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Premarital Screening and Genetic Counseling Program, Sickle Cell Anemia and Thalassemia in Saudi Arabia

Abdullah Mohammed Hussain (1) *, Suha sulimani (2), Emtenan Mohammed Makki Banjar (3), Eman E Abd-Ellatif (4)

(1) Director of Comprehensive Screening Center, MBBS, FETP, MOH, Saudi Arabia.

(2) Healthy Marriage Program Director, Deputy of Public Health, MOH, Saudi Arabia.

(3) Registered Nurse, MOH, Saudi Arabia.

(4) Lecturer of Public Health & preventive medicine, Mansoura University, Faculty of Medicine, Department of Public Health & community medicine, Mansoura, Egypt.

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***Corresponding author**

Abstract

Introduction: Sickle cell disease and thalassemia are common haemoglobinopathies among Saudi as the consanguineous marriages make up 42-67 % of all marriages in Saudi Arabia. In an attempt to decrease the high number of haemoglobinopathy in Saudi Arabia, the country's Ministry of Health introduced mandatory premarital screening and genetic counseling (PMSGC) in 2004. The process of PMSGC is characterized as the testing of couples who plan to marry for common genetic blood disorders.

Methods: This descriptive study drew on the national data of the Saudi PMSGC Program and its aim were an assessment of how the people using the governmental outpatient clinics felt concerning the Saudi PMSGC and to investigate the outcomes of mandatory Saudi PMSGC for couples with compatible hemoglobinopathies, namely sickle cell anemia and thalassemia, in terms of (diseased or carrier, compliant or non-compliant, satisfied or dissatisfied) in the Makkah, Qunfudah, Jazan, Al-Hasa and Eastern regions of Saudi Arabia during the duration of the program (between 2017-2018). Research data was gathered using a structured interview questionnaire designed by the Healthy Marriage Program in the MOH. The validity and reliability of the questionnaire were not, however, tested.

Results: In terms of assessing the program and the advice it offered, over 90% of those who took part gave a score of "excellent" or "very good" for the way in which the dangers and transmission of haemoglobinopathy were explained. Over 90% scored the materials used to raise awareness as "excellent". However, Couples who were planning at-risk marriages differed broadly in their reactions to the medical advice given: 20.3 % decided to cancel the marriage, while 79.9 % went ahead.

Conclusions: In this study found that satisfaction levels were high in relation to the PMSGC program, whereas advice acceptance levels were low within the population and responses were not very positive. It is essential to spread knowledge about the program and encourage individuals to understand its importance and comply with its requirements, and this can best be achieved by running campaigns on the subject in schools and universities.

Keywords: Sickle cell, Awareness, Genetic, Screening, Thalassemia, Saudi

Introduction

Sickle cell anemia and thalassemia disorders are genetic blood diseases affecting the efficiency of oxygen flow through the body (1, 2). Each condition is caused by inheriting mutant hemoglobin genes from parents, who may or may not know that they carry the disease. Epidemiological data indicates that genetic disorders have quickly become large-scale public health concerns in various regions of the globe (2, 3). Roughly five % of the global populace carries hemoglobin disorder trait genes, the majority of which are for thalassemia and sickle cell disease (4). In excess of 300,000 children are born annually with severe hemoglobin disorders, 80% of whom are born in developing countries (3).

In the Gulf region and nearly all Arab countries, sickle cell disease and thalassemia are extremely common, causing the children diagnosed with these diseases a great deal of suffering (5, 6). The issue's prevalence is attributable to two main factors: One is the high number of children per family, which can mean a higher number of children afflicted with one of the diseases; and the second is a cultural factor, of preference for consanguineous marriage, which is associated with a reasonably high occurrence of recessively inherited disorders (6-9).

Arabic countries have, since the 1950s, made great progress areas such as infant mortality rates, life expectancy and health care. However, congenital disorders and inherited diseases are responsible for a high amount of neo- and perinatal mortality in Arab populations which, as well as having a significant effect on general health, also have related extreme financial, psychological and social issues, greatly impacting life quality for both the individuals and their families (6, 10, 11). These related issues can be addressed with a high amount of success through the use of preventative measures, focusing mainly on a variety of primary health care approaches, together with the provision of strong education programs (12).

