QATAR UNIVERSITY

COLLEGE OF HEALTH SCIENCES

PARENTAL KNOWLEDGE AND ATTITUDES TOWARDS GENETIC COUNSELING AND CHILDHOOD GENETIC TESTING FOR CONGENITAL ANOMALIES IN QATAR

BY

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ABSTRACT

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Title: Parental knowledge and attitudes towards genetic counseling and childhood genetic testing for congenital anomalies in Qatar

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Background: Understanding parental baseline knowledge of the implications of genetic counseling and genetic testing may unveil educational gaps or circumstantial fear and reluctance towards this important component in the management of children with congenital anomalies. This study was designed to investigate parental knowledge of and attitudes towards genetic counseling and genetic testing as it pertains specifically to pediatric plastic surgery practice in Qatar.

Methods: The study employed a prospective face-to-face questionnaire that was administered online to parents who met inclusion criteria and attended the pediatric plastic surgery clinic at Sidra Medicine between October 2022 and February 2023. The questionnaire consisted of 38 questions, the questionnaire considered (i) demographics, (ii) knowledge, and (iii) attitudes (perceived benefits vs. perceived barriers) towards genetic counseling and genetic testing. Statistical analyses were performed using SPSS software v28.0.

Results: A total of 160 participants filled out the questionnaire. Parents were from Asia 27%, North Africa 25%, Middle East 22%, and America/Europe 6%; only 22% were Qatari nationals. Consanguinity account for 22.9%. About 6% of children were presented with minor anomalies, 73% with major isolated anomalies, and 21% with major syndromic anomalies. 37% of children had undergone genetic testing in the past. American/European parents and all parents holding undergraduate and graduate degrees P=0.003; P=0.001 respectively) scored higher on genetic knowledge than did

the rest of the cohort. Moreover, American/European parents (P=0.028) and all parents with a higher knowledge score (P=0.048) had a higher positive attitude score towards genetic counseling and genetic testing. Qataris (46%) n=35 demonstrated strong knowledge but lower positive attitudes score towards perceived benefits and higher perceived barriers score than other ethnicities. Parents who were consanguineous (P=0.003) or whose child had already been referred for counselling and genetic testing by a medical provider (P<0.001) had a higher positive attitude score regarding possible benefits of genetic counseling and genetic testing. In turn, parents whose child had not been previously underwent genetic testing tested *(*P*<0*.001) and parents who did not have another child with a genetic disorder (P=0.002) had a higher negative attitude score towards genetic counselling and genetic testing

Conclusion: This study highlights the need for cultural sensitivity and tailored education about genetic counseling and genetic testing for parents of children with congenital anomalies. Healthcare providers should consider parental education levels and consanguinity when providing information about the benefits of and the barriers to genetic testing. By addressing barriers and providing accurate information, healthcare providers can help parents make informed decisions about genetic testing and counseling.

Plastic surgery physicians play a crucial role in advocating for genetic testing for their patients. By recognizing the benefits of genetic testing and referring their patients to genetics professionals, plastic surgery physicians can help identify patients who may be at an increased risk for genetic conditions and provide them with personalized care. Through proactive screening and early intervention, plastic surgery physicians can improve patient outcomes and help reduce the burden of genetic conditions on individuals, families, and society as a whole. It is essential for plastic surgery physicians

to stay informed about advances in genetics and genomics and to collaborate with genetics professionals to provide the best possible care for their patients, as genetic testing becomes more accessible and affordable.

DEDICATION

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1: INTRODUCTION

Throughout human history, congenital anomalies have been studied in various ways both from the scientific and artistic perspectives [1, 2]. From the 17th century onward, the concept of epigenesis (the notion that an embryo develops progressively from a fertilized but undifferentiated egg) emerged amongst eminent academics. This understanding paved the way for the study of both conventional and atypical patterns of growth and development [3].

Congenital anomalies are structural abnormalities that are present before or at the time of birth regardless of the cause [4, 5]. They have been discovered to be a major cause of infant and child morbidity and mortality in addition to a significant cause of lifelong disability [6, 7]. While 2-3% of liveborn neonates are born with congenital abnormalities, stillbirths and miscarriages have been found to have much higher rates of anomaly [8, 9]. Congenital anomalies are caused by a wide range of factors including genetic issues such as alterations in the number or structure of chromosomes and pathogenic variations in single genes, infection, radiation exposure, the use of particular medications during pregnancy, or other environmental factors [4]. A combination of genetic and environmental factors have been shown to cause the majority of common birth defects such as cardiac defects, neural tube defects, and cleft lip and palate [4].

The field of medical genetics has been significantly impacted by recent advancements in molecular biology technology, most notably chromosomal microarray analysis (CMA) and next generation sequencing (NGS) [10]. Genetic testing has become more routinely accessible to clinicians, helping in the diagnosis of individuals with anomalies that may have a defined genetic basis. Early identification, focused surveillance, and preventative efforts could reduce the occurrence of these conditions. One such approach involves preimplantation genetic testing (PGT), which is a procedure used to test

embryos conceived by in vitro fertilization (IVF) for a known familial genetic or chromosomal disorder before transferring them back to the mother's womb. The goal of PGT is to discard embryos affected with detectable genetic or chromosomal disorders to increase the chances of implantation of an unaffected embryo and achievement of a successful pregnancy[10].

The role of genetic counselors is becoming increasingly important in the era of genomic medicine. According to several studies, genetic counselors play a crucial role in providing patients and their families with relevant medical education, important information about genetic risk and clinical health treatments, , and emotional support, all of which assist parents and couples in making well informed, autonomous decisions regarding their reproductive and health care options [11, 12]. It is important for genetics counselors to keep in mind that genetic testing can pose significant ethical considerations in terms of appropriateness of indications, interpretation of results, and unique individual and familial perspectives and judgment [13]. One must be aware that there may be a lack of clinical utility or uncertainty arising from any genetic test such as with variants of uncertain significance. Moreover, genetic testing may yield secondary findings that were entirely unanticipated [13, 14], which can lead to greater patient confusion or anguish than expected. Genetic testing of children is another topic that requires particular attention [15, 16]. Because children lack the capacity to give voluntary informed consent, the decision to undergo genetic testing is made by the child's parent(s) or legal guardian(s). The implications of genetic testing can be significant and long-lasting, leaving a child with a diagnostic label that may be welcome or unwelcome. Clearly, pre-test genetic counseling is crucial. The benefits, risks, limitations, and long-term consequences of genetic testing must always be carefully discussed with patients and/or their parents ahead of testing. It is indeed essential for

parents and clinicians to bear in mind the physical, psychosocial, and reproductive consequences that a particular genetic finding may have on a child's future [17]. Despite challenges in approaching the subject of childhood genetic testing, there is a clear potential benefit in trying to identify patients at risk of life-threatening conditions when such knowledge could inform treatment and surveillance plans and improve prognosis [17]. For instance, prenatal genetic diagnosis for a suspected underlying genetic cause can help parents prepare for maternal-fetal interventions, delivery, and early postnatal interventions, as well as gather prognostic and supportive information in addition to seeking social support such as meeting other families impacted by the same condition [18].

Numerous studies have been conducted in the Western world on the topic of genetic testing uptake in children, examining parental attitudes and knowledge. These existing studies all point towards a similar conclusion: parents are more likely to consent to their children undergoing genetic testing when they anticipate gaining knowledge of potential clinical benefit. The parental educational level also appears to have an impact on decision-making. For instance, parents with higher educational levels are more likely to be in favor of genetic testing [17]. It is worth noting that only a few studies have explored parental attitudes and knowledge regarding genetic counseling and various genetic testing indications among populations in the Middle East [19-23]. A survey conducted among university students in Saudi Arabia found that they expressed a favorable view towards genetic testing for pregnant women, fetuses, children, and adults. The survey also revealed that their perception of genetic testing was most significantly influenced by factors such as their gender, academic year, grade point average, and prior knowledge of the topic [24]. A population-based study conducted in Jordan examined knowledge, attitudes, and practices related to genetic testing and

found that younger age, higher education level, and better health awareness were associated with a higher uptake of genetic testing. This study also found that gender and health insurance had no significant effect on genetic testing uptake [25]. Both studies emphasized the need for youth-focused initiatives for genetic education that could improve genetic knowledge and increase public acceptance of genetic testing.

In recent years, Qatar's population has grown to include a diverse range of ethnic groups, while native Qataris account for approximately 22% of Qatar's 2.7 million population [26]. The native Qatari population has always had a high rate of consanguinity, estimated at 54% in 2006, which is predictably associated with a high rate of occurrence of autosomal recessive diseases [27]. Qatar's national health strategy prioritizes the health of seven population groups, including children, adolescents, and pregnant women [28]. As a result, investments in premarital screening, genetics and genomics, as well as early and widespread adoption of new diagnostic and related technologies, have been implemented into the health system in order to provide state-of-the-art care to the Qatari and regional populations.

The Division of Pediatric Plastic Surgery (PPS) at Sidra Medicine, Qatar, brings on the expertise of a distinguished team to provide world-class care to children with congenital and acquired anomalies. In 2018, this is where the first multidisciplinary clinic for patients with clefts and craniofacial anomalies was established in Qatar. The team includes providers from Plastic Craniofacial Hand Surgery (PCFHS), Otolaryngology (ENT), Neurosurgery, Orthodontics, Speech and Language Pathology, Audiology, Feeding/Lactation, Dietetics, and Nursing. Although a clinical geneticist and a genetic counselor are not members of the team, the service provides direct in-house referrals to Clinical Genetics and Genetic Counseling. Based on our clinical observations, only a few patients attending the PCFHS clinic at Sidra Medicine have received genetic

counseling or underwent genetic testing. Investigating the clinic's parent population – in terms of their knowledge of the genetic contribution to their child's congenital anomalies and their attitudes toward genetic counseling and genetic testing – may lead to a better understanding of factors that encourage or discourage them from seeking consultations with clinical geneticists and genetic counselors. This new information may have a direct impact on the development of Qatar's current PPS services as well as clinical genetics and genetic counseling services.

Further qualitative research will provide a more in-depth understanding of the barriers associated with referral to genetic counseling and the uptake of genetic testing. By delving into the experiences and perspectives of individuals, families, and healthcare professionals, we can gain valuable insights into the factors that influence these decisions. This deeper understanding will allow for the development of targeted interventions and strategies to overcome these barriers and enhance the utilization of genetic services and testing.

CHAPTER 2: LITERATURE REVIEW

2.1 Congenital anomalies history

Throughout the course of human history, congenital anomalies have been interpreted as supernatural omens, portents, or curses. This idea is reflected in the origin of the word "monster," which comes from the Latin verb *monstrare*, meaning "to show or reveal" [1]. Congenital abnormalities were once thought to be triggered by a variety of different causes including witchcraft, astrological constellations, and the feelings of the pregnant mother [1].

The disfigured forms of humans and animals served as inspiration since ancient human history for a wide variety of characters in literature, mythology, art, and religion. Cleft palate for example is one of the congenital anomalies that were seen in an Egyptian mummy [29]. Although malformations were still viewed with a superstitious attitude in the 18th century, physicians and biologists had already started studying them during that same period [1]. In the 17h century onward, the idea of epigenesis emerged. This idea states that all developing entities start out as unformed material, and during development, shape emerges gradually and steadily over time [3]. This concept became widely accepted by prominent academics, opening the way for inquiries into both typical and unusual patterns of growth and development [1]. Subsequently, it was hypothesized that cellular interactions and intracellular determinants were jointly responsible for shaping the final form of an organism [3]. In the setting of Mendelian genetics and the Weismann hypothesis of heredity, studies of these determinants became vital while embryology maintained its emphasis on cell cytoplasm research [3]. According to the Wiseman hypothesis, the "germplasm" theory of genetic inheritance states that an organism's cells are divided into body cells (soma) and germ cells (germ), cells that produce the gametes. He proposed, importantly, that the two cell types don't

share information with each other; instead, the germ cells are the ones that make changes [30].

2.2 Congenital anomalies prevalence

In 1989, Nelson and Holmes examined over 70,000 stillborn and liveborn babies in the United States and discovered that the prevalence of major congenital anomalies was around 2% [9]. Similarly, congenital abnormalities were also found to be a major cause of child mortality in a European population investigated between 2003 and 2007 [8]. The estimated prevalence of congenital abnormalities in the latter study was 2%-3% in livebirths who died at first week of life and 2.0% in stillbirths or fetal deaths after 20 weeks of gestation [8]. Most infants with congenital defects are those who make it past the neonatal period and therefore have significant medical, social, or educational requirements [8, 9].

2.3 Types of congenital anomalies

In the literature, numerous classification methods have been suggested. The National Birth Defects Prevention Study (NBDPS) developed one of these classifications, which emphasizes the difference between major and minor anomalies, as well as syndromic and non-syndromic congenital anomalies. These classifications are crucial in order to make case groups more homogeneous for the success of birth defect studies (see below) [31].

2.3.1 Major anomalies

The majority of morbidity, mortality, and disability caused by congenital defects is caused by major anomalies [32]. A major anomaly is one that has an impact on a newborn's life expectancy, current health status, can lead to long-term disability with limited physical function, or can lead to social stigma and discrimination. In addition to the physiologic and/or functional implications of major anomalies, some of the structural defects can result in deformity that can make people feel embarrassed, alone,

and less likely to interact with others [33]. Furthermore, a major anomaly can cause a physical defect that necessitates expensive medical attention. Patients, their families, the healthcare system, and society as a whole are all affected by the burden of long-term disability [32]. Examples of major craniofacial congenital anomalies include cleft lip and/or palate (an opening through the upper lip and/or the roof of the mouth), craniosynostosis (premature fusion of cranial sutures), microtia/anotia (hypoplastic/absent external ear), and hemifacial microsomia (hypoplasia of one side of the face) [31].

There are two other ways to categorize major congenital abnormalities: isolated and syndromic (group of symptoms that collectively indicate or characterize a disease). The underlying molecular basis of several anomalies, ranging from isolated congenital cardiac defects to commonly seen patterns of malformations such as VACTERL association (vertebral defects, anal atresia, cardiac defects, tracheoesophageal fistula, renal anomalies, and limb abnormalities), remains unknown [34, 35]. Advancement in the fields of human genetics and genomics have transformed our understanding of congenital abnormalities. Several lines of evidence suggest that single-gene abnormalities are more likely to be involved in cases of multiple congenital defects (syndromic) than in cases of isolated malformations. [9]

As an example, orofacial clefts are the most common orofacial malformations in humans, affecting 1 to 25 per 10,000 newborns worldwide. They include cleft lip (CL), cleft lip with or without cleft palate (CL/P), and cleft palate only (CPO) [36]. CL/P can be divided into the syndromic and non-syndromic categories, respectively, according to whether the condition is present in isolation or in conjunction with a certain set of malformation patterns [37]. There is a strong genetic component to both types of CL/P. Many syndromic forms of CL/P are caused by chromosomal changes or single-gene

changes, for example Van der Woude syndrome is the most common type of syndromic CL/P. It is caused by heterozygous pathogenic changes in the IRF6 gene and accounts for about 2% of all CL/P cases. On the other hand, non-syndromic CL/P is caused by a combination of genetic and environmental factors [37].

Craniosynostosis, for example, is a premature fusion of the cranial sutures. It can be either isolated or part of a syndrome such as Apert syndrome, which is characterized by bicoronal synostosis, bilateral symmetrical complex syndactyly of the hands and feet, and other common complications such as cleft palate and learning disabilities. It is linked to heterozygous pathogenic changes in the FGFR2 gene [38]. Pathogenic variants in single genes or chromosomal abnormalities were observed to be responsible for 20% of craniosynostosis cases, with the vast majority of cases being syndromic [39].

2.3.2 Minor anomalies

Minor anomalies have little to no effect, if any, on either the short-term or long-term function of the body [31]. Minor abnormalities are structural changes to the body that, while noticeable, do not usually cause serious medical problems and have only minor psychological or cosmetic effects on the affected person such as singular palmar crease and clinodactyly (mild curvature of a finger) [40].

2.4 Causes of birth defects

Over the past 50 years, advances in embryology, teratology, reproductive biology, and human and medical genetics have helped scientists and physicians better understand the causes of congenital anomalies, but there were still families of children with congenital abnormalities that could not establish a definitive diagnosis and etiology [4]. According to the Institute of Medicine in the United States 2003 report (Reducing Birth Defects: Meeting the Challenge in the Developing World), the causes of only about 30% of birth defects are reasonably well recognized genetically, and knowledge of those causes is sometimes incomplete [41]. In addition, the fact that 70% of the causes

of birth defects are unknown shows that environmental factors may play a significant influence in the development of birth defects [41]. The Institute of Medicine also stated in its 2003 report that there are numerous factors that might contribute to birth defects, and these factors can be divided into three groups: environmental influences, complex or unidentified genetic factors, and genetic factors such as single gene pathogenic variants and chromosomal aberrations [42].

2.5 Environmental factors

Malnutrition, maternal illnesses such as diabetes, infectious agents such as TORCH infections (toxoplasmosis, other agents, rubella also known as German measles, cytomegalovirus, and herpes simplex virus), and teratogenic medicines such as epileptic drugs are all examples of environmental factors that can result in birth defects. The type of exposure, such as radiation, can contribute to congenital anomalies such as spina bifida, cleft palate, and abnormal extremities growth. Other factors that may affect whether an exposure to these environmental factors is harmful include the timing of the exposure, whether it occurs during or shortly after conception, the gestational period, and the person's genetic makeup [42, 43]. It has also been found that families and countries with lower and middle incomes have a higher incidence of congenital abnormalities due to the exposure to a variety of illnesses in the context of insufficient healthcare delivery systems [44].

2.6 Genetic factors

Single-gene defects and chromosomal abnormalities are the two most frequent genetic causes of congenital malformations; furthermore, there are numerous forms of chromosomal abnormalities, but they can be classified as numerical or structural. Numerical anomalies include aneuploidies, which refer to entire chromosomes that are either absent from the usual total number or present in excess, as well as microdeletions and microduplications, which refer to loss or gain of smaller chromosomal segments.

Structural abnormalities occur when a chromosome takes on an abnormal shape (e.g., ring chromosome), a portion of a chromosome is transferred to another chromosome (e.g., translocation), or a piece of a chromosome is found in reverse orientation (e.g., inversion).

Several studies looking at the most common causes of congenital anomalies, such as the one that was carried out in Saudi Arabia, found that chromosomal aberrations (changes in the structure or number of chromosomes) are the leading cause of congenital anomalies in newborns. The nondisjunction form of Down syndrome was one of the most common chromosomal abnormalities [45]. This type of Down syndrome results in an embryo having three copies of chromosome 21 rather than the two normal copies because the duplicated chromosome 21 fails to split during the formation of the sperm or the egg that contributed to the pregnancy. In addition, a substantial association was unsurprisingly discovered between chromosomal abnormalities and advanced maternal age (defined as at least 35 years) [45, 46]

Copy number variants (CNVs) are made up of chromosomal microdeletions and microduplications. CNVs happen when a stretch of DNA is added to or lost from the reference human genome. They can be as small as one kilobase or as big as several megabases. CNVs can involve one, numerous, or no genes at all. Some CNVs cause disease, but many others are common and/or harmless in the general population [47-49]. An instance is the 22q11.2 area, which is vulnerable to copy number changes that can result in congenital defects and intellectual disability. 22q11.2 deletion syndrome is a condition that affects most people with a harmful loss of genetic material in this region. The disorder can display a vast array of characteristics that can vary significantly, even among members of the same family. The clinical manifestations may include congenital heart disease, particularly conotruncal malformations (such as

ventricular septal defect, tetralogy of Fallot, interrupted aortic arch, and truncus arteriosus), palatal abnormalities (like velopharyngeal incompetence, submucosal cleft palate, bifid uvula, and cleft palate), velopharyngeal insufficiency, characteristic facial dysmorphic features, language impairment, developmental delay/learning difficulties, and conotruncal cardiac anomaly [50].

Pathogenic variants in single genes have also been documented as causes of birth abnormalities [9]. These pathogenic variants can be inherited from one or both parents, or can happen by chance as a new occurrence in the offspring (de novo) [9]. For instance, a single gene disorder of craniofacial development is Treacher Collins syndrome (TCS), which is caused by a pathogenic change in the Treacher Collins–Franceschetti 1 (TCOF1) gene and inherited in an autosomal dominant manner. TCS is characterized by hypoplastic facial bones, microtia, micrognathia, other deformities of the external and middle ears, auditory pits, hearing loss, and cleft palate[51].

