Acceptance of Premarital Counseling, Prenatal Diagnosis and Abortion of Affected Fetus by Parents of BetaThalassemia Children; A Systematic Literature Review.

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Abstract

Introduction: Thalassemia, a hereditary autosomal recessive disorder, imposes a major public health burden in an area known as the thalassemia belt. The thalassemia belt extends from Mediterranean region to middle east and south east Asia. To avert the fiscal and social burden on health system, countries have devised and adopted preventive strategies. Although, WHO developed and disseminated a preventive strategy for prevention of hemoglobinopathies, including thalassemia, countries must adjust it according to the prevailing sociocultural determinants within countries.

Objectives: This study aims to investigate acceptance of the preventive measures for thalassemia i.e. premarital counseling, prenatal diagnosis and abortion in existing body of literature. Furthermore, it seeks barriers towards successful implementation of these preventive approaches.

Methodology: Online search engines (Google scholar and PubMed) were used for exploring related studies that meets the inclusion criteria. Studies conducted from 2000 onwards were illegible for the study.

Result: With strictly following PRISMA methodology, 11 studies were included for the full-text reading from the total of 4097 articles. The results of studies varied widely; for instance, the acceptance of premarital counseling ranged from about 59% to 84% by different studies that had been investigated fully. Similarly, Acceptance of prenatal diagnosis was reported from 100% to as low as 74% by studies conducted in India. This study found out that acceptance of premarital counseling was higher in Muslim majority countries compared to PND and abortion whereas the opposite is true in India. Furthermore, preventive strategies and social mobilization can significantly transform the acceptability of prohibited preventive measures such as PND (El- Beshlawy et al, Egypt).

Conclusion: With the wide discrepancies found in the results of studies that have been conducted, further investigations are crucial to reflect the true acceptance of each of preventive approach within India. Although, the results of the study highlights that Muslim communities are in favor of premarital counseling whereas prenatal diagnosis and abortion of affected fetus is welcomed in multiethnic countries like India. This will contribute in successful development of strategies that can halt the raising trend of thalassemia in India effectively.

Key words: Thalassemia prevention, premarital counselling, prenatal diagnosis, Thalassemia parents.

1. Introduction

Thalassemia, a hereditary hematological disease, is highly preventable. Prevention of new births of the thalassemia can be ensured through screening, genetic counseling in combination with prenatal diagnosis (PND)
and abortion of an affected fetus [1]. This approach is cost-effective and is proving remarkably successful in reducing the frequency of thalassemia in many countries [2-3]. While counties such as Cyprus and Iran have achieved considerable reduction of thalassemia cases through implementation of premarital genetic counselling and prenatal genetic diagnosis, it is still a major problem in India. Existing literature suggests that the best approach for combating the disease varies from one culture to another because of the disparate acceptability of preventive approach. This is because marriage is a complex social phenomenon, and the selection of marriage partners are based on a strong personal preference, family or traditional reasons. It is stated that unlike Iran and Cyprus, Indian communities are less receptive toward premarital genetic counselling, rendering prenatal diagnosis in spotlight for preventive measures [4]. Hence in the endeavor to halt and reverse the trend of thalassemia, the acceptability of these approaches must be evaluated. It is important to find feasible approaches for prevention since despite noticeable efforts for the provision of screening and genetic counselling services, India is still struggling with the burden of thalassemia.

2. Methodology

Online search engines [google scholar and PubMed] were used for screening the existing literature. All types of study designs were included in condition to be conducted from 2000 onwards. While the priority was given to the research conducted in India, countries within Thalassemia belt (in middle and South East Asia) were included. Keywords used for search engines were: prenatal genetic diagnosis, premarital genetic counselling, and attitude towards beta thalassemia. The articles were selected through using PRISMA model of systematic review. The PRISMA flowchart depicting the systematic search used in this article is illustrated in Diagram 1.1

<table>
<thead>
<tr>
<th>Table 2.1</th>
<th>inclusion and exclusion criteria for the study.</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>Criteria</td>
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<td>1</td>
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<td>Location</td>
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<td>3</td>
<td>Gender</td>
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<td>4</td>
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<tr>
<td>5</td>
<td>Study design</td>
</tr>
<tr>
<td>6</td>
<td>Study area</td>
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</table>

