Barriers to Premarital Thalassemia Screening in Asia

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Abstract

Thalassemia is a genetic disorder of hemoglobin synthesis. Every year 70,000 infants are born with beta thalassemia globally. Its incidence can be reduced by premarital thalassemia screening This review aims to focus on barriers to premarital thalassemia screening and to observe the current thalassemia practices in Asian countries.

This study was conducted on six countries of Asia based on economic status according to World Bank criteria. High income states included Kingdom of Saudi Arabia, and Oman, Iran constituted an upper middle-income country and in lower middle-income category Sri Lanka, Pakistan and Bangladesh were considered. Search engines like PubMed, Research Gate and Google scholar were used to look for relevant articles from 2005 to 2019. A total of (89) articles were reviewed and (61) articles were finally selected to be included in this review.

In Saudi Arabia, major obstacles for premarital thalassemia screening included planned weddings (43%), fear of social disgrace (21%), pressure from family (17%), and religious factors (14%). While in Oman, 4% of the people feared positive results and also considered it as an insult. Amongst the Iranian population, financial burden on couples, disease phobia, fear of positive results, difficulty in accessibility, tribal variances and sociodemographic factors were frequent hindrances to a screening program. Religious factors, financial constraint and lack of awareness cause reluctance in Pakistan and Bangladesh. Moreover, in Sri Lanka, factors like cancellation of marriage and sociocultural norms were identified as negative outcomes of the screening.

In conclusion, a negative attitude and reluctant response to premarital thalassemia screening was observed in people belonging to all the countries included. Major contributing factors were religious misconceptions, social stigma, varying ethnicities, low financial status and poor accessibility to screening programs.

Key words
Beta thalassemia, thalassemia screening, premarital screening, consanguineous marriage, social impact

Introduction

Global Overview

Thalassemia is a genetic disorder of hemoglobin synthesis, in which there is a decreased production of one or more globin chains. It is classified into alpha and beta-thalassemia which are further grouped into thalassemia major and thalassemia minor(1). Abnormal hemoglobin synthesis results in asymptomatic to clinically apparent severe anemia. Thalassemia major poses a huge economic burden on families individually and on the government as a whole(2). The goal of mass screening for this hereditary disorder is to reduce its incidence by identifying individuals at risk(3).

Worldwide, every year around 70,000 infants are born with beta-thalassemia. About 270 million carriers of haemoglobinopathies exist globally. Beta-thalassemia is mostly prevalent among individuals of Mediterranean countries, as well as in Southeast Asia, India, Africa, Central America, and the Middle East. According to the World Health Organization (WHO) guidelines, published in 1998, genetic screening should not be compulsorily carried out. However, some countries including Iran, Saudi Arabia, Palestinian Territories, and Cyprus now have mandatory premarital screening laws for hemoglobin disorders for all couples before marriage. Successful awareness programs have been carried out in countries like Greece, Italy, and Cyprus to reduce high carrier rates(3).

Developed Countries

The incidence in Turkey is 2.1% for beta-thalassemia trait (4). In Malaysia, 1/20 of people are carriers of ßeta-thalassemia trait with a prevalence of 6-10%(5). In Greece, the average frequency is 7.4% for carriers of Beta-thalassemia(6). The Turkish Parliament passed a law in 1993 for the determination of inherited disorders. Since 2003, premarital screening services are provided at forty-one centers in provinces with the highest prevalence of hemoglobinopathies (4). In 2004, Malaysian thalassemia registry was founded and voluntary screening was introduced at primary health centers, where the response in the population was 94% (7). Moreover, in Greece, a countrywide screening program was implemented approximately forty years ago for recognition of carriers, which is providing promising outcomes(6).

In Malaysia, the reasons behind the reluctance to screen are poor availability of screening tests, fear of positive results, and social stigma (8). Whereas in Greece and Turkey, the Ministry of Health has played an important role in the prevention of thalassemia(6-9).

