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ORIGINAL ARTICLE

Consanguinity, awareness, and genetic disorders among female university students in Riyadh, Saudi Arabia

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ABSTRACT

Background: There is a high rate of consanguinity and related genetic diseases in the general population of Saudi Arabia. Studies have been conducted to address the level of awareness about consanguineous marriages (CM); however, targeted young female studies are still limited. The association between consanguinity and socio-demographic information and the prevalence of consanguinity among educated female university students of Princess Nourah Bint Abdulrahman University (PNU), Riyadh, Saudi Arabia, is being addressed in the present study.

Methodology: A cross-sectional web-based questionnaire study was conducted randomly among PNU students from October 3 to November 2, 2019. Multivariable data analysis was conducted, and an odds ratio was calculated to identify factors associated with CM and health outcomes.

Results: Among the 637 students who completed the questionnaire, consanguinity was significantly higher among participants than their parents, as 37.88% of the 293 married participants had CM. A strong correlation was found between parents and their daughters; consanguinity was highest (52.27%) in the daughters of parents who were in consanguineous marriages themselves. The general high level (91.51%) of awareness about CM's consequences, and their link to genetic diseases was found. However, a lack of knowledge about the type of diseases was noted among participants. Diabetes and blood diseases were the most common diseases in different CM groups.

Conclusion: Despite the high levels of awareness, more targeted awareness campaigns are needed, especially among the younger generation.

Keywords: Consanguinity, consanguineous marriage, genetic diseases, awareness, female, Riyadh, Saudi Arabia.

Introduction

Consanguinity is used to describe a marriage relationship between a man and a woman with at least one common ancestor (1). Historically, consanguineous marriages (CMs) have been widespread in many communities throughout the world. Despite being illegal in some religions, including Catholicism and Hinduism, and prohibited by law in other countries, CMs are widely practiced in the Middle East, Northern Africa, and South Asia with variable rates that can reach 70% in some regions (2). Sociocultural factors, including similar culture, religion, ethnicity, and geography, play a crucial role in the preference of consanguinity in Arab and Middle Eastern populations (3). CM in the form of cousin marriages revolved around the beliefs of assuring

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a better married life, as consanguinity strengthens family ties, enforces family solidarity, and provides excellent opportunities for the transmission of cultural values and continuity (4). Moreover, CM has been recently practiced in Europe and North America among emigrants from communities with high consanguinity rates (1). Saudi Arabia is one of the highest countries in practicing CM; recent reports indicated high rates, reaching 60% and 70% (5). However, despite the socioeconomic benefits of CM, it is positively linked to an increased risk of autosomal recessive genetic diseases in resulting offspring. The more the population is ethnically similar, the higher the risk of developing such diseases. Autosomal recessively inherited diseases include metabolic disorders, liver disease (Wilson), blood diseases, polycystic kidney disease, phenylketonuria (PKU), and immunodeficiency disorders, which are common among CM communities (6). Among blood diseases are sickle cell disease (SCD) and Mediterranean anemia (thalassemia), which are the most common favorably reported severe blood disorders in Saudi Arabia (7). Also, CM can increase the risk of developmental genetic disorders, as reported in a study that found an increased number of children with Down syndrome (DS) in CM families, despite the fact that more research is needed to prove the link between DS and CM (3,8). Alongside autosomal inherited diseases, mental illnesses were also higher in CM families, such as depression, autism, schizophrenia, and anxiety disorders (9). The primary source of information about CM in Saudi Arabia is mass media and medical personnel from hospitals and local general practices. Additionally, couples' examination can predict the possibility of inheriting disease(s), and individuals can be aware of their conditions and disease-related consequences. Despite the general increase in awareness and the establishment of premarital testing in 2003, still reports suggested high CM levels. A recent study found a lack of knowledge about the link between CM and genetic diseases among participants, despite their high education level (10). The study's main objective is to determine the prevalence of CMs and the level of awareness among well-educated female students of Princess Nourah Bint Abdul Rahman University (PNU).

Subjects and Methods

This cross-sectional survey was conducted among 637 students attending PNU for about 4 weeks, starting from October 3 and ending on November 2, 2019. The subjects' ages were between 19 and 26 years. This study's overall goal was to shed light on the prevalence of consanguinity regarding socio-demographic factors and the associated genetic diseases. The questionnaire was designed in accordance with previously published studies in which questions were addressed and validated (3,11). Ethical approval was obtained from the Institutional Review Board's Committee of Princess Nourah bint Abdulrahman University (PNU) (IRB-19-0073). All methods were carried out in accordance with the relevant guidelines and regulations of the National Committee of Bioethics, Saudi Arabia. All participants signed a consent form before filling the questionnaire to inform their willingness to participate in the study. Participants were given the freedom to terminate the survey anytime. Participants who did not consent to participate in the study and/or did not answer the study's questions were excluded from the study. The survey was conducted in English and Arabic, depending on the respondent's preference, and took about 5-7 minutes to be completed.

