

**The experiences of couples undergoing Preimplantation Genetic Diagnosis  
(PGD) at the Genetic and Developmental Medicine Clinic, Sultan Qaboos  
University Hospital (SQUH) in Oman**

By

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## Declaration

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## Abstract

Preimplantation genetic diagnosis (PGD) is an alternative reproductive technology integrated with in-vitro fertilisation (IVF). It is a well-established technique offering reproductive options for families at a high risk of transmitting a genetic disorder, allowing them to avoid a termination of pregnancy (TOP). Consanguineous unions are common and encouraged in many Arab communities. This can lead to an increased risk of one or more autosomal recessive disorders that may occur within the family. Traditional prenatal testing involves testing fetal cells with the option of TOP of an affected fetus. In Arab communities where TOP is restricted under Muslim law, such testing is not acceptable. For these couples and their family members, PGD is a feasible option as the fetus is diagnosed before implantation and allows for only healthy embryos to be implanted. However, undergoing PGD is relatively new in the Arabic Muslim countries and Omani patients have only recently had access to the service. This study utilised a phenomenological approach to explore the experience of Omani families who had selected to undergo PGD as a means of reducing the risk of having a child affected with a genetic disorder. Fourteen participants from eight families who underwent PGD were interviewed. Data collected were analysed using thematic analysis. The research identified five main themes; *Desire for a Healthy Child*; *Anxiety “Taraqub”*; *Unforeseen*; *Secrecy*; *Me and My Partner*. The PGD experience was reported as physically and emotionally distressing. Some participants felt attached to their embryos regardless of health status, while the majority did not anticipate the loss of intimacy, autonomy and control they experienced, particularly related to the insemination process. The social and religious background of participants played a significant role in the participant’s perception of PGD, which has both practical and psychosocial implications. The findings of the research have provided insight into the PGD experiences of Omani families and can be used to improve the services that are currently available to these families.

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## Appendix A : Abbreviations

PGD	Preimplantation Genetic Diagnosis
PGS	Preimplantation Genetic Screening
IVF	In Vitro Fertilization
TOP	Termination of Pregnancy
PND	Prenatal Diagnosis
HLA	Human Leukocyte Antigen
aCGH	Array comparative Genomic Hybridisation
SNP	Single Nucleotide Polymorphism
GDM	Genetic and Developmental Medicine Clinic
SQU	Sultan Qaboos University
SQUH	Sultan Qaboos University Hospital
OHSS	Ovarian hyper-stimulation syndrome
GDM	Genetic and Developmental Medicine clinic at SQUH
ESHRE	European Society of Human Reproductive and Embryology
HFEA	Human Fertility and Embryology Acta
US	Unites States of America
UK	United Kingdom
PCR	Polymerase Chain Reaction
FISH	Fluorescence in situ hybridisation
PGDIS	PGD International Society
ICSI	Intra cell sperm injection
ADO	Allele drop out
mtDNA	Mitochondrial DNA
NGS	Next generation sequencing
WES	Whole exome sequencing

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## Chapter 1

### Introduction

Preimplantation genetic diagnosis (PGD) is a technique combined with In Vitro Fertilization (IVF) that has come into existence in the last 20 years (Harper, 2009). PGD aims to evaluate a known genetic defect in an embryo (Brezina et al., 2012). It is a well-established technology offering a reproductive option for families at a high risk of transmitting a genetic disorder enabling them to avoid a termination of pregnancy (TOP) (Harper, 2009).

Consanguineous unions are common and encouraged in many Arab communities, and can lead to an increased risk of one or more autosomal recessive disorders that may occur within families. The chance of homozygosity in progeny of first double cousins is  $1/8$ , first cousins  $1/16$  and for the second cousins  $1/32$  (Harper, 2004). For these couples and their family members, avoidance of recurrence is particularly important (Hamamy, 2012; El-Toukhy, 2014a). Consanguinity is a respected tradition with strong social and financial benefits that is practiced among a number of communities within North Africa, the Middle East and West Asia (Bittles & Black, 2010; Hamamy, 2012). In Oman 56% of marriages are consanguineous unions of first or second cousins or between relatives within the same tribe (Rajab & El-Hazmi, 2007; Al-Thihli et al., 2014). A 2008 publication by the Omani Ministry of Health claimed that 39% of perinatal deaths were due to malformations and genetic disorders (Rajab, Al Rashdi & Al Salmi, 2013). Al-Thihli et al (2014) furthermore reported that 95% of a cohort of 285 Omani patients with inborn errors of metabolism were identified to be the product of consanguineous unions (Al-Thihli et al., 2014). Preventative options such as prenatal genetic diagnosis (PND), TOP and PGD can reduce the burden of caring for a diseased child or in many instances children with a serious debilitating disorder. In contrast to PGD, PND is a method of testing a pregnancy for a genetic disorder and if the results indicate an affected fetus the only option for avoidance would be TOP. This can cause physical and emotional trauma which may be compounded by grief and guilt (Katz et al., 2002). Therefore, PGD is often seen as an alternative to avoid the stress of PND and trauma of TOP (El-Toukhy, 2014b).

In Islam, PGD is allowed when performed by an embryologist who is aware of the Islamic regulations in handling human embryos. Individuals in whom the egg and

sperm are retrieved must have a recognized Islamic marriage, live together and be alive (Atighetchil, 2007; Serour, 2013).

However, preimplantation genetic diagnosis (PGD) services are not available within Oman and families considering PGD have to travel to neighbouring countries to access the service. The Genetic and Developmental Medicine Clinic (GDM) at Sultan Qaboos University Hospital (SQUH) facilitates the counselling and logistic arrangements for families undergoing PGD. On average, the procedure can take as long as 12 to 18 months before a cycle is started. This has a major psychosocial impact on families because of the cultural significance of a large family (El-Hazmi, 2004; Rajab & El-Hazmi, 2007).

The demand for the PGD service in Oman has grown exponentially. During 2014/2015, the GDM clinic received more than 30 requests, compared to only three in 2013 (local database). To date, there has been no study on the attitudes and perceptions of Omani families towards PGD, and the patients' needs from the service. This situation demands an understanding of the experiences of these families. By gaining insight into the impact of the procedure, it is hoped that genetic counselling for future families can be improved. Furthermore, knowledge derived from the investigation can be extrapolated to developing regulations and guidelines for counselling and enrolment of PGD families in Oman.

### Aim of the study

To explore the experience of Omani families who have selected to undergo PGD as a means for reducing the risk of having a child affected with a genetic disorder.

### Objectives:

- To identify the factors affecting the decision to undergo PGD
- To explore the couples' expectations of the PGD procedure
- To explore the couples' experience of the PGD enrolment procedure
- To identify the facilitators and barriers to accessing PGD
- To determine the recommendations the couples make to improve the service.

### Organisation of the study

This thesis is organised as follow

- Chapter 2 contains an overview of the current literature on PGD, including information on the technology, its use and limitations. The author in this chapter additionally explores published literature concerning the experiences of families undergoing PGD while at the end of the chapter presents information on the Islamic perspectives of PND and PGD, and discusses Oman and the country's healthcare system.
- In chapter 3, the author explains the research design and methodology used in the current study. It also describes the participants, the selection criteria, validity and trustworthiness. The data collection and analysis are described and the ethical issues involved in the study are considered.
- Chapter 4 contains a discussion of the research study results. The analysis and discussion are included in the same chapter to prevent unnecessary repetition of information. It will also integrate comparison with the published literature.
- In chapter 5, the conclusion and summary of the main findings of the study is presented. At the end recommendations in practice and recommendations for future research and study is discussed.

## Chapter 2. Literature review

### 2.1. Introduction

This chapter will explore the literature with regards to the historical overview of PGD development and utilisation. It will present an overview of the reported motives, perspectives and experiences of families who have undertaken PGD. Religious aspects regarding PND and PGD will be presented as well in this chapter. This chapter will also present the demography of Oman, law, religious and service provided for PGD users.

### 2.2. Literature review

The number of studies concerning PGD experience in Islamic and Middle Eastern cultures are limited and no literature is available for Omani families. Literature searches were conducted using the search terms ‘preimplantation genetic diagnosis’, ‘PGD’, ‘PGD in Arab countries’, ‘PGD and Muslims’, ‘PGD Oman’, ‘PGD Saudi Arabia’, ‘PGD Lebanon’, ‘PGD Qatar’, ‘PGD Bahrain’, ‘PGD Egypt’, ‘PGD Tunis’, on EBSCO, ProQuest, Wiley, Pubmed, google search, google scholars, google books, Web of Science, ScienceDirect, Scopus, SciVal and Springer.

#### 2.2.1. *Introduction to PGD*

PGD was first successfully performed in a human embryo in 1989 for a sex-linked disorder (Handyside et al., 1990). In this first PGD, the pioneering team extracted DNA from a biopsy of the cleavage cells for Y- specific DNA amplification polymerase chain reaction (PCR) (Flinter & Stewart, 2014; Harper & SenGupta, 2012). The embryos with absent Y allele were considered female and returned to the uterus (Handyside et al., 1990). In 1989 the first unaffected child was born following PGD for an X-linked disorder (Harper & SenGupta, 2012). Since then, PGD has been used widely for different autosomal recessive and dominant disorders (El-Toukhy, 2014a). To date, PGD has been implemented for more than 400 disorders - the most common include cystic fibrosis, spinal muscular atrophy and hemoglobinopathies (Kuliev & Rechitsky, 2015).

While IVF entails the fertilization of mature oocytes outside the uterus (in a cell culture setting) and implanting them back into the uterine cavity (Coughlan, Ledger & Ola, 2011), PGD aims to evaluate a known genetic defect in an embryo before implantation (Brezina et al., 2012). The technology is well-established and offers a reproductive

option for families at a high risk of transmitting a genetic disorder which enables them to avoid TOP (Harper, 2009). Preimplantation genetic diagnosis is considered an early form of PND but without the risk of the procedure-related miscarriage (Ben-Nagi et al., 2016; Brezina et al., 2012).

In addition, there are other benefits such as reduction of parental anxiety as PGD is capable of providing a couple with the possibility of starting a pregnancy with the knowledge that the fetus is free of the familial genetic disorder (El-Toukhy, 2014a). Furthermore, the anxiety related to the decision making process of TOP is removed when utilising PGD (Ben-Nagi et al., 2016; Brezina et al., 2012).

In recent years, different technologies have been developed to provide highly accurate methods for genetic testing of the fertilised egg (Brezina et al., 2012; Flinter & Stewart, 2014; Renwick & Altarescu, 2014). These include fluorescence in situ hybridization (FISH) that can be used to target a chromosomal rearrangement; PCR for single gene mutations and array CGH for chromosomal aneuploidy (El-Toukhy, 2014a). Each procedure is discussed in detail in section 2.2.3. After the introduction of PGD, preimplantation genetic screening (PGS) was initiated to exclude chromosomal aneuploidies which could reduce the success rate of achieving a healthy pregnancy. PGS can be offered to couples with multiple miscarriage or advanced maternal age or even together with PGD for couples at risk of transmitting a genetic disease (Ben-Nagi et al., 2016; El-Toukhy, 2014a; Harper & SenGupta, 2012; Flinter & Stewart, 2014). PGS is provided through FISH or more recently through microarray (Ben-Nagi et al., 2016; Brezina et al., 2012; El-Toukhy, 2014a). However, PGS technology is very new and remains controversial for clinical use (Harton et al., 2011a).

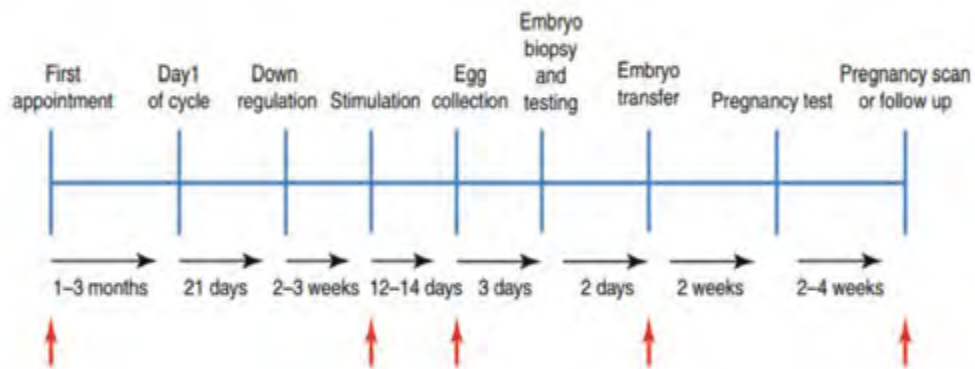
### *2.2.2. PGD procedure*

In practice, as recommended by ESHRE and the PGD international society (PGDIS), facilitating PGD requires a multidisciplinary team including medical and administrative staff (Harton et al., 2011a; Khalaf & Grace, 2014; Lashwood, 2014). The couple should be counselled by a qualified geneticist or genetic counsellor and provided with psychosocial support. The majority of PGD families have undergone a stressful history of disease occurrence or recurrence; loss of affected individuals; experience of PND and/ or TOP in addition to being at a high risk of transmitting a genetic disease (Harton et al., 2011a; Lashwood, 2014). Genetic counselling is

essential to ensure that the couple understands the mode of transmission and recurrence risk of the condition affecting their family and to support an informed decision for an alternative reproductive option. Limitations of testing and success rate of the procedure as well as the potential risk of short or long term effects should be provided prior to referral to a PGD centre (Harton et al., 2011a). Preimplantation genetic diagnosis (PGD) counselling may occur over several visits as the couple experiences the different phases of decision making (Hershberger et al., 2012). Genetic counselling should additionally address the potential that no healthy embryos may be available for implantation following testing. They should also be informed that the biopsy may cause harm to the morphology of the tested embryos rendering them unsuitable for implantation.

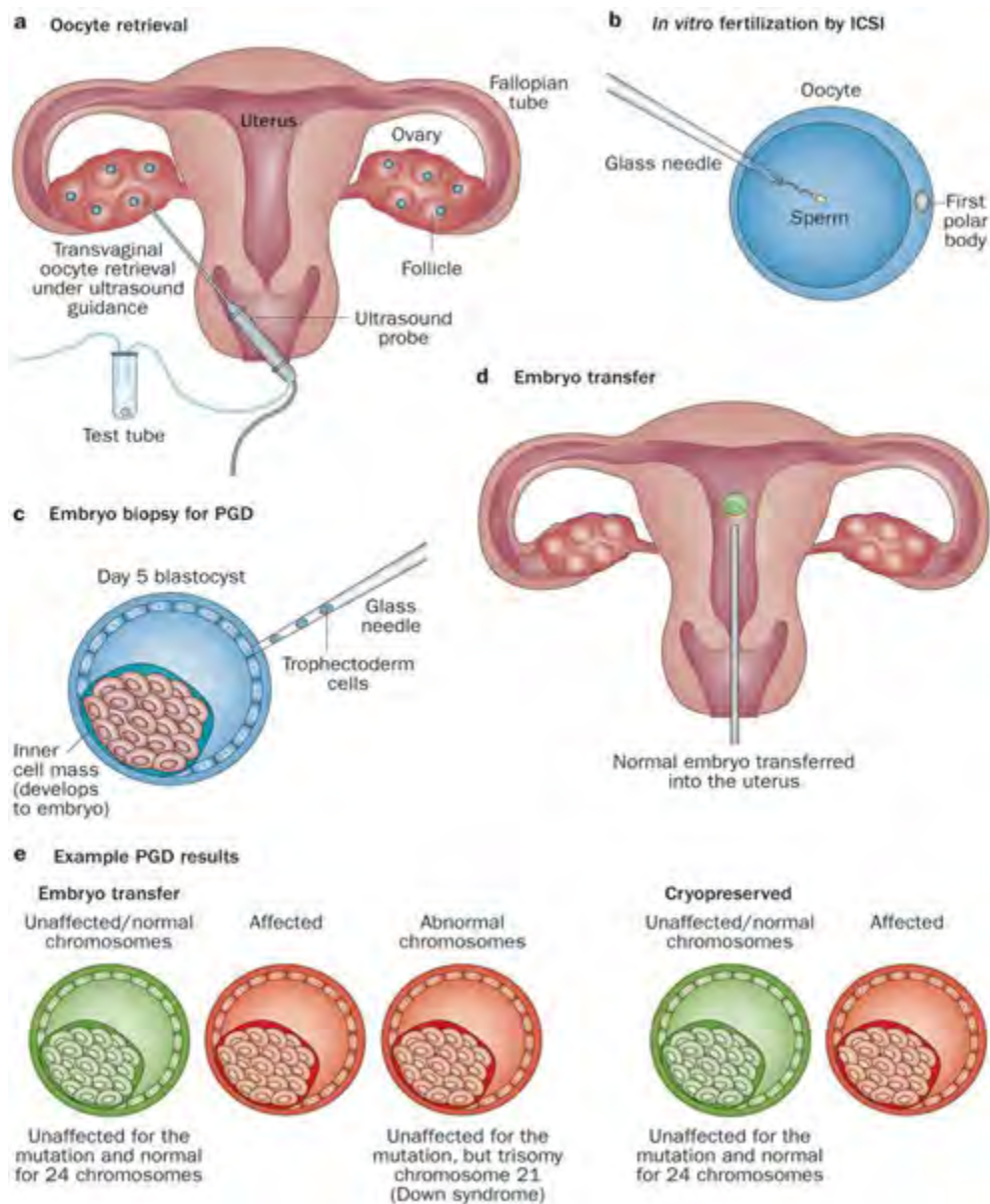
Couples interested in PGD usually have no fertility concerns but still require assessment and treatment from the infertility/reproductive specialists to ensure that they are medically suitable for treatment (Ben-Nagi et al., 2016). However, in a study by Horton et al 2011, it was found that 30% of PGD families actually had some infertility concerns when the infertility work-up was initiated (Harton et al., 2011a). Importantly, the reproductive specialist should provide information regarding the IVF treatment, details about IVF/ICSI procedure, risk of medical treatment (ovarian hyperstimulation risk) and potential complications during the oocyte retrieval procedure (Harton et al., 2011a; Lashwood, 2014). In addition, the chance of potential spontaneous pregnancy and need for contraceptives should also be addressed (Harton et al., 2011a).

