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THE EFFECT OF CONSANGUINITY ON CONGENITAL DISABILITIES IN THE KUWAITI POPULATION

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Summary. Consanguinity has been shown to increase homozygosity and to reduce genetic variation in a group, which may protect against the expression of recessive genes that can lead to genetic disorders. Consanguineous marriages are practised widely in Kuwait. The major aim of this study is to delineate the association of consanguineous marriages with congenital disabilities in different Kuwaiti population subcultures. A total of 9104 married Kuwaiti females aged 15–79 years from different backgrounds were selected at ten primary health care centres from six governorates in Kuwait. Data were collected using a questionnaire and analysed with chi-squared tests. The data indicate significant differences in the occurrence of genetic diseases in consanguineous couples' offspring (4.88%) compared with those of non-consanguineous couples (4.13%) ($p<0.002$). The results also show significant differences in frequencies of genetic/environmental diseases in consanguineous couples' offspring (8.59%) compared with those of non-consanguineous couples (8.23%) ($p<0.005$). No significant differences between the two groups regarding environmental diseases were observed. A higher frequency of genetic diseases was found in first- (6.97%; $p<0.001$), second- (6.78%; $p<0.001$) and third-cousin (6.46%; $p<0.022$) couples' offspring compared with those of non-consanguineous couples. The frequency of congenital disabilities in the offspring of couples from consanguineous marriages (2.9%) is higher than that in the offspring of non-consanguineous marriages (2.3%). But this difference is not significant at the 0.05 level. First-cousin marriages have the highest frequency (3.5%) of congenital disabilities compared with other kinds of marriages (2.1–2.3%). Differences across groups are significant ($p<0.036$). Significant differences are found for first-cousin couples in both physical (2.37; $p<0.042$) and mental (0.74; $p<0.037$) disabilities compared with non-consanguineous couples. No significant differences were observed in deafness and blindness disabilities. The data show no significant differences between second- and third-cousin and non-consanguineous couples in physical, mental or deafness and blindness disabilities. There are no significant differences in

the percentages of offspring with congenital disabilities in consanguineous and non-consanguineous marriages across sub-population groups for the total of four types of congenital disability.

Introduction

Consanguinity is prevalent in many Middle Eastern and Arab cultures and societies (e.g. Hafez *et al*., 1983; Khlat & Halabi, 1986; Hamamy & Al-Hakkak, 1989; Al-Salem & Rawashdeh, 1993; El-Hazmi *et al*., 1995; Demirel *et al*., 1997; Al-Abdulkareem *et al*., 1998; Hamamy *et al*., 2005; Bener & Hussain, 2006; Barbour & Salameh, 2009, Akrami *et al*., 2009). Some studies have shown significant differences in genetic disorders between children born to consanguineous marriage partners and those born to non-consanguineous parents (Zlotogora, 1997; Hamamy *et al*., 2007; Jaouad *et al*., 2009), while others have found no significant differences (Al-Awadi *et al*., 1986; Al-Abdulkareem & Ballal, 1998; El-Mouzan *et al*., 2008). Consanguinity has been shown to increase homozygosity and to reduce genetic variation in a group, which may protect against the expression of recessive genes that can lead to genetic disorders (Denic & Nicholls, 2007).

Kuwaiti society is not different from other Middle Eastern and Arab societies. It has been shown that consanguineous marriages are practised widely in Kuwait. Over the last three decades, three studies reported consanguinity in Kuwait to be in the range of 44.8% (Al-Kandari, 2006), 48% (Al-Thakeb, 1982) and 54.3% (Al-Awadi *et al*., 1985), which is considered rather high.

El-Najjar (1996) assumed that there must be a relationship between consanguinity and physical and mental disabilities, including deafness and blindness. However, he provided no data to support this conclusion. Other studies have shown a relationship between consanguinity and some genetic conditions and health problems such as phenylketonuria (PKU) (Teebi *et al*., 1987), immunodeficiency disorders (White *et al*., 1988; Al-Herz, 2008), children's hypertension (Saleh *et al*., 2000), beta-thalassaemia (al-Fuzae *et al*., 1998), protein-C and protein-S deficiency (Mohanty *et al*., 1996), low birth weight (Al-Awadi & Amin, 1992) and Down's Syndrome (Alfi *et al*., 1980). Other studies show higher rates of miscarriages and prenatal and neonatal losses among children born to consanguineous parents in Kuwait compared with those born to non-consanguineous parents; however, these differences were not statistically significant (Al-Awadi *et al*., 1986; Egbase *et al*., 1996).

