A long-term follow up of premarital counseling in the Israeli Arab population

Joël Zlotogora · Stavit A. Shalev

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Abstract A follow up study of 168 Arab counselees that received premarital genetic counseling between 2001 and 2009, mostly since they planned to marry with a relative, was performed in 2013. Among the 156 cases in which the counselee married, 30 changed their marital plans (19.2 %). Those who changed their marital plans were more often Muslim Arabs that came for counseling since they were related in particular first cousins. Among the 126 counselee that married as planned, 66 were interviewed. From these interviews, it appears that many of the counselees that were related as first cousins or closer came to premarital genetic counseling in order to decide whether to marry. Most of the couples interviewed followed the recommendations concerning the use of folic acid and genetic tests. Among the 53 consanguineous couples interviewed, 49 women had 118 children. Among these 118 children, 8 (6.8 %) were born with a severe disease in 8 different families. This rate of malformations/genetic diseases is similar to the one observed for consanguineous couples from the general Arab population in the region, suggesting therefore that the premarital

counseling and the adherence to the recommendations did not change the final risk to the counselees.

Keywords Premarital genetic counseling · Consanguinity · Arabs

Introduction

While consanguineous marriages are relatively frequent in specific populations worldwide (Bittles 2012), there are only few studies assessing the impact and the outcome of voluntary premarital genetic counseling from the counselees perspectives (Hamamy 2012). Several studies about the decisions of couples that received premarital genetic counseling in the context of mandatory screening preventive programs for haemoglobinopathies have been performed (Ahmadnezhad et al 2012; Al-Allawi et al 2013; Alswaidi et al 2012). However, in these studies, the couples were referred to genetic counseling because of the mandatory program and therefore the comparison with couples who request by themselves genetic counseling is not fruitful.

A study of couples that came for voluntary premarital counseling because of consanguinity was performed in Israel in the years 1984–1990 based on records of a single genetic clinic (Shiloh et al 1995). Among the 72 consanguineous Jewish couples who received premarital counseling, 52 (72 %) subsequently proceeded with their marriage plan. Most of those that were interviewed later in life, reported that the genetic counseling influenced their decisions to some degree. The purpose of the present study was to assess the possible impact of voluntary premarital genetic counseling on Israeli Arab couples.

J. Zlotogora
Department of Genetic Community, Public Health Services Ministry
of Health, Jerusalem, Israel

J. Zlotogora
Hebrew University, Jerusalem, Israel

S. A. Shalev
Genetic Institute, Emek Medical Center, Afula, Israel

S. A. Shalev
Rappaport Faculty of Medicine, Technion, Haifa [SAS], Israel

J. Zlotogora (✉)
Department of Community Genetics, Building 67 Sheba Medical
Center, Ramat Gan, Israel
e-mail: zlotogora@gmail.com

Subjects and methods

The genetic institute in the Emek Medical Center in Afula, which is located in the north part of Israel, is responsible for most of the genetic services in a region which includes a relatively large Arab population. In the last decade, in order to improve the genetic services, the genetic institute opened several outreach clinics in the community. The present study includes counselees who voluntarily came for premarital counseling between 2002 and 2009 in two of these community clinics, aimed exclusively for the Arab population (Zlotogora et al 2006). Those clinics were situated in two Arab localities: Nazareth and Kafr Kana, and the genetic counseling was given solely by one of the authors (JZ).

Data related to the counselees were updated up to the end of 2013 according to the Israeli population registry, the files from the genetic institute in Emek Medical Center, and follow up interviews. In 2013, a trial to contact all the counselees was made by phone calls according to the details that were given during the genetic counseling session, and those who responded were interviewed according to a same questionnaire. The main questions addressed the motivation of the counselees for having premarital counseling; whether or not they were satisfied by the information they received and did they recommend their friends to apply for such counseling. In addition, they were asked whether the information given during the counseling was considered in their final decisions. Several other questions dealt with the utilization of folic acid, the performance of genetic tests, the existence of fertility problems, and the number of pregnancies, still births and live births. The questionnaire was also aimed to learn whether there has been any medical problem diagnosed during a pregnancy or after birth in any of the offspring.