Following the infertility work-up and investigation, pre-PGD can be initiated. This step involves the preparation for PGD testing of the particular genetic mutation and can take between six weeks and six months to complete. The actual PGD procedure starts after the preparation stage and includes IVF treatment with hormonal induction to stimulate oogenesis (Fig1). Counselling should include informing the couple about the complications of the treatment and side effects such as the 7.5% risk of ovarian torsion, 2.3% risk for ovarian hyper-stimulation syndrome (OHSS); 4.5% risk for early pregnancy bleeding, ovarian cancer risk (1:1000) and increased breast cancer risk for BRCA1/2 mutation carriers (El-Toukhy, 2014a; El-Toukhy, 2014b; Källén, 2008; Madill, Mullen & Harrison, 2008).



**Fig. 1: Timeline for a typical PGD treatment cycle (Khalaf & Grace, 2014)**

On day 14 to 16, oocytes are retrieved under anaesthesia (Fig 1). At the same time, semen is collected and in vitro fertilization takes place through intra cellular semen injection (ICSI) to avoid supernumerary semen contamination (Fig 2) (El-Toukhy, 2014b). A biopsied sample is collected from fertilised embryos either at day three (blastomere) or day five or six (trophectoderm of the blastocyst) (Fig 2). The latter is thought to be less traumatic to the cell and, as more cells can be removed than with a blastomere biopsy, provides more genetic material to test. As a result, the majority of centres have modified their protocol to include blastocyst trophectoderm biopsy. (Kuliev & Rechitsky, 2015). Healthy embryos will be implanted into the mother's uterine under ultrasound guidance. Surplus unaffected embryos can be cryopreserved for future implantation based on the couple's preferences (Harton et al., 2011a).



**Fig. 2: Illustrative Procedure of PGD (Tur-Kaspa, Jeelani & Doraiswamy, 2014)**

### 2.2.3. Indications for PGD and technology used

PGD can be provided for autosomal and sex linked disorders where mutations can be single base pair substitutions, insertions, or deletions or even large deletions or insertions and trinucleotide repeat expansions (Ben-Nagi et al., 2016). Different techniques may be required depending on the targeted mutation or the purpose of PGD-IVF (Brezina et al., 2012; El-Toukhy, 2014a).

#### *2.2.4. PGD for chromosomal anomalies*

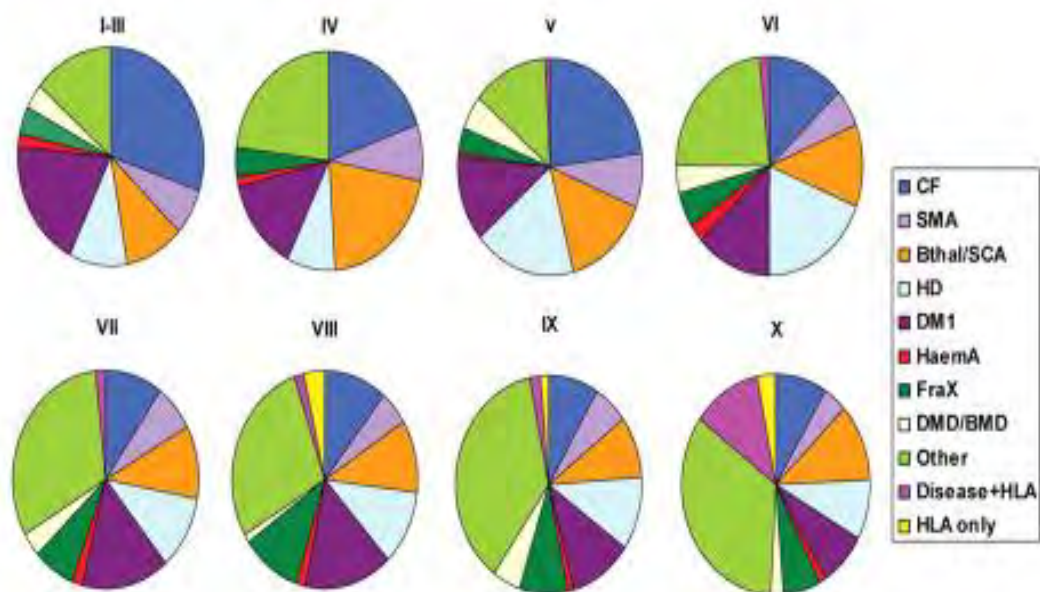
If the target is avoidance of chromosomal aneuploidy or unbalanced chromosomal product, FISH is the most suitable technique (Brezina et al., 2012). Parents carrying a chromosomal rearrangement can have a reciprocal translocation, Robertsonian translocation, pericentric inversion or a paracentric inversion (Brezina et al., 2012). According to ESHRE data XIII 60% of tested chromosomal rearrangements were reciprocal translocations and 28% were Robertsonian translocations (De Rycke et al., 2015). Carrier individuals are healthy and generally have no health concerns. These individuals are however at risk of producing gametes with unbalanced chromosome numbers which may result in infertility, live-births with congenital anomalies or developmental delay, multiple miscarriages or stillbirths (Brezina et al., 2012; El-Toukhy, 2014a). **PGD** centres under ESHRE have reported the least viable embryos are those from parents who carry a reciprocal translocation (De Rycke et al., 2015). FISH is also used to screen for aneuploidy (PGS) in couples with infertility; recurrent miscarriage or advanced maternal age where both parents have a normal karyotype. In these cases PGS is used in an attempt to improve implantation rate (Brezina et al., 2012). Despite the above mentioned advantages of FISH, the technology has limitations, including the possibility of culture failure, hybridisation failure and the inability to differentiate between unbalanced rearrangements unless specifically targeted with a spectrum of probes (Brezina et al., 2012; Kuliev & Rechitsky, 2015).

Recently, the development of microarray technology has allowed aneuploid embryos to be excluded and is available in most IVF centres (fig 2) (Ben-Nagi et al., 2016; Flinter & Stewart, 2014). Microarray (PGS) allows screening of all chromosomes and can identify complex rearrangements in addition to aneuploidy (Scriven & Ogilvie, 2014). Microarray (PGS) is done either through comparative genomic hybridization (aCGH) or through single nucleotide polymorphism (SNP) hybridisation. The two techniques are distinctly different: SNP array provides dense genotyping while aCGH provides a ratio between a labelled reference DNA and the tested DNA (Brezina et al., 2012; Scriven & Ogilvie, 2014). While array CGH cannot differentiate ploidy status, SNP array can identify haploidy, triploidy, diploidy and uniparental disomy (UPD) plus regions of loss of heterozygosity (Repping, Mastenbroek & Scriven, 2014). In addition, SNP array is able to identify clinically relevant deletions and duplications that can be missed through aCGH or FISH. The disadvantage of SNP array is the high

monetary and time (30 to 40 hours) cost of the technique when compared to aCGH (12-15 hours) (Brezina et al., 2012).

### 2.2.5. PGD for single gene disorders

Single gene mutation is most likely to occur in autosomal recessive and dominant disorders (El-Toukhy, 2014a). In autosomal recessive conditions, the couple is healthy but are carriers for a disease with a recurrence risk of 25% while for the dominant disorders, one parent is affected and the risk of having an affected child is 50% (Ben-Nagi et al., 2016). Testing for a monogenic mutation can be done via direct sequencing, genotyping or SNP array (El-Toukhy, 2014a; Ben-Nagi et al., 2016). More than 300 monogenic disorders have been tested for PGD. The most frequently tested conditions are cystic fibrosis, the haemoglobinopathies and myotonic dystrophy (Fig 3) (Harper et al., 2012; Kuliev & Rechitsky, 2015). However, conditions that are often tested in western populations may not be common in other countries, especially in the Middle East where rare autosomal recessive disorders are more frequently found (Bittles & Black, 2010; Hamamy, 2012). Optimisation for these rare (novel) mutations remains a challenge and can reduce the opportunity for consanguineous families to embark on PGD. Another consideration for families undergoing PGD for monogenic diseases is the fact that a healthy embryo can still not be guaranteed due to the risk of birth defects such as chromosomal anomalies that are unrelated to the condition being tested.



**Fig. 3: PGD for common monogenic disorders reported by ESHRE data I-X (Harper et al., 2012)**

The common technical limitations of PCR are exacerbated in PGD due to the limited sample size. Errors of diagnosis have been reported. Analysis of ESHRE data identified 12 misdiagnosed cases over a period of ten years; 10 of them with monogenic autosomal disorders such as B-thalassemia, Charcot Marie Tooth and myotonic dystrophy (Harton et al., 2011a; Kuliev & Rechitsky, 2015; Wilton et al., 2009) and two cases with X-linked disorders. Ten cases were identified following PND while two were identified after birth (Wilton et al., 2009).

These errors were mostly linked to allele dropout (ADO). ADO occurs as a result of the failure of amplification of one or both alleles and results in a false negative result (Brezina et al., 2012; Ben-Nagi et al., 2016; Konstantinidis et al., 2015).

Misdiagnosis can also happen as a result of failure of PCR amplifications and DNA contamination (Ben-Nagi et al., 2016; Konstantinidis et al., 2015). Limitations of sample size (biopsy of a single cell as occurs with blastomere biopsy) can increase the risk of amplification failure or ADO (Kuliev & Rechitsky, 2015; Wilton et al., 2009). Contamination of DNA can occur from maternal cumulus cells or paternal supernumerary sperm (Wilton et al., 2009). Harper et al (2012) collected data from all ESHRE centres over a ten-year period and reported the misdiagnosis rate for monogenic testing via PCR was 0.27% (Harper et al., 2012). As a result of the technique limitations of direct PCR, guidelines recommend that a second test is always done for confirmatory purposes. This may include either multiplex PCR or linkage analysis by using polymorphic markers in close proximity to the gene of interest (Thornhill et al., 2005; Wilton et al., 2009). Linkage analysis is however not always possible as it requires samples from other family members. Samples are not always obtainable due to the unavailability of individuals or the couple being unwilling to reveal their genetic status or their intention for PGD to family members (El-Toukhy, 2014a).

Karyomapping is a new technique developed and optimised through an array platform which integrates 300,000 SNPs (Konstantinidis et al., 2015). It allows for the diagnosis of more than one monogenic disorder and is capable of identifying chromosomal rearrangements (Ben-Nagi et al., 2016). Karyomapping's main advantage is that it provides a single protocol applicable to a wide range of patients which reduces the time required for pre-PGD test optimisation (Konstantinidis et al., 2015). Karyomapping does however have limitations and it should be run in parallel with a

conventional PCR when a high degree of homozygosity is expected (as in consanguineous families), for genes with low SNP coverages (CFTR & SMN1) and genes in telomeric regions (Ben-Nagi et al., 2016; Konstantinidis et al., 2015).

#### *2.2.6. PGD for mitochondrial disorders*

Mitochondrial disorders are inherited either through nuclear DNA (thus follow an autosomal recessive mode of inheritance) or via mtDNA mutations which are transmitted through the maternal line only. The latter is associated with pleiotropic expression (variable phenotypes depending on the threshold of the mutation load on the tissue) and variable expression due to heteroplasmy (different amounts of mutated mtDNA versus normal mtDNA within the cell) (Nussbaum et al., 2007). The poor correlation between mutation load and the phenotype plus the uncertainty of which tissue carries a greater load of mutated mtDNA limits the scope of testing for PND and PGD. An option available to non-Muslim couples is oocyte donation fertilised by the male partner's sperm (Bredenoord et al., 2009). Gamete donation is not allowed in most of the Islamic sects and would therefore not be an option for most Muslim couples (El-Hazmi, 2004). A recent development that may be allowed for Muslim couples includes nuclear genomic transfer from the carrier maternal oocytes to a surrogate nucleus-free oocyte to provide a biologically related embryo (Serour, 2013). However, the Fatwa has not yet been released and it is uncertain if this option will be accepted by the religion.

#### *2.2.7. PGD for HLA matching*

Other couples might consider PGD for the purposes of HLA matching to facilitate donor compatibility (saviour sibling) for an existing affected sibling in the absence of a well-matched family member or cord blood (Ben-Nagi et al., 2016; El-Toukhy, 2014a). Combining HLA typing with genetic testing complicates the technical procedure and reduces the chances of identifying a genetically and HLA suitable embryo among the existing fertilized cells (Brown & Gaspar, 2014; El-Toukhy, 2014b). This option raises several ethical concerns related to the fate of healthy embryos who are not HLA matched; the desire to have another child for the sole purpose of saving the affected child; complications of PGD/IVF with potential pregnancy failure; limitations of PGD and misdiagnosis rate (Ben-Nagi et al., 2016; Brezina et al., 2012).

### 2.3. PGD policy and regulations

Following the expansion of the practice of PGD after 1990, there was a need to set regulations to control the newly developing reproductive technology (Roberts & Franklin, 2004). The Human Fertilisation and Embryology Act was established in the UK in 1990 after the birth of the first PGD child. It regulates the practice of creation and use of human embryos (including PGD), the use of donated gametes or embryos and their storage (El-Toukhy, 2014a). In 1997 the European Society of Human Reproduction and Embryology was established to construct best practice guidelines; to stimulate research in reproductive medicine; to enhance teaching and training; and to collect data on PGD, pregnancy and children born through IVF/PGD (De Rycke et al., 2015; Harper et al., 2012).

The ESHRE PGD consortium has published collective data including ten years of experience from 57 PGD centres distributed in 29 countries (Harper et al., 2012). The participating centres are from Europe, North and South America, Asia, Africa, Russia and Australia (Harper et al., 2012). Among these centres were two from the Arab Middle Eastern countries (one centre from Jeddah, Saudi Arabia and one from Al-Ain, United Arab Emirates). The data included a total of 27,000 cycles, 5187 pregnancies and 5135 live born babies. Out of the reported cycles, 61% were for aneuploidy screening (PGS), 16% oocytes were tested for chromosomal disorders, 4% for X-linked diseases, 17% for single gene disorders and 2% for social sexing (Harper et al., 2012).

PGD is prohibited in many countries, including Germany, Ireland, Switzerland and Italy (since 2003) due to ethical and religious concerns (Gourounti & Glentis, 2012). The religious influence has played a major role in the prohibition of embryo manipulation in some countries and permission in other countries. The new approach of polar body testing may facilitate PGD for X-linked disorders in restrictive countries as the polar body is not considered part of the fertilized egg according to Catholic religious law (Kuliev, 2012). Preimplantation genetic diagnosis (PGD) is not restricted by Islamic law, on the contrary, it is encouraged as it replaces the termination of an affected fetus which is prohibited in some sects (Atighetchil, 2007; el-Hazmi, 1999). However, few centres are available in Arab countries and none are available in Oman. Couples who would like PGD must travel abroad for the procedure.

### *2.3.1. PGD Success Rate and Limitations*

According to the statistics provided by ESHRE, the overall success rate of PGD is 22% and the misdiagnosis rate 2.2% (De Rycke et al., 2015; Gourounti & Glentis, 2012). The misdiagnosis rate may be attributed to a number of factors, particularly the limited sample size as only one or two blastomeres can be utilised for testing and a single cell biopsy cannot exclude mosaicism (more than one cell line) in an embryo at the cleavage stage (Brezina et al., 2012; Harper et al., 2012; Konstantinidis et al., 2015). It has been reported that 40- 60% of embryos at cleavage stage (day 3 after fertilisation) are mosaic which increases the risk of false diagnosis (Harton et al., 2011b; Kuliev & Rechitsky, 2015). As mentioned, most PGD centres have moved to blastocyst biopsy (day 5 after fertilisation) where more cells (trophectoderm) can be biopsied to overcome the mosaicism issue and eliminate the risk of false negative/positive diagnosis (Harton et al., 2011b; Kuliev & Rechitsky, 2015). However, not all embryos reach this stage and biopsied embryos at blastocyst stage require cryopreservation or vitrification (instant freezing) to allow enough time to test before implantation has to occur. Polar bodies can also be used to overcome the sample limitations particularly when there is a concern for maternal chromosomal aberrations (Kuliev & Rechitsky, 2015). Countries, such as Germany and Italy, who have strict regulations concerning the discarding of embryos, are able to use polar body testing.

Other factors contributing to the failure rate of PGD include general IVF treatment challenges: the possibility of poor ovarian response to stimulation, failure of fertilization and poor embryo quality or absence of genetically suitable embryos for transfer (Brezina et al., 2012; Khalaf & Grace, 2014; El-Toukhy, 2014a). To ensure transparency, a couple should be provided with all the details related to the procedure and counselled by a specialist in reproductive medicine prior to PGD (El-Toukhy, 2014a). Considering the misdiagnosis rate, a follow up PND is recommended. However, many couples may decline PND as they would not consider termination of an affected fetus (Lashwood, 2014). According to Lavery et al (2002), 63% of couples who achieved a successful pregnancy following PGD did not opt for confirmatory PND (Lavery et al., 2002).

## 2.4. Motivations for PGD

### 2.4.1. *Avoidance of recurrence risk and TOP*

PND is often considered by couples who may have experienced a pregnancy loss or had an affected child with a genetic disorder. In the event that prenatal testing indicates the fetus is affected the only option aimed at avoidance includes TOP. This can be associated with physical and emotional trauma compounded by grief and guilt (Katz et al., 2002). Therefore, PGD is often seen as an alternative to avoid the stress of PND and trauma of TOP (El-Toukhy, 2014a). Most studies report that couples prefer PGD to TOP which is often against their moral, religious or cultural beliefs (Karatas et al., 2010a). Other families who have experienced previous termination of an affected pregnancy consider PGD to avoid a second termination (Karatas et al., 2010b; van Rij et al., 2011).

Many studies have investigated the attitudes, experiences and motivation for undertaking PGD in western countries (Australia, UK, Spain, Sweden and USA) (Cunningham, Goldsmith & Skirton, 2015; Hershberger et al., 2012; Hershberger & Pierce, 2010; Järholm, Broberg & Thurin-Kjellberg, 2014; Karatas et al., 2010a; Karatas et al., 2010b; Katz et al., 2002; Kalfoglou, Scott & Hudson, 2005; Lavery et al., 2002). Very few explored motives and attitudes toward PGD in Muslim and Arab groups (Saudi, Lebanon and Malaysia) (Alsulaiman et al., 2010; Alsulaiman & Hewison, 2006; Farra et al., 2008; Olesen, Nor & Amin, 2015) and none have been conducted on Omani families.

