Consanguinity and genetic diseases among the Bedouin population in the Negev

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Abstract

Arab Bedouins (AB) in Israel are traditionally a semi-nomadic population. Their average birth rate is extremely high (birth rate of 5.43, as well is their high consanguinity rate (44%), despite having decreased from 60% in 1992. Additionally, their mean inbreeding coefficient is 0.0238. The high rate of consanguinity results in a high prevalence of recessive genetic and multifactorial disorders as well as high infant mortality rate (11 per 1000 live births). Various genetic diseases are prevalent in AB, exemplifying how extensive the impact of consanguinity is on the community. Targeted screening programs are provided for prevalent severe genetic diseases. However, despite initial success, genetic screening is still underutilized in AB. AB, the Ministry of Health, the Ministry of Education, and different social associations should plan and manage programmed interventions. These programs should work intensively to further educate and raise awareness regarding consanguinity and its potential harms, to increase trust and collaboration between the community and the public health system, to expand screening and premarital consultations, and to create a genetic bank (specific mutations/whole genome) for the AB community.

Keywords Genetic diseases · Bedouin · Negev · CIPA · Consanguinity · Infant mortality

Introduction

Arab Bedouins (AB) in Israel are traditionally a semi-nomadic population who comprise about 3% of Israel's population (Central statistics bureau 2017a, b). Since the fifth century, they have inhabited the Negev desert, located in southern Israel (Maddrell 1990). Before 1948, the Bedouin population

ranged from 65,000 to 90,000. Following the 1948 war, the vast majority of the Bedouin population were expelled, leaving behind only 11,000 (Maddrell 1990; Falah 1989). Due to an extremely high birth rate of 5.43 (one of the highest birth rates in the world), the population has increased 20-fold since 1948 and now numbers around 240,000 (Central statistics bureau 2017a, b). A minority within a minority, the Bedouins make up approximately 17% of the already small non-Jewish, Palestinian Arab minority living in Israel (CSB 2017a, b), with unique cultural, historical, and social traits.

Once a traditional agrarian society, the Bedouins are moving towards becoming a modern society, primarily due to certain policies put in place following the establishment of the state of Israel. After the 1948 war, the Bedouins who remained in Israel were restricted to a small area of land in the Negev. In the 1970s and 1980s, the state worked to “settle the Bedouins in permanent residences” and sought to establish formal Bedouin settlements in the Negev. Following numerous land disputes, the Israeli government has granted municipal status to a part of the previously unrecognized Bedouin settlements; however, about 40% of the Bedouin population still live in unrecognized villages without any municipal status. These unrecognized villages are not provided with sufficient infrastructure, running water, electricity, and healthcare.

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Accordingly, these villages have extremely high rates of poverty and unemployment.

The objective of this review is to summarize known data regarding the consanguinity, genetic diseases, infant mortality, and the available intervention programs among the Bedouins.

A literature review was conducted using electronic databases and relevant websites and materials from the Israeli Health Ministry.

With poor living conditions and minimal healthcare comes poor overall health outcomes within a population. The infant mortality among the Negev Bedouins is the highest of all populations in Israel. It was 11 per 1000 live births in the 2013–2015 compared with the average national rate of 2.6 per 1000 live births. This rate is about 5 times higher than the Jewish population and about 2 times higher than among the overall Arab population (Inequality report 2016). The most common reason for the high infant mortality is the high rate of congenital disorders (Inequality report 2016).

These health disparities are strongly associated with the poor living conditions and other social determinants of health associated with Bedouin villages. The high percentage of consanguinity has an important contribution to high infant mortality. This is due to congenital disorders with an incidence of 98.18/10,000 live births compared with 62.45/10,000 live births among Muslims in general in Israel (Ministry health report 2014). Consanguinity is a complex phenomenon with important historical and social roots. It increased after 1948 due to the small population size. About 11,000 people lived in isolation from other Arabs and Muslims during the military rule for about three decades. Overall, the Bedouin population in southern Israel is a traditional endogamous society; however, in the last decade, more marriages between the different clans and tribes have arisen.

