressing this burden.

Advances in Therapeutics and Molecular Diagnostics

Salama et al. discuss novel gene therapies and molecular diagnostics for spinal muscular atrophy in the GCC, highlighting both opportunities and challenges.[13] Our results confirm the utility of gene therapy in severe genetic disorders and emphasize the need for robust genetic screening infrastructure to identify candidates early. Aldossary et al. reinforce this by demonstrating the evolving therapeutic landscape for mitochondrial diseases, a category relevant to some patients in our cohort.[15]

Current Status and Future Directions

Saudi Arabia has a unique genetic epidemiology due to high rates of consanguinity and complex socio-cultural determinants. Following the analysis of 205 patients' information from different genetic hospitals, the research illuminates several significant aspects of the current situation of genetic healthcare service provision, clinical work, and research activity in the country.

- Gene Therapy Eligibility and Severity of Disorder: Our findings indicate an extremely strong correlation between the severity of disorder and eligibility for gene therapy ($p < 0.001$). More severe phenotypes receive preference for new gene therapy treatment, an observation which follows clinical triage guidelines that maximize treatment benefit. The observation is consistent with international practices as seen in the US and Europe,[20,21] where indication of clinical need offers access to the treatment. The strategy, however, reveals an issue with initial treatment of cases with moderate or mild severity, which would greatly benefit from new treatments before the condition becomes irreversible.
- Impact of Consanguinity and Family History: Consanguineous marriages that are prevalent in Saudi Arabia and the Middle East have a well-documented impact on the severity and prevalence of autosomal recessive disease. The evidence from our study confirms a statistically significant correlation between positive family history, consanguinity, and disorder severity ($p < 0.001$), and justifies the utilization of culturally modified genetic counseling and premarital screening programs. Preventive interventions are needed to reduce the burden of genetic disease and are consistent with earlier regional studies.[22,29]
- Geographic disparities in access to gene therapy: This study shows strong regional variability in the provision of gene therapy ($p < 0.001$), with higher levels of treatment being reported in metropolitan nodal cities such as Riyadh and Jeddah than in more remote provinces such as Abha and Qassim. This finding is in agreement with earlier reports of unequal distribution of healthcare services in Saudi Arabia.[30,31] Such disparities are most likely being driven by infrastructural limitations, availability of specialists, and logistic challenges in transporting novel therapies to more remote areas. Addressing such inequalities remains a current priority for national healthcare.
- Clinical trial participation and treatment access: Clinical trial patients were also significantly more likely to have been treated with gene therapy ($p < 0.001$), confirming the role of clinical research as a gateway to new therapies. These results concur with what clinical trials have reported globally, establishing the value of research participation within therapy availability.[32] Continued growth in Saudi Arabian biomedical research infrastructure and regulatory reform are needed to enable enhanced patient access and the establishment of gene therapy innovation.
- Disease Spectrum and Treatment Outcomes: The prevalence in this category of genetic disorders—predominantly thalassemia, sickle cell anemia, G6PD deficiency, Tay-Sachs disease, and cystic fibrosis—is representative of the Gulf's epidemiolog.[33] Regimens for treatment are presently largely supportive, with blood transfusions, bone marrow transplant, and emerging gene therapies. Clinical improvement occurred in approximately 46.3% of the patients, 41.5% were stable, while a smaller percentage worsened or expired (5.9%). These results reflect ongoing challenges in disease control, treatment response, and reduction in mortality.
- Economic Cost of Gene Therapy: The expenses of gene therapies varied widely, with a mean expenditure of over 930,000 SAR per patient, mirroring the extremely high price of these new therapies. This economic factor highlights the urgent need for financially sustainable models of financing within the Saudi healthcare system, especially as

gene therapies transition from the experimental to the standard of care.

Future Directions

On the basis of these findings and the broader literature, we suggest several future directions as being crucial in advancing access to genetic healthcare and gene therapy in Saudi Arabia.

1) Expansion of Genetic Counseling and Preventive Programs

With the huge contribution of consanguinity to the prevalence and severity of genetic disease, an increase in genetic counseling services must be provided. This includes the increase in the number of genetic counselors, integration of genetic services into primary care, and expansion of premarital screening programs with culturally sensitive education campaigns. Public awareness campaigns must be directed toward de-stigmatizing genetic disease and encouraging forward-looking risk screening, as has been previously proposed.[11,34]

2) Reducing Healthcare Disparities between Regions

Strategies for geographic disparity reduction will need to include upgrading healthcare infrastructure and specialist care in underserved areas. Mobile genetic clinics, telemedicine, and regional genetic centers could offer equal access. Workforce incentives and training positions will also need to be enhanced to entice specialists to practice in lower urbanized areas. Collaborations between governmental health departments and private providers will be required to overcome systemic obstacles and ensure uniform standards of care.

