Alya Qari et al. JBC Genetics. 2021;4(2):100-111
https://doi.org/10.24911/JBCGenetics/183-1619687090



ORIGINAL ARTICLE

# Ethical solicitude in medical genetics as perceived from a genetic counselor's perspective in the tribal-based community of Saudi Arabia

Alya Qari[1,2]*, Moeen Al-Sayed[1,2,3], Zuhair Al-Hassnan[1,2,3], Amin Kashmeery[4]

## ABSTRACT

**Background:** The genetics domain is witnessing great advances in diagnosing and predicting genetic diseases. In a clinical setting, autosomal recessive genetic disorders are frequently observed as a result of the high rate of consanguinity. The advances in genomic technologies and methods in recent years have facilitated new tools for gene discovery in humans. There is a debate over the ethical dilemmas and challenges behind providing families with the genetic test results and incidental findings. Thus, this vast source of information can have a multitude of ethical, social, legal, and political implications.

**Objectives:** To study how families of the affected children respond when they receive incidental findings. Also, we aimed to identify how healthcare professionals descriptively abide by their role and the information-sharing procedures.

**Methods:** This qualitative study was conducted at King Faisal Specialist Hospital and Research Centre in Riyadh. It included a total of 14 participants and 14 healthcare providers.

**Results and conclusion:** Six strong themes emerged in this study. This study explored the experiences of parents of children affected with genetic diseases and the experiences of healthcare providers attending these families; their observations and the ethical challenges they faced during their practice.

**Keywords:** Genetic results, ethical issues, genetic counseling, incidental findings, whole exome sequencing.

## Introduction

In the past, the problems of genetic disorders were hidden within the high infant mortality statistics because most affected infants died without being diagnosed (1). However, nowadays, the genetics domain is witnessing great advances in diagnosing and predicting genetic diseases and ailments carried through the genes from one generation to another (2). In a population with a high rate of consanguinity, whose genetic pool extends over millennia, these phenomena become more exacerbated. According to the latest census (2021), the population of Saudi Arabia is 35.34 million (3). There is a high birth rate in the country every year. Furthermore, some of the Saudi population has maintained their tribal lineage over a long period of time and, therefore, Saudi Arabia retains many tribal customs. Each tribe could have hundreds or thousands of members. Some tribes in the country have an extremely high consanguinity rate and may be considered "genetic isolates" (4). A cross-sectional study in a smaller urban area, Dammam city, carried out on 1,307 married Saudis showed that the rate of consanguineous marriage was 52% (5). Another study by El-Hazmi et al. (6) was conducted on 3,212 Saudi families and showed that the overall rate of consanguinity was

**Correspondence to:** Alya Qari
*Medical Genetics Department, King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia.
**Email:** abc@def.com
*Full list of author information is available at the end of the article.*
**Received:** 29 April 2021 | **Accepted:** 02 August 2021

57.7%. In the most extensive survey over a 2-year period (2004-2005), it was found that, of 11,874 mothers, 56% were in consanguineous relationships (7). According to El-Hazmi et al. (6), the overall consanguinity rate could reach >80% in certain rural areas of the country. The first cousin marriage rate ranged between 28.4% and 39.3% (5-7). The combination of the tribal structure of society with a high rate of consanguinity and the large family size has raised the prevalence of autosomal recessive diseases (8). Consanguinity possibly increases the prevalence of multifactorial conditions such as congenital heart defects and common adult-onset disorders (9).

Despite the tremendous amount of research and clinical efforts, some of the molecular roots causing a large number of patients with autosomal recessive conditions are still unknown. Next-generation sequencing has dramatically reduced the cost and increased the output of sequencing (10). These are influential new tools for gene discovery in human and medical genetics research (11). The emergence of whole exome sequencing (WES), whole genome sequencing (WGS), their growing speed, and their low cost, as well as developments in informatics, have facilitated the automated analysis of potentially new variants. Moreover, computer-supported communication with clinicians and participants has generated vast amounts of high-resolution data. These sequencing methods enable the capture of the full extent of genetic variations in an individual's genome or their entire gene coding region. Such approaches have already proven to be beneficial for the identification of the genetic causes of several Mendelian disorders (12). On the other hand, WES and WGS and their increasing integration into clinical care have raised several ethical concerns. One of these concerns is what to report to patients from the resultant findings (13), particularly since these advances in diagnostic tools and methodologies can also reveal mutations that reflect certain hidden personal traits that are sensitive in nature, such as those with behavioral/ psychological implications (14). In this paper, we studied how families of affected children respond when they receive WES results and incidental findings. We also investigated how healthcare professionals working within genetic counseling fields descriptively abide by their role and the information-sharing procedures.

