Original Article

Strategies to Decrease the Incidence of Genetic Disorders in Arab Countries

Hossam E. Fadel, MD, PhD, FACOG
Maternal Fetal Medicine
University Hospital
Clinical Professor
Medical College of Georgia
Augusta, Georgia

Abstract

Genetic disorders are responsible for a significant proportion of perinatal morbidity, mortality, infant deaths, and handicaps. Their incidence in Arab countries is higher than in the developed world. This is attributed to ethnic diversity, consanguineous marriages, large family size, advanced maternal and paternal age, lack of resources that deal specifically with genetic diseases, lack of public awareness of the significance of genetic disease, reluctance of couples to receive preconception counseling and prenatal diagnosis, and religious and cultural concepts related to causation and dealing with diagnosed malformations.

Suggested strategies to reduce the incidence of genetic diseases include: (1) public education, specifically about the role of consanguineous marriages and the correction of religious misconceptions; (2) providing premarital counseling services, family-oriented carrier screening, and family planning services; (3) improving preconception and prenatal care to include prenatal diagnostic services; (4) augmenting genetic services resources to include the human as well as lab components; (5) neonatal screening for metabolic disorders; (6) providing preimplantation genetic diagnosis services; (7) establishing databases of cases of genetic diseases; and (8) establishing ethical and religious guidelines for prenatal genetic diagnosis and for termination of pregancies complicated by fetal genetic diseases or malformations.

Keywords: Genetic diseases, Arabs, consanguineous marriages, premarital counseling, preconception counseling, prenatal diagnosis, termination of pregnancy, Islam, medical ethics.

Congenital malformations and genetic disorders are responsible for a significant proportion of perinatal morbidity, mortality, infant deaths, and handicaps in the Arab world.[1-3] The incidence of genetic diseases is higher than in the developed world. As a matter of fact, several new genetic diseases were identified in Arabs. According to Teebie,[1] there are 115 such new syndromes. More than 100 syndromes are autosomal recessive, 10 are autosomal dominant, and 5 are possibly x-linked or autosomal recessive. Some autosomal recessive disorders characteristically have a higher prevalence among Arabs, e.g. Meckel-Gruber syndrome, Bradelt-Biedl syndrome.

Several factors contribute to this increased incidence of genetic disorders. Despite its linguistic, reli-

gious, and cultural cohesion, the Arab region is rich in ethnic diversity. Present-day Arabs represent a mixture with other ethnicities such as Persians, Turks, Berbers, Southeast Asians, Europeans, and Africans. Another factor is the preponderance of consanguineous marriages. Its incidence ranges from 25% in Beirut[4] to 90% in the Bedouin community of Kuwait[5] or Saudi Arabia.[6] The average is probably 40%. The most common form of intermarriage is that between first cousins, particularly paternal first cousins, and also includes the marriage of double first cousins. Consanguineous marriages are more common in rural than in urban areas and do not correlate with the socioeconomics status.[1] Consanguineous marriages are more common among Muslims than among Christians in the Arab countries, but this is a cultural, not religious, trait. While Islam does not prohibit it, Islam appears to discourage it. This high rate of consanguineous marriage undoubtedly causes an increase in autosomal recessive genetic disorders. Sickle cell diseases and thalassemias are relatively common in Arab countries. There is also some evidence to suggest the presence of a recessive nondisjunctional predisposing gene(s), which may be preferentially expressed with advancing maternal age.[7] This results in a higher incidence of aneuploidies, specifically Down syndrome (DS), among children of closely related parents. The incidence of DS in Arab countries is slightly higher than in the West. The incidence of DS among Egyptians was estimated to be 1.26/1000 live births.[8] The incidence of DS in Saudi Arabia was reported to be 1.81/1000 live births. The mean maternal age was 33.1 years with a range from 19-50. The incidence of DS births was 0.98/1000 for mothers < 35 years and 7.6/1000 for those aged > 35.[9] Faraq et al reported an incidence of DS of 3.6/1000 live births in Kuwait.[10] While in industrialized countries, the majority of DS babies are born to younger women, up to 50% of children with DS in the Arab world are estimated to be born to mothers 40 years old or older.[2,11] In addition there is an increased incidence of autosomal dominant disorders. This may be related to the higher paternal age. Arabs tend to marry younger and to continue to reproduce at an older age. This results in larger sized families. A study showed that the total fertility rate in the period 1990-1994 in the Arab world was 5.37 children per woman but varied from 3 in Lebanon to 8.6 in Yemen.[12] During the 1987-1993 period, another study showed that the average family size (including the parents) varied from 5.3 in Egypt to 8.8 in Kuwait.[1]

