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PRENATAL SCREENING AND DIAGNOSIS OF THALASSEMIA: PREVENTING THALASSEMIC BIRTHS

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ABSTRACT

Background: Thalassemia is one of the most common hereditary disorders in India. Early antenatal screening, spousal testing, and prenatal diagnosis (PND) are key strategies to prevent thalassemia major births.

Objectives: To assess the role of antenatal screening, spousal testing, and PND in identifying carrier couples and reducing thalassemia major births.

Methods: A cross-sectional study was conducted at RNT Medical College, Udaipur, including 1,280 pregnant women in the first and early second trimester. Screening was done using high- performance liquid chromatography (HPLC). Carrier women were advised spousal testing; at- risk couples were offered PND through chorionic villi sampling (CVS) or amniocentesis.

Results: The total 1,280 pregnant women were screened, of wich 92 (7.2%) were identified as carriers. The most common abnormality was beta-thalassemia trait (5.0%), followed by sickle cell trait (1.25%) and rare variants such as Hb-D, Hb-E, Hb-C, and alfa-thalassemia. Among 68 spouses tested, 5 (7.4%) had beta-thalassemia trait and 1 (1.5%) had sickle cell trait. Five couples were classified as “at risk”; four underwent prenatal diagnosis, which detected one fetus with thalassemia major, two with thalassemia minor, and one normal fetus. The acceptance rate of prenatal testing was 80%. **Conclusion:** Antenatal screening with spousal testing and PND is feasible and effective in preventing thalassemia major births. Integration of such programs into routine maternal care, especially in high-prevalence tribal areas, is essential.

Keywords: Thalassemia, Antenatal Screening, Prenatal Diagnosis, Hemoglobinopathies, β-thalassemia Trait, Pregnancy

INTRODUCTION

Thalassemia is a common inherited hemoglobin disorder caused by reduced or absent alpha or beta globin chain synthesis, leading to anemia and multi-organ complications. Globally, about 1.5% of the population are carriers, with nearly 60,000 children born annually with thalassemia major, posing significant health and economic burdens.[1] India carries one of the heaviest burdens of thalassemia worldwide, with an estimated 42 million carriers and about 10,000–15,000 births of thalassemia major annually[2] In India, the prevalence of thalassemia carriers ranges from 3– 17%, with higher rates in certain states and tribal populations. However, in the absence of a comprehensive national prevention program, screening remains fragmented, leading to late diagnosis and continued births of affected children[3,4].

The cornerstone of thalassemia prevention lies in early identification of carriers through premarital or antenatal screening, followed by genetic counseling and prenatal diagnosis[5]. Evidence from Mediterranean countries such as Cyprus and Sardinia demonstrates that well- structured national programs can reduce the birth of thalassemia major children by more than 90%. In India, smaller regional studies have confirmed the feasibility of antenatal screening programs, yet their implementation remains inconsistent[6]. For example, Mandirata S L et al (2012)[7] reported a 7% prevalence of beta thalassemia trait among pregnant women in Indore, Madhya Pradesh, while Gupta et al. (2015) highlighted the success of integrating partner testing and prenatal diagnosis in reducing affected births in Jodhpur, Rajasthan. However, these studies also noted challenges such as poor compliance of spouses, limited awareness, and late antenatal registration.[8]

First-trimester antenatal screening using CBC and red cell indices, followed by HPLC, enables early detection of carriers. If both partners are carriers, prenatal diagnostic methods such as CVS or amniocentesis can identify the fetal genetic status, allowing informed reproductive decisions[9]. Advances in molecular diagnostics and non-invasive prenatal testing (NIPT) are further improving the accuracy and safety of such programs[10]. Despite this, major gaps remain in India's public health response. Awareness about thalassemia is low, particularly in rural and tribal populations, and misconceptions about genetic disorders often create stigma and hinder participation in screening programs[11]. The high cost of lifelong treatment makes prevention through screening and prenatal diagnosis both medically and financially vital. This study was conducted among antenatal women in Southern Rajasthan to evaluate the effectiveness and feasibility of integrating carrier detection and prenatal diagnosis into routine maternal care.