3) Enhancing Clinical Trial Infrastructure and Participation

To benefit from the pivotal role of research participation in accessing gene therapy, Saudi Arabia must enhance its clinical research infrastructure. Steps must be taken to simplify regulatory pathways to expedite trial approvals without compromising safety for patients. Public campaigns to de-mystify the advantages of clinical research and dispel cultural fears will improve recruitment and retention of patients. Facilitating a partnership between academic centers, pharmaceutical industry, and regulatory agencies is critical to develop sustainable, high-quality networks of trials.

4) Widespread Use of Advanced Genetic Diagnostics

The study points out the diagnostic value of whole genetic testing. Broader access to next-generation sequencing technologies, e.g., whole-exome and whole-genome sequencing, will improve diagnostic yields and allow for earlier identification of genetic disease. Harmonization with genomic databases across the nation will allow personalized medicine projects and epidemiological surveillance to support precision medicine based on the Saudi population's needs.

5) Constructing Sustainable Models for Healthcare Financing

The costly aspect of gene therapy requires new mechanisms for healthcare financing. The potential models include government subsidies, expanded insurance coverage, public-private partnerships, and outcome-based payment. Policy decisions need to be informed by health economic evaluations and health technology assessments to optimize allocation of resources and make novel therapies affordable without compromising quality or access.

6) Promoting Patient and Community Participation Education

Families, advocacy groups, and support networks empower patients to receive therapies, improving disease management and treatment compliance. Culturally appropriate communication is a key component of community-based participatory approaches that can enhance trust and reduce stigma against genetic diseases and research studies.

7) Embracing Technological Developments and Translational Research

Saudi Arabia's dedication to genomics and biotechnology research has the promise of introducing new therapies such as CRISPR gene editing and the treatment of mitochondrial diseases to the clinic. Translational research needs to continue to bring global advances to local population needs and establish tailored therapeutic regimes.

8) Building Strong Ethical and Legal Foundations

With improvements in genetic testing and gene therapy technologies, ethical dilemmas related to data privacy, informed consent, and equitable access must be addressed aggressively. Saudi Arabia must develop comprehensive guidelines that are culturally sensitive as well as safeguard patients' rights. Public debate and professional education on ethics will support ethical research and clinical practice.

Limitations

We note several limitations with our analyses. The retrospective design of this study limits causal inferences and missing data, especially on the cost of therapy, limits economic evaluations. Region-level availability of treatment was established from hospital data and may not capture informal care pathways that many patients use. Additionally, social determinants and patient preference data were unavailable, limiting detailed analysis of access barriers.

Implications and Recommendations

This study's findings underscore the need to determine and implement standardized gene therapy eligibility criteria that include severity and genetic risk factor analysis. Implementing public health interventions for genetic counseling, particularly in highly consanguineous populations, can help prevent disease

incidence and reduce severity. Disparities between regions could be improved through the establishment of gene therapy facilities, investments in training healthcare professionals, and using new technologies such as telemedicine to increase equal access. Facilitating patient participation in genetic study programs through raising awareness and simplifying the recruitment process may also improve access to novel therapeutics. Improved health data collection, including cost and outcome information, is needed to enhance policy and economic analyses.

Table 1.

Study No.	Focus Area	Region	Methodology	Key Findings	Gaps Identified	Reference (Author, Year)
1	Genetic counseling landscape	Qatar	Review, program analysis	Expansion of services, academic programs	Limited data on long-term outcomes	Abiib et al., 2024
2	Oncology early-phase clinical trials	MENA	Review	Infrastructure/regulatory challenges	Need for unified regulatory framework	Alotaibi et al., 2024
3	SMA genetics and therapy	GCC	Genetic and clinical review	High prevalence linked to consanguinity	Limited population-wide screening data	Salama et al., 2024
4	Genetic disorders prevalence	Saudi Arabia	Retrospective study, molecular testing	High diagnostic yield, consanguinity influence	Lack of longitudinal outcome data	Alqahtani et al., 2023
5	Mitochondrial disease molecular insights	Global (including GCC)	Review	Molecular mechanisms and therapies	Translation to clinical practice limited	Aldossary et al., 2022
6	Genetic screening & precision medicine	GCC	Review	Growing role of genomics	Integration in routine care incomplete	Chancellor et al., 2023
7	Rare disease epidemiology	Saudi Arabia	Epidemiological analysis	High burden of rare diseases	Policy implementation challenges	Fasseeh et al., 2025
8	Clinical trial participation barriers	MENA	Systematic review	Identified patient and institutional barriers	Limited practical solutions implemented	Alotaibi et al., 2024
9	Genetic counseling ethics	Arab countries	Ethical review	Need for cultural sensitivity and confidentiality	Insufficient counselor training programs	Hosen et al., 2021