Consanguinity in Kuwait is higher among the sub-population with Bedouin tribal roots (Radovanovic *et al*., 1999; Al-Kandari, 2006). The Kuwaiti population has special characteristics. The population originally came from three different surrounding areas: Saudi Arabia, Iraq and Iran. The Bedouin tribal sub-population came from the *Najd* (the middle of the Arabian Peninsula) and Iraq. Some belong to the same tribe although they come from different regions. Muslim Shiites originally came from southern Iraq and southern Saudi Arabia, but the majority came from Iran. Muslim Shiites are the minority in Kuwait, while the tribal groups are the majority. Al-Kandari (2006) reported differences between Muslim Sunnis and Shiites in practising of consanguineous marriages, with a higher incidence reported by Sunnis. One explanation is that a majority of Kuwaitis come from tribal Muslim Sunnis

roots. Compared with other groups, Bedouins also have a higher fertility rate (Al-Kandari, 2007). In the Al-Jahra region of Kuwait, for instance, which has a high proportion of its population with ancestors with tribal Bedouin roots (68% of the studied sample), the occurrence of offspring with congenital malformations is high in consanguineous marriages (Madi *et al*., 2005).

The major aim of this study is to delineate associations of consanguineous marriages with congenital disabilities in the Kuwaiti population. It examines (1) whether pattern of marriage (relatives versus non-relatives) and congenital disorders in children are statistically significantly related; (2) whether pattern of marriage (relatives and non-relatives) is significantly associated with the total prevalence of four types of congenital disability (physical, mental and deafness and blindness combined); and (3) whether differences in prevalences of disabilities occur among different population groups in Kuwait (Muslim Sunni vs Shiite, Bedouin vs non-Bedouin roots, Arabic vs non-Arabic origin).

Methods

A total of 9104 married Kuwaiti females aged 15–79 years from different backgrounds were selected at ten primary health care centres from six governorates in Kuwait (Al-Kandari, 2006). Centres were selected randomly from a total of sixty facilities. Data were collected by a well-trained research assistant. The questionnaire was prepared for a large project study funded by Kuwait University (Al-Kandari, 2006); additional data were collected specifically for this study.

Four major marriage categories were reported in this questionnaire: first-cousin marriage (including five sub-categories: double first-cousin marriage where the couple share their four grandparents; man marrying his mother's brother's daughter; man marrying his mother's sister's daughter; man marrying his father's brother's daughter; and man marrying his father's sister's daughter), second-cousin marriage, third-cousin marriage and non-consanguineous marriage. Participants were asked to report their religious background and roots: Muslim Sunni or Shiite, and original tribal or non-tribal affiliation. Respondents were asked to report whether their offspring suffered from congenital disabilities of four different types: physical, mental, deafness and blindness. Respondents were asked to report on four different types of congenital disabilities of their offspring. Respondents only reported disabilities their offspring were born with to ensure that these did not have environmental causes. The research assistants ensured the validity of the respondents' answers. Offspring were defined as disabled when they had physical and mental impairment that meant having any congenital physiological and mental disorder. The deafness and blindness disabilities were defined as a vision and hearing impairment or loss as a result of a congenital condition. SPSS was used for data analysis. Chi-squared analysis was the major tool of statistical analysis.

Results

Differences in frequencies of congenital disabilities were examined by pattern of marriage (relatives and non-relatives) with regard to offspring, including four types of disability: physical, mental, deafness and blindness (Table 1).

Table 1. Frequencies of congenital disabilities among offspring of consanguineous and non-consanguineous marriages using chi-squared test

Marriage type	% (*n*)	*p*
Consanguineous	2.9 (121)	0.066
Non-consanguineous	2.3 (113)	
Non-consanguineous	2.3 (113)	0.036
First cousin	3.5 (80)	
Second cousin	2.3 (20)	
Third cousin	2.1 (21)	

Table 2. Frequencies of different types of congenital disabilities among offspring of consanguineous and non-consanguineous marriages using chi-squared test

	Physical disabilities		Mental disabilities		Deaf/blind disabilities	
Marriage type	% (*n*)	*p*	% (*n*)	*p*	% (*n*)	*p*
Non-consanguineous	1.70 (84)		0.36 (18)		0.22 (11)	
Consanguineous						
First cousin	2.37 (54)	0.042	0.74 (17)	0.037	0.39 (9)	0.309
Second cousin	1.61 (14)	0.481	0.48 (4)	0.480	0.23 (2)	0.476
Third cousin	1.68 (17)	0.548	0.38 (3)	0.429	0.10 (1)	0.121

The frequency of congenital disabilities in the offspring of couples from consanguineous marriages (2.9%) is higher than that of non-consanguineous marriages (2.3%) (Table 1). But this difference is not significant at the conventional 0.05 level. When consanguineous marriages are divided into three categories (first-, second- and third-cousin marriages), first-cousin marriages have the highest frequency (3.5%) of congenital disabilities compared with other kinds of marriages (2.1–2.3%). Differences across groups are significant ($p<0.036$). By dividing consanguineous couples into three sub-groups (first-, second- and third-cousin couples) and comparing them with non-consanguineous couples by four disability categories (physical, mental, deafness and blindness disabilities), significant differences are found for first-cousin couples in both physical (2.37; $p<0.042$) and mental (0.74; $p<0.037$) disabilities from non-consanguineous couples (Table 2). No significant differences were observed in deafness and blindness disabilities. The data show no significant differences between second- and third-cousin and non-consanguineous couples in physical, mental, deafness and blindness disabilities.