The questionnaire consisted of 30 questions in total and categorized into two sections; the first section focused on socioeconomic information, including age, education level, and marital status. Simultaneously, the second section focused on the participants' awareness and knowledge about the link between consanguinity and genetic diseases. Respondents were asked about the level of consanguinity in their families, given the following four choices: first-degree cousins, second-degree cousins, a distant relative relationship, or no blood relationship. Additionally, a group of autosomal recessive genetic diseases was listed, including inherited blood diseases, gastrointestinal diseases, hearing impairments, and cancer. Also, multifactorial diseases, including diabetes and mental diseases, were added to the questionnaire and participants were asked if they or their family members have them.

First, a pilot study of the questionnaire was conducted using 70 participants to check for any misinterpretation or difficulty in understanding the survey questions. In light of the feedback from all the 70 participants, some questions were amended or clarified. The researchers distributed the questionnaires, which were filled by the participants online through Google Forms; the researcher's clarified questions for the participants if needed. Before the participant started to give their feedback, they were given a short introduction about the study and its purpose. Subjects were assured confidentiality of their answers and were not requested to provide any personal information. In this study, participants were not provided with any vouchers or given money for filling the questionnaire. The questionnaires were distributed through PNU's different faculties, including Medicine, Science, and Humanities, and communication between the researchers and the participants was in Arabic or English if needed. The sample size used to conduct this research was 637, with a 3.1% margin of error and a 90% confidence level. The sample size was calculated based on the total number of students in the Science (4,600), Medicine (375), and Humanities (3,400) faculties, which is in total 8,375 students; the dean of each Faculty retrieved the number of students. Data were refined and organized by Excel version (16.0.6769.2017)/2016 and were cross-checked before and after data entry. Simple Random Imputation Approach was used to impute missing values (random. imp R package). To identify factors associated with CM and health outcomes, data were analyzed using R Software (R 3.5.3 for Windows 64 bit)/2018 with (fmsb package). Multivariable data analysis was conducted, and the odds ratio (OR) and their corresponding 95% confidence interval (CI), and p-value were calculated. All variables showed association with practices at the bivariate level, with *a p*-value less than 0.05 were considered statistically significant and highly significant, respectively, and the 95% confidence level.

Results

In this study, a total of 637 students from Princess Nourah University responded to the questionnaire. From this number, 51.81% (n = 330) of the students' or/and their families were consanguineous. Among all the CMs, first cousins' marriages were the highest with 48.79% (n = 161), then third cousins' marriages with 34.24% (n = 113), and finally, second cousins' marriages with 16.97% (n = 56). More than third 36.42% (n = 232) of the participants were among the age group 19-20 years, and the majority 59.3% (n = 378) were between 21 and 25 years. 43.80% (n = 279) were from the Faculty of Science, while 34% (n = 217) were from the Faculty of Medicine and 22.1% (n = 141) from the Faculty of humanities. About three-quarters of the participants, 75.82% (n = 482), were from an average income family, while 21.9% (n = 139) were from high-income families. Approximately 68.13% (n = 284) of the respondents' mothers received higher education, while 84.30% (n = 345) of the fathers received higher education (Figure 1).Most of the participants, 91.37% (n = 528), are aware and well informed of the link between genetic diseases and CM. About half of the participants, 55.57% (n = 354), supported premarital counseling.

Medical students in CM were more likely to support consanguinity (OR 8.95% CI 1.00 63.9) compared to sciences students in CM (OR 3.95% CI 0.58, 15.3). Analyzing the data found that medical students in CM were more likely to have more awareness of the risk factors connected to consanguinity than humanities students (OR 3.55 95% CI 0.13, 90.9).

The OR of medical students involved in non-CM supporting consanguinity was slightly higher, 4.66 (95% CI 0.29, 73.3), than humanities students. On the other hand, science students who have had non-CM were found more likely to support consanguinity by OR 0.29 (95% CI 0.008, 9.857) than humanities students. Medical students who have had non-CM were found more likely (OR 1.42 (95% CI 0.03, 51.4) to have an awareness of consanguinity than humanities students. The OR of having an awareness of consanguinity among sciences students involved in non-CM was higher (OR 3.42, 95% CI 0.10, 15.8) than humanities students. Participants whose husbands' income was high or average were found more likely [(OR 1.75, 95% CI 0.15, 20.2) and (OR 1.32, 95% CI 0.12, 14.1)] to support consanguinity than students whose husband's income was less than average (Table 1).