2.7 Consanguinity

Consanguinity (descending from the same ancestor) increases the prevalence of rare genetic congenital anomalies, particularly those with recessive inheritance patterns [52]. A study carried out in the United States between the years 1967 and 1997 on newborns who were diagnosed with congenital anomalies found a significant association between parental consanguinity and three different types of congenital anomalies: hydrocephalus, postaxial hand polydactyly, and bilateral CL/P [53]. Another study was carried out in Norway between the years 1967 and 1995 with the purpose of estimating and comparing the recurrence risk of birth defects among offspring of first cousins vs. nonconsanguineous parents. The researchers concluded that the risk of recurrence of birth defects is higher for subsequent children of first cousin parents than it is for subsequent children of nonconsanguineous parents. This

difference illustrates the degree to which the higher homozygosity among offspring of consanguineous parents increases the probability of recurrence of birth abnormalities [54]. A study conducted in Saudi Arabia between 2004 and 2005 to investigate the role of consanguinity in genetic disorders discovered that congenital heart disease (CHD) had the most significant association with first cousin consanguinity [55].

2.8 Genetic counseling for congenital anomalies

The National Society of Genetic Counselors (NSGC) defines the clinical scope of practice of genetic counselors as including medical roles (medical and family history taking, risk assessment, education about genetics and patterns of inheritance, and coordination and ordering of genetic testing, including cascade testing), psychosocial roles (assessing patient adaptation to genetic risk/diagnosis, providing anticipatory guidance, and short-term client-centered counseling), and case management roles, all of which can be offered prenatally or postnatally to parents and couples [56]. While genetic counselors perform these roles globally, there is variation in how genetic counseling services are implemented and the degree of psychotherapeutic intervention involved [57]. As a result of recent scientific, technological, and bioinformatic developments, genetic counseling is rapidly evolving, and demand for genetic counselors is high in various industries and academic settings as a part of an ongoing efforts to interpret genomic data in ways useful to both patients and clinicians [58].

Better identification and a reduction in long-term morbidity and mortality of patients with congenital abnormalities have resulted from relevant diagnostic and therapeutic tools that have been steadily improving over the last decades [35]. Thus, it is fitting that genetic counseling services be made available to parents whose unborn child or infant has been diagnosed with a congenital abnormality [59].

Genetic counselors offer prenatal and/or postnatal genetic counseling to individuals,

couples, and families concerned about their babies' health, in particular those with congenital anomalies [60]. Most of the genetic information is complex and should be clarified and simplified for the parents. In addition to addressing parents' concerns, genetic counselors have in-depth conversations with parents and couples in simple clear terms about their needs and support them to make informed decisions [59, 61].

For instance, in prenatal genetic counseling sessions, genetic counselors help couples who are at increased risk for birth defects to understand the purpose of the session, which is to determine whether there is a reason to suspect a congenital anomaly in the current pregnancy, and to make informed decisions by providing accurate, objective, and thorough information about screening, diagnostic, and therapeutic options [62]. When congenital anomalies are detected in pregnancy, genetic counselors lay out the options that couples have for monitoring the pregnancy and discuss the feasibility of prenatal testing as well as the different procedure and testing options available to look for the cause of the congenital anomalies [63]. In the event that a couple decides to pursue prenatal diagnosis, the genetic counselor is required to discuss the purpose, benefits, risks, limitations, and costs associated with each of the procedures and genetic tests that are available. A recommendation may be accepted or rejected by the couple. It must be clear that genetic testing is voluntary, i.e. not mandatory, at all times [63]. After genetic testing has been initiated, patients should receive post-test counseling in which the meaning of the result – positive, negative, uncertain, or unexpected – and its implications are thoroughly explained [62]. The patients' options and desires are always supported by the genetic counselors, who honor patient autonomy.

2.9 Clinical diagnosis

Congenital abnormalities are serious problems in healthcare due to the extensive resources required to provide the necessary interdisciplinary care; therefore, the first

step in providing useful genetic counseling to parents is to establish that a congenital abnormality exists [35].

The relevant diagnostic and treatment methods have been steadily advancing over the course of the previous several decades, which has contributed to an improvement in identification of patients with congenital anomalies as well as a reduction in the long-term morbidity and mortality of these patients. In other words, the prognosis for these patients has become significantly more optimistic [64].

Because of the improvements in ultrasound technology, structural congenital defects can now be detected earlier in pregnancy, allowing mothers/parents and clinicians to make informed decisions about pregnancy management, delivery, and postnatal medical and surgical interventions [65].

In the first trimester of pregnancy, biochemical screening and ultrasonography can be used to identify pregnancies at increased risk of congenital anomalies or genetic disorders, as is the case with prenatal screening [66]. During the first trimester of pregnancy, biochemical screening that is based on the determination of maternal serum markers associated with an increased risk of chromosomal diseases reveals variations in several serological components; however, only free human chorionic gonadotropin (hCG) and pregnancy associated plasma Protein-A (PAPP-A) are linked to the presence of a trisomy 21 [67, 68]. Ultrasound examination, on the other hand, is an excellent method for detecting morphological abnormalities in genetically abnormal fetuses; the most common soft markers are increased nuchal translucency (NT) and absent/hypoplastic nasal bone (NB) [69]. Based on the combination of maternal age and the results of this sonographic scan, roughly 75% of pregnancies with trisomy can be detected, with a false positive rate of only 5% [70].

There are several soft markers that clinicians can look for during prenatal ultrasound

that could indicate a higher chance of a genetic problem. While hyperechoic bowel is more commonly seen in pregnancies affected by aneuploidy (particularly trisomy 21), it is nonspecific and may be seen in as many as 0.5% of otherwise healthy fetuses [71]. Shortened limbs, clinodactyly, and a broad pelvic angle are skeletal abnormalities linked with trisomy 21 that can be detected in the second trimester of pregnancy [71]. Moderate pyelectasis (hydronephrosis) is also associated with a high risk for aneuploidy, especially for trisomy 21 [71, 72]. The marker echogenic intracardiac focus (EIF) can be identified in 3-4% of otherwise healthy fetuses, with an incidence that is three times higher in Asian cultures [73]. Ventriculomegaly is when the size of the ventricles grows to be more than 10 millimeters, it may possible that trisomy 21 or another aneuploidy is present [74].

Furthermore, according to the 2016 recommendations of the World Health Organization (WHO), pregnant women should get "one ultrasound scan before 24 weeks of pregnancy (early ultrasound)" in order to estimate the gestational age of their unborn child, improve the identification of fetal malformations and multiple pregnancies, prevent the induction of labor for post-term pregnancies, and enhance the overall experience of being pregnant for the woman [75]. In 2022, a new update to the previous WHO report stated that a "routine second trimester (14-24 weeks of pregnancy) ultrasound scan" probably increases the detection of fetal anomalies before and after birth, and it was recommended that because ultrasound may detect fetal abnormalities, the provision of associated support services for parents is important. If an abnormal diagnosis is suspected or confirmed, parents may require counseling and access to social support networks [75].

2.10 Genetic testing

The human genome project with the development of the molecular technologies are the

main factors that helped both researchers and clinicians to identify potential genetic disease variants and develop new drugs and therapies [76].This paved the way to a new era in medicine, marked by cutting-edge technologies, widely accessible clinical genetic testing, and personalized medicine [77].

There are several reasons to conduct genetic testing, these include newborn screening, prenatal testing, carrier testing, diagnostic testing, and pre symptomatic/predictive testing , and preimplantation testing [78]. Additionally, there are pharmacogenetic tests that reveal the presence or absence of a certain genetic variation that may affect a person's response to a particular drug [78]. Over 1000 genetic tests are used now, and more are being developed [78, 79].

The first step in selecting the most appropriate genetic test is identifying the reason(s) for referral to genetic testing or the phenotype(s) in order to specify the genetic cause(s) that need to be investigated [78]. Evaluation and interpretation of genetic testing findings will be limited in the absence of detailed characterization of the phenotype, medical and family history, in addition to ethnicity of the patient [78] .

According to a study that looked at genetic testing strategies for newborns, early diagnosis can help families obtain accurate information about the baby's health and give them the opportunity to receive precise care, both of which can improve the baby's outcome[80]. As a result, understanding the various genetic testing modalities and their limitations has become critical for health care providers working with neonates, especially in intensive care units [80] .

2.10.1 Chromosome analysis (karyotype or KT)

The karyotype (KT) was the first clinically available cytogenetic test, and it continues to this day to be the test of choice for evaluating aneuploidies and other structural chromosomal abnormalities. KT requires a short-term culture of cells that have been

arrested during metaphase. These cells are typically lymphocytes taken from a sample of peripheral blood. Following this step, the cells are treated, fixed, and stained so that the structural characteristics of the chromosomes may be seen. After that, the chromosomes are placed in a karyogram, which shows the autosomes arrayed in order of decreasing size from 1 to 22, followed by the sex chromosomes [80]. For instance, Down syndrome (also known as trisomy 21), Edward syndrome (also known as trisomy 18), Patau syndrome (also known as trisomy 13), and Turner syndrome (also known as monosomy X) can be diagnosed by karyotyping. Furthermore, KT can confirm if the syndrome is caused by a sporadic nondisjunction event or by an unbalanced translocation, which may or not be inherited from a parent carrying a balanced translocation [80].

2.10.2 Fluorescence in situ hybridization (FISH)

Fluorescence in situ hybridization (FISH) is a cytogenetic technique that uses fluorescent DNA probes to target specific chromosomal sites within the nucleus, resulting in colored signals that can be spotted using a fluorescent microscope. One advantage of this technique is that no cell culture is required. SRY and X chromosomal FISH probes, for example, can be used to quickly determine the sex of a newborn with ambiguous genitalia; however, the disadvantage is that it requires a high index of suspicion for a specific disease and a specific probe [80].

2.10.3 Chromosomal Microarray Analysis (CMA)

Neurodevelopmental disorders and multiple congenital anomalies are the most common conditions that could benefit from chromosomal microarray analysis (CMA); this test can be performed prenatally or postnatally and is considered the first-tier genetic test for these indications [81]. CMA is a microchip-based testing technology that automates high-volume DNA analyses that are used to measure patient genetic material and compare it to a reference sample in order to identify CNVs [82]. CNVs

can be either a gain or a loss when compared to the diploid (two-copy) genome. Every person's genome contains CNVs; however, the vast majority are polymorphic variants with no phenotypic or clinical significance. In contrast, CMA seeks to determine whether a CNV is likely or definitely known to be associated with disease or clinical significance [82].

The assessment of the clinical significance of a CNV is usually decided based on guidelines from the American College of Medical Genetics and Genomics (ACMG) and the Association for Molecular Pathology (AMP) [83]. These guidelines classify the CNVs into different categories: Pathogenic (disease-causing CNVs); Likely Pathogenic (CNVs with substantial evidence to imply that they will ultimately be determined to be disease-causing, but there is not yet enough data to firmly establish pathogenicity); Uncertain significance (CNVs of uncertain clinical significance represent a broad category that may include results that are later proven, with the accumulation of additional information, to be either pathogenic or benign); Likely benign (there is a large body of evidence that points to the likelihood that these CNVs do not have a role in Mendelian disease; nevertheless, there is not yet sufficient evidence to declare this with certainty); Benign (CNVs that are definitely not involved in Mendelian disease) [83].

2.10.4 Next generation sequencing (NGS)

Next generation sequencing (NGS) uses new technologies for sequencing DNA that take advantage of massively parallel computing [84]. NGS offers extraordinarily high throughput analysis, in addition to scalability and speed. NGS can be used to sequence entire genomes (whole genome sequencing a.k.a. WGS) and all 22,000 protein-coding genes (whole exome sequencing a.k.a. WES), or it can be constrained to specific areas of interest (multi-gene panels) [84]. This technology can be used to determine the order

of nucleotides in targeted areas of DNA or in the whole genome by mapping the individual reads to the human reference genome [84]. The three billion bases that make up the human genome are sequenced numerous times. This provides a high depth that allows for the delivery of reliable data as well as insight into unanticipated DNA variation [84]. Findings are also usually classified according to the ACMG guidelines [85]. Although NGS diagnostic yield is overall high, an overwhelming proportion of the reported variants are variants of uncertain clinical significance (VUSs) [86].

2.11 Ethical issues

Although ethical problems surrounding genetic testing have been long known [87], they have recently taken on a more relevant role as a result of the tremendous advances made in the field of genomic medicine especially in pediatric settings [88]. Furthermore, the improvement of genetic tests has made accurate and low-cost screening of embryos, fetuses, children, and adults possible [13]. Genetic testing has primarily highlighted ethical concerns about fundamental ethical principles such as autonomy, nonmaleficence, beneficence, and justice [87, 89]. For instance, in regard to the concept of autonomy, because of the inherent and unconditional value that each person possesses, individuals should all be given the ability to make their own rational decisions and moral choices, and they should all be given the opportunity to use their capacity for self-determination. Nonmaleficence refers to the duty of a clinician to avoid causing unnecessary suffering to a patient. The principle of beneficence requires clinical providers to act for the benefit of their patients and uphold a set of moral principles to protect and defend the rights of others, prevent harm, and get rid of circumstances that would cause harm. The concept of justice can be loosely defined as the application of standards that are fair, equitable, and acceptable to the treatment of individuals [90].

Furthermore, the gap between the ability to collect extensive genetic information and the ability to give decisive treatment based on that information poses ethical concerns, especially in children [13]. For example, a study looking at challenges in pediatric WES found that the uncertainty as to whether a VUS is benign or pathogenic might induce anxiety. It may be time-consuming and financially burdensome for patients and their families to undergo segregation analysis on extended family members in order to try to clarify whether a VUS segregates with the disease phenotype in the family [91].

Multiple platforms that analyze multiple targets at once are used in clinical diagnostic testing such as CMA, WES, and WGS[13]. Testing generates a large amount of data, which increases sensitivity in detecting causative variations but also produces uncertain and secondary/unexpected results that must be managed [13]. Two factors contribute to the ethical dilemmas that arise with children while using diagnostic testing: (1) the potential lack of clinical utility of genetic testing outcomes as is the case with VUSs and (2) the possible detection of secondary or unexpected findings [13, 14].

In terms of clinical utility, a study that looked at how parents perceive their children's CMA test results found that the most important part of the test is its ability to give parents the answer they have been looking for about the etiology of their child's condition. This is also a key part of the test's ability to guide care, access to services, and family planning [92]. Furthermore, parents of children who had a CMA finding of uncertain significance appeared to adapt to uncertainty and the limited availability of information, and they valued honesty and empathic ongoing support from medical professionals in the hope that more information could become available in the future [93]. Every single genetic expert highlights the significance and the importance of thoroughly counseling parents about the complexities and limitations of genetic testing prior to doing the test, i.e., pre-test genetic counseling [92-94].

When it comes to secondary findings the intentional search for pathogenic variants in genes that do not appear to be associated with the diagnostic indication for which the NGS test was ordered [95] the ACMG recommended in 2022 that laboratories routinely examine and report variants in 78 genes linked with major and medically actionable disorders including adult onset conditions when genome scale sequencing is employed, regardless of the indication [96]. The *BRCA1* gene, for example, is known to increase an individual's risk of adult-onset breast and ovarian cancer among others [97].

Disclosing an unexpected secondary finding in a child is different from testing a child for an adult-onset illness in a high-risk family [13]. If a child is unexpectedly found to harbor a *BRCA1* pathogenic variant for example, his/her family is unlikely to have previous knowledge about it; in this instance, withholding the child's results will prevent other at-risk adult family members from seeking genetic testing and benefitting from preventive and early detection measures [13]. This is different from testing a child for a known familial pathogenic variant in *BRCA1* gene when his/her family members already know about the child's hereditary risk of harboring the *BRCA1* variant [13]. The American Society of Human Genetics (ASHG) report from 2015 various recommendations within the scope of this discussion. It was suggested that testing should be as focused as possible, based on the clinical context, to reduce the possibility of secondary findings [94]. Furthermore, secondary findings for conditions that manifest in adulthood should be disclosed, but only after parents have been informed and consented, further emphasizing the need for pre-test genetic counseling [94]. An exception to this rule is when a secondary finding has immediate and serious implications for the child's health, in which case the ASHG recommends that results should be shared with parents regardless of their earlier wishes regarding disclosure [94]. As an example, the result of a child unexpectedly found to have a homozygous

pathogenic variant in *BRCA2* gene must be urgently disclosed to parents, as this is consistent with autosomal recessive Fanconi anemia (FA) characterized by birth defects, short stature, bone marrow failure, hypersensitivity to DNA crosslinking agents, and an increased chance of childhood malignancy including pediatric hematological cancers such acute myeloid leukemia [98].

2.12 Literature from GCC and Qatar about knowledge of and attitudes toward genetic testing and counseling

As mentioned earlier, it is important to highlight that only a limited number of studies have focused on investigating parental attitudes and knowledge regarding genetic counseling and different genetic testing indications within populations in the Middle East. This indicates a significant gap in the current understanding of these specific cultural contexts and their impact on genetic healthcare decision-making. Conducting research in this region would contribute to the existing body of knowledge, enabling a more comprehensive understanding of the unique factors and challenges that influence attitudes and knowledge related to genetic counseling and testing. Such insights are crucial for the development of culturally sensitive and effective genetic healthcare interventions in the Middle East.

2.13 Study Aim

The aim of this research project is to gauge parents' a knowledge and attitudes towards genetic counseling and childhood genetic testing. In a related fashion, we are interested in determining how those attitudes differ depending on sociodemographic factors such as parental education level, gender, and income

2.14 Study Objective

1. Assess parents' knowledge of the genetic contribution to congenital anomalies and parents' willingness to pursue genetic counseling and childhood genetic testing for

these conditions.

2. Identify factors (demographic, socioeconomic, familial, psychological, social, etc.) that influence parental attitudes towards genetic counseling and childhood genetic testing.

3. Explore parents' perceived benefits and barriers to genetic counseling and childhood genetic testing, ethical concerns, and psychosocial issues.

CHAPTER 3: METHOD

3.1Study design

The study was based on a prospective face-to-face questionnaire Real-time data collection allow a direct interaction between researchers and participants, facilitating real-time data collection. This method enables immediate clarification of questions, reduces misunderstandings, and ensures accurate responses.

3.2 Study Participants Recruitment

Any parent who fulfilled the inclusion criteria was approached to participate in the survey between October 2022 and February 2023. The survey was installed on an iPad, which was handed over to the parent who agreed to participate after obtaining the signed consent. If both parents of a child showed an interest in filling out the survey, the questionnaire was filled separately by each parent (to increase the sample size) .

In total, we have approached 174 parents. Only 10 of them refused to participate for the following reasons: no time (6 parents), illiterate (3 parents), and language barrier (1 parent). In addition, 4 questionnaires were discarded due to too many missing answers/values. In total, 160 questionnaires were analyzed including 66 questionnaires from 33 couples (and 94 questionnaires from one parent only

3.4 Study Setting and Population

It was offered to parents who met the inclusion criteria (please see section 3.4) and attended the Pediatric Plastic Surgery clinic at Sidra Medicine between October 2022 and February 2023.

3.5 Inclusion Criteria

- Parent of a patient attending the pediatric plastic surgery clinic at Sidra Medicine for a first or follow-up visit between October 2022 and February 2023.
- Parent of a pediatric patient, i.e., a child between the age of 1 day and 17 years.
- Parent of a patient with one or more congenital anomaly.

- Parent of a patient who was previously seen or not seen by a geneticist or a genetic counselor at Sidra Medicine or Hamad Medical Corporation (HMC).
- Parent of a patient who previously underwent or not genetic testing at Sidra Medicine or HMC.

3.6 Exclusion Criteria

- Parent of a patient of 18 years of age or above.
- Parent of a patient attending the pediatric plastic surgery clinic at Sidra Medicine with an acquired anomaly due to non-congenital reasons such as trauma, burn, skin flap, etc.

3.7 Sampling and Data collection

The research questionnaire was provided in both English and Arabic. The questionnaire was translated from English to Arabic by a licensed medical translation company, under the authorization of Sidra Medicine. Sample size calculation target is 200 questionnaires.

The questionnaire was completed using the SurveyMonkey® online tool (https://www.surveymonkey.com/).

3.8 Overview of the questionnaire.

The questionnaire used in this study was adapted from previously reported studies in scientific literature. These studies were conducted to investigate similar topics or research questions related to the subject at hand. By adopting a questionnaire that has been previously used and validated, it ensures that the data collected in this study can be compared and analyzed in a consistent and reliable manner [99-106] , the questionnaire had also been tailored to our patient population with the assistance of a certified genetic counselor Ms. Karen El-Akouri and under the supervision of Dr. Houssein Khodjet Elkhil, dissertation supervisor, to address the objectives of the current thesis.

The questionnaire included 38 questions divided into the following 6 sections : Questions (1-9) about patient and parent demographics; Questions (10-12) about family

history; Questions (13-16) about previous experience with genetic counseling and genetic testing; Questions (17-22) about parental knowledge of genetics and its contribution to disease/congenital anomalies; Questions (23-28 and 35) about parental attitudes towards genetic counseling and genetic testing (perceived benefits); Questions (29-34 and 36-38) about perceived barriers to genetic counseling and genetic testing.