MATERIALS AND METHODS

Study design: It was a cross-sectional observational, hospital based study.

Study setting: This study was conducted in the Department of Paediatrics with collaboration of Obstetrics & Gynecology, RNT Medical College and Maharana Bhupal (MB) Government Hospital, Udaipur, Rajasthan.

Study duration:

Participants: - Pregnant women attending routine antenatal care (ANC) in the 1st and early 2nd trimester who provided written informed consent were eligible.

Exclusions criteria like known HIV infection on zidovudine/stavudine therapy; history of blood transfusion within the preceding 3 months; known epilepsy on antiepileptic drugs; and refusal to consent.

Sample size and sampling: - The minimum required sample size was 1,276, assuming an expected beta-thalassemia carrier prevalence of 7% (Mendiratta S L et al)[7], two-sided $\alpha=0.05$ ($Z_{1-\alpha/2}=1.96$), and 20% relative precision. Consecutive eligible attendees were approached until the target was met; ultimately 1,280 women were enrolled (exceeding the target). Screening was done using HPLC. Carrier women were advised spousal testing; at-risk couples were offered PND through CVS or amniocentesis.

Data management and statistical analysis: - Data were entered in Microsoft Excel and analyzed in IBM SPSS version 25. Quantitative variables are reported as mean ± SD; categorical variables as frequency (percent). Associations between HbA2 category and categorical factors (e.g., consanguinity, need for PND) used Chi-square or Fisher's exact tests. Two-sided $p < 0.05$ was considered statistically significant.

Ethical considerations: - The protocol received approval from the Institutional Ethics Committee of RNT Medical College, Udaipur (IEC Approval no. RNT/ACAD./IEC/2024/367 dated 11.07.2025). All procedures adhered to the Declaration of Helsinki and national guidelines for biomedical research. Confidentiality was maintained throughout.

RESULTS

Among the 1,280 antenatal women screened, 92 (7.2%) were found to have abnormal hemoglobin patterns, while the majority (92.8%) showed normal profiles. Mean age participants was 25.22 ± 4.109 years. Majority of women (72.1%) were screened in first trimester. Beta-thalassemia trait was the most common abnormality, accounting for 5.0% of cases, followed by sickle cell trait (1.25%). Rare variants such as Hb-D, Hb-E, Hb-C, α-thalassemia, and sickle-β thalassemia were also identified. Among the 68 spouses screened, 5 (7.4%) were beta- thalassemia carriers and 1 (1.5%) had sickle cell trait, while 6 spouses (8.8%) declined testing. (Table 1)

Table 1. Hemoglobin Variants and Hemoglobinopathies in Women and Their Spouses

Group	Category	Type	Frequency (n)	%
Women (n= 1280)	Hemoglobinopathies	Normal	1188	92.8
		β-thalassemia trait	64	5.0
		Sickle cell trait (SCT)	16	1.25
		Hb-D	3	0.23
		Hb-E	1	0.07
		Hb-C	1	0.07
		α-thalassemia	3	0.23
		S/β-thalassemia	4	0.32
Spouses (n = 68)	Hemoglobinopathies	Normal	56	82.3
		β-thalassemia trait	5	7.4
		Sickle cell trait (SCT)	1	1.5
		Refused HPLC	6	8.8

Among five identified at-risk couples, four underwent prenatal diagnostic testing—three via chorionic villus sampling and one via amniocentesis—while one couple declined further testing. Prenatal diagnosis revealed one fetus with thalassemia major, two with thalassemia trait, and one unaffected fetus. The overall acceptance rate for prenatal diagnosis was 80%.(Table 2)

Table 2. Prenatal Diagnostic Procedures and Outcomes in At-risk Couples

Variable	**Frequency (n=5)**	**%**
At-risk couples identified	5	100
CVS performed	3	60.0
Amniocentesis performed	1	20.0
Refused for PND	1	20.0
Fetal genetic outcomes (n=4)		
– Thalassemia major	1	25.0
– Thalassemia minor	2	50.0
– Normal	1	25.0

DISCUSSION

The study of "Prenatal Screening and Diagnosis of Thalassemia: Preventing Thalassemia Major Births" was conducted in the Department of Paediatrics in collaboration with the Department of Obstetrics and Gynecology at RNT Medical College, Udaipur. A total of 1,280 study subjects were analyzed.

