IJBC 2015; 7(2): 75-78

Hereditary Spherocytosis among Neonates with Jaundice in Bandar Abbas, South Iran

Nazemi A[1], Molavi MA[1], Raeisi E[2]*

1. Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
2. Student Research Committee, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.

***Corresponding Author:** Raeisi E, **Email:** eraesi@yahoo.com*

Submitted: 16-09-2014 , Accepted: 25-11-2014

Abstract

Background: Neonates affected by hereditary spherocytosis may suffer from significant jaundice. This study was conducted on neonates with jaundice hospitalized at the Children's Hospital in Bandar Abbas, South Iran, to determine the frequency of hereditary spherocytosis among them.

Patients and Methods: In this cross-sectional study, 814 neonates with jaundice hospitalized at the Children's Hospital in Bandar Abbas, South Iran, were studied from August 2013 to August 2014. Neonates with serum bilirubin levels requiring phototherapy were included in the study, while those whose parents did not consent to their children entering the study, those with congenital abnormalities, infections, bile duct obstruction, and ill neonates were excluded from the study. Peripheral blood smears were prepared for neonates with MCHC≥ 36g/dl, and osmotic fragility tests were carried out if spherocytes were found in the blood smear.

Results: Of the 814 studied neonates, 58.1% were boys and 41.9% girls. Their average bilirubin, hemoglobin, and MCHC levels at the start of the study were 16.96 ± 3.49, 14.69 ± 2.19, and 34 ± 1.37, respectively. Ninety eight percent (798 neonates) had MCHC levels below 36 and 2% (16 neonates) had MCHC levels equal to or over 36, but the osmotic fragility tests of all these 16 neonates were normal.

Conclusion: In the present study none of the hospitalized neonates with jaundice had hereditary spherocytosis. More studies with larger sample size and longer duration are recommended to further study the causes of jaundice and the prevalence of hereditary spherocytosis in Iran.

Keywords: Hereditary spherocytosis, neonatal jaundice, Iran.

Introduction

Hereditary spherocytosis (HS) is a prevalent hemolytic disease among populations in northern Europe [1, 2], affecting approximately one in every 5000 live births. There is no correct estimate of its prevalence in other societies, but it is less common in African, American, and Southeast Asian populations [3]. HS is the most prevalent hereditary disorder of the red blood cell and causes cell-wall fragility. The most common molecular defects are ankyrin, α-spectrin, β-spectrin, band-3, and protein 4.2 defects [1, 2]. HS causes red blood cells to take on abnormal shapes, to have greater metabolic needs, and to be destroyed more readily in the spleen [4].

HS has autosomal dominant and autosomal recessive types, and in 75% of the cases is inherited as the autosomal dominant type [5, 6], and passed on less frequently as the autosomal recessive type.

Anemia is the most frequent presenting complaint, followed by splenomegaly, jaundice, and a positive family history [4]. HS often manifests itself with jaundice in the first few days of life. Fifty percent of HS patients with spherocytosis may have a history of neonatal jaundice, and in 91% of them jaundice appears in the first week of life (bilirubin > 10 mg/dl) [3].

Jaundice also happens in healthy neonates, and it must be monitored and followed-up to prevent bilirubin encephalopathy [7]. The importance of the role hemolysis plays as a risk factor for jaundice and neurotoxicity increases the need to identify hemolysis in children with jaundice who are referred to hospitals.

In a study conducted by Christensen et al.[8], from January 2004 to December 2008 on 670 neonates with serum bilirubin levels of over 20 mg/dl, 8 neonates who had MCHC levels of 35.1-37 were identified with hereditary spherocytosis. In another study conducted by Johnson et al.[9], it was found that kernicterus was the cause of 2.4% of HS cases despite the fact that timely diagnosis and simple treatment prevented this complication. Considering the importance and complications of neonatal jaundice, and due to the intensification of jaundice in the presence of hereditary hemolytic diseases such as HS, we decided to study the frequency of HS in neonates affected by jaundice who were hospitalized at the children's ward of the Children's Hospital, Bandar Abbas, Iran.

Patients and Methods

This was a cross-sectional study carried out at the Children's Hospital in Bandar Abbas, South Iran, from August 2013 to August 2014. The target population was neonates hospitalized with Jaundice in the children's ward. Neonates with high serum bilirubin levels requiring phototherapy and hospitalized in the children's ward entered the study, while those whose parents did not consent to their children's participation in the study, those with congenital abnormalities, infections, bile duct obstruction, and ill neonates were excluded from the study.