Questions 1, 2, 4, and 6 are free text questions. For the purpose of analysis, we have grouped the answers to these questions into categories as follows:

- Question 1: Reason of the referral answers were grouped into 3 categories:
    - Major single/non-syndromic anomalies such as CL/P, microtia, and craniosynostosis.
    - Major multiple/syndromic anomalies such as Apert syndrome, Crouzon syndrome, 22q deletion syndrome.
    - Minor anomalies such as ear deformity and syndactyly.

For significant statistical analysis, the categories were further combined to ‘‘single anomalies’’ and ‘‘multiple anomalies’’ due small number of questionnaire with minor anomalies.

In our study, we have classified the children into age groups based on Piaget’s theory of intellectual development, which describes a series of 4 stages that define the typical progression of children’s level of knowledge as they grow up [107]. The intellectual development of children is reflected in each stage. These stages have been classified as follows: (1) the sensorimotor stage, which occurs between birth and the age of two years; (2) the preoperational stage, which occurs between the ages of two years and 7 years; (3) the concrete operational stage, which occurs between the ages of 7 years and 11 years; and (4) the stage of formal operations, which goes from 11 or 12 years through adulthood [107].

- Question 2: Age of child answers were grouped into 4 categories:
    - 1 day to < 24 months
    - 2 years to < 7 years
    - 7 years to <12 years
    - 12 years to < 18 years
- Question 4: Age of parent filling the survey answers were grouped into 4 categories:
    - < 30 years
    - 30 years to < 40 years
    - 40 years to <50 years
    - 50 years and above
- Question 6: Nationality of non-Qatari answers were grouped into 4 categories:
    - Middle Eastern
    - North African
    - Asian
    - American/European

For question 13 (Did your child ever undergo a genetic test in the past?) and question 15 (Did any health care provider ever offer you/your child a referral to genetics/genetic counseling?), if the participant chose "No" as an answer, then question 14 (The genetic test helped me understand the contribution of genetics to my child's congenital anomaly(ies) and question 16 (The genetic/genetic counseling consultation helped me understand the contribution of genetics to my child's congenital anomaly(ies) become nonapplicable.

In questions 14, 16-22, and 25-37, answers were collected through 5-point Likert scales (Strongly Agree, Agree, Undecided, Disagree, and Strongly Disagree). For the 6 questions assessing parental knowledge of genetics (questions 17-22), each correct

answer was given a score of 2, an ‘‘Undecided’’ answer was given a score of 1, and a wrong answer was given a score of 0 (Appendix 1) [108]. The total score of knowledge level if all answers are correct is 12. The knowledge level was classified as ‘‘high knowledge level’’ if the score was between 9 and12, ‘‘moderate knowledge level’’ if the score was between 6 and 8, and ‘‘low knowledge level’’ if the score was less than 6.

For questions 10 and 11 collecting patients’ family history, the data regarding part 2 of these 2 questions (if yes, specify who) were excluded from analysis due to a low percentage of responses.

For questions (23-28 and 35) assessing parental perceived benefits of genetic counseling and genetic testing, a score of 2 was given to those who answered (Strongly Agree or Agree), a score of 1 was given to those who answered (Undecided), and a score of 0 was given to those who answered (Strongly Disagree or Disagree). Due to the small sample size, we recorded the parental attitudes towards perceived benefits in three groups: Agree, Undecided, and Disagree). The higher the score on the scale for perceived benefits, the higher the perceived benefit of genetic counseling and genetic testing, and thus the more positive the parental attitude.

For questions (29-34 and 36-37) assessing parental perceived barriers, a score of 2 was given to those who answered (Strongly Agree or Agree), a score of 1 was given to those who answered (Undecided), and a score of 0 was given to those who answered (Strongly Disagree or Disagree). Due to the small sample size, we recorded the parental attitudes towards perceived barriers in three groups: Agree, Undecided, and Disagree. A higher score on the scale for perceived barriers represents a higher perceived barrier against genetic counseling and genetic testing.

Additionally, question 38 (Can you think of any other reason that would stop you

from meeting a genetic counselor or considering genetic testing?) was left open-ended as free text for the participants to list other reasons that would stop them from meeting a genetic counselor or consider genetic testing for their child. The answers were later grouped, and themes were extracted. Out of 160 participating parents, only 24 provided additional perceived barriers. The main themes were lack of time, lack of knowledge towards benefits, lack of medical evidence, lack of support from family members, focus on current medical issues, increasing stress and anxiety, and God 'destiny.

3.9 Statistical Analysis

All data was coded and analyzed in the SPSS software v28.0. All categorical variables were presented as frequencies and percentages. The continuous variables were tested for normality using the Shapiro Wilk test and presented as mean and ± (standard deviation). All missing data were considered to be 0 . After checking for normal distribution, parametric tests were used as follows: One-way analysis of variance (ANOVA) was used to compare the parental knowledge score according to demographic characteristics where number of categories were more than two. In case of significant main effect was found, post-hoc pairwise comparisons were made after adjusting for Bonferroni correction. An independent sample t-test was used to compare parental knowledge score among two groups (Major single and Multiple anomalies) A chi-square test was used and P-value <0.05 was considered cutoff for statistical significance for all categorical data. To assess the relationship between two continuous variables a Pearson's correlation coefficient was used along with scatter plot. Similar analyses were conducted for other outcome variables including the perceived benefits scores and perceived barriers scores. A multiple linear regression was conducted to determine the factors associated with knowledge score, perceived benefits scores, and

perceived barriers scores. Only those factors that were significant were considered for multiple regression as factors or covariates, but only significant factors were retained. A P-value <0.05 was used as a cutoff for statistical significance for multiple regression analysis.

To further evaluate the strength of the observed relationships, multiple regression analysis has been performed between our outcome variable (knowledge score, perceived benefits scores, and perceived barriers scores) with each predictor variables such as demographics and other factors such as family history listed after adjusting for other significant predictors. The main goal of multiple regression is therefore to eliminate confounding.

3.10 Ethical Approval

Ethical approval was obtained from Qatar University's Institutional Review Board (IRB) under the number: 1967276-1, as well as from Sidra's IRB under the number: 1916398. Prior to participation, all participants signed a consent form.

Ethical Considerations

IRB and confidentiality.

CHAPTER 4: RESULTS

4.1 Study Participants demographics

A total of 160 participants filled out the questionnaire. The reason of the referral was mainly due to major isolated/non-syndromic congenital anomaly (n=117, 73.1%), followed by major multiple/syndromic anomalies (n=33, 20.6%) and only (n=10, 6.3%) with minor anomaly (Table 1). The mean age in years for children included in the study was 5.2 years and most children were between the ages of 2 and 7 years (n= 56, 35.0%). Males accounted for 56.3% (n=90) of children included in the study; in contrast, most of the parents who answered the questionnaire were females (n=101, 63.1%). The mean age of parents responding to the survey was 37.4 years and most of the participant ages fell between 30 and 39 years (n=67, 46.2%). In total, 22.2% (n=35) of the participants were Qatari. Among the non-Qatari participants, Asians (n=42, 26.6%) and North Africans (n=40, 25.3%) represented the majority, followed by Middle Eastern (n=32, 20.3%), and Americans/Europeans (n=9, 5.7%). Almost 50% of parents who responded to the survey had an educational level corresponding to College/Undergraduate level/ Bachelor's, followed by 21.3% with a Graduate level/Master's/PhD education, 18.8% with a high school or less education, and 10.0% with a Diploma education. About 31.1% of parents reported a household income above 20,000 QAR, and 12.1% with a household income below 5,000 QAR. Nearly half (n=79, 49.4%) of the participants lived less than 30 minutes away from Sidra Medicine, and only 5.6 % (n=9) living more than 60 minutes away (Table 2).

4.2 Family History

A total of 19 participants, comprising 12.3% of the sample, reported having another child or family member with a similar congenital anomaly (ies). Participants with children or other family members with a genetic disorder accounted for 12.6% (n=20) of our study sample. About 23% of our participants were consanguineous. When asked

for the type of parental consanguinity, the majority reported being first cousins (n=18), 3 were double first cousins, 6 were second cousins, 4 reported belonging to the same tribe, and 5 did not specify (Table 2).

4.3 Previous experience with genetic counseling and genetic testing

Of the 160 participants, 36.9% (n=32) had a child who underwent genetic testing in the past at HMC, while other children had genetic testing at Sidra Medicine (n=18) or outside Qatar (n=5), and 4 did not mention where genetic testing was done. Furthermore, out of the 59 participants whose child had genetic testing in the past, 69% found that genetic testing helped them understand the contribution of genetic to their children's congenital anomaly(ies), while 27.6% were undecided to answer this question, and only 3.4% didn't feel any contribution from genetic testing to their understanding of their child's anomaly (Figure 1). In addition, out of 160 participants, 33.8% (n=54) were offered by their medical provider a referral for their child to see a geneticist/genetic counselor. Out of these 54 participants, 72.5% found that the genetic/genetic counseling consultation has helped them understand the contribution of genetic to their child congenital anomaly(ies), while 23.5% were undecided, and about 4% didn't agree (Figure 1).

Table 1. *Reason of the referral classification*

Reason of referral	n (%)
Minor Single Anomaly	10 (6.3%)
Major Isolated/Single Anomaly	117 (73.1%)
Major Syndromic/Multiple Anomaly	33 (20.6%)

***Table 2**. Demographic characteristics of the parents participating in the survey*

Questions	n (%)
Age of the child (years)	
<2	49 (30.6)
2- <7	56 (35.0)
7- <12	36 (22.5)
12- <18	19 (11.9)
Sex of the child	
Male	90 (56.3)
Female	70 (43.8)
Age of the parent (years)	
<30	19 (13.1)
30 - <40	67 (46.2)
40 - < 50	53 (36.6)
>50	6 (4.1)
Missing	15
Sex of the parent	
Male	59 (36.9)
Female	101 (63.1)
Nationality of the parent	
Qatari	35 (22.2)
North African	40 (25.3)
Middle Eastern	32 (20.3)
Asian	42 (26.6)
American/European	9 (5.7)
Missing	2
Education level of the parent	
High school or less	30 (18.8)
Diploma	16 (10.0)
College/Undergraduate level/Bachelor's	80 (50.0)
Graduate level/Master's/PhD	34 (21.3)
Household income (both parents)	
< 5000 QAR	19 (12.1)
5000 – <10000 QAR	42 (26.8)
10000 - 20000 QAR	46 (29.3)
>20000 QAR	50 (31.8)
Missing	3
How far do you live from Sidra Medicine?	
<30 minutes	79 (49.7)
30 - 60 minutes	71 (44.7)
>60 minutes	9 (5.7)
Missing	1
Other child or family member with similar congenital anomaly(ies)	
No	136 (87.7)
Yes	19 (12.3)
Missing	5

***Table 3**. Demographic characteristics of the parents participating in the survey*

Questions	n (%)
Other child or family member with a genetic disorder	
No	139 (87.4)
Yes	20 (12.6)
Missing	1
Parental consanguinity	
No	121 (77.1)
Yes	36 (22.9)
Missing	3
Parental consanguinity relationship	
1st cousins	18 (11.5)
2nd cousins	6 (3.8)
Double 1st cousins	3 (1.9)
Same tribe	4 (2.5)
Not mentioned	5 (3.2)
Missing	3
Did your child ever undergo a genetic test in the past?	
No	101 (63.1)
Yes	59 (36.9)
Genetic testing location	
HMC	32 (20.5)
Outside Qatar	5 (3.2)
Sidra	18 (11.5)
Missing	4
The genetic test helped me understand the contribution of genetics to my child's congenital anomaly(ies)	
Strongly agree	21 (36.2)
Agree	19 (32.8)
Undecided	16 (27.6)
Disagree	1 (1.7)
Strongly disagree	1 (1.7)
Did any health care provider ever offer you/your child a referral to genetics/genetic counseling?	
No	106 (66.3)
Yes	54 (33.8)
The genetic/genetic counseling consultation helped me understand the contribution of genetics to my child's congenital anomaly(ies).	
Strongly agree	21 (41.2)
Agree	16 (31.4)
Undecided	12 (23.5)
Disagree	1 (2.0)
Strongly disagree	1 (2.0)

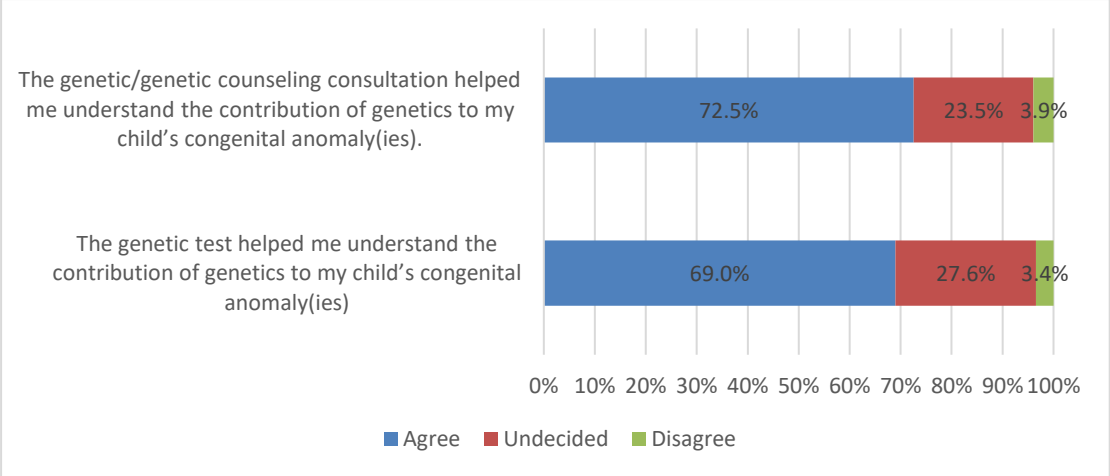

Figure 1. *Attitudes towards previous experience with genetic counseling and genetic testing*

4.4 Parental knowledge of genetics and its contribution to disease/congenital anomalies

Parental responses were given scores of 2, 1, and 0 for each correct answer, each undecided answer, and each false answer, respectively. Parental knowledge level was then categorized based on the knowledge scores as follows: High level (knowledge score between 9 and 12), Moderate level (knowledge score between 6 and 8), and Low level (knowledge score less than 6). The parental mean knowledge score was 8.7±2.0 out of 12. About 53.7% of participants scored with a high level of knowledge, 40.6% scored with a moderate level of knowledge, and only 5.63% scored with a low level of knowledge, as illustrated in Figures 2 and 3.

As shown in Table 3, when we looked at the knowledge score and the demographic factors, we found that the age of children had an overall significance on parental knowledge score (P= 0.037). Furthermore, a post hoc pairwise comparison showed that parents of children from the age group 2- < 7 years have significantly higher knowledge than those with children less than 2 years (P= 0.024). The knowledge score was also

significantly different between ethnicities (P= 0.003). A post hoc comparison showed that American and European parents' knowledge score is higher than that of Qatari (P= 0.008), Middle Eastern (P= 0.017) and Asian (P= 0.004) parents. The knowledge score was also found to be significantly different with the level of education (P= 0.001): parents with only a high school or less education level had lower knowledge in comparison with those who have a diploma (P = 0.046), undergraduate level (P< 0.001), and postgraduate level (P=0.03) education after a post hoc comparison. When it comes to the reason of referral (single anomaly vs. multiple anomalies), there was no significant difference between the two groups. Additional analysis was done looking for the association of the knowledge level with demographic factors. We have found that ethnicity (P=0.016) and parents' education level (P=0.006) were maintained significantly associated to knowledge level similarly to what was found when knowledge score was considered, while the reason of the referral showed a border value of significance (P=0.005) and conversely age of children did not show any more significant association. When it comes to ethnicity, post hoc pairwise analysis showed that American and European parents had a higher knowledge level than Asians. Similarly, post hoc pairwise analysis also revealed that the proportion of parents with a low knowledge score was larger for those with a high school or less education level compared to those with a diploma, undergraduate degree, and postgraduate degree (P=<0.05). Moreover, parents of children with single congenital anomalies were found to have higher knowledge level than parents of children with multiple congenital anomalies (Table 3).

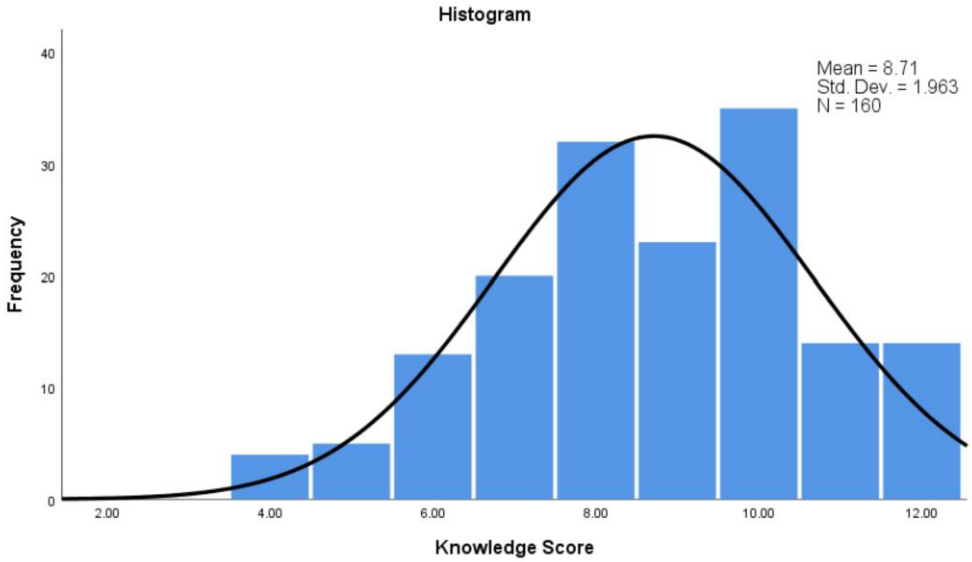

Figure 2. *Parental knowledge score distribution*

The above figure shows the distribution of parental knowledge score as a histogram, which confirms that it has a normal distribution. The scores ranged from 4 to 12 with the average score being 8.7±2.0.