Katz et al (2002) evaluated the range of moral and social concerns prior to undertaking PGD in Australian couples with three different obstetric and genetic histories (PGD for single gene, PGD+ PGS for aneuploidy screening and for IVF due to infertility issues). The majority - 95% of participants - found PGD/IVF acceptable and the discarding of embryos to be less harmful and morally more acceptable than terminating an affected pregnancy (Katz et al., 2002). A similar study was conducted on Arab Muslim Lebanese mothers of affected children with thalassemia. The study identified that 68% of participants felt that PGD was more favourable than PND for religious reasons (Farra et al., 2008). More than half of the participants (58%) consider the main advantage of PGD to be avoidance of termination (Farra et al., 2008). Likewise, Van Rij et al (2011) reported that 53.4% of couples out of a cohort of 264 referred for PGD

in The Netherlands favoured PGD (van Rij et al., 2011). The experience of one or more miscarriages, the loss of an affected child and the absence of (acceptable) alternatives for the female partner positively contributed to PGD intention (van Rij et al., 2011). Similar findings were identified among Malaysian patients considering PGD (Olesen, Nor & Amin, 2015) and Australian women (Karatas et al., 2010b).

Jarvholm, Broberg and Kjellberg.K (2014) explored the psychological and health system considerations that influenced Swedish men and women's PGD decisions (Järvholm, Broberg & Thurin-Kjellberg, 2014). They observed three themes of decision-making; related to self; related to the child and related to the society. In relation to self; an affected parent would consider PGD in order to have a better life for their children. The intention of reducing the burden on family or siblings by preventing the birth of an affected child was a common reflection among the participants. Those that had experienced termination found this was a key reason to undergo PGD (Järvholm, Broberg & Thurin-Kjellberg, 2014). Despite the stressful situation, some were able to think of the impact on others and the cost burden on the society (Järvholm, Broberg & Thurin-Kjellberg, 2014).

Alsulaiman et al (2010) explored the attitudes towards PGD among a group of Saudi Muslim couples who had affected children with haemoglobinopathies. The study reported different attitudes among individuals who experienced genetic disorders (haemoglobinopathies and deafness) as compared to a control group of individuals undergoing IVF (Alsulaiman et al., 2010). Eighty-nine percent of the individuals who had a history of a genetic disorder were enthusiastic about PGD and had no concerns about the technical limitations. For half of these individuals confirmatory PND would have been considered if PGD was successful while only 18% of the IVF group found it acceptable. The difference among the PGD and IVF groups related to different perceptions and attitudes which could be correlated to "the chief aim of the genetic groups was probably to have a healthy child, rather than to avoid miscarriage of a particular pregnancy" (Alsulaiman et al., 2010; Lashwood & Say, 2014). Similar findings have been identified by other studies conducted on western populations (De Krom et al., 2015; Katz et al., 2002; Lashwood & Say, 2014).

Couples appear to undergo a conceptual framework composed of cognitive appraisal, emotional responses and moral judgments when considering PGD (Hershberger & Pierce, 2010). These decisions are influenced by success rate, procedure risk, financial

costs and time while emotional responses capable of influencing the decision-making process may include regret, guilt, shame, sadness and despair (Hershberger & Pierce, 2010).

#### *2.4.2. Emotional and psychological experience of PGD*

Different studies report the PGD journey as "emotionally draining" (Cunningham, Goldsmith & Skirton, 2015). Lavery et al (2002) reported that 41% of their cohort found the treatment cycle to be extremely stressful (Lavery et al., 2002).

In a systematic review of literature related to the psychological and broader psychosocial impact of PGD, Karats et al (2010) confirmed the psychological and psychosocial impact of PGD (Karatas et al., 2010a).

After then, Karatas et al., (2011) measured the level of anxiety and depression using a validated measure on a cohort of 50 women (Karatas et al., 2011). Results identified that anxiety and depression levels fluctuated during the PGD cycle and were highest following embryo transfer and pregnancy testing irrespective of a negative or positive outcome (Karatas et al., 2011). Similar findings were reported by Lavery et al., (2002) and Alsulaiman et al (2010) and karatas et al (2010b) where participants identified the pregnancy test to be the most stressful part (Alsulaiman et al., 2010; Karatas et al., 2010b; Lavery et al., 2002).

However, some PGD users find the time prior to implantation as stressful as post implantation in order to identify the availability of unaffected embryos. Negative results were reported to cause and acute disappointment and distress (Karatas et al., 2010b).

In a study by Roberts & Franklin (2004), participants expressed that PGD consumed their time, energy, attention and money (Roberts & Franklin, 2004). Although the participants felt fortunate to have the choice of PGD, the decision-making process was complex and required careful consideration of social and personal issues (Roberts & Franklin, 2004). Such a stressful life decision can impact on a couple's relationship (Lashwood & Say, 2014). Lavery et al., (2002) reported that one third of the families experienced a negative effect on their relationship while for another third a positive effect was identified (Lavery et al., 2002) .

Drazba et al (2014) focused on the psychological and financial impact of PGD and identified that these factors could complicate the PGD decision making process

(Drazba, Kelley & Hershberger, 2014). The study by Roberts & Franklin (2004) and that of Olesen, Nor & Amin (2015) emphasised the financial burden reported by PGD consumers (Olesen, Nor & Amin, 2015; Roberts & Franklin, 2004).

Despite the stressful and negative emotions associated with PGD, some studies have highlighted the positive effects including the relief (Roberts & Franklin, 2004) and hope (Karatas et al., 2010a; Karatas et al., 2010b) when arriving at the PGD clinic.

## 2.5. PND and PGD perspectives in Islam

Despite the fact that there are different sects in Islam, termination of an affected pregnancy is prohibited by the majority. Sharia' in Islam is the word given to the perfect divine Islamic Law and is derived from the Holy Quran, Prophet Mohammed's opinions and sayings (Sunna or Hadith) (Atighetchil, 2007) and agreed opinion and analogy of Islamic scholars "which is the intelligent reasoning, used to rule on events not mentioned by the Quran and Sunna, by matching against similar or equivalent events ruled on" (Serour, 2013). Islam has many sects with minor differences (Sunna, Shi'a and Ibadism which is a conservative form of Sunna but closer to Shi'a). Omani Muslims are mostly Ibadism and Sunna while Shi'a present as minorities in some colonies of communities (U.S. Department of State, 2010).

Two main Fatwa's (Islamic decrees) are derived from the interpretation of the timing of the ensoulment period. One Fatwa, embraced by most of the Islamic scholars, at the Islamic Fiqh Academy, describes the breath of ensoulment to occur 120 days after conception and therefore would permit TOP up to 120 days of gestation (Atighetchil, 2007; Bruwer et al., 2014). The other Fatwa, which is followed by the Omani Grand Mufti (Highest Islamic scholar), believes that an embryo is a living human once a pregnancy is confirmed and would not permit TOP at any stage unless continuation of pregnancy could harm the mother's physical or mental health (Atighetchil, 2007; Bruwer et al., 2014). Islam is the predominant religion in Oman and plays a major role in Omani's life and sociocultural beliefs (U.S. Department of State, 2010). The law in Oman states that Islam is the basic state of religion and Sharia' is the basis of the religious legal system (Rajab, Al Rashdi & Al Salmi, 2013). Both Fatwa are recognised by Omani Muslims, however the official law in the country follows the Fatwa of the Grand Mufti of Oman. Consequently no hospitals in Oman are able to offer TOP (Bruwer et al., 2014) and couples have to travel abroad for termination which further

burdens the family emotionally and financially. Thus, PGD offers an alternative reproductive option for those who do not consider PND with TOP to be a preventative option.

In Islam, PGD is allowed when performed by an embryologist who is aware of the Islamic regulations for handling human embryos. Individuals from whom the egg and sperm are retrieved must have a recognised Islamic marriage, live together and be alive (Atighetchil, 2007; Eskandarani, 2009). This permission interpreted as PGD does not conflict with God's desire and wish, therefore, the technology used to select embryos is not considered a modification of God's creation (Alsulaiman & Hewison, 2006). Micromanipulation during the IVF procedure is allowed to overcome infertility issues (Atighetchil, 2007; Eskandarani, 2009). Furthermore, freezing of embryos, sperm, eggs, ovarian and testicular tissue is permitted in Islam providing that it will not be used for a different marriage, for donation or for surrogacy (Atighetchil, 2007; Eskandarani, 2009).

Although PGD can serve as a reproductive substitute in most Islamic countries where TOP is not an option, few PGD centres are available in the Arab and Muslim countries (Atighetchil, 2007; Eskandarani, 2009). Saudi Arabia, United Arab Emirates, Iran, Malaysia and Turkey have established PGD centres while others like Jordan have a satellite PGD service in which IVF is done locally and the zygote biopsy is tested in an international centre for assays such as microarray (Eskandarani, 2009; El-Toukhy, 2014a).

Cryopreservation for healthy embryos is allowed in Islam under some restrictions; the marriage has to be ongoing; both couples need to be alive and the embryos may not to be used for another couple (Atighetchil, 2007; Serour, 2013; Serour, 2008). Couples are allowed to donate excess embryos for research providing informed consent is signed. This was confirmed in 2007 by different Muslim scholars who encourage using embryos for the development of knowledge for the advantage of humans. However, donated embryos have to be used before day 14 after fertilization (not to be allowed for further embryonic stages development) and may not be implanted in a woman's uterus (Serour, 2008).

## 2.6. Health care system in Oman

Oman; officially the Sultanate of Oman; is an Arabian country located in Southwest Asia on the South Eastern coast of the Arabian Peninsula bordered by the United Arab Emirates, Saudi Arabia and Yemen (Rajab, Al Rashdi & Al Salmi, 2013; World Population Review, 2016). The majority of the Omani population consists of Arabs, ethnic Balochis (from Baluchistan/ Pakistan), ethnic Lurs (From Iran), Swahilis (East African), Hindus and Mehri (from India) (World Population Review, 2016).

Health care in Oman is provided free of charge to all Omani citizens. There are more than 200 primary health centres, 50 secondary regional hospitals with specialised care distributed throughout the country and five main tertiary hospitals (Rajab, Al Rashdi & Al Salmi, 2013). A genetic service is integrated in two main centres; the National Genetic Centre under the ministry of health and the GDM under SQUH. Each of the centres consist of a clinical genetic team and diagnostic laboratories for cytogenetics and molecular genetics. However, as the molecular laboratory associated with the GDM clinic is underdeveloped, the majority of tests are outsourced to overseas diagnostic laboratories. The cost for molecular genetic testing is financed by the government.

## 2.7. PGD procedure in Oman

No PGD services are available within Oman and families considering PGD have to travel to neighbouring countries such as United Arab Emirates, Saudi Arabia, Jordan, Iran, Turkey or the United Kingdom (UK). Families with a molecularly confirmed genetic diagnosis are offered genetic counselling at the GDM clinic and reproductive options aimed at the prevention of disease recurrence are discussed. These options include premarital genetic testing and, for those who are already married, PND and PGD. The majority of families in Oman avoid PND with the option of TOP due to moral and religious beliefs and thus prefer PGD. However, PGD is expensive and this contributes to a decreased uptake of this preventative measure. Prior to 2015, families who had no living healthy children were eligible for full coverage of the cost of one PGD-IVF cycle. Following budget constraints in 2015 all families interested in pursuing PGD, even if previously eligible for funding, have to cover the costs themselves. Although these families are no longer financially covered, the process of embarking on PGD is still facilitated by the clinic. If governmental financial strategy

integrated PGD services, this could be cost effective by alleviating expenditure on the medical care provided for an affected child (Tur-Kaspa et al., 2010).

To date, 33 families have requested PGD through the GDM service. The role of the genetic counsellor, in addition to the genetic counselling and psychosocial support, involves preparation of the administrative work including communication with the PGD centres, counselling and consenting the couple for the procedure. In addition, the collection and shipment of requested samples for pre-PGD test optimisation is handled by the counsellor. On average the procedure can take as long as 12 to 18 months before a cycle is started.

The GDM clinic refers patients to three centres. These centres have been selected as the embryologists are licensed, the laboratory is accredited, prices are competitive and centres are within an Arabic Muslim country. One centre is in Amman in Jordan and two in the United Arab Emirates (one in Abu Dhabi and one in Dubai).

The cohort in this study received genetic counselling in the GDM clinic for a minimum of three counselling sessions lasting on average one hour per session. The couples had also been referred to the infertility team at SQUH and seen for infertility investigations. Counselling was also received at the PGD centre. Despite extensive counselling, it is not uncommon to find that individuals perceive success rates as higher than the actual figures given by counselling (Kalfoglou, Scott & Hudson, 2005; Karatas et al., 2010b; Lashwood, 2014).

## Chapter 3. Methodology

### 3.1. Method and Instrumentation

This chapter will describe the methodological process of the research. It will include a discussion of the sampling method used, instrumentation, data collection and analysis. The chapter will conclude with a description of the measures taken to ensure validity and trustworthiness and ethical considerations.

### 3.2. Research Design

As described in chapter 2, minimal literature exists on the experiences of families undergoing PGD in Arab and Islamic populations (Alsulaiman & Hewison, 2006; Farra et al., 2008; Eskandarani, 2009) and to date no published research exists on this topic for Omani families. The research design was therefore selected to allow for an in-depth understanding of the main research question - the experience of Omani families undergoing PGD (Creswell, 2012; Macfarlane, 2014). Hence, this study utilised a qualitative, descriptive, phenomenological approach. Qualitative methods, in contrast to quantitative methods, are able to provide insight into the individual's thoughts and perceptions and are not concerned with exploring cause and effect relationships (Macfarlane, 2014). This particular qualitative research paradigm is defined as a study in which the researcher attempts to understand a complex phenomenon based on a perspective that individuals' lived experience is a valuable data source (Creswell, 2012; Ellis et al., 2008; Macfarlane, 2014).

The approach uses an interpretive framework to enable the researcher to explore the experiences of the participants so as to uncover meaning and generate understanding (Lapan, Quartaroli & Riemer, 2012). The qualitative researcher immerses him/herself in the data in order to view the meaning of the articulated experience through the eyes of the participants (Lapan, Quartaroli & Riemer, 2012; Macfarlane, 2014). Phenomenology has also been described as "an approach that focuses on how life is experienced" (Denscombe, 2003). Furthermore, it does not primarily investigate the cause of the problem, but rather investigates how individuals experience the problem (Denscombe, 2003). This approach is best suited to the research question as it can provide insight into human experience through the use of dense descriptions provided by the individuals affected by the phenomenon under study (Baillie, 2015).

A cross sectional design was utilized which meant that information from participants was captured at one point in time. Although this meant that changes over time would not be identified, as in a longitudinal study, the limited resources and time available for the study made this an ideal approach (Creswell, 2012; Denscombe, 2003).

### 3.3. Population and Sampling Method

The GDM unit has facilitated 33 requests for PGD cycles since the inception of the service in 2014. Three families have achieved a successful pregnancy - two of them from the first PGD cycle, and the third after the second cycle. Four families have undergone multiple PGD cycles without achieving a successful pregnancy and four families' plans were interrupted by a spontaneous conception. The remaining 22 were in different stages of the PGD process but have not yet reached the implantation phase.

The researcher identified eligible families from the GDM PGD database and purposive sampling was used to recruit individuals that lived in close proximity (less than 200 km from GDM). Purposive sampling allows for the identification and selection of information-rich cases related to the phenomenon of interest (Creswell, 2012). Individuals were selected on the basis of being easily accessible and willing to participate (Denscombe, 2003). According to Denscombe (2003), from a group of equal samples, it is reasonable to select the participant who is available first and in closer proximity to the researcher (Denscombe, 2003).

To obtain broadest range of information, the researcher looked for variable samples that might offer contrary opinions and evidence as this would facilitate in-depth study while avoiding any appearance of biases (Patton, 1990). Bringing people of the same background and experience together to participate in in-depth interviews enables the researcher to shed light on the major issues affecting them (Patton, 1990; Denscombe, 2003).

Macfarlane et al (2014) propose that "8-13 participants in individual interviews are typically sufficient for saturation" (Macfarlane, 2014). Once saturation is reached, no new description or explanation arises from further exploration and increasing the sample size only results in duplication or redundancy of ideas (Creswell, 2012; Macfarlane, 2014; Patton, 1990). Furthermore, larger samples do not necessarily enhance the research as they may lack the depth and richness of a smaller group (Creswell, 2012). The target for this study was therefore to recruit 10 couples in order

to achieve data saturation (Macfarlane, 2014). Although all families were enthusiastic to participate, many were unable to commit to an interview due to their ongoing PGD procedures and/or family circumstances related to the needs of their affected children. Thus, considering the time constraints associated with a mini-dissertation the number was reduced to eight couples (14 interviews; two female partners could not commit due to health or social issues). However, it was felt that data saturation was achieved where no new themes identified in the last two interviews.

In this study, each partner of the Omani couple was interviewed separately to enable a comparison of the PGD experience from both the female and male perspectives. Although several studies have assessed perspectives, attitudes and experiences surrounding PGD, they have been limited to female participants (Farra et al., 2008; Karatas et al., 2010b; Wah Hui et al., 2002). Only a limited number of studies have considered the couple's perspective, but in these studies, information was obtained from joint interviews (Alsulaiman et al., 2010; Järholm, Broberg & Thurin-Kjellberg, 2014; Lavery et al., 2002).

### *3.3.1. Setting*

When an individual is requested to discuss sensitive issues, a private venue is more likely to result in a true representation of the situation (Lapan, Quartaroli & Riemer, 2012; Macfarlane, 2014). Interviews therefore took place in the participants' homes or a private venue of their choice. Six of the eight families preferred to be seen in a private room at the GDM clinic before or after one of their frequent hospital appointments and two families were interviewed at home.

The researcher obtained the data for her study during face-to-face interviews. Face-to-face interviewing is time intensive as it focuses on extended interaction, and requires transcription of the interview material, as well as familiarisation with the data and the coding process (Lapan, Quartaroli & Riemer, 2012; Macfarlane, 2014). Lapan et al (2012) describes this method "as one that allows for a collection of richer data with nuance" (Lapan, Quartaroli & Riemer, 2012). It additionally allows for the observation of non-verbal behaviour and builds rapport more quickly and deeply (Macfarlane, 2014).

### 3.3.2. *Inclusion criteria*

- Individuals with a molecularly confirmed genetic diagnosis identified in the proband or family member
- Individuals counselled about the genetic diagnosis and option of PGD
- Individuals enrolled in the PGD request process (any stage of process)
- Individuals willing to be interviewed and audio-recorded by the researcher
- Individuals accessible for a personal interview

### 3.3.3. *Exclusion criteria*

- Individuals who have previously undertaken PGD without been counselled or seen by the GDM team

## 3.4. Measurement Instruments

### 3.4.1. *Interviews*

A semi-structured interview schedule including the researcher's observations was used to gather data for the study (Appendix C) (Creswell, 2012; Lapan, Quartaroli & Riemer, 2012; Macfarlane, 2014).