Other factors that contribute to the increased incidence of genetic disorders in the Arab population include the relative lack of health facilities that deal specifically with genetic disorders, lack of lab facilities to perform the necessary tests for proper diagnosis, lack of genetic counselors, relatively poor prenatal care in many countries, inadequate maternal nutrition, as well as the lack of awareness among the population of the significance of genetic disease and the means to decrease its incidence. Another significant factor contributing to the increased incidence of genetic disorders and congenital malformation in the Arab population is the reluctance of couples to receive preconception counseling, and especially to seek prenatal diagnosis because of the religious/legal prohibition of termination of pregnancies (TOP) of affected fetuses and the cost involved. The Arab family, whether Muslim or Christian, generally speaking has strong faith in God. Muslims believe that disease is God's will. They refer to the Qur'anic verse:

مَا أَصَابَ مِن مُّصِيبَةٍ فِي الْأَرْضِ وَلَا فِي أَنفُسِكُمْ إِلَّا فِي كِتَابٍ مِّن قَبْلِ أَن نَّبْرَأَهَا

> No misfortune can happen on earth or in your selves but it is recorded in a decree before we bring it into existence.[13]

Such a belief helps to alleviate parents' feelings of guilt by relating a child's problem to God's will rather than to a blind probabilistic event and thus the reluctance to have genetic counseling and prenatal diagnosis.

Excerpts from this paper were presented at the First Global Knowledge Forum, held in Madinah, Saudi Arabia, June 22-24, 2008.

Correspondence should be directed to
Hossam E. Fadel, MD, PhD, FACOG
1348 Walton Way, Suite 5500
Augusta, GA 30901
email: hefadel@comcast.net

Strategies to decrease the prevalence of genetic disorders

Public education: The public should be educated about genetic disease, its modes of inheritance, and its increased incidence in consanguineous marriages. These educational programs have to take into account cultural and religious sensibilities. While it is true that Muslims believe in destiny and accept whatever ill befalls them, they still need to try to avoid harm to themselves and to their community. Allah ﷻ gave us the intellect to develop the medical sciences. It is narrated that the Prophet ﷺ said:

إن الله تعالى أنزل الداء والدواء وجعل لكلِّ داءٍ دواءً فتداووا ولا تداووا بحرامٍ

> Allah ﷻ created disease and treatment, and He made for each disease a treatment. So seek treatment but do not use forbidden things.[14]

So trying to prevent genetic disease is a worthwhile goal. Programs should also address consanguinity. Although it is not prohibited in Islam, it appears that it may be discouraged. There is a hadith that recommends marrying from afar and avoiding near relatives because the pregnancy (in the latter situation) will be weak.[15] It is also reported that Umar ibn al-Khattab gave a similar advice.[16] It should be noted that this hadith is weak and only mentioned in books of "strange" ahadith. However, in the current state of medical knowledge, it maybe worthwhile to consider. The culture of endogamy is still well engraved. Its proponents cite "The spouse that you know is better than the one you did not know", "A cousin takes better care of you", and "It increases the bond between the two families". It will be difficult to change this perception and will take time to accomplish that.

Premarital counseling: Premarital counseling should include detailed genetic history, screening for the more common genetic disorders such as hemoglobinopathies, especially when a consanguineous marriage is contemplated, and calculating the risk for having an affected fetus. Couples have to decide if the risk is acceptable.

