GENETICS

Consanguineous Marriage and Its Effect on Offspring Congenital Malformation: A Study among Palestinian Rural Community

Farid AW Ghrayeb

ABSTRACT

Objective: **Consanguineous marriage is a long-standing socially accepted practice among Palestinian population. It is proposed that consanguineous marriages increase the risk of congenital malformations and genetic disorders. This study aimed to determine the health consequences of consanguinity on congenital malformations in Yata rural population, Hebron, Palestine.**

Methods: **A cross-sectional household-survey study was conducted on 500 married women. All the women were interviewed personally using a structured questionnaire. A family pedigree was constructed to study the type of consanguineous marriages.**

Results: **The prevalence rate of consanguineous marriages in the present study was 61%, where first-cousin marriages representing 34.8% of all marriages. The genitourinary system was the most common malformation, where was reported by 17.4% of the 305 consanguineous married parents, and 15.2% of the 105 non-consanguineous married parents. The gastrointestinal system defects was the second most affected anatomical system in frequency in 6.2% of the 305 consanguineous married parents, and 13.3% of the 105 non-consanguineous married parents.**

Conclusion: **The study revealed that consanguinity has adverse health consequences on offspring of consanguineous couples. There is a need for genetic counseling to increase the awareness of the health consequences of consanguineous marriages.**

KEY WORDS

consanguinity, congenital malformation, genetic disorder, consequences, Palestine

INTRODUCTION

Consanguineous marriage is the union between biologically related individuals, where first cousins are the most common prevailing form worldwide[1]. It is estimated that more than 10.4% of global population are either of consanguineous marriage or are of consanguineous union progeny[2].

Consanguineous marriages are recognized as being associated with higher risk for inheriting abnormalities and diseases due to homozygous recessive genes, thus suffer autosomal recessive genetic diseases than non-consanguineous unions[3,4], where brothers and sisters share commonly 50% of their genetic make-up. Uncle and niece share 25% and first cousins 12.5% of their inherited genetic material[5]. As a result, the offspring of consanguineous marriages are more often homozygous by descent than those of non-consanguineous parents. Consequently, that consanguineous marriage have almost higher risk of producing offspring with congenital malformations, and increased perinatal and child mortality and morbidity, caused by the inheritance of rare recessive genes from common ancestors compared with general population[6-8].

Surprisingly, the results of the previous studies toward the association between consanguinity and offspring genetic disorder are controversial. On one hand, literature reported that offspring's of consanguineous couple had higher rates of perinatal and child mortality and morbidity[9], congenital malformation[10-12], increased risk of abortions, stillbirths[13], chronic diseases such as, hypertension, diabetes, certain cancer, obesity, mental disorders, heart diseases, and deafness[14-17]. On the other hand, some scholars believe that a long practice of inbreeding over several generations leads to elimination of deleterious recessive alleles from the population gene pool due to the death of an affected child[2,18].

Although consanguineous marriage is deeply rooted and widely practiced in Palestine, there is paucity in available information regarding the possible linkage between parental consanguinity and offspring mortality. Consequently, this paper aims to determine the prevalence of genetic consequences of parental consanguinity on offsprings malformation in Palestine.

MATERIALS AND METHODS

This study is part of a cross sectional household survey. A convenience sample of 500 married women was personally interviewed using a structured questionnaire in Yatta to determine the prevalence of consanguineous marriages and the associated health consequences on mother and children. An Arabic version questionnaire was used and included four areas of interest: Personal information, socioeconomic factors, obstetric profile, family pedigree, the level of consanguinity, if any (that is, first cousin, second cousin, or others), and offspring morbidity and mortality.

Fieldswork techniques

Data was collected by female fieldworkers whom were selected at the regional level to ensure familiarity with local norms and locations of sampling areas. The three selected field workers were working with the

Received on April 8, 2014 and accepted on December 25, 2015
School of Public Health, Al Quds University
Jerusalem, Palestine
Correspondence to: Farid Abdulwahab Ghrayeb
(e-mail: ghrayeb2000@yahoo.com)

Table 1 Prevalence of consanguineous marriage among study population

Consanguineous marriage		
variable	No.	%
Yes	305	61.0
NO	105	39.0
Degree of consanguinity among consanguineous married women		
First degree	174	34.8
Second degree	60	12.0
Third degree	71	14.2
Total	305	61.0