The researcher started the interview by providing the participant with an information sheet, before discussing the aims and objectives of the research and answering any queries. The consent form was then discussed with an explanation about the research, the need for audio-recording, potential publication and the strategy to maintain anonymity and confidentiality. The interview began with closed-ended questions about demographics. These basic questions helped to establish some rapport with the participant prior to discussing more sensitive issues (Patton, 1990; Denscombe, 2003). Open-ended questions within the interview schedule were grouped into six main categories. These included motivations for PGD and how participants learnt about the procedure; how the decision was made and the impact of the decision on the couple's relationship and lifestyle. The researcher also explored the religious and social impact of the couple's decision based on their population background. The last question dealt with the availability and accessibility of support for couples undertaking PGD. As the researcher gained experience with interviews, she was able to pick up on issues as the participant discussed them. If the answer to the main question was insufficient, the researcher enquired further with open-ended questions. Prompts were additionally used to clarify responses or to facilitate greater exploration of a particular topic when

required. Probes were included to enable the researcher to cover each topic in enough depth before the participant moved onto the next topic. As suggested by Denscombe (2003), probes were handled in a sympathetic and subtle manner (Denscombe, 2003). Validity of the questions, probes and/or prompts were reviewed by the researcher's supervisors to ensure they were understandable and neutral.

The order of the questions in the interview schedule varied according to the trend of conversation, however the same interview schedule was used for all participants to explore the story of their PGD experience (Alsulaiman et al., 2010; Hershberger et al., 2012; Katz et al., 2002; van Rij et al., 2011). The researcher used other data sources, such as the GDM database and hospital records, to collect and verify demographic details, family history of recurrence, age of the couple and number of affected versus living healthy children.

#### *3.4.2. Audio recording*

A digital recording device was used to record the interviews for documentation and transcription. This also allowed the researcher to wholly engage with the participants instead of having to write down their answers. Audiotaped digital files were dated and labelled with codes and the participant's names were kept separate from both the tapes and interview schedules. Only the researcher had access to these, thus preserving participant confidentiality. The recordings were directly translated from Arabic to English after each interview by the researcher who is fluent in both Arabic and English. Any non-verbal cues, identified during the interview, such as facial expressions or gestures, were noted during the discussion and written down immediately after the interview from the field notes.

### *3.5. Procedure*

#### *3.5.1. Testing interview*

A test interview was conducted as a role-play scenario with two Arabic speaking colleagues and observed by the co-supervisor. This allowed the schedule to be refined and identified changes needed to improve clarity. Furthermore, questions were tested for difficulty of comprehension, ensuring that data would be observable and measurable (Creswell, 2012). A second test interview was then undertaken with a participant who met the inclusion criteria. The interview schedule was adapted after these test interviews to aid the clarity of the questions and subsequently rechecked by

the researcher's supervisors. As a result of the time constraints and limited participants available for interviewing during the study period, the data from the second test interview was included in the write-up. However, a follow-up interview was arranged with the participant to supplement the previously collected data. The length of the interviews were between 50 and 60 minutes as assessed through the test interviews.

### *3.5.2. Recruitment*

Participants were selected on the basis of having undergone experiences about which the researcher wanted to gain insight and were selected from the GDM database. Potential candidates meeting the inclusion criteria were invited to participate in the study telephonically or during their clinical visit. The purpose of the research and expected length of interviewing was explained and interested participants were given the choice of place and time for an interview. Every individual invited to participate in the study consented to interviewing, audio-recording and potential publication of anonymised data.

### *3.5.3. Implementation of interviews*

The researcher conducted every interview personally during the months of February to May in a private venue of the participant's choice. Where both members of the couple were available, separate individual interviews were conducted to exclude partner pre-dominance (Hershberger et al., 2012). However, the researcher had to consider meeting the couple together, as opposed to interviewing the husband separately, if the interview was conducted in the home setting. This was to respect the cultural and religious aspects applying to a female researcher when interviewing a male participant. By Islamic law, a woman is not allowed to be in a closed or isolated area with anyone other than her father, brother, husband, son, uncle, grandfather/grandchild and nephew. In essence the people whom she is forbidden to get married to (Atighetchil, 2007). However, only one couple had been interviewed together.

All interviews were conducted in Arabic, the first language of the participants. If any distress was experienced by the participants during the discussion of their experience of PGD, they were given the option of further counselling with a qualified genetic counsellor or clinical geneticist.

A total of 14 interviews were conducted to reach data saturation. Eight males and six females were interviewed. Two females, of the eight couples, could not be interviewed

as a result of social or medical reasons despite rescheduling the interview three times. Due to the time limitations associated with the study and after discussion with the supervisors it was decided to exclude these individuals from the interviewing process. The majority of interviews were conducted in a private venue in the clinical setting (85% of participants; 12/14) while two participants (15%; 2/14) preferred to be seen at their home.

### 3.6. Data Analysis and Interpretation

On average a one hour interview took four to six hours to transcribe and produced eight to nine pages of data. Transcription and translation was carried out by the researcher and this allowed for repeated listening and proof reading of the data. As the studied group was small and to maintain the confidentiality the researcher did the transcription and translation herself. The first seven transcripts were used as a guide to the initial recording. The researcher went back and forth between the transcripts and the audio records, which is ultimately the data, to refine the themes. The more the researcher listened to the audio-recordings the more familiar she became with the data enabling the comparison of translated transcripts to identify nuances (Yin, 2011). The researcher continued with the re-listening during the interpreting, coding and theme identification phase.

Data was analysed using thematic analysis. During this process the researcher analyses the data and interprets patterns of responses to bring order, structure and understanding to the mass of collected information (Braun & Clarke, 2006). Raw qualitative data by itself is not informative and certain steps are required to organise the collected information into meaningful and descriptive data. Creswell (2012) recommends several steps for thematic analysis. These include:

- Reading the written transcripts several times and listening to the recordings to obtain an overall feeling
- Identifying significant meaning linked directly to the experience
- Formulating meanings into clusters of themes

The collected themes can then be integrated into a thorough text description of the phenomenon (Braun & Clarke, 2006; Creswell, 2012). The researcher followed the

seven steps described by Colaizzi (1978) and integrated in Creswell's recommendation for data analysis (Edward & Welch, 2011). These steps are described as follow:

1. Transcribe the participant's narrative descriptions from the audiotape (Multi steps of writing through different individuals can threaten the data by losing the original meaning (van Nes et al., 2010))
2. Extract statements from the participant's narratives that are directly related to the phenomenon under study. Significant statements are numbered and assembled in a list
3. Attempt to formulate more common statements or create a meaning of each statement
4. Organise formulated statements or meanings into clusters of themes (groups of similar types)
5. Develop comprehensive descriptions for the clustered themes
6. Rigorously analyse the comprehensive description of the themes to identify a fundamental structure for the phenomenon
7. Validate the essence of the phenomenon.

Immersion in the data can help the researcher comprehend the meaning of the participant responses (Creswell, 2012). As the interviews went on, the researcher could identify common words, events or ideas shared by participants (Step 2 of Colaizzi's approach). The initial coding procedure was guided by the literature and observations from clinical experience (Patton, 1990; Braun & Clarke, 2006). Commonalities and differences that were observed in patterns were then defined as themes (Braun & Clarke, 2006; Creswell, 2012).

The researcher met regularly with her co-supervisor to review the identified codes during the interpretation and categorisation of the analysis phase. The emerging themes were also discussed and finalised with the supervisors.

Quotes were included to substantiate participants' responses. As all interviews were conducted in Arabic, the meaning of the sentence, rather than the exact wording, was included. This was done to ensure the meaning was not lost during the direct translation into English (van Nes et al., 2010). Although this process may mean that some of the authenticity is lost, it is more important to ensure the meaning of the data is conveyed to the reader rather than the actual words (Carpenter & Suto, 2008; Denscombe, 2003). However, to uphold validity, supervisor checks were included to

ensure that the interpretation did not alter the participant's meaning during this process.

### 3.7. Trustworthiness and rigour

#### 3.7.1. *Validity*

Qualitative research requires different techniques to enhance rigour compared to the ones used in quantitative research. Rigour in qualitative research uses one or more validation procedures to ensure accuracy. These may include prolonged time in the field, member checking, validation, use of peer-review or external auditors and/or negative case analysis (Baillie, 2015; Creswell, 2012).

This research used some of the suggested techniques, appropriate to the research design, to maintain validity. Data were validate by cross-checking the information and observing reactions or responses of patients seen but not participated in the study. A Different combination of data sources used for the study included interviewing, observations and analysis of the GDM database records. This technique describes the use of different methods of data collection, where the strength of one approach compensates for the weakness of another approach (Baillie, 2015).

In order to establish external validity of the research, a rich description of the research methodology was ensured so that it could help the reader decide whether the research would be transferable to their setting or not (Beeson, 1997; Creswell, 2012). Many qualitative researchers are more meticulous about validity - "the degree to which data and interpretation fit with the situation" - than with generalisability (reproducibility and regeneration of the data in other contexts) (Lapan, Quartaroli & Riemer, 2012). The researcher additionally used rich description to support the development of a clear audit trial to provide a transparent and detailed account of the sampling method and sampling size (Baillie, 2015; Creswell, 2012). Thus readers can determine if the same research findings could be applied to reflect key concepts or experiences in other cohorts or situations.

Peer review was used to ensure credibility and the researcher met with her supervisors on a regular basis to check the data collection and transcription. In addition, regular meetings also took place with the neutral co-supervisor during the analysis phase. This was undertaken to eliminate any bias in the interpretation and categorisation of the

data and content analysis and promoted confidence in the truth of the findings of the study.

The content validity of the interview schedule was reviewed by the supervisor and co-supervisor for the English version and by two Omani genetic counselling colleagues at the GDM clinic for the Arabic version. This ensured that the sequencing of questions was appropriate and easily comprehensible and understandable. The role-play conducted with the Omani GDM staff members could additionally serve to validate the translated interview schedule in terms of the sensitivity and reliability of the words used in the Arabic interview schedule.

### *3.7.2. Reflexivity*

In qualitative research, the researcher is the main instrument for data collection and can potentially influence how data is collected and interpreted (Baillie, 2015). Therefore, reflexivity during the field work is of importance. Finlay (2002) described reflexivity as "a confessional account of methodology or as examining one's own personal, possibly unconscious, reactions" (Finlay, 2002; Finlay & Gough, 2008). The focus is on exploring the dynamics of the researcher–researched relationship (Finlay, 2001). Reflexivity can be a valuable tool to:

- examine the perspectives of the researcher;
- investigate personal interaction and interpersonal dynamics
- create self- awareness of unconscious drives and hidden biases;
- qualify external auditing;
- examine the integrity of the research approach and interpretation (Finlay, 2002).

The researcher took field notes before, during and after each interview. A conscious effort was made to differentiate between the researcher's personal values and those of the participants and she obtained repeated affirmations from the participants related to the information that was heard. This ensured that the findings were as a result of the research and not related to subjectivity or personal bias (Denscombe, 2003).

The researcher faced a professional challenge in her dual roles as a health care provider involved in counselling families through the lengthy PGD procedure, and as a researcher interested in uncovering meaning from their experiences and accessing their accounts of events she has not witnessed (for instance during the PGD procedure

abroad or at the family's homes). As the researcher was heavily involved with helping the families with the PGD arrangements there was an assumption that, as rapport had already been established, there would be minimal obstacles to conducting the research. However, difficulties were encountered during the research. The first occurred during the initial telephonic contact inviting the selected individuals to participate in the study as calls were integrated with pending issues for the PGD arrangements (there was a risk of confusing the request as a requirement for the procedure). Therefore, the researcher had to alert the call recipient to separate the two distinctly different discussions. This also occurred during the appointment setting, where the researcher had to prioritise the research interviews due to the time limitations associated with the mini-dissertation. These concerns were discussed with the supervisors but are not unique in research. The same issues have been described as part of the experience of doing qualitative research at home which can be labelled as "switching on and off" or "entry and exit" of daily professional life and research (Nordquest, 2007). The researcher had to ensure that she did not take on the genetic counselling role during the interview as she had been involved in direct counselling or observation of the interviewed patients. To overcome this issue, an agreement was made with the interviewee to set up a counselling session if a need was identified during the interview. On the other hand, the researcher had to take off the researcher hat while counselling couples that were identified as potential research participant. Awareness of the different roles of researcher and counsellor ensured that an ethical framework for dealing with this concern was established prior to the study. Thus the researcher's professional activity did not interfere with the data-collection process and she was capable of maintaining the professional standards and codes of conduct of a practicing genetic counselling student.

Families were excited and enthusiastic to participate in the research as most of them "had something to share with others". However, agreeing on an interview time and venue was also difficult. Most of the families had frequent hospital appointments for their affected children as well as for their PGD preparations. Some had ongoing unplanned spontaneous pregnancies and were emotionally traumatised at having to consider/plan for prenatal diagnostic testing. Others achieved a successful PGD pregnancy which required that the researcher had to see them for post PGD counselling

and referrals to other departments. All these factors played a role in the number of participants available to participate in the research study.

### 3.8. Ethical Considerations:

The research was approved by two ethical committees before the data was collected: College of Medicine and Health Science at SQU where the study was undertaken and UCT research and ethics department at UCT where the master's program was undertaken (HREC/REF: 009/2016 and SQU-EC.244/15 MERC 1215) (Appendix F).

Participants were informed of the following points when invited to participate in the study:

- Aims and objectives of the research study
- Participation was voluntary
- The participants were assured that they had the right to withdraw at any stage of the study with no impact on their current or future health care.

Written informed consent was obtained for the interviewing and audio-recording process and all participants were over the age of 18 years and legally competent to sign consent. The consent forms are provided in Appendix E.

Participant confidentiality was maintained. Transcripts of the interviews were coded with numbers and locked in a cabinet where only the researcher had access to the actual data. The interview recordings were kept after the transcription process as the researcher needed to re-listen to the data several times to maintain rigour of data analysis. The records were discarded after the analysis and theme identification phase. Maintaining anonymity was challenging in this group as the number of patients enrolled in PGD is small and the genetic conditions are rare. Therefore, in an attempt to maintain anonymity, the researcher provided select information in the table of demographics of the participants. For example, the genetic conditions were grouped as neurodegenerative or metabolic rather than listing the exact conditions and the participants were coded as P1 to P14. In addition, the quotes were labeled as family and not participant and losses were described as "many" rather than stating the exact number. It is acknowledged that this may affect the validity of the study but it was thought that this was the best compromise to being transparent and protecting the participant's privacy. Participants were reassured that their data would remain confidential apart from possible future publication in a scientific journal, when names

or any identifiable characteristics would not be included. If distress was expressed during the interview, participants were referred for genetic counselling.

### 3.9. Risk and benefits to subjects:

Participants were informed that their confidentiality would be respected and data kept anonymous. As the researcher explored intimate and sensitive decisions, participants were assured that they had the right to choose to decline to answer any questions. In addition, early withdrawal from the study would not cause any harm or alter the provision of care. However, participation in the study would also neither benefit or privilege the individuals. All participants were treated equally and offered referral to counselling by a qualified genetic counsellor if potential harm or emotional distress was expressed.

### 3.10. Strengths and Limitations of the Study

As with all research this study has its own strengths and limitations and the details are discussed below:

#### 3.10.1. *Limitations*

- The use of a cross-sectional design meant that participants' experiences could not be assessed over a period of time. It is therefore possible that certain views may have changed over time;
- Sample selection was believed to include the informative families who experienced PGD. However, there could be a bias in selection as the samples were chosen based on the researcher's background and knowledge of the families based on her previous interaction with the participants;
- Although most of the invited candidates were willing to be enrolled in the study, the researcher experienced difficulties recruiting more than eight couples. The reasons related to frequent hospital appointments for their affected children or for PGD investigation, ongoing pregnancy or emotional distress due to failure of a cycle;
- Minimal literature was available on the experiences of PGD in Arab and Muslim societies, particularly in Omani patients. Therefore, a limited amount of data was available for comparison purposes.

Comparison with non-Muslim and other ethnic groups was possible but may not have been as informative;

- The researcher's level of counselling skills could have missed salient points.

### *3.10.2. Strengths*

- Each interview was conducted by the researcher in a venue of the participant's choice and in his/her first language;
- Face-to-face interviewing is known to improve response rates;
- Semi-structured interviewing is more flexible than a structured questionnaire and allowed participants the opportunity to express their personal views;
- Audio-recording of the interview reduced researcher bias in reporting the articulated interview as it captured the exact words of the participant and allowed for re-visiting of the data;
- Reflexivity of the researcher supported self-identification and was believed to reduce personal bias and subjectivity.

The findings of the interviews will be presented and discussed in the next chapter. Validation for the findings will be presented with quotes from translated interview. The results will be contrasted to the findings in the literature to identify similarities and differences with other PGD users from other countries. The presentation of the analysis, findings and discussion are combined in Chapter Four. This format is customary in qualitative research (McMillan & Schumacher, 2001) and prevents unnecessary repetition of information.

## Chapter 4. Results and discussion

### 4.1. Introduction

This chapter will describe the sociodemographic characteristics and reproductive history of participants. This study identified five main themes emerging from the data collected through interviewing couples who had experienced the process of PGD. Partners were interviewed separately; mostly on the same day. One couple was interviewed together (as discussed in chapter 3). Quotations from the participants' interviews have been included to enhance the validity of the identified themes. Some participants mentioned their history and for confidentiality, information that does not add value on the study or would not decrease the validity of the data, has been removed from the quotations. As discussed in chapter 3, translation for meaning rather than wording was conducted to reduce the chance of losing the nuances contained in the original meaning. The quotes used are therefore not verbatim. To maintain anonymity and ensure confidentiality, a code was assigned to each participant. The names of the disorders were not included as this is a small group of very rare disorders where individuals could be identified from this information (as explained in chapter 3). However, a general classification has been provided to offer the reader insight into the disease type and prognosis.

### 4.2. Description of participants:

All participants (n=14) were Omani Muslims of Arab descent who speak Arabic as their first language. Six couples out of eight families participated in the study. This section will describe participants in two separate tables; table (1) contains demographic information for each participant and is labelled with alpha-numerical code. Table (2) summarises the reproductive histories of all families. Separation of the tables was done to reduce identification of individuals by their reproductive history.

