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ORIGINAL RESEARCH

At-Risk Marriages after Compulsory Premarital Testing and Counseling for β-Thalassemia and Sickle Cell Disease in Saudi Arabia, 2005–2006

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Abstract Results from a screening program for sickle cell disease and β-thalassemia suggest about 90% of couples in Saudi Arabia at risk of having affected children still decide to marry. This study determined the rate of at-risk marriages and identified several factors that may prevent at risk couples from marrying. The marriage status of 934 at-risk couples was determined from original screening program records in the Ministry of Health. Of 934 couples, 824 married (88.2%) and 110 (11.8%) did not. A case–controlled study was conducted on 104 couples who did not marry (cases) and 478 couples who did marry (controls) in order to assess relationships between various cultural and social factors and marriage decisions. In the case-controled study, 28.8% of couples (30/104) who did not marry (cases) knew their disease or carrier status before screening compared to 18% (86/478) of those who married (controls). Reasons couples gave for proceeding with marriage included: wedding plans could not be canceled, and fear of social stigma. Couples who did not marry reported being influenced by prior knowledge of their disease or carrier status and whether they or family members were affected. Approximately half of the cases and controls ($n=270$, 46.4%) thought it best to undergo screening before proceeding with the engagement and wedding plans. Most couples received no advice to participate in genetic counseling services. Marriage decisions for the small number who received genetic counseling ($n=168$, 27.6%) did not differ significantly from those that received no counseling. Recommendations are made for improving the effectiveness of this screening program.

Keywords Premarital · Screening · At-risk marriages · Decision factors · Thalassemia · Sickle cell disease · Saudi Arabia · Genetic counseling

Introduction

Thalassemia and sickle cell disease (SCD) are common autosomal recessive heritable hemoglobinopathies. Both are difficult to treat, they cause significant morbidity and mortality, and they pose a financial burden on society (Tosun et al. 2006). Premarital screening can detect carriers of these diseases so that at-risk couples can be identified and advised about the possibility of bearing affected children. Since the 1970s screening programs have become mandatory in many countries (Alswaidi and O'Brien 2009). Factors that limit their success include religious beliefs, cultural norms, traditions, literacy, education, government policy and attitudes of the couples themselves (World Health Organization 2006).

In Saudi Arabia there was a royal decree in 2003 calling for premarital screening results for genetic diseases to be available before the marriage contract was written. β-thalassemia and SCD were targeted because they are the most common hereditary blood disorders in Saudi Arabia, with high medical costs and social support needs (El-Hazmi 2004). Screening started in February 2004 with mandatory blood testing at designated centers and laboratories, and a network of government facilities providing free testing and counseling for couples wanting to marry (Al-Hamdan et al. 2007). Couples were defined as "genetically incompatible" or "at-risk" if both partners were affected with or were carriers of

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either disease. Couples were free to marry regardless of their test results.

A network of 20 main health care facilities (reception centers) connected to another 103 peripheral centers, 70 laboratories, and 20 genetic counseling clinics (for incompatible couples only) have been developed in the government sector in the Ministry of Health. They provide testing and counseling facilities to all potential couples at no cost.

The primary aim of the counseling is to avoid the at-risk marriage. If an at risk couple decides on marrying and having children, possible preventive measures like Preimplantation Genetic Diagnosis are explained to prevent the birth of ill children.

Due to the limited number of qualified genetic counselors in Saudi Arabia, a majority of counseling clinics are run by pediatricians. Counseling sessions are supposed to be delivered in the form of one-to-one counseling with the incompatible couple after which a "mismatch certificate" (indicating genetic risk) is given to the couple. There are no standardized national guidelines for the content of counseling sessions and materials, but the counselor should undertake the following:

- Review and affirm the test results and the file number of the tested person before interviewing him/her.
- Check the tested person's identity according to the civil registrar.
- Adhere to a practice of breaking bad news sensitively.
- Explain positive carrier testing results and cancel requests for further confirmation testing.
- Identify the tested person's questions and concerns.
- Affirm for the tested person/couple that he/she/they are at risk of having children with hemoglobinopathies in the future.
- Inform incompatible couples of ways to avoid at-risk marriage in the case of hemoglobinopathies.

The main objectives of the screening program were to reduce the occurrence of marriages among at-risk couples and the incidence of both diseases in the population. In the first year, 241,825 people were screened, and 2,441 at-risk couples were identified. Tracking their marriage decisions through Ministry of Health records was difficult, but data were available for 1,213 of these at-risk couples. About 90% (1,101/1,213) of these couples did marry despite the risk of having affected offspring (Al-Hamdan et al. 2007). The second year of the screening program yielded similar outcomes.

Although Al-Hamdan et al. (2007) analysis provides important information about some couples' decisions, the marriage decisions for many at-risk couples are still unknown. Therefore, the first objective of the current study was to locate these at-risk couples and determine what decision they made regarding marriage. The second objective was to identify sociodemographic and cultural factors that influenced their marriage decisions, including the role of genetic counseling in their decisions. The third objective was to develop recommendations based on the findings to improve the program's success in preventing high-risk marriages.

Methods

Materials

After obtaining administrative and ethical approval, all available Ministry of Health (MoH) records for the premarital screening conducted between February 20, 2004 and February 21, 2006 were reviewed. Data collection was restricted to this time period because in subsequent years, most of the records were maintained by regional health centers and were extremely difficult to access.

Based on MoH records, a list was compiled of at-risk couples along with their contact information. Their marital status (Married, Not married, or Unknown) was established from the records or by contacting one partner from each couple. A decision to not marry was uncommon after testing, so the case–control study aimed to identify factors influencing that decision. A "case" refers to an at-risk partner of a couple who did not marry (Did Not-Marry). A "control" refers to an at-risk partner of a couple who did marry (Did-Marry).

Sampling and Sample Size Calculation

Based on all at-risk couples contacted by telephone, a two-section sampling frame (Did-Marry and Did Not-Marry) was constructed, as shown in the flowchart (Fig. 1). The required sample size of 582 was calculated by using StatCalc (Epi Info Software) based on an unmatched case–control design. Only 104 potential cases (Did Not-Marry) agreed to participate in the study. The 478 couples used as controls (Did-Marry) were chosen randomly. Only one partner from each couple was included in the study. So, "couple" refers to the "partner" who participated in the study.

