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Original article

Global distribution of consanguinity and their impact on complex diseases: Genetic disorders from an endogamous population

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ABSTRACT

Background: Marriage between close relatives has been practised globally since the early existence of human society. The role of consanguinity and inbreeding affecting human health is a topic of great interest in medical genetics.

Objective: The objective of the study was to investigate the extent of consanguinity and its effects on common non-communicable diseases, the related risk factors, its role in human health and susceptibility to various chronic and complex diseases in Qatari population.

Subjects and methods: The study design was a cross-sectional and multi-stage sampling based on Hospitals and primary health care [PHC] centres. A representative sample of 1626 subjects were approached and 1228 subjects (75.5%) consented to participate in the study between January 2013 and May 2014. The questionnaire based on socio-demographic data and for responses, on the Premarital Screening and Genetic Counseling [PMSGC] program knowledge, attitude and practice statements. Additionally, questions were asked regarding services, activities, how to attract and motivate the genetics counseling and screening for the hereditary diseases programme.

Results: The mean age ± S.D of the 1228 women interviewed was 39.25 ± 9.57 years. The rate of consanguinity in the present generation was 43.5% [95% CI = 47.7–54.4]. There were statistically significant differences between males and females with regards to age, educational status, occupation status, household income, consanguinity, BMI, cigarette smoking and sheesha (water pipe) smoking. The consanguinity rate and coefficient of inbreeding in the parental was significantly higher than the maternal rate (44.3% versus 41.4%; $p < 0.001$) (0.018738 versus 0.017571 maternal). The current generation of consanguineous parents had a slightly higher risk for diseases such as diabetes mellitus, cancer, blood and mental disorders, heart diseases, asthma, gastro-intestinal disorders, hypertension, hearing deficit, G6PD and common eye diseases.

Conclusion: The present study revealed a higher incidence of certain diseases in consanguineous population with a high significant increase in the prevalence of common adult diseases such as diabetes mellitus, cancer, blood disorders, mental disorders, heart diseases, asthma, gastro-intestinal disorders, hypertension, hearing deficit, G6PD and common eye diseases. This confirms the role of genetic factors across the full spectrum of disease and not only for Mendelian disorders.

1. Introduction

Consanguineous marriages have been practiced since the early existence of humans. At present, accounting for 20% of world populations live in communities with a preference for consanguineous marriage [1–3]. Consanguinity rates vary from one population to another, varying with differences in religion, culture and geography [3–8]. A number of factors govern the influence of endogamy on community gene pools. There is an important cluster of countries with high levels of consanguinity observed in most communi-

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ties of North Africa, the Middle East and Western Asia, a transverse belt that runs from Pakistan and Afghanistan in the east to Morocco in the west, and also in South India, with intra-familial unions collectively accounting for 20−50+% of all marriages [3–8]. Noticeably, many Arab countries display some of the highest rates of consanguineous marriages. The rate of consanguineous marriage varies in different countries and is usually associated with demographic features, such as religion, educational level, socioeconomic status, geography (including urban/rural community, size of the area, isolation of the population), consanguinity among the parents' marriages and the respondents' attitudes towards consanguinity [6–11].

There is a long tradition of consanguineous marriage in many communities throughout the world, [9–12] especially in countries of the Middle East, Northern Africa and South Asia [4–9]. While the rate of consanguinity varies within the Middle East region, the difference is usually related to religion, race, ethnicity and sociocultural factors, including socially accepted norms of endogamy in tribal societies [1,2,4–18]. Among the major populations studied, the highest rates of consanguineous marriages have been associated with socioeconomic levels, illiteracy and rural residence [1,2,4,7–8]. Recent studies show that the prevalence of consanguineous marriages varies from 51–58% in Jordan [10], to 54% in Kuwait [4], 49% to 33% in Tunisia and Morocco [12], 58% in Saudi Arabia [13], 50% in United Arab Emirates [11], 52% in Qatar [1–2,14], 40–47% Yemen [16], 50% in Oman [18]. and as high as 68% in Alexandria, Egypt [19].

Genetic carrier screening programmes are systematic programmes, generally being recommended by government health bodies, advising the entire population of asymptomatic individuals of reproductive age to have a screening test to identify those who are carriers of autosomal recessive disorders. In some contexts, the screening programme may be recommended for subpopulations whose risk of particular genetic diseases is known to be increased [1–8]. These programmes are designed to determine whether individuals carry a genetic predisposition that may produce a disease in their offspring [2,3].