#### 4.2.1. *Demographics*

The age of participants ranged from 26 to 41 years with an average of 36 years for males (26 - 41) and 33.5 years (range 28 - 37) for females. The majority (57%; 8/14) of the participants had completed a college degree or higher diploma certificate and have a full time job with an average household income of 24,900- 46,700 USD per annum. According to the National Centre for Statistics and Information (NCSI) of Oman, yearly statistics book: 2016, the average Omani household income is 37,000 USD per annum (NCSI, 2016). Five (35.7 %) participants were school graduates in

full-time employment with incomes ranging between 15,500 and 23,800 USD per year (lower middle income) (NCSI, 2016). The only participant who did not complete schooling (for social reasons) runs a private family business generating an average income within the low income (11,444 – 15,588 USD annually).

Since the PGD procedure is very expensive (10,400 – 18,000 USD), financial assistance for the intervention was required by the majority of participants. The cost of the procedure, excluding travelling expenses, was close to half the average annual income. The majority of participating families requested a financial grant but only five (62.5 %) were eligible (had no living healthy child) and successful in obtaining financial assistance from the government. The remaining three families (37.5 %) who financed PGD themselves were from a similar income category. They were not eligible for governmental funding as they had one healthy living child. Table 1 summarises the sociodemographic information of participants.

**Table 1. Sociodemographic information of participants (n=14)**

	Age	Level of Education	Disorders	No. unaffected children	PGD cycles
<b>P1</b>	37	School	Neurodegenerative	0	1
<b>P2</b>	36	College	Neurodegenerative	1	1
<b>P3</b>	41	College	Neurodegenerative	1	1
<b>P4</b>	28	College	Metabolic	0	0
<b>P5</b>	37	College	Chromosomal imbalance	0	2
<b>P6</b>	28	School	Neurodegenerative	0	1
<b>P7</b>	34	School	Neurodegenerative	0	1
<b>P8</b>	37	College	Metabolic	1	0
<b>P9</b>	26	School	Metabolic	0	0
<b>P10</b>	35	College	Chromosomal imbalance	1	3
<b>P11</b>	40	College	Chromosomal imbalance	1	3
<b>P12</b>	37	College	Metabolic	1	0
<b>P13</b>	40	Did not complete schooling	Neurodegenerative	0	3
<b>P14</b>	34	School	Chromosomal imbalance	0	2

All families had at least one affected child with a lethal genetic disorder. Four families were at risk of having a child with an autosomal recessive neurodegenerative disorder (Aicardie Goutier, Warburg Micro syndrome and iron brain accumulation gyrate atrophy). Two families had a history of chromosomal imbalances due to a carrier parent (t (5:13) and t (15:18)). The remaining two families were at risk for an autosomal recessive metabolic disorder (Glutaric acid urea and hydrops fetalis due to a novel as yet unreported founder gene involved in metabolic / mitochondrial cardiomyopathology). The pregnancy-related history and clinical outcome is summarised in Table 2.

**Table 2. Summary of reproductive and PGD family history**

<b>Reproductive health status of families</b>	<b>No. of families/ 8</b>
Families with history of still birth/ miscarriage	2
Families with a history of neonatal death	1
Families with a history of early childhood death	2
Families with a history of adolescent death	2
Families never experiencing a loss	1
Affected with autosomal recessive condition	6
Affected with chromosomal imbalance	2
TOP	2
Approved for financial grant	5
Completed PGD cycle	6
PGD successful pregnancy	2
Interrupted by natural conception	3 (2 never started a cycle)

All the participating families were at different stages of the PGD procedure. Six had completed at least one cycle (75%) while two (25%) had not yet had a PGD cycle as they had conceived spontaneously before starting the IVF treatment. Another family had conceived spontaneously after several unsuccessful PGD attempts.

Despite counselling families at risk and emphasising the need to utilise different methods of birth control, unplanned pregnancies occurred in three families prior to initiating PGD (one had experienced previous unsuccessful cycles). This meant that

PGD had to be postponed until after the birth of the child. One of the three families had a healthy term child, one had an affected child and the other was currently pregnant (uncertain status). None of the participants requested PND. Interruption of a PGD cycle by spontaneous pregnancy is a common occurrence (Lashwood & Say, 2014; Lashwood, 2014).

#### 4.3. Themes identified

This section will discuss the themes emerging from the data collected through interviewing fourteen participants. Headings are organised according to the main theme and followed by the sub-themes. The themes were extracted by the researcher after reading the translated transcripts and re-listening to the audio-records several times (as described in chapter 3). Themes and sub-themes were validated by the supervisor and the co-supervisor. Themes are organised according to the stages of the PGD as experienced and reported by the participating families. The section headings describe themes as follows: the desire for healthy child; anxiety; unforeseen; secrecy and me and my partner. Excerpts from participants are used when appropriate to strengthen the argument and compared to the published literature when required to highlight any similarities or differences. Table 3 is a summary of the identified themes and sub-themes.

**Table 3. Description of themes**

<i>Theme</i>	<i>Sub-theme</i>
<i>Desire for healthy child</i>	<ul style="list-style-type: none"> <li>- Longing for a child (window of hope)</li> <li>- Can't have another affected</li> <li>- Avoidance of TOP</li> </ul>
<i>Anxiety "Taraqub"</i>	<ul style="list-style-type: none"> <li>- Road to PGD</li> <li>- Waiting for exam results</li> <li>- She was not herself</li> </ul>
<i>Unforeseen</i>	<ul style="list-style-type: none"> <li>- Loss of intimacy and autonomy</li> <li>- Piece of me</li> <li>- Never expected a failure</li> </ul>
<i>Secrecy</i>	<ul style="list-style-type: none"> <li>- PGD baby "Haram"</li> </ul>
<i>Me and my partner</i>	<ul style="list-style-type: none"> <li>- Impact on the relationship</li> </ul>

### 4.3.1. Theme 1

#### 4.3.1. Desire for a healthy child

In this study, the primary motive for undertaking PGD was related to a poor reproductive history. All participants embarked on the procedure of PGD based on their reproductive history of having an affected child or losing an affected pregnancy. Males and females agreed that the reproductive history was a primary reason for pursuing PGD.

##### 4.3.1.1. *Longing for a child (window of hope)*

All couples had between one and four affected children (Table 2.). Five families had no healthy living children before enrolling in PGD while three had only one healthy child. Patients who had experienced miscarriages or pregnancy losses were as motivated to undergo PGD as the couples who had lost children during infancy. Family 5 lost many affected children and expressed that the losses had motivated them to consider an alternative reproductive plan so that they could have a healthy pregnancy.

***” First time I heard about the treatment I was excited, it gave me a hope, a new hope, my main motive is that I don’t have many children now, I want to have children”*** (Fm5-M, lost affected term pregnancies, have one healthy child).

Another family who presented with multiple miscarriages and affected full term children (with survival limited to one month) expressed the importance of PGD consideration for risk avoidance:

***“I think any mature adult parent who has a genetic disorder and knows about this option should consider it rather than having an affected child”*** (Fm6-M, multiple miscarriages, lost affected term children).

Similarly, family 2 lost many affected children and found the option of PGD to be their only choice if they were to consider having more children. The family would rather avoid having future children than take the risk of having another affected child.

***“Living without a child is better than bringing to life another affected child. Definitely PGD is the window of hope for me and my wife and we will not stop trying”*** (Fm2-M, one live child, lost many children, experienced a PGD cycle).

Religious beliefs were a major driving force in pursuing PGD for all 14 participants. Having healthy progeny is particularly important in Islam as the main Islamic teachings encourage followers to maintain self, health, wealth, mind and progeny (El-Hazmi, 2009). Many (n=5) quoted phrases from the Quran or Hadith (prophet Mohammed's opinions) which say that having a large healthy family and many offspring is more favoured by God and the Prophet Mohammed who will be proud of them on the day of resurrection. This phrase was quoted by four males and one female participant.

***Messenger of Allah (peace be upon him) said, "Get marry and multiply, for I shall be proud of you in the day of resurrection".***

One of the participants stated that he would like to proceed with a second PGD cycle as soon as financially possible although his wife was content with one healthy child after their first PGD. He expressed that this was hurtful to him as he would have liked to have had more children. However, he did report that this did not raise conflict in their decision making.

***"Children are the wealth of the life. I would like to go for another cycle as soon as financially afforded, but my wife does not. This hurts me due to my longing for many children"*** (Fm1-M, lost affected children, went through a successful PGD cycle).

A small family size has a major psychosocial impact on many individuals from Middle Eastern and Muslim backgrounds due to cultural expectations and preference for having many children (El-Hazmi, 2004) and this was clearly observed in these families' motivations, as they reported the need to have more children.

A participant with one healthy child, had gone through several pregnancy losses as a result of natural conception and experienced multiple PGD cycles expressed her desire to have many healthy children and be a mother

***"My desire to be a mother cannot stop for one child, I will continue at least for one more and then consider permanent sterilisation /.../Time passes and I understand that as I get older the risk increase to lose my eggs and have more syndromes like Down syndrome plus my main problem. This pushes me forward to not stop searching for the chance"***. (Fm6-F, lost affected children and had multiple miscarriages).

Similarly, another family expressed their motivation for PGD is based on the desire to have a large family, however the male partner find his desire to be greater than that of his partner. However, the PGD process was later interrupted by a naturally conceived pregnancy.

***“It is natural to want to have many children, this is similar to one’s desire for wealth”*** (Fm5-M, lost affected children and PGD cycle is interrupted by natural conceiving).

It was previously highlighted that the desire for a biologically related healthy child, loss of at least one affected child, multiple miscarriages or experiencing years of complex medical and obstetric histories were the main reasons for considering PGD (Karatas et al., 2010b; Kalfoglou, Scott & Hudson, 2005; Lavery et al., 2002; Roberts & Franklin, 2004; Farra et al., 2008; Alsulaiman & Hewison, 2006). These factors also seemed to play a role in motivating families in this study as all of them had experienced at least one affected child or multiple losses at the same time it had delayed some families from parenting another child; thus delayed their PGD plan.

Some participant mentioned that despite the strong wish for a healthy child, it took them a while to consider parenting another child. They felt that they had a responsibility to their affected child(ren) as a result of the intensive care and medical attention required. The following participant describes the amount of suffering they experienced with their affected children, and how this made them defer having more children for couple of years:

***“The disease my children suffers is really horrible; the child is distressed and irritated all the time. Spasticity made the care very difficult, difficulties in feeding, washing, sleeping and even to get them calm. The required care keeps us occupied. We had to suspended our pregnancy plan for eight years, which deprived our desire to have many children”*** (Fm1-M, no healthy, many affected children, experienced a PGD cycle).

Procreation and establishment of a family is a fundamental purpose of marriage in Islam. The Quran itself describes both riches and children as “allurements of the life of this world” (18.46; 63.9; 64.15) and, at the same time, progeny is considered a blessing and a reward. However, when Islamic Shari’a suggested procreating, they emphasised the importance of the role of parents as the providers of adequate

nourishment, protection and wealth for their children so that they could be of benefit to the family and society. As a result, children would be raised as virtuous, civil and healthy, and therefore responsible in society (Atighetchil, 2007). On the other hand, Islam discourages raising children in situations in which they may become a source of harm to the society (Atighetchil, 2007). In The Holy Quran, Allah said: ‘Do Beneficence, Allah likes Beneficent people’ and the Messenger of Allah said: “The most gruelling trial is to have plenty of children with no adequate means.” This was also a motive to have healthy rather than many sick children which is non-beneficent to the family and the society.

Many Muslims believe the interpretation relates to having many children. Others refer to physical strength and health as being important in order to worship and be of benefit to the nation (Serour & Dickens, 2001). Utilising a procedure such as PGD was therefore particularly important to the participants, as it would ensure health in future offspring by being able to select against disease.

The desire for a healthy child was reported to be equally motivating for most partners. However, three shared a different view point - these cases had reported disagreements due to logistical issues such as financial burden and partner concern about the side effects of the treatment on his wife, as the following partners reported:

***“At some stages, I felt my partner is not motivated for a new cycle and takes me time to get the other party engaged but cannot say not supportive, he mostly thinks of the financial burden as well the side effects of the treatment on me”*** (Fm6 F; several cycles with no healthy embryos).

Overall, participants were equally motivated for PGD. There was no gender dominance although carrier partners (n=2) felt more motivated. In contrast to this finding Van Rij et al (2011) reported that females dominated the decision-making process in a cohort of Dutch PGD users (van Rij et al., 2011). Since the majority of couples in this study are carriers for autosomal recessive conditions, they may feel that they share the burden of being a cause of the defect in their progeny. In contrast in the Dutch group, 56% are carrier females while the AR carriers make up only 18% of the group. However the group in this study is small and the findings from the study may not be representative of the population.

#### 4.3.1.2. *Can't have another affected*

The experience of having an affected child was described as emotionally and physically draining and avoidance of similar suffering in the future (for both the parents and future children) was highlighted as a significant motivating factor (Farra et al., 2008; Lavery et al., 2002). A similar finding was identified in this study where most families had taken care of a chronically ill child who was frequently hospitalised and for whom there was no cure. For the genetic conditions included in this study individuals had a shortened lifespan, often associated with pain and suffering in the final stages of the disease. Family 4, who has affected children described the trauma of the child never achieving any developmental milestones due to the disease.

***“When I see other children play and talk, I feel sorrow for my children who never had such an opportunity and for me who never had the pleasure of the experience”*** (Fm4- F, had affected children, no healthy).

The couple in family 8 who lost a pregnancy presenting with multiple anomalies and had no living children found their experience was difficult and felt they could not go through it again:

***“It was a difficult experience; my first pregnancy took all the joy away. Every visit was to watch for death, more warning signs. No single sign of joy. It was horrible, I can't go through it again”*** (Fm8-F, lost a child with congenital anomalies).

This feeling was also reported by family 3 who had an affected child but had not experienced loss.

***“My first child was affected, we struggled for the diagnosis and on his care. We were afraid to have another child that can be similarly affected and live the same experience”*** (Fm3-M, have an affected child, but never experienced PGD as it was interrupted by an unplanned natural conception).

These participants felt overwhelmed by the thought of having another affected child and thought that it would be sensible to prevent suffering in a future child.

In addition, all families reported that having an affected child had changed their family and social dynamics. It was typical for the mother of an affected child to become more isolated and less involved in social activities and for the father to have frequent absences from work or be less productive in the work environment. One participant

expressed that his low productivity at work had become noticeable to his work colleagues after having several affected children.

***“I am not focused at work. My mind is scattered and my work colleagues noticed that I became less productive than before. My mind is always occupied by my sick children”*** (Fm4-M, had affected children, no healthy).

#### ***4.3.1.3. Avoidance of TOP***

Another motivating factor common to all participants was the avoidance of termination of an affected pregnancy. Three families (37.5%) had considered prenatal diagnosis in a previous pregnancy but had found travel abroad for a TOP overwhelming. Two families received a result indicating an affected fetus and terminated a pregnancy overseas. For both of these families the experience was distressing both due to the nature of the procedure and being unfamiliar with the foreign country’s healthcare service.

Here one of the couples described their experience with a TOP done abroad plus their experience of the loss. They feel they would not consider this option again:

***“It was difficult, very difficult experience. I can’t explain how much we struggled with the emotions of going through termination. I would not consider it again”*** (Fm4-F, had affected children, went through TOP).

This experience was similarly described as difficult by family 7 who lost multiple affected children in their first year of life and went through TOP following the news that another pregnancy was affected after undertaking PND.

***“It was difficult, too difficult to see your child die in your lap and there is nothing that you can do. We tried termination, and I am telling you it was the hardest experience we went through”*** (Fm7-M, lost affected children, has no healthy children, went through TOP).

Five families (62.5%) were from an Islamic sect that did not consider TOP an option. For these individuals PGD was the only option available to avoid affected children.

***“I am willing to go through 20 cycles rather than go through termination which I cannot accept morally or religiously”*** (Fm2- M, has affected children, went through a PGD resulting in no pregnancy). This family finds that TOP conflicts with their religious background and moral perceptions.

Views concerning TOP are strongly influenced by the perception of the period of ensoulment. TOP is permissible in certain Islamic sects prior to the period of ‘the breath of life’ however the interpretation of this ranges from 40 to 120 days. The majority of participants (57 %; 8/14) reported that their consideration of TOP was complicated by the uncertainty of the time period in which ensoulment could take place. Serour (2008), in the symposium of religion in assisted reproduction, stated that “Most Muslims adhere to the view that human life requiring protection commences two weeks from conception and uterine implantation” (Serour, 2008). The authors believe that few Muslims are aware that fatwas (Islamic permission) do exist that enable them to consider TOP until 120 days. All participants in this study were however aware of the permissible Fatwa. It is not unexpected that the study group was more informed than the general population given the fact that they had received extensive genetic counselling and maybe because they were educated and did thorough research.

In contrast to TOP, the religious guidelines concerning PGD in Islam are clearer as the majority of Muslim jurists approve PGD and IVF as not against the will of God and not modifying creation (Atighetchil, 2007). A consensus of several Islamic conferences encouraged PGD, where feasible, as an option for couples at exceptionally high risk to avoid clinical pregnancy termination (Serour & Dickens, 2001).

Participants had further researched information about ethical and religious aspects of PGD to aid their decision-making process. Three participants (21.4%) additionally contacted a religious scholar to obtain further insight into the religious acceptance of the procedure. However, another three (21.4%) reported that it was enough for them to receive the information from the genetic team.

Of interest is the fact that partners in some couples had different perspectives on the guidance from a religious leader. An example of this can be seen in the case below where, although the wife had contacted a religious leader for guidance of proceeding with PGD, her husband had based his decision on his own interpretation of Shari’a.

*“I believe every person should assess their family dynamics and consequences without crossing the red lines such as termination of pregnancy. I know that sometimes religious leaders are diplomatic and cannot give an open fatwa as a precaution of misusing the permissions. That is why reading about the basics*

*of Shari'a (Islamic Law) helped me to make my own decisions that suited my circumstances"* (Fm6-M, lost affected children, went through several PGD cycles).

