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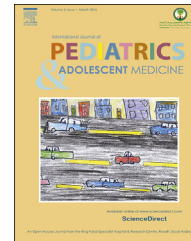


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REVIEW ARTICLE

# Genetic counselors' scope of practice and challenges in genetic counseling services in Saudi Arabia



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**Abstract** Genetic counseling is an evolving field in Saudi Arabia. In 2015, genetic counseling was recognized as a Master's program by the Saudi Commission for Health Specialties. Our genetic counselors combine their knowledge of genetics, counseling theory and interpersonal communication to serve Saudi and non-Saudi patients affected with a range of genetic conditions and/or birth defects. Most patients are referred to the clinic from different clinics at King Faisal Specialist Hospital and Research Centre (KFSHRC) and outside of KFSHRC for various indications. Carrier testing and preventative reproduction options rank highly on the reasons for referral to our clinics.

The Saudi population has unique customs and beliefs, such as consanguinity and the evil eye. Challenges that are routinely encountered in our genetic counseling clinics include, but are not limited to, preventative reproductive options and termination of pregnancy, manifesting carriers, stigmatization of women and approaches to complex molecular findings. Working with families from different backgrounds and beliefs undoubtedly requires professionals with a distinctive set of skills and a structured clinical setting. This review article presents the scope of genetic counseling practice and tackles some of the challenges faced in providing genetic counseling in Saudi Arabia.

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## 1. Introduction

The term “genetic counseling” was first introduced in 1947 by Sheldon Reed [1]. The American Society of Human Genetics proposed a definition of genetic counseling in 1975, which was redefined after the professional society of genetic counselors known as “The National Society of Genetic Counselors” was incorporated in 1979. Genetic counseling is a “process of helping people understand and adapt to the medical, psychological and familial implications of genetic contributions to disease” [2]. The first genetic counseling program was established by Professor Melissa Richter in 1969 at Sarah Lawrence College, which is located in New York, in the United States [3]. At present, there are several genetic counseling Master’s programs in the United States, Canada, Europe and South Africa.

Training in genetic counseling was not available in the Middle Eastern countries until 2003, when the late Professor Ahmed Teebi was hired by King Faisal Specialist Hospital and Research Center (KFSHRC) as Head of the Department of Genetics. He championed the development of a training program in the kingdom and hired a Canadian genetic counselor, Shelley Kennedy, as supervisor of the program to develop its curriculum. One year later, with Professor Moenaldeen Al-Sayed, as Medical Director, a diploma in genetic counseling was established at KFSHRC in Riyadh, Saudi Arabia [4]. Nine years later, Saudi Arabia witnessed the birth of a Master’s program in genetic counseling. As an expansion of the successful development of this field in Saudi Arabia, the Master’s program in genetic counseling was recognized and accredited by the Saudi Commission for Health Specialties in 2015. The inclusion of this Master’s program in the Ministry of Higher Education in Saudi Arabia will provide genetic counselors throughout the Kingdom, which will alleviate the burden placed on non-geneticist health care providers who have little training in medical genetics. The availability of genetic counselors in many of the governmental hospitals in the Kingdom of Saudi Arabia will provide tremendous advantages to patients and to other health care providers. This article reviews the genetic counselor’s scope of practice at KFSHRC, placing particular emphasis on the challenges encountered in our genetic counseling service.

### 1.1. Genetic counselors’ scope of practice

Genetic counselors are Master’s trained health care professionals who combine their knowledge of basic science, medical genetics, epidemiological principles, counseling theory with their skills in genetic risk assessment, education, interpersonal communication and counseling to provide services to patients and their families for a diverse set of genetic or genomic indications. Some genetic counselors offer general genetic counseling, while others specialize in a particular area of interest, such as cancer or prenatal care, assisted reproduction, cardiovascular health, research, public health and education.