## Subjects and Methods

This study is a qualitative study conducted at King Faisal Specialist Hospital and Research Center (KFSHRC) in Riyadh between 2014 and 2015. Ethical approval for the study was sought and obtained from the local Research Ethics Committee at KFSHRC (RAC# 2141020). It included a total of 28 participants (Table 1): 14 parents of children with genetic conditions treated and followed at the genetic/ metabolic clinics and 14 healthcare providers working with children diagnosed with genetic diseases (Table 2). Each subject signed a consent form approved by an institutional review board. The eligibility criteria for the parents of the affected children included that couples should be at their reproductive age; have children affected by genetic diseases; and have their samples sent for genetic testing (WES) for diagnosis purposes. They must have positive pathogenic gene mutations in their results and a confirmed diagnosis to be included in the study. The eligibility criteria for the healthcare providers specified that only healthcare providers who attend families with a history of autosomal recessive genetic diseases at a range of different hospitals in Riyadh, Saudi Arabia, will be enrolled in the study.

Parents were recruited through the Medical Genetics Clinics at KFSHRC. The healthcare providers were recruited through the Department of Medical Genetics at KFSHRC, the Saudi Society of Medical Genetics, and through Prince Sultan Military Medical City. The data were analyzed by using a thematic analysis method (15). All the interviews were conducted face to face with the participants.

## Results

Six strong themes emerged: 1) recall of strong emotional responses; 2) the existence of cultural beliefs; 3) the extent of faith; 4) family and social influences; 5) ethical challenges; and 6) healthcare providers' perspective on common mutations. These themes describe different aspects of the participants' experiences with having children with genetic diseases. It also describes different aspects of the healthcare providers' experiences with the families of the affected children.

### *Emotional responses*

A wide range of emotional responses for the parents were evident in their stories. There were three stages for their emotional responses.

a) First stage of emotional responses was at the time of discovering that a genetic disease existed within the family.

b) Second stage of emotional responses was at the time of receiving the WES test results.

c) Third stage of emotional responses was at the time of informing the parents of the incidental findings in their children if any were discovered.

The sequence of theses emotional responses started when these families first came to the genetic clinic and were informed that their children are affected with inherited diseases and these diseases run in the families. Moreover, there is a chance of recurrence in the future. 11 of the 14 parents of affected children recalled the feeling of shock at the time of receiving their child's diagnosis.

- *He was the first affected child in the family; I was shocked when the doctor told me (Participant 04).*

However, two parents who already had a positive family history reported that the news was somewhat expected and experiencing lesser amount of shock.

- *It was in the family, so I was expecting one of my children to be affected. When I was told by the healthcare provider, I was only worried about taking care of the affected child alone because my husband has special needs (Participant 08).*

The second stage of emotional responses started at the time of receiving the WES test results. All the parents were satisfied with the WES results and thought that this new technology is very important.

- *The WES test is especially important because now we know the cause of the problem and the diagnosis, although they were late. We have been waiting for 3 years (Participant 11).*

The third stage of emotional responses was at the time of informing the parents that there is a chance of receiving incidental findings with the WES results if any were discovered. Eight of the parents expressed difficulties in accepting the incidental findings in their children if any were discovered.

- *It is going to be very difficult; because it is something new, which I am not aware of (Participant 06).*

Ten of the parents were interested in knowing the incidental findings. The other four showed no interest in knowing the incidental findings as they were afraid of not being able to cope with these findings.

### *Cultural and religious beliefs*

Four of the parents who were interviewed in the study explained that they were expecting the disease to be caused by the evil eye.

- *We never had this problem in the family, we could not believe from the beginning, we though it is evil eye. When the results came back, we realized that it is an inherited disease (Participant 07).*

### *Extent of faith*

All the parents showed acceptance of the problem because of their faith in God.

- *I was shocked and maybe this was not right, but my faith in God helped me to accept the situation (Participant 1).*

### *Family and social influences*

Seven of the parents decided not to tell their relatives about the genetic problem they had in the family, which had been identified by the WES test.

- *We decided not to tell anybody to protect our normal daughters* (*Participant 05).*
- *I consider it a private issue. I do not want it to affect my life. Nobody is going to give me a solution so why to tell. I can deliver the information in a different way without mentioning my children (Participant 07).*

However, the remaining seven parents indicated that they have told their relatives about the genetic condition of their child to prevent the recurrence in future children in the family. All the parents who delivered the information to their family members experienced rejection of the fact that an inherited disease existed in the family by their relatives.

- *My husband has a low IQ, and his mother is not showing any understanding of my daughter's situation; she asked me to stop following at the hospital although she knows that she has four other affected grandchildren (Participant 08).*

### *Ethical challenges faced by healthcare providers*

*Breaking bad news*

Nine out of the 14 healthcare providers considered that providing families with the diagnosis of their affected children is a difficult process because of its impact on the family.