Developing Countries

In Yemen, the prevalence of Beta-thalassemia trait is 4.4%(10). In Lebanon, the prevalence rate of thalassemia major is 64%(11). In the Tunisian population, the estimated carrier incidence rate is 4.48% for the thalassemia trait. Mandatory premarital services are available in Tunisia since 1995 and in Lebanon (11, 12). While in Yemen optional premarital screening services are available, although it is not practiced commonly(10). The obstacles towards this program can be due to marriages among relatives, influenced by many religious and cultural factors (10, 11, 13).

Asian Countries

The approximate prevalence of beta-thalassemia major was 0.7/1000, 12.9/1000 for the trait, and 13.6/1000 calculated in total for beta-thalassemia in Saudi (14). Oman shows a 2.4% prevalence rate of thalassemia(15). WHO reported that the carrier rate in Iran is estimated to be 4% which means about 2 to 3 million people have been affected by the syndrome in Iran (16). In Pakistan an estimated 9.8 million carriers have been reported (17) with a carrier rate of 5.3% and greater than 4,000 cases of beta-thalassemia observed annually(18). In Bangladesh, WHO estimates a 3% carrier rate of beta-thalassemia and more than 7,000 children are born with thalassemia each year(19). There are half a million carrier cases and over 3,500 children affected with thalassemia in Sri Lanka (20) and gene frequency of thalassemia was observed as 2.8% in Sri Lanka (21).

Saudi Arabia, in 2003 made premarital screening a compulsory procedure before marriage (22). Similarly, Iran also implemented premarital screening in all provinces in 1997(23). Voluntary premarital services are widely distributed in Oman (24). Screening practice has also been started in the states of Pakistan, Sri Lanka and Bangladesh (25-27).

Regional Countries

The prevalence rate of β thalassemia carriers is 3–4% in India(28) , 2.21% in China (2), 4% in Iraq (29), and 16-18% in the Maldives(30).

Prevention programs have been started in India almost 3 decades ago (31). Whereas the first premarital screening program in China was conducted in 1986(32). In Iraq, a mandatory premarital screening program for hemoglobinopathies was set up in 2008 in the Kurdistan region in Northern Iraq(29). In the Maldives, the non-governmental organization, Society for Health Education (SHE) started thalassemia screening and awareness program in 1992. According to the law implemented in 2012 for thalassemia screening, every individual under the age of 18 has to be tested for thalassemia and it is compulsory to provide the results before marriage (30).
Various factors have contributed as a hindrance factor in implementing thalassemia screening programs, globally. In India, it has been observed that pre-marital screening of partners is usually not accepted because marriage decisions are influenced by family members, and due to the social stigma caused by calling off a marriage(31). In China, some people showed a negative attitude towards screening; reasons included fear of tests, lack of knowledge, dislike towards hospitals (32). In Iraq limitations to this program were consanguineous marriages and other social factors(33). The main reasons influencing marriage decisions and thalassemia screening in the Maldives were social and religious factors, lack of awareness, and some personal misbeliefs (30).

Rationale

This review aims to study the literature available on premarital thalassemia screening surveys, carried out in six different countries of Asia according to their economic status(34). We grouped countries into three levels, high income, upper-middle income, and low-middle income state. High-income countries include Saudi Arabia and Oman, upper-middle-income comprises Sri Lanka and Iran, while low-middle income includes Pakistan and Bangladesh. This selection will allow us to compare the impact of social and financial aspects, availability, and accessibility of health care services that vary accordingly with the class of the country. Through this study, we aim to identify various communal perspectives, traditional practices, and different causative factors that lead to the negative perception and poor compliance of the public to the premarital screening test. Suggestions regarding premarital screening laws, awareness campaigns, and future genetic counseling are targeted goals to conduct this review article.

Objectives

1. To observe the current thalassemia screening practices in the selected countries.
2. To identify the social, religious, and cultural barriers that adversely affect response and behavior towards thalassemia screening.

Inclusion criteria:
• Published literature between 2005 – 2020 in peer-reviewed research journals.
• Published articles related to selected countries.

Exclusion criteria:
•Articles published before 2005.
•Data not published in research journals.
•Reports of the local clinics.