One approach is that of pre-marital screening, which can identify carriers of hemoglobinopathies with good

accuracy, even if the carrier presents no symptoms. Another method is the provision of 'genetic counseling' to couples, enabling them to have a healthy reproductive life (13). A reduction in the number of high-risk marriages and subsequent birth of afflicted infants can be the result of these two different methods, as long as factors including cultural, religious, ethnic and social are addressed sufficiently (12, 14, 15).

In an attempt to decrease the high number of haemoglobinopathies in Saudi Arabia, the country's Ministry of Health introduced mandatory premarital screening in 2004. It is called Premarital screening and genetic counseling (PMSGC) program. As well as mandatory testing, which was decided on after conversations with several religious, social and technical organizations. At the time of writing, over 100 health centers have been established in Saudi Arabia, together with 70 laboratories for testing blood and a further 20 clinics focused on providing education and genetic counselling. Counselling and screening services are both provided free of charge. There is also a specialist center based in Riyadh which, working with the King Faisal Specialist Hospital, aims to instruct all healthcare professionals working within the program. Moreover, The program guidelines are updated regularly (16).

These services would have to function at the grass roots to be accepted by the community to be successful in maintaining and enhancing public health. An increase in public literacy on consanguineous marriages could also prove effective through the provision of suitable education services for relevant adults and training to the workforce in primary care in all health and social conventions related to marriages between close relatives. This study aims to assess how the people using the governmental outpatient clinics felt concerning the Saudi PMSGC and to investigate the outcomes of mandatory Saudi PMSGC for couples with compatible hemoglobinopathies, namely sickle cell anemia and thalassemia, in terms of (diseased or carrier, compliant or non-compliant, satisfied or dissatisfied) in the Makkah, Qunfudah, Jazan, Al-Hasa and Eastern regions of Saudi Arabia during the duration of the program during 2017-2018.

Methods

This descriptive study drew on the national data of the Saudi PMSGC Program, a mandatory targeted screening, as part of a program of primary prevention, available to all Saudi couples who wish to marry (17). The PMSGC primarily aims to prevent or reduce the number of at-risk marriages, to evaluate the size and distribution of those who are sickle cell anemia and thalassemia carriers, or suffer from the diseases. It also sets out to ensure non-compatible couples are made aware of their chances of having offspring with the diseases, as well as providing them with alternatives to cancelling their planned marriage (17).

This study included all the couples who were incompatible for haemoglobinopathies - sickle-cell anaemia and thalassemias - who were registered with PMSCGS consultation clinics affiliated to the Saudi MOH across five health sectors (Makkah, Qunfudah, Jazan, Al-Hasa and Eastern Region) between 2017 and 2018. PMSGC clinics have been authorized to carry out premarital screening by the Saudi MOH, and provide testing and counselling for couples who have decided to apply for a marriage license. All the tests are free for Saudi nationals, and non-Saudi nationals alike. PMSCG guidelines state that every couple who intends to marry must register with the nearest healthcare center, in order to apply for a marriage certificate. The clinic staff attached to the program gather demographic information, take a blood sample (containing ethylene-diamine tetraacetic acid [EDTA] anticoagulant) and offer couples educational materials, which explain the program. Blood samples are sent for analysis to a laboratory designated for testing for sickle cell disease and b-thalassemia, using haemoglobin electrophoresis.

In addition, other blood tests are also carried out, including a full blood count, a peripheral blood film, a reticulocyte count and a sickling test. The results are compiled by using standard laboratory practices (17, 18). The couples are given the test results and then premarital certificates are issued. Couples are divided into three categories: free (healthy), carriers (carrying the trait) or cases (they have the disease), in relation to sickle cell disease and/or b-thalassemia. If one of the

partners is healthy, the marriage is said to be safe. Marriages are declared at-risk, if both of the individuals are carriers or cases - or if one is a carrier and the other a case - of sickle cell disease or b-thalassemia. Any couple who are declared safe are instantly provided with their compatibility certificates, whereas at-risk couples have to attend personal genetic counselling sessions, and only once this is done are they given incompatibility certificates. During the sessions, couples are given information about the health hazards they are risking through marriage, and the fact that any agreement is voluntary. Finally, the program staff telephone the at-risk couples to see what they have decided to do, and keep in contact with the Ministry of Justice - who issue the marriage certificates - for updates on whether the at-risk couple have married, or not.

Counseling is provided to the couple who intend to marry, or to the male partner, alongside someone who is representing the female. The session will cover the serious risks of having children with a high risk of the disease, and the consequences. The couple are each given health education materials to take away with them, and issued a certificate of incompatibility, once they have both provided their signatures. Couples are permitted to marry, irrespective of their test results, and every high-risk couple is followed up, to get an idea of whether the program is proving successful.

