ISSN NO. 2320-5407

Journal homepage: http://www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

RESEARCH ARTICLE

Neonatal screening for sickle cell disease in Taif governorate, KSA

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Manuscript Info

Manuscript History:

Received: 12 January 2015
Final Accepted: 25 February 2015
Published Online: March 2015

Key words:

Sickle cell disease- Neonatal screening.

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Abstract

Sickle cell disease (SCD) is a group of inherited conditions of red blood cells affecting mainly individuals of African origin but also Indian , Saudi and some Mediterranean populations .

Neonatal screening and early diagnosis of sickle cell disease (SCD) is essential to prepare preventative and management program as the greatest mortality in SCD occurs in the first year of life. Major causes of death at this age include pneumococcal sepsis, acute splenic sequestration, and chest syndrome.

This paper presents cross sectional study from newborn child whose come to immunization unit in Prince Mansur hospital to take the first dose of immunization program in Taif, Saudi Arabia, between the period of August 2014 to January 2015. A 860 newborn child was tested for early detection of sickle cell disease, 450 (52,3%) male newborns child and 410 (47,6%) female newborns child. A self-administrated questionnaire and a venous blood sample (3 ml) for complete blood count and hemoglobin electrophoresis to all newborn children participate in the study. The questionnaire includes questions about socio-demographic data, gestational age, family history, positive consanguinity of parents. Also weight and height and categorize it underweight, normal, overweight according to WHO classification. All collected data was been statistically analyzed using SPSS version 16.

INTRODUCTION

Sickle cell disorders (SCD) are genetic blood disorders that affect the Hemoglobin in red blood cells(Kate S.L., Lingojwar D.et al., 2002) Sickle cell disease (SCD) is one of the most common inherited chronic hematological disorders (Okpala IE et al.,2004).Sickle cell disease (SCD) consists of a group of life-threatening, genetically inherited disorders, characterized by large amounts of abnormal hemoglobin in the red blood cells. Most infants with SCD are healthy at birth and become symptomatic later, in infancy or childhood. Affected infants generally present clinically during infancy or early childhood with painful swelling of the hands and feet , pneumococcal sepsis or meningitis, severe anemia and acute spleen enlargement, acute chest syndrome, pallor, jaundice, or splenomegaly (American Academy of Pediatrics (AAP)2002).

Hemoglobin is the main substance of the red blood cell which helps red blood cells to carries oxygen from the air in our lungs to all parts of the body. Normal red blood cells contain hemoglobin A. Hemoglobin S and hemoglobin C are abnormal types of hemoglobin. The Normal red blood cells are soft and round and can squeeze through tiny blood vessels. Normally, red blood cells live for about 120 days before new ones replace them (U.S. Preventive Services Task Force 1996).

People with sickle cell disease have abnormal red blood cells that contain mostly hemoglobin(S) which is an abnormal type of hemoglobin (Lees C, Davies SC, Dezateux C et al., 2000). Sometimes these red blood cells become sickle-shaped (crescent shaped) and have difficulty passing through small blood vessels (Lorey F, Cunningham G et al., 1994).

People who have hemoglobin S do not live as long as normal red blood cells (normally about 16 days). They also become stiff, distorted in shape and have difficulty passing through the body's small blood vessels. When sickle-shaped cells block small blood vessels, less blood can reach that part of the body. Tissue that does not receive a normal blood flow eventually becomes damaged. This is the causes the complications of sickle cell disease. There is currently no completely cure for sickle cell disease (Kaye CI, Accurso F, La Franchi S et al., 2006).

Carriers of SCD are asymptomatic and often unaware that they carry the gene (Eboh & van den Akker et al., 1994). If made aware of this carrier status before they contemplate having children they could make an informed choice not to go ahead with a pregnancy if at risk of having an affected child (Laird et al., 1996). This depends on good screening and counseling services being in place. However, even in areas of the UK with a high prevalence of relevant ethnic minority groups, haemoglobinopathy screening and counseling services have been criticised for being fragmented (Anionwu & Atkin et al., 2001; Atkin & Ahmad et al., 1998).

You inherit the abnormal hemoglobin from your parents, who may be carriers with sickle cell trait or parents with sickle cell disease. You cannot catch it. You are born with the sickle cell hemoglobin and it is present for life. If you inherit only one sickle gene, you have sickle cell trait. If you inherit two sickle cell genes you have sickle cell disease (Halasa NB, Shankar SM, Talbot TR, et al., 2007).

Sickle cell trait is a person who carries one sickle hemoglobin producing gene inherited from their parents and one normal hemoglobin gene. Normal hemoglobin is called type A. Sickle hemoglobin called S. Sickle cell trait is the presence of hemoglobin AS on the hemoglobin electrophoresis so This will NOT cause sickle cell disease (Halasa NB, Shankar SM, Talbot TR et al., 2007).