Research question designed for this research

- What is the acceptability of prenatal diagnosis among people?
- What are barriers against adoption of prenatal diagnosis?
- How likely parents of a thalassemia child encourage their extended family to practice premarital counseling.
- Whether parents accept termination of an affected fetus following prenatal diagnosis.
Diagram 1.1 PISMA Figurative Illustration

**Identification**
Number of article identified by search engines google scholar and PubMed
N=4097

**Screening**
Records after removing duplicates and irrelevant titles
N=2020

Excluded articles
N=2077

**Eligibility**
Number of articles after screening abstracts
N=43

Excluded articles
N=1977

**Full-text reading**
Number of articles after full text reading
N=11

Excluded articles
N=32
### 2.1 Data extraction table

<table>
<thead>
<tr>
<th>No</th>
<th>Author</th>
<th>Title</th>
<th>Study Design</th>
<th>Sample Size</th>
<th>Study population</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Dr. Sarita Agarwal et al. (2002), India</td>
<td>Prenatal diagnosis in beta thalassemia: an Indian experience</td>
<td>experimental</td>
<td>53 couples</td>
<td>Couples with one affected child</td>
<td>29% (14 pregnancies) thalassemia affected fetuses diagnosed via PND were all aborted; hence, the acceptance of PNC was 100% following PND. All patients were amenable to attend PND counseling to avoid another thalassemia child.</td>
</tr>
<tr>
<td>2</td>
<td>Parag M. Tamhankar et al. (2009), India</td>
<td>Prevention of thalassemia by premarital screening and prenatal diagnosis in India</td>
<td>experimental</td>
<td>1348 Anemic OPD patients 939 college students 400 extended families</td>
<td>OPD patients College students Extended families</td>
<td>99 percent of identified high risk couples proceeded with the marriage. However 66.5% of these couples admitted for PND, whereby, 33 births of thalassemia children were avoided. After counselling From the recognised high risk couples 74.3, 37.5 and 100 percent of extended family members, OPD and college students admitted for PND, respectively (64.7% overall admission rate).</td>
</tr>
<tr>
<td>3</td>
<td>Asha Baxi et al. (2012), India</td>
<td>Carrier screening for beta thalassemia in pregnant Indian women</td>
<td>experimental</td>
<td>1320</td>
<td>Pregnant women in antenatal care</td>
<td>76 percent of pregnant women accepted screening for beta thalassemia, 99 percent of which were willing for PND if required.</td>
</tr>
<tr>
<td>4</td>
<td>Swati Chawla et al (2017), India</td>
<td>Attitudes and beliefs among high- and low-risk population groups towards β-thalassemia prevention</td>
<td>cross-sectional descriptive study</td>
<td>926</td>
<td>Arura Rural (AR) population from both male and female from house to house visits from Rohtak</td>
<td>73.3% were amenable towards screening for beta thalassemia. Moreover, while 59.4% conceded that they would do premarital genetic testing, 76.3% accepted PND if required. Acceptance of abortion following PND was 67.3%. Higher proportions of AU (54.7%) are not willing for premarital screening than those of AR and CC. Furthermore AR preference for abortion is the highest (96.4%) followed by AU (72.9%) and CC (62.9%). A great</td>
</tr>
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</table>
District, Haryana state in north India, and Arora Urban (AU) and cosmopolitan commoner (CC) from New Delhi Kalanur village of numbers of CC have willingness to share knowledge about β-thalassemia with others, whereas half of the AR and AU groups are not willing to share the same.