Table 2. The Prevalence of Congenital Malformation in Consanguineous and Non Consanguineous Marriages (n = 305 consanguineous, 195 non-consanguineous marriage)

variables	Consanguinity						
	Yes		NO		Total		
	No.	%	No.	%	No.	%	P Value
Cleft lip and palate							
Yes	12	2.4	7	1.4	20	4.0	0.723
NO	293	58.6	188	37.6	480	96.0	
Imperforated anus							
Yes	3	0.6	3	0.6	7	1.4	0.811
NO	302	60.4	192	38.4	493	98.6	
Pyloric Stenosis							
Yes	4	0.8	4	0.8	8	1.6	0.922
NO	301	60.2	191	38.2	492	98.4	
Congenital hip dislocation							
Yes	10	2.0	6	1.2	16	3.2	0.943
NO	295	59.0	189	37.8	484	96.8	
Clubfoot							
Yes	2	0.4	1	0.2	3	0.6	0.801
NO	303	60.6	194	38.8	497	99.4	
Congenital heart disease							
Yes ≥ 1	5	1.0	3	0.6	8	1.6	0.921
NO	300	60.0	192	38.5	492	98.4	
Down syndrome							
Yes ≥ 1	4	0.8	3	0.6	7	1.4	0.834
NO	301	60.2	192	38.4	493	98.6	
Hypospadias							
Yes ≥ 1	20	4.0	6	1.2	26	5.2	0.082
NO	285	57.0	189	37.8	474	94.8	
Undescended testis							
Yes ≥ 1	18	3.6	5	1.0	23	4.6	0.084
NO	287	57.4	190	38.0	477	95.4	
Hydrocele							
Yes ≥ 1	15	3.0	5	1.0	20	4.0	0.084
NO	290	58.0	190	38.0	480	96.0	
Hydrocephalus							
Yes ≥ 1	2	0.4	1	0.2	3	0.6	0.800
NO	303	60.6	194	38.8	497	99.4	
Total	81	16.2	20	10.3	121	24.2	

Palestinian Census Bureau of statistics system; they were given adequate training using role play techniques and small group discussion of the questionnaire.

Furthermore, appropriate means for maintaining close and open contact between the researcher and fieldworkers was established. The inclusion criteria included married couples with at least one child. The data were analyzed by SPSS version 12.0. Standard procedures of chi-square test and fisher's exact test were employed to analyze the data. The data collected throughout face to face interview between the interviewers and the interviewees, but the data and answers were registered by the interviewers only.

Pilot study

A small pilot test was conducted prior to administration in order to assess readability, understanding, response bias, respondent burden, time required for completion and analysis of potential social desirability bias by correlation between the summed social desirability measure and individual questionnaire items (internal consistency and factor analysis were not conducted on the pilot test data). Internal consistency for these variables, as represented by Cronbach's alpha was tested prior to the implementation of the environmental education program, was 0.88.

Ethical considerations

The study was approved by the higher education ethical committee of Al Quds University, permission was obtained from the Municipality of Yatta, and consent form was signed by the participants.

RESULTS

The prevalence rate of consanguineous marriage in the present study population was 61% (Table 1). The most common type of consanguineous marriage was first-cousin marriage (174, 34.8%). The second most common category of consanguineous marriages was third degree cousin marriages (71, 14.2%), whereas the second degree cousin marriage was the least common category (60, 12.0%)

The overall prevalence of reported congenital malformation was 24.2%, where higher in consanguineous in 16.2% than non-consanguineous in 8.0% marriages. Although, the prevalence of congenital malformation was more likely reported in consanguineous marriages than non-consanguineous marriages, there was no significant difference between the two groups.

Table 2 shows the frequency of these malformations by consanguinity. The abnormalities were divided the anatomical system. The genitourinary system was the most commonly affected, where was reported by 17.4% of the 305 consanguineous married parents, and 15.2% of the 105 non-consanguineous married parents. Among this group the most frequent reported anomaly were undescended testis, hypospadias and hydrocele, representing 5.2%, 4.6% and 4.0% of the malformations respectively.

The gastrointestinal system defects was the second most affected anatomical system in frequency in 6.2% of the 305 consanguineous married parents, and 13.3% of the 105 non-consanguineous married parents. Among this group the most frequent reported anomaly were cleft lip and palate, pyloric stenosis, and imperforated anus, representing 4.0%, 1.6% and 1.4% of reported gastrointestinal malformations.