#### 4.3.2. Theme 2

##### 4.3.2. Anxiety "Taraqub: Arabic metaphor"

###### 4.3.2.1. Road to PGD

PGD became an option to all participants once a genetic diagnosis was obtained. Many families (43%; 6/14) underwent a long journey to reach a diagnosis due to a lack of genetic facilities and resources in the country. The recent establishment of a genetic clinic in 2012 has enabled easier access to genetic testing in Oman (Rajab, Al Rashdi & Al Salmi, 2013; Al-Thihli et al., 2014). Following the diagnosis of a genetic disorder, families are counselled about the available reproductive options including PND and PGD. However, due to the restrictions on termination in Oman, PGD is often preferred and requested more frequently compared to PND to avoid moral and religious dilemmas (Bruwer et al., 2014). This was found in this group and discussed in the previous theme. Currently both options require travelling abroad and are associated with emotional and physical stressors. However, PND is associated with a lower financial burden on the family. Nonetheless, families who have experienced PND find it difficult to consider in future pregnancies (as discussed in theme 1).

All families learnt about their risk after having an affected child or pregnancy. The journey to diagnosis varied from four months to twelve years among families. As previously discussed, the availability of genetic diagnosis in recent years, and accessibility to expertise, enabled affected families to obtain a diagnosis more quickly than before. Furthermore, the availability of new testing techniques such as next generation sequencing (NGS) and whole exome sequencing (WES) increased the rate of diagnosis further. Being aware of the genetic diagnosis, and hence the recurrence risk, led families to consider alternative reproductive plans such as PGD. An example of this is illustrated in the following quotation:

*"We lost many children with the same disease and it took us more than 10 years to know what was going on. The first time we met the geneticist in this clinic three years back was the first time we heard about a potential diagnosis. She mentioned PGD and we felt this would be our hope to have a healthy child. It took*

*us two years to get an answer from the geneticist and after that we immediately started the arrangements for PGD”* (Fm2, lost affected children, unsuccessful PGD cycle).

Similarly, a participant who waited for five years to obtain a diagnosis for his affected children explained that the diagnosis helped them to consider an alternative reproductive option:

***“I had many affected, no diagnosis was available for more than five years. Once I got the diagnosis in 2013 and counselled about the option; I felt this is my best to consideration”*** (Fm4-M, had affected children, unsuccessful PGD cycle).

PGD is expensive and many couples found it overwhelming to consider such an expenditure. Six participants (43%) stated that the availability of the financial support from the government was a facilitator for considering PGD. Till early 2015, couples at risk with no healthy children were eligible for financial coverage of one PGD cycle. Couples who had been sponsored and experienced a failure, would have to consider self-payment for future cycles. However, due to budget constraints since mid-2015, caused by the decrease in oil prices, funding has been suspended.

***“I would not be able to make it without receiving the fund. However, for the next trial I will need more time to make my own budget. You know it is an expensive procedure”*** (F4M/F, no healthy embryos).

Drazba et al (2014) reported that “cost is salient” in decision making for PGD (Drazba, Kelley & Hershberger, 2014). The couples in Drazba’s study who lived in states with IVF financial coverage did not report cost as a concern while those who were not supported commented that cost delayed their decision-making process (Drazba, Kelley & Hershberger, 2014). Although financial funding was a facilitator in the current study, families who received governmental support had to go through a time-consuming administrative process. This meant waiting for the funds to be released before they could start the procedure. The average waiting time to start the IVF-PGD arrangements, among the participants who accessed governmental support, was one year. Four families took less than one year (four to six months) to start the actual procedure. Three of them were self-funded and one, despite receiving financial support and therefore being delayed by the lengthy administrative procedure, accessed PGD

earlier as no pre-PGD optimisation was required (they had a chromosomal rearrangement).

All participants suggested that the government should consider bringing the technology into the country to facilitate accessibility. The health care system should be made aware of the fact that the amount paid for PGD would be incomparably lower than the amount required for providing care to a chronically sick child with a genetic disorder necessitating intensive medical treatment and investigations. All Omani citizens are provided with full free health care for all medical appointments, treatments, interventions and hospitalisations. Therefore, participants in this study were surprised by the restriction of funding for PGD since they felt that PGD was a cost effective strategy. Couples emphasised that if PGD was subsidised it would significantly reduce hospital expenditure and the burden on the medical care system. This is clearly described by Fm2-M who was not granted funding for PGD because they did not meet the criteria even though they had lost many children with a neurodegenerative disease:

***“Having the support of the government would mean that less money would be spent treating an affected child. Look how much they paid to take care of my affected children while if I have the support for PGD they could avoid such an expense”*** (Fm2-M, lost affected children).

Tur-Kapa, 2010 suggested that providing PGD for American CF carrier partners would save 2.3 millions of dollars spent on providing care per affected individual for an average life of 37 years (Tur-Kaspa et al., 2010). Similar comments were made by the participants for a cost effective strategy plan. All participants recommended that the government should be more directly involved in establishing regulations concerning procedures required in the PGD and IVF process. Three participants (21.4 %) felt that they had undergone unnecessary investigations and that the centre may have had a more commercial (financial) rather than patient-based interest. Similarly, American PGD users in Kalfoglou’s study wanted regulations and guidelines but did not want them to be imposed by the government. The users argued that the government could make it too restrictive, reducing the chance of accessing PGD (Kalfoglou, Scott & Hudson, 2005).

Twelve participants (85.7%) recommended bringing the technology to Oman and establishing the service within the country. They considered travelling abroad an obstacle, even though this was only to a neighbouring country. For one family, the choice of centre was largely dependent on location so that they could travel back home and look after their affected children during the treatment period. Another family stated that they had to consider the proximity of a centre to reduce the time required to be abroad due to their work obligations.

In addition to the treatment itself, families had to consider the issues of travelling abroad such as choice of centre and accommodation. Some families selected a PGD centre due to proximity to Oman, either to reduce financial costs associated with travelling or because they needed to return to Oman to care for affected children:

***“We had to come in between to check on my children. It was not a good decision, but I couldn’t leave my children for three weeks”*** (Fm4 M/F, had living affected children). The parents were the primary carers and unable to leave their children in the care of others who were inexperienced with the disease management.

Another family reported that travelling abroad was physically draining:

***“We had to select a place that was close to the centre which was not easy as it was more expensive. As a result, we had to walk for more than 20 minutes every day including the day of the last injection and due to the hospital appointment it meant it was after midnight. We did not feel safe“*** (Fm1 M, successful PGD cycle).

This has also been highlighted in western populations where PGD was found to consume energy, time, attention and money (Roberts & Franklin 2004). These families were confronted with many stressful factors that they had to consider when undergoing PGD. All these add further stress to the already stressful treatment.

#### ***4.3.2.2. Waiting for exam results***

Anxiety was a persistent feeling during the treatment and found to be highest prior to and after implantation. High levels of anxiety were also reported during the wait for the test result of the embryos. Participants described waiting to hear if they had healthy embryos as “waiting for a final exam result”.

Similarly, another participant described the stressful time waiting for embryos test results as a hard time where the time moves slowly.

***“You feel the time does not move, hardly move in these five days”*** (Fm8-M, several unsuccessful cycles).

Similar feelings were expressed by a participant who went through several cycles before having a successful pregnancy.

***“It was the most difficult time, you went through all the effort, tolerated and managed the stress of the treatment and the travel, paid all the money and then waited for the outcome of this effort without having any input. As if you had a difficult exam and had to wait for five days counting the time waiting for the results”*** (Fm7-M, several cycles, successful pregnancy).

It had been reported that the anxiety prior to and after implantation of embryos (Järholm, Broberg & Thurin-Kjellberg, 2014; Karatas et al., 2010b; Karatas et al., 2010a). Many families find themselves confronted by the unavailability of embryos to be transferred (Karatas et al., 2010b) which was acute distresses and disappointment. This research did not focus of the level of anxiety and this area remains unexplored in our patients. Nevertheless, it would valuable for the future study to explore the levels of anxiety before and after embryo implantation in a larger sample.

Families who had healthy embryos described the waiting period before the pregnancy test as another stressful event. Some families who had a negative pregnancy test explained that despite the negative result, knowing the answer reduced the anxiety and afforded relief as mentioned by the couple in family 2:

***“You know, it is very stressful, but once you have the results you get less stress, no matter what is the result, just to know the result is a relief”*** (Fm2M/F, went through unsuccessful cycle).

In contrast to family 2's experience, the couple in family 7 felt distressed after a negative test and not relieved. Here they describe one of the failed trials:

***“When we received the test results, which was negative we didn't know what to do or what to say. We were confused, kept silent and went home. After that my wife was distressed for many days”*** (Fm7-M, went through several cycles, had one successful).

But they found the whole experience emotionally and physically stressful as did others who reported a distressing experience:

***“It was stressful time, not an easy step”*** (Fm4-M, unsuccessful PGD cycle).

Similarly, another participant who went through several unsuccessful cycles also reported that the experience was stressful. She was emotional while expressing her feelings as she recalled stressful memories. The researcher offered to stop the interview, but she expressed her willingness to continue:

***“I can’t say it was easy, it was too difficult and stressful (was emotional) I am sorry but it brought stressful memories”*** (Fm8-F, more than one cycle, no healthy embryos).

The couple who did not report a stressful procedure believed that their experience was in line with their expectations. They had a successful pregnancy which could have normalised their emotions or could have been due to good preparation as they reported. As mentioned in chapter 3, the female partner did not attend the interview, and she could have a different perception as it is usually the female who experiences the invasive and stressful treatment in PGD. However, the male partner explained that they read a lot and met with other families who had experienced IVF. Two participants who were cautious of the procedure delayed the start of the treatment as a result of their uncertainty and both of these couples became pregnant spontaneously and were unable to initiate a treatment cycle.

Despite the stress, PGD remains a better option for the majority. Eleven families would consider using PGD for future pregnancies (78.6 %) and expressed a strong desire to do so. For the three (21.4 %) that would not consider PGD for future pregnancies, the outcome of the procedure (being unable to achieve a healthy pregnancy) and financial burden were reported as the main reasons. Two couples had no healthy embryos following several PGD cycles. Both were reluctant to consider another PGD cycle due to emotional and financial concerns. Nevertheless, they reported that they did find PGD to be an easier option than TOP which was restricted in Oman and by their interpretation of the Islamic sect of their belief (Bruwer et al., 2014). One family who experienced TOP following a PND of an affected fetus still believe PGD is better but might consider PND again due to financial concerns. Similar figures were reported in Lavery’s study where 77% of the couples who undertook PGD would consider PGD again while only 15% would opt for PND (Lavery et al., 2002). In this study 78% of couples find PGD a better option for their next pregnancy.

However, this participant felt it would be emotionally overwhelming to go through another cycle after experiencing several unsuccessful cycles:

***“I went through many cycles; none had worked. It was difficult, very stressful and exhausting. I’m hesitant to have another one shortly”***. (Fm8-F, despite finding PGD stressful still believe it was easier than termination).

#### *4.3.2.3. She was not herself*

Four females reported that they had experienced mood swings and emotional fluctuation during the treatment. Some examples follow:

***“I read a lot, I thought I’m ready but I realised that there was more than that. It was painful and stressful”*** (Fm4-F, PGD cycle no healthy embryos).

Another participant experienced mood swings, pressure and stress during the treatment to the extent that she wanted to discontinue the treatment:

***“I had severe mood swings, I felt strong pressure and exhausted. I was about to stop the treatment”*** (Fm8-F, many PGD cycles no healthy embryos).

Interestingly, their partners reported that they observed this but that it had taken them time to connect it to the treatment.

***“She was not her usual self. She was totally different; mostly angry, anxious and tired. She spent most of the day sleeping and depressed. First few days, I thought she is psychologically sick, then I realised it is a side effect of the hormonal injection”*** (Fm4-M, unsuccessful PGD cycle).

Another male partner who observed changes in his wife was surprised at the beginning until he noticed these changes elevated after every hormonal injection. He then appreciated the stress his wife went through, became more tolerant and started to provide more support.

***“She was different, anxious, stressed and nervous. If you don’t appreciate what they are going through, you will lose it. I just had to be calm so she can be calm”*** (Fm8-M, many unsuccessful PGD cycles).

The PGD journey has often been reported as "emotionally draining" (Cunningham, Goldsmith & Skirton, 2015). Lavery et al (2002) identified that 41% of their participants found the treatment cycle to be extremely stressful (Lavery et al., 2002).

It is not unusual for couples to be emotionally affected during the PGD journey (Katz et al., 2002; Drazba, Kelley & Hershberger, 2014; Karatas et al., 2011; Karatas et al., 2010a). Similarly, couples in this study experienced the emotional burden of stressful treatment cycles.

Half of the families reported a painful experience as a result of side-effects or complications of the procedure. This participant who developed some side effects, did not require hospitalisation:

***“I had strong pain on my lower abdomen which increased with time. I reached the stage where I was not able to walk”*** (Fm8-F, several unsuccessful cycles).

While this participant developed chronic health problems after many PGD cycles, she expressed her desire for continuation of trials while her husband was concerned about her health status (as mentioned earlier).

***“I had different side effects, I developed a chronic vascular problem, my husband is always worried about my health and potential side effects “*** (Fm6-F, unsuccessful cycles).

Male partners also find it difficult to watch their wives going through such invasive treatment. This participant expressed his emotions about seeing his wife being given daily injections and undergoing thorough investigations:

***“it was hard for me to see her injected several times; daily injection for sixteen days: that was hard for me”*** (Fm-1-M, successful PGD cycle).

### 4.3.3. Theme 3

#### 4.3.3. Unforeseen

Couples undergoing PGD treatment experienced unexpected issues that they felt conflicted with their religious and cultural beliefs. Such issues had not been addressed in the booklets, websites and forums they researched and were concerning for them.

##### 4.3.3.1. *Loss of intimacy and autonomy*

Most participants (62.5%) realised that the procedure involved different teams which meant that their medical information had to be disclosed. Female participants felt uncomfortable being treated by a male doctor and expressed their preference to be seen by a female doctor. Male participants also reported that they felt uncomfortable with their wives being seen by male doctors although they accepted this as there were no

alternative options. The main practice and preference in Oman, based on Shari'a, is that female patients are examined by female gynaecologists and obstetricians. As a result, being examined by a male was not a comfortable experience.

***“...when they told, you have only one healthy embryo, my mind was occupied what if pregnancy does not happen and then my wife has to repeat the treatment and seen again by male doctors. It was harsh for me, but you know (sadly/.. /with slurred voice) I can't see another solution”*** (Fm1-M, successful cycle).

Gender preference of care providers by PGD users may be unique to this study as a result of the conservative religious and cultural backgrounds of the population group. Nonetheless, the topic remains unexplored in the literature.

Two families expressed the desire to be involved in the embryo selection decision. One of them wanted to select a non-carrier embryo with a gender different to their affected children as a 'fresh start'. They understood the disease was not linked to gender but felt that having a healthy child of the opposite sex would erase the painful image of the previous affected children. A couple may request the opposite gender to their affected child if, for example, it had an X-linked condition where they would consider avoiding a brother to protect the affected child from seeing a younger brother achieving what he would not do (Lashwood & Say, 2014). According to ESHRE guidelines PGD should not be used as a method to provide sex selection for non- health indications (De Rycke et al., 2015; Thornhill et al., 2005). This finding and that of Katz et al (2002) highlight the participant's interest in being involved in the selection process of embryos (Katz et al., 2002). The concern around implanting a healthy carrier has been raised in previous literature (Katz et al., 2002) and was raised by one participant who felt disappointed to know that a carrier embryo had been implanted.

Participants were also interested in being more involved in decisions related to their treatment process:

***“I wish I could have been given the chance to understand the treatment procedure. I felt that I had to follow their recommendations and go through steps whereas I read later that could have been altered based on my conveniences; like timings of the injections”*** (Fm2-, unsuccessful cycle).

This was not unique to this participant as Kalfoglou, Scott & Hudson (2005) had reported that their patients would limit questions to avoid being perceived as a difficult

patient (Kalfoglou, Scott & Hudson, 2005). The feeling of losing the control and autonomy to decide on the treatment was an unexpected issue and was inconvenient.

Likewise, men reported feeling shocked when informed that they would have to provide a semen sample. Those participants also mentioned that the request underscored the reality of the procedure - very artificial as compared to the natural conception process.

***“I was shocked when asked to provide a semen sample. It was not easy and made me feel insecure. I realised at that moment this is a very un-natural procedure, you cannot compare it to the natural procedure with warm feelings”*** (Fm1-M, a successful cycles).

Masturbation is against Shari’a law as it could lead to an illegal sexual desire. When sexual intercourse takes place within the marriage it maintains the legal sexual desire (Inhorn, 2007). This reflection was reported by Muslim males in Lebanon and Egypt, where they experienced anxiety associated with semen collection through masturbation for IVF. Their anxiety was compounded by the guilt associated with masturbation (Inhorn, 2007). Similar concerns were highlighted among the males in this study. Such a concern might be unique to certain religious groups such as Muslims and Orthodox Jews, due to their religious restrictions (Inhorn, 2007).

#### *4.3.3.2. A piece of mine*

Families who completed cycles of treatment and had fertilised zygotes felt some degree of attachment to the embryos. These participants reported that they felt emotionally and mentally attached to their embryos. Fm1-M described it as follows:

***“I followed them to the lab, wanted to see my embryos. I was not allowed. I wish they could show us the embryos and involve us in the selection procedure”***

Another participant who went through one cycle with no healthy embryos felt attached to the embryos and was described them as viable babies: ***“they are my babies in an incubator”*** (Fm4-M, had unsuccessful cycle). A similar finding was described were women call their embryos as live children (Karatas et al., 2010b).

Attachment was so strong that some participants reported that they wanted to implant an affected embryo when no healthy embryos were available:

***“They did test for everything (PGS) plus the mutation we have and we got one free of the mutation but the other test showed something wrong. My wife wanted to implant that one but I had to convince her that we came to avoid having a sick child.”*** (Family 4, unsuccessful cycle).

One couple, in separate interviews, expressed that they would struggle with the concept of discarding the embryos if they had been given a choice. They described the affected embryos as:

***“a piece of mine had been discarded”.*** (Fm8-M, unsuccessful cycles).

This sentiment was echoed by another participant (Fm6-M) who went through several cycles and experienced difficulties every unsuccessful cycle:

***“Went through several cycles and no healthy embryos, we came to select healthy however knowing that those, the affected, will be discarded, felt as throwing a piece of mine”.*** (Fm6-M, unsuccessful cycles).

Similar findings were reported among 62% of Saudi couples who felt attached to embryos, however did not mind discarding embryos (Alsulaiman et al., 2010). This could be explained by the main reason to undergo such an invasive procedure being to avoid having an affected child. Most families would not consider implanting a child identified with a potential disability. Such an attitude was evident in some couples in this study.

