Awareness and Prevention: The Need for Genetic Screening in the Syrian Jewish Community

Farha Zibak

Syrian Jewry originated from the combination of two different populations. One segment of Syrian Jewry, often referred to as the Mizrahi Jews, ascribes its origins to the time of King David. His army general, Joab, conquered Aram Zoba (II Samuel 10), an area of Syria that was tentatively identified as Aleppo. In Roman times, approximately 10,000 Jews lived in Damascus [1]. The other segment of Syrian Jewry, known as the Sephardi Jews, arrived in Syria after their expulsion from Spain in 1492. In the beginning of the 20th century, with anti-Jewish sentiment rising, many Syrian Jews migrated from Syria to the United States, Latin America, and Israel [2]. The next major emigration occurred in 1948, after Israel declared its independence. Those Jews who remained in Syria were permitted to leave in 1992, with most settling in Brooklyn, New York, the world's largest Syrian Jewish community [3].

Because the Syrian Jewish community is a close-knit community, there is a tendency for close blood-relatives to marry. Marriages between an uncle and a blood-related niece or between blood-related first cousins are common. Such blood related marriages may be clinically problematic, as these individuals share 1/8 of their genes and there is a greater probability of recessive deleterious genes for a specific disorder being transmitted from each partner to a common offspring. Even in Biblical times this was an issue, as we see in in *parashat Acharei Mot* (*Vayikra* 18:6-23) the prohibition of *arayot*, or illicit sexual conduct between close relatives, such as between a father-in-law and a daughter-in-law, between a mother-in-law and a son-in-law, between a parent and a child, or between a sister and a brother are noted. Marriages between uncles and blood-related nieces and between first cousins are not in the category of *arayot* and are *halachically* permitted. Yet, such marriages lead to increased incidence of genetic defects in the offspring. Recognizing this, Rav Waldenberg recommends that one abstain from such marriages [Tzitz Eliezer 15: *simon* 44]. Rav Avigdor Miller notes that such marriages were common in biblical times and thereafter, without the worry of producing children with adverse health effects [14]. However, those generations were closer to *Adom HaRishon*, whose genome was perfect, as it was created by *HaShem*. Over the generations, defective genes arose and accumulated within the human genome, making marriages between close-blood relatives clinically problematic, and increasing one's risk of producing offspring with hereditary diseases.

Marriage between first cousins is still very common in many cultures today , particularly in Moslem countries. For example, in Qatar, the current rate of marriage between first cousins is 22% [6]. First cousin parents have about a twofold higher risk than unrelated parents of having a child with a multifactorial polygenic disease which is a disease that is affected by multiple genes and can be influenced by environmental factors [7]. Consanguineous marriages (a union between two individuals related as second cousins or closer) are also linked to increased risk for fetal death and infant mortality, congenital heart disease, coronary arterial disease, deafness, and for preterm birth at less than 33 weeks of gestation [8, 9, 10, 11, 12]. In the mid-1970s, a study was published showing that the increased incidence of leukemia in females within the Syrian Jewish community in Brooklyn correlated with first cousin marriages [13].

This article will shed light on several common genetic disorders in the Syrian Jewish community, as well as issues (*i.e.*, consanguineous marriages) that magnify the incidences of genetic defects within the community. As an isolated population within the Middle East, the Syrian Jewish community developed genetic disorders unique to their specific group. According to the Victor Center for the Prevention of Jewish Genetic Diseases [4], the five most prevalent genetic disorders within the Syrian Jewish community are glucose-6-phosphate dehydrogenase (G6PD) deficiency, anophthalmia, renal tubular acidosis, Roberts syndrome, and striate keratoderma.

The first of these five genetic disorders, glucose-6-phosphate dehydrogenase (G6PD) deficiency, is the most common among the Syrian Jewish population. It is characterized by a yellowish colorization of the skin, as well as the possibility of anemia. Individuals with this disorder are advised to avoid consumption of fava beans and aspirin, both of which may induce anemia. The defective gene for G6PD deficiency is located on the X chromosome. Because males have only one X chromosome, Syrian Jewish males either carry or do not carry the defective gene. As females carry two X chromosomes, Syrian Jewish women may be homozygous (both X chromosomes carry the defective gene or neither X chromosome carries the defective gene) or heterozygous (only one X chromosome carries the defective gene). The carrier frequency for this defective allele which is one of two or more alternative forms of a gene that arise by mutation and are found at the same place on a chromosome, is 1 in 27 within the Syrian Jewish population .