- *Relatively difficult but there are benefits, delivering the bad news is a challenge; dealing with expectations like trying to find a cure is another challenge. Some think that the disease is the responsibility of one parent and others think of evil eye but never tell, most of the time they try to keep it confidential (Doctor 01).*

Four of the healthcare providers thought that providing families with the diagnosis of their affected children depends on the type of the family.

- *It is a routine process because of the type of our patients, a good percentage of them accept whatever they are told (Doctor 04).*

*Stigmatization*

Eight of the healthcare providers expressed that families feel stigmatized after being informed of their child's genetic condition and afterward receive genetic counseling.

*Confidentiality*

Ten of the healthcare providers explained that most of their patients like to keep information related to genetic conditions confidential and do not like to share it with extended family members.

- *The families feel like it is a secret; they do not want anyone to know, especially when it is marriage time. It is an issue with them (Doctor10).*

***Table 1.*** *Profiles of the 14 parents recruited in the study.*

| Incidental findings | No. of affected children | Condition | Age of affected child | The interviewed parent | # |
|---|---|---|---|---|---|
| N/A | 1 | Dihydropyridine dehydrogenase deficiency | 5 years | Mother | 1 |
| Carrier for methylmalonic acidemia | 1 | Temtamy syndrome | 13 years | Father | 2 |
| N/A | 2 | Gerodermia osteodysplastica | 1 year | Mother | 3 |
| N/A | 2 | Spastic paraplegia | 9 years | Father | 4 |
| N/A | 2 | Neuronal ceroid lipofuscinosis | 5 years | Mother | 5 |
| N/A | 2 | Sodium leak channel | 6 years | Mother | 6 |
| Carrier for sickle cell disease | 1 | Galactosemia | 2 years | Mother | 7 |
| N/A | 3 | Goldberg Shprintzen megacolon syndrome | 8 years | Father | 8 |
| N/A | 3 | Mitochondrial depletion syndrome | 1 year | Mother | 9 |
| N/A | 3 | Combined oxidative phosphorylation deficiency 14 | 3 years | Father | 10 |
| N/A | 2 | Alazami syndrome | 8 years | Father | 11 |
| N/A | 4 | Mitochondrial complex III deficiency | 4 years | Father | 12 |
| N/A | 2 | AR osteopetrosis | 1 year | Father | 13 |
| N/A | 1 | Skeletal dysplasia | 7 years | Father | 14 |

***Table 2.*** *Profiles of the 14 healthcare providers recruited in the study.*

| Participant | Speciality | Hospital | The number of requested exome tests |
|---|---|---|---|
| 1 | Medical Genetics | KFSHRC | 100 |
| 2 | Medical Genetics | KFSHRC | More than 50 |
| 3 | Medical Genetics | KFSHRC | 100 |
| 4 | Clinical Genetics | PSMMC | 10 |
| 5 | Medical Genetics | MNGHA | 100 |
| 6 | Clinical Genetics | KFSHRC | 50 |
| 7 | Medical Genetics | KFSHRC | 500 |
| 8 | Medical Genetics | KFSHRC | 4 |
| 9 | Genetic Counseling | MNGHA | 3 |
| 10 | Clinical Genetics | KSMC | 1 |
| 11 | Pediatric Metabolic | KKH | 30-50 |
| 12 | Neuorology | PSMMC | 9 |
| 13 | Neuorology | PSMMC | 10 |
| 14 | Genetic/Metabolic | PSMMC | 5 |

*Carrier testing for minors*

Eleven of the healthcare providers mentioned having difficulties with the carrier testing results of minors identified by WES.

### *Healthcare providers' perspective on common mutations*

All the healthcare providers expressed observing common pathogenic mutations in certain tribes that could lead to stigmatization. In addition, they all agreed that the common pathogenic mutations should be saved in a registry and shared by the various healthcare professionals.

- *Yes, it should be saved in a registry, someone else could benefit from this registry (Doctor 01.)*

They all observed good traits in certain tribes that could lead to high self-esteem.

- *As medical professionals, we are more concerned with pathogenic mutations. Certain tribes have certain genetic characteristics that are unique to them and when they marry from each other, these unique genetic characteristics are going to stay between them; for example, variants associated with high performance in certain areas, variants that are associated with good body stature. However, we as people are more involved in medicine; we do not look at these characteristics; we investigate pathogenic variants (Doctor 06).*