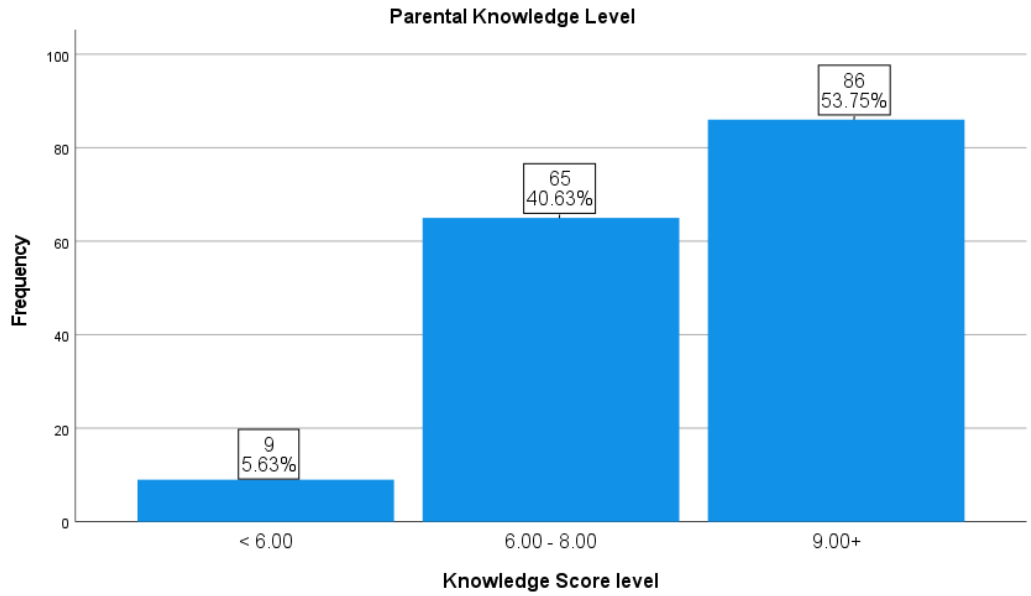

Figure 3. *Parental knowledge level*

Table 4. *Parental knowledge score and parental knowledge level in association with demographic factors.*

Demographic factors	Valid N	Mean score ± SD	P-Value	Low (<6)	Moderate (6-8)	High (9-12)	P-value
Overall score				9 (5.6)	65 (40.6)	86 (53.8)	
Age of the child (years)							
< 2	49	8.7±2.0		2 (4.1)	23 (46.9)	24 (49.0)	
2 - < 7	56	9.2±1.8①	0.037	2 (3.6)	19 (33.9)	35 (62.5)	0.347
7 - < 12	36	8.0±2.1		4 (11.1)	17 (47.2)	15 (41.7)	
12 - <18	19	8.8±1.8		1 (5.3)	6 (31.6)	12 (63.2)	
Sex of the Child							
Male	90	8.7±1.9	0.928	4 (4.4)	38 (42.2)	48 (53.3)	0.724
Female	70	8.7±2.1		5 (7.1)	27 (38.6)	38 (54.3)	
Age of the parent (years)							
<30	19	9.1±1.9		0 (0.0)	9 (47.4)	10 (52.6)	
30 - <40	67	8.9±1.9	0.723	3 (4.5)	25 (37.3)	39 (58.2)	0.910
40 - < 50	53	8.6±2.0		3 (5.7)	22 (41.5)	28 (52.8)	
>50	6	8.3±2.1		0 (0.0)	3 (50.0)	3 (50.0)	
Sex of the parent							
Male	59	8.4±1.9	0.156	4 (6.8)	27 (45.8)	28 (47.5)	0.468
Female	101	8.9±2.0		5 (5.0)	38 (37.6)	58 (57.4)	
Ethnicity of the parent							
Qatari	35	8.3±1.9		1 (2.9)	18 (51.4)	16 (45.7)	
North African	40	9.2±1.6		0 (0.0)	15 (37.5)	25 (62.5)	
Middle Eastern	32	8.5±2.1	0.003	4 (12.5)	11 (34.4)	17 (53.1)	0.016
Asian	42	8.3±2.1		4 (9.5)	21 (50.0)	17 (40.5)	
American and European	9	10.8±1.3②		0 (0.0)	0 (0.0)	9 (100.0)④	

Table 5. *Parental knowledge score and parental knowledge level in association with demographic factors.*

Demographic factors	Valid N	Mean score ± SD	P-Value	Low (<6)	Moderate (6-8)	High (9-12)	P-value
Education level of the parent							
High school or less	30	7.4±2.0③		5 (16.7)	17 (56.7)	8 (26.7) ⑤	
Diploma	16	9.0±1.8		0 (0.0)	7 (43.8)	9 (56.3)	
College /Undergraduate level /Bachelor's	80	9.1±1.8	0.001	2 (2.5)	26 (32.5)	52 (65.0)	0.006
Graduate level / Master's /PhD	34	8.7±2.0		2 (5.9)	15 (44.1)	17 (50.0)	
Household income (both parents)							
<5000 QAR	19	8.5±2.4		2 (10.5)	7 (36.8)	10(52.6)	
5000 – 10000 QAR	42	8.5±1.7	0.536	1 (2.4)	23 (54.8)	18 (42.9)	0.221
10000 - 20000 QAR	46	8.9±1.9		4 (8.7)	15 (32.6)	27 (58.7)	
>20000 QAR	50	9.0±1.9		1 (2.0)	19 (38.0)	30 (60.0)	
How far do you live from Sidra Medicine?							
<30 minutes	79	8.8±1.8		3 (3.8)	32 (40.5)	44 (55.7)	
30 - 60 minutes	71	8.6±2.2	0.692	6 (8.5)	29 (40.8)	36 (50.7)	0.638
>60 minutes	9	9.1±1.5		0 (0.0)	3 (33.3)	6 (66.7)	
Other child or family member with similar congenital anomaly(ies)							
No	136(87.7)	8.7±2.0		7 (5.1)	56 (41.2)	73 (53.7)	
Yes	19(12.3)	8.4±1.8	0.612	2 (10.5)	7 (36.8)	10 (52.6)	0.634
Missing	5						
Other child or family member with a genetic disorder							
No	139(87.4)	8.7±2.0		7 (5.0)	61 (43.9)	71 (51.1)	
Yes	20(12.6)	8.9±1.9	0.636	2 (10.0)	4 (20.0)	14 (70.0)	0.112
Missing	1						

Table 6. *Parental knowledge score and parental knowledge level in association with demographic factors.*

Demographic factors	Valid N	Mean score ± SD	P-Value	Low (<6)	Moderate (6-8)	High (9-12)	P-value
Parental consanguinity							
No	121(77.1)	8.7±2.0		8 (6.6)	47(38.8)	66 (54.5)	0.624
Yes	36(22.9)	8.8±1.9	0.680	1 (2.8)	16 (44.4)	19 (52.8)	
Missing	3						
Parental consanguinity relationship (n=36)							
1st cousins	18 (50.0)	8.7±2.0		1 (5.6)	8 (44.4)	9 (50.0)	
2nd cousins	6 (16.7)	10.2±1.3		0 (0.0)	0 (0.0)	6 (100.0)	
Double 1st cousins	3 (8.3)	7.3±0.6	0.316	0 (0.0)	3 (100.0)	0 (0.0)	0.341
Same Tribe	4 (11.1)	9.0±1.4		0 (0.0)	2 (50.0)	2 (50.0)	
Not mentioned	5 (13.9)	8.6±2.8		0 (0.0)	3 (60.0)	2 (40.0)	
Did your child ever undergo a genetic test in the past?							
No	101(63.1)	8.6±2.0	0.157	6 (5.9)	45 (44.6)	50 (49.5)	0.366
Yes	59(36.9)	9.0±1.9		3 (5.1)	20 (33.9)	36 (61.0)	
Did any health care provider ever offer you/your child a referral to genetics/genetic counseling?							
No	106(66.3)	8.6±2.1	0.523	7 (6.6)	44 (41.5)	55 (51.9)	0.671
Yes	54(33.8)	8.9±1.8		2 (3.7)	21 (38.9)	31 (57.4)	
Reason for referral							
Single anomaly	96 (60.0)	8.9±1.8	0.063	1 (1.0)	38 (39.6)	57 (59.4)	0.005
Multiple anomalies	64 (40%)	8.4±2.2		8 (12.5)	27 (42.2)	29 (45.3)	

①After post hoc comparison, 2-<7 age group had significantly higher level of knowledge compared to age group <2 years (P= 0.024)

②After post hoc comparison, the knowledge score of American and European parents was higher than Qatari (P= 0.008), Middle Eastern (P= 0.017), and Asian (P= 0.004) parents.

③ After post hoc comparison, the knowledge score of parents with only high school or less education level was lower compared to those with Diploma (P = 0.046), undergraduate level (P < 0.001), and postgraduate level (P=0.038).

④ After post hoc comparison, the parents who were American or European were more likely to have a

knowledge score >9 compared to others (P<0.05).
⑤ After post hoc comparison the parents with a high school education level were less likely to obtain high knowledge score (9+) compared to parents with Diploma, Undergraduate, and Postgraduate education level (P <0.05).

4.5 Attitudes towards genetic counseling and genetic testing (Perceived benefits)

There was a total of 7 questions in the survey that examined the attitudes of parents towards genetic counseling and genetic testing, particularly in how they perceive their benefits and if they would be willing to go through this service. The data obtained shows that 74.7% of the participants said that they would be open to consider genetic testing for their child if it were suggested by a healthcare provider, 13.9% said they would not, and 11.4% were undecided. Similarly, the majority (70%) of parents who replied to the study said they would be open to being referred to genetic counseling if they hadn't already been, 13.8% said they wouldn't be open to a referral, and 16.3% weren't sure (Figure 4). Furthermore, most respondents (above 85%) are in favor of agreeing with perceived benefits, with the exception of the question asking if genetic test results are always accurate where 41% agreed, 50% were undecided, and only 8.9% disagreed.

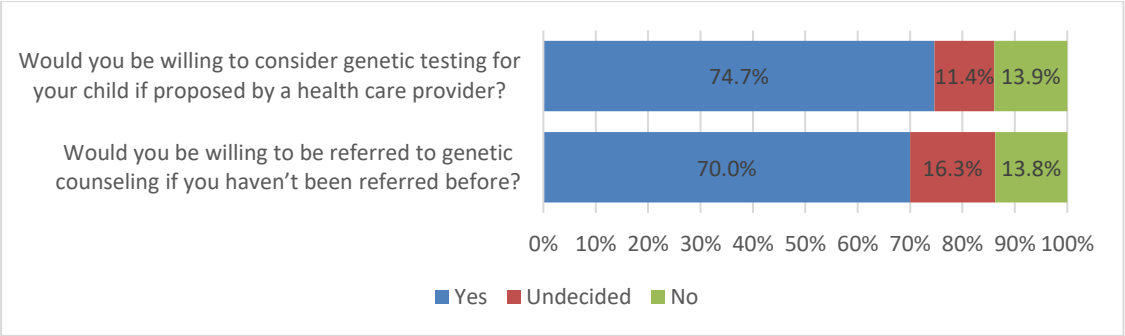

Figure 4*. Willingness to undergo genetic counseling and genetic testing.*

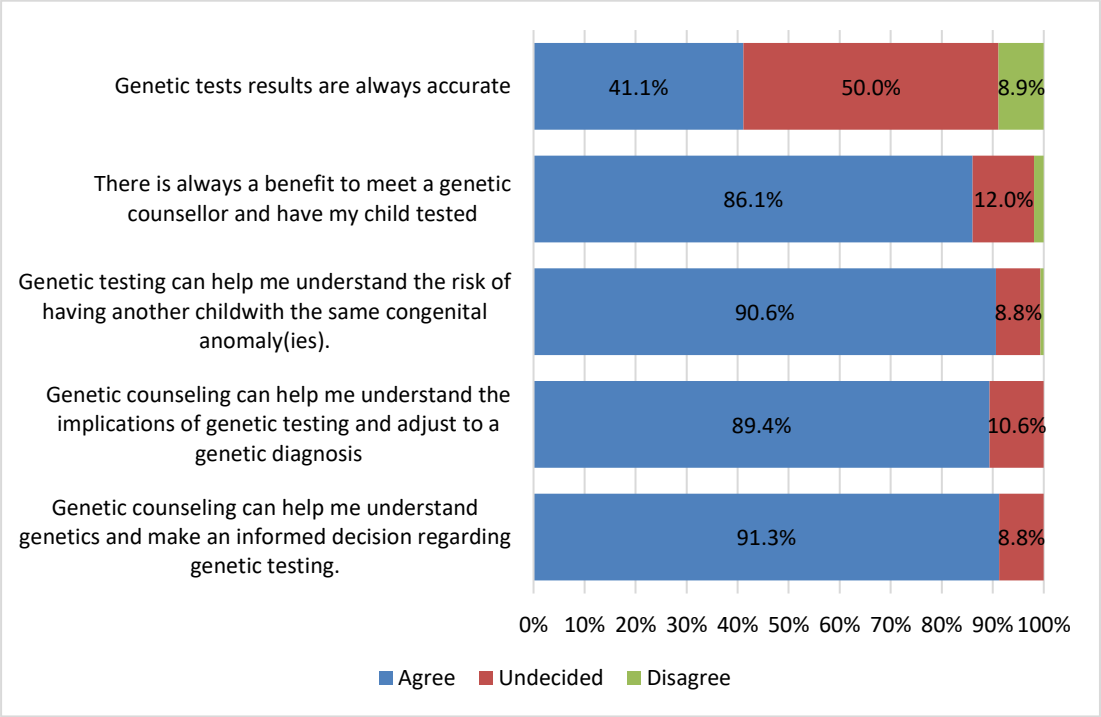

Figure 5. Attitudes towards genetic counseling and genetic testing (Perceived benefits)

The figure shows the percentage of respondents who agreed with each attitude question.

4.5.1 Attitudes towards genetic counseling and genetic testing (Perceived benefits) vs. demographic factors.

We wanted to know if any demographic factor could be associated with the attitudes of the participants regarding their perceptions of the benefits they could get from genetic counseling and genetic testing. Scores of 2, 1, and 0 were given for the three types of answers, Agree, Undecided, and Disagree, respectively. The data show that parental consanguinity (P=0.003), children who had previously undergone genetic testing (P=0.009), and parents whose medical provider referred them to genetic counseling (P=0.001) were found to be significant factors that could have an impact on parents' positive attitudes towards genetic counseling and genetic testing since they showed higher scores with more positive attitudes. When parental attitudes scores were compared based on the reason of referral, no significant difference was found between the groups (Table 4).

Table 7*. Attitudes towards genetic counseling and genetic testing (Perceived benefits) and (Perceived barriers) vs. demographic factors*

Attitude	Perceived benefits			Perceived barriers		
Demographic factors	N	Mean score±SD	*P*-Value	n	Mean score±SD	P-Value
Age of the child (years)						
< 2	49	12.3±2.0		49	5.6±3.3	
2 - < 7	56	12.2±1.7	0.102	56	5.2±2.9	0.112
7 - < 12	36	11.6±2.2		36	4.8±3.2	
12 - <18	19	11.2±2.4		19	7.0±4.7	
Sex of the Child						
Male	90	12.2±1.8	0.188	90	5.8±3.4	0.086
Female	70	11.7±2.3		70	4.9±3.3	
Age of the parent (years)						
< 30	19	13.0±1.3		19	5.9±3.1	
30 - <40	67	11.8±2.1		67	5.1±3.3	
40 - < 50	53	12.1±1.9	0.074	53	5.1±3.1	0.659
>50	6	11.0±1.9		6	6.2±5.6	
Sex of the parent						
Male	59	12.2±1.8	0.252	59	5.9±3.5	0.129
Female	101	11.8±2.1		101	5.1±3.3	
Ethnicity of the parent						
Qatari	35	11.8±2.1		35	6.5±4.2	
North African	40	12.2±1.9		40	5.9±2.9	
Middle Eastern	32	12.4±2.0	0.482	32	5.0±3.0	0.028
Asian	42	11.6±2.2		42	5.0±3.3	
American and European	9	12.0±1.9		9	2.8±1.9①	
Education level of the parent						
High school or less	30	12.2±2.1		30	6.4±4.0	
Diploma	16	12.3±2.4	0.658	16	4.6±2.1	
College/Undergraduate level /Bachelor's	80	12.0±2.1		80	5.1±3.3	0.237
Graduate level / Master's /PhD	34	11.6±1.5		34	5.6±3.4	
Household income (both parents)						
< 5000 QAR	19	12.3±2.1	0.481	19	4.2±2.8	
5000 – 10000 QAR	42	12.3±1.8		42	5.3±3.5	
10000 - 20000 QAR	46	12.0±2.1		46	5.8±3.0	0.372
>20000 QAR	50	11.7±1.9		50	5.4±3.8	

Table 8*. Attitudes towards genetic counseling and genetic testing (Perceived benefits) and (Perceived barriers) vs. demographic factors*

Attitude		Perceived benefits			Perceived barriers	
How far do you live from Sidra Medicine?						
<30 minutes	79	12.1±2.0		79	5.3±3.7	
30 - 60 minutes	71	11.8±2.1	0.599	71	5.6±3.1	0.844
>60 minutes	9	12.4±1.6		9	5.1±2.7	
Other child or family member with similar congenital anomaly(ies)						
No	136 (87.7)	11.9±2.1	0.560	136 (87.7)	5.4±3.3	
Yes	19 (12.3)	12.2±1.4		19 (12.3)	5.1±3.5	0.637
Missing	5			5		
Other child or family member with a genetic disorder						
No	139 (87.4)	11.9±2.1	0.443	139 (87.4)	5.6±3.5	
Yes	20 (12.6)	12.3±1.5		20 (12.6)	3.8±2.1	0.018
Missing	1			1		
Parental consanguinity						
No	121 (77.1)	11.8±2.0	0.003	121 (77.1)	5.4±3.5	
Yes	36 (22.9)	12.8±1.4		36 (22.9)	5.3±3.1	0.804
Missing	3			3		
Did your child ever undergo a genetic test in the past?						
No	101 (63.1)	11.7±2.1	0.009	101 (63.1)	6.1±3.6	<0.001
Yes	59 (36.9)	12.5±1.8		59 (36.9)	4.2±2.4	
Did any health care provider ever offer you/your child a referral to genetics/genetic counseling?						
No	106 (66.3)	11.5±2.2	<0.001	106 (66.3)	5.8±3.6	<0.001
Yes	54 (33.8)	12.8±1.3		54 (33.8)	4.6±2.8	
Reason for referral						
Single anomaly	96 (60.0)	9.0±1.8	0.132	96 (60.0)	5.5±3.4	0.856
Multiple anomaly	64 (40%)	8.4±2.1		64 (40.0)	5.4±3.4	

① After post hoc comparison, parents who were of American or European ethnicity scored significantly lower on perceived barriers score compared to Qatar nationals (P=0.031)

4.5.2 Attitudes towards genetic counseling and genetic testing (Perceived benefits) vs. knowledge level

We wanted to investigate any impact of knowledge level on positive attitudes of our participants. The data obtained showed that there were no significant differences in knowledge level and attitude score (P= 0.349) (Figure 6). However, when we looked at the answers for each knowledge question and the parental attitude score, data for question 1 (K1) ‘‘Congenital anomalies refer to a wide range of problems with the way the body looks or works that are present at birth’’ showed that parents who answered correctly had a higher attitude score in overall perceived benefits (P=0.001) in comparison to parents who answered incorrectly (Figure 7). To further explore the potential association between knowledge scores and positive attitudes, we analyzed the level of correlation between them. The resulting data showed no correlation between attitude scores and knowledge scores (Correlation = r = 0.067, P= 0.400) (Figure 8).

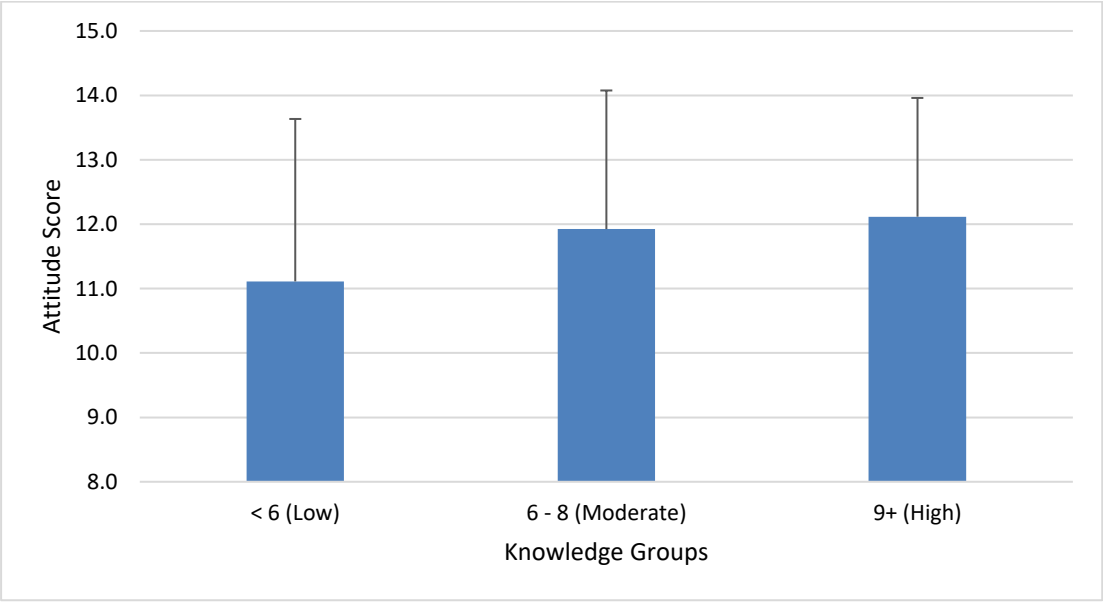

Figure 6. *Parental attitudes (Perceived benefits) vs. Knowledge level.*

One-way ANOVA p-value = 0.349

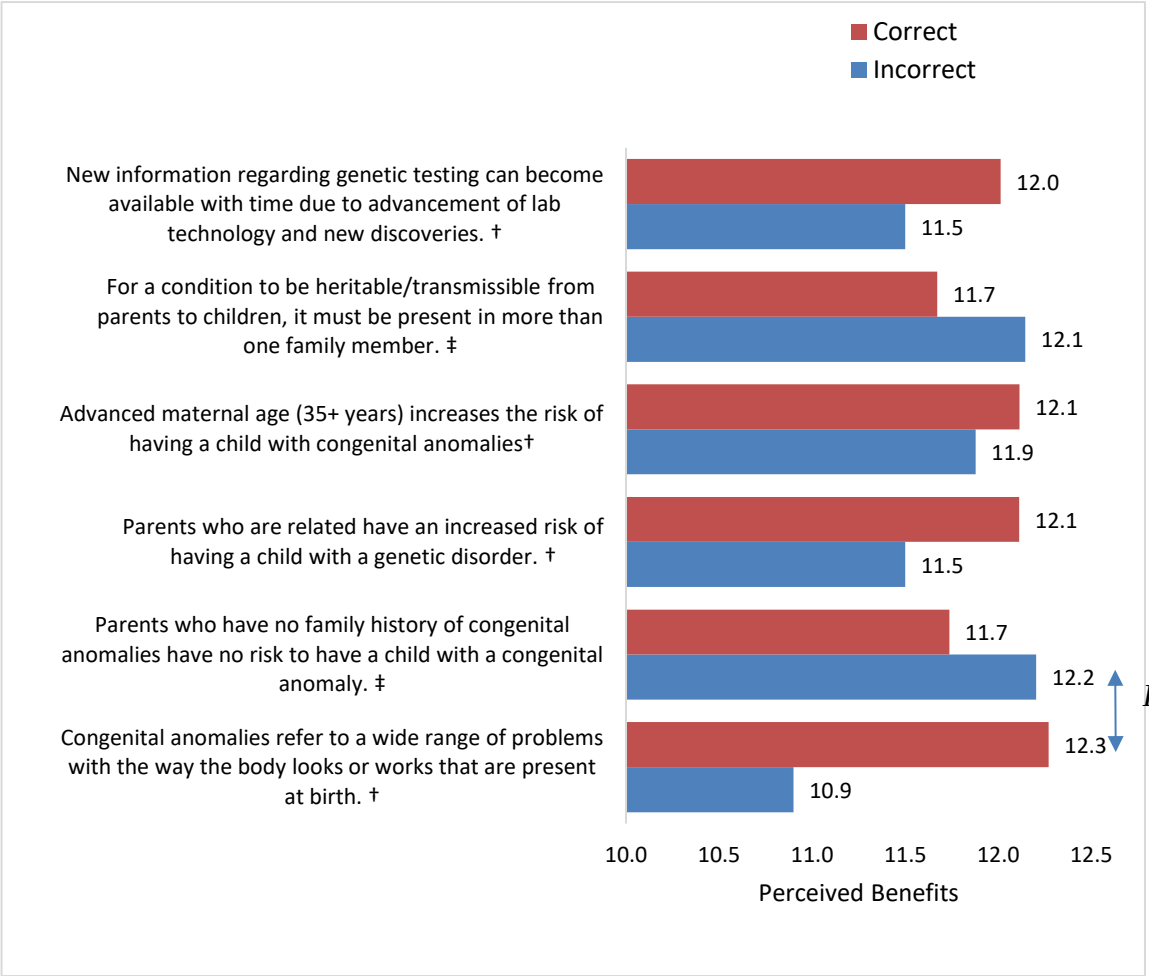

Figure 7. Answer to knowledge questions vs. Attitude score using t-test

† The correct answer is when participants agree or strongly agree.