Table 3 lists differences in the prevalence of the total of four types of congenital disability. There are no significant differences in the percentages of offspring with congenital disabilities in consanguineous and non-consanguineous marriages across sub-population groups for the total of four types of congenital disability.

Table 3. Frequency of congenital disabilities among offspring in different sub-groups using chi-squared test

Sub-group	%	*p*
Origin		
Arabic	2.6	0.190 (ns)
Non-Arabic	3.2	
Roots		
Bedouin	2.6	0.497 (ns)
Non-Bedouin	2.6	
Religion		
Muslim Sunni	2.5	0.169 (ns)
Muslim Shiite	2.9	

Discussion and Conclusion

Of congenital disabilities of offspring, the results show that the offspring of first-cousin marriages only have significantly higher percentages of physical and mental disabilities. No significant differences were found among couples in sub-population groups by origin, roots and religion. These results reflect the impact of sociocultural factors associated with choice of marriage partners on the health status of offspring within one society with different types of marriages.

Genetic-related conditions are more frequent in the offspring of consanguineous marriages, as shown in some studies in the region (Abdulrazzaq *et al.*, 1997; Al-Kandari, 2007). The relationship between type of marriage and congenital disabilities is reinforced by the positive relationship between health symptoms in general and type of marriage. Kinship is an influential factor in determining symptoms of health within this community. This is supported by previous studies (Teebi *et al.*, 1987; Al-Kandari, 2007). In addition, the study by Al-Awadi *et al.* (1986) pointed to the high incidence of reproductive wastage as a potential factor contributing to disabilities in children; however, this finding was not statistically significant.

It is stated that 'the closer the biological relationship is between relatives, the more likely that they will have the same faulty gene in common' (Barlow-Stewart & Saleh, 2007, p. 2). Although differences in disability among offspring of consanguineous and non-consanguineous marriages are only borderline significant, there is a clear statistically significant difference when consanguinity is divided into three categories (first-, second- and third-cousin). First-cousin marriages only show a higher percentage of congenital disabilities among their offspring than those of second- and third-cousin marriages. By comparing each cousin couple group with non-consanguineous couples in each disability type, the data show the only significant differences are found for first-cousin couples in both physical and mental disabilities. No significant differences were found between second- and third-cousin and non-consanguineous couples. Not finding differences in other cousin types could be explained by the effect of natural selection over time in the larger kinship group,

which could be faster than in small ones, especially for fetal diseases, of which disabilities could be one. This result has been supported by another study which 'shows no significant differences in the death of offspring between consanguineous and non-consanguineous marriages' (Al-Kandari, 2007, p. 82). The lack of significant difference in deafness and blindness disabilities in first-cousin couples' offspring compared with other types may be related to the low frequency of these two disabilities. As stated by Al-Merjan *et al*. (2005), only 412 people are registered as blind in Kuwait.

As shown in this study, first-cousin marriage is an important contributor to congenital disabilities in Kuwait. This finding confirms those of other studies (Jain *et al*., 1993; Nasir *et al*., 2004; Kanaan *et al*., 2008; Khabori & Patton, 2008). As explained by Bittles (2002), a population with a high rate of consanguinity will be expected to have higher rates of recessive genetic disorders, but this pattern will be negated by urbanization, which causes family size to be smaller. Marriages happen within and across all ethnic groups within Kuwait and often between those without any blood relationship. This may in part explain the lack of relationship between the second- and third-cousin marriages and congenital disabilities in their offspring, as these relationships may be more similar to the background level of consanguinity in the population. In the case of first-cousin marriages, the relationship is clear. Genetic isolation clearly increases homozygosity, leading to congenital diseases. More studies are highly recommended.

The findings of the current study show that there is no statistical significant association between pattern of marriage between groups or various social strata in the Kuwaiti population and the prevalence of disability in their offspring. This may be due to the fact that all social strata in Kuwaiti society regularly marry relatives. In spite of disparity in the relative numbers of each sub-group, consanguinity is widely practised in all social strata of Kuwait. As shown in three different studies in Kuwait, the range is from 44.8% to 54.3% (Al-Thakeb, 1982; Al-Awadi, 1985; Al-Kandari, 2006). It is found that first-cousin marriage is highly practised in Kuwait. Al-Thakeb (1982) found that 48% of the total marriages are among relatives and 79% of them (almost 38%) are first-cousin marriages, while Al-Awadi stated 30.2% and Al-Kandari (2006) 24.3%. It is clear that first-cousin marriage is highly practised, although data from these studies show a decline in recent years.

A possible explanation for lack of a relationship among sub-groups in Kuwait with regard to congenital disabilities may relate to several factors. For one, as stated by Barakat (2008), different tribes in the Arabian Peninsula and the Arab world are not necessarily composed strictly along kinship lines and genetic relationships. Thus, 'third-cousin' marriages may not reflect an actual close genetic kinship, but rather may include fictive kin who introduce heterozygosity rather than additional homozygosity into the 'family'. Second, as hypothesized by Sanghvi (1966), consanguinity may be practised over time, which can reduce the frequency of recessive genes for a disease, and even eventually eliminate recessive traits.

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