Materials and Methods

Our study is a systematic review of the literature regarding premarital screening of thalassemia. We selected six countries of Asia based on the level of economic status as defined by WHO(34). We grouped countries into three levels, high income, upper -middle income, and low-middle income states. High-income countries include Saudi Arabia and Oman, upper-middle-income comprises Sri Lanka and Iran, while low-middle income includes Pakistan and Bangladesh. The literature search was carried out in PubMed, Research Gate, and Google Scholar websites to find relevant published articles in English. It is a simple analysis. Relevant articles in reference lists of published articles were also searched. We collected and retrieved a total of (89) publications out of which we selected a total of (61) references. Data were independently extracted from each article, evaluated, and further processed.

Results

1 Premarital screening
Premarital screening is a method for examining couples before marriage for the diagnosis of communicable and non-communicable diseases. In this regard, Saudi Arabia, in 2003 made premarital screening compulsory in order to reduce the incidence of disease (22). In Oman premarital screening has been in action since 1999 and is available voluntarily and free of cost at all governmental healthcare centers (24). In 1991, the Iranian screening program was started and through later years, was carried out in all provinces of Iran (23). Similarly, Pakistan, Bangladesh, and Sri Lanka, also started practicing premarital screening. Although the government of Pakistan is working to make pre-marital screening mandatory, still very few studies are found regarding pre-marital thalassemia screening and work is still in progress(25). In Sri Lanka, thalassemia screening is proposed for teenagers from 15 years of age(35). According to AL Farsi, 89.3% of adults of Oman were aware of premarital screening while 30.5% were strictly against this test (24). A study conducted on youngsters regarding premarital screening in Pakistan showed around 60.9% were aware of this screening test, while 60.4% wished to get screened before marriage. (36). Results compiled from a Sri Lankan study showed that the number of individuals who had gone through screening was 17%; 14% of partners have been tested and 79% had not taken the screening test(26). Several procedures have been proposed in different countries including CBC, Hb, Electrophoresis, and PCR based analysis. In a South Asian rural area one tube fragility test (OF) associated with dichlorophenol indophenol (DCIP) dye test is used to detect the presence of Hb E (27). For B Thalassemia, the technique which is effective is electrophoresis or high-pressure liquid chromatography (HPLC), recommended by Cao et al. Nowadays PCR is used to detect thalassemia. Screening policy is made at the national level in Sri Lanka where the government provides accessible screening by MCV and MCH analysis. HPLC technique is used (26). The screening method in the Islamic Republic of Iran is by performing a complete blood count (CBC) and many variables in the report are evaluated without specific measures or standard criteria (37). Although Saudi Arab has a mandatory screening program it was unable to minimize both the incidence of disease as well as the rate of high-risk patients' marriage. It was believed to be due to the late stage of screening when couples were already committed and engaged(22). In Oman and Sri Lanka, premarital screening facilities are provided at low cost and sometimes free of charge, but still, people are not motivated to practice screening(24, 26).

2 Practice of premarital screening
Saudi Arabia and Iran have mandatory premarital thalassemia screening laws for couples. They believe that by making screening mandatory, the practice of premarital screening would be more effective(3). Iranian Ministry of Health passed an obligatory screening policy at the national level for premarital testing; all couples

were screened who registered themselves for marriage (38). From a study conducted at Taif University, 95.3% of students had a positive attitude and good intended practices toward premarital screening (39). The results observed from a study conducted in Oman in 2010 showed that 2.9% of people had undergone screening before marriage(40) . In Sri Lanka, a study conducted, on medical students, showed that only 10.2% had tested their blood for thalassemia and only 4.6% had screened their siblings (26). The results from a study performed in Dhaka showed a dearth of knowledge and practice among parents. The percentage of individuals who practiced thalassemia screening was merely 13.37%. However, the knowledge and practice among the prosperous and literate families were significantly high(27). Data from Saudi Arabia and Oman revealed that premarital screening was not practiced properly despite having mandatory screening(24, 41). In Pakistan and Bangladesh people were reluctant mostly because of financial constraints, lack of awareness regarding thalassemia and some simply ignored screening despite being advised by doctors(27, 42). Furthermore, in Sri Lanka premarital screening was not practiced significantly despite adequate knowledge about thalassemia and free diagnostics facilities(43).