The limited number of cases was the main determinant of sample size. The maximum number of cases verified by telephone interview was 104; therefore the ratio was set at approximately four controls for each case. On the assumption that the least exposure among controls was 20% and the least odds ratio (OR) to be detected was 2, then the sample size of 104 cases and 478 controls would have an approximate power of 78%.

Data Collection Procedures and Analysis

The rate of at-risk marriages in the MoH was confirmed. Before commencing the interviews, training and demonstration sessions were given to all data collectors. The team

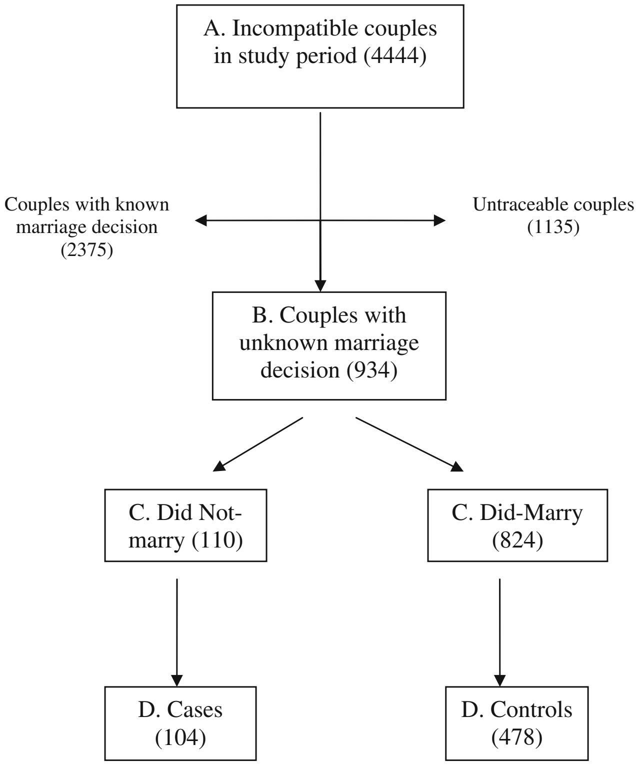

Fig. 1 Selection of cases and controls. **a** Study population. **b** Sampling population (all were contacted to confirm their marital status). **c** Sampling frames (based on marital status Not-Marry and Did-Marry). **d** Required sample size (one partner from each couple)

of data collectors, which included both male and female physicians, and varied in number from two to four people during the data collection period, interviewed one partner from each couple by telephone from the MOH headquarters. A couple (one partner) was dialed a maximum of three times in a day; if there was no response, another three re-dials were tried in the next session/day. Informed oral consent was obtained before each interview, and the average time spent in the interview was about 10 min.

A telephone-based questionnaire was designed to collect the following information:

- Confirmation of decision to marry or not–What was the outcome of the engagement/proposed marriage for which premarital screening was done? (already married, decided to marry, decided to not marry, not decided yet)
- Socio-demographic and medical history data–Includes age, gender, region, education, relationship to the partner, source and level of income, marital status and number of children at time of premarital screening, participant's medical status (thalassemia/SCD), participant's family history for thalassemia and SCD.
- Knowledge about the premarital screening test–Knowledge about the existence of compulsory premarital screening, source of this knowledge (media, family), the purpose of the premarital screening, the diseases for which screening was done.
- Effect of the counseling services on the decision regarding marriage–Did the health staff advise you to visit the counseling clinic? Did you actually visit the clinic? With whom did you visit the clinic? What type of counseling did you receive?
- Cultural and familial factors–Who made the decision about marriage (couple/family)? When was the decision about marriage made? Why was the decision to proceed with an at-risk marriage made (family pressure/fear of stigma/religious considerations/uncancellable wedding)? Participants' financial support (independent/family support).

Bivariate (single factor risk) analysis was performed to identify the association of each factor with the outcomes and odds ratios were computed for any relationships. Multivariate logistic regression analysis demonstrated the adjusted effect of each variable on the outcome, while controlling for all other entered variables. Partial or complete confounding effects of all factors were controlled for (but not measured). The stepwise backward Wald method allowed identification of the minimum number of variables that were significantly associated with the outcome. Adjusted ORs were calculated for all variables. For a variable to enter the model a probability of 0.05 (0.10 for removal) was required.

Results

Identifying At-Risk Couples from Records

Data were obtained for 4,444 at-risk couples. Marriage status was known for 2,375 and unknown for 2,069. Of the unknown 2,069, 1135 were untraceable or did not respond, and 934 stated their decision either to marry (824 Did-Marry; 88.2%) or not (110 Did Not-Marry; 11.8%).

Case–Control Results

Demographic Characteristics

Of the 934 couples, 582 (62.3%) were included in the case–control study. The demographic characteristics of the participants in this study are reported in Table 1. There were 104 participants in the Did Not-Marry group (17.9%) and 478 (82.1%) in the Did-Marry group. The age ranges of the Did Not-Marry and Did-Marry participants were 19–39 (mean 26.1±6.56) and 15–46 years (mean 25.2±5.30), respectively. There were 299 males (51.4%), of which 205 (68.6%) were 25 years old or less, and 283 females (48.6%), of which 160 (56.5%) were more than 25 years old. Being older or younger than 25 years was not

Table 1 Relationship of sociodemographic characteristics to marriage decision for 582 at-risk couples from the Saudi premarital screening program in 2005–2006