The OR of participants supporting consanguinity was slightly higher among those whose parents were in CM of first cousins (OR 2.83, 95% CI 1.77, 4.54) more than students with non-consanguineous parents. On the contrary, CMs of third cousins (OR 1.84, 95% CI 1.06, 3.20) were less likely to support CM than students with non-CM (Table 2). The OR of having awareness among students whose parents were in CM third cousin was (OR 1.01, 95% CI 0.43, 2.34) greater than students with non-CM (Table 2). Students who had diseases linked to consanguinity were found more likely to be involved in a family of CM of first cousins (OR 1.01, 95% CI 0.67-1.52) than those who had non-CM (Table 2).

Discussion

The prevalence of consanguinity in communities is an important phenomenon to be addressed, particularly in Saudi Arabia. Cultural norms still encourage relative's marriage despite the high incidents of different genetic

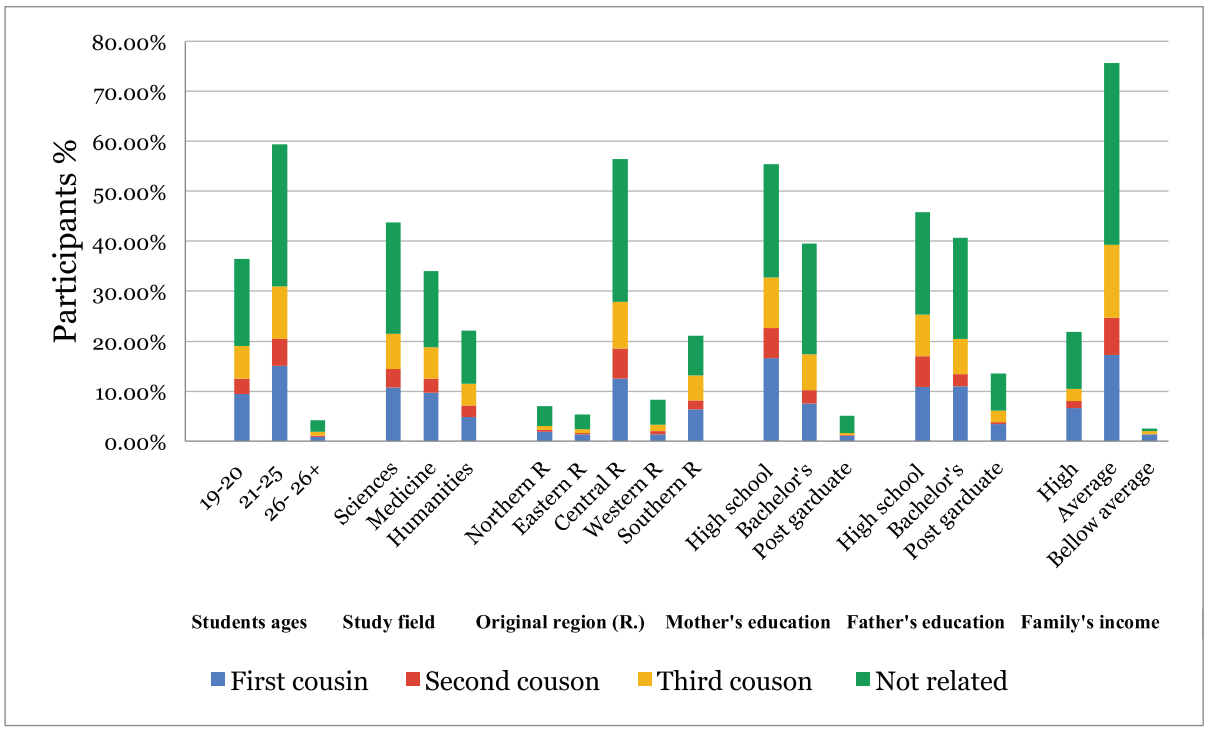

Figure 1. *Socio-demographic information of the participants (n = 637).*

Table 1. *The associated factor for consanguineous and non-consanguineous Married students (n = 59).*