‡ The correct answer is when participants disagree or strongly disagree.

Undecided responses were classified as incorrect.

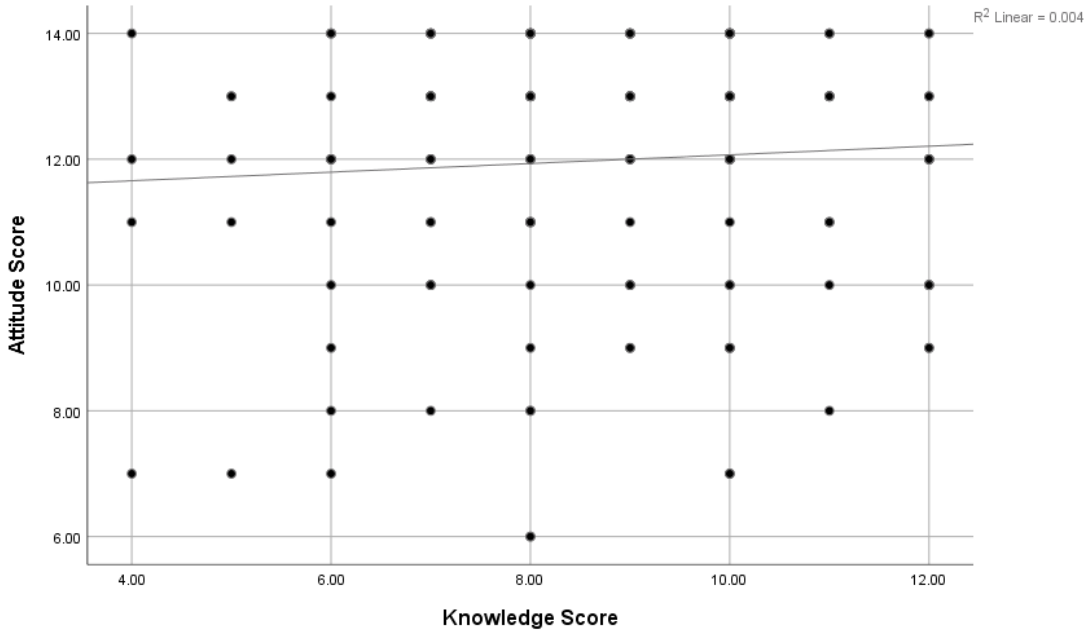

Figure 8. *Correlation of attitude score and knowledge score using scatter plot.*

Correlation = r = 0.067 (p = 0.400)

There is no correlation between the knowledge score and the attitude score.

4.6 Attitudes towards genetic counseling and genetic testing (Perceived barriers)

The last questions of the survey were designed to assess parents' perception of barriers that could represent obstacles to genetic counseling and genetic testing. The majority of the respondents to the questionnaire (above 55%) were disagreeing with most suggested barriers to genetic counseling and genetic testing, except when they were asked about the cost of genetic testing and the impact of genetic testing on private insurance where approximately 50% of respondents were undecided and about 47% agreed to the high cost of genetic testing (Figure 9). It is also interesting to note that about 75% of the parents do not see that having genetic counseling or genetic testing contradicts their religious beliefs. However, there are still around 15% of parents who perceive that genetic counseling and genetic testing could harm their child or their family or create social stigma.

Out of 160 parental responses, only 24 provided additional barriers (free answer) that they felt might prevent them from moving forward with genetic counseling and genetic testing. We have identified the following main themes: lack of time, lack of knowledge towards benefits, lack of medical evidence, lack of support from family members, focus on current medical issues, increasing stress and anxiety, and God's will.

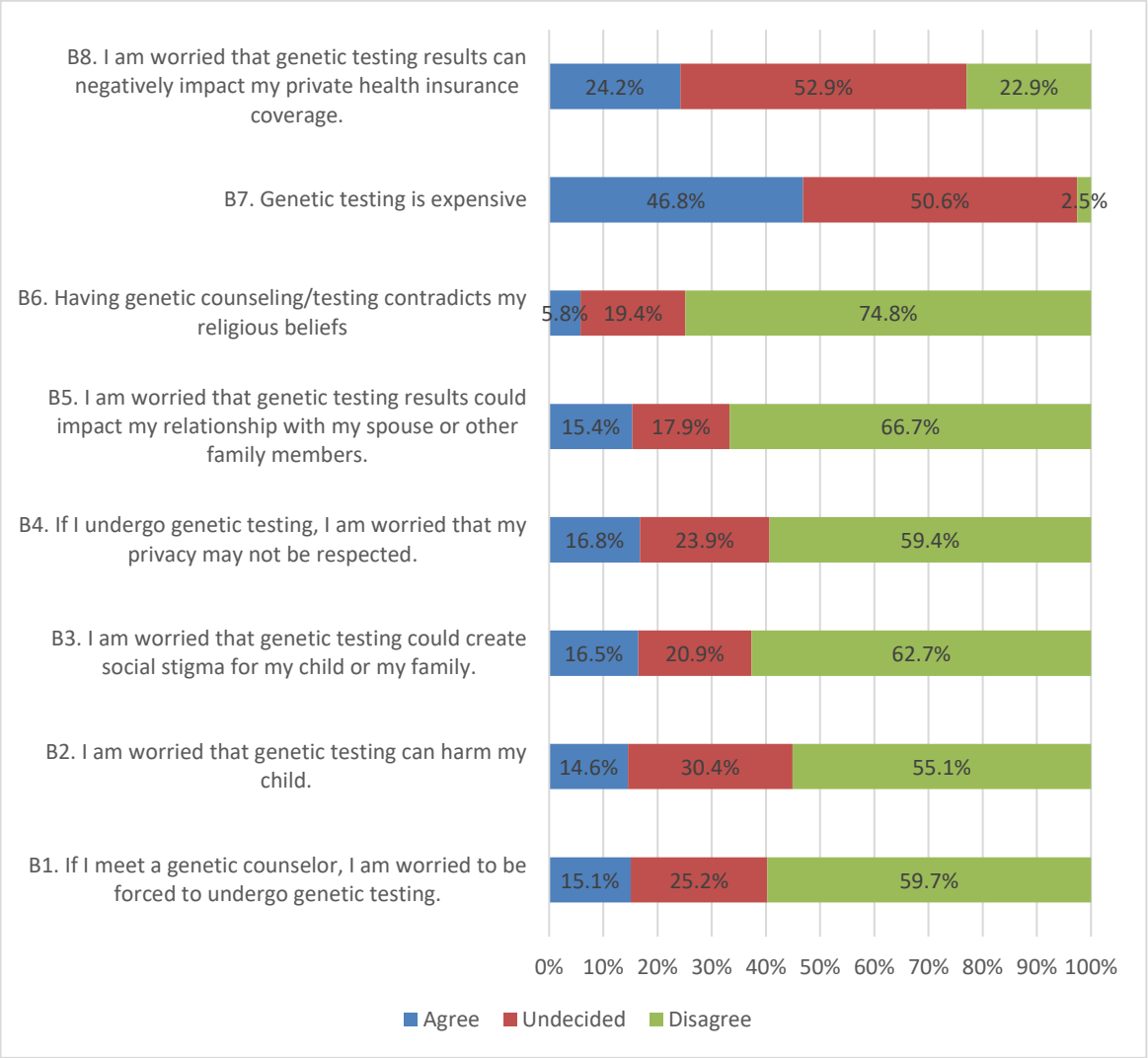

Figure 9. Attitudes towards genetic counseling and genetic testing (Perceived barriers)

4.6.1 Attitudes towards genetic counseling and genetic testing (Perceived barriers) vs. demographic factors

Along the same lines of our analysis of parental attitudes towards benefits of genetic counseling and genetic testing, we wanted to explore what demographic factors could impact parental attitudes and perception of possible barriers to genetic counseling and genetic testing. Scores of 2, 1, and 0 were given for the three types of answers, Agree, Undecided, and Disagree, respectively. The data showed that the ethnicity of the parent (P=0.028), children who had not previously undergone genetic testing (P=> 0.001), and parents whose medical provider did not refer them to genetic counseling (P=< 0.001) were found to be significant factors that could have impacted parental negative attitudes. However, after post hoc testing, Qatari parents had the highest score with negative attitudes in comparison to another ethnicities (P=0.031). American/European parents had the lowest score with negative attitudes. When parental attitude scores were compared based on the reason of referral, no significant difference was found between the groups (Table 6).

4.6.2 Attitudes towards genetic counseling and genetic testing (Perceived barriers) vs. knowledge level

To investigate the impact of knowledge level on the perception of barriers to genetic counseling and genetic testing, we did an association analysis that showed no significant association between knowledge level and barrier perception scores p=0.058 (Figure 10). However, when we considered answers for each question related to barriers, the data showed that the parents who answered incorrectly to question K2 “Parents who have no family history of congenital anomalies have no risk to have a child with a congenital anomaly” scored higher on overall barrier scores with a P-value slightly near significance (P=0.048) (Figure 11).

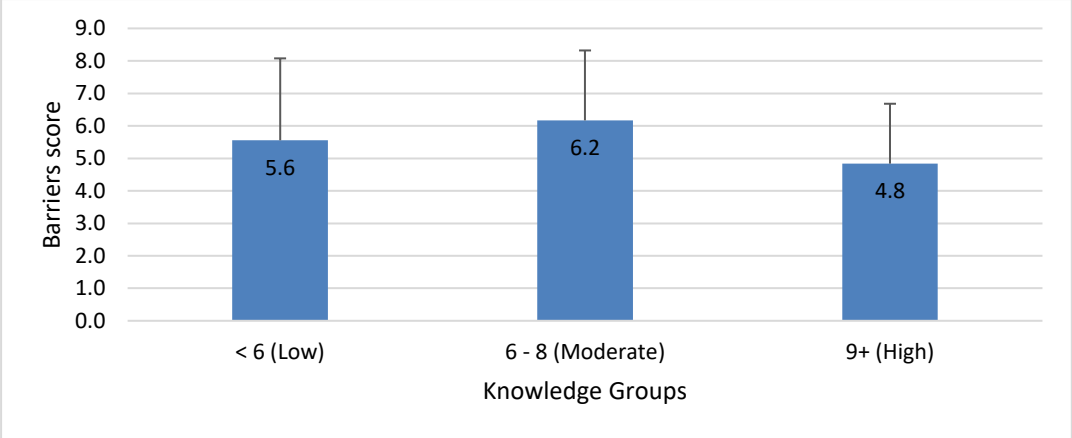

Figure 10. *Attitudes towards genetic counseling and genetic testing (Perceived barriers) vs. Knowledge level.*

One-way ANOVA p-value = 0.058

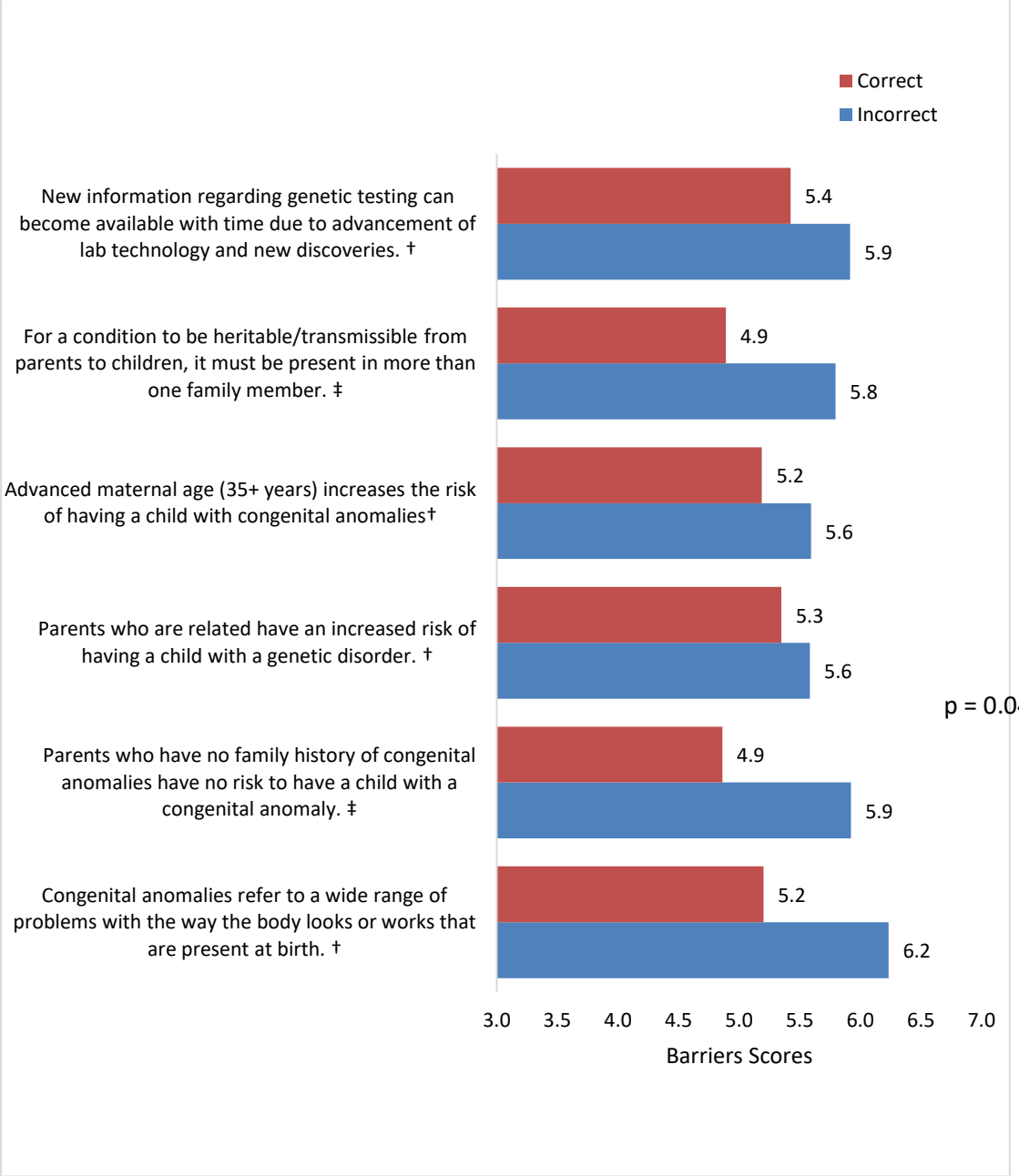

Figure 11. *Attitudes towards genetic counseling and genetic testing (Perceived barriers) vs. Answer to knowledge question.*

† The correct answer is when participants agree or strongly agree.
‡ Correct answer is when participants disagree or strongly disagree.
Undecided responses were classified as incorrect.

When a correlation analysis was done between knowledge scores and barrier scores, the plot showed that the knowledge score was higher compared to the barrier scores, which were lower. The correlation was negative ($r = -0.157$, $P = 0.048$) (Figure 12). This indicates that if the knowledge score is higher, there will be less perceived barriers

to genetic counseling and genetic testing.

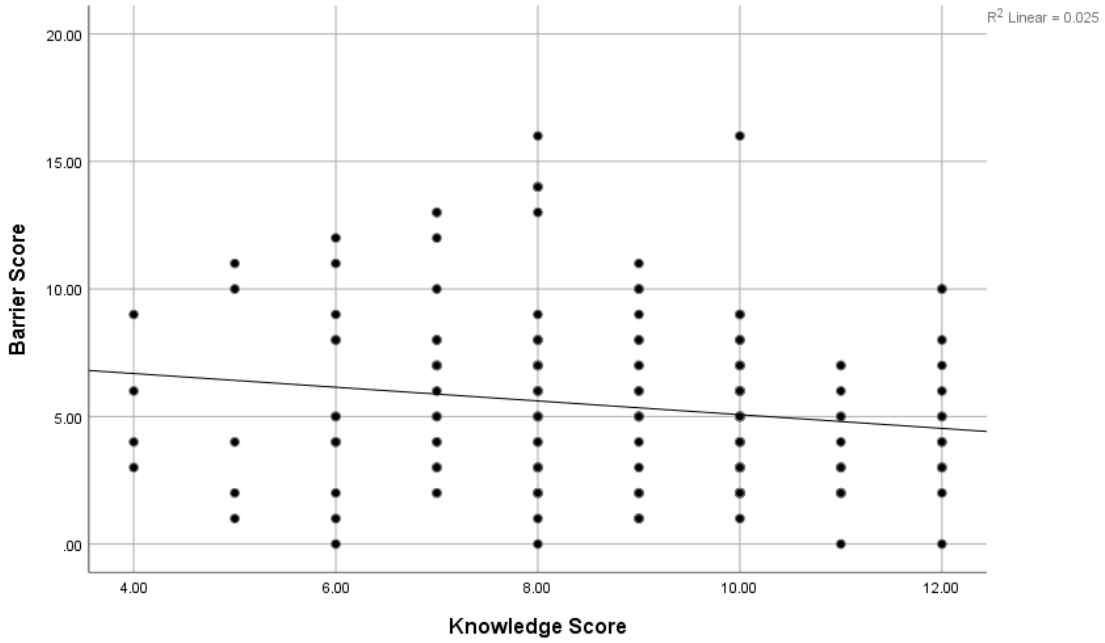

Figure 12*. Correlation analysis between barrier score and knowledge score*

4.7 Multivariable regression analysis

Ethnicity, education level, and age of the child were significant factors in the univariate analysis. However, in the regression analysis, the age of the child was no longer a contributing factor, so it was excluded from the overall analysis shown in Table 4. Parental knowledge was significantly associated with ethnicity after adjusting for education level. The parents from Qatar, North Africa, Middle East, and Asia had significantly lower knowledge score compared to American and European parents regarding genetic counseling and genetic testing. Education level was significantly associated with parental knowledge. After adjusting for ethnicity, having a diploma or more education level resulted in better knowledge compared to high school or less (Table 5).

After adding attitudes regarding benefits and barriers scores as independent covariates,

the final model did not improve. Both attitudes' scores were not significantly associated with parental knowledge.

Table 9*. Multiple regression analysis of parental knowledge score with only the significant factors*

Parameter	B	*P*-value	95% Confidence Interval	
			Lower Bound	Upper Bound
Intercept	9.34	0.000	7.88	10.79
Ethnicity				
- Qatari	-1.84	0.011	-3.24	-0.43
- North African	-1.61	0.019	-2.95	-0.26
- Middle Eastern	-1.99	0.005	-3.38	-0.61
- Asian	-2.28	0.001	-3.62	-0.94
- American/European	0[a]			
Education level				
- Diploma	1.41	0.018	0.25	2.57
- Undergraduate	1.54	0.000	0.69	2.39
- Postgraduate	1.28	0.012	0.29	2.28
- High School or less	0[a]			

β: coefficient from the regression model, Std Error: standard error of the coefficient. The 95% CI (confidence intervals) of the coefficients are also shown. P-value is significant if the 95% CIs do not overlap zero. For example, the intercept coefficient 9.34 refers to constant score in parental knowledge where ethnicity and education levels are set to reference values (i.e., 0). 0[a]: Are set as reference categories for ethnicity and education level. For example, the coefficient (-1.84) should be interpreted as average parental knowledge of Qatari parents is significantly lower by 1.84 when compared to the reference category (American/European) P=0.011 after controlling for education level. The t statistics help to determine whether the coefficient of regression is significant or not. A positive t value indicates a positive relationship and a negative coefficient a negative relationship.