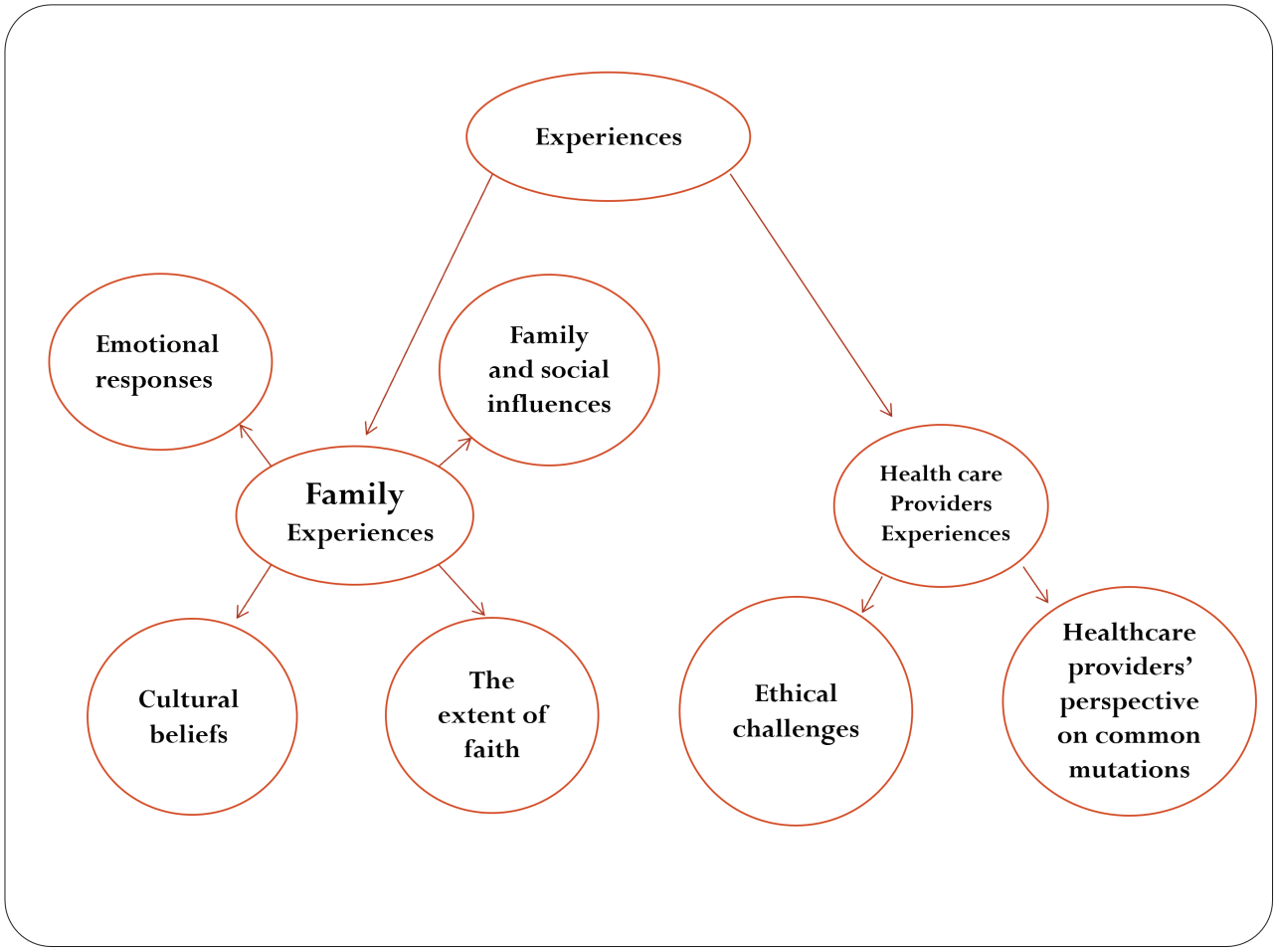


*Figure 1. The six strong emerging themes.*

## Discussion

The importance of this study stems from the fact that it has been conducted in a tribal-based community, such as that of Saudi Arabia, and shows how these families would react when they receive genetic test results identified by WES or any incidental findings that run in the families. It also explored these families' beliefs and reactions based thereupon. This study has also investigated healthcare providers' experiences in a tribal-based society. Such an impact could be amplified when the populations constitute a tribal bond of common of a genetic pool. The current study aimed to address these experiences in the Saudi population in central Arabia, which is tribal-based and highly consanguineous.

Analysis of the interview data revealed several major themes (Figure 1). The theme of emotional responses at the stage of discovering an inherited disease in the family showed that the parents of affected children in this study were experiencing shock at the time of discovering an inherited disease in the family. That was due to the fear of the recurrence risk in the future and the fear of not ever being able to have normal children. This was consistent with a previous study, which revealed that returning genetic information to patients differs from returning other health-related information, because learning genetic information has the potential to change someone's life, especially if it is unexpected and serious. It also revealed that participants suggested that conveying "bad news" must be executed with the support of a psychologist (16). The present study also discovered that the parents who already had a positive family history of the same condition reported experiencing less shock at the time of receiving the WES results. All the parents in this study explained that they are glad to finally receive the diagnosis of their affected children. All of them thought that the WES test was extremely important because they have been waiting for years for this diagnosis. They all wished they could prevent the inherited disease from occurring again in the future. Most of the parents were interested in knowing the incidental findings. This was also found by Strong et al. (16) that there is a desire among study participants to receive information about incidental findings, both for themselves and for their children for all categories of findings. On the other hand, most parents in the present study expressed difficulties in accepting incidental findings in their children if any were discovered. Some of the parents in the present study related the inherited diseases in the family to the belief of the evil eye. Some cultures believe that the evil eye can suddenly bring bad luck by looking