The study was performed according to a protocol approved by the institutional review board of the Emek Medical Center.

Results

Between 2001 and 2009, data were available regarding 168 Arab counselees (123 Muslim, 44 Christian, and one Druze) who received premarital counseling (Table 1). Among the 123 Muslim counselees, in 101 the prospective partners were related (82.1 %); out of those, 74 partners were first cousins and 13 were double first cousins. Out of the 44 Christian counselees, 26 of the prospective partners were related (59.1 %); out of those, 21 were first cousins but none had a closer relationship. The partners of the Druze couple were double first cousins. Few of the counselees in whom the prospective partners were related and almost all the counselees, in whom the prospective partners were not related, requested premarital counseling because of a medical condition affecting either one of the partners or a member of their family.

The marital decisions

Data about the final marriage decisions were based on the Israeli population registry for all of the counselees. In 12 cases, the partners remained single up to the end of the study. Among the other 156 cases in which the counselee married, 30 changed their marital plans ending by marrying someone else. The 30 counselees that married with another partner included 27 out of the 113 Muslims counselee (23.9 %), 2 out of the 42 Christians (4.8 %), and the single Druze couple. Among the counselees in whom the prospective partners were first cousins or closer, all the 19 Christian Arab counselees married as planned while 19 out of the 78 Muslim Arab counselees changed their marital plans (24.4 %) (chi-square, 5.76; $p=0.0164$). The highest percentage of Muslim counselees that changed their marital plans was among those in whom the prospective partners were first cousins, children of brothers (8 out of 28 counselees, 29 %).

Data obtained by the interviews

We did not succeed to interview any of the counselees that had premarital genetic counseling and later changed their marital plans. Among the other 126 counselees, we were able to interview one spouse from 66 couples (52.4 %). The 66 couples interviewed included 44 Muslim couples out of the 86 who married and 22 Christian couples out of the 40 who married.

Aspects related to the motivation of consanguineous for requesting premarital genetic counseling

Fifty three out of the 66 interviewed couples came to premarital counseling since they were related. Among these 53 couples, 33 came either since they were told to do so or in order to increase their chances for a normal child, and 15 of them used the information for their final decision (44 %). The other 20 consanguineous couples came in order to decide whether or not to marry a specific partner, and among them 17 (85 %) stated that they used the information to reach their final decision (chi-square, 8.14; $p=0.00043$). Among the 29 couples in which the partners were first cousins, those who were the children of brothers declared more often that they came in order to decide whether or not to marry (5 out of 7) than all other types of first cousin marriages (7 out of 22) (chi-square, 0.03; $p=0.8625$).

Degree of satisfaction of the counselees

As an indirect measure of the satisfaction of the counselees, they were asked whether they recommended their friends to have premarital genetic counseling. Among the total 66 couples that were interviewed, 46 said that they recommended their friends

Table 1 Summary of the data on premarital counseling

	Married			Remained single	Total	
	PGC partners	Different partners	% marriage with different partners		N	% total couples
Muslims						
Double first cousins	8	3		2	13	10.6 %
FC, father brother daughter	20	8		4		
FC, mother sister daughter	15	4		1		
FC, father sister daughter	8	1		1		
FC, Mother brother daughter	6	1				
FC unknown	2	2		1		
<i>All first cousins</i>	<i>51</i>	<i>16</i>		<i>7</i>	<i>74</i>	<i>60.2 %</i>
Related, more distant	9	5			14	
<i>All related</i>	<i>68</i>	<i>24</i>	<i>26.1 %</i>	<i>9</i>	<i>101</i>	<i>82.1 %</i>
Not related	12	3			15	
Unknown	6			1	7	
Total	86	27	23.9 %	10	123	
Christians						
FC, father brother daughter	7			1		
FC, mother sister daughter	5				5	
FC, father sister daughter	4			1	5	
FC, mother brother daughter	2				2	
FC, unknown	1				1	
<i>All first cousins</i>	<i>19</i>			<i>2</i>	<i>8</i>	<i>47.7 %</i>
Related, more distant	4	1			5	
<i>All related</i>	<i>23</i>	<i>1</i>	<i>4.3 %</i>	<i>2</i>	<i>26</i>	<i>59.1 %</i>
Not related	12	1			13	
Unknown	5				5	
Total	40	2	4.8 %	2	44	