<table>
<thead>
<tr>
<th>No.</th>
<th>Authors</th>
<th>Title</th>
<th>Methodology</th>
<th>Sample Size</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Jahnavi Hatti (2015), India</td>
<td>Genetic counseling in Anemia and Thalassemia</td>
<td>Cross Sectional Study</td>
<td>71</td>
<td>Parents of beta thalassemia patients Consanguinity was detected in 42 (59%) of cases whereas 29 (40.84%) was non consanguineous marriages culminating in Thalassemia children 30 percent of families did not opted for prenatal counseling because they considered the given information inadequate however, 11 percent did so for the fear of stigma. 24 and 35 percent of those who refused prenatal diagnosis had misconception of cost and financial hardships respectively.</td>
</tr>
<tr>
<td>6</td>
<td>Ahmed I. Gilani et al. (2007), Pakistan</td>
<td>Attitudes towards Genetic Diagnosis in Pakistan: A Survey of Medical and Legal Communities and Thalassemic Children parents</td>
<td>Cross sectional study</td>
<td>902</td>
<td>570 doctors, 49 lawyers, 178 medical students, 89from parents of thalassemic children and 16 members of parliament (MPs) 11% did not considered genetic screening acceptable of which 38.3% did so due to prioritization of other morbid diseases, 26% and 34% did so because of stigmatization and stimulation of a surge in abortion rate respectively. 77% were in favor of premarital genetic screening and 94.4% of parents were in favor of prenatal screening, compared with 77.4, 51 and 70.8% of doctors, lawyers and medical students, respectively. In case of a scenario of a child expected to have a life of disability due to a genetic disease only 1 MP (6%) was in support of any sort of prenatal screening.</td>
</tr>
<tr>
<td>7</td>
<td>Fouzia Ishaq et al. (2009), Pakistan</td>
<td>Awareness Among Parents of β-Thalassemia Major Patients, Regarding Prenatal Diagnosis and Premarital Screening</td>
<td>Descriptive cross sectional study</td>
<td>115</td>
<td>Parents of beta thalassemia patients Comprising of 74 men and 41 women</td>
</tr>
<tr>
<td>8</td>
<td>El-Beshlawy et al (2012), Pakistan</td>
<td>Prenatal diagnosis for thalassaemia in Egypt: what changed parents' attitude?</td>
<td>Experimental study</td>
<td>71</td>
<td>pregnant mothers at risk for β-thalassaemia</td>
</tr>
<tr>
<td>9</td>
<td>Ching Fang Ngim et al (2013), Malaysia</td>
<td>Attitudes towards prenatal diagnosis and abortion in a multi-ethnic country: a survey among parents of children with thalassaemia major in Malaysia</td>
<td>Cross sectional study</td>
<td>116</td>
<td>parents of children suffering thalassemia major</td>
</tr>
<tr>
<td>10</td>
<td>Mehran Karimi et al</td>
<td>Attitude toward prenatal diagnosis for β-thalassemia</td>
<td>Cross-sectional descriptive study</td>
<td>764</td>
<td>Parents of thalassemia children (66.7%) and</td>
</tr>
</tbody>
</table>
(2006-2007), southern Iran | major and medical abortion in southern Iran | thalassemia patients (33.2%).

11 Ayman Alsulaiman et al (2006), Saudi Arabia | Attitude determination to prenatal and preimplantation diagnosis in Saudi parents at genetic risk | Cross sectional study | 30 | Families with a child with morbid thalassemia gene

Eight of the 30 couples (27%) would only accept PGD; four (13%) only PND; three (10%) either technology; the remaining half (50%) would accept neither test, or were undecided. Twenty three parents declared disagreement with abortion following PND and stated religious reasons as driving factor.

Abbreviations: prenatal diagnosis (PND), prenatal genetic counselling (PNC), outpatient department (OPD), urban and rural Arora (UA & RA respectively), cosmopolitan commoners (CC).

2.2 Quality assessment of studies using AXIS (Appraisal Tool for Cross-sectional Studies) guidelines

From the 11 studies that were included in the article, 7 were cross-sectional study which, for quality assessment (QA) purpose, the AXIS guideline was used. AXIS tool examines survey articles in terms of their introduction, methodology, result, discussion and conclusion and other (funding and conflict of interest, and consent). The aims and hypothesis are scored one each in introduction (total 2 scores), similarly, appropriateness of study design, justification of sample size, generalizability of sample frame, representativeness of sample, definition of target population, validity, reliability, non-responders measures, explanation of statistical methods and statistical significance individually merit one score in methodology (total score of 10). Result carries 5 marks which is determined based on clearly explanation of results, concerns about non-responders, measurements of non-responders, consistency of results and the compliancy with methodology. Furthermore, whether the study’s discussion and conclusion was in accordance with results and whether it mentioned the limitations of the study a total score of 2 was assigned for each respective part. Finally, one score is given if either the funding or conflict of interest was mentioned, besides, one extra one mark was allotted for the consent form for respondents in the study. Eventually, the highest score a study can get is 21 marks which 9 is the yardstick for a study to be considered qualified in this article. Once studies were assessed using Axis tool, one scored below the quality standard while the others were found to be quality assured. The results are depicted in the table 2.3

