

# What is the Impact of Genetic Counseling and Prenatal Diagnosis in Genetic Diseases Prevention in an Arab Muslim Population?

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## Abstract

Genetic counseling remains the best and the most efficient action for genetic diseases prevention. Based on families' education, and sometimes followed by prenatal or preimplantation diagnosis, genetic counseling is relevant by reducing the incidence of hereditary and congenital disorders. The development of medical care, the accumulation of laboratory techniques and the legality of pregnancy termination will help largely to decrease the severity and the frequency of inherited diseases. In daily practice, we are sometimes surprised by parents' attitude. After genetic counseling, why do parents decide to stop reproduction despite the availability of prenatal testing or the absence of recurrence risk? While, some other parents at very high risk continue to have children. To reply to such questions, we surveyed during three years, couples who were referred to the genetic centre for genetic counseling. We considered only couples at risk of affected children. We evaluated the impact of genetic counseling on parents' attitude by analyzing two parameters, the occurrence of pregnancies and the acceptance of prenatal screening and prenatal diagnosis. These parameters were correlated to parents' characteristics: age, socioeconomic situation, education level; to the number and children health status and to the kind and severity of the disease. We analyzed simultaneously the same parameters in the group of couples who were referred for prenatal diagnosis during this period. The aim of the presentation is to evaluate the real impact of genetic counseling and prenatal diagnosis on genetic diseases prevention in an Arab Muslim country and to determine how to increase the acceptability of the role of genetic counseling in the welfare of the family. Legislation for genetic counseling: In areas with high risk of genetic diseases for example where consanguinity rate is increased, it would be necessary to establish genetic counseling facility as obligatory. In premarital stage each partner has to be informed about risk for his progeniture. Each couple will of course be responsible for his decision making. Legislation for pregnancy termination in countries where it is accepted have to be established taking account of the community culture.



# ما هو دور الاستشارة الوراثية والفحص الجيني للجنين في التقليل من نسبة الإصابة بالأمراض الجينية والوراثية في المجتمع العربي المسلم؟

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## ملخص

تلعب الاستشارة الوراثية الدور الأهم والأكثر فاعلية في المساهمة بالوقاية والتقليل من نسبة الإصابة بالأمراض الوراثية والاضطرابات الجينية وذلك من خلال توعية الأسر بالمخاطر المحتملة. تُعطى الاستشارة الوراثية في بعض الأحيان عقب إجراء الفحص الجيني للجنين قبل الولادة أو قبل انفرازه في الرحم. كما يساعد تطوير الرعاية الطبية والتقنيات المخبرية ومشروعية إنهاء الحمل بشكل كبير على الحد من نسبة الإصابة بالأمراض الوراثية. ومن خلال ملاحظتنا اليومية، نفاجاً بالمواقف التي يتخذها الآباء بعد إعطاء الاستشارة الوراثية. حيث يقرر بعض الآباء التوقف عن الإنجاب بالرغم من إمكانية إجراء الفحص الجيني للجنين قبل الولادة أو عدم وجود خطر تكرار الإصابة. وعلى النقيض من ذلك، يقرر بعض الآباء استمرار إنجاب الأطفال بالرغم من وجود احتمال كبير لتكرار الإصابة في عائلاتهم. ومن أجل الإجابة على هذه التساؤلات، قمنا بإجراء دراسة رسمية استمرت مدة ثلاث سنوات للأزواج المراجعين لمركز الوراثة من أجل الحصول على الاستشارة الوراثية. وأخذنا بعين الاعتبار فقط الأزواج المحتمل إنجابهم لأطفال مصابين. وكان تقييمنا للتأثير الذي تحدثه الاستشارة الوراثية على الموقف الذي يقرره الآباء من خلال دراسة معيارين هما: حدوث الحمل وقبول الفحص والتشخيص الجيني للجنين قبل الولادة. ثم تم مقارنة هذين المعيارين مع مواصفات الآباء التالية: العمر، الوضع الاقتصادي، المستوى الثقافي، وأيضاً مع عدد الأبناء ووضعهم الصحي ونوع المرض المصابين به ومدى شدته وخطورته. وفي نفس الوقت قمنا بدراسة هذه المعايير على مجموعة من الأزواج المراجعين من أجل إجراء الفحص الجيني للجنين قبل الولادة. والهدف من هذه الدراسة هو معرفة مدى التأثير الحقيقي الذي تحدثه الاستشارة الوراثية والتشخيص الجيني للأجنة قبل الولادة في التقليل من نسبة الإصابة بالأمراض الوراثية والاضطرابات الجينية في الدول العربية والمسلمة. كما كان للبحث هدفاً آخر وهو تحديد كيف يساهم قبول دور الاستشارة الوراثية في تحقيق مصلحة الأسرة. ونشير إلى ضرورة وضع القوانين التي من شأنها أن توجب توفير خدمة الاستشارة الوراثية في المناطق التي تنتشر فيها الأمراض الوراثية بنسب عالية والمناطق التي يحدث فيها زواج الأقارب بكثرة. كما يجب إخبار كل فرد من الشريكين المقبلين على الزواج بالمخاطر المحتملة عند الإنجاب وذلك من خلال الفحص الوراثي قبل الزواج. وبالتالي يصبح كل منهما مسؤولاً عن القرار الذي اتخذه. كما يجب سن القوانين والتشريعات التي تنظم عملية إنهاء الحمل مع مراعاة ثقافة وحضارة المجتمع.