Three factors were discovered as significant with attitudes regarding perceived benefits scores in the univariate analysis: parental consanguinity, having genetic testing in the past, and having a referral for genetic testing/genetic counselling by a medical provider. In the regression analysis, only parental consanguinity and having a referral to genetic testing/genetic counseling by a medical provider were significant. After adjusting for parental consanguinity, those having a referral for genetic testing/genetic counseling

had a significantly higher positive attitude score. After adjusting for having a referral for genetic testing/genetic counseling, parents with parental consanguinity had significantly higher scores related to positive attitudes towards perceived benefits compared to non-consanguineous parents.

In the below model Table 6, we considered perceived barrier as a covariate. Other important factors were more significant. Some factors will be significant in univariate model but need to be significant in the multiple regression. These are excluded from the final model.

Table 10. *Multiple regression analysis of parental attitudes (Perceived benefits) with only the significant factors*

			95% Confidence Interval	
Parameter	B	P-value	Lower Bound	Upper Bound
Intercept	13.36	0.000	12.68	14.04
Parental Consanguinity				
No	-0.82	0.025	-1.53	-0.10
Yes	Reference			
Did any health care provider ever offer you/your child a referral to genetics/genetic counseling?				
No	-1.12	0.001	-1.75	-0.49
Yes	Reference			

β: Coefficient from the regression model. Std Error is the standard error of the coefficient. The 95% CI (confidence intervals) of the coefficients are also shown. P-value is significant if the 95% CIs do not overlap zero. The t statistics help to determine whether the coefficient of regression is significant or not. A positive Beta value indicate positive relationship and a negative value indicate a negative relationship.

In the univariate analysis, ethnicity, having other children or family member with a genetic disorder, having undergone genetic testing in the past, and having received a referral to genetic testing/genetic counseling by a medical provider were significantly associated with barrier scores. In the multiple regression analysis, only three factors remained. After adjusting for family history of genetic disorder and having a child who

had undergone genetic testing, American/European parents had significantly lower barrier scores compared to the Qatari and North African parents. After adjusting for ethnicity and previous genetic testing experience, parents with no family history of genetic disorder showed higher barrier scores. Obviously, parents who had already undergone genetic testing perceived less barriers towards genetic testing after adjusting for ethnicity and family history of genetic disorder.

In the below model Table 7, knowledge and attitude scores were also added but were not significant; hence, they were not included in the final model. Knowledge and attitude do not contribute to barriers in this study.

Table 11. *Multiple regression analysis of parental attitudes (Perceived barriers) with only the significant factors*

			95% Confidence Interval	
Parameter	β	P-value	Lower Bound	Upper Bound
Intercept	0.62	0.637	-1.96	3.20
Ethnicity				
Qatari	3.39	0.006	1.00	5.78
North African	2.88	0.017	0.52	5.24
Middle Eastern	2.00	0.100	-0.38	4.38
Asian	1.92	0.110	-0.44	4.29
American/European	Reference			
Other child or family member with a genetic disorder				
No	1.64	0.041	0.07	3.21
Yes	Reference			
Child undergone genetic testing				
No	1.57	0.005	0.48	2.66
Yes	Reference			

β: is the coefficient from the regression model, std error is the standard error of the coefficient. The 95% CI (confidence intervals) of the coefficients are also shown. P-value is significant if the 95% CIs do not overlap zero.

CHAPTER 5: DISCUSSION

The purpose of this study is to investigate the genetic knowledge and attitudes of parents regarding genetic counseling and genetic testing for children with congenital anomalies attending the Pediatric Plastic Surgery (PPS) Clinic at Sidra Medicine, Qatar. To our knowledge, this study is the first of its kind in Qatar targeting parents of affected children. The reason behind this study is to identify the gaps in parents' knowledge and attitudes towards genetic counseling and genetic testing, in order to provide better education and support for families. Ultimately, the goal of this study is to improve the quality of care for children with congenital anomalies and their families in Qatar. By understanding parents' perspectives and experiences, we hope to develop more effective strategies for providing genetic counseling services and supporting families throughout the genetic testing process.

Additionally, collaboration between PPS and clinical genetics/genetic counseling is essential for the provision of multidisciplinary care to children with congenital anomalies. These children often require complex, coordinated care from multiple specialists, and a collaborative approach can help ensure that they receive comprehensive, high-quality care.

Introducing a clinical geneticist/genetic counselor to the PPS team could be a valuable addition, as it would enable more seamless collaboration and communication between PPS and genetics/genetic counseling. This would also help ensure that genetic evaluation and counseling are integrated into the overall care plan for children with congenital anomalies.

The study found that most participating parents were females, with a percentage of 63.1%. Additionally, most parents, accounting for 60.0%, visited the clinic due to their children having a single congenital anomaly. Qataris constituted 22.2% of the sample

population, and 50.0% of the participants had completed an undergraduate or bachelor's degree. Furthermore, the study revealed that only 36.9% of parents reported that their child had undergone genetic testing before – 20% of those genetic tests having been performed at HMC – and 33.8% of parents reported having been previously referred by their medical provider to genetics/genetic counseling.

Participants whose children had previously undergone genetic testing were surveyed to determine their attitudes towards the benefits of genetic counseling and genetic testing in understanding the contribution of genetics to their child's congenital anomalies. Of those surveyed, 69.0% agreed that genetic testing was beneficial, while 72.5% found that genetic counseling helped them comprehend the contribution of genetics to their child's condition. These findings are consistent with two other studies, one conducted in Ontario and the other in the United States, which found that individuals who had undergone genetic testing had a favorable attitude towards both genetic counseling and genetic testing [109, 110]. Our findings suggest that there is an overall acceptance and appreciation of genetic counseling and genetic testing among those who have utilized these resources in the context of congenital anomalies.

Knowledge level/score and impact of demographic factors

Our study found that a significant proportion (53.75%) of people in our cohort had a high level of knowledge of genetics, while 40.6% had a moderate level of knowledge, and only 5.65% had a low level of knowledge. This variability in knowledge level could be attributed to several factors, including education level, access to information, and previous exposure to genetic counseling and genetic testing. Another study investigating Qataris' attitudes regarding genetic testing and their willingness to participate in the Qatar genome project found that 56.1% of the sampled representative public population had a high level of knowledge [111]. The results of both studies

indicate that a significant proportion of the population in Qatar has a high level of knowledge regarding genetics and its applications in healthcare. This highlights the importance of providing accessible and accurate information about genetic counseling and genetic testing to the public, which could lead to increased awareness and utilization of these services.

We observed that ethnicity and education level were significantly the most influential factors in determining genetic knowledge level. Our results align partly with previous studies. For example, a study conducted in Malaysia that explored genetic knowledge, awareness, and perception of genetic testing for hereditary diseases among Malaysians found that education level, field of study, and prior exposure to genetic testing were all linked to knowledge level [108]. Similarly, a study conducted in China reported that higher levels of education and household income per capita were associated with greater knowledge [112]. Generally, most similar studies emphasized the significance of education level in enhancing genetic knowledge, which is somewhat expected [100-103]. However, unlike previous studies, our findings do not support the idea that previous experience with genetic counseling or genetic testing increases genetic knowledge [101]. There are a few possible explanations. One explanation could be that the questions in the study were focused more on fundamental concepts of genetics, such as inheritance risk and basic genetic terminology, rather than on specific details pertaining to genetic counseling or genetic testing. Therefore, previous experience with genetic counseling and genetic testing may have not provided participants with the knowledge needed to answer the questions in the study.

Another possible explanation is that many of the participants had undergone genetic testing in a non-genetic setting for example in pre-marital screening without receiving formal genetic counseling. In this case, it is possible that participants may have received

information about their genetic condition during or after the genetic testing process, but not necessarily in the context of a genetics/genetic counseling consultation. This could explain why previous experience with genetic counseling or genetic testing did not have a significant impact on genetic knowledge in this study.

Furthermore, in a study conducted in Saudi Arabia, respondents' knowledge of genetics was found to be associated with various demographic factors, such as gender, age, education level, marital status, household income, and family history [113], which was not found in our study. We cannot exclude the effect of the small sample size of our study in revealing such associations.

Our study found that individuals of American and European ethnicity had significantly higher genetic knowledge levels than those of Asian, Qatari, Middle Eastern, and African ethnicities. This is a novel finding that could be attributed to cultural and lifestyle factors, including a higher public awareness of genetics and genetic diseases in certain cultures/societies. A related article highlights the importance of understanding the cultural and social contexts in which genetic information is communicated and received, and advocates for culturally sensitive approaches to genetic counseling and genetic testing, especially in diverse populations with differing beliefs and attitudes towards genetics [114].

In a recent systematic review examining ethical, social, and cultural issues related to clinical genetic testing and counseling in low- and middle-income countries, one of the key themes that emerged was the influence of cultural beliefs and practices on the uptake of information and understanding of genetic disease [115]. This underscores the complex interplay between genetics and cultural, social, and economic factors.

Attitudes towards perceived benefits of genetic counseling and genetic testing and impact of demographic factors

Our study showed that parents held overall a positive attitude towards the potential benefits of genetic counseling and genetic testing, with 70% expressing a willingness to be referred to genetic counseling even if they had never been referred before. This is consistent with another study that assessed the Qatari general population for public attitudes and willingness to undergo genetic testing and participate in the Qatar genome project [111]. Furthermore, we found that 74% of the parents in our cohort expressed their willingness to have their child undergo genetic testing if recommended by a healthcare provider. A study focusing on 30 parents with 24 deaf children in the United States found that only 46% of them underwent genetic testing despite it being recommended by their pediatricians. However, the study also indicated that having a supportive pediatrician played a significant role in the decision to undergo genetic testing. This emphasizes the crucial role that medical providers can play by referring patients to genetics/genetic counseling [116]. This highlights the importance of PPS clinics in recognizing the role of genetics in the etiology of many congenital anomalies and providing families with referrals to genetics/genetic counseling services as needed. Collaboration between PPS and clinical genetics/genetic counseling is essential for the provision of multidisciplinary care to these children and introducing a clinical geneticist/genetic counselor to the PPS team could help facilitate this collaboration.

Moreover, we found that 50% of the parents surveyed were unsure about the accuracy of genetic testing results, while 41.1% believed in their accuracy. This raises an important question about the appropriateness of using the term "accuracy" in our question and how the parents may have comprehended and interpreted it differently. For example, since it is possible for a VUS to be reclassified as pathogenic or benign based on additional evidence becoming available from new publications, functional

studies, and/or family segregation analysis, the uncertainty could potentially cause confusion among parents who could then reasonably consider genetic testing to be as lacking ‘‘accuracy’’.

To further explore the issue of parental knowledge regarding variant reclassification, we looked at a study that was carried out at a pediatric neurology and developmental clinic in the United States. The study emphasized the importance of pre-test genetic counseling and highlighted the need for increased community and informational support for parents whose children receive inconclusive genetic testing results [117]. To make informed decisions about their children's health, it is essential for parents to have access to accurate and up-to-date information that helps them comprehend the complexity of genetic testing results. Genetic counselors are essential in providing this type of information and emotional support; but more research is necessary to determine the most effective ways of providing this assistance to families who receive inconclusive genetic testing results, especially when such results are received in non-genetic clinics.

After adjusting for confounding variables, only two demographic characteristics were significantly correlated with a positive attitude towards perceived benefits of genetic counseling and genetic testing, namely parental consanguinity ($P=0.003$) and being previously referred to genetics/genetic counseling by a healthcare provider ($P<0.001$). In a Saudi Arabian study, the authors found that individuals born from consanguineous marriages generally had positive attitudes towards genetic testing ($P=0.005$) but may need to improve their knowledge of genetics. Furthermore, the study revealed that 80.2% of the respondents knew that consanguineous marriages increased the likelihood of producing children with a genetic disorder [113]. These findings are consistent with results of another study where consanguineous couples in Saudi Arabia had a high

knowledge level of genetic testing and were more likely to seek genetic testing than non-consanguineous couples [118]. In addition, the authors of the study suggested that the higher incidence of genetic disorders among consanguineous marriages in Saudi Arabia led to greater awareness and acceptance of genetic testing among that community [109]. In Qatar, the situation could be the same. However, we cannot exclude the possibility of the increased awareness among consanguineous parents being attributed to the establishment of the Qatari national newborn screening (NBS) program in 2003 and the Qatari national premarital screening (PMS) program in 2009, which could have led to greater awareness in the community as a whole. Based on the experience and expertise of the clinical genetics and metabolic team at Sidra Medicine and HMC, the NBS program has an impressively high uptake (close to 100%) and the PMS program is mandatory.

The second significant demographic factor associated with a positive attitude towards perceived benefits of genetic counseling and genetic testing was found to be previous referrals to genetics/genetic counseling from medical providers. A study surveyed parents who had experience with genetic counseling and genetic testing for their child in the United States found that those who were referred by their child's physician had a higher knowledge level of genetics and genetic testing and a higher likelihood of having a positive attitude towards benefits of genetic testing for their children. This study further supports the idea that healthcare providers have an important role in promoting understanding and acceptance of genetic testing by referring patients to genetic counseling and genetic testing services [119].

Impact of knowledge level/score on attitudes towards perceived benefits of genetic counseling and genetic testing

Upon examining the association between knowledge level and attitude score of the participants, we did not find a significant association (P=0.349). Similarly, when we

analyzed the correlation between the knowledge score and attitude score of parents, we could not find a significant association correlation (r=0.067, P=0.400). Our findings contradict a Chinese study that partially found a significant association (P=0.48) between knowledge and positive attitude towards perceived benefits of genetic testing [112] , additionally a cross sectional study conducted in Qatar looking at Knowledge and Perception of and Attitude toward a Premarital Screening Program in Qatar found that college student had higher knowledge level with positive attitude towards premarital screening [120]. Furthermore, two additional studies shed light on the correlation between genetic knowledge and attitudes towards genetic testing. According to one study, even with a relatively high level of education and genetic knowledge, there still existed a lack of comprehension regarding scientific and medical concepts related to genetics, as well as a disparity in understanding the medical applications and societal implications of genetic testing. [121]. This suggests the need for more effort to educate people about the benefits, risks, and limitations of genetic testing, at both the social and individual levels, to ensure informed decision making. Another study conducted on attitudes towards genetic testing found that participants held a consistent attitude towards genetic testing. However, interestingly, it was observed that those participants who reported lower levels of perceived medical genetic knowledge and higher levels of perceived social genetic knowledge were more inclined to have a reserved attitude towards genetic testing. This suggests that the perceived social and cultural implications of genetic testing can also influence people's attitudes towards it [122] .

This finding highlights the significance of taking a broader view of genetic testing, beyond just the technical aspects. Medical professionals and genetic counselors should consider social and cultural factors when educating patients about the potential benefits

and risks of genetic testing. This can help increase patients' understanding of the implications of genetic testing and ensure that they make informed decisions about whether or not to undergo genetic testing. By doing so, healthcare providers can provide better care that is tailored to the unique needs and perspectives of each patient.

A study conducted in Jordan demonstrated that people have a positive attitude towards genetic testing and a good understanding of genetics, but not without highlighting certain disparities. These included a greater understanding of gene-related scientific facts than disease-related concepts, as well as discrepancies between people's perceived and actual genetic knowledge [123]. These findings emphasize the need to improve public awareness about genetic testing to ensure that individuals can make informed decisions that contribute to the implementation of personalized medicine. It is important to note that increased knowledge in genetics does not necessarily indicate a positive overall perception of genetic testing and genetic services.

Our study may have been limited by the small sample size, which could have hindered our ability to detect significant associations. We wanted to explore more in depth this lack of association by analyzing the responses of each question about genetic knowledge and the corresponding attitude score of parents. We found that correctly answering Question 1, which pertains to the definition of congenital anomalies as "a wide range of birth defects and developmental disorders," was associated with a more positive attitude towards the perceived benefits of genetic counseling and genetic testing (P=0.001). This highlights the importance of ensuring that parents have a basic understanding of genetic concepts and terminology to promote a positive attitude towards genetic counseling and genetic testing.

By providing parents with accurate and accessible information about genetics and its contribution to congenital anomalies, healthcare providers can help improve parental

knowledge and understanding of these topics. A study conducted in Jordan highlighted the importance of collaboration and interaction between various partners of genetic services, including healthcare professionals and patients, in order to facilitate the use and implementation of genetics in clinical practice [124]. This, in turn, may increase families' willingness to consider genetic counseling and genetic testing as a way to identify and address potential health issues in their children.

Attitudes towards perceived barriers to genetic counseling and genetic testing and impact of demographic factors

There are several factors that may contribute to perceiving barriers to genetic counseling and genetic testing including cultural beliefs and values, access to healthcare services, and historical experiences with genetic testing. After adjusting for confounding variables, our study revealed three significant factors that were found to be associated with attitudes towards perceived barriers to genetic counseling and genetic testing. These factors are ethnicity, family history of genetic disorders, and previous experience with genetic testing.

Ethnicity plays a significant role in shaping attitudes towards perceived barriers to genetic counseling and genetic testing. People from certain ethnic backgrounds may encounter unique cultural, social, and economic challenges that impact their willingness to undergo genetic counseling and testing. Our study found that American and European individuals perceived fewer barriers compared to those from Qatar, North Africa and Asia. Another study showed that African American women had more negative attitudes towards genetic testing for breast cancer than white women due to a lack of trust in the healthcare system, fear of discrimination, and cultural beliefs about fatalism and faith in illness [125]. Similarly, a systematic review of Asian Americans' attitudes towards genetic testing and counseling showed that language and communication barriers were widespread among these groups, and the communication

of results and risk information to family members was lower than in other ethnic groups. Therefore, healthcare providers must recognize and address such barriers by offering culturally sensitive and inclusive services tailored to different ethnicities [126].

Having a family history of genetic disorders was shown to have a significant impact on attitudes towards genetic testing and counseling. Parents who had a child or another family member with a genetic disorder were more inclined to have a positive outlook on genetic counseling and genetic testing, with less perceived barriers compared to those who did not have such history. This could be due to their heightened awareness of the potential benefits and risks of genetic testing, as well as their proactive approach towards managing their family's health. In the same context, a study conducted in Saudi Arabia revealed a correlation between a positive family history of genetic disorders and a favorable attitude towards genetic testing. Individuals with a family history of genetic disorders were more likely to perceive genetic testing as an important tool for disease prevention and early detection [113].

Individuals who had previously undergone genetic testing were also more likely to have a positive attitude towards genetic counseling and genetic testing, and they perceived less barriers compared to those without previous experience with genetic testing. This suggests that personal experience and education may play a significant role in shaping attitudes towards genetic counseling and genetic testing and highlights the importance of providing access to educational resources and genetic counseling services to all individuals.

Overall, these findings suggest that healthcare providers need to consider a variety of demographic factors when working with patients to address potential perceived barriers to genetic counseling and genetic testing. By understanding the demographic characteristics of their patient populations, providers can tailor their services to meet

the unique needs and concerns of each individual patient and help to promote greater awareness and acceptance of genetic counseling and genetic testing.

When we examined the percentage of people who considered different factors as barriers to genetic counseling and genetic testing, we found that 24% of participants agreed that health insurance was a barrier, while 52.9% were undecided. It is important to note that health insurance is a relatively new require in Qatar. Not all individuals have private insurance, and many individuals may lack exposure to or knowledge of how health insurance works, which may explain the high percentage of undecided responses. Additionally, 46.8% of parents believed that genetic testing was expensive, which is consistent with previous studies that have identified cost as a significant barrier to genetic testing [127, 128].

In the context of genetic counseling and genetic testing, religious beliefs can play a significant role in determining an individual's attitudes and behaviors. In Qatar, where most of the population is Muslim, one could suspect that there may be concerns about the religious implications of genetic testing. However, our study found that only a small percentage (5.8%) of parents agreed that religious beliefs would prevent them from pursuing genetic counseling and genetic testing. On the other hand, a systematic review study conducted on a global worldwide population found that religious principles can pose significant barriers to the acceptability and utilization of genetic services [115]. These barriers may include concerns about interfering with God's plan, fear of stigmatization and discrimination, and discomfort with the use of reproductive technologies. These concerns can lead to resistance towards genetic counseling and genetic testing and may result in individuals not seeking and/or not receiving appropriate care and treatment. For example, social stigma was found to be often associated with genetic disease, which may lead to fear and reluctance to undergo

genetic testing [114].

