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From Classical Molecular Diagnostics to Genomic Medicine: Evolution of Medical Genetics Education at Mashhad University of Medical Sciences

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ABSTRACT

This research aims to evaluate the evolutionary trajectory of the MSc in Medical Genetics program at Mashhad University of Medical Sciences (MUMS), focusing on the transition from classical biochemical screening to modern genomic analysis. The field of medical genetics in Iran has transitioned from basic biochemical screening to the analysis of complex genomic architecture. Mashhad University of Medical Sciences (MUMS) has played a seminal role in this evolution. We specifically examine the foundational molecular diagnostic work on phenylketonuria (PKU) and beta-thalassemia (β-thalassemia), which established the regional mutation spectrum and continues to inform current educational practices. We discuss how these classical molecular techniques provided the foundation for modern next-generation sequencing (NGS) and precision medicine education. Furthermore, we highlight current challenges, including the bioinformatics bottleneck, ethical considerations in genetic counseling, and the need to integrate whole-exome sequencing (WES) data with traditional targeted methods. The main conclusion is that maintaining competence in classical diagnostic techniques while simultaneously integrating NGS, bioinformatics, and genetic counseling is essential for sustainable medical genetics education in populations with high rates of consanguinity.

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Abbreviations

ARMS-PCR, Amplification-refractory mutation system polymerase chain reaction; ELSI, Ethical-legal-and social implications; ID, Intellectual disability; IEMs, Inborn errors of metabolism; MUMS, Mashhad University of Medical Sciences; NGS, Next-Generation Sequencing; PKU, Phenylketonuria; PND, Practical prenatal diagnosis; PRSs, Polygenic risk scores; RFLP, Restriction fragment length polymorphism; SVs, Structural variants; VUS, variants of uncertain significance; WES, Whole-exome sequencing

Introduction

Medical genetics education in Northeast Iran is shaped by the high prevalence of autosomal recessive disorders, which is partly attributable to historically high rates of consanguinity [1]. To address this issue, the MSc program at Mashhad University of Medical Sciences (MUMS) was established to create a cadre of specialists capable of navigating the "diagnostic odyssey" associated with rare diseases. The program's success is built upon a legacy of molecular epidemiology that established the mutation spectrum of the most common regional genetic conditions [2]. However, a comprehensive review of how this educational framework has adapted to rapid advances in genomic technologies has been lacking. The Department of Medical Genetics at MUMS owes much of its diagnostic infrastructure to the early research of Hamzehloei and colleagues. Their work in the late 1990s and early 2000s provided the first molecular maps of genetic disorders in Khorasan Province, moving the department toward a modern molecular paradigm. In this review, we examine both the educational development and the diagnostic infrastructure of the MUMS medical genetics program, with particular emphasis on the integration of classical and cutting-edge technologies. The primary focus is on how historical molecular diagnostic achievements have shaped the current MSc curriculum and how future directions can build upon this foundation.

Molecular Diagnostics of β-Thalassemia

β-Thalassemia remains the most common monogenic disorder in Iran. Hamzehloei et al. conducted extensive studies to identify the specific mutation spectrum in Northeast Iran [2].
Allelic Heterogeneity: Their research utilized amplification-refractory mutation system polymerase chain reaction (ARMS-PCR) and restriction fragment length polymorphism (RFLP) techniques, revealing that the mutation pattern in Mashhad is distinct from those in other regions of Iran, with a high prevalence of the IVS-I-5 (G>C) mutation [2, 6]. Pedagogical Impact: This research allowed the MSc curriculum to move from theoretical Mendelian genetics to practical prenatal diagnosis (PND) and carrier screening, which remain cornerstones of student laboratory training at MUMS.

