

# Ethical Concerns to the use of Pre-implantation Genetic Diagnosis in the Gulf Cooperative Council States

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## Abstract

Assisted reproductive technology (ART) makes pre-implantation genetic diagnosis (PGD) possible, allowing embryos to be screened genetically before placement in the uterus, by analyzing the DNA from a single cell after amplification by polymerase chain reaction and/or the use of fluorescence *in situ* hybridization (FISH) technique. However, many objections have been raised against genetic screening of embryos, giving the practice an uncertain ethical, legal, and social status. We have, therefore, aimed to survey the possible presence and compliance to any legislation for the PGD practice in the existing sixty IVF centres in the GCC States. The PGD techniques, mainly FISH analyses, were practiced in three centres in Saudi Arabia only, even though many IVF centres were contemplating the PGD program. The under utilization of PGD testing was the result of the high cost of tests and the sophisticated technology involved in such program, and the poor returns of the investment. In general, however there were some deficiencies in the legislation which regulated the PGD practice and its compliance to guidelines. Consequently, the involved medical team often faced difficulties on what rights to exercise in some PGD cases.



# التطلعات الأطلاقية لهستقبل استخدام التشخيص الجيني للجنين قبل انفرازه في الرحم في دول مجلس التعاون الخليجي

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## ملخص

جعلت تقنيات الحمل المساعد التشخيص الجيني للجنين قبل انفرازه في الرحم ممكناً وذلك عن طريق تحليل الحمض النووي للجنين في مرحلة الخلية الواحدة باستخدام تقنية مضاعفة الحمض النووي. كما يمكن استخدام التقنيات الحديثة المطبقة في مجال الوراثة الخلوية والتي يقوم مبدأ عملها على استخدام مجس مشع مصنع من الحمض النووي، ويمكن استخدام هذه التقنية بمفردها أو مع تقنية مضاعفة الحمض النووي. ولقد نشأت العديد من الاحتجاجات التي تعارض المسح الجيني للأجنة بعد الحمل من الناحية الأخلاقية والقانونية والاجتماعية مما أدى إلى صعوبة تطبيقها عملياً. ولذلك كان الهدف من هذه الدراسة بحث امكانية سن قوانين للمسح الجيني للأجنة في مراكز التخصيب الموجودة في دول الخليج العربي والتي يبلغ عددها ستون مركزاً. وبالرغم أن العديد من مراكز التخصيب فكرت في تطبيق برنامج المسح الجيني للأجنة إلا أن ثلاثاً من تلك المراكز فقط طبقت هذا البرنامج في المملكة العربية السعودية باستخدام تقنيات الوراثة الخلوية. ويبقى تطبيق برنامج المسح الجيني للأجنة باهظ التكاليف بسبب استخدام تقنيات متطورة وبالإضافة إلى ذلك يعتبر استثماراً مالياً غير مربح لأن عائده المادي قليل. وبشكل عام توجد بعض الصعوبات في سن القوانين ووضع الارشادات التي تنظم عملية التطبيق العملي لبرامج المسح الجيني للأجنة حيث تواجه في الغالب الطاقم الطبي القائم في برنامج المسح الجيني للأجنة صعوبة في اتخاذ القرارات الحساسة في بعض الحالات.



## Introduction

Pre-implantation genetic diagnosis (PGD) has been in use since 1990 to screen embryos for aneuploidy and genetic disease (Grifo *et al.*, 1990). In vitro fertilization (IVF) paved the way for PGD to be established within assisted reproductive technology (ART) setup. Nevertheless, PGD technology was made possible through the use of microinjection of oocyte with a single spermatozoon as in intracytoplasmic sperm injection (ICSI) technique and the micromanipulation of the resulting embryo. Moreover, the technology involves removing 12- cells from each of the 68- cell stage embryos (usually three days after ICSI procedure), study each cell for chromosomal anomalies or screening using fluorescent in situ hybridization (FISH) technique and/or look for certain single-gene defect using polymerase chain reaction (PCR) technique. Normal (or appropriate) embryos are then transferred into the uterus while unwanted ones are discarded or used for research.