unintentionally at people unlucky enough to be cursed with the power (17). All the parents in the present study reported the acceptance of the problem because of their faith in the divine will. They all explained that it is God's will, which they must accept. Half of the parents decided not to tell their relatives about the genetic problem that had occurred within their family and had been identified by the WES test. Some were trying to protect their normal children from being stigmatized. This is consistent with a previous study undertaken in Greece where the experts interviewed suggested that being diagnosed with a genetic condition could lead to stigmatization. This could discourage parents from disclosing the genetic diagnosis of the affected child even to their other children (18). However, the other half of the parents in our study had no problem with delivering the information to the extended family members and considered it important to protect the future children of the family. This was also discovered by Fernandez et al. (19) when they explained that the majority of the parents in their study indicated that they would want results shared with extended family members, either directly or with the assistance of a physician. The parents in the current study who delivered the information to their family members experienced rejection by their relatives of the fact that an inherited disease existed in the family.When the healthcare providers working by families of children affected with genetic diseases were interviewed, the majority explained that delivering the diagnosis is a difficult process because of its impact on the family. As mentioned earlier, Gourna et al. (18) stated that breaking bad news is difficult and requires the assistance of a psychologist. The healthcare providers in the current study considered it to be a challenge. Most of the healthcare providers in the present study illustrated that some of the families feel stigmatized by being informed of their child's genetic condition. In a tribal-based society like Saudi Arabia, when a particular genetic condition becomes well known in a certain family or a certain tribe, the females in this tribe become labeled and this could defer these females from getting married and living a normal life. A similar situation was mentioned by Kashmeery. When a trend was established that clan members had a neurogenic locus notch homolog 4 gene triplet repeat polymorphism, which is associated with a serious psychological defect, such as schizophrenia (20), rumors spread swiftly and people in the clan were ordered to stop being tested to protect women from being haunted by the state of spinsterhood. Another ethical issue was faced by the healthcare providers in the present study, which was confidentiality. Most of the healthcare providers explained that the majority of the patients requested to keep information related to genetic conditions confidential and not to share it with other family members. One of the participants in our study even asked the healthcare providers to keep this information confidential from her sister, who was also at risk but, however, had a child with a different genetic condition. As mentioned earlier, some parents want to protect their normal children from labeling, while others want to protect the family dynamic. Most of the healthcare providers in the present study mentioned having difficulties with not disclosing carrier testing results of minors identified by WES. Carrier testing is an important part of prevention and has been applied in different countries to prevent some common genetic diseases. Just like any other country, Saudi Arabia considers disclosing carrier testing of minors identified by WES to be an ethical issue; there are pros and cons. Although carrier testing results will help parents to make decisions regarding their children's future, it may have psychological effects on the child, such as the loss of long-term autonomy - the so-called "open future" - or it might change family dynamics if the child is found to have a threatening condition.Finally, healthcare providers have explained that paternalistic medicine is an ethical challenge they face in their practice. Some healthcare providers think that it is the right of the family to decide what information they receive regarding the WES test results or the incidental findings. However, others think that the healthcare provider should be the one to decide what information to relay to the family. In addition, some healthcare providers think there should be clear local guidelines about this issue. This is consistent with the study by Grove et al. (21) in which a consensus was reached regarding the importance of developing evidence-based professional guidelines and regularly revising them to assist in consistently and appropriately providing genomic results to patients (22). Furthermore, another study in Greece stated that there is no framework to guide practice in Greece. All experts noted the lack of any legal documents, guidelines, or other supportive mechanisms to support clinicians, geneticists, or laboratories using sequencing technologies if incidental findings are discovered (18).

The healthcare providers in this study also expressed observing common pathogenic mutations in certain tribes that could lead to stigmatization. As mentioned by Al-Hamid et al. (23), eight tribes are responsible for 10% of the Saudi population and common pathogenic mutations are known in some tribes. They all agreed that the common pathogenic mutations should be saved in a registry and shared by healthcare professionals. However, producing a data registry could lead to the labeling of some tribes if misused.