This study excluded couples at low risk of hemoglobinopathy who had been issued with compatibility certificates. If both partners are positive for sickle cell trait/disease, and/or thalassemia trait/disease, they are automatically viewed as high-risk and form part of this study.

Research data was gathered by giving every incompatible couple for haemoglobinopathies a structured interview questionnaire to fill in. All the data was treated as anonymous and confidential. The questionnaire itself was designed by the Healthy Marriage Program in the MOH. The validity and reliability of the questionnaire were not, however, tested. The questionnaire was made up of 24 questions and participants were given ten minutes to fill it in. An

assistance was on hand to answer any questions respondents might want to ask. The questionnaire was drawn up in English, and then had to be translated into Arabic - the target group's spoken language.

Statistical and data entry analysis carried out using SPSS (statistical package of social sciences) version 23 (SPSS Inc., Chicago, IL, USA), and relevant statistical tests carried out. The normality of data will be tested by a single sample K-S test, and parametric data recorded in mean \pm standard deviation. and the results presented in frequency tables and/or groups - as suitable. The Ministry of Health provided Institution Review Board (IRB) approval for this study. The aim of the research study, its major objectives and each step of the procedure were all set out and explained in relation to the Healthy Marriage Program.

Results

This study included 886 participants who met the criteria for eligibility, covering five areas in Saudi Arabia: Alhasa (n=355) Alqunfudah (n=14) Eastern province (n=108), Jazan (n=48) and Makkah (n=361). Of the participants involved, 490 visited the clinics in 2017, and 396 in 2018, 65.8 % of them were sickle cell anemic (n=583), and 33.7 % had thalassemia (n=299), while four participants (0.5 %) had both diseases - see Figure 2. In Overall participants age range 13-78 (mean (SD)= 28.2(8.6). However, the participants from Alqunfudah were younger than other participants with age range 19-33 withy mean age (SD)= 24.2(5.3), as illustrated in Figure 1 and 2. Among the participants, 60.8 were male (n=539) and 39.2% were female (n=347), and sickle cell disease was found more often in male than female participants. When the questionnaire was handed out, 76.2% of the respondents were single, with 9 % being married, 12.6% divorced and 2.1% widowed. In terms of work, 512 of 886 respondents (57.7%) were either working in the government sector (14.5%), the private sector (32%) or in the military (11.2%) (Table 1). Education levels varied, with 41.4% of the participants having a high school qualification, and 33.7 % having attended university. A family history of haemoglobinopathy was reported by 40.6% of the respondents (n=360), and 59.1% of the participants stated they had no family relationship with their incompatible partner (table 1).

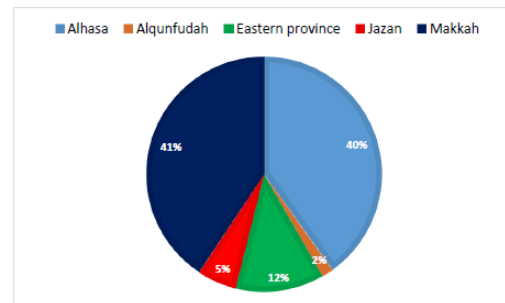


Figure [1]: Participants distribution based on province (2017-2018)

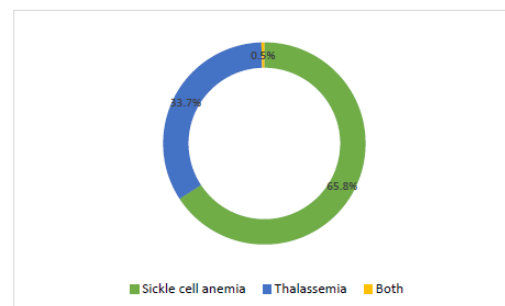


Figure [2]: Province Participants diagnoses (2017-2018)

Regarding gender, males formed a higher %age of participants in the provinces of Alhasa, Eastern province and Makkah, accounting for 58.9, 53.7 and 66.8% respectively. The balance between men and women was equal in the other two provinces. Figure 6 shows that the majority of the participants were single in every province, as well as illustrating that the majority of the participants had high school or university qualifications and were in work. There were no relationships between the majority of incompatible couples in four cities, with 58.2 % of the couples in Makkah and 80% in Eastern Province stating this was the case. The majority of the incompatible couples in Alqunfudah (42.9 %) were linked by a family relationship, and most of the participants in the five cities suffered from sickle cell disease.