## The Utilization of PGD

Although PGD screening has been available for nearly two decades in Western Europe and North America, only a small number of people using assisted reproduction utilized this advanced service to screen embryos (Robertson, 2003a). The main reason is that accessing embryos through IVF is intrusive and expensive, and for some people raises serious ethical concerns. The average cost of an IVF/ICSI cycle in the USA is approximately \$9,000 - 12,000 and additional \$4,000 - 8,000 for a PGD test, while such costs in the GCC States are \$3,000 - 5,000 and \$1,500 - 2,000 respectively. However, it has been estimated that the level of need equals 3000 IVF/ICSI cycles per million per annum cpm (Collins, 2002) while the optimal demand equals 1500 IVF/ICSI cpm (ESHRE Capri Workshop Group, 2001). Based on a more recent study which showed that approximately 3,000 PGD cycles had been performed in 2003 (Sermon *et al.*, 2007), we have estimated the optimal demand to approximately 10 PGD cpm as depicted in Table 1.

## PGD Dilemmas

There are many quandaries of various aspects which still exist even after nearly two decades of PGD practice amongst which are the ethical, legal, and social dilemmas (Robertson, 2003b). This is because of three main reasons: (1) the unclear position for the medical team on certain aspects of treatment modes which often alternates with reproductive medicine, (2) not enough information supplied by the authority which alternates with reproductive health, and (3) the subject of molecular diagnosis is rather tabooed that alternates with reproductive awareness.

## Ethical Dilemma

The ethical dilemma has two main sets of ethical concerns to the use of PGD program (Robertson, 2003a). The first is embryo status and embryo manipulation which is concerned with the safety and reliability of the techniques used in PGD. Moreover, patients who think that the embryo is a person will object to creating and destroying embryos, and oppose most uses of PGD. However, others accept

**Table 1.** Worldwide IVF centres and their offered services for 2003.

IVF Centres	3300
IVF/ICSI Cycles/annum	800,000
PGD Centres	50
*PGD Cycles/annum	3,000
PGD setup/IVF Centre %	1.5%
PGD cycle/IVF Cycle %	0.4%

\*(Sermon *et al.*, 2007).



PGD, as embryos are too rudimentary in development to have interests or rights. Hence, PGD may prevent selective abortions for genetic diseases. Nevertheless, the second set of ethical concerns is the genetic selection itself. It poses a deontological concern because human reproduction is a gift of life. Therefore, it is wrong to choose traits of offspring whatever the intention. On the other hand, the consequential concern will move many people toward a eugenic world as a result of the obsession with genetic screening of prospective children.

## Legal Dilemma

The advent of new technology especially in reproductive medicine necessitated legislative measures in many countries to regulate its uses. Furthermore, PGD and stem cell research instigated tighter control over the practice in general. For instance, in the UK, the human fertilization and embryology authority (HFEA) has regulated both the ART and PGD practice (HFEA, 2006). It is quite surprising, however, that in the United States, there was universal state or federal statutory body for PGD regulations (Levine, 2005). The practice is thus left largely to the discretion of providers offering those services and the patients who seek it. On the other hand, the GCC States have been surveyed, as presented in this study, for PGD regulations and guidelines, and the extent of their implementations.

## Social Dilemma

Different societies approach the PGD program with different perspective which depends on how well they are supplied by relevant and updated information by both the media and the health authorities. The GCC States have no exemption; quite the contrary they have many qualms which stem from the fact that definition of certain medical and technical terminologies are not yet fulfilled, related procedures are not understood and shortage of clear religious standpoints to the demanding aspects of the treatment and technology involved in both ART and PGD such as sex pre-selection (Eskandarani, 1996). The situation is doomed further by restricting the cryopreservation of gametes/embryos due to fear of possible mix-up and nuclear transfer misconception.

## The PGD Study

The presented study was aimed to survey the possible presence and implementation of rules and regulations for the PGD practice in the GCC States, which include Saudi Arabia, the United Arab Emirates, Kuwait, Oman, Qatar, Bahrain, and Yemen. Also to show the standpoint to any effects, which could have been generated by compliance/noncompliance to such regulations.