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 improved both morbidity and mortality. The aim of this study was to estimate the incidence of hemoglobin S (HbS) by blood screening in Taif city in K SA.

Sickle cells are destroyed rapidly in the body of people with the disease causing anemia, jaundice and the formation of gallstones. The sickle cells also block the flow of blood through vessels resulting in lung tissue damage (acute chest syndrome), pain episodes (arms, legs, chest and abdomen), stroke and. It also causes damage to most organs including the spleen, kidneys and liver. Damage to the spleen makes sickle cell disease patients, especially young children, easily overwhelmed by certain bacterial infections (American Academy of Family Physicians 2007)

Clinical manifestations of SCD are extremely varied. Some patients are asymptomatic, whereas other patients suffer from painful episodes Pearson HA et al, 1998).)

SCD, a condition that has variable clinical manifestations, is characterized by:

(1) Severe obstruction of blood vessels by sickled cells preventing oxygen supply reaching tissues and organs

(2) Hemolytic anemia where the body breaks down damaged blood cells, which have become permanently sickled (Frewin & Provan et al., 1997)

Major causes of death at this age include pneumococcal sepsis, acute splenic sequestration, a plastic crisis and acute chest syndrome – some of which can be prevented or effectively treated if the underlying diagnosis is known. SCD can be diagnosed in the newborn period by hemoglobin electrophoresis using umbilical cord blood(Schneider RG, Hosty TS, Tomlin G et al., 1974).

Neonatal screening and early diagnosis is essential to prepare preventative and management programs as the greatest mortality in SCD occurs in the first year of life. Without early screening, the mortality from SCD approaches 20% by 3 years of age(Rodgers D, Clarke J, Cupidore et al., 1978).

Newborn screening is now integrated into routine neonatal practice in many parts of the world, and the overall ethical acceptability of newborn screening programmes is well recognized (Kerruish, N.J. and, Robertson, S.P et al., 2005).

The WHO considers that newborn screening should be mandatory if early diagnosis and treatment will benefit the newborn(World Health organization) (WHO 1997).

Screening linked to timely diagnostic testing, parental education, and comprehensive care markedly reduced mortality and morbidity from SCD in infancy and early childhood (Vichinsky E, Hurt D, Earles A, Kleeman K, Lubin B et al., 1988).

Health maintenance for patients with sickle cell disease starts with early diagnosis, preferably in the newborn period and includes penicillin prophylaxis, vaccination against pneumococcal bacteria and folic acid supplementation(Lorey F, Cunningham G, Shafer F, Lubin B et al., 1994).

Treatment of complications often includes antibiotics, pain management, intravenous fluids, blood transfusion and surgery all backed by psychosocial support. Like all patients with chronic disease patients are best managed in a comprehensive multi-disciplinary program of care (Daniel YA, Turner C, Haynes RM et al., 2005).

A simple blood test followed by a laboratory technique called Hemoglobin Electrophoresis will determine the type of hemoglobin you have. When you pass an electric charge through a solution of hemoglobin, distinct hemoglobin move different distances, depending on their composition. This technique differentiates between normal hemoglobin (A), Sickle hemoglobin (S), and other different kinds of hemoglobin (such as C, D, E, etc.) (Halasa NB, Shankar SM, Talbot TR et al., 2007).

The goal of newborn screening is early identification of children at increased risk for Selected metabolic or genetic diseases so that medical treatment can be promptly initiated to Avert metabolic crises and prevent irreversible neurological and developmental squeals, Early identification of these conditions is crucial, as timely intervention can lead to a Significant reduction of morbidity, mortality, and associated disabilities in affected infants.1 Today every state in the world provides newborn screening for sickle cell disease and Congenital hypothyroidism. These two disorders set the scope for the classical benefits Newborn screening can achieve, whereby early identification and treatment change the Potential course of the infant's life from dependent mental retardation to Functioning near full normalcy(A Report et al., 2000).

I. **Clinical manifestation and complication of sickle cell disease**

- *Hemolytic crises*

Hemolytic crises, as a result of accelerated RBC death, occur rarely(Beutler E. et al, 1995) A plastic crises cause massive suppression of normal erythropoiesis, with absent reticulocytes and a hemoglobin level which falls by about 1 gram per day. A number of different infections are implicated including parvovirus B19, pneumococci , Salmonella species, streptococci and Epstein–Barr virus. With prompt diagnosis and transfusion, the outcome of a plastic crises is predictable and benign, with bone marrow activity recovery after 7–10 days being the rule (Serjeant GR et al., 1997)

- *Splenic sequestration crises*

Acute splenic sequestration may occur in the first five years of life. many numbers of RBCs are sequestered in the child's large spleen leading to a precipitous drop in the hemoglobin level. Hemoglobin levels less than 6 g dl and are considered major and these children may require fluid resuscitation and blood transfusion (Beutler E et al., 1995).