Several authors reported the common effect of inbreeding on health which focused mainly on its impact on reproduction, childhood mortality and rare Mendelian disorders [1,2,6,9,20–26]. Nevertheless, some limited information is available on the possible role of consanguinity and recessive genes in multi-factorial or polygenic common adult diseases [1,2,20–26], also known as the common, complex degenerative disorders. The aim of the study was to determine the extent and nature of consanguinity in the Qatari population and its effects on the common non-communicable diseases, especially susceptibility to a range of chronic, complex diseases.

2. Subjects and method

This is a cross-sectional based on survey conducted at the Primary Health Care (PHC) Centres and Hospitals in the State of Qatar. The survey was conducted among Qatari national and Arab women aged 18–40 years old.

The data was collected through a validated questionnaire [1,2] based on face-to-face interviews by physicians and qualified nurses using the local language and perviou. The nurses were aware of the Arabic culture and were able to assist the study participants if they were unable to answer the questions. Data collection took place from January 2013 to May 2014. The sample size was determined on the *a priori* presumption that the prevalence rate Premarital Screening and Genetic Counseling [PMSGC] in neighbouring countries would be similar to the rates found in other countries in the Arab Gulf Counties [1–8,11]. The reported prevalence of consanguinity in Arab and Middle-East Countries were vary between 35–40% with the 99% confidence interval for 3% error of estimation, a sample size of 1626 subjects would be required for this study to achieve objective. Of the 22 primary health care centres available, we selected 13 health centres on a random sampling basis. A multi-stage sampling design was used and a representative sample of 1626 women aged 18–45 years were approached and 1228 subjects agreed to participate (75.5%) and responded to the study. Furthermore, content validity, face validity and reliability of the questionnaire were tested in a sample of 100 subjects and demonstrated high levels of validity and a high degree of reliability (Kappa = 0.84); 72% and-reported diseases were confirmed in medical charts. All information was gathered based on structured face-to-face interviews by physicians and qualified nurses using the local language. The relationship between the spouses was recorded and whether their parents were consanguineous. Marriages between relatives were classified in six groups: double first cousins; first cousins; first cousin once removed; second cousin; less than second cousin (third cousin); and non-consanguineous marriage.

Odds ratios were computed for the likelihood of disease by consanguinity status in the current generation as well as the respondent's children. For the current generation, cases were defined as respondents who were an offspring of consanguineous unions (disease report limited to either self or siblings having the disease) and controls were defined as respondents who were an offspring of non-consanguineous unions (disease report limited to either them-self or siblings having the disease).Similarly definitions were adopted for responder's offspring. Chi-square test was used to ascertain the association between two or more categorical variables. In 2×2 tables, the Fisher exact test (two-tailed) was used when the sample size was small. Relative risk and 95% confidence interval were calculated using Mantel-Haenszel method. All statistical tests were two-sided and $P < 0.05$ was considered statistically significant.

3. Results

The mean age ± S.D of the 1228 women interviewed was 39.25 ± 9.57 years. The rate of consanguinity in the present generation was 43.5% [95% CI = 47.7–54.4]. The socio-demographic characteristics of consanguineous and non-consanguineous distribution in the study population is shown in Table 1. There were statistically significant differences between consanguineous and non-consanguineous participants with regards to age, educational status, occupation status, household income. BMI, cigarette smoking and sheesha smoking. Although a similar pattern between consanguinity and husband's education was observed, the differences were smaller and not statistically significant. Table 2, give some characteristics of studied subjects according to life-style habits, No. of parity, number of gravid and number of children are alive.

Data on trends in levels of consanguinity in the current generation compared to the parental generation and the associated coefficient of inbreeding are presented in Table 3. The most common type of consanguineous marriage was first cousin marriage (284, 23.1%). The second most common category of consanguineous marriages was double first cousin marriages (41, 3.3%). The coefficient of inbreeding in the respondent, husband's parents and respondent's parents were 0.017591, 0.018738 and 0.06794 and, respectively. All types of consanguineous marriages were higher in the respondent's generation, particularly first cousin (23.1% versus 22.1% paternal and 21.3% maternal) and double first cousins (3.2% versus 3.1% paternal and 2.9% maternal).