Genetic counselors see patients and their families for several reasons, including but not limited to, a family

history of an inherited condition, a previous child with intellectual disability, multiple congenital anomalies or birth defects, repeated pregnancy loss or infertility, a positive newborn screening test, a newly diagnosed abnormality or genetic condition and to enroll patients in research studies. Moreover, they provide carrier testing, premarital genetic testing and counseling regarding preventative reproductive options, which include prenatal diagnosis (PND) and pre-implantation genetic diagnosis (PGD) for various underlying genetic defects and chromosomal abnormalities.

### 1.2. Genetic counseling clinics: the KFSHRC experience

Our genetic counseling clinics serve patients from different provinces of Saudi Arabia, the gulf and Arab countries. We have six genetic counseling clinics per week. These clinics are separate from the genetic and metabolic clinics, which are operated by geneticists. The time allocated for each patient ranges from 25 min for a follow-up to 75 min for a new case. Some cases require multiple counseling sessions, whereas other cases require only one or two visits to the genetic counseling clinic.

Cases are referred to our clinics from different specialties both within and outside of KFSHRC, such as medical genetics, high risk obstetric gynecology, cancer, dermatology, neurology, hematology, pediatrics and in vitro fertilization clinics. Referrals are primarily for extensive genetic counseling, molecular and cytogenetic testing, premarital screening, carrier testing and preventative reproductive options.

Many families seek genetic counseling to understand the nature and consequences of genetic conditions, the risk of recurrence and preventative reproductive options and to address their uncertainty regarding genetics and inheritance. Our teams provide support for these families by identifying their concerns, addressing their needs, providing psychosocial counseling and promoting their decision-making process regarding testing or methods of prevention.

### 2. Challenges in genetic counseling services: the KFSHRC experience

Genetic counseling often raises ethical and professional challenges. The most frequently encountered challenges among physicians in Western countries such as in Austria have been informed consent, organizational constraints, withholding information, and attaining/maintaining proficiency. [5].

The major ethical principles that govern the attitudes of genetic counselors include respect for the patients’ autonomy and right to make their own decisions, beneficence, i.e., taking actions to help others, non-maleficence, i.e., to do no harm, and justice, or administering services fairly between others [6].

There are several unique and difficult issues that are faced routinely in genetic counseling clinics in Saudi Arabia. Below is an overview of these issues based on several experiences at KFSHRC.

## 2.1. Consanguinity

Consanguineous marriage is a common practice in Saudi Arabia. Consanguinity refers to the marriage of parents with a recent common ancestor [7]. The overall prevalence of consanguineous marriage in Saudi Arabia is 56% and is 33.6% between first-degree cousins [8]. When families with a positive family history for an autosomal recessive condition are seen for genetic counseling, the role of consanguinity in increasing the chances of having children with genetic disease is always discussed; however, most of the time these families continue practicing consanguineous marriage and have more affected children. In addition, it is not uncommon to see more than one genetic disease segregate with a family.

In Saudi Arabia, the high rate of consanguinity may be attributed to different social and traditional factors, in addition to the desire to keep property within families. Main factors that inspire consanguinity include social and economic benefits and the stability of marriage between cousins. When the man and woman are raised in the same or a similar family environment, it is believed that they will adjust more easily to the marriage. In addition, marriage between relatives is considered to be beneficial because it maintains family fortunes within the same family structure. Anthropologists have long agreed that the primary achievement of consanguineous marriages is the inheritance of family structure and property [9–11]. Another cultural belief is in polygamy, which the husbands in some Saudi families believe is the practical solution to this situation.