## Introduction

The main aim of genetic counseling is to reduce the incidence of genetic disorders in the population. The aim of prenatal diagnosis is to evaluate the fetus status for a defined genetic or congenital severe disease, in order to alert parents about their affected fetus status, to treat the fetus and to propose pregnancy termination if treatment is not available.

To evaluate the impact of genetic counseling on population, different techniques are used. Most methods are based on population behavior study such as couples attitude for union type choice; reproduction, acceptance and refusal of affected offspring.

The analysis of epidemiological variation in genetic disorders in the population is the best scientific method. In order to evaluate the impact of genetic counseling on the decreasing occurrence of genetic disorders, we need epidemiological data from the population, before and after genetic counseling application. Such data are rare and, if available, biased, since in most cases investigation of genetic disorders is always followed by genetic counseling.

The analysis of population behavior is possible using questionnaire-based method; several studies were carried out in Arab populations (UAE, Lebanon, Palestine), but the analysis was limited to opinion (Zahed *et al.*, 1999). We report here the survey and the analysis of couples' and families' attitude toward genetic counseling, and the evaluation of its impact on the Tunisian population.

## Material and Methods

Tunisia is a Muslim Arab country situated on the North African Mediterranean coast. It is the easternmost and smallest of the nations situated along the Atlas mountain range, bordering Algeria, to the west, and Libya to the south. The population size in Tunisia is about 10.5 million; with two millions inhabiting the capital, Tunis. Modern Tunisians are the descendents of indigenous Berbers and of people from various civilizations that have invaded, occupied, migrated to, and been absorbed into the population over the centuries (The Library of Congress).

Nearly all Tunisians, 98% of the population, are Muslim. Arabic is the official language; however a mix of local Tunisian dialect and French is most commonly used (National Statistics Institute of Tunisia, 2004). Mean marriage age is about 25.9 years for females and 32.1 years for males. The population growth rate is about 0.99% with a birth rate of 15.5 births/1,000 population. Life expectancy at birth is 74.89 years. The mean family size is 1.75 and consanguinity rate is 32%. In Tunisia, education is mandatory; thus, 98% of children go to school and literacy in the total population is estimated at 74.3%. Contraception is encouraged and pregnancy termination for medical reason is allowed (Chaabouni *et al.*, 2001; National Statistics Institute of Tunisia, 2004).

## Population Samples

Our study was carried out at the "hereditary and congenital disorders department", Charles Nicolle hospital in Tunis. Patients, couples and families are referred to the department from different regions; but most people come from the northern half of the country. The main demand for referred patients consists of genetic counseling, investigation of a suspected genetic disease followed by genetic counseling and prenatal diagnosis when indicated.

Our sample is divided into three groups. Group 1 includes all couples and families referred to the department during one year, 2005. These patients and families were referred for the first time in 2005 and their medical dossier was established during the period from January 1st to December 31st. A total of 2862 patients/families, were referred with a mean number of 57 new patients/families per week. Group 2, includes parents of Down syndrome (DS) diagnosed during 2005 at postnatal or prenatal stage. Group 3 includes parents /families with one or more affected member. Two diseases were considered: spinal muscular atrophy (SMA) and congenital adrenal hyperplasia (CAH). Each group served to evaluate the impact of genetic counseling and prenatal prevention, by answering one of the three main questions. The group 1 analysis was to answer to the first question: do people ask for genetic counseling? The group 2 analysis was to answer to the second question: do people follow genetic counseling? The group 3 analysis was to answer to the third question: does genetic counseling reduce the frequency of severe genetic disorders?