2: Barriers

2.1 Consanguineous Marriages

The culture of consanguinity is common in all the countries of the Middle East, with a prevalence rate from 10.6% to 67.7%. A study from Saudi Arabia, comparing the rate of consanguineous marriages among two generations, indicated the total consanguinity (first and second cousins) was 29.7% in the parents. Consanguinity was significantly higher among the daughters than the parents, where 37.9% of married women had consanguineous marriages. The prevalence of consanguinity among the second generation is relatively high compared to the first (44). The prevalence of first-cousin marriages is about 35% of Omani marriages(15). In Iran, about 88% of participants (marriage partner volunteer) were reported to be blood-related (45). Another study carried out in 2016 to determine the prevalence of consanguinity among Iranian Mandaeans living in Khuzestan Province, south-west Iran, showed that the overall frequency of consanguinity was 50.7% in urban and 86.2% in rural areas. First cousin marriages (51.8%) were the most common type of marriages, reported in the study. (46). Pakistan also has a prevalence of consanguineous marriages. The study conducted in District Bannu indicated the rate of consanguineous marriages among B- thalassemia major patients is about 74% (47). A study conducted on Bangladeshi children in 2015-2016 indicates a consanguineous marriage prevalence rate in 14% of parents(27). In Oman, a study in (2010-2012) compared results from previous studies which indicated that no remarkable change is found in prevalence rates of consanguineous marriages. Furthermore, studies clearly described more prevalence of first cousin marriages among individuals as compared to second cousin marriages. There is a prevalence of Arab culture and customs, of consanguineous marriages and they still prefer consanguinity regardless of the rising risk of autosomal disorders and congenital defects(48). Cultural, racial factors, and insufficient knowledge regarding consanguineous marriages have an important role in the high prevalence of consanguineous marriages in Iran(45). In summary, the main factors behind consanguineous marriages are social and cultural reasons, not religious beliefs (49). To the best of our knowledge, we could not find evidence of the culture of consanguineous marriages among Sri Lankan families. By far the most common practice of consanguinity was observed in Muslim societies.

2.2 Culture

A study conducted on university students in Taif, Saudi Arabia showed that according to most of the participants the major barriers to premarital carrier screening were found to be the fear of positive results and religious misconceptions which may lead to termination of a planned marriage (39). The major barriers to the Saudi premarital screening programs were found to be pressure from society, family, and religious factors. Although a majority took the screening test before the marriage, 52% of them agreed to marry despite the unfavorable results, mainly due to expensive wedding preparations (50). A study in Oman showed overall barriers that included young age, female gender, single status, and poor literacy (40). Data from Iran showed that in Sistan and Baluchistan province there is a high prevalence of thalassemia due to their tribal variances and misconceptions regarding premarital screening (45). Studies conducted in Pakistan in 2013 (36) and 2018 (42) on non-medical university students and Thalassemia Centre of Pakistan Institute of Medical Sciences, Islamabad respectively, concluded that due to the religious and cultural factors people usually show reluctance for screening. A review on Bangladesh also showed a similar pattern of consanguinity as seen in Saudi, Oman, and Iran. Furthermore, some individuals accept it as a fortune resolute by God and take the risk of having a thalassemic baby (51). In Sri Lanka, marriage is largely determined by parents and stakeholders, and it is very hard to cancel a planned marriage due to disgrace and social and cultural norms (35).