In contrast, some participants were confused as to how to deal with the extra healthy embryos. It was a dilemma for those travelling to Jordan, where the option was available. This was experienced by family7 who was hesitant to freeze excess healthy embryos. Although these individuals were initially against freezing, they were later convinced by the medical team to freeze their healthy embryos. As it turned out, the decision to freeze embryos was particularly important for this couple as the first implantation failed.:

***“I was against freezing embryos. I was worried about potential mistakes of mixing embryos as we had one healthy and I was afraid to keep it. Drs assured me about their storing procedure. Thanks God, I was encouraged by them and other families who had experience. That really helped!”*** (Fm7 had successful pregnancy after implanting a cryopreserved embryo from a previous cycle).

However, this is not an option for couples undergoing PGD in the UAE, where freezing embryos is restricted by Law (Inhorn, 2016). A couple who underwent PGD in UAE followed by unsuccessful implantation had to change their clinic to a country such as Jordan where they can cryopreserve their embryos.

***“ we had been in a country that restricted freezing (UAE) and we had no pregnancy. We thought as they implanted many embryos we will have at least one that may stick there, but it didn’t. The next plan is to Jordan where we can freeze if we had excess healthy”*** (Fm1F/M, unsuccessful cycle).

Moreover, couple who had implanted embryos felt attached to the healthy embryos when implanted and took extra precautions. These included the avoidance of sexual activity, hard work, heavy lifting and some foods that are culturally believed to cause miscarriage as shared by this participant:

***“I was taking extra care after returning my eggs, I was even avoiding some food my friend was restricted to eat when she was pregnant to avoid miscarriage”*** (Fm2-F, had implantation, no pregnancy).

Participants expressed attachment to the healthy implanted and frozen embryos but did not object to discarding the affected embryos as they believed the purpose was to avoid an affected pregnancy:

***“I feel attached to implanted embryos and I take precautions when implanted, however, I have no objection to discard the affected as the affected embryos are meant to be avoided”*** (Fm6- F, went through several unsuccessful PGD cycles).

Attachment to transferred embryos in PGD was less than that with IVF (Karatas et al., 2010a). This can be corresponding to the motive behind the IVF/PGD; as achieving pregnancy in the IVF and looking for a healthy child in the PGD (Karatas et al., 2010b).

Overall participants felt attached to their embryos at different levels; prior and after implantation. Some had been attached even to the affected embryos. However, to the researcher's knowledge, no study has examined the attachment of PGD couples to their healthy versus affected embryos. This could be another area for research and study.

#### 4.3.3.3. *Cannot remember a failure rate*

Most participants understand that PGD is a means of achieving a healthy baby. The majority were not concerned about the technical aspects or success rate before starting the procedure and were focused on achieving their main target: having a healthy child. It is common for couples undergoing PGD to believe that it is a promise of having a healthy child and not just a method of avoiding a disease (Karatas et al., 2010b; Järholm, Broberg & Thurin-Kjellberg, 2014). Despite being counselled about the success rate the couple can figure the reality when they experiencing failure of a PGD cycle. Some examples of this are seen below:

***“I never expected a failure. It was too harsh to hear it. I don’t think I heard the potential of failure before, maybe I didn’t want to. Please advise people in my position not to be optimistic”*** (Fm4-M, lost affected children, went through PGD cycle resulted in no healthy embryos).

Achieving an unsuccessful pregnancy after implantation was also reported as an unexpected event. This can be correlated to the prior expectation of a high success rate as previously discussed.

***“when we had the genetic results, we were very enthusiastic and rushed in the arrangements for a PGD cycle. I was too optimistic that by the end of the treatment, I will have a healthy baby. I can’t remember anything about the failure risk”*** (Fm2F, lost affected children, went through PGD cycle with no successful pregnancy).

Another participant who believed the success rate was 80%, but he was shocked with the failure and figured it can be only 20%:

***“I heard the information of low success rate; however, in my mind this was up to 80% or more. May be I was very enthusiastic and pushing to undergo the treatment”*** (Fm2-M, lost affected child, went through PGD cycles with no pregnancy).

***“I never expected to not have a healthy embryo. All my thoughts were how to prepare for the coming baby and what the name would be”***. (Fm4-F, had affected children, PGD cycle no healthy embryos).

Although this participant acknowledged that the failure rate had been discussed in several counselling sessions, the hope for success and a healthy pregnancy remained.

The higher expectation of success rate, despite extensive counselling, has been reported by other PGD users (Kalfoglou, Scott & Hudson, 2005; Karatas et al., 2010b). Furthermore, couples may believe that failure rates may be lower for them as they do not present with infertility concerns. However, many publications report a lower pregnancy rate within the PGD group as compared to the IVF group due to the exclusion test to avoid the genetic risk (Kuliev & Rechitsky, 2015; Lashwood, 2014; Moayeri et al., 2016). This research finding finds similar attitudes of couples towards the expected success rate. Couples could be strongly driven by the end outcome hoping for a successful pregnancy.

***“I used to believe it is 90% successful, after many trials, I came to believe it is less than 50%. But I am still motivated even with lower chance”*** (Fm8-M, went through many unsuccessful trials).

#### 4.3.4. Theme 4

##### 4.3.4. Secrecy

###### 4.3.4.1. PGD child “Haram” (sinful)

Cultural acceptance was found to vary based on the perception of other family members. For example, if a family member had experienced infertility and therefore utilised IVF, PGD was acceptable within the family or surrounding society. In this situation, the couple would openly share their intention for using PGD to resolve their genetic problem. However, if the couple were the first to undergo such a treatment within their surrounding society or social network, they were more reluctant to share their intention of undertaking PGD. Initially they faced the difficulty to ask their parents for DNA samples; as a requirement for pre-PGD optimization. Some explained that this is requirement to establish a genetic diagnosis. As stated:

***“ we didn’t want our parents to know. We told them we want to know what is the genetic problem; which is the truth for our future children”*** (Fm3 F/M, interrupted).

For those couples (62.5%; 5/8) who had not informed any family or did not openly discuss the use of PGD, the main reason for non-disclosure was for the benefit of the child so as to protect him/her from possible stigmatisation in the future (by the family members or society in general).

For instance; this participant expressed that he would not share the uptake of this treatment with any of his circle as he believes people can be judgmental since they don't know about their major problem and what the alternative would be:

***“I’m quite sure that this is the best option for me. However, I will not disclose it with any, even my parents, you know, I mean people can be judgmental and stigmatise the child in the future. So if I keep it secret, it is for the child’s protection”*** (Fm6-M, lost affected children, unsuccessful PGD).

Similarly, another participant feels that she wouldn't mind disclosing the information if society is well aware that this is a treatment and is allowed, not forbidden, in Islam. She herself had heard people describe the child born through IVF as a “Haram” baby. Therefore she would keep it secret as she wanted to avoid the child being stigmatised.

***“I am happy to educate people about PGD, to advocate for this treatment as any other treatment, but at this stage I cannot risk my PGD child to be stigmatised in ignorant society /.../I wish I can go out in public or out in the media and talk to people telling them that PGD is a treatment, not a luxury selection. I wish I can correct their perceptions that this is something correct under Islamic permission and not Haram (Haram: forbidden in Islam which can be sinful) to do it”*** (Fm3-F, PGD interrupted).

Another family believed that there was no advantage to disclosing the fact that they had gone for PGD. They are comfortable sharing with relevant people like health care providers or religious scholars, but it would be unnecessary to share with other people. As stated:

***“You are a health care provider and he is a religious leader, other than that no point to share even with my siblings and my friends”*** (Fm7-M, had a successful pregnancy after different trials).

Family 5 also shared similar concerns were they believe that the PGD child could be stigmatised as a designer baby.

***“ I know people who labels that child as the designer baby or tube baby or Haram baby, many labels. I am not happy to inform. This is very private issue where me and my wife decided not to disclose with anyone”*** (Fm5, interrupted).

Although the majority of participants expressed their concern about society's perceptions, disclosure to parents and close siblings did occur. This was reported by a participant who did thorough reading and understood the risk of the treatment to his wife. Therefore, he had to inform her parents and ask for a permission:

***“I informed my wife’s parents. It is a responsibility that I am taking her for a treatment; which has many side effects and complications; what if something wrong had happened! I wanted their approval and they didn’t resist. I urged them not to share the information to anyone”.*** (Fm1-M, successful pregnancy through PGD).

The reported perception contrasts that of the Saudi couples in which 100% of the studied group stated that their extended family and friends were informed and supportive of PGD/IVF (Alsulaiman et al., 2010). This could be because the PGD service is established in Saudi whereas in Oman it is relatively unknown. This could have played a role in cultural awareness and acceptance.

#### 4.3.5. Theme 5

##### 4.3.5. Me and my partner

All participants except two reported that their journey through IVF-PGD had strengthened their relationship. They believed that the struggle provided them with a greater appreciation of their partner. In a third of the participants in Lavery's study the treatment had a negative impact on their relationship, while for the other third it brought them closer together (Lavery et al., 2002).

***“though I was stressed, but I tried to hide my worries to make my wife calm. It wouldn’t work if both of us were nervous, someone should be calmer and support the other”.*** (Fm8-M, many unsuccessful cycles).

Participant (Fm8-M) felt the experience had brought him closer to his wife and strengthened his faith in God. He expressed that his faith had strengthened and also helped him to tolerate the stress and understand his wife's stress during the treatment (mentioned earlier). His wife reported independently that his faith was a big help and support for her during their unsuccessful experiences (Fm8-F).

***“His faith was a power for me. He was always positive and able to keep me calm and renew my hope”*** (Fm8-F, went through several unsuccessful cycle).

However, one partner reported PGD to be a burden on their relationship as the carrier partner was preoccupied with having a healthy child. In his opinion, this led her to ignore the potential side effects and harm that could occur from repeated cycles. This partner also believed that the financial burden had acted as an additional stressor on their relationship.

***“I believe it was the obsession to have another child and ignored other important things. Going for consecutive cycles without considering the risk and not even consider the financial burden and the time required”.*** (Fm6, went through different unsuccessful cycles).

As discussed before, in Middle Eastern societies procreation is highly valued and can therefore influence the dignity and self-esteem of a woman if she cannot bear healthy children (Serour, 2008). In contrast, an infertile man is not faced with the same pressure due to societal privileges. Furthermore, the blood line is culturally important in the Islamic societies where it serves as a strong ideological support of a progeny kinship for the paternal family. In addition, males are allowed to marry a second wife if the first is unable to achieve a pregnancy (Inhorn, 2007).

One participant reported that their relationship was under strain due to the accumulation of stressful circumstances of unsuccessful PGD in addition to the burden of having many living affected children and the amount of care that this required. On the other hand, the partner did not report a threat to their relationship, but did express a stressful dynamic.

***“me and my partner went through a very stressful life full of challenges, every child born was a shock, all came sick. We never thought to break our relation. As the life goes on, we accepted our fate, tolerated the pain and continued the care needed. Now we were hoping for a big success, but it did not happen. The treatment was stress, a big stress”*** (Family 4, affected children, PGD cycle, no healthy embryos).

Two participants described their experience with an impression of happiness and satisfaction, however this was not surprising as they were from families who had had a successful pregnancy. Unfortunately, the wives of both couples were not available and the female’s perspective may have been different.

Four participants out of the ten who completed treatment stated that they had a good experience (40%). Two of them (20%) felt it was a “good start” which gave them

insight and improved understanding of the treatment. Although the couples were unsuccessful in achieving a pregnancy they were motivated to continue with another cycle. The other two felt that PGD was an acceptable experience but disappointing as they were not prepared for the unsuccessful outcome. One participant felt it was just a solution, and the experience was fine while the partner felt it was exhaustive. In contrast, one couple felt it was a difficult experience.

***“It was difficult, very difficult. Emotionally and physically. I had lots of embryos and none were healthy. I had to be in a treatment that caused many side effects. I had to be in all this stress and the result was distressing”*** (Fm4-F, went through PGD cycle with no healthy embryos).

Overall most families (60%; 6/10) reported that the treatment experience was stressful. The two participants with the successful pregnancy were motivated and happy. As expected, families with no healthy embryos or where healthy embryos had failed to implant were disappointed. The reported perceptions are congruent with other studies where couples describe the experience as distressing or joyful depending on the outcome (Järholm, Broberg & Thurin-Kjellberg, 2014; Lavery et al., 2002). Some participants felt that they would be more anxious if future trials were to be considered. In general, disappointing news associated with unsuccessful PGD cycles correlated with the length of time required to make a decision for another trial. This was seen in three of the four families with an unsuccessful outcome. Two participants felt that they would not be able to tolerate another cycle if it did not result in an unaffected pregnancy. As a result, they considered natural conception for the future pregnancy hoping for the 75% chance of having an unaffected child (as for autosomal recessive inheritance).

***“I still find PGD best option, I’m not sure if I am ready to go again for my next pregnancy. I will go for a natural pregnancy, though I am concerned about taking the risk. Yes, we have 75% opportunity for healthy, but I never had it. PGD also was disappointing”*** (Fm4-F, had affected, no healthy, unsuccessful PGD)

Two of the couples, who went through unsuccessful trials, wanted to delay the decision before considering another cycle. All families, including those who oscillated between PND and PGD, considered PGD the best option for future pregnancies. Six participants associated the actual decision with availability of financial resources (42%). On the

other hand, some linked the next plan with their emotional readiness (21.4%; 3/14). Two families were waiting till after delivery (naturally conceived pregnancy) before considering arrangements for future PGD plans. The participant who felt that repeating PGD 20 times (mentioned earlier) would still be better than having an affected child, emphasised that the PGD stress was short lived while living with an affected child could bring suffering and stress for years:

***“the stress of living with an affected child stays for years. It is very difficult to see your children suffer. Yes, PGD is stressful but still better than having another affected child”*** (Fm2-M, one healthy, lost many affected, unsuccessful PGD cycle).

As reported in many studies, the burden of having an affected child motivated the family to consider PGD (Alsulaiman & Hewison, 2006; Farra et al., 2008; Järholm, Broberg & Thurin-Kjellberg, 2014; Kalfoglou, Scott & Hudson, 2005; Karatas et al., 2010b; Lavery et al., 2002; Wah Hui et al., 2002). However for some families, if that desire cannot be achieved through PGD, they would rather not have a child who might be at risk to be affected.

In general, Participants reported stressful experience of PGD motivated by desire for healthy child, avoidance of termination which conflicts with their religious beliefs. They experienced anxiety during several stages of the treatment procedure, and mostly to the embryos and pregnancy test. They were confronted with unforeseen conflicts with their religious and cultural backgrounds such as insemination, loss of intimacy and freezing or discarding embryos. Majority of the families consider the treatment very private and were secretive to avoid society stigma on the child. Despite having a stressful experience most families felt it brought them closer and strengthen their relation. The trauma of distressing outcome had impacted negatively on some participants as they felt overwhelmed and hesitant to consider another cycle. Nevertheless, even oscillating between PND and another PGD, 78% would consider PGD as their preference for future pregnancy. All participants would recommend PGD as an option for families who suffer from a genetic problem. Two participants were motivated to become a support resource for other families considering PGD. Of importance, none of the participants discouraged others from considering PGD as an option despite their stressful experiences.

## Chapter 5. Conclusion

### 5.1. Introduction

This chapter will discuss the conclusion of the study findings and recommendations for future practice. It will also provide suggestions for potential areas for further research.

### 5.2. Conclusion

The aim of this study was to explore the experience of Omani families who have elected to undergo PGD as a means for reducing the risk of having a child affected with a genetic disorder. The service of PGD is very new to Omani patients and the factors that affected the decision making, facilitators and obstacles had not been explored before. Therefore, understanding these factors might help to improve the current service. The current research is thus valuable as it highlighted these issues. Furthermore, the study explored these families expectations of PGD and the impact of their preconceived ideas on their real experience.

This study was conducted using semi-structured interviews with fourteen participants from eight families. Five main themes were identified from the collected data:

- Theme one was the desire for healthy child, which was considered the main motivating factor for PGD. It was chosen to avoid a stressful reproductive experience considering the restriction of TOP imposed by their religious belief. The desire to procreate was encouraged by religious and cultural mores.
- Theme two was anxiety during the whole journey of PGD due to: waiting for the genetic diagnosis; waiting for financial grants; waiting for enrolment at the PGD centre and having to travel abroad. It was found that although couples long for a healthy child, the amount of time and care dedicated to the affected child played a role in the timing of PGD. It also affected the selection of the centre as some families had to consider neighbouring countries so that they could visit their children when necessary. Couples found themselves being nervous and anxious during the entire lengthy treatment. They also reported stress during the procedure because of side effects from the treatment. The biggest concerns were for the status of embryos and their suitability for implantation. This was reportedly as stressful as waiting for pregnancy test results. Sixty percent of the participants who completed at least one PGD cycle felt the treatment was stressful.

- Theme three was the unexpected traumatic experiences, such as loss of intimacy and privacy, masturbation for “semen sample collection”, freezing or discarding of embryos and unexpected attachment to their embryos.
- Most participants considered the PGD-IVF treatment private and dealt with it secretly. This was addressed in the fourth theme where 62% of participants believed that they could be stigmatised for undergoing unnatural procreation and that their child could be labelled as a *Haram* ("sinful") baby.
- Theme five describes the impact of the treatment on the participants' relationship. Most reported that the treatment brought them closer and made them more appreciative of one another. However, three felt the treatment experience was sometimes stressful enough to negatively impact on their life dynamic.

Although this study focused on a small group of PGD users in Oman and reported on the experiences of a single hospital centre, valuable insights have been identified. Nonetheless, the findings of this study cannot be generalised to PGD users seen in other hospitals or from other Middle Eastern population groups. Further study would be required to research these aspects. It would also be useful to explore the correlation between the natural history of a disease, reproductive history, recurrent miscarriage and termination of an affected pregnancy in terms of their roles as facilitators or barriers to PGD in a larger cohort.

