

small sample size and lack of work-up for viral and bacterial pneumonias. We conclude that circulating levels of copeptin are significantly increased in children with pneumonia, and are higher in children dying of the disease. Copeptin levels might predict unfavourable outcome in pediatric pneumonia.

*Contributors:* All authors have contributed, designed and approved the study.

*Funding:* None; *Competing interest:* None stated.

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## Screening for Thalassemia Carrier Status in Pregnancy and Pre-Natal Diagnosis

This hospital-based study reports the results of antenatal screening for thalassemia in pregnant women visiting a hospital in Jodhpur, Rajasthan, India. Eighty-eight (5.9%) of 1500 women screened for thalassemia had thalassemia trait. Twenty at-risk couples were identified and two fetuses were detected to be having thalassemia major.

**Keywords:** *Abortion, Pregnancy, Prenatal diagnosis.*

The most effective and feasible approach to reduce the incidence of thalassemia major is implementation of carrier screening program to test the mothers antenatally as early as 8-12 weeks of pregnancy, offering genetic counseling, prenatal diagnosis and selective termination of affected fetuses. This study was planned to determine the frequency of carrier status of thalassemia in pregnant females visiting our hospital to identify “at-risk” couples, and to prevent birth of new cases of thalassemia major.

This observational study was conducted over 18 months in Departments of Pediatrics, and Obstetrics and Gynecology, Umaid Hospital, Dr. Sampurnanand Medical College, Jodhpur, India. Pregnant women in first trimester and early second trimester (<16 weeks), who were willing for carrier screening, were screened by hematological indices after an informed consent. Detailed history to ascertain the ethnic descent, and any history of blood transfusion was obtained. Complete blood count was done on automated cell counter (Sysmex K-100) and hematological parameters were recorded for 1500 women. HbA<sub>2</sub> estimation was done in females with either of the following: (a) MCV <77 fL (b) MCH <27 pg, (c) Mentzer Index <13, (d) family history of thalassemia, (e) high risk ethnic groups – Punjabis, Sindhis, Gujaratis, Bohris and Malis, (f) history of blood transfusion, or (g) unexplained chronic anemia. Women who attended the antenatal clinics in late second trimester and third trimester or those who did not consent were excluded. HbA<sub>2</sub> estimation was performed using HPLC (High Performance Liquid Chromatography). HbA<sub>2</sub> >3.5% confirmed the diagnosis of β-thalassemia trait. Those with HbA<sub>2</sub> in the borderline range (3.3-3.4%) were screened for thalassemia mutations by ARMS-PCR (Amplification Refractory Mutation

System - Polymerase Chain Reaction). Chorionic villous sampling (CVS) was done if gestational age was <12 weeks and amniocentesis was preferred for cases detected in later weeks of pregnancy. ARMS-PCR was used for genetic analysis.

Out of 1500 pregnant women, 450 required HbA<sub>2</sub> estimation, and 88 (5.9%) were diagnosed as  $\beta$ -thalassemia trait. Mean (SD) age and gestational age of these women was 25.2 (4.2) y and 11.8 (1.4) wk, respectively. Forty-five (45%) had family history of thalassemia. Husbands of 80 of these women responded for screening and 20 proved to be thalassemia trait. Seventeen out of 20 at-risk couples agreed for prenatal diagnosis. Amniocentesis was done in thirteen and CVS in four pregnancies. Two fetuses were detected as having thalassemia major, and medical termination of pregnancy was done. Eleven fetuses were detected as having thalassemia trait and 4 without any  $\beta$ -globin chain abnormality. The mutations detected are depicted in **Table I**. Most common mutations were IVS 1-5 (G-C) > Fs8/9  $\beta$ -globin > 619bpdel=fs41/42=codon 30G-C > codon  $\beta$ 8 > Cap+1 (A-C). Five most common mutations were present in 77% of alleles. No complication occurred in CVS/amniocentesis conducted.

**TABLE I** RESULTS OF MUTATION ANALYSIS IN THE STUDY CHILDREN (N=17)

Mutation	Mother	Father	Fetus
IVS 1-5 (G-C) heterozygous	6	6	6
Fs 8/9 $\beta$ -Globin heterozygous	5	6	5
619 bp del $\beta$ -Globin			
heterozygous	1	1	-
homozygous	-	-	1
Codon $\beta$ -8 (-AA) heterozygous	1	1	1
Codon 30 G-C heterozygous	1	1	1
Fs 41/42 heterozygous	1	1	1
Cap+1 (A-C) heterozygous	1	-	-
Compound heterozygous (Fs 8/9 and IVS 1-5(G-C))	-	-	1
No Mutation	1	1	1

The sample size of our study was small and three couples could not be persuaded for prenatal diagnosis despite repeated counseling. Colah, *et al.* [1] conducted prenatal diagnosis on only 15 out of 37 at-risk couples over a period of 7 years, and Xu, *et al.* [2] carried prenatal diagnosis in 11 out of 12 at-risk couples. Five common mutations were reported to be present in 89% thalassemia patients in an earlier study [3] from India. Saxena, *et al.* [3] reported abortion rate of 3.9% following prenatal diagnosis. Antenatal screening of pregnant females is the most feasible and effective method to reduce birth of children with thalassemia. Carrier screening for thalassemia and hemoglobinopathies should be offered and genetic counseling should be done to women at-risk of these disorders.

*Contributors:* VD: design of the study, analysis, drafting and final approval of the manuscript; PS: data acquisition, data analysis, revision of the manuscript for important intellectual content and final approval; RJ: data analysis, revision of the manuscript and final approval; MA: analysis of data, data acquisition, drafting of the manuscript and final approval; AK: analysis of data, data acquisition, drafting of the manuscript and final approval.

*Funding:* Marwar Thalassemia society, Rajasthan; *Competing interests:* None stated.

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