Factors	Study groups				Odds ratio	95% CI	*p*-value
	Did not-marry (n=104)		Did marry (n=478)				
	n	%	n	%			
Age							
≤25 years	53	51.0%	279	58.4%	0.74	0.48–1.13	0.168
>25 years	51	49.0%	199	41.6%	reference	–	
Gender							
Male	54	51.9%	245	51.3%	1.03	0.67–1.57	0.902
Female	50	48.1%	233	48.7%	ref	–	
Educational status							
Secondary/lower	71	68.3%	309	64.6%	1.78	0.75–1.85	0.482
University/higher	33	31.7%	169	35.4%	ref	–	
Region							
East	84	80.8%	297	62.1%	2.65	1.56–4.51	0.000
Central	1	1.0%	3	0.6%	3.12	0.31–31.53	0.334
West	19	18.3%	178	37.2%	ref	–	
Income[1]							
Self-dependent	64	61.5%	303	63.4%	ref	–	
Family-dependent	40	38.5%	175	36.6%	1.1	0.70–1.68	0.723
Average monthly income (Riyals)[1]							
<5000	22	21.2%	84	17.6%	1.26	0.74–2.13	0.392
>5000	82	78.8%	394	82.4%	ref	–	
Blood relationship (consanguinity)							
Third-degree (first cousin)	34	32.7%	180	37.7%	0.73	0.45–1.18	0.195
Fourth-degree (second cousin)	17	16.3%	93	19.5%	0.71	0.39–1.29	0.256
None	53	51.0%	205	42.9%	ref	–	
Marital status at screening							
Never married	95	91.3%	448	93.7%	ref	–	
Married/divorced/widowed	9	8.7%	30	6.3%	1.42	0.65–3.08	0.382
Children at time of screening							
No children	95	91.3%	448	93.7%	ref		
Have children	9	8.7%	30	6.3%	1.41	0.60–3.24	0.379

[1] Others and missing values are not included

significantly related to marriage likelihood for either males or females (OR = 0.74).

Most participants (n=236, 40.5%) had a secondary education, and they were more likely to avoid an at-risk marriage than those with a university or higher education (OR = 1.78). Couples in the eastern province were more likely to not marry than participants from elsewhere in the country (OR = 2.65) (n=84, 80.8% Did Not-Marry vs. n= 297, 62.1% Did-Marry). Those who were family-dependent were more likely to not marry than those who were financially self-dependent (OR = 1.1).

The average monthly income of the men and women in the study was 4,468 and 4,034 Saudi Riyals, ($1190 and $1076) respectively. Low-income participants were less likely to marry than high-income participants (OR = 1.26). Those designated as "Married/Divorced/Widowed" also were less likely to marry (OR = 1.42) (Table 1).

Consanguinity/Relatedness

Around half (n=52, 51%) of the Did Not-Marry couples and 42.9% (n=205) of the Did-Marry couples were unrelated. Among related couples, 223 were third-degree blood relatives. Of these, 43 (32.7%) Did Not-Marry vs. 180 (37.7%) that Did-Marry (OR = 0.73). One-hundred ten were fourth-degree blood or other relatives. Of these, 17

(16.3%) Did Not-Marry vs. 93 (19.5%) that Did-Marry. Blood-related couples had a significantly higher probability of getting married than unrelated couples (OR = 0.71) (Table 1).

Reasons for Deciding to Proceed with the "At-Risk" Marriages

The 478 participants from an at-risk couple were asked to identify the primary reason they proceeded with the marriage. As shown in Table 2, they identified a total of six different reasons. In descending order of prevalence, they are: completed and non-cancellable wedding plans (*n*=207, 43.3%); social stigma (*n*=101, 21.1%), especially among females (*n*=91, 19% of females, vs. *n*=10, 2.1% of males); familial commitment or pressures (*n*=80, 16.7%) and religious considerations (*n*=68, 14.2%).

Knowledge of the Diseases

Knowledge of Disease or Carrier Status A total of 116 couples knew their disease or carrier status before screening. Of these, 30 (28.8%) were in the Did Not-Marry group, and 86 (18%) were in the Did-Marry. Of those who did not know their status, 65 (62.5%) were in the Did Not-Marry group, and 392 (82.0%) were in the Did-Marry group. Knowledge of one's status prior to screening was significantly associated with a decision to not marry (OR = 1.85).

Family History of Disease Family history of SCD was not known by 65 (62.5%) of the Did Not-Marry couples vs. 348 (72.8%) of the Did-Marry couples; and it was known by 39 (37.5%) of the Did Not-Marry couples and 130 (27.2%) of the Did-Marry couples. Knowledge of family history of SCD was significantly associated with not marrying (OR = 1.61). Family history of β-thalassemia was not known by 89 (85.6%) of the Did-Marry couples vs. 425 (88.9%) of the Did-Marry couples; and it was known by 15 (14.4%) of the Did Not-Marry vs. 53 (11.1%) of the Did-Marry couples. Knowledge of family history of β-thalassemia was significantly associated with likelihood to not marry (OR = 1.35).

Affected Family SCD affected family members of 169 (29.03%) couples. In the Did-Marry group, 11 (28.2%) couples had affected parents, 19 (48.7%) had affected siblings or children, and 9 (23.1%) had other relatives that were affected. SCD among close family members was associated with greater likelihood of a decision to get married (OR = 0.88). β-thalassemia affected the families of 68 (11.7%) couples. Of those with affected parents, 6 (40.0%) were in the Did Not-Marry group and 16 (30.2%) were in the Did-Marry group. Four (26.7%) with affected other relatives were in the Did Not-Marry group vs. 18 (34.0%) in the Did-Marry group. Having a close relative with β-thalassemia was significantly associated with a decision to not marry (OR = 1.69) (Table 3).

Disease Status among Couples

SCD affected both partners in 30 (55.6%) of the Did Not-Marry couples and 60 (31.9%) of the Did-Marry couples. These couples were more than twice as likely to not marry (OR = 2.67) than couples where both persons were carriers [*n*=24 (44.4%) Did Not-Marry vs. *n*=128 (68.1%) Did-Marry]. β-thalassemia affected both partners of 32 (72.7%) Did Not-Marry couples and 80 (42.1%) Did-Marry couples. They were more than three times as likely to not marry (OR = 3.67) than couples who were carriers [*n*=12 (27.3%) Did Not-Marry vs. *n*=110 (57.9%) Did-Marry] (Table 4). The study sample did not include couples of mixed partners with thalassemia and SCD.