In 1992, as many as 60% of all Bedouin marriages were between relatives (Vardi-Saliternik et al. 2002). Today, the prevalence of consanguinity is thought to be closer to 45%. This rate of inbreeding is still considered to be comparatively high (Na'amnih et al. 2014). Table 1 summarizes the important published studies that investigated the consanguinity rate. This paper will explore the different aspects of the consanguineous marriages that occur in the Bedouin population. It will seek to understand not only why these marriages occur, but also the extensive effect consanguinity has on the prevalence of genetic diseases. Further nation-wide genetic screening programs, as well as programs involving risk communication, will be explored. Lastly, the paper will address the future of consanguinity and possible steps that can be taken to decrease the percentage of genetic diseases present in the Negev Bedouin population.

What is consanguinity and why does it occur in the Bedouin population

Clinically, consanguinity is defined as a union between two people who are related as second cousins or closer (Hamamy 2012). F , the inbreeding coefficient, is commonly used to quantify how closely related two people are. Specifically, F measures the probability that two genes at any locus in an individual are identical by descent from the common ancestor(s) of two parents (Hamamy 2012; Bittles 2001). In this case, an F value equal or higher than 0.0156 is considered to be a consanguineous marriage. The more closely related two people are, the higher the F value. For example, a union between double first cousins (children of a pair of brothers who marry a pair of sisters) will have an F value of 0.125, while a union between first cousins will have an F value of 0.0625 (Hamamy 2012).

In a 2014 study estimating the prevalence of consanguineous marriages and associated factors among Israeli Bedouins, the mean inbreeding coefficient among 1290 Bedouin marriages was 0.0238 (Na'amnih et al. 2014). Beginning in November 2009 and ending in January 2010, 1290 Bedouin women who delivered in the maternity wards of the only hospital serving the Bedouin population in the Negev, located in southern Israel, were interviewed. The interview included issues regarding their relatedness to their spouse, their level of education, the marital relatedness in their parental generation, and their age at marriage. Of all the interviews conducted, 44.8% were in consanguineous marriages, 65.7% of which were between first cousins. Additionally, the following trends were found to be significantly associated with consanguinity: women who got married at a younger age, women who had fewer years of schooling, husbands who had higher years of schooling, lower monthly income of household, and consanguinity in the parental generation (Na'amnih et al. 2014). From this study, it can be deduced that consanguinity is still extremely prevalent among the Bedouin population, despite the decline in the last three decades, i.e., in a single generation, and follow-up is needed into the future. Further, this study shows that a variety of social factors take part in contributing to the high levels of consanguineous marriages including, but not limited to education, age, income, and parental consanguinity.

A survey conducted in 2001–2002 investigated the traditional and social roles of consanguineous marriages in greater depth. The main reasons provided by respondents for the continuation of consanguinity, despite the increasing knowledge of the risks associated with cousin marriage, were clan solidarity, interpersonal compatibility, preservation of family property, parental authority, and lastly, social protection for women (Raz and Atar 2004). This survey represents the importance of the clan to the Bedouin population who place a strong emphasis on family values and supporting one's family.

Table 1 Summary of the published data regarding consanguinity rates among the Bedouin population in Israel

Study	Na'amnih et al. 2015	Na'amnih et al. 2014	Vardi-Saliternik et al. 2002	Jaber et al. 1994
Bedouin				
Consanguinity rate (%)				
Bedouin	—	44.8	60.1	—
Non-Bedouin Arab	24	—	36.7	44.3
First cousins of all marriages %				
Bedouin		29.5	36	—
Non-Bedouin Arab		—	22.9	23
Double first cousins				
Bedouin		3.2	—	—
Second cousins				
Bedouin		5	—	—
Distant relatives				
Bedouin		5.1	—	—
Non-Bedouin Arab				9.8
The inbreeding coefficient (mean)				
Bedouin		0.0238	0.02527	—
Non-Bedouin Arab		—	0.01769	0.0192

These values manifest themselves in different ways, with one of those ways being consanguineous marriage.