The majority (64.7 %) of the participants stated that they had received medical advice at the same center and 98.9 % reported that they had been informed about the method of transmission, the dangers associated with the disease and the social, psychological and economic impact it could have on them and their families (see figure 3 and 4).

Table [1]: Province Demographic characteristics of the included participants (n=886) (2017-2018)

Criteria	Number (%)
Gender	
Male	539 (60.8%)
Female	347(39.2%)
Social status	
Single	675 (76.2%)
Married	80(9%)
Divorced	112(12.6%)
Widowed	19(2.1%)
Education	
Illiterate	13 (1.5%)
Primary School	53(6%)
Middle school	89(10%)
High school	367(41.4%)
University stage	299(33%)
Post-graduate stage	26(2.9%)
Other	39(4.4%)
Occupation	
Student	177(20%)
Government employee	129 (14.5%)
Military	100(11.2%)
Private employee	283 (32%)
Unemployed	74(8.4%)
Housewife	87(9.8%)
Other	36 (4%)

In addition, 92.2 % of the participants noted that they had been provided with awareness materials alongside medical advice. When questioned about the awareness materials, 48.1 % of participants mentioned brochures, 22.8 % referred to videos and 20.3 % spoke of the handbook - posters and charts were, collectively, only reported by 16.3 % of participants. Figure 5 illustrates how long the participants spent in the medical advice session, with just under 50 % spending over 20 minutes.

There was a wide variation in the answers from different provinces in relation to the medical advice participants were given. For example, 53.2 % of the Makkah participates and 31.8% of the Alhasa participants stated that the medical advice session took place in a different centre, while 92.9, 98.1 and 89.6 % of the participants from Alqunfudah, Eastern province and Jazan, respectively, stated that the advice had been provided in the same medical center. Over 95 % of the participants from Alhasa, Eastern province, Jazan and Makkah asserted that they had been provided with a clear explanation of the transmission and dangers of haemoglobinopathy, whereas a far lower 85.7% of

participants from Alqunfudah agreed, and 14.3% strongly disagreed. Figure 13 shows that over 90 % of participants from each province agreed that they had been given a full explanation of the dangers of the disease and its potential social, psychological and economic impact.

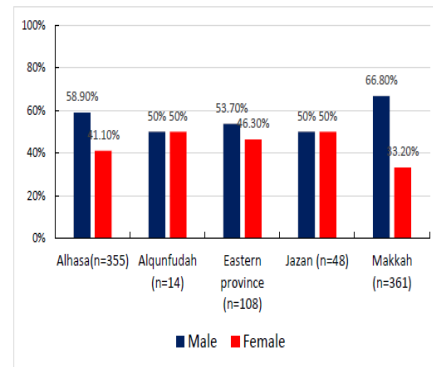


Figure (3): Percentage of male and female participants in different provinces (2017-2018)

The majority of the participants spent over 20 minutes at the clinic and virtually all of them report that the doctor answered their questions fully, while 92.2% confirm that awareness material was used - mainly brochures, the handbook and posters. Overall, 96.4% of the participants stated they were satisfied with the premarital screening program (figure 6). About 20% of the participants decided to accept the medical advice and not to marry the incompatible partner: 13.7% stated that this was a logical and reasonable decision; 7.4 % wanted to have a life free of disease. There was a significant difference between the provinces in terms of advice acceptance rates, with the East province having an acceptance rate of 68.5%, and Al-hasa reporting 2% acceptance. There was also variance between cities in term of the reason for advice acceptance and rejection. About 79.7 % of the study participants rejected the advice, either because they believed the marriage was predestined, or because they believed the likelihood of transmission of the disease was low. Next, participants stated that family relations and emotional links with their partner made them disinclined to accept the advice, as a finding which applied across all five provinces (Figure 7).