Family-oriented carrier screening: A child diagnosed with a genetic disease identifies a family at increased risk. Carrier screening should be offered to all family members, including the extended family members. This will lead to the identification of current and future couples at risk for producing affected children.

Family planning services: Family planning services should be offered in the primary health care system. It is especially important to offer contraception to older women who may think they are beyond their reproductive years and who, if they conceive, have a high risk of carrying DS and other chromosomally abnormal fetuses.

Preimplantation genetic diagnosis (PGD): Preimplantation genetic diagnosis is a procedure where preembryos obtained through in vitro fertilization (IVF) are tested for genetic diseases/chromosomal abnormalities and only preembryos free of these are implanted in the uterus.[17-19] Preimplantation genetic diagnosis may be an acceptable strategy in Muslim countries as it does not involve termination of pregnancy when a genetic disease or a chromosomal abnormality is later detected. While PGD is accepted by most Muslim scholars, there are still some concerns about discarding affected embryos, use for sex selection for non-medical reasons, and its availability only to the wealthiest segments of the population.[20]

Preconception and prenatal care: Improving nutrition, smoking cessation, and avoidance of alcohol and recreational drugs are important factors in reducing fetal malformations. A detailed medical history, including the use of medication, is very important. Medications that may be teratogenic, e.g. coumadin, should be discontinued and substituted with nonteratogenic medications, e.g. heparin. Strict diabetic control before and during pregnancy would reduce the incidence of birth defects in the offspring. Following an alanine-free diet in phenylketonuric women before and throughout pregnancy will reduce the incidence of mental retardation in the offspring.

Prenatal diagnosis: Serum markers screening identifies women with high risk of carrying fetuses with chromosomal anomalies, specifically DS. For those women, invasive testing can be offered to rule in or out such abnormalities. This can be by chorionic villous sampling (CVS) at 11-13 weeks or amniocentesis at 15-18 weeks. Termination of pregnancy

may then be offered if the fetus is affected.[21] This strategy is of questionable value because TOP is not allowed in most Arab countries.

Alternatively, targeted ultrasound[22] detects many malformations, sometimes in the first trimester, e.g. anencephaly, but mostly in the second trimester. Some of these detected malformations are lethal e.g. bilateral renal agenesis or result in severe deformities/birth defects e.g. hydrocephaly, skeletal dysplasia. Other detected malformations are serious but can be corrected in utero, either medically, e.g. cardiac arrhythmias, or surgically, e.g. diaphragmatic hernia or bladder outlet obstruction. Other detected malformations can be corrected surgically neonatally e.g. gastroschisis, omphalocele, and heart defects.[23] When a fetus is diagnosed with these abnormalities, plans to have the delivery in the appropriate medical facility with proper neonatal management will result in a significant improvement of outcomes.

Neonatal screening: Metabolic genetic diseases cause a significant percentage of neonatal and infant deaths. Neonatal screening for some of the common diseases will result in detection and early treatment that may reduce the morbidity and mortality.

Creating Databases for Researchers: Databases for genetic disease research will provide timely information on the occurrence of genetic disorders in Arabs and are essential tools to promote scientific research on genetic disorders in the region. A good example of such a database is the Catalogue of Transmission Genetics in Arabs (CTGA) in the United Arab Emirates. This database hosts entries for 692 phenotypes and 235 related genes described in Arabs and offers Web-based basic and advanced research approaches.[3]

Increasing the Number of Specialists: The pool of specialists to address these issues can be increased by encouraging specialization in genetics, both as clinical geneticists, genetic technology researchers and genetic counselors and by introducing and augmenting genetic education into medical, nursing, and social service curricula.

Coming to a Consensus Around Genetic Services: The ethical, legal, religious, and cultural factors in formulating genetic services, including guidelines for prenatal genetic diagnosis and for TOP of fetuses affected by genetic diseases or malformations, should be defined in more detail.