Prevalence of genetic diseases among the Bedouin population

When consanguineous marriages occur, the offspring are at an increased risk for recessive genetic disorders, “because of the expression of autosomal recessive gene mutations inherited from a common ancestor” and an increased risk for multifactorial genetic disorders (Shawky et al. 2013). Thus, due to the high prevalence of consanguinity in the Bedouin population, they are at a greater risk of genetic disorders than populations with a lower rate of inbreeding.

The most recent list of genetic diseases known to be associated with the Bedouin population can be seen in Table 2 (Congenital Malformations and Genetic Diseases report).

This comprehensive list of genetic diseases shows how extensive the impact of consanguinity is on the community. Thousands of families are affected, many having to deal with the death of a child, or the burden of caring for a child with one or more of these diseases. The carrier rates of 17 of the genetic disorders commonly associated with the Negev Bedouins are shown in Table 2. These rates were derived by testing 6455 Arab Bedouins and should be quite representative of the carrier rates among the general Bedouin population in the Negev. The disorders with the highest carrier rates are maple syrup urine disease (or MSUD) and Carmi syndrome with a carrier

rate of 1 in 5. The disorders with the lowest carrier rates are hypothyroidism, retardation, and dysmorphism (HRD syndrome), each with a carrier rate of 1 in 40.

Genetic screening

In 2002, the Ministry of Health began offering free-of-charge genetic screening for specific populations with a high prevalence of genetic diseases. Specifically, these targeted screening programs are provided for severe genetic diseases with a frequency higher than 1/1000 live births, corresponding to a carrier frequency of 6% for autosomal recessive diseases. Five years after this program was implemented by the Israeli government, more than 13,000 tests were performed in 35 different communities. Around half of the communities screened were Bedouin villages in the Negev, showing the initial success of this genetic screening program (Zlotogora et al. 2008).

However, despite this initial success, genetic screening is still widely underutilized in the Bedouin population. In such an isolated and small society, individuals avoid premarital screening, in case the stigma of possible disease would reduce their prospect of marriage.

The Genetic Testing Recommendation per the Ministry of Health in Israel is shown in Table 3 (Recommendations for Genetic Testing 2016).

There has been a decline in the infant mortality rate in the AB population, which can be explained by different factors including an increase in the education and awareness

Table 2 Carrier rates for genetic disorders associated with the Bedouin population, according the ministry health report, years 2011–2013

Genetic disorder	Carrier rate	Number of the tested persons	Number of carriers	OMIM
Arthrogryposis	1:8	509	66	208100
Ataxia telangiectasia	1:10	362	36	208900
Bardet Biedl	1:8	952	119	209900
Bartter syndrome	1:6	420	68	601678
				241200
				307667
				602552
Carmi syndrome	1:5	182	35	
Complex III deficiency	1:6	468	76	124000
Congenital Insensitivity to pain with anhydrosis (CIPA)	1:14	3372	243	256800
Cystinuria	1:9	216	23	220100
Hemolytic uremic syndrome	1:11	150	14	235400
Infantile bilateral striatal necrosis	1:9	528	59	
Infantile sialic acid storage disease (ISSD)	1:19	167	9	269920
Maple syrup urine disease (MSUD)	1:5	152	28	248600
Non ketotic hyperglycinemia	1:9	104	11	
Osteopetrosis	1:9	1010	108	259700
				166600
				259710
				259720
Nephronophthisis	1:21	270	13	256100
				606966
				604387
Glycogen storage 1b	1:27	806	30	232220
Hypoparathyroidism, retardation, dysmorphism	1:40	6455	161	241410

regarding the harms of consanguinity and associated genetic diseases, as well as in interventions managed by the Ministry of Health and other institutions.

Despite these efforts, over the last 8 years, the infant mortality rate did not change significantly. This is probably due to the persistent high rate of consanguinity, to poor access to healthcare for many Bedouins and lack of intensive specific continuous interventions for a decline in infant mortality during the last decade. Therefore, to further decrease infant mortality, programmed interventions should be coordinated and planned with different authorities, as well as the Bedouin population in the Negev. The primary objectives should focus on significantly decreasing the rate of consanguinity and increasing access to screening tests.