- *Acute pain crises*

Acute pain in SCD is thought to be caused by vascular occlusion and, in the case of bone pain, the consequent release of inflammatory mediators that results in raised intramedullary pressure and stimulation of nociceptors. Greater than three pain episodes per year are an indicator of more severe disease and hence, risk of early death (Platt OS, Brambilla DJ, Rosse WF et al., 1994).

- Cardiopulmonary manifestations of sickle cell disease

Acute chest syndrome:

The acute chest syndrome (ACS) is the leading cause of death and hospitalization among patients with SCD, being responsible for up to 25% of sickle related deaths (Vichinsky EP, Styles LA, Colangelo LH et

al.,1997). It is caused by a spectrum of pathology including elements of infection, infarction, pulmonary sequestration and fat embolism (Vichinsky EP, Williams R, Das M et al., 1994).

- Cardiac changes in sickle cell disease

  Cardiomegaly is a frequent finding in patients with SCD and may occasionally be the presenting feature(Falk RH, Hood WB Jr et al., 1982).

- Neurological manifestations of sickle cell disease

  Cerebrovascular accident (CVA) is a severe complication of SCD that may impair both motor and intellectual function. Clinically overt CVAs affect about 5% of children with SCD (hene-Frempong K, Weiner SJ, Sleeper LA et al., 1998).

- Renal problems in sickle cell disease

  Urological problems encountered are haematuria and urinary tract infection (Tarry WF, Duckett JW Jr, Snyder HM et al.,1987).

II. Material and Method

- Study setting:

The study was be conducted in immunization unit Prince Mansur hospital, Taif governorate,. It will include all neonate children attending immunization unit of the hospital between the period of August 2014 to January 2015.

- Subject of the study:

860 newborns children whose come to immunization unit in Prince Mansur hospital 450 (52,3%) male newborns and 410 (47,6%) female newborns.

- Study design:

-The study will be a cross-sectional study including all neonate children in order to find out the prevalence of sickle cell disease.

- Ethical clearance:

This study was approved by the Institutional Ethical Committee (IEC).

- Data collections and tools:

The purposes of the study was be explained by the research team to all parents of the newborn children included in the study.

All parents of the newborn children included in the study was be interviewed personally and asked to:

1. Fill the self- administrated questionnaire after initial training. This self- administrated questionnaire was include the following:

A. Socio-demographic data such as age of parent's residence, family size.
B. Family history: such as consanguinity, blood disorder,chronic diseases as diabetes and heart diseases.
C. Anthropometric measurement: weight, height be used to classify underweight, normal, overweight.

2. Blood sample for analysis:
   Venous blood sample (3ml) was be drawn from each newborn children into tubes with ethylene-diamine tetra acetic acid (EDTA).EDTA blood sample was be used to analyzed hemoglobin electrophoresis which was be used to screened the newborn children for detection sickle cell anemia and beta thalassemia.
3. Statistical analysis:
   Data entry and Statistical analysis was been performed using statistical package for the social science (SPSS) program for windows version 16. Frequency and range checks was been performed. Descriptive statistics was been used for the quantitative variables. Percentage was been used to determine the rate of sickle cell anemia and thalassemia.

III. Results and Discussion

We screened 860 neonates at the age of one day to seven days in prince Mansur hospital when they come to the hospital to take the first dose of immunization between the period of August 2014 to January 2015 for early detection of sickle cell disease by using electrophoresis blood test.

The study was done on 450 (52,3%) male newborns and 410 (47,6%) female newborns.

Table 1: sex distribution and diagnosis of 860 newborns (N=860)

Variables	NO	%
Sex:		
Males	450	52,3
Females	410	47,6
Diagnosis:		
S-S	38	4,4
Males	24	2,79
Females	14	1,6
S-β thalassemia	16	1.8
Males	9	1
Females	7	0.8

S-S is sickle cell anemia ,S-β thalssemia is beta thalassemia.

Among our newborns (n=860), 38 (4,4%) was diagnosed with sickle cell anemia,24 males (2,79%) and 14 female (1,6%) and 16 (1,8%) was diagnosed with beta thalassemia ,9 males (1%) and 7 females(0,8%).