2.3 Social

In Saudi Arabia, a lot of sociocultural factors influencing premarital screening are found such as inability to find another compatible match, the loyalty of the couple, or negligence of the health staff to provide sufficient knowledge to couples. According to Alswaidi et al, the main barriers to the Saudi premarital screening included planned weddings (43%), fear of social disgrace (21%), pressure from family (17%), and religious factors (14%). The timing of screening also plays an important role in the success of this program (22). In Oman, a study showed that 4% of the people feared that the test results may be positive; some considered it as an insult (4%). Similarly, about 3% thought that positive results would cause difficulties in the continuation of their wedding, the remaining 1% were apprehensive about the cancellation of their engagement(52). A study in Iran concluded that premarital screening results in financial burden on

couples, they get disease phobia, the stigma associated with the condition, fear of positive results, difficulty in the accessibility of screening and other socio-demographic factors i.e. ethnicity, sex, and language(53). In Pakistan, premarital screening programs are more successful in urban areas in comparison to the rural areas, mainly because of differences in financial status and accessibility of programs(54) . In Sri Lanka, A survey showed that marriage is a sensitive matter in the country, where decisions are taken by parents. So, at the time just before marriage, couples won't agree on screening due to stigma and other social and traditional beliefs attached to it(35). A review on Bangladesh premarital screening programs, concluded some strong social and cultural norms influence the decision to get tested and accept the results, which include religious beliefs, consanguineous marriages, literacy rate, and reduced intervention programs(51).

2.4 Religious

Data from Saudi Arabia showed that around 14% of the population make wedding decisions according to the religion (55). As demonstrated by a study in Oman, a minority of the participants refused this program, because they believed that they would be intruding with God's will by doing so, and almost a quarter of these patients decided to continue with the marriage(52). A similar study in Nawabshah, Pakistan showed that religious factors have a strong influence on deciding about premarital screening(56). In Iran, these programs are not successful, which may be due to religious and cultural issues(23).A literature review on Bangladesh also showed a negative attitude towards screening due to religious views(51). According to two studies in Sri Lanka (Mudiyanse RM et al 2015 and Mudiyanse RM 2015)(36), cessation of pregnancy is illegal and disagreeable due to religious reasons, so a safe marriage program was implemented as a preventive measure(35).

Discussion

Inherited hemoglobin disorders are arising as a global health burden. Roughly 320,000 babies are born annually with clinically important hemoglobinopathy. About 80% of these births take place in developing countries(57).
The international perspective of thalassemia was reviewed. In India, it is observed that premarital screening is usually not accepted because marriage decisions are influenced by family members(31). In China, some people showed a negative attitude towards screening; reasons included fear of tests, lack of knowledge, and some people considered it unnecessary(32). In Iraq limitations to this program were arranged and consanguineous marriages, late timing of screening, and other social factors(33). In Malaysia, the reasons behind reluctance for screening were lack of adequate knowledge, poor availability of screening tests, fear of positive results, and social stigma (8).

We reviewed published literature to determine barriers towards premarital thalassemia screening in Asia. Perceived barriers observed in Saudi Arabia are level of education, cultural, religious factors, different ethnic groups, and psychological issues (45, 58, 59). Different studies showed a positive attitude of the participants regarding premarital screening in order to prevent further disease transmission to the next generations (52, 60). The Oman population showed a poor response due to fear of test results, resulting insult, cancellation of marriage, and other socio-cultural aspects (24, 52). Rural areas in Iran also showed a negative attitude towards screening programs(59). The negative attitude found in Pakistan was based on fear of discrimination, a rise in the abortion rate, and some stress factors(60). In Sri Lanka, people considered it as inhuman advice(35). However, in Bangladesh, attitude is affected by a lack of knowledge (27). In Saudi Arabia and Oman premarital screening has not been practiced properly (24, 41). In Pakistan and Bangladesh, people refused premarital screening advice by health care practitioners because of financial constraints and insufficient knowledge about thalassemia (27, 42). However, in Sri Lanka also, premarital screening was not practiced significantly despite having adequate knowledge and free facilities(43).