## 2.2. The evil eye

The evil eye is a “folk belief elicited by the good luck of fortunate people whether in the form of material possessions including livestock, or possessing beauty, health, or offspring, may result in their misfortune” (Evil eye Encyclopedia). Some families relate their children's inherited disease to belief in the evil eye. The evil eye belief is widespread, according to which people can cause harm by merely an envious glance at desired objects or their owners [12]. The belief in the evil eye is ancient and present in every culture. The oldest reference appears in the cuneiform texts of the Sumerians, Babylonians and Assyrians around 3000 BC (Ancient History Encyclopedia). At that time, it was called “drishti” or “nazar” in India, and it was also called “nazar” in Turkey. Some people believe that the evil eye can place a curse on victims through a malevolent gaze of their magical eye. Others believe that envying others through the use of the evil eye can happen unintentionally. Furthermore, some cultures believe that the evil eye can suddenly bring bad luck by looking unintentionally at people who are unlucky enough to be cursed with the power. The evil eye was mentioned in the Quran in Sorat Al-Nisa verse: “or envy people for what God has given them of His bounty gave Ibrahim the Book and Wisdom and gave him the great king”. In Islam, Prophet Muhammad states: “The influence of an evil eye is a fact.” All Muslims believe in the evil eye because it is mentioned in the Quran. Some of the families at the

genetic counseling clinics explained that they expected the disease to be caused by the evil eye. According to some health care providers, others held this belief but they did not share it.

## 2.3. Preventative reproductive options and termination of pregnancy

Preventative reproductive strategies are urgently needed to combat the medical, financial and social burden of genetic diseases in Saudi Arabia. Preventative reproductive options are governed by religious rulings and/or political influence worldwide. While PGD and PND diagnoses are permitted in majority of countries worldwide, the practice of PGD is prohibited in Germany to protect embryos [13,14].

In the past few years, several studies have been conducted in Saudi Arabia to compare the Saudi preference for PGD versus PND. In a study conducted in 2006, 30 couples who had been treated at KFSHRC were surveyed regarding their attitudes towards preventative reproductive options. It was found that 27% of the couples preferred PGD compared to 13% who accepted PND. In addition, 10% were reluctant to choose any preventative options [15]. Similar findings were observed in a study conducted with a Lebanese population that examined their attitudes towards PGD as an alternative option to PND. The results indicated that 68% of the participating women accepted PGD [16]. The factors that contributed to the avoidance of PGD included receiving an IVF procedure, long waiting lists, fear of mixing embryos, the possibility of misdiagnosis and/or failure to conceive. However, the aforementioned studies showed an overall preference for PGD compared with PND primarily due to religious rulings that govern the termination of pregnancy in Arab countries.

The potential benefits of PGD are not confined to preventing the occurrence of genetic disease; they expand to include advantages that are strongly valued by families. One advantage is the use of unaffected IVF-embryos for affected siblings who would benefit from hematopoietic stem cell transplantation for different genetic diseases, such as Fanconi Anemia and hemoglobinopathies [17]. Another benefit is the use of sex selection for medical reasons, e.g., in case of an affected child with X-linked conditions. This practice is permitted in Islam [18]. However, some families request sex selection in genetic counseling session because of social preferences, which is not accepted in Saudi Arabia. Similarly, sex selection for social reasons is prohibited in other countries, such as in Turkey [19].

Prenatal diagnoses are accepted in Islam before 120 days of conception if the fetus is grossly malformed with an untreatable severe condition and are based on the parent's request [20]. Cases that receive consensus by three geneticists can be terminated before 120 days; other patients that do not fulfill the criteria for termination of pregnancy are provided with a letter describing the medical aspects of the disease to seek support from scholars by getting a Fatwa. PND and termination of an affected pregnancy present a real challenge to genetic counselors, geneticists and maternal fetal medicine consultants, especially when

the pregnant woman reports to the clinic late in her first trimester and/or with a lack of identifiable pathogenic mutations underlying the cause of the index case.