Quality assessment of cross-sectional studies using AXIS guideline
<table>
<thead>
<tr>
<th>Name of the author /year of publication</th>
<th>Introduction (2 scores)</th>
<th>Methods (10 scores)</th>
<th>Results (5 scores)</th>
<th>Discussion (2 scores)</th>
<th>Other (funding source, conflicts of interest, ethical approval) (2 score)</th>
<th>Total (21 scores)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swati Chawla et al 2017</td>
<td>2</td>
<td>8</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>17</td>
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<tr>
<td>Jahnavi Hatti et al 2015</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>6</td>
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<tr>
<td>Ahmed I. Gilani et al. (2007)</td>
<td>1</td>
<td>9</td>
<td>6</td>
<td>3</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td>Fouzia Ishaq et al. 2009</td>
<td>1</td>
<td>6</td>
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<td>2</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>Ching Fang Ngim et al 2013</td>
<td>1</td>
<td>4</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>Mehran Karimi et al 2006-2007</td>
<td>1</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Ayman Alsulaiman et al 2006</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>10</td>
</tr>
</tbody>
</table>
3. Results:

4097 studies were retrieved from the search result, 4054 got excluded because the study titles and abstracts did not address the research questions, 43 articles were assessed for eligibility from which 32 studies were excluded because they had inappropriate study population, did not include neither premarital nor prenatal genetic counselling. As a result, a total of 11 studies were recruited in this study.


Population study for Swati Chawla et al (2017) was Arura urban and rural population and Delhi cosmopolitan students, whereas Parag M. Tamhankar (2009) did his study among OPD patients, college students and extended family members. Pregnant women in antenatal care made up study population in studies conducted by Asha Baxi et al (2012) and El-Beshlawy et al (2012). Ahmed I. Gilani et al (2007) included doctors, lawyers, and parents of thalassemia patients, college students and parliament members in his study. Study population and sample size of each study is shown in the bar graphs.

1.1 Study population of included articles

![Classification of studies according to study population](image-url)
4. Discussion

4.1 Perception and practice of premarital screening and counselling

From all studies entailed in this article two (Swati Chawla et al from India and Ahmed I. Gilani from Pakistan) reported willingness towards premarital genetic counselling for prevention of beta thalassemia. Out of 926 respondents in Swati Chawla’s cross sectional study, 59.4% expressed adoption of premarital genetic counselling. Supporters of this initiative was reported higher (77%) by another cross sectional study by Ahmed I. Gilani in Pakistan. Fouzia et al (2009) reported awareness of premarital genetic counselling 84.3% among parents with a thalassemic child in Lahore, Pakistan.

4.2 What is the acceptability of PND among parents of thalassemia patients?

In all five studies that were conducted in India acceptance of PND was reported in four of them (100 % by Sarita Agarwal et al 64.7% by Parag M Tamhakar, 99% by Asha Baxi et al and 76.3% by Swati Chawla et al). Acceptance of PND was 71.6 percent in a study in Malaysia carried out by Ching Fang Ngim et al in 2003. 28.1% of Muslim participants were against termination of pregnancy compared to 50 % of Christians and 11.8% of Buddhists and 100% Hindu in that study. In a cross sectional study conducted by Ahmed I. Gilani et al in Pakistan Islamabad on 902 respondents of specified groups (doctors, parents, lawyers, members of parliament and medical students) found that 89% of respondents were receptive of the PND. In Iran, another Islamic majority country, Mehran Karimi reported acceptance of PND 93% through a cross-sectional study performed in southern Iran. In Saudi Arabia, Ayman Alsulaiman published the result of his study as 13 % were amenable toward prenatal diagnosis whereas 27 % were supportive of pre-implementation genetic counselling for prevention of beta thalassemia.