The results showed that, there were 8 (1.6%) of the 500 participated women reported that they had infant with congenital heart disease, where 1.0% was reported by women of consanguineous marriage, and 0.6% was reported by non-consanguineous married women.

Overall, 19 (3.8%) of the women in this study reported that they had one or more infants with musculoskeletal system defects. Among this group the most frequently reported defects were hip dislocation and club foot, representing 3.2% and 0.6% of the reported musculoskeletal abnormalities.

DISCUSSION

The prevalence rate of congenital malformations in the reported birth varies from one country to another and within the same country between geographic areas, or these could vary over time. These differences might be due to ethnic and environmental factors or survey meth-

odology. Therefore, comparison between different study results should be done with caution. The highest and lowest prevalence rates of congenital malformations in this study were hypospadias and club foot/ Hydrocephalus, representing 5.2% and 0.6% respectively. The prevalence of the overall major congenital malformations in this study was 24.2%, which concurs with results from previous study in Oman[19], and in Palestinian Arab Israeli[20], but is in contrast with the results of other previous studies, 12.9% for Abu Dhabi[21], 7.9% for United Arab Emirates[22], and 2.8% for Iran[23].

The risk of inheriting the autosomal recessive disorder in the offspring of a consanguineous parent is inversely proportional to the frequency of the disease allele in the total gene pool. In other words, the less common the disease allele is in the gene pool, the higher the risk will be in the expression of an autosomal recessive disorder in the offspring of consanguineous couples[8,24,25]. Therefore, the increased prevalence of congenital abnormalities in the offspring of consanguineous couples was attributed to the increase in the rate of homozygous expression of recessive genes inherited from their common ancestors[6,26,27].

It is believed, but not fully examined or confirmed, the long term of practice of consanguinity over multiple generations, might eliminate the detrimental recessive genes from the gene pool, and the population might be able to get rid of those genes due to the death of an affected progeny[28,29]. However, in several previous studies, it has been reported that, the prevalence rate of congenital abnormalities was higher in offspring of consanguineous than non-consanguineous marriages[30-33], these results were in agreement with our study results.

CONCLUSION

The study findings showed a higher prevalence of congenital malformation in the offspring of consanguineous parents and that, in a population where consanguinity is in high rates. Consequently, genetic counseling before marriage must be applied for consanguineous couples to increase their awareness of the health burdens of consanguineous marriages, and premarital and preconception carrier testing should be integral parts for any couples that may have a family history of genetic disorders. More researches are needed to determine the factors underlying the different types of congenital malformation encountered in Palestine, and to determine accurately the association between consanguinity and congenital anomalies.

ACKNOWLEDGEMENT

The authors of this paper would like to thank the School of Public Health, Al Quds University in Palestine. As well as, the authors would like to thank both the all participants of this study, the field workers, the Municipality of Yatta, and the higher education ethical committee of Al Quds University.