Characteristics	Unadjusted odds ratio	95% confidence interval	*p*-value
Consanguineous wife education with support			
Humanities	Reference		
Medicine	8.0000	1.0005 63.9625	0.0452
Sciences	3.0000	0.5858 15.3622	0.1881
Consanguineous wife education with awareness			
Medicine	3.5555	0.1389 90.9696	0.4327
Sciences	1.4444	0.1705 12.2316	0.7399
Non-consanguineous education with support			
Medicine	4.6666	0.2967 73.3838	0.2713
Sciences	0.2916	0.0086 9.8578	0.482
Non-consanguineous wife education with awareness			
Medicine	1.4285	0.0396 51.4274	0.8505
Sciences	3.4285	0.1014 115.8796	0.482
Husband's income with wife's support of consanguinity			
Less than average	Reference		
High	1.7553	0.1513 20.2314	0.6585
Average	1.3280	0.1231 14.1441	0.8203

diseases. Eliminating such burdens of genetic disorders is positively linked to improving public knowledge and practice toward CM (12). CM and its association with genetic diseases has been addressed lately in Saudi Arabia (13). Nevertheless, more public awareness is still needed, especially among young generations. This study investigated the prevalence and attitude toward CMs among PNU students. Correspondingly, the association between consanguinity and genetic disorders was addressed through methodical surveys of the selected participants. CM has been reported to increase the occurrence of genetic mutations compared to the general population. In countries where people are practicing CMs, including Saudi Arabia, more genetic disorders were reported (14). Different reports addressing the phenomena have associated higher rates of CM with poor socio-economical and educational factors (15). Studies from several Arabs countries, including Jordan, Yemen, and Tunisia, showed reduced consanguinity rates among educated males and females (16). Additionally, reports from Middle Eastern countries showed lower consanguinity rates in urban compared to rural settings (17). A significant number of the participants were interested in the subject, and 91.37% were aware of the correlation between CM and genetic disorders. Nearly all of the participants, 97.1%, showed their support for premarital counseling, highlighting the importance of education to alter people's behavior. The recent increased attention on providing information to new couples was through pre-marriage counseling and premarital medical examination. However, when participants were asked if raising awareness will decrease CM rates in Saudi, 19% were negative, suggesting that they think that people's preferences will not change toward cousin's marriages even with awareness programs. In this study, we found a positive correlation between high income and awareness about CM. Better socioeconomic conditions can reduce CM rates, as parents will not tend to accept CM to reduce marriage expenses (15). However, better income can be linked to higher CMs rates, as wealthy parents prefer to keep money within their families, as also found in this study. Living in urban areas is another factor that can help to reduce CMs and associated genetic diseases. The ongoing developments in genetic diagnostic tests in cities and the advanced technologies to detect genetic disorders, and awareness programs are all well established in cities (18). These factors are likely to provide new couples with information related to their carrier status of autosomal recessive disorders and also to educate and prepare them (19). In our study, 51.8% of the participants were in CM families, which was lower than an older study as 57.7% of the participants were in CMs (20). In terms of the most prevalent causes of CMs concerning regions, the southwestern region was the highest in the rate of CMs with 80.6%. A previous study indicated a high rate of CM in the southern region (69%) and the northern region (60%) (21). These results place Saudi Arabia among the countries of the world with a high rate of consanguinity. When the correlation between university programs studied by participants and their levels of awareness was addressed, we found that Medicine students had better awareness about CM and its association with genetic diseases than Science and Humanities students. However, unexpectedly, despite their high level of awareness, they were the most group supporting CMs, despite knowing the risks involved, as they had the highest percentage of

***Table 2**. According to the support of consanguinity and awareness of risk factors (n = 637).*

Characteristics	Unadjusted odd ratio	95% CI	*p*-value
Parents' marriage with students' support of consanguinity			
Non-consanguineous	Reference		
First cousin	2.8384	1.7741 4.5411	0.0000
Second cousin	0.7785	0.3138 1.9310	0.5888
Third cousin	1.8431	1.0605 3.2031	0.0287
Parents' marriage with students' awareness			
First cousin	0.7513	0.3783 1.4918	0.4132
Second cousin	0.3550	0.1579 0.7980	0.0095
Third cousin	1.0131	0.4378 2.3458	0.9757
Type of parents' marriage with the existence of diseases			
First cousin	1.0126	0.6736 1.5221	0.9519
Second cousin	0.8695	0.4789 1.5788	0.6463
Third cousin	0.7864	0.5021 1.2315	0.2938
Students awareness of genetic diseases linked to consanguinity			
No knowledge	Reference		
Yes	1.4599	0.8314 2.5634	0.1860
Students approval of adding the family medical history record			
No adding the history	Reference		
Yes	5.3461	2.4780 11.5335	0.0000
Students support premarital medical test of genetic diseases			
No	Reference		
Yes	2.5243	0.9815 6.4924	0.0473
Students support CM despite knowing the risks			
Yes	0.1833	0.1033 0.3253	0.0000
Student support of CM with the existence of diseases in the family			
No	Reference		
Yes	0.8298	0.5496 1.2526	0.3746
Student's family Income related to support of consanguinity			
Less than average	Reference		
High	0.5800	0.1866 1.8018	0.3433
Average	0.484557	0.1641 1.4301	0.1812