Table 2: data of 38 diagnosed newborns of sickle cell anemia included in the study using the screening test (n=38)

variables	Males (No=24)	Males %	Females (No=14)	Females %
Gestational age				
Preterm	2	8,3	1	7,1
fullterm	22	91,3	13	92,8
History of neonatal jaundice	16	66,6	9	64,2
+ve consanguinity of parents	18	75	10	71,4
History of kernictrus	2	8,3	0	0
+ve family history	3	12,5	1	7,1

In our study we show that there is positive relationship between sickle cell anemia and neonatal hyperbilirubinemia that has been confirmed by several studies, in our study we have 16 male neonates (66,6%) and 9 female neonates (64,2%) had history of neonatal jaundice , and we also we have 2 males (8,3) had complication of kernictrus . In our study we show also a positive relationship between consanguinity of parents and sickle cell anemia as we have 16 male neonates (75%) and 10 female neonates (71,4%) which had been positive consanguinity of parents.

Table 3: data of 16 diagnosed newborns of beta thalassemia included in the study using the screening test (n=16)

variables	Males (No=9)	Males %	Females (No=7)	Females %
Gestational age				
Preterm	1	11,1	0	0
fullterm	8	88,8	7	100
History of neonatal jaundice	5	55,5	3	42,8
+ve consanguinity of parents	6	66,6	4	57,1
History of kernictrus	0	0	0	0
+ve family history	2	22,2	1	14,2

In our study we show that there is positive relationship between beta thalassemia and neonatal hyperbilirubinemia that has been confirmed by several studies, in our study we have 5 male neonates (55,5%) and 3 female neonates (42,8%) had history of neonatal jaundice. In our study we show also a positive relationship between consanguinity of parents and beta thalassemia as we have 6 male neonates (66,6%) and 4 female neonates (71,4%) which had been positive consanguinity of parents.

Table 4: Anthropometric data of 54 diagnosed newborns of sickle cell disease included in the study using the screening test (n=54)

variables	No	%
Height percentile		
<5th percentile	21	38,8
>5thpercentile-<25 thpercentile	22	40,7
>25thpercentile-<75 thpercentile	9	16,6
>75thpercentile	2	3,7
weight percentile		
<5th percentile	10	18,5
>5thpercentile-<25 thpercentile	27	50
>25thpercentile-<75 thpercentile	15	27,3
>75thpercentile	2	3,7

Interpretation of height and weight respectively according to international growth curves showed that patients below 5thpercentile were 38,8%,18,5% respectively. And patient between 5thpercentile and 25thpercentile were 40,7%,50% respectively. And patient between2 5thpercentile and 75thpercentile were 16,6%,27,3%respectively. And patients above7 5thpercentile were 3,7% for height and weight.

The study in this paper was done on 450 (52,3%) male newborns and 410 (47,6%) female newborns. Among our newborns (n=860), 38 (4,4%) was diagnosed with sickle cell anemia,24 males (2,79%) and 14 female (1,6%) and 16 (1,8%) was diagnosed with beta thalassemia ,9 males (1%) and 7 females(0,8%). In our study we show also a positive relationship between consanguinity of parents and sickle cell anemia as we have 16 male neonates (75%) and 10 female neonates (71,4%) which had been positive consanguinity of parents. In our study we show also a positive relationship between consanguinity of parents and beta thalassemia as we have 2 male neonates (22,2%) and 1 female neonates (14,2%) which had been positive consanguinity of parents. In our study we show the interpretation of height and weight respectively according to international growth curves showed that patients below 5thpercentile were 38,8%,18,5% respectively. And patient between 5thpercentile and 25thpercentile were 40,7%,50% respectively. And patient between2 5thpercentile and 75thpercentile were 16,6%,27,3%respectively. And patients above7 5thpercentile were 3,7% for height and weight.

IV. conclusion

Sickle cell disease should be detected by screening program at the first week of life further work-up should be offered to early detection of blood disorder will lead to prepare preventive and management. ***From the course of this study*** we can entail that; prevalence of neonatal screening of sickle cell anemia was 4,4% and prevalence of neonatal screening of beta thalassemia was 1,8%. Therefore Sickle cell disease should be detected by screening program at the first week of life further work-up should be offered to early detection of blood disorder will lead to prepare preventive and management. Most of those diagnostic patients had positive consanguinity of parents as 75% of diagnostic males and 71,4% of diagnostic females with sickle cell anemia and 66,6% of diagnostic males and 57,1% of diagnostic females had positive consanguinity of parents. Also we show the relationship between the diagnostic patients and underweight and under height as 38,8% of the diagnostic patients was under height (less than 5 percentile)and 18,5% of the diagnostic patients was underweight (less than 5 percentile).

V. Recommendations

(1) We recommend to do screening program for sickle cell disease at the first week of life.

(2) Further work-up should be offered to early detection of blood disorder in neonates.

(3) Put a guideline plan strategy for prevention and control of complication of sickle cell disease and thus decreasing morbidity and mortality from anemia.

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