Phenylketonuria (PKU) and Metabolic Genetics

Mashhad is a primary center for the management of inborn errors of metabolism (IEMs). The work of Hamzehloei et al. on the PAH gene provided the first detailed examination of the molecular basis of PKU in the region [5, 7]. Their identification of common regional mutations, such as p.Arg261Gln (NM-000277.3.782G>A), allowed for the implementation of rapid molecular screening in newborns [7]. These foundational data enable current MSc students to perform genotype-phenotype correlations, which are essential for predicting clinical severity and responses to tetrahydrobiopterin (BH4) cofactor therapy.

Current Research Pillars and Advanced Technologies: From Targeted Testing to Next-Generation Sequencing (NGS)

While Hamzehloei's legacy focused on targeted mutation detection, the current MSc curriculum at MUMS has expanded to include whole-exome sequencing (WES). Students are now trained to interpret the vast amounts of data generated by NGS, particularly in "undiagnosed" cases involving neurodevelopmental delay and intellectual disability (ID) [3, 4]. Building on the regional focus on esophageal cancer, faculty members have integrated oncogenetics into the MSc program. Research focuses on both genetic predisposition, including germline mutations, and the epigenetic silencing of tumor suppressor genes through DNA methylation in the "Asian Esophageal Cancer Belt" [3, 8].

Discussion

The evolution of medical genetics at MUMS mirrors the global shift from "gene-at-a-time" diagnostics to "genome-wide" analysis. This transition from targeted ARMS-PCR/RFLP-based diagnostics to current NGS/WES education represents a fundamental pedagogical shift. However, this transition is uniquely colored by the socio-genetic landscape of Northeast Iran.
While the seminal work of Hamzehloei et al. [6, 7] successfully mapped the most common mutations for β-thalassemia and PKU using targeted molecular techniques, modern MSc students often encounter "negative" WES results.

This highlights the challenge of "missing heritability" or "hidden variants," particularly in consanguineous populations such as those in Razavi Khorasan. There is an increasing need to focus on deep intronic mutations and structural variants (SVs) that standard WES pipelines may overlook. This represents a critical pedagogical shift: teaching students to move beyond the exome and consider the impact of the non-coding genome [3, 11]. The diagnostic protocols established by Hamzehloei et al. [8] for β-thalassemia and PKU were highly cost-effective and well suited to high-throughput carrier screening in resource-limited settings. A key point of discussion for current MSc students is the economic efficiency of diagnostic approaches. In the era of NGS, there is a risk of "over-testing." Students must be trained to understand the clinical utility of maintaining classical techniques, such as ARMS-PCR, for detecting known familial mutations, as these methods remain faster and more affordable for PND than WES [9, 11].

Perhaps the most significant challenge facing the MUMS MSc program is the "bioinformatics gap." As laboratory work becomes increasingly automated, the primary role of the medical geneticist is shifting toward variant interpretation. At MUMS, there is a pressing need for formalized training in the following areas:

• ACMG/AMP Guidelines: Standardizing the classification of variants as pathogenic, likely pathogenic, or variants of uncertain significance (VUS).

• Protein Modeling: Understanding how a mutation such as p.Arg261Gln in the PAH gene disrupts protein folding, thereby bridging the gap between biochemical alterations and clinical severity. [7, 9].

The history of research on PKU and β-thalassemia at MUMS emphasizes that a diagnosis is only as valuable as the family's ability to act on it.

In Eastern Iranian culture, genetic results carry considerable social weight and may affect marriage prospects and family dynamics. MSc students must be trained not only as laboratory technicians but also as clinical interpreters who can navigate the ethical, legal, and social implications (ELSI) of genomic data. This includes the sensitive task of discussing incidental findings identified through NGS, a concern that did not arise during the era of targeted testing pioneered by Hamzehloei *et al* [10].