Knowledge of Compulsory Screening (Table 5)

Knowledge about the Program A total of 104 couples [*n*=21(20.2%) Did Not-Marry vs. *n*=83 (17.4%) Did-Marry]

Table 2 Reasons at-risk couples proceeded with marriage despite knowing the risk of bearing affected offspring (*n*=478)

Reason	Men		Women		Total	
	n	%	n	%	n	%
Wedding already arranged/non-cancelable	187	37.2%	20	4.2%	207	43.3%
Fear of social stigma	10	2.1%	91	19%	101	21.1%
Familial commitment/pressure	60	12.5%	20	4.2%	80	16.7%
Religious considerations	40	8.3%	28	5.8%	68	14.2%
Availability of preventive measures	12	2.5%	8	1.6%	20	4.2%
Wedding was cancelled for unknown reason	1	0.2%	0	0	1	0.2%
Wedding was postponed to unknown time	1	0.2%	0	0	1	0.2%

Participants were asked to identify the most influential reason for proceeding with the at-risk marriage

Table 3 Relationship of participants' knowledge of disease status and family history of sickle cell disease and β-thalassemia in cases (Did Not-Marry) and controls (Did-Marry) groups to marriage decision

Factors	Study groups				Odds ratio	95% CI	*p*-value
	Did not-marry (*n*=104)		Did-marry (*n*=478)				
	n	%	n	%			
Awareness of disease status before screening							
Yes	30	28.8%	86	18.0%	1.85	1.14–3.00	0.013
No/not sure	74	71.2%	392	82.0%	Ref	–	
Family history of Sickle Cell Disease (SCD)							
Yes	39	37.5%	130	27.2%	1.61	1.03–2.51	0.037
No/don't know	65	62.5%	348	72.8%	ref	–	
Family members with SCD (*n*=169)							
Parents (one or both)	11	28.2%	39	30.0%	0.88	0.32–2.40	0.799
Sibling or child	19	48.7%	63	48.5%	0.94	0.38–2.33	0.891
Other relative	9	23.1%	28	21.5%	ref	–	
Family history of β-thalassemia							
Yes	25	24.4%	53	11.1%	2.45	1.44–4.46	0.000
No/don't know	79	75.6%	425	88.9%	ref	–	
Family members with β-thalassemia (*n*=68)							
Parents (one or both)	6	40.0%	16	30.2%	1.69	0.43–7.07	0.474
Sibling or child	5	33.3%	19	35.8%	1.18	0.27–5.12	0.821
Other relative	4	26.7%	18	34.0%	ref	–	

were unaware of compulsory screening. They were more likely to not marry (OR = 0.83) than the 478 who did know about compulsory screening [*n*=83 (79.8%) Did Not-Marry vs. *n*=395 (82.6%) Did-Marry].

Knowledge about Screening Aims Among the 104 Did Not-Marry group, 86 couples (82.7%) knew that screening aimed to prevent diseases among offspring, 17 (16.3%) did not know its purpose, and 1 couple (1.0%) knew that it aimed to detect disease in couples. Of the Did-Marry group, 396 couples (82.8%) knew screening aimed to prevent diseases in offspring, 85 (17.8%) did not know its purpose, and 17 (3.6%) knew it aimed to detect diseases in couples. Those who knew screening aimed to prevent disease in offspring were more likely to marry (OR = 0.83).

Knowledge about Disease Of the 367 couples who knew about the diseases concerned, 61 (58.7%) were in the Did Not-Marry group, and 306 (64.0%) were in the Did-Marry

Table 4 Relationship of screening test results with marriage decision among case (Did-Not-Marry) and control (Did-Marry) groups

Factors	Study groups				Odds ratio	95% CI	*p*-value
	Cases		Controls				
	n	%	n	%			
SCD (*n*=242)							
Both affected	30	55.6%	60	31.9%	2.67	1.44–4.95	0.002
Both carriers	24	44.4%	128	68.1%	ref	–	
β-thalassemia (*n*=234)							
Both affected	32	72.7%	80	42.1%	3.67	1.78–7.59	0.000
Both carriers	12	27.3%	110	57.9%	ref	–	

Table 5 Relationship of participants' knowledge about premarital screening program to marriage decision among cases (Did Not-Marry) and controls (Did-Marry)

Factors	Study groups				Odds ratio	95% CI	*p*-value
	Cases (*n*=104)		Controls (*n*=478)				
	n	%	n	%			
Awareness of compulsory screening							
Aware	83	79.8%	395	82.6%	0.83	0.49–1.42	0.091
Unaware	21	20.2%	83	17.4%	ref	–	
Understanding the purpose of screening							
Possibility of disease in offspring	86	82.7%	396	82.8%	0.83	0.46–1.49	0.532
Detecting disease in couples	1	1.0%	17	3.6%	0.23	0.03–1.81	0.161
Do not know/not sure	17	16.3%	65	13.6%	ref	–	
Knowledge about the diseases in the screening							
Yes	61	58.7%	306	64.0%	0.80	0.52–1.23	0.305
No	43	41.3%	172	36.0%	ref	–	
Sources of knowledge about screening							
Media	32	30.8%	157	32.8%	0.68	0.58–1.44	0.682
Others (family members and friends)	72	69.2%	321	67.2%	ref	–	
Participant's opinion of best time for screening							
During secondary school	20	20.8%	103	23.4%	ref	–	
When 18 years old	18	18.8%	90	20.4%	1.03	0.51–2.07	0.934
When planning engagement	50	52.1%	220	49.9%	1.17	0.66–2.07	0.588
After engagement and before marriage	8	8.3%	28	6.3%	1.47	0.59–3.69	0.411
Other	8	7.7%	37	7.7%	1.47	0.58–3.69	0.815

group. Of those who knew little, 43 (41.3%) were in the Did Not-Marry group, and 172 (36.0%) were in the Did-Marry group. Knowing about the diseases was associated with a greater likelihood to not marry (OR = 0.80).

Sources of Knowledge The 104 couples in the Did Not-Marry group gained information from a number of sources. In descending order of prevalence they include: newspaper/magazines (n=40, 38.5%), their family (n=30, 28.8%), the marriage official (n=12, 11.5%), their partner (n=10, 9.6%), television (n=10, 9.6%), or their partner's family (n=2, 1.9%). The 478 couples in the Did-Marry group gained information from: their family (n=172, 36%), newspaper/magazines (n=80, 16.7%), television (n=80, 16.7%), the marriage official (n=76, 15.9%), their partner (n=42, 8.8%), their partner's family (n=24, 5%), or the radio (n=4, 0.8%). In general, those learning about the program from the media were less likely to not marry compared with those informed by other sources such as family and friends (OR = 0.68).

Timing of Screening Of the 270 couples who thought that the screening should be undertaken before engagement, 50 (52.1%) Did Not-Marry vs. 220 (49.9%) that Did-Marry. The opinion that screening should be done prior to an engagement was related to a greater likelihood to not marry (OR = 1.17) Of the 123 couples who believed screening should be done during secondary school education, 20 (20.8%) Did Not-Marry vs. 103 (23.4%) that Did-Marry.