Peripheral blood smears were prepared for neonates with jaundice who entered the study and whose MCHC levels were ≥ 36 mg/dl in the CBC test. With the consent of parents, blood samples were taken from neonates who had spherocytes in their smears. One milliliter of venous blood was taken from each of these neonates, poured into a tube containing EDTA anticoagulant, and sent to the Pasteur Laboratory, Iran, for osmotic fragility test. There several dilutions were first prepared using 10% physiological serum and distilled water, and the neonates' washed blood was added to the dilutions. The samples were incubated for half an hour at room temperature, low speed centrifugation was performed, and light absorption by the supernatant was read against a blank tube (or a dilution with no lysis) using a spectrophotometer. The percentage of lysis was then calculated by dividing the amount of light absorbed by the sample tubes to those absorbed by tubes with total lysis. Tubes with 50% lysis were considered positive results. The collected data was entered into SPSS version 16 (SPSS Co, Chicago, IL) and means, standard deviations, frequencies, and other descriptive indices were used for data analysis.

Results

Of the 998 neonates with jaundice hospitalized at our hospital in study's time period, 814 who met the requirements entered the study. There were 473 (58.1%) boys and 341 (41.9%) girls in the study, and the average age of their mothers was 25.67±4.79 years. The mean bilirubin level of the neonates at the start of the study was 16.96± 3.49 (with the range of 8-34). The average hemoglobin and MCHC levels of the neonates were 14.69±2.19 (with the range of 7.3-20.3) and 34.00±1.37 (with the range of 28.7-38), respectively. In this study, 789 (98%) of the neonates had MCHC levels below 36 and 16 neonates (2%) had MCHC levels equal to or higher than 36.

Exchange transfusion was performed for only 29 neonates (3.6%), and phototherapy was employed

Table 1: Baseline characteristics of neonates entering the study.

Variable	Number	Minimum	Maximum	Mean± standard deviation
Bilirubin	814	8	34	16.96± 3.49
Mother's age	814	15	42	25.67± 4.79
Hemoglobin	814	7.30	20.30	14.69± 2.19
MCHC	814	28.7	38	34.00± 1.37

for treating the remaining 785 neonates (96.4%). Osmotic fragility tests were conducted on all of the 16 neonates with jaundice who had MCHC ≥ 36, and who had no family history of HS, splenectomy, gallstones, or anemia requiring treatment. The average bilirubin level in neonates with MCHC < 36 was 16.96± 3.49 and 16.88± 3.2 in neonates with bilirubin levels ≥ 36. However, these differences in serum bilirubin levels between the two groups were not statistically significant (p = 0.43). The average hemoglobin level in neonates with MCHC < 36 was 14.63 ±2.16 and 17.45 ± 1.88 in neonates with MCHC ≥ 36. However, the differences in the hemoglobin levels between the two groups were also not statistically significant (p = 0.79).

In the present study 57.9% of neonates with MCHC<36 were boys and 42.1% were girls, and 68.8% of the neonates with MCHC ≥ 36 were boys and 31.2% were girls. The difference between the two groups regarding the gender was not statistically significant (p=0.27).

We found that 25.7% of the neonates with MCHC <36 had G6PD deficiency but among neonates with MCHC ≥ 36 this percentage was 12.5%. The differences between the two groups in G6PD deficiency was not statistically significant (p= 0.48).

In the present study 96.5% of the neonates with MCHC < 36 were treated with phototherapy and 3.5% with exchange transfusion. Also 93.8% of the neonates with MCHC≥ 36 were treated with phototherapy and 6.2% with exchange transfusion, however, the difference between the two groups regarding the treatment method was not statistically significant (p= 0.44).

Discussion

Eight hundred and fourteen neonates with jaundice who met the study's criteria were evaluated. Ninety eight percent (798) of them had MCHC levels below 36 and two percent (16) had MCHC levels of equal to or higher than 36. Considering several other studies regarding the prevalence of HS [8, 10, 11, 12], we predicted a prevalence level of 2% for HS among the studied neonates, which was close to the 2.4% Johnson et al.[9], found in their study in the United States. However, although the MCHC levels among hospitalized neonates in our study were equal to or higher than 36 in 16 neonates, results of osmotic fragility tests for all of them were negative and, therefore, no cases of HS were found among them.

There was no family history of HS, splenectomy, gall stones, or anemia requiring treatment among our patients. This finding conforms to those reported by Dehdashtian et al. [13], conducted in Ahvaz, Iran.

Contrary to our study results, Christensen et al.[8], have suggested that the possibility of HS in neonates with jaundice and high HMCH should be considered. Moreover, in a study carried out by Kaplan et al.[14], high MCHC was found to be a good indicator for diagnosis of HS. The reason for this discrepancy may be lysis resulting from ABO and Rh incompatibility that increases MCHC levels. In our research, 5 out of the 16 neonates with jaundice and higher than 36 MHCH levels, had ABO incompatibility. Also the presence of Heinz bodies and incorrect hematocrit evaluation may show MCHC levels in patients with G6PD deficiency to be higher than the normal level. In our study, 6 of the 16 neonates with high MCHC levels and jaundice had G6PD deficiency. Moreover, normal blood parameters in neonates are usually not available and often a range of values is considered for them.