Termination of pregnancy of fetuses affected by genetic disease or malformations is the most controversial aspect. In Islam, TOP is permissible for preservation of the life and health of the mother. There is a difference of opinion about TOP for fetal malformations. While some completely prohibit it, others will allow it up to 40 days after conception. Yet others allow it up to 120 days. Some will allow it only for clearly lethal conditions e.g. anencephaly or bilateral renal agenesis, while they prohibit it for chromosomal anomalies compatible with life such as DS. There is also controversy about TOP in cases of birth defects that are compatible with life but result in significant morbidity for example hydrocephaly, neural tube defects, etc.[16,24]

The Islamic Jurisprudence Council of the Islamic World League at its 12th session held in February 1990 in Makka, Saudi Arabia, agreed by a majority vote to allow for the option of abortion, when requested by the parents, if a committee of specialized competent physicians decide that the fetus is grossly malformed, that the malformation is untreatable, and that the life of the baby if born alive will be extremely difficult/disturbing for the individual and the family. The abortion may be performed within 120 days of conception.[25]

However, many unanswered questions remain. Is it permissible to abort a DS fetus or fetuses affected by ß-thalassemia major or sickle cell disease? What about myelomeningocele, which can be surgically corrected but may still cause permanent disability, mental retardation, etc?[16]

It would be helpful if Muslim scholars and physicians involved in these fields of medicine confer and possibly establish more specific guidelines for different conditions or establish acceptable procedures as to how to deal with prenatally diagnosed birth defects, for example establishing specialized committees of physicians, Muslim scholars, social workers, etc. This would help physicians to make recommendations to their patients, help their patients to know the religious opinion about their specific problem, and help the healthcare administrators to plan for programs to decrease the incidence of birth defects in Arab countries.

Finally, effective genetic counseling requires an appropriate infrastructure with adequate genetic diagnostic facilities. The counselors should be chosen from the community so that they have the confi-

dence of the population. Such services are available in some Arab/Muslim countries including Saudi Arabia, United Arab Emirates, Tunisia, and Iran.

However, the response has been generally poor mainly because of cultural and religious beliefs, unchanging traditional practice of consanguineous marriages, and most important the lack of options available to carrier couples. In Iran, carrier screening for couples for thalassemia has been offered for some time without good response. Only beginning in 2001, when TOP up to 15 weeks for affected fetuses was permitted, were there more couples going to obtain these services. Since then there has been a 70% reduction in the annual birth rate of affected infants.[26]

In a descriptive study of the attitudes of families attending a genetic clinic in the United Arab Emirates, it was concluded that most parents did not accept the inheritance of disease unless the family history was quite obvious. In a follow-up visit only 10% remembered the calculated risk of recurrence, only 40% will avail themselves of prenatal diagnosis if it were available, and only 25% of those would have an abortion if it were available at 10 weeks. Almost half preferred consanguineous marriages even though they were made aware of the risk. The majority agreed with carrier screening and preconception diagnosis.[27] Public education and the other strategies discussed above will hopefully make these services more utilized and more effective.

Another important aspect to consider is the fact that in other Arab countries genetic services i.e. counseling, carrier screening, and prenatal diagnosis are not generally available in the public sector. Most of the couples cannot afford its high cost. It behooves the government in these countries to allocate the funds necessary for these services. In the long run, whatever the cost, it will be offset by the savings in health care provided to physically and mentally disabled individuals who will be born in the absence of these services, not to mention the alleviation of human suffering, which cannot be valued monetarily.