4.3 What is the acceptance of abortion following prenatal diagnosis for beta thalassemia major?

Both of studies conducted in India by Sarita Agarwal et al (2002) and Parag M Tamhankar et al (2009) showed a 100 percent acceptance of abortion among those who had undergone PND and the fetus was diagnoses to have beta thalassemia major. However, another study by Swati Chawla et al (2017) yielded that only 67.3 % of respondents were agreeable about abortion of an affected fetus. The former two studies are among parents with one affected child or were previously screened for beta thalassemia trait, the later on, the other hand, was conducted using door to door survey method. Fouzia et al(2009) under her cross sectional study in Pakistan reported 69% of population accepting abortion. While Mehran Karimi et al claimed that 86.8% of his subjects accepted early termination of affected pregnancy , Study of Ayman Alsulaiman in Saudi Arabia, another Muslim majority country, contended that 76.7% of 30 couples who had one affected child refused to terminate an affected
pregnancy. El-Beshlawy et al (2012) asserted that as a result of in-depth counselling on religious aspect of abortion 100 percent of pregnancies with affected fetus adopted abortion as a means to evade a beta thalassemic child. He mentioned that a noticeable improvement had occurred in the attitude of parents towards termination of thalassemia major pregnancy since it was reported 36% acceptance of abortion by previous studies.

4.4 Socio-economic, religion and education influences

Parag M. Tamhankar (2009) in his study suggested that all college students who had screened for thalassemia admitted for prenatal diagnosis after marriage compared to extended family members and OPD patients (74.3% and 37.5% respectively). Moreover, Swati Chawla et al (2009) carried out a study among rural and urban Arura population and cosmopolitan commoners of New Delhi. Her findings were as follows: rural Arura with 81% acceptance of premarital screening was the highest in this term. Similarly, abortion was widely accepted among rural Arura (96.4) followed by urban Arura (72.9%) and cosmopolitan commoners (62.9%). In the study conducted by Ahmed I. Gilani et al. (2007) 77% were in favor of premarital genetic screening and 94.4% of parents were in favor of prenatal screening, compared with 77.4, 51 and 70.8% of doctors, lawyers and medical students, respectively. In case of a scenario of a child expected to have a life of disability due to a genetic disease Only 1 member of parliament (6%) was in support of any sort of prenatal screening.

A cross-sectional study by Ching Fang Ngim et al. (2013) in Malaysia yielded the results that reflect the religious constructs on the matter of prenatal diagnosis of thalassemia. He and his team reported that 28.1% of Muslim participants were against termination compared to 50% of Christians, 11.8% of Buddhists and 100% Hindus.

5. Conclusion

There is less literature regarding acceptance of premarital counselling by parents of thalassemia children in India. In the past twenty years only one study that was conducted among residents of Arora by Swati Chawla, acceptance was 59%. However it does not reflect the acceptability among parents of thalassemia children. Overall, the acceptability of premarital counseling is higher than PND and abortion while the opposite trend can be seen in India.

Acceptance of PND is reported with remarkable variations in the studies in India ranging from 64.7 to 100%. Similarly, it varies among Muslim majority countries (93% in Iran and 71.6% in Malaysia), indicating that other social factors determines the acceptability of PND in communities.

In order to effectively halt the rising trend of thalassemia, PND must be adopted only when the acceptance of abortion of a severely diseased fetus is acceptable. The acceptance of abortion among parents of beta thalassemia children is reported high in studies by Sarita Agarwal et al (2002) and Parag M Tamhankar et al (2009), while in studies in other countries the acceptance was significantly lower. This shows the need for reassessment of the acceptance of abortion among Indians. The relationship between socioeconomic factors and acceptability of premarital counselling and prenatal diagnosis has not been investigated enough since the study done by Swati Chawla et al. rural area showed a higher acceptance compared to urban area and no other study has been repeated to confirm its validity and the underlying cause.

References


6. Parag M Tamhankar et al. prevention of homozygous beta thalassemia by premarital counseling and prenatal diagnosis in India. Wiley InterScience; 2008.