CMs. The parents' education level was an essential factor in the prevalence of CMs; low mothers' education levels are linked to higher CMs rates among their daughters. In this study, we found that genetic diseases such as blood diseases and diabetes were higher in participants of CMs than the non-CM participants. Other studies have reported high incidents of blood diseases in association with CMs (22). In Saudi Arabia, pre-marriage testing was implied in 2005, mainly to reduce two types of blood diseases including, Sickle cell anemia and thalassemia (23). Blood diseases are the most common inherited disorders globally, as it is estimated to affect 800 million women and children globally, of which SCD and thalassemia are included (24). Saudi studies have shown reduced blood inherited disease rates, as they are no longer the most prevalent genetic diseases in Saudi Arabia (25). However, it is worth mentioning that there is a lack of accurate statistics to represent the states of genetic disorders resulting from CMs (26). A mega retrospective study on more than 700,000 screened newborns indicated the prevalence of autosomal diseases, including endocrine disorders: congenital hypothyroidism and congenital adrenal hyperplasia, brain atrophy propionic acidemia, carbohydrate disorder like galactosemia, and

aminoacidopathies, like PKU (27). Type 2 diabetes is also one of the most common diseases in Saudi Arabia. Reports suggested that Saudi is one of the world's highest countries in type 2 diabetes (28). However, other genetic diseases, including neurological diseases, gastrointestinal diseases, and kidney diseases, are common in CMs families in Saudi Arabia (29). These genetic diseases have a high cost, time, and social burden for patients and their families. Thus, raising awareness among younger generations of CM's risks is still a need, at least for the next few decades. In our study, the level of awareness among participants was high, which is understandable because of the high level of participants' education. This can also be attributed to the high level of education in most participants' parents, influencing their children's knowledge about consanguinity-related health issues. The level of awareness in this regard was improved compared with a similar study that was conducted on the students of King Abdulaziz University, as 84% of their respondents believed that consanguinity could increase the risk for genetic diseases compared with (91.36%) of the participants from this study (30). Understanding technical terminologies of genetic disorders were variable among participants depending on their specialist; Medical and Science students had a better understanding of disease conditions and terminologies compared with Humanities students. There is a need for awareness programs regarding CM and their pitfalls. It is believed that improving the level of awareness among the young generation can change the upcoming generations' attitude on this deeply rooted tradition. Awareness programs can help to educate people about the outcomes which might occur in those involved in CMs. The best methods of preventing genetic disorders are focused on prenatal tests, which help predict the possibility of transmitting genetic disorders to children. It was shown that there is a relatively positive change in the Saudi community towards CM; incompatibility results among respondents in the Premarital Screening Program led many couples to cease their marriage (31). However, the cultural sensitivity of the issue, especially among individuals in CMs families, can be challenging to overcome. Many couples can be derived from CM because of family pressure and social stigma (32).This study helped clarify the role consanguinity plays as a risk factor in the occurrence of genetic diseases and raise awareness of this issue. However, the study has some limitations, including that it was conducted with a limited number of participants, which can be attributed to the researchers' short time collecting data. Another limitation is that most of the participants were originally from the central region, considering the study's location. Also, all the participants were female, considering that the PNU is a female university. Information obtained from participants in the study can point to the association but cannot be causative.

Conclusion

The prevalence of genetic disorders due to consanguinity is still an issue in Saudi Arabia. In this study, the level of awareness about the association between CM and genetic diseases was high. About half of the participants were in CMs, with high incidents of diabetes and blood diseases. Although the phenomenon of CMs is slightly decreased, educational attempts are a necessity to reduce the spread of genetic disease in Saudi Arabia. More targeted awareness programs are needed, especially among the young female generation.

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List of Abbreviations

CM	Consanguineous Marriages
PKD	Polycystic Kidney Disease
Wilson	Liver disease
SCD	Sickle Cell Disease
Thalassemia	Mediterranean anemia
DS	Down syndrome

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Ethical approval
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Consent for publication
Written consent was obtained from the patients.

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