

# Neonatal Screening for Sickle Cell Disease in South West Iran: a Pilot Study

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## Abstract

**Background:** Children affected with sickle cell disease (SCD) are at increased risk for severe morbidity and mortality, especially during the first 3-5 years of life. It is suggested that early treatment can improve the condition. The aim of this pilot study was to estimate the incidence of hemoglobin S (HbS) by umbilical cord blood screening in Khorramshahr and Abadan cities in southwest of Iran.

**Materials and Methods:** Cord blood sample (10 ml) was collected and stored in ethylenediaminetetraacetic acid (EDTA) pre-coated tubes and transported to the reference laboratory in Ahwaz. Samples were analyzed for presence of HbS by hemoglobin electrophoresis. Positive specimens were confirmed by sickle preparation test.

**Results:** Four patients (1.3%) with sickle cell disease were identified among 308 screened newborns, all with Arabian ethnic origin.

**Conclusion:** We concluded that HbS is a common disease in Khuzestan Province.

**Keywords:** Sickle cell anemia, Neonatal screening, Iran.

## Introduction

Sickle cell disease (SCD) is one of the most common inherited chronic hematological disorders.<sup>1</sup> SCD has been the first human disease to be described at the molecular level. The feasibility of accurate molecular diagnosis encouraged epidemiological studies which revealed that SCD was more prevalent than it was initially estimated.<sup>2</sup> This inherited condition affects people of European, Arabian, Indian, Oriental, and African origin.<sup>3</sup> The clinical manifestations of SCD are extremely varied. Some patients are entirely asymptomatic, whereas other patients suffer from painful episodes.<sup>4</sup> A report in 1986 which described prophylactic penicillin in sickle cell disease markedly reduced the incidence of pneumococcal sepsis provided a powerful incentive for widespread neonatal screening. Screening linked to timely diagnostic testing, parental education, and comprehensive care markedly reduced mortality and morbidity from SCD in infancy and early childhood.<sup>5</sup> However, neonatal screening system is not foolproof. A few infants, even in the United States with nationwide screening, may not be screened. Some other infants with SCD may be missed because of mislabeled specimens, personal errors, extreme prematurity,

blood transfusion prior to screening, or inability to locate affected infants after discharge from the nursery.<sup>6,7</sup> To have a perfect screening system, all infants including those born at home must be screened and the initial screening test should always be obtained prior to any blood transfusion. Hemoglobin FS in newborn and infancy reflects a variety of genotypes with a wide range of clinical severity. Most infants with FS on screening have homozygous SS genotype; but other genotypes including sickle beta-0-thalassemia, sickle beta-(+)-thalassemia, sickle delta thalassemia, and sickle HPFH are also possible. The co-inheritance of alpha-thalassemia may complicate diagnosis of genotype in some infants.<sup>8</sup> Infants and children affected with SCD are at increased risk for severe morbidity (e.g. splenic dysfunction, pain crisis, and bacterial infections) and mortality, especially during the first 3-5 years of life. It is suggested that early treatment (before symptoms development) can improve both morbidity and mortality.

## Materials and Methods

As sickle cell disease is much more prevalent in Arabian ethnic groups,<sup>9-12</sup> we selected

Khoramshahr and Abadan cities where most people have Arabian ethnic origin. In this cross-sectional pilot study, demographic data were collected by a questionnaire which was designed specifically for this study. Written consent form was obtained prior to any sample collection. Cord blood samples were obtained from all normal newborns born via vaginal delivery.<sup>6</sup> Three hundred and eight samples (158 from Khoramshahr, and 150 from Abadan) were collected.

Cord blood samples (10 ml) were collected in ethylenediaminetetraacetic acid (EDTA) pre-coated tubes in maternity hospitals,<sup>13</sup> and transported to the reference laboratory affiliated to Ahwaz Jondishapour University of Medical Sciences. Samples were placed in edetic acid containers and stored at 4°C until reaching to the laboratory. Samples were analyzed for the presence of HbS. Hemoglobin electrophoresis was performed by Helena Aparatus. To confirm the positive specimens, those were re-evaluated by sickle preparation test by sodium bisulfate (2%). They were read after 1 and 24 hours by macroscopic and microscopic methods.<sup>9</sup>

## Results

Screening was carried out in 308 infants (147 males and 161 females) by cord blood sampling during the first week of life. About 54.5% were outcome of consanguineous marriage. Screening was "missed" in 92 infants, because of some problems in sample transfer. Table 1 shows the number of infants screened in each city and the number of infants with HbS.