In this study, 7.19% (92) of antenatal women were identified as carriers of hemoglobinopathies, while 92.81% (1188) had normal HPLC profiles. The most common abnormality was β-thalassemia trait (64, 5.0%), comparable to national prevalence estimates (3–6% in the general population, up to 10–15% in high-risk groups). Similar prevalence rates have been reported by **Madan et al. (2010)[4]** in Rajasthan (4.95%), **Kulkarni et al. (2013)[12]** in Maharashtra (8.5%). Other variants included Sickle Cell Trait (1.25%), Sickle-β-thalassemia (0.32%), Hb-D (0.23%), Hb-E (0.07%), Hb-C (0.07%), and α-thalassemia trait (0.23%), reflecting the genetic heterogeneity across India. The presence of α-thalassemia trait, although infrequent, is notable given its underdiagnosis on routine HPLC and frequent misclassification as iron deficiency anemia (IDA) or beta thalassemia trait BTT.

Among 68 spouses screened, 7.35% (5) were BTT carriers and 1.47% (1) carried SCT. Importantly, five couples were at risk of having children with thalassemia major, underscoring the necessity of partner testing. Acceptance of prenatal diagnostic procedures (PND**)** was encouraging, with 80% undergoing either CVS or amniocentesis. Outcomes revealed one fetus with thalassemia major, two with trait, and one normal. The couple with an affected fetus was counselled and underwent termination, consistent with global best practices. Similar high-risk couple prevalence and PND acceptance trends have been documented in multicentric Indian studies **Jain et al., 2012[13]** and international reports **Shojaeian et al.,2020**.[14]

Notably, 8.82% of spouses refused testing, highlighting barriers such as stigma, financial constraints, and cultural hesitancy—barriers previously described by **Samra et al. (2015)[15]** and others. While the 80% acceptance rate of PND in this cohort is encouraging, refusal by one couple reflects persisting challenges, particularly related to cost, awareness, and religious beliefs, as reported in studies from **Iran (Samavat et al., 2004; Moudi et al., 2025)[16,17]**. However, limitations include the single-center design, lack of molecular confirmation for α-thalassemia, and partial refusal of spousal screening, which may underestimate true prevalence.

Overall, these findings confirm that antenatal hemoglobinopathy screening, coupled with partner testing, genetic counselling, and PND, is feasible and effective in preventing thalassemia major births. The detection of diverse variants further emphasizes the need to broaden screening beyond BTT. Integration of systematic screening into routine antenatal care, supported by culturally sensitive counselling and affordable diagnostic services, remains a critical strategy to reduce the burden of hemoglobinopathies in high-prevalence regions such as India.

CONCLUSION

The present study demonstrates that antenatal screening for hemoglobinopathies, followed by spousal testing and prenatal diagnostic procedures, is a practical and effective strategy to prevent births affected by thalassemia major. The carrier prevalence of 7.2% observed in our cohort aligns with regional and national estimates, reaffirming the clinical importance of routine screening in high-burden regions such as Southern Rajasthan. Spousal screening successfully identified at-risk couples, and prenatal diagnostic techniques such as chorionic villus sampling and amniocentesis enabled early fetal risk assessment. The 80% acceptance rate of prenatal diagnosis highlights growing awareness and willingness among couples to adopt preventive measures when supported with adequate counseling. Despite some barriers including refusal of partner testing and invasive diagnostic procedures, the program proved feasible within routine antenatal care. Strengthening public awareness, improving access to diagnostic facilities, and policy-level integration are essential to eliminate preventable thalassemia births in India.