Counseling (Table 6)

Attendance A total of 160 couples [n=48 (46.2%) Did Not-Marry vs. n=132 (27.6%) Did-Marry] were advised to visit a counseling clinic. Advice to visiting a counseling clinic was associated with a greater likelihood to not marry (OR = 2.25). Of the couples who were not advised to visit a counseling clinic, 56 (53.8%) Did Not-Marry vs. 346 (72.4%) that Did-Marry. Actual attendance at counseling was associated with a less likelihood to not marry (OR = 0.79). Of those who did attend counseling, 26 (25.0%) Did Not-Marry and 142 (29.7%) Did-Marry. Of those who did not attend counseling, 78 (75.0%) Did Not-Marry vs. 336 (70.3%) that Did-Marry.

Table 6 Relationship of participants' visit to counseling clinic to marriage decision for case (Did Not-Marry) and control (Did-Marry) groups

Factors	Study groups				Odds ratio	95% CI	*p*-value
	Cases (*n*=104)		Controls (*n*=478)				
	n	%	n	%			
Advised to attend counseling							
Yes	48	46.2%	132	27.6%	2.25	1.42–3.55	<0.001
No/Not sure	56	53.8%	346	72.4%	ref	–	
Attended counseling session							
Yes	26	25.0%	142	29.7%	0.79	0.47–1.31	0.337
No	78	75.0%	336	70.3%	ref	–	
Attendees at counseling (*n*=165)							
Participant alone	6	24%	18	12.9%	ref	–	
Both partners	17	68%	107	76.4%	0.48	0.17–1.37	0.162
Family	1	4%	11	7.8%	0.27	0.03–2.58	0.257
Friend	1	4%	4	2.8%	0.75	0.03–10.45	0.812
Decision-maker							
Couple	77	74.0%	389	81.4%	0.65	0.40–1.07	0.091
Family	27	26.0%	89	18.6%	ref	–	
When decision was made							
Immediately after positive result	55	52.9%	256	53.6%	ref	–	
After discussion with partner/family	42	40.4%	178	37.2%	1.10	0.70–1.71	0.680
After counseling session	7	6.7%	44	9.2%	0.74	0.32–1.73	0.488

One or both Partners Of 165 couples, only one partner out of 24 couples attended the counseling session [6 (25.0%) Did Not-Marry vs. 18 (13.2%) Did-Marry]. Where both partners attended, 17 (70.8%) were in the Did Not-Marry group and 107 (78.7%) were in the Did-Marry group (OR = 0.48). The family attended on behalf of some couples [1 (4.2%) Did Not-Marry vs. 11 (8.1%) Did-Marry; OR = 0.27]. Either the participant was accompanied or not, at the time of counseling, was not associated with the likelihood of not to marry.

Decision-Maker The decision to marry or not was made by the participant in this study for 232 couples [*n*=32 (30.8%) Did Not-Marry vs. *n*=200 (41.8%) Did-Marry], by the participant's partner in 222 couples [*n*=38 (36.5%) Did Not-Marry vs. *n*=184 (38.5%) Did-Marry] and by the participant's family in 86 couples (*n*=26 (25%) Did Not-Marry vs. *n*=60 (12.6%) Did-Marry). Overall, 77 (74%) couples in the Did Not-Marry group made their decision themselves, while the families made the decision for 27 couples (26%). Among the Did-Marry couples, the decision was made by 389 (81.4%) couples themselves and 89 (18.6%) by their families. A family decision was associated with a greater likelihood of not marrying (OR = 0.65).

Fifty-five couples (52.9%) in the Did Not-Marry group and 256 couples (53.6%) in the Did-Marry group made a marriage decision immediately after receipt of a positive screening test result. Of those couples who decided after discussions with a partner or family, 42 (40.4%) Did Not-Marry vs. 178 (37.2%) that Did Marry. An immediate decision was associated with less likelihood to not marry (OR = 1.10)

Seven couples (6.7%) in the Did Not-Marry group and 44 couples (9.2%) in the Did-Marry group made a marriage decision after participating in a counseling session rather than immediately after receiving positive test results. A decision made after counseling was associated with greater likelihood to not marry. Couples who made a decision after counseling were less likely to get married than those deciding immediately after receiving positive results (OR = 0.74).

Multivariate Analysis

In the bivariate (single variable risk) analysis, most variables had statistically non-significant close associations to unity. Variables with positive significant associations with the decision to not marry were (in order of the strength of association): positive test for β-thalassemia (OR = 3.67); family history of β-thalassemia (OR = 2.83); positive test for SCD (OR = 2.67); geographic region; advised to have counseling (OR = 2.25); prior disease awareness (OR =

1.85); and family history of SCD (OR = 1.61). Young age, consanguinity, and prior knowledge of the program were not significantly associated with the decision to not marry.

Seven variables showed statistically significant associations and minimal changes in their adjusted odds ratios. Five were also significantly associated in the bivariate analysis. Two were significant only in the multivariate analysis (marital status at screening; decision-maker). Five showed increased association with the decision to not marry (positive test for β-thalassemia (OR = 4.13); region (OR = 3.00); positive test for SCD (OR = 2.86); marital status at screening (OR = 2.51); and known disease status (OR = 1.87)). Two variables [family history of β-thalassemia (OR = 2.45), and decision-maker (OR = 0.58)], showed lower but significant associations with the decision to not marry (Table 7).

Discussion

Marriage Decisions among At-Risk Couples

This premarital screening program is relatively new in Saudi Arabia, only becoming mandatory in 2004. Although it has successfully reached its intended target group, its efficacy depends on the proportion of marriages that are averted among couples who are identified as being genetically incompatible (at-risk). The present findings suggest the program was not as successful as hoped for in that respect as almost 88% of at-risk couples did marry or decided to marry after testing.

By tracing at-risk couples whose marriage decision was unknown, this study showed no significant difference in the percentage of couples deciding to marry compared with MoH records. These results illustrate the accuracy of the program's reporting system. The number of at-risk marriages is higher among couples who are at risk for having a child with SCD than among those who are at risk for having a child with β-thalassemia. A similar prevalence of at-risk marriages occurred among at risk SCD-incompatible couples in Saudi as among at risk genetically incompatible couples of Arabic ethnicity in the Turkish premarital screening program (Tosun et al. 2006). One possible reason is that medical complications from SCD are less severe than those from β-thalassemia.