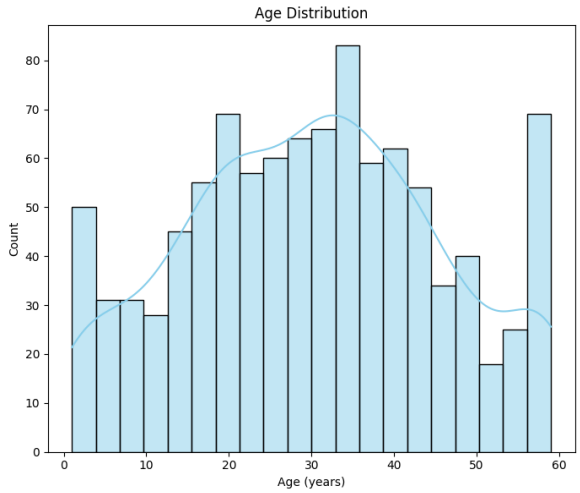
Table 2: Patient Demographics and Characteristics.

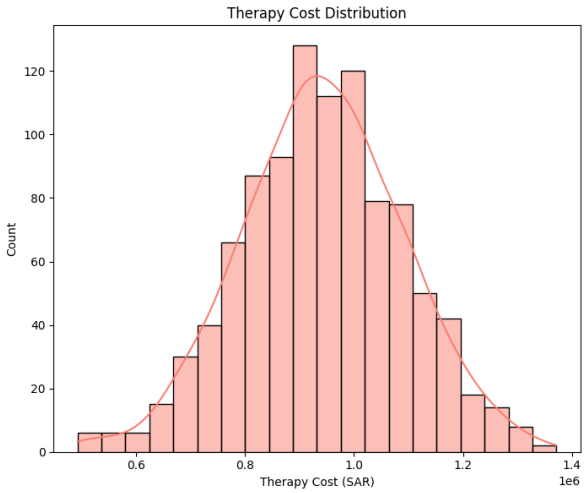
Variable	Category	Count	Percentage (%)
Nationality	Saudi	185	90.2
	Non-Saudi	20	9.8
Region	Madinah	34	16.6
	Riyadh	28	13.7
	Tabuk	28	13.7
	Jeddah	26	12.7
	Qassim	26	12.7
	Makkah	24	11.7
	Eastern Province	22	10.7
	Abha	17	8.3
Genetic Disorder	Thalassemia	51	24.9
	Sickle Cell Anemia	41	20
	G6PD Deficiency	39	19
	Tay-Sachs	37	18
	Cystic Fibrosis	37	18
Severity Level	Moderate	79	38.5
	Severe	75	36.6
	Mild	51	24.9
Treatment Type	Supportive care	75	42.4
	Blood transfusion	74	41.8
	Bone marrow transplant	28	15.8
Gene Mutation	*HBB*	92	44.9

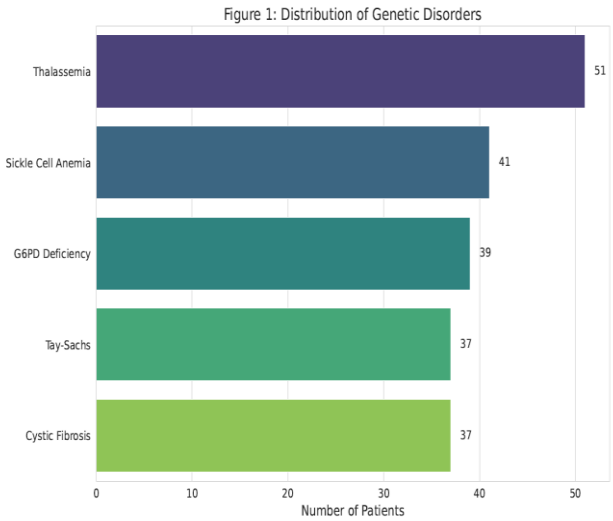
	G6PD	39	19
	HEXA	37	18
	CFTR	37	18
Treatment Outcome	Improved	98	47.8
	Stable	59	28.8
	Worsened	36	17.6
	Deceased	12	5.9
Mortality Risk	Low	101	49.3
	Medium	61	29.8
	High	43	21