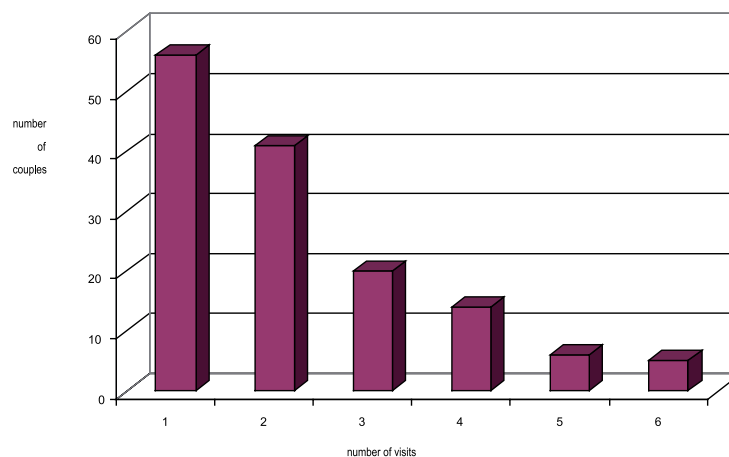


## Results

Among the 2862 patients/families (group 1), referred during one year, 143 Patients/families, came to clinics to get genetic counseling only. Asking for genetic counseling was subsequent to a family history or a personal history (advanced maternal age excluded). Among these 143 patients/families, 55% came before their first conception, they had no children, and their demand was based on family history of genetic (or suspected) disease in 64% and on consanguinity, in 36%. The remaining 45% came after abnormal child (fetus) conception. The pathologies which pushed people to ask for genetic counseling are reported on table 1. The mean age of parents/couples is of 29 y (19 - 43) for females and 36 y (24 - 56) for males. The socio-economic level is high for 15%, medium for 41% and low for 44% cases. Consanguinity was present in 64%. Most people had the genetic counseling after one visit only (figure 1).

**Table 1.** List of pathologies for which patients requested genetic counseling.

Two associated diseases
Cerebral malformation
Chromosomal abnormality
Congenital adrenal hyperplasia
Consanguinity
Current pregnancy at risk
Deafness
Dysmorphic syndrome
Genodermatosis
Heart disease
Hemoglobinopathies
Mental retardation
Metabolic disorder
Neonatal death/miscarriages
Neurologic disorder
Ophthalmologic disease
Renal disease
Other pathologies



**Figure 1.** Number of visits required by patients/couples before receiving genetic counseling.



For the second group, we evaluated whether patient/couple who received a genetic counseling, follow it or not. During the year 2005, we diagnosed 82 cases of Down syndrome (DS; subgroup A) in neonates or infants, and we diagnosed DS in 29 fetuses (subgroup B). The question was, did subgroup A receive genetic counseling or not? In case they received genetic counseling, did they refuse prenatal diagnosis? Genetic counseling was not provided for 94% of patients belonging to subgroup A while it was provided to 6% only, these patients refused prenatal diagnosis. If we consider genetic counseling for patients based on advanced maternal age, we found that only 10% of women aged over 35 years received genetic counseling with proposition of prenatal diagnosis.

The comparison between the two subgroups was based on different parameters. Patients of subgroup B had slightly higher socio-economic level; most of them were living in the capital (75% vs 52%). Pregnancy was followed in a university hospital in 65% for group B while the percentage was about 8% for group A. Finally maternal age was more than 35 years in 77% of group B vs. 60% for group A (table 2).

For group 3 we analyzed the parents' attitude toward prenatal diagnosis in case of a severe genetic disease. We selected two common diseases that are routinely diagnosed in the department of molecular biology; spinal muscular atrophy (SMA) and congenital adrenal hyperplasia. SMA is a neurological disorder with severe clinical features. In case of an affected fetus, PND is followed by pregnancy termination, as there is no available treatment. Among 63 SMA families, we performed PND for 78 pregnancies (2002 - 2007), one time for 68 couples; two times for 8 couples and three times for 3 couples. The fetus was affected in 20 cases and pregnancy was terminated for 19 cases.