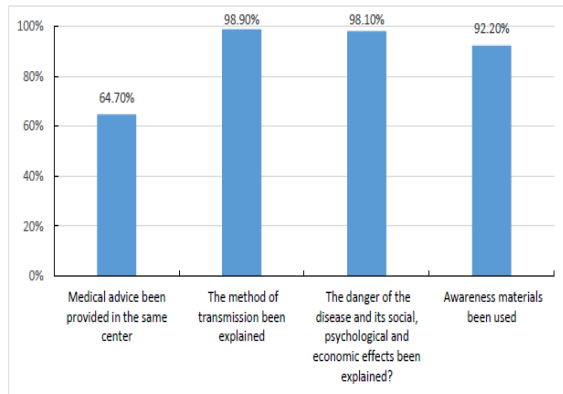


Figure (4): General description of the medical advice, as perceived by the participants

Discussion

Shaikha Al Arrayed, Amani Al Hajeri (17) point out that many countries are recognising the value of premarital counselling and implementing it as a public health measure. health Al Azeem, Elsayed (18) add that PMSGC provides couples who are considering marriage essential information about reproductive health. This is particularly relevant in the Arabian Peninsula, which has a high rate of consanguineous marriages shaped by tribal links (13, 19). According to Al-Aama (15) and Ibrahim, Al-Bar (25) the region's consanguinity rates fall between 25 and 60%, and first-cousin marriages are common. This study concurs with the above results, having found a consanguinity rate of 23.3% for first-cousin couples, and 12.6% for couples who are family-related.

Al-Aama (15) carried out a study which focused on community attitudes, and found that 94% of respondents viewed premarital testing and counselling as valuable and important in preventing genetic blood diseases, while 87% stated that it should be compulsory. Ibrahim, Bashawri (20) note that a study which was carried out in Jeddah, and involved 800 university students, showed the majority supported the test, but objections were raised to mandatory testing, on the basis this infringed the right to personal decision-making. Ibrahim, Al-Bar (25) found that the

female students at Riyadh's King Saud University who took part in an educational program also supported premarital testing and counseling.

Nevertheless, this research determined that incompatible couples rarely cancelled their marriages or took onboard the advice they were offered, in spite of the fact 96.4% expressed satisfaction that the service was available to them. Participants who refused to cancel their marriages most often cited predestination and their belief that the likelihood of transmission was low. In addition, they also stated that family relations made cancellation difficult, as did the emotional bond they had formed with their future partner. This finding emphasizes that it is essential to ensure couples are taught the importance of genetic counselling and realize that any decision they make will impact on their sibling/children. Bener, Al-Mulla (21) point out that genetic counselling provides families and individuals with information on potential genetic conditions which could affect them, and allows them to use this information to shape decisions they make about marriage, reproduction and ways of managing their health.

In terms of assessing the program and the advice it offered, over 90% of those who took part gave a score of "excellent" or "very good" for the way in which the dangers and transmission of haemoglobinopathy were explained. Over 90% scored the materials used to raise awareness as "excellent". In Bahrain, 70% of those who attended premarital counselling stated that the service was excellent, overall, and this was mirrored in the high levels of satisfaction provided in the feedback (17).

The poor rate of advice acceptance remains an issue, and one that must be addressed. Schumm, Walker (22) state that the aim of marriage education and medical advice is to provide individuals and couples with the information, skills and principles that will help them create and maintain a healthy marriage. Puri, Dhiman (13) and Williamson, Trail (23) argue that advice acceptance rates will only rise if the population is made aware of the advantages of counselling and the ethical issues it may throw up, so that people can make right choices for themselves and their own families. If this is done, the level of advice acceptance in Saudi Arabia will rise.