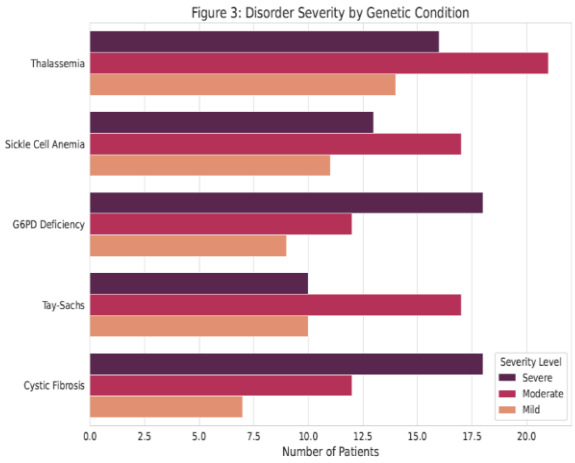
Table 3: Continuous Variables Summary.

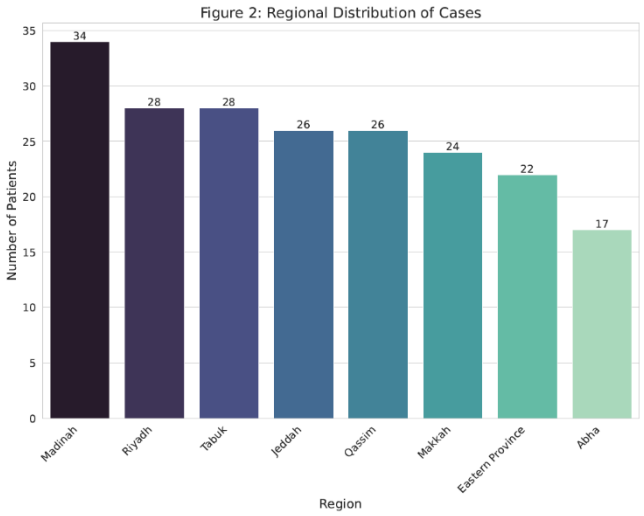
Variable	Mean	Median	SD	Min	Max	Missing (%)
Age (years)	29.98	32	17.07	1	59	0
Therapy Cost (SAR)	931,561	936,518	149,286	488,857	1,371,295	0