## Conclusion

This study explored the experiences of parents of children affected by genetic diseases at the time of receiving the WES results of their affected children. It investigated their emotional reactions to this difficult situation in the Saudi Arabian population, which has a tribal structure with a rate of consanguinity exceeding 55% (6). Especially that some of these families had to wait a few years to get these results. Moreover, it considered their perspectives of incidental findings if any were discovered. It investigated the parents' feelings, beliefs, and the influences of the extended families and the society on these parents. It also explored the experiences of the healthcare providers involved with these families. It investigated their observations in a tribal-based society and the ethical challenges they faced in their practice.

## Study's Strengths, Limitations, and Recommendations

This study has issued a random sampling selection method to use here to reduce bias in the study and to ensure the study collects the most accurate and relevant data that reflects the population. It highlighted different experiences regarding WES testing and incidental findings. However, there are several limitations. Most of the WES reports did not include incidental findings. Only two of the patients had incidental findings included in their WES reports. This means that our findings on incidental findings were based on hypothetical questions and may not represent how participants would act in the future. Moreover, guidelines for the WES tests, consenting patients, and data sharing need to be developed.

### List of Abbreviations

MMA Methylmalonic acidemia
WES Whole exome sequencing
WGS Whole genome sequencing


### Funding

None.


### Declaration of conflicting interests

The authors of this article have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

### Ethical approval

Ethical approval for the study was sought and obtained from the local Research Ethics Committee at KFSHRC via Ref # RAC# 2141020, dated March 8, 2014.

### Consent to participate

Written consent was obtained from all the participants.

### Authors' contribution

AQ conceived and designed the study, collected data, carried out the statistical analysis, and wrote and edited the manuscript. All authors reviewed, revised, and approved the final draft of the manuscript.


### Author details

Alya Qari[1,2], Moeen Al-Sayed[1,2,3], Zuhair Al-Hassnan[1,2,3], Amin Kashmeery[4]

1. Medical Genetics Department, King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia
2. Genetic Counselling Program, AlFaisal University, Riyadh, Saudi Arabia
3. College of Medicine, AlFaisal University, Riyadh, Saudi Arabia
4. Emeritus Professor of Physiology, Former Head, Biomedical Ethics Section, King Saud Bin Abdulaziz University for Health Sciences, King Abdulaziz Medical City, Riyadh/ Jeddah, Saudi Arabia


### References


1. Rajab A, Mohammed AJ, El-Hazmi M, Raeburn A, Raeburn S, Modell B. Medical ethics: dealing with families and communities affected by genetic disease. 2nd pan Arab human genetics conference. Dubai, UAE.
2. Crawford G, Foulds N, Fenwick A, Hallowell N, Lucassen A. Genetic medicine and incidental findings: it is more complicated than deciding whether to disclose or not. Genet Med 2013; 15(11):896–9. https://doi.org/10.1038/gim.2013.165
3. Stat G. General authority of statistics, Kingdom of Saudi Arabia. Riyadh, Saudi Arabia.
4. Al-Owain M, Al-Zaidan H, Al-Hassnan Z. Map of autosomal recessive genetic disorders in Saudi Arabia: concepts and future directions. Am J Med Genet A 2012; 158(10):2629–40. https://doi.org/10.1002/ajmg.a.35551
5. Al-Abdulkareem AA, Ballal SG. Consanguineous marriage in an urban area of Saudi Arabia: rates and adverse health effects on the offspring. J Community Health 1998; 23(1):75–83. https://doi.org/10.1023/A:1018727005707
6. El-Hazmi MA, Al-Swailem AR, Warsy AS, Al-Swailem AM, Sulaimani R, Al-Meshari AA. Consanguinity among the Saudi Arabian population. J Med Genet 1995; 32(8):623–6. https://doi.org/10.1136/jmg.32.8.623
7. El Mouzan MI, Al Salloum AA, Al Herbish AS, Qurachi MM, Al Omar AA. Consanguinity and major genetic disorders in Saudi children: a community-based cross-sectional study. Ann Saudi Med 2008; 28(3):169–73. https://doi.org/10.5144/0256-4947.2008.169
8. Al-Gazali L, Hamamy H, Al-Arrayad S. Genetic disorders in the Arab world. Bmj 2006; 333(7573):831–4. https://doi.org/10.1136/bmj.38982.704931.AE
9. Becker SM, Al Halees Z, Molina C, Paterson RM. Consanguinity and congenital heart disease in Saudi Arabia. Ame J Med Genet 2001; 99(1):8–13. https://doi.org/10.1002/1096-8628(20010215)99:1<8::AID-AJMG1116>3.0.CO;2-U
10. Bick D, Dimmock D. Whole exome and whole genome sequencing. Curr Opin Pediatr 2011; 23(6):594–600. https://doi.org/10.1097/MOP.0b013e32834b20ec
11. Karow M, Popp T, Egea V, Ries C, Jochum M, Neth P. Wnt signalling in mouse mesenchymal stem cells: impact on proliferation, invasion and MMP expression. J Cell Mol Med 2009; 13(8b):2506–20. https://doi.org/10.1111/j.1582-4934.2008.00619.x
12. Wright GE, Koornhof PG, Adeyemo AA, Tiffin N. Ethical and legal implications of whole genome and whole exome sequencing in African populations. BMC Med Ethics 2013; 14(1):1–5. https://doi.org/10.1186/1472-6939-14-21
13. Wolf SM. Return of individual research results and incidental findings: facing the challenges of translational science. Annu Rev Genomic Hum Genet 2013; 14:557–77. https://doi.org/10.1146/annurev-genom-091212-153506
14. Hogan J, Turner A, Tucker K, Warwick L. Unintended diagnosis of Von Hippel Lindau syndrome using Array comparative genomic hybridization (CGH): counseling challenges arising from unexpected information. J Genet Couns 2013; 22(1):22–6. https://doi.org/10.1007/s10897-012-9520-z
15. Aronson JA. A pragmatic view of thematic analysis. Qual Rep 1995; 2(1):1–3. https://doi.org/10.46743/2160-3715/1995.2069
16. Strong KA, Zusevics KL, Bick DP, Veith R. Views of nonmedical, health system professionals regarding the return of whole genome sequencing incidental findings. WMJ 2014; 113(5):179–84. https://doi.org/10.1111/cge.12390