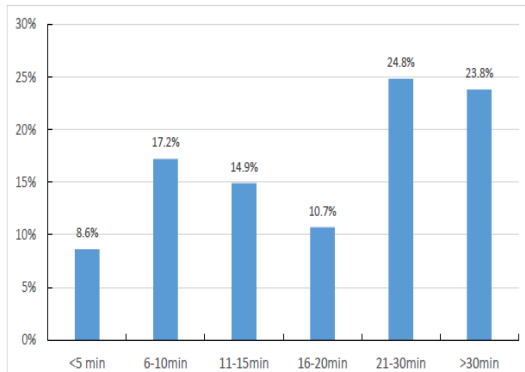


Figure (5): Length of time the participant spent in the medical advice session

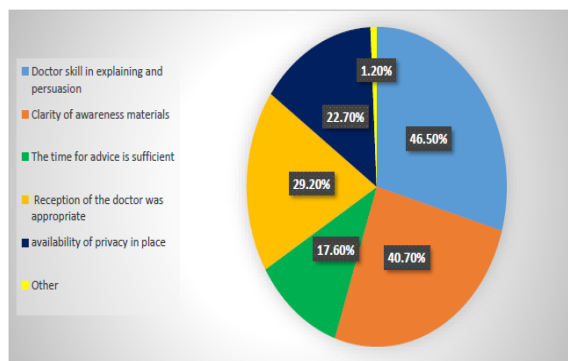


Figure (6): Different areas of participant satisfaction

In spite of the low level of advice acceptance, this study concurs with the findings of an Australian study which analyzed the expectations, psychological changes and satisfaction with genetic counselling - where the majority of participants stated they were "very satisfied". Muttappallymyalil and Sreedharan (24) evaluated the level of understanding of genetic advice provided by the UAE clinic, and came to the conclusion that it is essential to provide the whole population with this information, if it is to be effective. The authors also supported the idea of introducing carrier screening and preconception diagnosis among affected families, which could go some way towards preventing advice rejection in Saudi Arabia. Couples who were planning at-risk marriages differed broadly in their reactions: 20.3% decided to cancel the marriage, while 79.9% went ahead. These statistics

show that there has to be a cultural shift if more at-risk marriages are to be prevented, and this forms part of the counsellors' task. Those who attended counselling were generally pleased with the experience, but there are a number of issues which have to be addressed - for example, laboratory examinations have to be upgraded and counsellors have to improve their approach and add a number of subjects and areas to their presentations, if more at-risk marriages are to be prevented.

This study found that the marriage rate between first degree cousins was 23.3%, and while consanguinity does not necessarily always produce problems, the number of genetic disorders - sickle cell anemia, cystic fibrosis, spinal muscular atrophy, and several types of retardation and epilepsy - found in a population where cousin marriages are widespread can be 20 times higher (8). This study is not looking at cousin marriage as such, but is focusing on how to avoid the genetically determined diseases that can emerge from this practice. Genetic disorders are far less likely if second cousins or more distant relatives marry, but the children of first cousins share 12.5% of their genes, and this makes them 200% more predisposed to contract this type of disorder. As Kari, Bockenhauer (9) point out, this means that over a number of generations, populations which intermarry can find that the incidence of these disorders grows rapidly.

Wealthy families tend to marry their children to other wealthy families or within their own expanded family, possibly since the rich are protective of their own wealth. In Saudi Arabia, therefore, consanguinity is common, possibly for both cultural and economic reasons. One effective step might be to design a series of standardized procedures which deal with knowledge, understanding and practice in connection with the PMSGC program, and integrate them into daily clinical systems. Secondly, in order to increase outreach to the whole population, there should be more educational programs on the issue available in the media - such as internet web pages, religious programs, TV channels, radio stations and newspapers. The Saudi MOH has undertaken large-scale campaigns to prevent marriages at risk for sickle cell disease and b-thalassemia, and new initiatives are already in the pipeline. The number of specialized

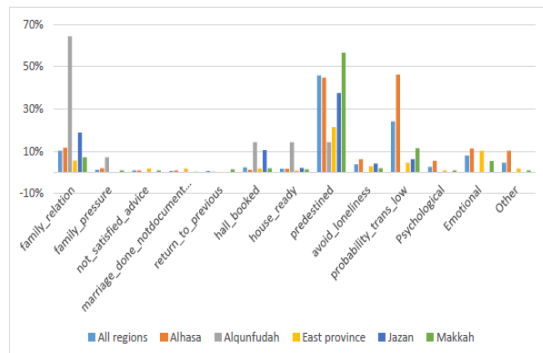


Figure (7): Reason for advice rejection among the participants

healthcare reception clinics will be expanded to include additional regions, and every clinic in the country will be linked through state of the art web-based database software, which will improve instantaneous rate calculation and research. This initiative will surmount the restrictions of aggregate data encountered in the present study, since it was not possible to access raw or individual data for analysis purposes.

The Saudi MOH could improve the effects of counselling by campaigning for couples to undergo tests early on in the marriage process, involve religious spokesmen in counselling, integrate program information into the curriculum at school, make it possible for single people to get genetic testing and encourage community figures to help with promoting and publicizing the program, both via the media and at religious gatherings.

Conclusions

This study found that satisfaction levels were high in relation to the PMSGC program, whereas advice acceptance levels were low within the population and responses were not very positive. It is essential to spread knowledge about the program and encourage individuals to understand its importance and comply with its requirements, and this can best be achieved by running campaigns on the subject in schools and universities. Reproduction and fertility are acknowledged to be extremely important areas of healthcare and have to be prioritized in this community.

Conflict of interests

The authors declared no conflict of interests.

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