The second disease was congenital adrenal hyperplasia (21 hydroxylase deficiency), 56 couples/parents received genetic counseling. For 29 pregnancies, the pregnant mother was given treatment (dexamethason) and PND was performed both for fetus sexing and molecular analysis of *CYP21B* gene. Eight fetuses were affected (4 males and 4 females), treatment was maintained along the pregnancy for female fetuses and all pregnancies were maintained.

## Discussion

It is clear that genetic disorders constitute a national health problem in Tunisia. These disorders have a great impact on morbidity; pose a burden on the health system, and on financial resources notwithstanding the present effort in diagnosis, prevention and care of affected patients and their relatives.

Our experience indicates that the response to genetic counseling is generally good in the country. First of all, patients ask for genetic counseling. In this report, people of the group 1 asked for genetic counseling by their own demand, based on family history even before reproduction. The demand comes from different socio-economic levels. The percentage of such demand remains low as it represents 5% of whole outpatients' clinics, but since more than 70% of the population is educated, we hope that they will be most receptive to health guidelines. For a long time, genetics was considered by physicians as an exclusive scientific and research activity. The low level of treatment availability for genetic disorders re-affirmed practitioners' beliefs. To assess the level of understanding of genetic advice given in the genetic clinic and attitudes toward consanguineous marriages, and prenatal, abortion

**Table 2.** Characteristics of subgroup A and subgroup B for genetic counseling in Down syndrome.

Reference centre where pregnancy was followed	Subgroup A (%)	Subgroup B (%)
University Hospital	8	65
Regional Hospital	46	13
PHCC	34	14
Private Clinics	37	22
Not Followed	9	-
<b>Maternal Age</b>		
< 35 Years	40	23
≥ 35 years	60	vv



and preconception diagnoses, Al Gazali and colleagues (2005) studied 100 couples in UAE, who were informed about the genetic origin of their children disease and they received genetic counseling. Three months later, the couples were asked open-ended questions about the perceived causation of the disease, recurrence risk, plans for births, and prenatal, abortion and preconception diagnoses. Half of the couples acknowledged a genetic basis for their child's condition, but only 10 remembered the risk given to them. The analysis of group 2 sample confirms physicians' beliefs. Genetic counseling is less provided in PHCC than in university hospital; it seems underestimated by practitioners. When genetic counseling is provided, people have the choice to accept or refuse PND, in our experience, the percentage of people who refuse PND is low. In most cases couples and parents follow the genetic counseling and its issues. This seems different from reported studies among Arab population. In a study evaluating the efficacy of prenatal testing for Down syndrome offered for women at risk, Davidov *et al.* (1994) found an increased acceptance of prenatal testing by Jewish women (67%) comparing with non-Jewish women (23%), especially for young women (0.6%).

To answer to the question: does genetic counseling contribute to reduce the frequency of people affected with severe genetic disease phenotype, we analyzed group 3 sample. The analysis showed that genetic counseling diffuses to other family members in case of severe disease. Parents ask for PND in case of severe disease such as SMA, when they belong to an affected family, even they do not have any affected children. PND is more needed by parents in case of lethal, incurable disease (SMA vs. CAH). PND is repeated more than one time, as much as necessary. These patients were referred to a genetic centre, here they were given genetic counseling and accepted prenatal diagnosis. In fact not all affected families had the PND available. The same problem may be encountered even in developed countries. Although antenatal screening and counseling for hemoglobin disorders are standard practices in the United Kingdom, they are delivered inadequately and inequitably (Modell *et al.*, 2000). In the same report, uptake of prenatal diagnosis when offered was 80% and varied with ethnic origin and gestation.

## Conclusion

Our experience indicates that the response to genetic counseling is generally good in the country. Genetic counseling remains the best and the most efficient action for genetic diseases prevention. The success of such action is based on people education and practitioners training. Followed by prenatal or preimplantation diagnosis, genetic counseling is relevant by reducing the incidence of hereditary and congenital disorders. Guidelines have to be defined for genetic counseling practice. Legislation for pregnancy termination in countries where it is accepted has to be established considering the community culture.

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