REFERENCES

1) Bittles AH, Speicher M, Antonarakis SE, *et al*. Consanguinity, genetic drift and genetic diseases in populations with reduced numbers of founders. Human genetics - principles and approaches. 4th ed. Heidelberg: Springer, 2009: 507-28.
2) Bittles A, Black M. Consanguinity, human evolution, and complex diseases. Proc Natl Acad Sci U S A 2010; 107(Suppl 1): 1779-86.
3) Kumaramanickavel G, Joseph B, Vidhya A, *et al*. Consanguinity and ocular genetic diseases in South India: analysis of a five-year study.
Community Genet 2002, 5: 182-185.
4) Sureender PB, Khan AG. "Mate selection and its impact on female age, pregnancy wastages, and first child survival in Tamil Nadu, India", Social Biology 1998; 45: 289-301.
5) Kumaramanickavel G. Problems with consanguineous marriages. The Hindu. 2004; Thursday, April 29.
6) Khlat M, Khoury M. Consanguinity and diseases: Demographic, Genetic, and epidemiologic perspectives. Epidemiol Rev 1991; 13: 28-30.
7) Teebi AS. Autosomal recessive disorders among Arabs: an overview from Kuwait. J Med Genet 1994; 31: 224-233.
8) Balkan M, Atar M, Erdal ME, *et al*. The possible association of polymorphisms in MTHFR, MTRR, and MTHFD1 Genes with Male Infertility. International Medical Journal 2013; 20(4): 404-408.
9) Sawardekar KP. Genetic analysis of lethal congenital malformations causing perinatal mortality at Nizwa Hospital, Oman. Clin Genet 2004; 66: 239-43.
10) Kushki AM, Zeyghami B. The effect of consanguineous marriages on congenital Malformation. J Res Med Sci 2005; 10(5): 298-301.
11) Yunis K, Mumtaz G, Bitar F, *et al*. Consanguineous marriage and congenital heart defects: a case-control study in the neonatal period. Am J Med Genet A 2006, 140:1524-1530.
12) Ramli RR, Shahrjerdi B, Hajmomenian M. Agenesis of Sphenoid Sinus: A Case Report. International Medical Journal 2013; 20(3): 378
13) Verma IC, Prema A, Puri RK. Health Effects of Consanguinity in Pondicherry. Indian J Ped 1992; 29: 685-92.
14) Abdulbari B, Rafat H, Ahmad ST. Consanguineous marriages and their effects on common adult diseases: studies from an endogamous population. Med Princ Pract 2007; 16: 262-267.
15) Dham K, Kaur J, *et al*. Dandy walker malformation, diagnosis by prenatal u Ultrasonography and Biochemical Investigations. International Medical Journal 2013; 20(3): 385-387.
16) Wnorlida WI, Norsa'adah B, *et al*. Associated Factors of Coronary Heart Disease in Patients with Type 2 Diabetes Mellitus. International Medical Journal 2013; 20(6): 668-671
17) Zheng Y-b, Guo H-t, Xie X-f, *et al*. A Population-Based Study of Obesity and its Complications in Children and Adolescents. International Medical Journal 2013; 20(6): 691-695
18) Khoury MJ, Cohen BH, Chase GA, *et al*. An epidemiologic approach to the evaluation of the effect of inbreeding on prereproductive mortality. Am J Epidemiol 1987; 125: 251-262.
19) Sawardekar KP. Profile of major congenital malformations at Nizwa Hospital, Oman: 10-year review. J Paediatr Child Health 2005; 41: 323-330.
20) Jaber L, *et al*. Marked parental consanguinity as a cause for increased major malformations in an Israeli Arab community. Am J Med Genet 1992; 44: 1-6.
21) Al-Jawad ST, Shubbar Al, Khafaji NA, *et al*. A survey of serious congenital morphological abnormalities in Abu Dhabi. Ann Trop Paediatr 1988; 8: 76-9.
22) Al-Gazali LI, Dawodu AH, Sabarinathan K, *et al*. The profile of major congenital abnormalities in the United Arab Emirates (UAE) population. J Med. Genet 1995; 32: 7-13.
23) Tayebi, N, Yazdani, K. Naghshin, N. The prevalence of congenital malformations and its correlation with consanguineous marriages. Oman Med J 2010; 25: 37.
24) Bittles AH, Grant J, Sullivan SG, Hussain R: Does inbreeding lead to decreased human fertility? Ann Hum Biol 2002; 29: 111-130.
25) Rudan I, Rudan D, Campbell H, *et al*. Inbreeding and risk of late onset complex disease. J Med Genet 2003; 40: 925-932.
26) Zlotogora J. Genetic disorders among Palestinian Arabs: effects of consanguinity. Am J Med Genet 1997; 68: 472-475.
27) Bittles AH: Consanguineous marriage and childhood health. Dev Med Child Neurol 2003; 45: 571-576.
28) Roberts JAF, Pembrey ME: Cousin marriage; in Roberts JAF, Pembrey ME (eds): An Introduction to Medical Genetics. New York: Oxford University Press, 1978: p 295.
29) Rao P, Inbaraj S. Trends in human reproductive wastage in relation to long term practice of inbreeding. Ann Hum Genet 1979; 42(3): 401-13.
30) Bener A, Al-Ali K: Consanguineous marriage in a newly developed country: the Qatari population. J Biosoc Sci 2006; 38: 239-246.
31) Ben Arab S, Masmoudi S, Beltaief N, *et al*. Consanguinity and endogamy in Northern Tunisia and its impact on non - syndromic deafness. Genet Epidemiol 2004; 27: 74-79.
32) Tamim H, Khogali M, Beydoun H, *et al*. National collaborative perinatalm neonatal network: consanguinity and apnea of prematurity. Am J Epidemiol 2003; 158: 942-946.
33) Saadat M, Ansari-Lari M, Farhud DD: Consanguineous marriage in Iran. Ann Hum Biol 2004; 31: 263-269.