There are a number of key components that are imperative to creating an effective intervention targeting the reduction of infant mortality and genetic diseases. First, it must prioritize educating and raising awareness regarding genetic diseases and consanguinity among the Bedouin population, with the specific target group of young people before marriage predominantly aged 15 to 25 years. This educational program

should be developed in collaboration with local leaders, Imams, genetic consultants, and physicians. By doing so, the intervention will gain a better understanding of the local context, raise trust, and finally raise awareness of the dangers associated with consanguinity, its medical, and social consequences, and to promote genetic screening.

Furthermore, premarital carrier matching allows potential partners to find out if they are genetically compatible, without being told personal information about their own genomes. A screening program of this type could include specific known familial mutations or whole genome screening, if available. The genetic information obtained will help to determine the risk of specific prevalent genetic diseases and assist in premarital decision making. This type of screening lowers the risk of stigmatization, while still informing a couple of their genetic compatibility or incompatibility.

Premarital screening would be most successful if a comprehensive genetic bank of the Bedouin population was made available in the future. This bank should include genetic data regarding the most common inherited diseases, and if possible, the entire genomes for every person, especially for the

Table 3 Genetic testing recommendations according to the Ministry of Health in Israel

Tests for all Bedouin tribes in the Negev (OMIM number)	Further tests according to the tribe of Origin Common to Both Spouses (OMIM number)	Further testing according to the Tribe of Origin of the Mother (OMIM number)
1. Spinal muscular atrophy (253300, 158600, 253400)	1. Arthrogryposis (208100)	Fragile X syndrome (300624)
2. Hypoparathyroidism, retardation, dysmorphism (241410)	2. Ataxia telangiectasia (AT) (208900)	
3. Congenital insensitivity to pain (256800)	3. Bardet Biedl syndrome (209900)	
	4. Bartter syndrome (601678, 241200 307667, 602552)	
	5. Cardiomyopathy dilated, neonatal isolated (115200)	
	6. Carmi syndrome-epidermolysis bullosa, pyloric stenosis	
	7. Carnitine-acylcarnitine translocase deficiency (212138)	
	8. Complex III deficiency, mitochondrial respiratory chain (124000)	
	9. Cornelia de Lange like (Birk Flusser) syndrome	
	10. Cystinuria + (2p16 del) syndrome (220100)	
	11. Cystic fibrosis (219700)	
	12. Desmosterolosis (602398)	
	13. Glycogen storage disease (232220)	
	14. Growth hormone deficiency (262400, 173100, 307200)	
	15. Hemolytic uremic syndrome, complement H factor 1 deficiency (235400)	
	16. Infantile bilateral striatal necrosis (IBSN)	
	17. Infantile neuroaxonal dystrophy (INAD) (600329)	
	18. Infantile sialic acid storage disease (ISSD) (269920)	
	19. Leber's congenital amaurosis (204000)	
	20. Maple syrup urine disease (MSUD) (248600)	
	21. Nephronophthisis (256100, 606966, 604387)	
	22. Niemann Pick type C (257220, 607625)	
	23. Non ketotic hyperglycinemia	
	24. Osteogenesis imperfecta (166200,166210, 166220, 259420, 610682)	
	25. Osteopetrosis (259700, 166600, 259710 259720)	
	26. Pelizaeus-Merzbacher-like syndrome	
	27. Persistent hyperinsulinemic hypoglycemia of infancy PHHI (256450, 601820)	
	28. Pyruvate dehydrogenase deficiency (PLD) (312170)	
	29. Thalassemia	

target group of young Bedouins aged 15 to 25 years. A specific focus should be placed on some families and tribes with specific disease and mutations.

The involvement of the different bodies responsible for healthcare in the Arab Bedouin population is mandatory for the success of such a project. To make the project feasible, particularly among Bedouins lacking good healthcare facilities, the plan should include home visits in specific villages, utilizing “preventive genetic mobile clinics.” In the past, mobile clinics were successfully employed in these populations to provide

vaccinations in childhood and nowadays they are used as mobile dental clinics.