We also found that some parents were concerned about the potential impact of genetic testing on their relationships with their spouse or family members. Specifically, 15.4% agreed and 17.9% were undecided. This finding is consistent with previous studies that have identified the potential for family conflict as a significant barrier to genetic testing [129].

Privacy concerns were also identified as a potential barrier, with 16.8% of parents worried that their privacy might not be respected if they underwent genetic testing. This finding is consistent with a previous study conducted in Qatar, which identified privacy concerns as a significant barrier to genetic testing [111].

Finally, it was found that a significant percentage of parents expressed concern about the potential negative consequences of genetic testing. Specifically, 16.5% of parents believed that genetic testing could lead to social stigma for their child, suggesting that a diagnosis of a genetic disorder might cause their child to be viewed negatively by others. Another 14.6% of parents expressed concern that genetic testing could cause harm to their child, potentially through physical or psychological harm.

Furthermore, our study found that 15.1% of parents were worried that meeting with a genetic counselor would force them to undergo genetic testing. This fear may stem from concerns about privacy, autonomy, or potential adverse outcomes of genetic testing in addition to a lack of understanding of the voluntary nature of genetic testing and a misconception that receiving genetic counseling necessarily means undergoing genetic testing. The results align with a systematic review that established a link between social determinants and awareness and knowledge of genetic diseases and genetic services. This review found that education and socioeconomic status were correlated with the uptake and comprehension of genetic services, highlighting their significant impact

[115] . Furthermore, the review pointed out that genetic services have the potential to disturb family values. For instance, the diagnosis of a genetic disorder may challenge a family's established beliefs about genetics and heredity. As an illustration, some families may attach importance to having an "ideal family size" in their family planning, which could be jeopardized by genetic services [115].

Overall, our study may highlight the importance of addressing these perceived barriers to genetic counseling and genetic testing in Qatar if we can extrapolate our finding to the general population, particularly regarding cost, privacy and autonomy concerns, and potential negative consequences. Healthcare providers and policymakers should work to address these issues to improve access to genetic services and ultimately improve health outcomes for individuals and families.

In our study, 24 out of the 160 responding parents provided information about additional potential barriers that may prevent them from moving forward with genetic counseling and genetic testing. After analyzing the responses, we identified seven main themes that were reported as potential barriers by the parents. One of the most reported barriers was a lack of time. Many parents stated that they simply did not have enough time to attend genetic counseling sessions or to follow through with genetic testing. This barrier was particularly prevalent among parents who had young children or busy work schedules. Another common barrier was a lack of knowledge of the benefits of genetic counseling and genetic testing. Some parents stated that they did not understand the potential benefits of these services or how they could help their families. This lack of knowledge often led to confusion and uncertainty about whether to pursue genetic counseling and genetic testing or not. Similarly, in a study conducted in Qatar, it was found that 55.5% of the reported barriers were related to practical issues rather than attitudes. These barriers included a lack of time and insufficient information about the

Qatar Genome Program [111]. A third barrier identified in our study was increasing stress and anxiety associated with the possibility of receiving genetic test results. Some parents stated that they were worried about what the results might reveal and how this information could impact their family's future. A lack of support from family members was also identified as a barrier. Some parents felt that their family members did not understand the importance of genetic counseling and genetic testing or were not supportive of their decision to pursue these services. In some ethnic groups, family dynamics play a critical and central role in decision-making processes. This has been highlighted in the literature, such as in a study on Palestinian perceptions of prenatal genetic counseling and how culture and acculturation influence these perceptions. The study found that family and society have a crucial role in prenatal decisions. The responses of native Palestinian and Palestinian American participants were similar in some respects, likely due to their shared cultural roots, but differed in others, potentially due to acculturation [130]. Moreover, our review revealed that some parents were not actively seeking out genetic counseling and genetic testing because they were preoccupied with existing medical problems and did not perceive it to be a pressing matter. These individuals may not prioritize genetic services as they perceive their current health concerns to be more immediate and pressing.

Furthermore, some parents may hold beliefs in the concept of predestination and feel that the outcomes of genetic testing are predetermined. Consequently, they may perceive the process of genetic counseling and testing to be unnecessary as they believe the results will have no bearing on their future or that of their children. Such attitudes can impact the uptake and utilization of genetic services, thereby limiting the potential benefits they offer. A study investigating the sociocultural challenges associated with the birth of children with beta-thalassemia major to carriers of beta-thalassemia in Iran

revealed that religious convictions, superstitious beliefs, and faith in a supernatural remedy were the primary reasons cited by 6 couples for declining prenatal diagnosis [131]. Finally, the lack of medical evidence reported by some parents can be a significant barrier to the uptake and utilization of genetic counseling and genetic testing. Without sufficient evidence supporting the benefits of genetic services in their particular situation, some parents may not feel motivated to undergo genetic testing or counseling, as they may not perceive it to be valuable or useful. Additionally, the perceived risks associated with genetic services, such as psychological distress or concerns about privacy, may further dissuade some parents from utilizing these services, especially if they do not perceive the benefits to be significant. Overall, these factors can contribute to the underutilization of genetic services and can limit their potential to improve health outcomes.

Overall, these themes provide important insight into the potential barriers that may prevent parents from pursuing genetic counseling and genetic testing and highlight the need for improved education and support for families who are considering these services.

Knowledge level/score and attitudes towards perceived barriers to genetic counseling and genetic testing

We did not observe a significant association between knowledge level and attitude towards perceived barriers score (P=0.058). However, when the correlation between knowledge score and barrier score was examined, we found a negative correlation (P=0.048), indicating that higher knowledge levels were correlated with lower perceived barriers towards genetic counseling and genetic testing. This finding aligns with a recent study, which investigated the knowledge of and willingness towards genetic testing for cancer prevention among low-income women and found that low knowledge levels were a significant barrier to testing [132].

Furthermore, when we analyzed each knowledge question and its corresponding barrier score, we found that parents who incorrectly answered knowledge question 2 (Parents who have no family history of congenital anomalies have no risk to have a child with a congenital anomaly) had higher overall perceived barriers scores (P=0.048). The results suggest that lack of knowledge of genetic risk factors and misconceptions about the nature of genetic disorders and the etiology of congenital anomalies may contribute to perceived barriers to genetic counseling and genetic testing. In our study specifically, for parents who incorrectly believed that having no family history of congenital anomalies eliminated the risk of having a child with a congenital anomaly, this misconception may be a significant factor in their decision-making process when it comes to genetic counseling and genetic testing.

This finding underscores the importance of addressing misconceptions about etiology and genetic risk factors in educational sessions and genetic counseling. By providing accurate information about the etiology of congenital anomalies, the nature of genetic disorders, and the ways in which genetic testing and counseling can be beneficial, healthcare providers may be able to alleviate some of the perceived barriers to genetic counseling and genetic testing. This may lead to increased uptake of genetic testing and ultimately improve health outcomes for both parents and their children.

CHAPTER 6: CONCLUSION AND RECOMMENDATIONS

The findings of this study have important implications for parents and healthcare providers who are involved in clinical genetics, genetic counseling, genetic testing. Although our participants are parents of children with congenital anomalies, our results could give insight into knowledge and attitudes of parents of children with any medical condition with a possible genetic etiology. Parents from Qatar, North Africa, Middle East, and Asia may require additional education and support to ensure they have accurate and sufficient information about genetic counseling and genetic testing. Additionally, parents with lower levels of education may need extra assistance in understanding concepts related to genetics and genetic testing.

Providers need to address perceived barriers such as lack of time, knowledge towards benefits, stress and anxiety, lack of support from family members, focus on current medical issues, God's will, and lack of medical evidence.

The study highlights the need for culturally sensitive and tailored education regarding genetic counseling and genetic testing. By providing accurate and sufficient knowledge and addressing perceived benefits and barriers, healthcare providers can help parents make informed decisions about genetic counseling and genetic testing.

In conclusion, identifying children and families who may benefit from genetic counseling is crucial for the provision of optimal care in pediatric plastic surgery. By working closely with genetic counselors, providing clear and accurate information, and offering referrals to appropriate resources and support, the PPS clinic can ensure that every patient receives the best possible care and outcomes by the multidisciplinary team.

CHAPTER 7: LIMITATIONS AND FUTURE DIRECTIONS

This study on genetic counseling and genetic testing in Qatar, similarly to studies conducted in other countries with high rates of consanguinity and ethnically diverse populations, provides valuable insight into the attitudes and experiences of individuals and families coping with medical conditions with a possible genetic etiology, however, there are limitations to the study that should be addressed in future research.

Firstly, this study sample was relatively small and is not representative of the broader population of Qatar. Future research should aim to include a larger and more diverse sample to ensure that the findings are generalizable to the broader population.

Secondly, this study relied on self-reported data and may be subject to response bias. Future research should consider incorporating objective measures of genetic literacy/ knowledge to provide a more accurate picture of participants' understanding of genetic information and genetic testing in addition conducting qualitative research can be highly valuable in gaining a deeper understanding of the barriers related to genetic counseling and genetic testing.

Finally, this study focused on the experiences and attitudes of parents and did not include the perspectives of healthcare providers or other stakeholders. Future research should incorporate a more comprehensive approach that includes the perspectives of healthcare providers, policymakers, and other stakeholders involved in the delivery of genetic counseling and genetic testing services.

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APPENDIXES

Appendix 1. Knowledge questions' answers

Question	Answer
Congenital anomalies refer to a wide range of problems with the way the body looks or works that are present at birth.	Correct
Parents who have no family history of congenital anomalies have no risk to have a child with a congenital anomaly.	False
Parents who are related have an increased risk of having a child with a genetic disorder.	Correct
Advanced maternal age (35+ years) increases the risk of having a child with congenital anomalies.	Correct
For a condition to be heritable/transmissible from parents to children, it must be present in more than one family member.	False
New information regarding genetic testing can become available with time due to advancement of lab technology and new discoveries.	Correct

Appendix 2. Qatar University IRB approval

Qatar University Institutional Review Board **QU-IRB**

QU-IRB Registration: IRB-QU-2020-006, QU-IRB, Assurance: IRB-A-QU-2019-0009

DATE:	November 20, 2022
TO:	Houssein Khodjet ElKhil , Associate Professor PhD
FROM:	Qatar University Institutional Review Board (QU-IRB)
PROJECT TITLE:	1967276-1 Parental knowledge and attitudes towards genetic counseling and childhood genetic testing for congenital anomalies in Qatar
QU-IRB REFERENCE #:	QU-IRB 1789-EA/22
SUBMISSION TYPE:	New Project
ACTION:	APPROVED
REVIEW TYPE:	Expedited Review
DECISION DATE:	November 20, 2022
REVIEW CATEGORY:	Expedited review category # 7

Thank you for your submission of New Project materials for this project. The Qatar University Institutional Review Board (QU-IRB) has APPROVED your submission. This approval is based on an appropriate risk/ benefit ratio and a project design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

This submission has received Expedited Review according to Qatar Ministry of Public Health (MoPH) regulations. This project has been determined to be a MINIMAL RISK project.

Please remember that informed consent is a process beginning with a description of the project and insurance of participant understanding followed by a signed consent form. Informed consent must continue throughout the project via a dialogue between the researcher and research participant. Qatar MoPH regulations require that each participant receives a copy of the consent document.

Please note that Expedited Review approvals are valid for a period of one year and renewal should be sought prior to October 21, 2023 to ensure timely processing and continuity. Moreover, any changes/ modifications to the original submitted protocol should be reported to the committee to seek approval prior to continuation.

All UNANTICIPATED PROBLEMS involving risks to subjects or others (UPIRSOs) and SERIOUS and UNEXPECTED adverse events must be reported promptly to this office. Please use the appropriate reporting forms for this procedure.

All NON-COMPLIANCE issues or COMPLAINTS regarding this project must be reported promptly to this office.

Please note that all research records must be retained for a minimum of three years after the completion of the project.

Documents Reviewed:

- Application Form - QU-IRB Brief Application Form_v5 HK.HM.docx (UPLOADED: 11/3/2022)
- Application Form - Sidra - IRB Application Form (stamped).pdf (UPLOADED: 10/24/2022)
- Consent Form - Research12 (RFQ4947) - IRB-400 Informed Consent Form English parental kn... (AR).pdf (stamped).pdf (UPLOADED: 10/24/2022)

Generated on IRBNet

Appendix 3. Sidra Medicine IRB approval

Tel: +974-4003-7747
Email: irb@sidra.org

Sidra IRB MOPH Assurance: IRB-A-Sidra-2019-0020
Sidra IRB MOPH Registration: IRB-Sidra-2020-009
Sidra IRB DHHS Assurance: FWA00022378
Sidra IRB DHHS Registration: IRB00009930

October 18, 2022

Approval

Dear Dr. Stotland,

On 18 October 2022 the IRB approved the following through 17 October 2023 inclusive.

IRB Number:	1916398
Protocol Title:	Parental knowledge and attitudes towards genetic counseling and childhood genetic testing for congenital anomalies in Qatar
Principal Investigator:	Mitchell Stotland
Type of review:	Initial Review
Sponsor/ Funding Agency:	None
Grant title and ID, if any:	N/A
Documents reviewed:	• IRB-400 Informed Consent Form (AR).pdf (UPDATED: 10/18/2022) • IRB-400 Informed Consent Form English parental knowledge and attitudes towards genetic counseling and childhood genetic testing for congenital anomalies in Qatar (English).pdf (UPDATED: 10/18/2022) • Questionnaire/Survey - questionnaire 01.09.2022 Final Version (English).pdf (UPDATED: 10/18/2022) • Questionnaire/Survey - Research12 (RFQ4947) - questionnaire 01.09.2022 Final Version_AR.pdf (UPDATED: 10/18/2022) • IRB-413- Research Proposal 11.09.2022 Final version.docx (UPDATED: 9/18/2022) • Information sheet for surveys-questionnaires 01.09.2022 final version.docx (UPDATED: 09/1/2022) • Sidra - IRB Application Form (UPDATED: 09/2/2022) • Training and Credentials
Level of review:	Expedited
Expedited Categories:	7
Pediatric Category:	Research does not involve greater than minimal risk
Approved sample size:	200

Appendix 4. Informed consent (English)

سدرة للطب
Sidra Medicine

IRB-400 Informed Consent Form For Research Study

Protocol Title:	Parental knowledge and attitudes towards genetic counseling and childhood genetic testing for congenital anomalies in Qatar
Protocol Number:	SDR600182 IRB Net # 1916398-1
Sponsor:	Not applicable
Principal Investigator:	Dr. Mitch Stotland Division Chief, Plastic/Craniofacial Surgery, Sidra Medicine
Site Address:	Sidra Medcine , Plastic surgery clinic
Telephone Number:	+974 40036478

1. Introduction

Before agreeing to participate in this research study, please read and understand the following explanation of the proposed study. This informed consent form describes the purpose, procedures and risks of the study. It also describes your right to withdraw from the study at any time, and that you are volunteering. Also, that no guarantees or assurances can be made as to the results of the study. Please feel free to ask questions.

2. Background and Purpose

The background and purpose of this research study the Plastic Surgery Department at Sidra Medicine and Qatar University are conducting this survey to Investigate parental knowledge of the contribution of genetics to their child's congenital anomalies as well as their attitudes towards genetic counseling and genetic testing. This study aims to understand parents' genetic knowledge levels, educational and awareness gaps, and factors that encourage or discourage them from seeking genetic counseling and genetic testing. Understanding these influencing factors would have a direct impact on Qatar's current expansion of clinical genetic and genetic counseling services.

The study is open to all parents visiting the pediatric plastics surgery clinic at Sidra Medicine with a child under the age of 17 who has one or more congenital anomaly.

you are invited to take part in an online questionnaire composed of 38 questions that should take approximately 20 minutes to complete. Your participation is anonymous and all information will be kept confidential.

3. Number of Subjects

About 200 subjects will participate in this study

4. Study Duration and Length of Participation

All activities related to your participation in this study will occur on one day at Sidra , online questionnaire composed of 38 questions that should take approximately 20 minutes to complete .

5. Procedures

Your participation will involve filling an online questionnaire composed of 38 questions that should take approximately 20 minutes to complete . If you agree to participate, there will be no other responsibilities required or expected from you after you complete the online questionnaire .

6. Alternative Procedures

This study is for research purposes only. The only alternative is to not participate in this study.

7. Risks, Side Effects and/or Discomforts

There is little in the way of risk to subjects who agree to particpate in this study . There is a small risk that some participant that might feel uncomfortable or embarrassed by some of the questions in the questionnaires you will be asked to complete.

8. Unforeseen Risks

There may be other risks of study participation that are unknown.

9. Pregnancy *(include if applicable)*

There is no risk for pregnant subjects who participate in this study

10. New Findings

Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be made available to you. This might include changes in procedures, changes in the risks or benefits of participation, or any new alternatives to participation that the researchers learn about.

11. Individual Results from the Research Tests/Surveys

Generally, tests/surveys done for research purposes are not meant to provide results or clinical information that apply to you alone.

12. Benefits

This study is for research purposes only. There is no direct benefit to you from your participation in the study. Information learned from the study may help other people in the future.

13. Costs

There will be no charge to you for your participation in this study. The study-related procedures and study visits will be provided at no charge to you or your insurance company.

14. Compensation for Participation

You will not receive any monetary compensation for your participation in this study.

15. Research Related Injuries

If you are injured or made sick from taking part in this research study, call Dr. Mitch Stotland immediately, T. +974-4003 3333, or alternatively contact Sidra Medicine Emergency Department. Page 3 of 4 Informed Consent Form For Research Study Version 1.5 / November 2019 Medical care will be provided to you at Sidra Medicine at no charge. In case we were unable to provide care to you at Sidra, we will arrange and pay for your care at Hamad Medial Corporation (HMC). If you receive care at another institution, you or your

insurance will have to pay for that care in accordance with the policies of that institution. Sidra Medicine has no program or funds set aside to compensate you for research-related injuries or to pay for medical care for research-related injuries at institutions other than HMC or Sidra. Contact the Principal Investigator for more information

16. Confidentiality

No personal information will be collected from you (NO names, medical record numbers, national identification numbers, etc.). We will record you demografic data such as age, gende and nationality . We may publish the results of this research.

17. Commercial Gain *(include if applicable)*

There is no commercial gain expected to be developed from this research.

18. Research Team Contact

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, contact the investigator, Dr. Mitch Stotland +974 40036478

19. IRB Contact

An Institutional Review Board (IRB) is an independent committee established to help protect the rights of research subjects. IRB at Sidra has reviewed and approved this study. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, Email: irb@sidra.org, or T. +974-4003-7747 during business hours Sunday- Thursday 7:30 a.m. to 4:00 p.m.

20. Voluntary Participation/Withdrawal

Your decision to participate in this study is voluntary. You may choose to not participate or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care.

21. Storing and Sharing Your Information or Samples for Future Use *(include if applicable)*

Not applicable

22. Place and Duration of Storage of Information or Samples *(include if applicable)*

1.Survey Monkey questionnaire will be linked to study user name and password that will be known by Research investigators only.
2. Account user name and Password will be saved in Dr. Mitch Stonalnd office in a locked cabinet.
3.IPADs used for data collection will be used for research purpose only and will be locked in Co-investigator Ms. Houda Kilani office during the data collection phase .

23. Consent

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions. All my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing this consent document. I will receive a copy of this signed consent document.

_____
Printed Name of Subject

_____ _____
Signature of Subject Date

_____
Printed Name of the Person Conducting the Consent Discussion

_____ _____
Signature of the Person Conducting the Consent Discussion Date

24. Consent for Subjects Who Cannot Read *(include if applicable)*

The study subject has indicated that he/she is unable to read. The consent document has been read to the subject by a member of the study staff, discussed with the subject by a member of the study staff, and the subject has been given an opportunity to ask questions of the study staff.

_____
Printed Name of Impartial Witness

_____ _____
Signature of Impartial Witness* Date

**Impartial Witness: A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the informed consent and any other written information supplied to the subject. Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance*

Appendix 5. Informed consent (Arabic)

سدرة للطب Sidra Medicine

نموذج موافقة مستنيرة IRB-400 لدراسة بحثية

عنوان البروتوكول:	معرفة الوالدين وسلوكهما تجاه الاستشارات الوراثية والاختبارات الجينية للأطفال لفحص التشوهات الخلقية في قطر
رقم البروتوكول:	SDR600182 IRB Net # 1916398-1
الجهة الراعية:	لا ينطبق
الباحث الرئيسي:	الدكتور ميتش ستوتلاند رئيس قسم جراحة التجميل والجراحة القحفية الوجهية، سدرة للطب
عنوان الموقع:	سدرة الطب، عيادة جراحة التجميل
رقم الهاتف:	+٩٧٤٤٠٠٣٦٤٧٨

1. مقدمة

قبل الموافقة على المشاركة في هذه الدراسة البحثية، يُرجى قراءة وفهم الشرح التالي للدراسة المقترحة. يوضح نموذج الموافقة المستنيرة هذا غرض الدراسة وإجراءاتها ومخاطرها. ويوضح النموذج كذلك حقكم في الانسحاب من الدراسة في أي وقت وأن مشاركتكم هي أمر طوعي. ويوضح كذلك أنه لا يمكن تقديم أي ضمانات أو تأكيدات بشأن نتائج الدراسة. يُرجى ألا تترددوا في طرح أي أسئلة لديكم.