17. Balobaid A, Qari A, Al-Zaidan H. Genetic counselors' scope of practice and challenges in genetic counseling services in Saudi Arabia. Int J Pediatr Adolesc Med 2016; 3(1):1–6. https://doi.org/10.1016/j.ijpam.2015.12.002

18. Gourna EG, Armstrong N, Wallace SE. Incidental findings from clinical sequencing in Greece: reporting experts' attitudes. J Community Genet 2014; 5(4):383–93. https://doi.org/10.1007/s12687-014-0194-0

19. Fernandez CV, Bouffet E, Malkin D, Jabado N, O'Connell C, Avard D, et al. Attitudes of parents toward the return of targeted and incidental genomic research findings in children. Genet Med 2014; 16(8):633–40. https://doi.org/10.1038/gim.2013.201

20. Wei J, Hemmings GP. The NOTCH4 locus is associated with susceptibility to schizophrenia. Nature Genet 2000; 25(4):376–7. https://doi.org/10.1038/78044

21. Grove ME, Wolpert MN, Cho MK, Lee SS, Ormond KE. Views of genetics health professionals on the return of genomic results. J Genet Counseling. 2014;23(4):531–8. https://doi.org/10.1007/s10897-013-9611-5

22. Allyse M, Michie M. Not-so-incidental findings: the ACMG recommendations on the reporting of incidental findings in clinical whole genome and whole exome sequencing. Trends Biotechnol 2013; 31(8):439–41. https://doi.org/10.1016/j.tibtech.2013.04.006

23. Al-Hamed MH, Al-Sabban E, Al-Mojalli H, Al-Harbi N, Faqeih E, Al Shaya H, et al. A molecular genetic analysis of childhood nephrotic syndrome in a cohort of Saudi Arabian families. J Hum Genet 2013; 58(7):480–9. https://doi.org/10.1038/jhg.2013.27

## Appendix A

## Families' interviews

Name: _____

Date: _____

Relationship with the participant: _____

The number of the participant:

_____

1. The age of the participant:

a. 26-30

b. 31-40

c. 41-60

d. More than 61

e. Other ----------

2. The gender:

a. Male

b. Female

3. Education:

a. Primary school

b. High school

c. Diploma

d. BSc

e. MSc

f. PhD

g. Other----------

4. Occupation:

a. Employed

b. Unemployed/housewife

c. Retired

d. Student

e. Other: ----------

5. Marital status:

a. Married

b. Divorced

c. Widowed

6. The number of affected children in the family

a. Alive: ----------

b. Deceased: ----------

7. The number of normal siblings:

a. No siblings

b. One sibling

c. Two siblings

d. Three siblings

e. Other: --------

## Parents' responses after receiving genetic counseling

8. Was your affected child diagnosed?
9. Who was the first healthcare provider to inform you of the diagnosis of your child and where was that?
10. How did you feel when you first found out that your child is affected with a genetic condition? Please explain
11. Were there any benefits in discussing the genetic condition with the healthcare provider? Please explain
12. Were there any challenges in discussing the genetic condition with the healthcare provider? Please explain
13. Did you wish to receive the information in a different way at that time?
14. What do you think could be done more to help you at that time?
15. By now, do you think that the term "consanguinity" is clear to you? Do you know what it means in your case?
16. What do you think of consanguineous marriages at the mean time?
17. Did you talk to other family members about the condition? And why?
18. If yes, how did they feel about it?
19. How did your partner feel about it?
20. Were you offered genetic counseling?
21. What was the effect of the genetic counseling on you?