PGC partners the partners as they were reported in the premarital genetic counseling 2001–2009, *FCX2* double first cousins, *FC* Father brother daughter, the fathers of the partners are brothers; *Mother sister daughter* the mothers of the partners are sisters, *Father sister daughter* the father of the male partner is the brother of the mother of the female partner, *Mother brother daughter* the father of the female partner is a brother of the mother of the male partner, *FC, unknown* first cousins, the exact relationship was not known. The rows in italics provide the summaries of premarital counseling for the total of partners that were first cousins, for those that were related and for those that were not related

have premarital genetic counseling. This recommendation was made more frequently when the spouses were not related (11 out of 13 couples, 85 %) than when they were related (36/53, 68 %).

Use of the recommendations regarding preventive measures

Among the 66 couples, 61 (92 %) said they had genetic tests before/during pregnancy and in 54 out of the 66 couples (82 %), the woman took folic acid prior to/at the beginning of pregnancy.

Fertility problems

Fertility problems which led to medical consultation were reported by a total of 11 of the interviewed couples

(21.2 %). The highest percentage of fertility problems was observed in spouses that were double first cousins (3 out of 6) (chi-square, 4.87; $p=0.0273$).

Outcome of the pregnancies

In 13 of the 66 interviewed couples, the spouses were not related and a total of 22 children were born to 10 of the women. No medical problem was reported in any of these 22 children.

Among the 53 couples in which the spouses were related, at the end of the present study 52 women had 158 pregnancies which included 39 spontaneous abortions (25 %) and one pregnancy that was medically interrupted. A total of 118 children were born to 49 women, of these 8 children had a significant medical problem (6.8 %). These 8 children were born to 8 different families in which the parents were first cousins. One

child had the diagnosis of congenital hypothyroidism after birth and another was diagnosed as affected with IDDM in early childhood. Three out of the 8 children died, two of them soon after birth. The last three children were intellectually disabled without an etiologic diagnosis. In one of these three cases, a medical problem in the family has been reported during the premarital counseling. This couple married even though they were given an additional risk for intellectual disability, based on the report that the brother of the male partner was intellectually disabled. The couple had two children, one of whom was intellectually disabled. It is probable that the intellectual disability in this family is due to an undiagnosed autosomal recessive disorder. The mother of another intellectually disabled child had a second pregnancy that was medically interrupted because of a diagnosis of agenesis of corpus callosum that was also present in the mentally affected child. We assume that in this family too, an undiagnosed autosomal syndrome exists.

Discussion

Consanguineous marriages are frequent in the Arab population in Israel, similarly to the surrounding populations in the Middle East. In a study performed among women who gave birth in the years 1990–1992, more than 25 % of Muslim Arabs and Druze marriages were of spouses that were first cousins with an additional 20 % related in other ways (Vardi-Saliternik et al. 2002). In the same study, consanguinity was less frequent among Christian Arabs, in which 21 % of marriages were between first cousins with an additional 11 % related in other ways. In a single Muslim village, located in the region where the present study was performed, while there were no major changes in the total frequency of consanguineous marriages over 50 years, a significant change in the pattern of marriages was observed (Zlotogora and Shalev 2014). The pattern shifted from a majority of marriages between first cousins, in particular children of brothers, to a majority of couples being distant relatives. At the beginning of the twenty-first century, all types of marriages between close relatives became rarer in this village, and for instance, marriages between first cousins represented less than 3 % of the total. While this village is likely representative of the Muslim population in the region, the couples that came for premarital counseling were significantly different. Among the Muslim couples who came for premarital genetic counseling, 70.8 % were first cousins or closer, and it is probable that the motivation of many stemmed from their concerns regarding the risks associated with close consanguinity. One of the influential factors may have been the public emphasis that has been placed in Israel on the adverse medical consequences of first cousins marriages (Strulov 2005). Indeed, among the Muslim Arabs, the highest percentage of couples who changed their marital