Four patients with sickle cell disease were identified among 308 newborns. All of them were from Arabian ethnic origin, and the outcome of consanguineous marriage. Demographic data of mothers is presented in table 2. The overall incidence of sickle cell disease was 1.3%.

## Discussion

Most SCD patients from Khuzestan have long been recognized to have mild disease with elevated levels of fetal hemoglobin (Hb F).<sup>9,11,12</sup> A newborn with SCD is not usually anemic, and is asymptomatic because of the protective effect of HbF.<sup>9,12</sup> Diagnosis of SCD in newborn can lead to prevention from mortality and morbidity. It is now recommended that all newborns at high risk should

be screened for HbS. Screening can be performed using umbilical cord blood or other blood samples.<sup>5,6</sup> Universal screening has been shown to identify more infants with the disease, prevent more deaths, and be more cost-effective.<sup>6</sup> Infants from high risk ethnic groups born in an area without routine neonatal screening should be screened by Hb electrophoresis, iso-electric focusing (IFE), high performance liquid chromatography (HPLC), or DNA analysis. Before 2 months of age, solubility testing methods and sickle cell preparation should not be used to screen for hemoglobinopathies.<sup>14</sup> Screening programs were widely implemented after a double-blind, randomized, placebo-controlled trial reported an 84 percent reduction in the incidence of pneumococcal sepsis, the most serious complication of sickle cell anemia in young infants, when prophylactic oral penicillin was initiated by three months old.<sup>15</sup> During the early months of the child's life, emphasis should be given to teaching the mother and other caregivers how to recognize early signs of serious complications. It is also important to ensure that prophylactic measures particularly oral penicillin VK and routine and specific immunizations are instituted in a timely fashion. New heptavalent conjugated pneumococcal vaccine should be given (if it is available) from two months old. All caregivers should be taught how to recognize specific signs and symptoms of the complications. Since acute splenic sequestration crisis is a leading cause of death in young children with SCD, the physician should carefully note the size of the child's spleen and teach the mother how to palpate it.

In the present study, among 308 newborn babies, 4 (1.3%) had HbS. All of them were Arabian in ethnic origin. They were outcome of consanguineous marriage. Approximately 30% of the population of Khuzestan Province are less than 15 years old. In Khuzestan Province, as in other parts of the country, the prevalence of sickle haemoglobinopathy is high, and a thorough knowledge of the mutation spectrum is critical for setting up effective prevention programs and improving molecular diagnosis. In a study performed in Shiraz city located in south of Iran, out of 1044 participants, 15 (1.4%) were heterozygous and 1 (0.09%) was homozygous for HbS.<sup>16</sup>

**Table 1.** The result of cord blood screening for sickle cell disease in 308 neonates from Khoramshahr and Abadan cities

Neonates	Khoramshahr	Abadan	Total
Female No. (%)	79 (52.7)	82 (52)	161 (52.3)
Male No. (%)	71 (47.3)	76 (48)	147 (47.7)
Patients with Hb S No. (%)	3 (2)	1 (0.68)	4 (1.3)
Total	150 (100)	158 (100)	308 (100)

**Table 2.** Demographic data of 308 newborns' mothers screened for sickle cell disease in Khoramshahr and Abadan cities

Characteristics	Khoramshahr	Abadan	Total
Number of mothers	150	158	308
Arabian race No. (%)	127 (84.6)	125 (79)	252 (81.8)
Consanguineous marriage	83 (55.5)	85 (54)	168 (54.5)
Mean of age (years)	26	25.15	25.45
Mean number of offsprings	2	1.26	1.56

## Conclusion

We concluded that SCD is a common disease in southwest of Iran, particularly in Arabian ethnic groups of Khuzestan. Therefore, we suggest that all newborns be screened for sickle cell disease in the early infancy or childhood. Also, medical counseling of affected high risk families seems to be indicated. Nevertheless, to determination true incidence of sickle cell syndrome, more extensive studies are recommended in the endemic north part of Persian Gulf and Oman Sea in south part of Iran.

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