**Parents' attitude toward the whole exome sequencing test**

22. Do you think that the whole exome test is important? And why?
23. Did you want to know the results of the whole exome sequencing test?
24. Whom do you think should know the results first; the mother, the father, or together? Why?
25. Did the healthcare provider give you enough information before the testing to enable you to retain consent?
26. Did you feel you had a free choice to decide about the whole exome sequencing test?
27. Do you accept that the healthcare providers speak to each other about your affected child's condition without taking consent from you?

**Parents' attitude toward incidental findings**

28. Were there any incidental findings when you received the results of the whole exome sequencing test?
29. Do you want the healthcare providers to give you the right to decide about knowing the incidental findings if any were discovered?
30. How would you feel if your child was found to be affected with another genetic condition when you received the incidental findings?
31. Will you share this information with your affected child? Does the age of the child make any difference?
32. What if your child was a carrier of another genetic condition; would you like to know this information? Why?
33. What if your child was identified to have a late onset genetic condition that cannot be prevented, would you still like to know this information? Why?
34. What if the incidental findings were unclear, would you still want to know this information?

**Appendix B**

**Healthcare providers' interviews**

Name: _____

Date : _____

Participant # _____

_____

**Biography:**

35. The gender:

a. Male

b. Female

36. Specialty:----------

37. Do you have a regular clinic where you see patients:

a. Yes

b. No

38. What type of patients do you usually see? (Please choose all that apply)

a. Pediatrics

b. Endocrinology

c. Neurology

d. Genetics & metabolic

e. Hematology

f. Oncology

g. Other----------

39. On average how many clinics do you have per week?

a. One

b. Two

c. Three

d. Four

e. More, specify ----------

40. On average how many patients do see per week?

a. Less than 10

b. 10 and 20

c. More than 20

41. How often do you order genetic testing (whole exome sequencing test) for your patients per month?

a. Less than 10

b. 10-20

c. 21-30

d. 31-40

e. More than 40

## The aims

The first aim: To explore the ethical dilemmas and challenges associated with providing genetic information through verbal counseling and written documentation to consanguineous Saudi families.

1. Do you offer genetic counseling through your practice?
2. According to the records, what is the percentage of consanguineous Saudi couples you see in your clinic?
3. How do you find it when you provide families with the diagnosis of their affected children?
4. Were there any benefits of explaining the diagnosis to the families? Please explain.
5. Were there any challenges in explaining the diagnosis to the families? Please explain.
6. Since Saudi Arabia is a tribal-based community, how do people react when they discover the existence of an inherited disease in their families?
7. Do you face any challenges or dilemmas when you give information about consanguinity to families?
8. How would you overcome these dilemmas?
9. What are the most difficult ethical issues/ onsequences of offering genetic counseling to Saudi families about inherited genetic diseases?

The second aim: To clarify how healthcare professionals working within genetic counseling fields, who provide the information to families, respond to their role and the information-sharing procedures (the attitudes of the healthcare providers toward providing families with genetic test results).

10. Do you have access to offer the whole exome sequencing test for your patients?
11. If you have this access, how many of your patients had undergone this testing so far?
12. In general, for what indications do you this test?
13. How do you find it to give information to couples about the genetic testing results (whole exome sequencing test results) of their children? Why?
14. How would you present this information to couples? Would you start by sharing this information with the father or the mother or both? Do you share it with anyone else such as other family members or healthcare providers?
15. What does it mean to the healthcare provider to disclose information like this to the families?
16. How do you support the families when you provide them with the genetic test results?

The third aim: healthcare providers toward incidental findings.

17. Do you think is it the responsibility of the healthcare provider to decide to share the incidental finding with the family? Or it is for the parents to decide if they want to know or not?
18. With whom would you start sharing this information within the family? Is that expected to include parents? Why?
19. Will you share this information with the affected child? Does the age of the child make any difference?

Informed consent

20. Do you think that you usually give enough information to the patients' families before genetic testing to enable them to provide informed consent?
21. Do usually ask them to sign any agreement in order to enable them to go for the testing?
22. Do you think they have a free choice to decide?
23. Do you think it is fine to share the patients' information with other healthcare providers without the patient's consent?

## Appendix C

## Amendment of healthcare providers' interviews

Name: _____

Date : _____

Participant # _____

_____

1. Do you observe pathogenic mutations that are common in certain tribal gene pools?
2. How frequent are these, if any?
3. Do you think that such mutations yielded through exome sequencing should be saved in a registry and shared by healthcare professionals?
4. What good practice could be followed by healthcare strategic planners and decision-makers to make use of such information on the tribal population?
5. Can you see a potential for tribal distinction in esteem, as much as there is stigma, if such information is made public?