The second of these five genetic disorders, anophthalmia, is the the absence of eye tissue in the socket, which along with microphthalmia, abnormally small eyes, is a birth defect occurring in 1 to 3 children of 10,000 births. In the Syrian Jewish community, this defective gene was traced to a mutation on autosomal chromosome 14.

Another Genetic defect found among the Syrian Jewish population is known as renal tubular acidosis. It is associated with defective kidney tubules, causing acid to accumulate in the blood. Rickets, poor growth, calcium deposition in kidney tubules, and hearing loss are some of the clinical symptoms of this disorder. About 33% of patients with this syndrome experience progressive and irreversible hearing loss, beginning as young as 3 months of age. The defective gene is located on the shorter arm of chromosome 2, an autosome. The carrier frequency of this defective gene is unknown.

Fourthly, Roberts syndrome is a prenatal condition of growth malformations of the bones of the skull, arms, legs, and face. Facial abnormalities are common, and most cases of Roberts syndrome are associated with mental retardation. The defective gene is located on the short arm of chromosome 2, and its carrier frequency is unknown. There is no cure for this disorder.

Lastly, Striate keratoderma is a dominant genetic disease affecting the palms, fingers, and soles of an individual and is manifested by a thickening and brown discoloration of the skin. The defective gene is located on chromosome 18, and the carrier frequency is unknown. As a dominant mutation, the carrier of this defective gene manifests the abnormal observable characteristics.

Some genetic disorders in the Syrian Jewish community are noted in other Sephardi communities as well such as G6PD deficiency. The commonality of a specific gene mutation may be indicative of gene flow (marriages) between these communities. However, G6PD deficiency is an interesting genetic defect as it shows advantage, with carriers of this mutation having increased resistance to malaria. This mutated gene is commonly expressed in Middle Eastern communities in which the climate and environment allow for the existence of malaria-carrying mosquitoes. Higher frequencies of this defective gene were noted both in Jewish and non-Jewish populations in regions where malaria is endemic [5].

Sephardi individuals and communities, including those in the Syrian Jewish community, need to be informed of these genetic disorders. With an awareness of the significant risks posed to their offspring, two recommendations be made: limit the incidences of these diseases by curtailing consanguineous marriages, and propose a genetic screening program for this population of Jewry.

Acknowledgements:

First and foremost I would like to thank *Hashem* for everything that I have and for this amazing opportunity. I would like to thank Dr. Babich for his help and his constant encouragement throughout this process. Last but not least, I would like to thank my parents for their constant support and dedication. I would not be where I am today without them.

References:

[1] Wikipedia, Syrian Jews, retrieved 6/17/2013.
[2] Wikipedia, History of the Jews in Syria, retrieved 6/17/2013.
[3] Tuttle, R., 2005, SyriaComment.com, October 25th
[4] Victor Center for the Prevention of Jewish Genetic Diseases, *www.victorcenters.org/*
[5] Diamond, J., 1993, Who are the Jews? Natural History, November, pp. 12-19.
[6] Lewis, R., 2013, Human Genetics. 10th edition, McGrawHill Co., Inc., NY, NY.
[7] Cummings, M.R., 2013, Human Heredity, 10th edition, Brooks/Cole, Belmont, CA.
[8] Mohammadi, M.M. *et al.*, 2012, The relationship between consanguineous marriages and death in fetus and infants, J. Res. Med. Sci., 17:448-451.
[9] Shieh, J.T. *et al.*, 2012, Consanguinity and the risk of congenital heart disease, Amer. J. Med. Genet., 158A:1236-1241.
[10] Youhanna, S. *et al.*, 2010, Parental consanguinity and family history of coronary artery strongly predict early stenosis, Atherosclerosis, 212:559-563.
[11] Feinmesser, M., Tell, L., and Levi, H., 1990, Decline in the prevalence of childhood deafness in the Jewish population of Jerusalem: ethic and genetic aspects, J. Laryngol. Otol., 104:675-677.
[12] Mumtaz, G. *et al.*, 2010, Consanguinity: a risk factor for preterm birth at less than 33 weeks' gestation, Amer. J. Epidemiol., 172:1424-1430.
[13] Feldman, J.G., Lee, S.L., and Seligman, B., 1976, Occurrence of acute leukemia in females in a genetically isolated population, Cancer, 38:2548-2550.
[14] Miller, A., 1994, Kingdom of Cohanim, Comments and Notes on *Vayikra,* Gross Printing Co., NY, NY.