REFERENCES

1. Weatherall DJ. The inherited diseases of hemoglobin are an emerging global health burden. Blood. 2010 June 3;115(22):4331–6.
2. Colah R, Gorakshakar A, Nadkarni A. Global burden, distribution and prevention of β-thalassemias and hemoglobin E disorders. Expert Rev Hematol. 2010 Feb;3(1):103–17.
3. Verma IC, Saxena R, Kohli S. Past, present & future scenario of thalassaemic care & control in India. Indian J Med Res. 2011 Oct;134(4):507–21.
4. Madan N, Sharma S, Sood SK, Colah R, Bhatia LHM. Frequency of β-thalassemia trait and other hemoglobinopathies in northern and western India. Indian J Hum Genet. 2010 Jan;16(1):16–25.
5. Angastiniotis M, Modell B. Global epidemiology of hemoglobin disorders. Ann N Y Acad Sci. 1998 June 30;850:251–69.
6. Cao A, Kan YW. The prevention of thalassemia. Cold Spring Harb Perspect Med. 2013 Feb 1;3(2):a011775.
7. Mendiratta SL, Mittal M, Naaz F, Singh S, Anand S. Role of thalassemia screening in prevention and control of thalassemia - a 5 year experience. Int J Reprod Contracept Obstet Gynecol. 2016;5(9):3107–11.
8. Gupta V, Sharma P, Jora R, Amandeep M, Kumar A. Screening for Thalassemia Carrier Status in Pregnancy and Pre-Natal Diagnosis. Indian Pediatr. 2015 Sept;52(9):808–9.
9. Tongsong T, Charoenkwan P, Sirivatanapa P, Wanapirak C, Piyamongkol W, Sirichotiyakul S, et al. Effectiveness of the model for prenatal control of severe thalassemia. Prenatal Diagnosis. 2013;33(5):477–83.
10. Yang X, Ye Y, Fan D, Lin S, Li M, Hou H, et al. Non-invasive prenatal diagnosis of thalassemia through multiplex PCR, target capture and next-generation sequencing. Mol Med Rep. 2020 Aug;22(2):1547–57.
11. Hasan MdM, Uddin KMdK, Lokman SM, Chakma K, Pulu ACU, Mannan A, et al. Knowledge and attitudes of thalassaemia among high-risk indigenous university students in Bangladesh: A pilot study. PLoS One. 2023 July 7;18(7):e0287630.
12. Kulkarni P, Masthi NRR, Niveditha S, Suvarna R. The prevalence of the beta thalassemia trait among the pregnant women who attended the ANC clinic in a PHC, by using the NESTROF test in Bangalore, Karnataka. J Clin Diagn Res. 2013;7(7):1414–7.
13. Jain BB, Roy RN, Ghosh S, Ghosh T, Banerjee U, Bhattacharya SK. Screening for thalassemia and other hemoglobinopathies in a tertiary care hospital of West Bengal: implications for population screening. Indian J Public Health. 2012;56(4):297.
14. Shojaeian Z, Khadivzadeh T, Sahebi A, Kareshki H, Tara F. Knowledge valuation by Iranian women with high-risk pregnancy: a qualitative content analysis. Int J Community Based Nurs Midwifery. 2020;8(3):243–52.
15. Abu Samra O, Auda W, Kamhawy H, Al-Tonbary Y. Impact of educational programme regarding chelation therapy on the quality of life for B-thalassemia major children. Hematology. 2015;20(5):297–303.
16. Samavat A, Modell B. Iranian national thalassaemia screening programme. BMJ. 2004;329(7475):1134–7.
17. Moudi Z, Mollashahi SS, Nouri N, Zaboli M, Arabnezhad L. Current use and barriers to healthcare service utilization among Afghan women refugees: a mixed-method study. Iran J Nurs Midwifery Res. 2025;30(2):182–91.