Recent results from the Saudi program show an overall decrease in the number of at-risk marriages, yet in some areas, the rates remain as high as 80%, according to the MoH records for 2008 (Saudi Ministry of Health 2009). Since the decision to marry after testing remains voluntary, this outcome might be expected, but it raises two important questions: What are the determinants of the decision either to proceed with or to decide not to marry? and How can couples' decision-making behaviors be modified? Some of the present findings offer insight about factors that influence couples' decisions, and those are discussed in the following section.

Sociodemographic and Cultural Factors Affecting Decision-Making

Saudi Arabia is a large country comprised of different cultures and social and demographic features that vary widely across different regions (and sometimes within regions). This study showed that the majority of SCD-incompatible and β-thalassemia-incompatible couples are from the eastern, western and southwestern parts of the country, in accordance with the prevalence pattern for both diseases in the country. The majority of couples were related to each other, indicating the degree of consanguinity present today, which explains how these illnesses are concentrated in certain communities (Shaikha et al. 1997). It is possible that the occurrence of specific hemoglobin mutations plays a role (Al-Odaib et al. 2003). Although the present results are congruent with the known high estimate (50%) of consanguineous marriages in Saudi Arabia (Rashad et al. 2005), consanguinity was not a significant predictor of likelihood of at risk marriage in this study.

Most of the couples in this study were young adults in their 20s embarking on a first marriage. Gender was not significantly related to the marriage decision, but this finding differs from the results of a study in Egypt in which men were found to have negative attitudes towards marriage decision after premarital testing (Eshra 1989).

The average age of marriage in Saudi Arabia has increased over the last two decades. The majority of marriages occur around the age of 22 (Rashad et al. 2005), but the average age of the participants in this study was 25. No important variations in age were detected between participants who decided to marry and those who decided not to.

This study showed that the educational status for both men and women ranged from the secondary school level or higher, but no significant association was found between education level and the marriage decision. These findings were expected because of the known social characteristics of the Saudi population in general. Moreover, collecting data via telephone, as in this study, is more readily accepted by educated young adults than by uneducated young adults or older age groups in Saudi. Health-education programs, especially those involving high-school students, are very effective for increasing awareness of genetic diseases and screening services (Cao et al. 2002), with known effects also in the UK, Cyprus, Italy and Canada (Modell et al. 2000; Modell and Kuliev 1998). The most successful program was in Canada, whereby over 90% of high-school students educated this way used premarital health services effectively over a 20 year period (Mitchell et al. 1996).

Table 7 Results of final multivariate analysis of factors affecting the probability of marriage among at-risk couples in the Saudi premarital screening program (2005–2006) using stepwise backward Wald technique

Factors	Bivariate analysis		Multivariate analysis		Adjusted *p*-value
	Crude odds ratio	95% CI	Adjusted odds ratio	95% CI	
Positive testing for β-thalassemia (*n*=234)	3.67	1.78–7.59	4.13	1.68–7.76	0.000
Region (*n*=582)	2.65	1.56–4.51	3.00	1.72–5.22	0.000
Positive testing for SCD (*n*=242)	2.67	1.44–4.95	2.86	1.09–5.11	0.002
Marital status at testing (*n*=582)	1.42	0.65–3.08	2.51	1.09–5.83	0.009
Family history of β-thalassemia (*n*=582)	2.83	1.17–6.80	2.45	1.10–6.60	<0.001
Prior knowledge of disease status (*n*=582)	1.85	1.14–3.00	1.87	1.13–3.10	<0.001
Decision-maker (couple vs. family) (*n*=582)	0.65	0.40–1.07	0.58	0.35–0.96	<0.001

Factors are arranged in descending order according to their strength of association

At-risk couples from the eastern region differed significantly from couples residing in other regions in terms of their decision to marry. Couples in the eastern region were more than twice as likely to decide not to marry. This region is highly endemic for hemoglobinopathies, so these couples are probably more aware of the hereditary risks.

Couples with low incomes also were likely to avoid at-risk marriages, probably because of the financial burden of a sick child(ren). Participants who were already married (males), divorced or lost their spouse (widows and widowers), or who had children during the screening period seemed to appreciate the risks associated with at-risk marriage. The social and demographic characteristics of the present sample generally are similar to those found in a voluntary premarital screening program in Bahrain (Shaikha et al. 1997). The similar demographic features and population structure in Middle Eastern countries, especially the high frequency of consanguineous marriages, increase the need for preventive genetic services that help avoid misinformation about and mismanagement of genetic diseases. Premarital screening programs are therefore important for reducing the incidence of such diseases in these countries (Bittles 2001; Shaikha et al. 1997).

We found that almost all the couples who intended to marry were screened just before the ceremony took place. Screening at an earlier stage, or age, independent of any marriage contract, may therefore help prevent some at-risk marriages. About half of the at-risk couples (51.9%) who proceeded to marry attributed their decision to the lateness of the test, inasmuch as the wedding arrangements were already made and cancellation was not an option. Wedding arrangements usually include offering a new house and paying a high bride-price. The same issue was reported in Iran with respect to premarital screening for β-thalassemia (Karimi et al. 2007).

The role of the couple's family in decision-making cannot be ignored. Couples who were related to each other were more likely to marry than those who were not, indicating the possibility of some sort of family pressure at play. However, for couples where decisions were frequently made by both partners together, other family members were in favor of stopping the marriage if it was at-risk. This observation might be valuable when promoting the screening program in the future. The program could include education that focuses on the couple's parents/families. The positive role of the wider family is lessened by the fact that most couples were financially independent, although it seems that financial independence had no significant bearing on the decision made by at-risk couples.

Another important finding in this study is that most women were prepared to continue with their marriages despite an identified risk because they feared the social stigma of remaining unmarried. Stigmatization following genetic screening is a well-known ethical problem, so confidentiality of the results must be guaranteed (Rennie & Mupenda 2008). The Saudi community is also greatly influenced by Islamic rules and regulations in all of its affairs. Many people believe their fate is determined by God, and they are prepared to accept the possibility of having a sick child (Monaghan 2007). The influence of religion was clear in this study, whereby around 14% of participants considered their marriage-decision in the context of their beliefs. These cultural, social and religious issues further underline the need for health education among the various communities.