Future Directions: Precision Public Health

Looking ahead, the MSc program at MUMS is uniquely positioned to lead precision public health initiatives in Iran. By combining historical carrier-screening data for β-thalassemia with modern polygenic risk scores (PRSs) for complex diseases such as esophageal cancer, the university could develop a Khorasan-specific genomic database. This database could facilitate the identification of founder mutations unique to Turkmen or Mashhadi populations, thereby further honoring and expanding the foundational work of the department's early researchers [6, 11]. However, the development of such a database requires careful attention to ethical considerations, including data governance, informed consent at the population level, and the protection of genetic privacy. These topics must be integrated into the MSc curriculum to prepare graduates for responsible data management. Moreover, incorporating these data into the curriculum would prepare graduates to design population-level screening programs rather than merely diagnose individual cases.

Conclusion

The MSc program at Mashhad University of Medical Sciences stands at a historical crossroads. It must maintain the rigorous molecular diagnostic standards established by pioneers, ensuring that every student masters the foundational techniques used to address regional priorities such as β-thalassemia and PKU. At the same time, the program must evolve to meet the computational and ethical challenges of the 21st century.

The main message is clear: maintaining competence in classical diagnostic methods while integrating NGS, bioinformatics, and genetic counseling is essential for sustainable medical genetics education in populations with high rates of consanguinity. By incorporating advanced bioinformatics and clinical counseling into its legacy of molecular epidemiology, MUMS can provide a global model for medical genetics education in such populations.

Declarations

Authors' Contributions

AH was responsible for conceptualization, data collection, manuscript preparation, and review.
KN contributed to the manuscript preparation, and critical revision. TH contributed to the conceptualization, supervision, project administration, manuscript review, and final approval.

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Conflicts of Interest

The authors declare that they have no competing interests.

Ethics Approval

Not applicable.

References

1. Hamamy H. Consanguineous marriages: Preconception consultation in primary health care settings. J Community Genet. 2012; 3:185-192.

2. Abbaszadegan MR, Keyvani V, Moghbeli M. Genetic and molecular bases of esophageal Cancer among Iranians: an update. Diagnostic Pathology. 2019;14(1):97.

3. Abolhassani A, Fattahi Z, Beheshtian M, Fadaee M, Vazehan R, Ahangari F, et al. Clinical application of next generation sequencing for Mendelian disease diagnosis in the Iranian population. NPJ Genomic Medicine. 2024;9(1):12.

4. Srivastava S, Love-Nichols JA, Dies KA, Ledbetter DH, Martin CL, Chung WK, et al. Meta-analysis and multidisciplinary consensus statement: exome sequencing is a first-tier clinical diagnostic test for individuals with neurodevelopmental disorders. Genetics in Medicine. 2019;21(11):2413-21.

5. Hamzehloei T, Hosseini SA, Vakili R, Mojarad M. Mutation spectrum of the PAH gene in the PKU patients from Khorasan Razavi province of Iran. Gene. 2012;506(1):230-2.

6. Mohajertehran F. The spectrum of mutations in 100 thalassemic carriers referred to Ghaem Hospital of Mashhad. Iranian journal of pediatric hematology and oncology. 2012 Jan 1.

7. Tayebeh H, Amir H. Mutation screening of whole PAH gene in the PKU patients from North east of Iran. Clinical Biochemistry. 2011;44(13):S64.

8. Hamzehloei T, Azimian H. A Novel Mutation in the α2-Globin Gene in Two Unrelated Iranian Families. Shiraz E-Medical Journal. 2014 Jan 1;15(1).

9. Ghanei M, Sadat Fatemi SH, Hamzehlouei T. A comprehensive study of disease-causing variants in PAH, QDPR, PTS, and PCD genes in Iranian patients with Hyperphenylalaninemia: A systematic review. Human Heredity. 2023;88(1):8-17.

10. Green RC, Berg JS, Grody WW, Kalia SS, Korf BR, Martin CL, et al. ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing. Genetics in medicine. 2013 Jul;15(7):565-74.

11. Akbari MR, Malekzadeh R, Shakeri R, Nasrollahzadeh D, Foumani M, Sun Y, et al. Candidate gene association study of esophageal squamous cell carcinoma in a high-risk region in Iran. Cancer research. 2009;69(20):7994-8000.

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