A study conducted with 32 families with hemoglobinopathies to explore their attitudes towards PND and termination of pregnancy found that 81.3% of the families accepted PND. However, termination of pregnancy was viewed differently because of religious differences, and no other factors were identified to contribute to the families' decisions [21]. Another study included a survey of 200 parents of affected Saudi children and explored their views on termination of pregnancy for 30 genetic conditions. The results indicated that mothers were more interested in termination of pregnancy than fathers of the patients [22]. Overall, PND is widely accepted by the Saudi population, but termination of pregnancy remains a dilemma for some families. Pregnancy at the time of mutation analysis is also common in Saudi Arabia. At the genetic counseling clinic, we routinely meet couples and review the preventative options with them. However, couples often indicate that an unplanned pregnancy has occurred. A similar problem arose when families were referred to the PGD clinic; this indicates lack of proper use of contraception, either intentionally or unintentionally.

Mitochondrial diseases due to mtDNA defects are a challenging category of genetic disease that present to genetic counseling for preventative reproductive options. The reasons these cases are difficult include social stigma for carrier mothers and technical limitations of PGD application. Tissue specificity, heteroplasmy, mutant load and bottleneck effect are barriers to performing PGD with no residual risk of recurrence for a concerned family [23]. The situation is different in Western countries such as in the UK, where parents of an affected child with an mtDNA defect have alternatives to PGD. These alternatives include oocyte donation and embryo manipulation to replace the defective mtDNA with unaffected mtDNA through different mitochondrial gene replacement techniques that have been approved ethically and legally (<http://www.nuffieldbioethics.org/mitochondrial-dna-disorders>) [24,25]. Both approaches are prohibited in Islam [26,27]. Accordingly, these families suffer physically and psychosocially due to their limited reproductive options in Saudi Arabia.

#### 2.4. Manifesting carriers

Our society is highly inbred, favoring first cousin marriages [28]. Therefore, most of our patients are affected with autosomal recessive conditions, in particular inborn errors of metabolism [29]. The carriers for autosomal recessive or X-linked conditions are typically asymptomatic. However, it is known that heterozygous individuals may manifest some signs of disease based on biochemical, radiological and clinical findings. Examples include hyperammonemia in case of carriers for X-linked conditions, ornithine transcarbamylase deficiency, calvarial thickening in heterozygote individuals with autosomal recessive disorders, Marshall syndrome reported by Khalifa et al [30] and phenotypic spectrums seen in heterozygotes for familial Mediterranean fever. The question that becomes apparent is whether we should provide management and treatment for the manifesting

heterozygotes. This demonstrates the crucial role of genetic counselors in providing pre-test and post-test counseling to enable these individuals to understand the implications of genetic testing and to adapt physically and cope psychosocially to carrier test results. Without proper education and counseling, this could lead to alterations in parenting, increased anxiety, negative self-concept and stigmatization. In Western countries, additional burdens on manifesting carriers include health insurance and/or employment discrimination [31].

Carrier testing identifies heterozygote individuals with autosomal recessive and X-linked conditions; these findings indicate additional family members who are at-risk for manifesting signs of the disease and/or having affected children, which elicits a complex counseling session. Ataxia telangiectasia (AT) is an autosomal recessive condition affecting 1:40,000–1:100,000 live births in the United States. Carriers of AT are at a four-fold increased risk of developing cancer and heart disease in comparison to general population [32]. AT carriers are often hypersensitive to radiation and radiomimetic drugs. Genotype–phenotype correlation may provide insight into at-risk carriers' predisposition to cancer. However, the lack of reported correlation between a novel genetic alteration and the risks mentioned above complicates genetic counseling. This ultimately affects individual's ability to make an informed decision regarding management. Urgent issues such as parental surveillance, referral to other specialties and carrier testing for unaffected offspring emerge and challenge the entire genetic counseling process.

#### 2.5. Emotional and social impact on carrier women

The emotional and social impact on parents with X-linked conditions differs from that of parents with recessive diseases. In a study conducted by James et al [33], they found that carrier mothers of X-linked conditions experienced more guilt, anger and self-blame while parents of children with autosomal recessive conditions worried more about reproductive risk. The social burden on female carriers in form of stigmatization is no longer a phenomenon that is uniquely related to X-linked conditions or mitochondrial disease due to maternal inheritance, as previously believed. Our clinical experience expands that list to include carrier mothers for autosomal recessive conditions. We believe that the stigmatization of carrier mothers of autosomal recessive conditions in our community is determined by the lack of adequate knowledge regarding the inheritance and etiology of the disease, the education level of the parents and social influence.

