Familial Mediterranean Fever: The Disease and the Need for Genetic Screening

By Rachel Faiena

Sephardic Jewry consists of people who originated from the Iberian Peninsula (Spain and Portugal). After their expulsion from Spain in 1492, the community migrated to Portugal and, soon thereafter, were expelled again and, as a result, migrated to the Middle East and North Africa. These communities were mainly isolated from European Jewry and married amongst themselves. There is a common misconception among Sephardim that hereditary diseases are solely an Ashkenazic health issue. Sephardim formed small and tight-knitted communities often isolated from one another, any hereditary diseases that may have developed were less numerous and varied much in their different communities. For example, a genetic disease common in Moroccan Jewry may be seldom seen in Syrian Jewry.

Until recently, little research and effort was directed towards discerning Sephardic genetic diseases, identifying the causative defective genes, and developing the molecular probes to screen for these disorders. Recently, extensive research was conducted to show that there is a broad spectrum of genetic diseases associated with Sephardim that are dependent on their country of origin. Amongst the various Sephardic conditions, Familial Mediterranean Fever (FMF) is one of the most common disorders found in most Sephardic populations [1].

FMF is an autosomal recessive disease that occurs in individuals who have multiple mutations in the MEFV gene located on chromosome number 16. When functioning normally, this gene is responsible for the presence of pyrin proteins which play a role in the immune system and regulating inflammation. Being homozygous is having two doses of the defective gene, thus an individual who possesses two copies on chromosome sixteen has the defective gene which causes an extended period of inflammation which reduces pyrin proteins in the body. Lack of treatment may lead to hazardous accumulation of proteins, termed amyloid fibrils in organs and tissues resulting in amyloidosis. In order to prevent amyloid formation, individuals take colchicine, an anti-inflammatory medication. People with amyloidosis experience fever along with recurrent attacks of painful inflammation of the serosal membranes in the abdomen, chest or joints. Additional symptoms include peritonitis, rashes and arthritis [2]. These painful episodes return in a variable pattern, and therefore occur often without warning [3].

The frequency of the FMF mutation has already been reported in several Arab countries, such as Lebanon, Saudi Arabia, and Jordan [4]. In Syria, specifically, there was a high percentage of people with FMF or at least who were carriers for the mutation. A study was conducted in which blood samples of 83 patients with FMF and 242 healthy individuals from different regions in Syria were collected. Restriction fragment length polymorphism (RFLP) analysis was used to screen the FMF patients for the five most common MEFV gene mutations. Amongst the 83 FMF patients, 89% were positive for at least 1 to 3 of the more common mutations and the remaining 11% had none of the common mutations. The carrier rate in the population of the FMF individuals was 17.5%. E148Q was the most common FMF mutation with a carrier frequency amongst healthy subjects of 1 in 5.7 individuals. In 45.8% of the patients with FMF, M684V was the most common mutation. Additionally, 58.3% of the patients had a family history of FMF. It was also determined that the age of onset is extremely high and was estimated to about 14 years old. This study demonstrated that the carrier rate for this disease was is above average, with FMF rated as one of the highest frequent familial disorders in the Syrian population [4]. Similarly, the carrier rate amongst Sephardic Jews is 1 in 5 individuals, [5], thus there is a 1 in 25 chance of a Sephardic couple with both the husband and wife being carriers of FMF. For such a couple, there is a 25% (1:4) chance of producing any one child with FMF.

Because of their reproductive isolation from the population of their host country, non-Ashkenazi communities have developed a unique set of genetic disorders. In the 2001 survey of the World Sephardi Federation, non-Ashkenazim comprised only 26% of world Jewry. This may be one of the contributing factors as to why there was a lack of attention...
towards involving Sephardim in screening programs for their unique genetic disorders. Through a collaborative effort between Dor Yeshorim, the largest Jewish genetic screening center, and the Syrian Jewish community in Brooklyn, NY, attention has focused to developing genetic screening for Sephardi Jewry. Dor Yeshorim, originally founded to prevent Tay-Sachs disease amongst Ashkenazim, has “spared 4,970 families from having children born with fatal or debilitating genetic diseases” [6].

According to Dor Yeshorim, 80% of children born with a genetic disease have no family history of the genetic issue. Thus, it is crucial to spread awareness and educate Sephardim on the severity and prevalence of those genetic diseases unique to their community in order to prevent the manifestation of these recessive genetic mutations. Many prominent rabbis such as Rabbi Ovadia Yosef, Rabbi Yitzchak Yosef, Rabbi Mordechai Eliyahu, etc., have approved and encouraged Sephardic families to have genetic screening by Dor Yeshorim. These rabbis ensure that the testing is done under halachic rule and there is always strict supervision while maintaining total confidentiality [6].

It is written in the Torah in the book of Devarim , “וְנִשְׁמַרְתֶּם מְאֹ֖ד לְנַפְשֹׁתֵיכֶ֑ם” which means that one should guard themselves very carefully [7]. According to Mesilat Yesharim, one should not put him/herself in danger even if he/she is righteous with many merits. A person should not depend upon miracles, rather he or she should be proactive in maintaining good health for themself and their families [8].

According to the Peleh Yoetz, the pasuk in Devarim is instructing people that when it comes to health, a person should ensure to seek the best medical treatment. Failure to do so is a punishable transgression before G-d, as commanded, “וְנִשְׁמַרְתֶּם מְאֹ֖ד לְנַפְשֹׁתֵיכֶ֑ם” that it will cause “death without judgment.” Consequently, the person will be held accountable for his/her death [9]. In the Talmud a mashal about a man who is praying while he is walking is described. An officer stops to greet him and the man does not respond due to his concentration in prayer. After finishing prayer, the officer asked why the man would endanger himself, if in the Torah it says that one must guard himself. The officer wanted to know why the man did not respond to him, as the officer could have killed the man for impudence. The officer then asked who will be accountable for this man’s death? Obviously, the man, not the officer [10]. This shows the extent to which a person should go in order to care for and prevent him/herself from facing danger, even if it may avert one from doing a mitzvah. Therefore, it can be understood that Sephardim have a responsibility to take control of their genes and be aware of genetic diseases present in their community.

FMF is a significant problem, yet we do not realize how common is it for people to inherit these diseases or become a carrier. FMF is but one of various genetic diseases in Sephardic communities. It is important to acknowledge the severe effects of some of these genetic disorders, because it will help educate people of the risks and to what extent they can prevent having children with these diseases.

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References


[7] Devarim 4:15
[8] Mesilat Yesharim 9:10
[9] Pele Yoetz 349:3
[10] Talmud Berachot 32B