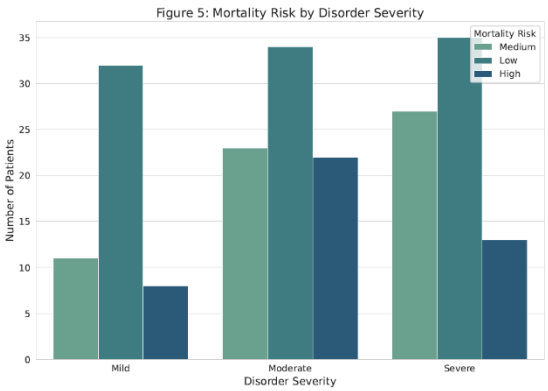


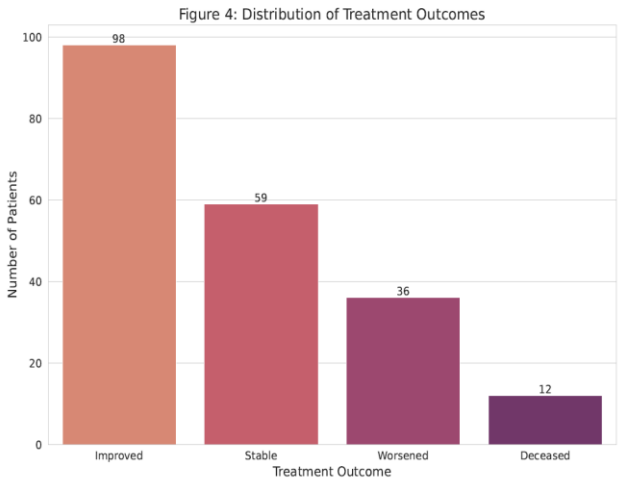


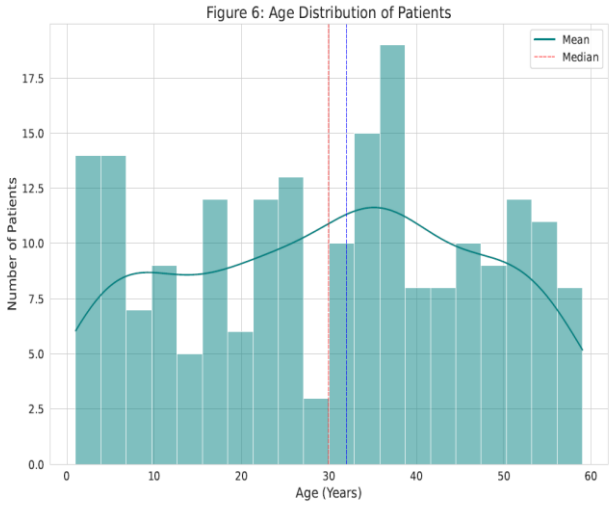


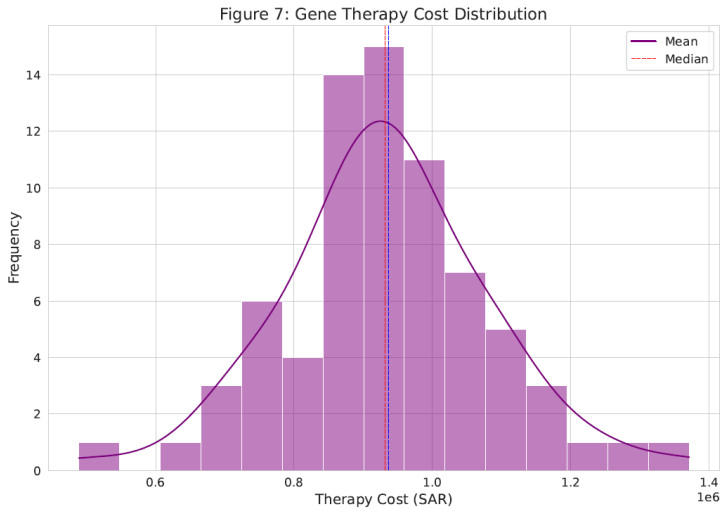












CONCLUSION

This research assessed data from patients with genetic diseases to assess gene therapy eligibility, healthcare access disparity, and clinical trial participation within the Saudi Arabian context. Consanguinity was determined to be a strong predictor of disease severity, and so targeted genetic counseling and screening programs should be established on the region's unique demographic landscape. This research also highlights important regional inequalities in access to healthcare, with patients

in rural or under-served regions of the country lacking access to specialist genetic services and gene therapy. These inequalities emphasize the imperative for changes in healthcare systems to decentralize and increase precision medicine access across the country. Moreover, increased patient enrollment in clinical trials was found to be an extremely important facilitating factor for patients to have access to new therapies, implying the need for the establishment of Saudi Arabia's clinical trials infrastructure and patient outreach networks.

Both local and international studies were compared to ensure representativeness of the findings and measure against international best practice in the provision of genetic healthcare. The results of this study provide useful information to policymakers, practitioners, and researchers by identifying key challenges as well as opportunities for the management of genetic disorders in such a highly consanguineous population.

In the future, closing the gaps noted with expanded genetic counseling services, equitable healthcare policy, and more participation in clinical research will be equivalent to driving patient outcomes and precision medicine in Saudi Arabia. Continued investment in genetic screening, infrastructure, and culturally adapted healthcare education will advance a more comprehensive and effective genetic healthcare system. Long-term outcome assessment, cost-effectiveness, and socio-cultural determinants should be the research agenda of the future to further enhance gene therapy access and delivery.

In summary, this study provides a benchmark for the advancement of genetic healthcare and the availability of therapy in Saudi Arabia, and more generally for similar nations with healthcare and genetic needs. With multi-disciplinary action across clinical, research, and policy fields, the vision for equitable and efficient treatment of genetic disease can be more and more realized.

Conflicts of Interest

The authors declare that they have no conflicts of interest with this work.

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Heba K. bin bisher: Investigation (supporting); Resources (equal).
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