The first premarital thalassemia screening was conducted in 1975 by Silverstroni and colleagues in Latium, Italy as a component of a school prevention program. Nationwide screening programs also started in Canada, Cyprus, Greece, Italy, and the UK during the 1970s. In Cyprus, Greece, and Italy, premarital thalassemia screening has been practiced for a long time due to the high consanguinity rate. Similar preventive programs have been initiated in Bahrain, China, India, the Islamic Republic of Iran, Indonesia, Malaysia, the Maldives, Singapore, and Thailand, and later in Saudi Arabia and the United Arab Emirates. Prenatal diagnosis is also available in the UK, Northern Ireland and other northwest European countries, and facilities for abortion as a prevention strategy(53).
Mandatory screening programs have been practiced in Saudi Arabia and Iran (22, 23). Voluntary screening services are available in Oman (24). Similarly, Pakistan, Bangladesh, and Sri Lanka, also started practicing premarital screening (25-27). Screening policy was made in Sri Lanka at a national level with easy accessibility(26).
Through studies, we perceived different social, cultural, and religious factors regarding premarital screening which result in financial burden on couples, the stigma associated with the clinical condition, difficulty in the accessibility of screening, and other socio-demographic factors. The culture of consanguineous marriages is high among Muslim countries because it is considered as a way to retain the wealth, to increase the compatibility between partners, and reduce the incidence of divorce, to preserve the relationships within a tribe.

We apprehended that in developed countries Saudi Arabia and Oman, although premarital screening services are offered nationwide, still the response is unsatisfactory because they prefer their religious customs over screening results. In middle-income countries like Pakistan and Iran, awareness is insufficient mostly in rural areas due to inadequate literacy rate, low financial status, and poor accessibility. In lower-income countries like Sri Lanka,

practice is insufficient to reduce the burden of thalassemia. Bangladesh is a country with low socioeconomic status and low literacy rate, where the success of the thalassemia prevention program is undermined due to a lack of awareness and screening policies.

Premarital screening is helpful for couples to decide regarding their future and building up a healthy family (24). In Islamic communities, abortion is considered as murder. Even in Sri Lanka abortion is illegal, so here premarital screening plays an important role in the prevention of a thalassemic child(26). Premarital screening can be a method for having safe motherhood for females, it can prevent psychosocial effects related to an affected child and can also lower the incidence of thalassemia and other hereditary disorders in the country(61).

Conclusion

The prevalence of thalassemia is high in Muslim countries due to consanguinity. Preventive management of thalassemia comprises premarital screening and genetic counseling. A good level of knowledge regarding screening was observed in Sri Lanka, Saudi Arabia, and Oman, a satisfactory level in Pakistan, while the level of knowledge in Iran and Bangladesh was not significant. Insufficient knowledge and negative attitude were observed in people due to religious misconceptions as they didn't want to interfere with God's will and various socio-cultural factors including timing of screening, and social stigma faced by the families, while breaking off a planned marriage, different ethnicities, low financial status, poor accessibility of programs and other various perceived barriers. A combination of these factors led to inadequate practice.

Recommendations

By reviewing different works of literature, we observed that the prevalence rate of thalassemia and the perception of people regarding premarital thalassemia screening is different in each country. In countries where lack of knowledge was reported, we recommend that more awareness should be provided by making it a part of the curriculum in schools, and mass awareness programs should be carried out through educational campaigns and media like TV, newspapers, and internet. As the timing of screening is an important determinant in the success of screening programs, so it is recommended that the test should be performed at an early stage, prior to engagement when it is easier for people to make a decision about their marriage. For this purpose, health education needs to be aimed at adolescents to change their opinion regarding genetic counseling. In Muslim countries, negative perceptions due to religious misbeliefs need to be addressed to increase the effectiveness of this program, and support from religious scholars is required in order to increase the trend of screening. People should be counseled about consanguineous marriages, which is an important factor in having thalassemic births in Muslim countries. The program should be made free of cost for its long term applicability. We recommend that premarital screening should be made mandatory in countries where it is not compulsory yet, as it seems a valuable measure to reduce the risk of thalassemia in high prevalence societies. Doctors and educated people of the society should participate in increasing awareness among people. The laws regarding screening programs should be in accordance with the social, cultural, traditional, and religious factors to be more effective.

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