Knowledge of the Diseases

β-thalassemia and SCD cause serious medical, social and economic problems for individual families and for the general public (El-Hazmi 2006). Participants in this study who knew about their disease or carrier status before they underwent screening were more likely to decide to not marry than those who did not know before testing. Participants with a family history of either SCD or β-thalassemia had a higher probability of not marrying compared to participants with no known family history. More participants who were affected by disease decided to not marry than those who were just carriers. This was especially true for β-thalassemia, and being a β-thalassemia patient was the most significant factor for avoiding at-risk marriages in this study. This likely is because β-thalassemia symptoms are manifested earlier and are more severe than those of SCD. Participants from families in which one or more members were affected by disease were very aware of the problems involved, yet the association between having ill family members and proceeding with the at-risk marriage was not statistically significant.

Knowledge of the Screening Program and Media Influences

Most participants seemed to be aware of the importance of early premarital testing. About 50% thought the best time for testing was before engagement, and 22% thought the best time was during secondary school. Similar opinions have been found in previous Saudi studies exploring public attitudes towards premarital testing and counseling (Al-Khaldi et al. 2002; Awatif 2006; El-Hazmi 2006).

A high degree of awareness is not enough to prevent many at-risk marriages, however, mainly because there are other prevailing cultural, social and religious factors, that override Government claims that its advertising campaign about the screening program and the guidance they provide has conveyed the right message to the target audience. The present findings show that most participants knew screening was mandatory before the marriage contract was drawn up, and many knew its main purpose was to avoid having children affected by thalessemia or SCD, but this knowledge was not significantly associated with a reduction in at-risk marriages.

Interestingly, the main source of knowledge was other family members or friends; television, radio and printed media were not strong influences. Because the program is mandatory, the health authority had decided to ignore the media in educating the public. Saudi Arabia is a developing country, whose efforts are mostly directed toward curative rather than preventive services, and health education has always been a low priority. Yet it is a wealthy country, and relying on counseling alone to educate at-risk couples does not offset the need for public health education. In Iran, the success of the β-thalassemia screening program was mainly attributed to an effective health campaign that spanned both television and radio (Karimi et al. 2007).

Effect of Counseling

Only one-third of at-risk couples were advised to undertake counseling, even though more than two-thirds of couples visited the counseling clinic. This was a missed healthcare opportunity, and is worrying because screening centers are required to direct all at-risk couples to counseling clinics. Such couples must attend all clinic appointments, not only to receive counseling but also to receive their "mismatch" certificates upon completion of counseling. It is possible that some screening centers may have been in breach of the regulations of the program. The present results indicate mismatch certificates have been distributed to some couples without genetic counseling as required by law. This problem indicates weak oversight of the program and revision is therefore necessary. The MoH should focus on educating healthcare personnel about the program and revising the system for issuing certificates.

Does counseling, when it takes place, actually have an effect on decisions to avoid at-risk marriages? The findings of this study suggest visiting the counseling clinic does not seem to significantly increase the decision to avoid at-risk marriage. This raises issues about how counselors are prepared professionally and about the content and processes that typify their sessions. Having worked in this program since its implementation in 2004, the first author reports that there are very few genetic counselors in Saudi Arabia. Most counseling is delivered by pediatricians instead, many of whom are unpaid for working overtime. Although the MoH organized regular training sessions for counselors, few were able to attend due to staff shortages in their workplaces. This likely has resulted in a significant lack of motivation and limited specialized training. If the counseling clinic is meant to be the cornerstone of the program, increased motivation and more extensive and intensive training are essential to its success. Since recruiting new full-time genetic counselors is problematic given their limited numbers currently, the MoH should focus on training and motivating those physicians who are available to work in the counseling clinics.

Genetic counseling sessions must include discussion about prenatal diagnosis as an option. The success of genetic counseling in reducing the incidence of sickle cell disease and thalassemia cases, in combination with premarital screening, has been proven worldwide (Theodoridou et al. 2008 and Strauss 2009). However, it is important to balance religious beliefs against the possibility of termination of fetuses with untreatable genetic diseases (Cowan 2009). The remarkable success of the β-thalassemia program in Cyprus mainly depended on the support given by the Church regarding prenatal diagnosis and abortion (Zlotogora 2009). In 2005, the health authority in Iran persuaded the religious establishment to permit termination of fetuses known to have β-thalassemia (Strauss 2009).

Regionally, communities in the surrounding countries where the majorities are Arabs and Muslims share virtually the same characteristics as those of the participants in the present study. Globally, many countries have Muslims and Middle-Eastern minorities. Therefore, findings from this study may be of value to premarital health services and counseling in other countries/communities with similar cultural characteristics.

This study evaluated various behavioral and cultural factors that affected the outcome of the premarital screening program, but numerous personnel and technical aspects should also be addressed in future research. Additional studies should assess the perspectives of both members of a couple as well as their family members' perspectives in order to more fully understand the effects of behavioral and cultural factors on marriage decisions among at-risk couples.

Conclusions

The premarital screening program for β-thalassemia and sickle cell disease is country-wide, but it appears to have very limited success in decreasing marriages among at-risk couples in Saudi Arabia. Factors that significantly influenced the decision to not marry included knowledge about disease or carrier status prior to screening, a family history of β-thalassemia, and both partners affected with either disease. Relationships between consanguinity, family influence, economic status, age, gender and knowledge about the diseases and the program itself and decisions to marry were not statistically significant. Most of the at-risk marriages proceeded because of the late timing of the test, some proceeded because of social stigma, and a few proceeded for religious reasons. About half of the participants recommended carrying out testing much earlier, certainly before the engagement. This study also showed that health personnel failed to advise many of the tested couples about specific counseling clinics. Moreover, when such counseling was provided, it did not significantly affect the marriage decisions of at-risk couples. Based on the results of this study, we recommend the following:

- Encourage public health education about genetic diseases, especially before individuals plan to marry, and possibly include this education in the school curriculum.
- Use mass media, especially print media, to access the target population.
- Conduct premarital screening well in advance of the wedding, in order to avoid social embarrassment by withdrawing from the marriage commitment at a late stage. One option to be explored is the introduction of screening in children during secondary school.
- Instruct staff of health facilities to advise at-risk couples to visit the genetic counseling clinic.
- Develop better educational materials and training programs for staff at the genetic counseling clinics.
- Conduct further studies to evaluate this screening program, including the genetic counseling clinics, technical facilities, and cost-effectiveness aspects.