### 5.3. Practical implications and recommendations

In the current study, some participants recommend having a centralised service with a clear referral system/pathway for communication and arrangements through genetics, obstetrics and gynaecology and the IVF-PGD centre (50%; n=7). They felt that there was a gap in counselling regarding the minor details of the IVF treatment (P3 and P6). However, most had reported that the current service was satisfactory and supportive. Perhaps it would be important to create awareness of the role of the genetic clinic being limited to providing genetic counselling about PGD testing, limitations and required referrals, while the IVF treatment should be discussed by the IVF-PGD centre. Incorporating the recommendations made by the participants as well as those identified by the researcher into service development for the PGD clinic at the GDM will

contribute towards an improved understanding of PGD and enhanced genetic counselling service. These suggestions include:

- a discussion of the experience of PGD based on previous users perspectives during the PGD counselling session. This could incorporate discussion about difficulties, stressors and unexpected experiences. Providing this information will aid couples in making well-informed decisions and in understanding the procedures;
- increasing public awareness and acceptance of PGD through social media, press, magazines, radio, e-forums and the internet;
- providing an information booklet with detailed descriptions of the PGD/IVF procedure and its limitations. The researcher has started compiling these booklets by contacting the PGD centres for information to be included. These booklets will include general information on the technology, treatment, preparations and investigations required, prices, time required for the treatment and the potential outcomes. It will also highlight salient topics raised by participants. The booklet will also contain religious perspectives on embryo selection, cryopreservation and masturbation which was found to be crucial for families awareness and preparation. The booklet will be available in Arabic;
- connecting new families considering PGD with the participants from this study who expressed interest in sharing their experiences. Being able to discuss the procedure with other families who have undertaken PGD will be important in facilitating decision-making. In addition, as families often keep their PGD procedure a secret from their own relatives, this will provide an additional means of support;
- the development of a flow-chart and tick-sheet of all the steps related to the PGD journey, which is lengthy and involves individuals being seen at multiple centres with different specialists. This will promote transparency around the service and procedure and prevent confusion;
- standard letters of support, for use to obtain financial assistance, are now offered to all families seen for genetic counselling of PGD since identifying this need in the study. These letters include information on the inherited nature of the disease, recurrence risk, lack of treatment as well as reasons for undergoing a PGD procedure.

Apart from concerns about PGD, three participants recommended creating public awareness about the importance of premarital genetic testing. These participants felt that it should be mandatory as is the case in some other Middle Eastern countries. Many countries in the Middle East have established compulsory premarital screening for haemoglobinopathies (sickle cell anaemia and B-thalassemia). To the researcher's knowledge, none of these programs achieved more than the 43% recurrence reduction of B-thalassemia which was reported in Bahrain (Saffi & Howard, 2015). Some countries such as Saudi Arabia, Iraq and Jordan reported that social pressures resulted in more than 80% of at risk couples not cancelling the marriage. Stressing the importance of providing PGD services might alleviate the recurrence burden from at risk couples who would not consider marriage cancellation due to social influences.

However, as this is one of the cornerstone strategies for the GDM clinic, building data for the common mutations would provide support for future premarital screening programs. At present, the PGD clinic offers targeted familial preventative programs. This embraces recommendations to create awareness among affected families for the importance of premarital genetic testing to reduce the burden of recurrence.

Some participants recommended avoidance of consanguinity (P1 and P7), while one participant promoted awareness of the importance of genetic counselling among his social circle (family, friends, neighbours and work colleagues) (P1). These individuals recommended avoiding intermarriage, using their own experience as an example.

#### 5.4. Recommendations for further study:

Based on the outcome of this study, the following points are recommended for future research :

- A longitudinal research study to explore the impact of the PGD experience at different stages of the treatment.
- A study on the process of decision making perhaps with a larger sample size to identify facilitators or barriers on the decision to undergo PGD.
- An in-depth study to measure the impact of factors such as natural history of the disease, miscarriages and PND experiences on the desire for PGD
- Further study to understand the perceptions of families who deferred PGD despite prior counselling. Understanding their viewpoints could help in further refining counselling practice.

- Further studies on couples who undertook PGD through different institutes to compare their experiences with the current study.
- In-depth study on the families who underwent unsuccessful PGD cycles, exploring how that impacted their future reproductive plans and motives for PGD.

In summary, participants reported stressful experiences of PGD motivated by the desire for a healthy child and avoidance of termination which conflicts with their religious beliefs. They were anxious throughout the treatment procedure, mostly due to worry about the embryos and the pregnancy test. They reported unexpected conflicts with their religious and cultural backgrounds including masturbation, loss of intimacy and freezing or discarding of embryos. Most of the families considered the treatment very private and were secretive to avoid societal stigma towards the child. The trauma of an unfavourable outcome impacted negatively on some participants, leaving them feeling overwhelmed and hesitant to consider another cycle. Nevertheless, 78% would prefer to consider another PGD before PND for a future pregnancy. All participants would recommend PGD as an option for families who suffer from a genetic problem. Two participants were motivated to become a support resource for other families considering PGD. Importantly, none of the participants would discourage others from considering PGD as an option despite their stressful experiences.

As this is the first in-depth qualitative study on Arab Muslim PGD users, many unique viewpoints were identified which need to be considered in future counselling of Omani couples considering PGD. These include issues that had not been addressed in previous counselling or reading materials provided prior to the PGD procedure. Being unprepared was traumatic for couples when it conflicted with their religious and cultural beliefs. Societal and religious beliefs on procreation, the desire for large families, and procedural aspects such as masturbation, embryo selection and cryopreservation were found to be major issues affecting Muslim PGD users.

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## Appendix D:

### Interview questions in English

The experiences of couples undergoing Preimplantation Genetic Diagnosis (PGD) at the Genetic and Developmental Medicine clinic, Sultan Qaboos University Hospital (SQUH) in Oman.

#### **Objectives:**

- Describe the reasons and motives for pursuing PGD
- Describe the participants' perceptions and expectations before enrolling into the PGD procedure.
- Explore the participants' experience of PGD enrolment and procedures.

#### **Interview questions**

##### **A. Demographic**

Age:

Education

Number of children:

Number of affected children (alive/dead):

History of miscarriages, stillbirths, etc. :

Name of the genetic disease:

Number of affected vs healthy

Name of the disease:

Region:

Stage in process

How many cycles

##### **B. Motives**

#### **1. Can you please tell me the story of your PGD?**

The researcher started with one open ended question like this one and the rest below will act as guide lines [As the researcher gained experiences with interviews, the researcher was able to pick up on issues as the participants speak].

If the answer of the main open ended question is not sufficient, the questions below were further used.

1. What options did you have for reproductive planning?
2. Would you consider any of these options (options besides PGD)?
3. Why did you decide on PGD?

4. Could you please describe what you understand about the actual PGD process (what PGD testing entails)?
5. Can you tell me about your view on PGD in terms of a religious, moral and cultural acceptability?

**C. Decision making experience**

1. Currently at what stage are you in the PGD process?
2. How long did it take to reach this stage (from the time you decided to undertake PGD)?
3. How do you feel about PGD now? (anxious, excited, upset, scared, nervous, hesitant, etc)?
4. Was there anything that made it easier to reach this stage of your PGD process (facilitators)?
5. What are the difficulties (barriers) you faced in reaching this stage of the PGD process?
6. What do you expect will happen next?

**D. Social dynamics**

1. In your social network did you discuss your PGD plans with anyone?
2. Did you receive sufficient support from your family and, or friends?
3. Which of both partners had the strongest wish for PGD? (male, female, both).
4. Did the experience impact on your family, marriage relationship, children, parents and siblings?
5. Did you receive sufficient support from professional team?

**E. Recommendations**

1. Overall, how do you describe this experience?
2. Do you recommend this option to others?
3. Has your experience been very different to your expectations?
4. How has the experience affected you?
5. Will you consider this option for your next pregnancy plan?
6. Do you have any recommendations or suggestions to improve the experience?

**F. Miscellaneous:**

- G. Would you like to share anything else related to PGD which you think might be useful for all of us?

## Interview questions in Arabic

### أسئلة ل قابلية

لوسة ت حبة ال عال ت التي اضا رلت لت لقي لهن ناع ي م ع ل ف حص قبال ل غر سول ك ي لة ل ل انجاب عن طريق ع ي ادة ال طب ال ورتي والتطور ي ب م س ت ف ي ج ا م ع ل ل ل ط ن ق ب ل و س

#### 1. ب ي ان ت ش خ ص ي ة

ال عمر :

ال ض ع ق ة :

م ح ل ة ال ط ف ي م :

ع د د ال ط ف ال :

ع د د ال ط ف ال ال ص ب ا ي ن ( ي ق ي ال ح ي اة / و ي ق ب ي ن ) :

ع د د ال ا ج ص ل ات / و ف ي ات ال ا خ ة :

ا س م ال م ر ض ال ل ش خ ي ص :

م ح ل ة ال ج :

ع د د د و ر ات ال ج :

#### 2. ل د و ف ل و ل م ح ر ك ات

1. ال ا ض ت و ن ي ن م ف ض ل ك ع ن ت ح ب ي ت ك م ع ال PGD؟ ال ب ا ح ش ه ي د ب ه ذ ل س و ال ال ف م و ح و ال ف ي ق ه ت غ ط ي

ا ج ل ت ه ف ي م ع ط م ق ا ط ال ح ش ف ي ح ل ة ع م ا س ت ف اء ال ا ج ل ق ي ل ج ل ل ا ح ث ل ل ا س ن ل ة ال م ك و ر ة ا د ن ا ه .

2. م ا ه ي ال خ ي ا ر ات ال ه ت ال ح ي ك ف ي خ ط ة ال انجاب؟

3. م ل ل ع ن ت س ق ت ا ر ا ي ا م ن م ذ ه ال خ ي ا ر ت ب ال ل ا ف ا ل ة ال PGD؟

4. ل م ا ن ف ض ل ت ه ل ل خ ي ا ر ؟

5. م ل ب ال ه ا ن ك ا ن ت ص ف م ا ذ ل ت ع ر ف ع ن خ ط و ات ال PGD ال ف ح ص ال ذ ي ت س ع ل ه ؟

6. م ل ب ال ه ا ن ك ا ن ت ض و ن ي ع ن و ج ه ق ن ظ ر ك ح و ل ال PGD م ن م ح ث ال ت ق ب ل ال ه ي ن ي ؟ ا خ ال ق ي ؟ و ال ا ج م ا ع ي ؟

#### 3. م ح و ب ة ص ن ع ل ق ر ا ر

1. ف ي ا ي م ح ل ة ل ت ال ا ن م ن م ر ا ح ل ال PGD ؟

2. ك م ال م د ة ال ز ي ن ة ال ي ا س ت غ ق ت ه ل ت ص ر ل ل م ذ ه ال م ح ل ة ف ي ذ ل ك خ ذ ت ل و ا ر ب ل ت خ ي ا ر ال PGD ؟

3. م ا ت ح س ال ا ن ب ش ا ن ال PGD ؟ م ت ح م س ؟ م ت خ و ف ؟ م ت ر د د ؟ م ت م ر ي ل ق ل ق ؟ م ت و ت ر ؟

4. م ل ك ا ن و ا ل ك ع و ا م ل م س ت ع ل ق ل و ص و ل ل م ذ ه ال م ر ل ج ة ؟

5. م ا ه ي ال ص ر و ع ا ت ال ت ي و ا ج ق ا ل ا ل و ص و ل ل م ذ ه ال م ر ل ج ة ؟

6. م ا ن ت و ق ع ي ال م ح ل ق ل م ل ة ؟

#### 4. ل م ح ا و ر ال ا ج م ا ع ي ة

1. م ع ن ت م ا ق ش ت ع ن ال PGD ف ي م م ح ل ق ا ت ك ال ا ج م ا ع ي ة ؟

2. م ل ل ي ك د ع م ا ج م ا ع ي ال ف ل ي ؟

3. ا ي ال ز و ج ي ن ك ا ن ل ه ال ر ي ف ال ق ي ف ي ل ت خ ي ا ر ال PGD ؟

4. ما هو نتائج هلكت جبة نعى اللعزل؟ ال القة الأسرية والزوجية؟ لوالين؟ الأخوة؟

5. لى فئدر نلت جبة عليك؟

6. لهت اقيت دعم كاف من لاطاقم للابى؟

#### 5. نوصيات

1. بهفة عامه لى فئتمس قللت جبة؟

2. هل رشح هذال خيار آل خرين؟

3. هل كنت جيتك ختفة جدا عن توقعاتك؟

4. لى متختر هذال طويق اقل حم للاق ادم؟

5. هل لىك قترحات أوتوصيات لتطوير الخدمة؟

## Appendix E:

### Invitation for participation in English

I am Khalsa Al-Kharusi, an Msc student in the MSc genetic counselling program at the Division of Human Genetics, Faculty of Health Science at University of Cape Town. As part of my study I am doing this research study of ***"The experiences of couples undergoing Preimplantation Genetic Diagnosis (PGD) at the Genetic and Developmental Medicine clinic, Sultan Qaboos University Hospital (SQUH) in Oman"***.

I am inviting you to participate in this study and would appreciate if you could attend an interview to be conducted by the researcher. Your confidentiality and personal information will be stored in a safe locked place where only be accessed by the researcher and supervisors.

The information to be collected from this study can be at a benefit of understanding the experience and needs of the families enrolled at PGD procedure and might be at a help to improve the current provided service.

If you have further questions kindly contact the researcher (Khalsa Al-Kharusi 24144384) or the supervisor (Dr. Zandre Bruwer 24144390).

## Invitation for participation in Arabic

### دعوة للمشاركة بمشروع بحث علمي

أن اخلصه الى خروصية طلبة ماجستير في تخصص الارشاد والارشاد في قسم علوم الوراثة والكيمياء في كلية الطب جامعة  
البيروت او اقرب اجراء بحث علمي لدراسة جبهه الوراثة والوراثة في اختصاصات الكيمياء في اختصاصات معاني حص  
قبل الخروصية في كل الانجاب و هي دراس قنوي تمسقيضة. هذا لراسمقش مل الوراثة التي يتم تبليغها من قبل  
عيادة الطب والوراثة والتطور في مستشفى جامعة القدس لطان قبيلوس.

أدعكم للمشاركة في هذه الدراسة وسأكون محققاً لمفوقكم لإجراء الأبحاث العلمية التي تهتم بها مراعاة  
خصوصية وسريته والعمل على انتشار خبرتي. سوف يتم تخزين المعلومات ومناقشة خبرتي والهدف من ذلك هو  
يطلع عليها سوا الباحث والشرف في البحث.

العمل ومات العمل من البحث في تخصص علم الوراثة والوراثة في اختصاصات الكيمياء في اختصاصات معاني حص  
جدوى في تطوير وتحسين خدمة العمل على التلخيص والتلخيص في اختصاصات الكيمياء في اختصاصات معاني حص  
الغرس.

لمزيد من العمل والتمويل المباشر من الجامعة (الخلاصة الى خروصية 24144384) أو المشرف على  
البحث. زان دريبوي 24144390)

## Appendix F:

### Research Consent Form in English

Study Title: ***The experiences of couples undergoing Preimplantation Genetic Diagnosis (PGD) at the Genetic and Developmental Medicine clinic, Sultan Qaboos University Hospital (SQUH) in Oman.***

I understand that I am participating in this research of study of "The experiences of couples undergoing Preimplantation Genetic Diagnosis (PGD) at the Genetic and Developmental Medicine clinic, Sultan Qaboos University Hospital (SQUH) in Oman".

I have been informed about the confidentiality and non- disclosure of my identity or that of my family. The interview will be digitally recorded and I have no objection regarding that. I have no objection of publication of the results of the research study in peer reviewed journals, presentation at conference or utilization for education and teaching purposes.

I am fully aware that this study is intended to improve the quality of the service and I have no conflict of interest. I am not receiving any payment or privileges of being part of this study and understand that this study will not cause me any harm. I have been assured that I can withdraw the study with no expected harm to me or my family and a psychological support will be provided if needed.

Name of participant:

Signature:

Date:



Appendix G:  
UCT ethical approval



**UNIVERSITY OF CAPE TOWN**  
**Faculty of Health Sciences**  
**Human Research Ethics Committee**



**Room E52-24 Old Main Building**  
**Groote Schuur Hospital**  
**Observatory 7925**  
Telephone [021] 406 6338 • Facsimile [021] 406 6411  
Email: [sumayah.ortefdien@uct.ac.za](mailto:sumayah.ortefdien@uct.ac.za)  
Website: [www.health.uct.ac.za/fhs/research/humanethics/forms](http://www.health.uct.ac.za/fhs/research/humanethics/forms)

11 February 2016

**HREC REF: 009/2016**

**Dr TM Wessels**  
Division of Human Genetics /Pathology  
Room 4.23- 4<sup>th</sup> Floor  
Falmouth Building-FHS

Dear Dr Wessels

**PROJECT TITLE: THE EXPERIENCES OF COUPLES UNDERGOING PREIMPLANTATION GENETIC DIAGNOSIS (PGD) THROUGH THE GENETIC AND DEVELOPMENTAL MEDICINE CLINIC AT SULTAN QABOOS UNIVERSITY HOSPITAL IN OMAN (MSc Candidate - K Al-Kharusi)**

Thank you for your response email dated 10 February 2016, addressing the issues raised by the Human Research Ethics Committee (HREC).

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

**Approval is granted for one year until the 28<sup>th</sup> February 2017.**

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

(Forms can be found on our website: [www.health.uct.ac.za/fhs/research/humanethics/forms](http://www.health.uct.ac.za/fhs/research/humanethics/forms))

**Please quote the HREC REF in all your correspondence.**

***We acknowledge that the following student, Khalsa Said Al-Kharusi will also be involved in this study.***

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Yours sincerely

**PROFESSOR M BLOCKMAN**  
**CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE**

Federal Wide Assurance Number: FWA00001637.

Institutional Review Board (IRB) number: IRB00001938

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical

HREC/REF:009/2016

Sultan Qaboos University



COLLEGE OF MEDICINE  
& HEALTH SCIENCES



جامعة السلطان قابوس

كلية الطب  
والعلوم الصحية

REF. NO. SQU-EC/244/15  
MREC #1215

TO: Ms. Khalsa Al Kharusi, MSc Student  
Department of Genetics  
Sultan Qaboos University Hospital

FROM: Prof. Mansour Al-Moundhri  
Chairman, Ethics Committee

SUBJECT: *Research Proposal "The Experience of Couples Undergoing Pre-implantation Genetic Diagnosis (PGD) through the Genetic and Developmental Medicine Clinic at Sultan Qaboos University Hospital in Oman"*

DATE: 22<sup>nd</sup> November 2015

I would like to inform you that the abovementioned proposal submitted to the Ethics Committee, College of Medicine and Health Sciences, Sultan Qaboos University for review and approval was presented and **approved** during its meeting of 19<sup>th</sup> November 2015.

I wish you a productive study with your research work.

: Irc  
cc: Dr. Khalid Al Balushi, Asst. Dean, Postgraduate Studies & Research, SQU