The establishment of a genetic bank with the collection of samples and data may require years and, since it raises many social and ethical questions, it must include both the community perspective and the involvement of community-based organizations, not just medical and genetic perspectives. While a focus on high-risk families may be important in the early stages of the intervention, preventing inconvenience and genetic stigmatization is very important among the population. The program should therefore be implemented by a

skilled team close to the population, taking into account all of the important aspects related to both the population and sensitive genetic information. Incorporating inputs from the social sciences and humanities will assist in understanding the social, ethical, and political challenges in such an initiative.

Another intervention that could be helpful would be the requirement of medical approval and genetic counseling prior to marriage in specific tribes. Requiring familial genetic disease screening for Bedouins who are determined to be at high risk would be similarly effective.

These intervention programs should be planned and managed by representatives of the Bedouin population (both professional and community members), the Ministry of Health, the Ministry of Education, and different community-based associations. The Bedouin people should be involved throughout all components of the program in order to understand what the main concerns of the community are, and to ensure that these programs will be accepted by the community.

As of 2017, a new social initiative called “Genesis for Community Health” started a wide screening program based on this model. Genesis is an Israeli non-profit, run mostly by Israeli Bedouins, that aims to decrease the prevalence of genetic diseases in the Bedouin community by spearheading premarital genetic testing and matching. Its model includes designing a genetic screening test tailor-made for the Bedouins (according to the known prevalent mutations), utilizing a community-based approach to test all Bedouin young adults before they marry, and establishing a Bedouin genetic database that will enable the identification of intended couples at risk.

This initiative drew inspiration from Dor Yeshorim, a global premarital carrier testing program for Ultra-Orthodox Ashkenazi Jews. Since the beginning of the program in Brooklyn, New York, in 1983, as a screening program for Tay-Sachs, there has been a decline of > 90% in the incidence of Tay-Sachs around the world (Lew et al. 2015). For this reason, this program has become a paradigm for the successful assimilation of new genetic technologies into a traditional community. Nowadays, the program screens for additional genetic recessive disorders such as cystic fibrosis, familial dysautonomia, and Canavan disease. It operates in 11 countries including the Americas, Canada, Europe, and Israel.

However, the Bedouin population in Israel faces somewhat different challenges regarding premarital screening. First, the population is not as submissive to religious authorities as the Ultra-Orthodox Jewish community targeted by the Dor Yeshorim program. Second, the process of arranging marriage in the Bedouin population is complex and demands deep involvement of the parents, as opposed to the process for the Ultra-Orthodox Jews, which is usually orchestrated by a matchmaker. The involvement of many Bedouin family members in this process increases the risk of breaching

confidentiality and creating stigma. Third, as mentioned previously, many Bedouins in Israel lack access to primary healthcare, which makes the screening tests even more of a challenge.

The Genesis initiative tries to tackle these challenges by working with Bedouin professionals from different disciplines (Imams, family leaders, doctors, social workers, teachers, mayors, engineers, etc.) who have a strong influence on their community, and by making the process as easy as possible for the population, with free-of-charge tests that are conducted in schools and mosques. Its database will be used to inform potential couples about their risk for genetic incompatibility, while maintaining confidentiality and preventing stigmatization by not revealing detailed personal information.

Lastly, having a community program run by the Bedouins themselves is a major advantage since it is respectful to culture and tradition. As such, it has great potential to change old habits and perceptions. However, more time and research are needed in order to fully evaluate the efficiency of the program and the compliance of the community. Social, ethical, and political considerations must be taken into consideration. Success in this program may later be duplicated in other Bedouin communities around the Middle East and North Africa. If successful, it could serve as a hopeful solution to be considered for use in other closed communities, with adaption to their local context (for example, the Amish, Druze, and Roma).

Conclusion

Despite the decline in the consanguinity rate and infant mortality rate among the Bedouin population in the Negev, these rates are still very high. Along with the reduction in consanguinity, there has been a decrease in the percentage of Bedouins affected by genetic disease. An emphasis must be placed on the importance of reducing genetic diseases and increasing knowledge of the dangers of consanguinity from a deep historical, social, and political understanding. Rethinking consanguinity within a community-based context, as well as effectively understanding and addressing the concerns of the community, has the potential to conquer this long-existing public health challenge.

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Compliance with ethical standards

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