Limitations of the Study

Only a limited number of cases were available for inclusion in the study during the assigned period, which reduced the power of the sample. The large confidence intervals observed in some variables reflect the low number of cases relative to controls. But the achieved total sample size and its statistical power (78%) were within the reasonable range. Some risk factors were statistically non-significant in this study, but this does not mean they are not meaningful in the community, possibly being dampened by the effect of other variables. It is also possible that the limited number of cases in this sample meant the power was insufficient for detecting significant associations. Furthermore, it is usual in case–control studies for the case to be the positive outcome and the control to be the negative outcome, but this study defined cases as the negative "Did Not-Marry" and controls as the positive "Did-Marry."

Other possible limitations include data collection from only one member of each couple. Although the participants likely were able to speak quite accurately for their partner, it cannot be presumed partners would have responded in exactly the same way as the participants. Also, more males than females participated in this study. It is possible that female partners might have had somewhat different perceptions (indeed, females in the present sample differed from males in identifying "fear of social stigma" as a reason for their marriage decision).

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Conflicts of interest None.

References

Al-Hamdan, N. A., AlMazrou, Y. Y., AlSwaidi, F. M., & Choudary, A. J. (2007). Premarital screening for thalassemia and sickle cell disease in Saudi Arabia. *Genetic Medical, 9*(6), 372–377.

Al-Khaldi, Y. M., Al-Sharif, A. I., Sadiq, A. A., & Ziady, H. H. (2002). Attitudes to premarital counseling among students of Abha Health Sciences College. *Saudi Medical Journal, 23*(8), 986–990.

Al-Odaib, A. N., Abu-Amero, K. K., Ozand, P. D., & Al-Hellani, A. M. (2003). A new era for preventive genetic programs in the Arabian Peninsula. *Saudi Medical Journal, 24*(11), 1168–1175.

Alswaidi, F. M., & O'Brien, S. J. (2009). Premarital screening programs for haemoglobinopathies, HIV and hepatitis viruses: Review and factors affecting their success. *Journal of Medical Screening, 16*, 22–28.

Awatif, A. (2006). Perception of female students of King Saud University towards premarital screening. *Journal of Family and Community Medicine, 13*(2), 83–88.

Cao, A., Rosatelli, M. C., Monni, G., & Galanello, R. (2002). Screening for thalassaemia: A model of success. *Obstetric and Gynecology Clinics of North America, 29*, 305–328.

Cowan, R. S. (2009). Moving up the slippery slope: Mandated genetic screening on Cyprus. *American Journal of Medical Genetics (Medical Genetics), 151C*(1), 95–103, 15.

Bittles, A. H. (2001). *A background summary of consanguineous marriage. Centre for human genetics. Edith Cowan University, Perth, Australia*. Available at: http://www.consang.net/images/d/dd/01AHBWeb3.pdf (last accessed June 2009)

El-Hazmi, M. (2004). The natural history and the national pre-marital screening program in Saudi Arabia. *Saudi Medical Journal, 25* (11), 1549–1554.

El-Hazmi, M. A. (2006). Pre-marital examination as a method of prevention from blood genetic disorders. Community views. *Saudi Medical Journal, 27*(9), 1291–1295.

Eshra, D. K., Dorgham, L. S., & el-Sherbini, A. F. (1989). Knowledge and attitudes towards premarital counselling and examination. *J Egypt Public Health Assoc*, 64(1–2), 1–15.

Karimi, M., Jamalian, N., Yarmohammadi, H., et al. (2007). Premarital screening for beta thalassaemia in Southern Iran: Options for improving the programme. *Journal of Medical Screening, 14*(2), 62–66.

Mitchell, J. J., Capua, A., Clow, C., & Scriver, R. C. (1996). Twenty-year outcome analysis of genetic screening programs for Tay–Sachs and beta-thalassemia disease carriers in high schools. *American Journal of Human Genetics, 59*, 793–798.

Modell, B., & Kuliev, A. (1998). The history of community genetics. The contribution of the haemoglobin disorders. *Community Genetics, 1*, 3–11.

Modell, B., Harris, R., Lane, B., et al. (2000). Informed choice in genetic screening for thalassaemia during pregnancy: Audit from a national confidential inquiry. *British Medical Journal, 320*, 337–341.

Monaghan, S. (2007). *For better or for worse. Middle East Health.* Available at: http://216.230.204.101/mehealth/sep03_article1.pdf (last accessed June 2009)

Rashad, H., Osman, M., Roudi-Fahimi, F. (2005). *Marriage in the Arab world. Population reference bureau*. Available at: http://www.prb.org/pdf05/MarriageInArabWorld_Eng.pdf (last accessed January 2010)

Rennie, S., & Mupenda, B. (2008). Ethics of mandatory premarital HIV testing in Africa: The case of Goma, Democratic Republic of Congo. *Developing World Bioethics, 8*(2), 126–137.

Saudi Ministry of Health. (2009). *General directorate of non-communicable diseases.* Unpublished annual report

Shaikha, S., Nada, H., & Samera, A. (1997). Premarital counseling: An experience from Bahrain. *Eastern Mediterranean Health Journal, 3*(3), 415–419.

Strauss, B. S. (2009). Genetic counseling for thalassemia in the Islamic Republic of Iran. *Perspectives in Biology and Medicine, 52*(3), 364–376.

Tosun, F., Bilgin, A., & Kizilok, A. (2006). Five-year evaluation of premarital screening program for hemoglobinopathies in the province of Mersin, Turkey. *Turkish Journal of Hematology, 23*, 84–89.

Theodoridou, S., Alemayehou, M., Prappas, N., et al. (2008). Carrier screening and prenatal diagnosis of hemoglobinopathies. A study of indigenous and immigrant couples in Northern Greece, over the last 5 years. *Hemoglobin, 32*(5), 434–439.

World Health Organization. (2006). *WHO secretariat report: Thalassemia and other hemoglobinopathies. Provisional Agenda Item 5.2, EB 118(5)*

Zlotogora, J. (2009). Population programs for the detection of couples at risk for severe monogenic genetic diseases. *Human Genetics, 126*(2), 247–253.