## Materials and Methods

A questionnaire, in the form of table, was sent to responsible persons of all 60 IVF centres in the GCC Countries. The collected data about the legalization and the guidelines of the PGD program were analyzed using SPSS. The following scoring system was applied: 0 = not applicable or available (NA), 1 = possibly, 2 = likely, 3 = strongly. The Wilcoxon Signed Ranks test was used for comparison of average scores for the regulations and/or guidelines of genetic services and for their implementations through surveillance system.

## Results

At present, there are 60 IVF licensed centres serving a total population of approximately 58 million people. All centres employ an IVF/ICSI program but only very few use a PGD program. When the questionnaire was passed to each of the concerned assisted conception centres, 16 (26.7%) of them have participated in the survey. Nine centres from Saudi Arabia, two from Bahrain, and one from each of Kuwait, Emirates, Oman, Qatar, and Yemen attempted the questionnaire as shown in Table 2. The PGD techniques, mainly FISH analyses, were practiced in three centres in Saudi Arabia. The major provider of the PGD service was King Faisal Specialist Hospital and Research Centre in Riyadh where more than 300 cases of FISH analyses and PCR screening for single-gene mutation tests had been performed. Nevertheless, the PGD service has just started in a centre in Dubai, UAE.

Whilst some regulations and guidelines have been introduced to participating IVF centres in all GCC countries, implementations to such guidelines were left to the discretion of the treating centre



**Table 2.** Average scores related to genetic services offered by the IVF centers.

Category	Average Score	
	X	SD
Are there any regulations and/or guidelines to the following?:		
Genetic counseling for severe male factor infertility	1.99	0.85
Mandatory submission of data for IVF centre to licensing office	1.08	1.40
Micromanipulation	1.84	1.28
Preimplantation genetic diagnosis	1.17	1.45
Moral status of the conceptus (embryo research)	1.33	1.44
Prior approval for research from ethical committee/licensing office	1.80	1.39
Sex preselection	1.62	1.37
Is there any surveillance by licensing body for the activities of the IVF centre?	0.32 <sup>*</sup>	0.64 <sup>*</sup>
Does your centre provide a PGD program?	0.25	0
Total score	11.40	9.81

\* Superscripts are significantly different (P<0.05)

as evident from the significantly low average score (Table 2) for surveillance by the concerned statutory body.

## Discussion

It can be drawn from the presented results that there was an introduction of controls over the PGD practice which could have been followed in their broadest terms. Whether such controls were effective was left to the discretion of the IVF centre that offered the PGD services as the mechanism of surveillance was somehow paralyzed. Similar study was conducted previously on fifty IVF centres for the ART regulations and guidelines and showed parallel results (Eskandarani, 2007). Again, the shortcoming of surveillance reflected on the lack of effective legislative regulations for the legalization of PGD practice and probably on the shortage of regulations/guidelines to the detailed PGD technology. Furthermore, ambiguity among professionals remained hovering over certain aspects of the PGD services (such as sex preselection) which in turn left them in uncomfortable situation with some of their patients.

The Gulf Cooperative Council (GCC) States have not, so far, capitalized on using the PGD technology although prosperity is quite well and level of need is high due to prevalence of consanguineous marriage which often passes on inherited diseases amongst the offspring. Besides, there are other reasons for under utilizing the PGD program amongst which are the requirement for high calibers of scientific team (complex setup), the demand for additional expensive assets and running costs (expensive investment), and the lack of genetic information-database in the area. These grim reasons have circumvented the demanded utilization of PGD tests to the extent that there are only four out of sixty IVF centres that have started recently offering the service. By comparison, however, to many developed countries it is fair to say that the PGD utilization has not been poorly undermined.

## Conclusions

Limitations of legislative regulations and proper guidelines for the PGD practice in the GCC countries has resulted in giving a cause for ethical and legal concerns. Consequently, effects at different levels can be demonstrated. The statutory body in each and every GCC country involved has compromised on surveillance as well as on the mechanism of imposing retribution to violations and dismissed the national or regional ART registry. On the other hand, if tighter controls were closely followed without necessarily being overzealous, many treating centres would have contemplated on certain aspects of PGD technology (e.g., sex preselection). Ultimately and because of mistaken beliefs, some patients might have found difficulties understanding PGD techniques. Nonetheless, the additional high costs of the PGD techniques could have caused financial burden for many deserving patients who can not afford the PGD testing; hence, is PGD targeting the rich?



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