The diagnosis of carrier status in mothers of affected boys with X-linked conditions has been found to affect their relationship with their daughters. Some mothers have reported a feeling of closeness, which enabled them to talk openly with their daughters, while others found that the results of the carrier test drove them apart [34]. In our population, the stigmatization that occurs when mothers receive a positive carrier test result may, in their opinion, justify mothers' choice to not inform at-risk daughters about the availability of genetic testing. Mothers who experience stigma from their husbands and relatives show



social isolation and tend to hide genetic test information from their daughters. These mothers clearly indicate that the underlying reason for their behavior is fear for their daughter's future (Personal communications).

One of the dilemmas we face in genetic counseling clinic is requesting carrier testing for the fiancé of a carrier female. In our clinical practice, the father of a carrier female brings the fiancé and requests us to perform carrier testing on him without providing information about the genetic disease in question. Nevertheless, some fiancés attend genetic counseling clinics unaware about the genetic condition in the female's family. This imposes a great challenge on the genetic counselors, who must value the ethical principles in practice for all of the involved parties while considering the burden placed on the woman's family, the confidentiality of the woman's test result and the right of the fiancé to be fully counseled before having the genetic test performed.

## 2.6. Complex molecular test findings

Advances in molecular testing have benefited families because it resolves the ambiguity associated with undiagnosed cases. It has simultaneously provided opportunities to extended family members to pursue premarital screening and to parents to pursue preventative reproductive options. In spite of these perceived benefits, advances in genetic testing will continue to become more complex [35]. In particular, exome sequencing presents challenges to genetic counselors. Examples of issues encountered in our routine clinical practice include the identification of variants of unknown clinical significance, which limits our ability to offer PND and termination of pregnancy, and the identification of pathogenic mutations in multiple genes causing a number of genetic conditions in a family. This certainly warrants careful and thorough genetic counseling. The major dilemma in these findings is related to PGD, as only two mutations are tested using the PGD approach. This places a large burden on geneticist to carefully review each case with the family and choose two candidate diseases for PGD based on several parameters, such as a disease severity and prognostic outcome. In such cases, PND would be offered to detect other causative mutations that would not be excluded by PGD, in the event that the pregnancy continued after PGD. The decision-making process for the parents becomes increasingly difficult as other issues arise, e.g., identifying at-risk family members and cascade genetic testing. Another issue encountered in the clinic was receiving negative results of exome sequencing, which required further consideration of reanalyzing the patient's sample with a platform characterized by in-depth coverage, homozygosity mapping if multiple affected family members are available or the use of another alternative molecular approach. Finally, incidental findings and ethical challenges of whether to report such findings were another challenge faced. The application of guidelines developed by The American College of Medical Genetics and Genomics (ACMG) helps address this dilemma and emphasizes the importance of pre-test genetic counseling in the era of exome sequencing [36]. It becomes apparent that the results from advanced molecular technologies in the field of medical genetics provide additional

complexity to the already complex family situation and reproductive history.

## 3. Conclusion

Marriage customs in Saudi Arabia present challenges to genetic counselors, as multiple diseases can segregate within a single family. This practice warrants cascade genetic testing for extended family members and raises ethical challenges. Genetic counseling becomes a very complex process in view of the available advanced molecular techniques and a lack of clinical significance of the reported variants. The profession of genetic counseling in the kingdom will continue to evolve to incorporate growing complexity due to molecular advances while addressing the unique social and cultural norms of the region.

## Conflict of interest

None declared.

## Ethical approval

There is no need for ethical approval for this review.

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