plans was observed among children of brothers (28.6 %), a type of marriage that was overrepresented among the couples who came for premarital counseling. In parallel, the majority of couples in which the spouses were children of brothers stated during their interviews, that they came in order to decide whether or not to marry their cousin. The first cousin marriages in which the father of the male partner is the brother of the father of the female partner are those that were traditionally preferred among the Muslim Arabs and therefore theoretically, those that have had the highest probability to have been arranged by the parents. Accordingly, the aim of at least some of these couples might be the use of premarital counseling as a stand against the parents' wishes. Indeed the counselees in one of the couples admitted during the counseling session that this was the reason for which they came to genetic counseling. A study of genetic counseling among the Bedouins in Israel indeed demonstrated that the real agenda of the counselee is not always the official one, and that there are often hidden purposes (Raz 2005). Even in this context, we find the premarital genetic counseling productive, since regardless the true motivation for the consultation, the meetings serve as an opportunity to educate and to shed light over the importance of prevention and the availability of genetic tests.

The proportion of Christian Arabs who came for premarital counseling (26.2 % of the couples) was significantly higher than their proportion in the Israeli Arab population (7.8 % in 2011). One reason is the larger number of Christian Arabs living in the geographic region in which the two clinics were located. In addition, it appears that the purpose of the genetic consultation was different between Christians and Muslims. Among the individuals interviewed, relatively fewer Christian Arab couples reported that they applied to genetic counseling in order to decide whether or not to marry according to their original plans (27.3 % compared to 43.2 % of the Muslim Arabs). In addition, less Christian Arab couples changed their marital plans (4.3 %) than Muslim couples (23.9 %).

One important aim of premarital counseling is focused on reproductive care including the importance of consumption of folic acid and performing genetic screening tests prior to future pregnancies, in order to reduce the risk of malformations and genetic diseases. From the interviews, it appears that the reported percentage of consumption of folic acid was high (82 %) as was the percentage of performing genetic screening tests (92 %). According to a survey based on interviewing women after birth in all the maternity departments in Israel, the range of reported utilization of folic acid was similar to the one found in the present study (Israeli Center for Disease Control 2011). Therefore, we cannot credit the premarital counseling in this regard; however, the rate of performance of genetic screening tests was significantly higher among the couples from the present study of premarital counseling (92 %) than in the survey performed in women interviewed after birth (less than 20 %).

In many of the couples, infertility problems lead to consultation in a specialized clinic. The highest percentage of fertility problems were reported by the couples that were double first cousins and therefore with the highest coefficient of inbreeding. While it is possible that the basis of the problems was related to consanguinity, no details are available and no conclusion can be drawn. In a review of the impact of consanguinity on fertility, Bittles (2012) pointed to the many problems existing in the studies of human fertilities and the high numbers of possible factors involved.

In the group of 53 couples, in which the spouses were related, among the 118 children born, 8 (6.8 %) were reported to have been affected with a severe disease in the first years of life and one pregnancy was interrupted because of fetal malformation. The rate of malformations and genetic diseases in the present prospective study are within the same range observed among consanguineous couples in the Arab population from the region (Zlotogora and Shalev 2010). While the genetic counseling included delivering information regarding the medical risks of consanguineous marriages allowing an informed decision regarding the marriage, it appears that in spite of the recommendations for preventive measures, and the fact that the recommendations were generally followed by the counselees, the medical burden of the consanguinity was not reduced. One of the reasons is that in spite of the efforts that have been made to delineate and diagnose the genetic diseases existing in the population, many are still unknown. Therefore, the genetic tests that have been offered during the study period were limited in terms of benefit, and indeed, at least in two of the families an undiagnosed autosomal recessive syndrome was probably present. It may be expected that with the introduction of whole exome/genome sequencing, in the near future premarital counseling for consanguinity will include the search for rare recessive mutations, allowing for a more precise counseling and more appropriate preventive measures (Teeuw et al 2010).

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