2. خلفية الدراسة والغرض منها

خلفية هذه الدراسة البحثية والغرض منها: يجري قسم جراحة التجميل بسدرة للطب وجامعة قطر هذا الاستطلاع للنظر في معرفة الوالدين بمساهمة الجينات في التشوهات الخلقية التي يعاني منها أطفالهم وكذلك دراسة سلوكهم تجاه الاستشارات الوراثية والاختبارات الجينية. تهدف هذه الدراسة إلى فهم مستويات معرفة الوالدين بالوراثة، والفجوات في التعليم والتوعية، والعوامل التي تشجعهم أو تثنيهم عن طلب الاستشارات الوراثية والاختبارات الجينية. وسيكون لفهم هذه العوامل المؤثرة أثر مباشر على التوسع الحالي لخدمات الاستشارات الوراثية والخدمات الجينية السريرية في دولة قطر.

الدراسة مفتوحة لمشاركة جميع الآباء الذين يزورون عيادة جراحة التجميل للأطفال في سدرة للطب ممن لهم طفل يقل عمره عن ١٧ عامًا ويعاني من تشوه خلقي واحد أو أكثر.

وأنتم مدعوون للمشاركة في استبيان عبر الإنترنت مكون من ٣٨ سؤالًا ينبغي أن يستغرق إكمالها حوالي ٢٠ دقيقة. ستكون هويتكم مجهولة في أثناء المشاركة وسيتم الحفاظ على سرية جميع المعلومات.

3. عدد الأشخاص الخاضعين للدراسة

سوف يشارك حوالي ٣٠٠ شخص في هذه الدراسة.

4. مدة الدراسة وطول فترة المشاركة

وستتم جميع الأنشطة المتعلقة بمشاركتكم في هذه الدراسة في يوم واحد في سدرة للطب، من خلال استبيان عبر الإنترنت يتكون من ٣٨ سؤالًا ينبغي أن يستغرق إكمالها حوالي ٢٠ دقيقة.

5. الإجراءات

ستشتمل مشاركتكم على إكمال استبيان عبر الإنترنت مكون من ٣٨ سؤالًا ينبغي أن يستغرق إكمالها حوالي ٢٠ دقيقة. في حالة موافقتكم على المشاركة، لن تكون هناك أي مسؤوليات أخرى مطلوبة أو متوقعة منكم بعد إكمال الاستبيان عبر الإنترنت.

6. الإجراءات البديلة

تُجرى هذه الدراسة لأغراض بحثية فقط. والخيار البديل الوحيد هو عدم المشاركة في هذه الدراسة.

7. المخاطر و/أو الآثار الجانبية و/أو الانزعاجات

تكاد تخلو هذه الدراسة من أي أخطار. قد يتعرض لها الأشخاص الموافقون على المشاركة. هناك خطر ضئيل لاحتمال شعور بعض المشاركين *بالانزعاج أو الإحراج بسبب بعض الأسئلة الواردة في الاستبيانات التي سيطلب منكم إكمالها.*

8. المخاطر غير المتوقعة

قد تكون هناك مخاطر أخرى غير معروفة للمشاركة في الدراسة.

9. الحمل *(يُرجى إدراج ذلك إذا كان ينطبق على هذا البحث)*

[illegible]

10. [illegible]

[illegible]

11. [illegible]

[illegible]

12. [illegible]

[illegible]

13. [illegible]

[illegible]

14. [illegible]

[illegible]

15. [illegible]

[illegible]

16. [illegible]

[illegible]

17. [illegible]

[illegible]

18. [illegible]

[illegible]

19. [illegible]

[illegible] irb@sidra.org [illegible]

20. [illegible]

[illegible]

21. [illegible]

[illegible]

22. [illegible]

[illegible] Survey Monkey [illegible]

٣. وسيتم استخدام أجهزة IPAD لجمع البيانات لأغراض البحث فقط وسيتم تخزينها في مكتب الباحثة السيدة هدى الكيلاني في أثناء مرحلة جمع البيانات.

23. الموافقة

لقد قرأت المعلومات الواردة في وثيقة الموافقة المستنيرة هذه وفهمتها. وقد أتيحت لي فرصة لطرح الأسئلة. وقد أجيب على جميع أسئلتي بشكل كافٍ ومُرضٍ. أنا أوافق طوعًا على المشاركة في هذه الدراسة إلى أن أقرر غير ذلك. ولا أتنازل عن أي من حقوقي القانونية بالتوقيع على وثيقة الموافقة هذه. وسوف أحصل على نسخة من وثيقة الموافقة الموقّعة هذه.

_____
اسم الشخص الخاضع للدراسة بأحرف واضحة

_____ _____ _____
توقيع الشخص الخاضع للدراسة التاريخ

_____
اسم الشخص الذي يُجري مناقشة الموافقة بأحرف واضحة

_____ _____
توقيع الشخص الذي يُجري مناقشة الموافقة التاريخ

24. موافقة الأشخاص الخاضعين للدراسة الذين لا يستطيعون القراءة *(يُرجى إدراج ذلك إذا كان ينطبق على هذا البحث)*

أشار الشخص الخاضع للدراسة أنه غير قادر على القراءة. ولذلك قرأ أحد أفراد طاقم عمل الدراسة وثيقة الموافقة للشخص الخاضع للدراسة وناقشها معه، وقد أتيحت للشخص الخاضع للدراسة فرصة لطرح الأسئلة على طاقم عمل الدراسة.

_____
اسم الشاهد المحايد بأحرف واضحة

_____ _____
توقيع الشاهد المحايد* التاريخ

*الشاهد المحايد: هو شخص مستقل عن التجربة، لا يمكن أن يؤثر عليه الأشخاص المشاركون في إدارة التجربة بطريقة غير عادلة، ويحضر هذا الشاهد عملية الموافقة المستنيرة إذا كان الشخص الخاضع للدراسة أو ممثله المفوّض قانونًا لا يستطيعان القراءة، ويقرأ هذا الشاهد الموافقة المستنيرة وأي معلومات مكتوبة أخرى تقدَّم للشخص الخاضع للدراسة. *Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance*

Appendix 6. Questionnaire (English)

Approval Date: October 18, 2022
Expiration Date: October 17, 2023

Demographic information

Questions	Answer
1. Reason for referral to pediatric plastic surgery clinic	Free text
2. Age of the child	Free text
3. Sex of the Child	Male Female
4. Age of the parent (responding to the survey)	Free text
5. Sex of the parent (responding to the survey)	Male Female
6. Nationality of the parent (responding to the survey)	Qatari Non Qatari – specify:
7. Education level of the parent (responding to the survey)	High school or less Diploma College \Undergraduate level \ Bachelor's Graduate level \ Master's \PhD
8. Household income (both parents)	< 5000 QAR 5000 – 10000 QAR 10000 - 20000 QAR >20000 QAR
9. How far do you live from Sidra Medicine?	<30 minutes 30 - 60 minutes >60 minutes

Family history

10. Other child or family member with similar congenital anomaly(ies)	Yes \ No If yes, specify who:
11. Other child or family member with a genetic disorder	Yes \ No If yes, specify who:
12. Parental consanguinity	Yes No

Previous experience with genetic testing and genetic counseling

Please specify the extent to which you agree with the following statements:

13. Did your child ever undergo a genetic test in the past?	Yes \ No If yes, specify where (Sidra, HMC, abroad)
14. The genetic test helped me understand the contribution of genetics to my child's congenital anomaly(ies)	Strongly Agree Agree Undecided Disagree Strongly Disagree Not Applicable (option for those who answer "No" to Q13)
15. Did any health care provider ever offer you\your child a referral to genetics\genetic counseling?	Yes \ No

16. The genetic/genetic counseling consultation helped me understand the contribution of genetics to my child's congenital anomaly(ies).	Strongly Agree Agree Undecided Disagree Strongly Disagree Not Applicable (option for those who answer "No" to Q15)

Parental knowledge of genetics and its contribution to disease/congenital anomalies

Based on your knowledge of the topic, please specify the extent to which you agree with the following statements:

Questions	Answers
17. Congenital anomalies refer to a wide range of problems with the way the body looks or works that are present at birth.	Strongly Agree Agree Undecided Disagree Strongly Disagree
18. Parents who have no family history of congenital anomalies have no risk to have a child with a congenital anomaly.	Strongly Agree Agree Undecided Disagree Strongly Disagree
19. Parents who are related have an increased risk of having a child with a genetic disorder.	Strongly Agree Agree Undecided Disagree Strongly Disagree
20. Advanced maternal age (35+ years) increases the risk of having a child with congenital anomalies.	Strongly Agree Agree Undecided Disagree Strongly Disagree
21. For a condition to be heritable/transmissible from parents to children, it must be present in more than one family member.	Strongly Agree Agree Undecided Disagree Strongly Disagree
22. New information regarding genetic testing can become available with time due to advancement of lab technology and new discoveries.	Strongly Agree Agree Undecided Disagree Strongly Disagree

Attitudes towards genetic counseling and genetic testing – Perceived benefits

Please choose the answer that best describes your opinion regarding the following statements:

Openness and perceived benefits:	

23. Would you be willing to be referred to genetic counseling if you haven't been referred before?	Yes / No /Undecided
24. Would you be willing to consider genetic testing for your child if proposed by a health care provider?	Yes / No /Undecided
25. Genetic counseling can help me understand genetics and make an informed decision regarding genetic testing.	Strongly Agree Agree Undecided Disagree Strongly Disagree
26. Genetic counseling can help me understand the implications of genetic testing and adjust to a genetic diagnosis.	Strongly Agree Agree Undecided Disagree Strongly Disagree
27. Genetic testing can help me understand the risk of having another child with the same congenital anomaly(ies).	Strongly Agree Agree Undecided Disagree Strongly Disagree
28. There is always a benefit to meet a genetic counsellor and have my child tested	Strongly Agree Agree Undecided Disagree Strongly Disagree

Attitudes towards genetic counseling and genetic testing – Perceived barriers

Please choose the answer that best describes your opinion/feeling regarding the following statements:

A. Worries about freedom of choices 29. If I meet a genetic counselor, I am worried to be forced to undergo genetic testing.	Strongly Agree Agree Undecided Disagree Strongly Disagree
C. Potential Harm 30. I am worried that genetic testing can harm my child.	Strongly Agree Agree Undecided Disagree Strongly Disagree
D. Social stigma 31. I am worried that genetic testing could create social stigma for my child or my family.	Strongly Agree Agree Undecided Disagree Strongly Disagree
E. Privacy 32. If I undergo genetic testing, I am worried that my privacy may not be respected.	Strongly Agree Agree Undecided Disagree Strongly Disagree

F. Family dynamic 33. I am worried that genetic testing results could impact my relationship with my spouse or other family members.	Strongly Agree Agree Undecided Disagree Strongly Disagree
G. religious beliefs 34. Having genetic counseling/testing contradicts my religious beliefs.	Strongly Agree Agree Undecided Disagree Strongly Disagree
Accuracy of genetic testing 35. Genetic tests results are always accurate	Strongly Agree Agree Undecided Disagree Strongly Disagree
Financial 36. Genetic testing is expensive.	Strongly Agree Agree Undecided Disagree Strongly Disagree
37. I am worried that genetic testing results can negatively impact my private health insurance coverage.	Strongly Agree Agree Undecided Disagree Strongly Disagree
38. Can you think of any other reason that would stop you from meeting a genetic counselor or considering genetic testing?	Free text

Appendix 7. Questionnaire (Arabic)

سدرة للطب Sidra Medicine
Approval Date: October 18, 2022
Expiration Date: October 17, 2023

المعلومات الديموغرافية

الأسئلة	الإجابة
1. سبب الإحالة إلى عيادة جراحة التجميل للأطفال	نص حر
2. عمر الطفل	نص حر
3. جنس الطفل	ذكر أنثى
4. عمر الوالد (القائم بالإجابة على الاستبيان)	نص حر
5. جنس الوالد (القائم بالإجابة على الاستبيان)	ذكر أنثى
6. جنسية الوالد (القائم بالإجابة على الاستبيان)	قطري غير قطري - حدد:
7. المستوى التعليمي الوالد (القائم بالإجابة على الاستبيان)	المدرسة الثانوية أو مرحلة أدنى شهادة الدبلوم الكلية/مستوى الدراسة الجامعية/البكالوريوس مستوى الدراسات العليا/الماجستير/الدكتوراه
8. دخل الأسرة (كلا الوالدين)	أقل من ٥٠٠٠ ريال قطري ٥٠٠٠ - ١٠٠٠٠ ريال قطري ١٠٠٠٠ - ٢٠٠٠٠ ريال قطري أكثر من ٢٠٠٠٠ ريال قطري
9. كم يبعد مقر سكنك عن سدرة للطب؟	أقل من ٣٠ دقيقة ٣٠ - ٦٠ دقيقة أكثر من ٦٠ دقيقة

التاريخ العائلي

10. طفل آخر أو أحد أفراد الأسرة مصاب بتشوه (تشوهات) خلقية مماثلة	نعم / لا إذا كانت الإجابة بنعم ، فحدد من:
11. طفل آخر أو أحد أفراد الأسرة مصاب باضطراب وراثي	نعم / لا إذا كانت الإجابة بنعم ، فحدد من:
12. قرابة بين الوالدين	نعم لا

التجارب السابقة للاختبارات الجينية والاستشارات الجينية

يُرجى تحديد مدى موافقتك على العبارات التالية:

13. هل سبق لطفلك أن خضع لاختبار جيني؟	نعم / لا إذا كانت الإجابة بنعم ، فحدد المكان (سدرة للطب، مؤسسة حمد الطبية، خارج البلاد)
14. لقد ساعدني الاختبار الجيني في فهم مساهمة الجينات والوراثة في التشوه (التشوهات) الخلقية لطفلي	أتفق بشدة أتفق لا أستطيع التحديد أختلف أختلف بشدة لا ينطبق (خيار لمن يجيبون بـ "لا" على السؤال ١٣)
15. هل عرض أي مقدم رعاية صحية عليك/على طفلك الإحالة إلى قسم طب الوراثة/الاستشارات الوراثية؟	نعم / لا
16. لقد ساعدني طب الوراثة/الاستشارات الجينية في فهم مساهمة الجينات في التشوه (التشوهات) الخلقية لطفلي	أتفق بشدة أتفق لا أستطيع التحديد أختلف أختلف بشدة

	لا ينطبق (خيار لمن يجيبون بـ "لا" على السؤال ١٥)

معرفة الوالدين بالجينات ومساهمتها في الأمراض/التشوهات الخلقية

بناءً على معرفتك بهذا الموضوع، يُرجى تحديد مدى موافقتك على العبارات التالية:

الأسئلة	الإجابات
17. تشير التشوهات الخلقية إلى نطاق واسع من المشكلات التي توجد منذ الولادة وتتعلق بشكل الجسم أو طريقة عمله.	أتفق بشدة أتفق لا أستطيع التحديد أختلف أختلف بشدة
18. الآباء والأمهات الذين ليس لديهم تاريخ عائلي من التشوهات الخلقية لا يواجهون خطر إنجاب طفل يعاني من تشوه خلقي.	أتفق بشدة أتفق لا أستطيع التحديد أختلف أختلف بشدة
19. الآباء والأمهات الذين بينهم صلة قرابة يواجهون مخاطر أعلى لإنجاب طفل مصاب باضطراب وراثي.	أتفق بشدة أتفق لا أستطيع التحديد أختلف أختلف بشدة
20. يزيد عمر الأم المتقدم (أكبر من ٣٥ عامًا) من خطر إنجاب طفل مصاب بتشوهات خلقية.	أتفق بشدة أتفق لا أستطيع التحديد أختلف أختلف بشدة
21. لكي تكون الحالة قابلة للتوريث/قابلة للانتقال من الآباء إلى الأبناء، يجب أن يكون أكثر من فرد واحد من أفراد الأسرة مصابًا بها.	أتفق بشدة أتفق لا أستطيع التحديد أختلف أختلف بشدة
22. يمكن أن تتاح المعلومات الجديدة المتعلقة بالاختبارات مع مرور الوقت بسبب تقدم تكنولوجيا المختبرات وبسبب الاكتشافات العلمية الجديدة.	أتفق بشدة أتفق لا أستطيع التحديد أختلف أختلف بشدة

المواقف تجاه الاستشارات الوراثية والاختبارات الجينية - الفوائد المتصورة

يُرجى اختيار الإجابة التي تصف بأفضل صورة رأيك في العبارات التالية:

الانفتاح والفوائد المتصورة: 23. هل يمكن أن توافق على إحالتك إلى الاستشارات الوراثية إذا لم تكن قد تمت إحالتك من قبل؟	نعم / لا / لا أستطيع التحديد
24. هل يمكن أن تفكر في إجراء اختبار جيني لطفلك إذا اقترحه مقدم الرعاية الصحية؟	نعم / لا / لا أستطيع التحديد
25. يمكن أن تساعدني الاستشارات الوراثية في فهم علم الوراثة واتخاذ قرار مستنير بشأن الاختبارات الجينية.	أتفق بشدة أتفق لا أستطيع التحديد أختلف أختلف بشدة
26. يمكن أن تساعدني الاستشارات الوراثية في فهم التبعات المترتبة على الاختبارات الجينية والتكيف مع التشخيص الناتج عن الاختبارات الجينية.	أتفق بشدة أتفق لا أستطيع التحديد

	أختلف أختلف بشدة
27. يمكن أن تساعدني الاختبارات الجينية في فهم مخاطر إنجاب طفل آخر قد يعاني من نفس التشوه (التشوهات) الخلقية.	اتفق بشدة أتفق لا أستطيع التحديد أختلف أختلف بشدة
28. هناك دائمًا فائدة من مقابلة مستشار وراثي وإجراء اختبار لطفلي.	اتفق بشدة أتفق لا أستطيع التحديد أختلف أختلف بشدة

<u>المواقف تجاه الاستشارات الوراثية والاختبارات الجينية - العوائق المتصورة</u>

يُرجى اختيار الإجابة التي تصف بأفضل صورة رأيك في/شعورك تجاه العبارات التالية:

A. المخاوف بشأن حرية الاختيارات 29. إذا قابلتُ مستشارًا وراثيًا، أكون قلقًا من أن يتم إجباري على الخضوع للاختبار الجيني.	اتفق بشدة أتفق لا أستطيع التحديد أختلف أختلف بشدة
ج. الضرر المحتمل 30. أنا قلق من أن الاختبارات الجينية يمكن أن تضر بصحة طفلي.	اتفق بشدة أتفق لا أستطيع التحديد أختلف أختلف بشدة
د. الوصمة الاجتماعية 31. أنا قلق من أن الاختبارات الجينية يمكن أن تخلق وصمة اجتماعية لدى طفلي أو عائلتي.	اتفق بشدة أتفق لا أستطيع التحديد أختلف أختلف بشدة
هـ. الخصوصية 32. إذا خضعت للاختبارات الجينية، فأنا قلق من احتمال عدم احترام خصوصيتي.	اتفق بشدة أتفق لا أستطيع التحديد أختلف أختلف بشدة
و. ديناميكية الأسرة 33. أشعر بالقلق من أن نتائج الاختبارات الجينية ربما تؤثر على علاقتي مع زوجتي أو أفراد أسرتي الآخرين.	اتفق بشدة أتفق لا أستطيع التحديد أختلف أختلف بشدة
ز. المعتقدات الدينية 34. يتعارض الحصول على استشارات/اختبارات وراثية مع معتقداتي الدينية.	اتفق بشدة أتفق لا أستطيع التحديد أختلف أختلف بشدة
دقة نتائج الاختبارات الجينية 35. نتائج الاختبارات الجينية تكون دقيقة دائمًا	اتفق بشدة أتفق لا أستطيع التحديد أختلف أختلف بشدة
<u>الجانب المالي</u> 36. تكاليف الاختبارات الجينية باهظة.	اتفق بشدة أتفق لا أستطيع التحديد أختلف

37. أنا قلق من أن تؤثر نتائج الاختبارات الجينية سلبًا على تغطية خدمة التأمين الصحي الخاصة بي.	أختلف بشدة أتفق بشدة أتفق لا أستطيع التحديد أختلف أختلف بشدة
38. هل يمكنك التفكير في أي سبب آخر يمكن أن يمنعك من مقابلة مستشار وراثي أو التفكير في إجراء اختبارات جينية؟	نص حر