References

1. Teebi AS, Farag TI, editors. Genetic disorders among Arab population. New York: Oxford University Press; 1997.
2. Al-Gazali L, Hamamy H, Al-Arrayad S. Genetic disorders in the Arab world. BMJ. 2006;333:831-4.
3. Tadmouri GO, Al Ali MT, Al-Haj Ali S, et al. CTGA: the database for genetic disorders in Arab populations. Nucleic Acids Res. 2006;34:D602-6.
4. Klat M, Khudr A. Cousin marriages in Beirut, Lebanon: is the pattern changing? J Biosoc Sci. 1984;16:369-73.
5. Al-Roshoud R, Farid S. Kuwait Child Health Survey. Kuwait: Ministry of Health Publication; 1991.
6. Panter-Brick C. Coping with an affected birth: genetic counseling in Saudi Arabia. J Child Neuro. 1992;7:S69-72.
7. Hashem N. Population indices and markers of value as prospective monitors for prevention of genetic morbidity. In: Hashem N, Gerald PS, editors. Preventable aspects of genetic morbidity: proceedings of first international conference. Cairo: Al-Ahram Press; 1978.
8. Hashem N, Sakr R. Mongolism among Egyptian children. In: Proceedings of the second international congress on mental retardation, Wien, 14-19 August, 1961. Basel and New York: S. Karger; 1963, Part 1, pp 387-403.
9. Niazi MA, al-Mazyad AS, al-Husain MA, et al. Down's syndrome in Saudi Arabia: incidence and cytogenetics. Hum Hered. 1995;45:65-9.
10. Faraq TI, Al-Awadi SA, Al-Othman SA, et al. Down syndrome and trisomy 18 in the Bedouins. Am J Med Genet. 1988;29:943-4.
11. Wahab AA, Bener A, Teebi AS. The incidence patterns of Down syndrome in Qatar. Clin Genet. 2006;69:360-2.
12. Courbage Y, Khlat M. Population structure and growth in the Arab world: recent trends. Amman, Jordan: United Nations, Economic and Social Comission for Western Asia; 1993.
13. Glorious Qur'an, Chapter 57, Verse 22.
14. Sunan Abī Dāwūd. Kitāb al-ṭibb (27). Bāb fī al-adwiyya al-makrūha (11). Hadith 3870. Available from http://www.muhaddith.org.
15. Hathout H. In: Genetic disorders among Arab population. Teebi AS, Farag TI, editors. New York: Oxford University Press; 1997.
16. Albar MA. Counseling about genetic disease: an Islamic perspective. East Mediterr Health J. 1999;5:1129-33.
17. Kuliev A, Rechitsky S, Verlinsky O, et al. Birth of healthy children after preimplantation genetic diagnosis of thalassemias. J Assist Reprod Genet.

1999;16:207-11.
18. Traeger-Synodinos J, Vrattou C, Palmer G, et al. An evaluation of PGD in clinical genetic services through 3 years application for prevention of beta-thalassaemia major and sickle cell thalassaemia. Mol Hum Reprod. 2003;9:301-7.
19. Xu K, Shi ZM, Veeck LL, et al. First unaffected pregnancy using preimplantation genetic diagnosis for sickle cell anemia. JAMA. 1999;281:1701-6.
20. Fadel HE. Preimplantation genetic diagnosis: rationale and ethics – an Islamic perspective. J Islam Med Assn. 2007;39:150-7.
21. ACOG practice bulletin no. 77: screening for fetal chromosomal abnormalities. Obstet Gynecol. 2007;109:217-27.
22. Nyberg DA, McGahan JP, Pretorius DH, Pilu G, editors. Diagnostic imaging of fetal anomalies. Philadelphia, USA: Lippincott Williams and Wilkins; 2003.
23. Evans MI, Adzick NS, Holzgreve W. The unborn patient: the art and science of fetal therapy. 3rd edition. New York: W.B. Sanders Company; 2001.
24. Athar S, Fadel HE, Ahmad WD, et al. Islamic medical ethics: the IMANA perspective. J Islam Med Assn. 2005;37:33-42.
25. Islamic Jurisprudence Council of the Islamic World League. Feb 1990, 12th Meeting, Makka, Saudi Arabia. The fourth decision: Regarding aborting a defective fetus. Available from http://www.themwl.org/Publications/default.aspx?d=1&cidi=116&l=AR (p. 277-8).
26. Samavat A, Modell B. Iranian national thalassaemia screening programme. BMJ. 2004;329:1134-7.
27. Al-Gazali LI. Attitudes toward genetic counseling in the United Arab Emirates. Community Genet. 2005;8:48-51.