Based on our study, G6PD deficiency was present in 25.4%, ABO incompatibility in 20%, and Rh incompatibility in 3% of the neonates with neonatal jaundice. This finding is in agreement with those reported by Cheng et al. [15], from Taiwan. However, it was reported in their study that HS was the cause of 1.2% of cases of neonatal jaundice (and this does not conform to our findings). The reason for this disagreement may be the short duration of our study and the fewer cases of HS diagnosis in neonates with bilirubin levels of lower than 20 mg/dl [8].

In a study carried out by Mariani et al. [16], the sensitivity of the osmotic fragility test for diagnosing of HS was reported to vary from 48 to 95 percent, and this sensitivity was independent of cytoskeletal abnormalities and the degree of protein deficiency. Other tests such as the cryohemolysis test, the osmotic gradient ektacytometry test, and the eosin-5 maleimide test may be more sensitive, but they are not available at the present 4 and the main test for diagnosing of HS is the SDS-PAGE test [17].

Conclusion

No cases of HS were detected in our study on neonates hospitalized with jaundice at the

Children's Hospital in Bandar Abbas, South Iran, probably because of the short duration of the research and the unavailability of more sensitive diagnostic tests. Considering the limitations of the present study and the high prevalence of neonatal jaundice in Iran, and due to the complications jaundice and HS may cause, it is suggested that studies with larger sample size and longer duration be conducted to further study the causes of jaundice and the prevalence of HS in Iran.

References

1. Gallager PG, Glader B. Hereditary spherocytosis, hereditary elliptocytosis, and other disorders associated with abnormalities of the erythrocyte membrane. In: Greer JP, Foerster J, Rodgers GM, et al, eds. Wintrobe's Clinical Hematology. 12th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009: 91120.
2. Perrotta S, Gallagher PG, Mohandas N. Hereditary spherocytosis. Lancet. 2008; 372(9647):1411-26.
3. Orkin SH, Nathan DG, Ginsburg D, Look AT, Fisher DE, Lux S IV. Nathan and Oski's Hematology of Infancy and Childhood. .7th ed. Phyladelphia PA. Saunders Elsevier. 2009:714-46.
4. Kliegman RM, Nelson textbook of pediatrics.19th ed. Saunders Elsevier press;2011:1659-62.
5. Bolton-Maggs PH. Hereditary spherocytosis; new guidelines. Arch Dis Child. 2004; 89(9): 809-12.
6. Barcellini W, Bianchi P, Fermo E, Imperiali FG, Marcello AP, Vercellati C, et al. Hereditary red cell membrane defects: diagnostic and clinical aspects. Blood Transfus. 2011;9(3):2747.
7. Kaplan M, Bromiker R, Hammerman C. Severe neonatal hyperbilirubinemia and kernicterus: are these still problems in the third millennium? Neonatology. 2011;100(4):354-62.
8. Christensen RD, Henry E. Hereditary spherocytosis in neonates with hyperbilirubinemia. Pediatrics. 2010;125(1):120-5.
9. Johnson L, Bhutani VK, Karp K, Sivieri EM, Shapiro SM. Clinical report from the pilot USA Kernicterus Registry (1992 to 2004). J Perinatol. 2009;29 Suppl 1:S25-45.
10. Schroter W, Kashnitz E. Diagnosis of herediatary spherocytosis in newborn infants. The Jornal of pediaterics.1983;103(3):460-3.
11. Akar N, Gokce H. Red blood cell indexes in patients in with herediatary spherocytosis and beta-thalassemia combination. Pediateric hematology and oncology.2002;19(8):569-73.
12. Eberle SE, Sciuccati G, Bonduel M, Diaz L, Staciuk R, Torres AF. Erythrocyte indexes in herediatory spherocytosis. Medicina (B Aires). 2007;67(6 Pt 2):698-700. (Article in Spanish)
13. Dehdashtian M, Aramesh MR, Malakian A, Aletayeb MH, Salehi Z. Is Elevated Mean Corpuscular Hemoglobin Concentration Valuable for Neonatal Hereditary Spherocytosis Screening? Shiraz E-Medical Journal. 2013;14(3): 220-5.
14. Kaplan M, Bromiker R, Hammerman C. Hyperbilirubinemia, hemolysis, and increased bilirubin neurotoxicity. Semin Perinatol. 2014;38(7):429-37.
15. Cheng SW, Chiu YW, Weng YH. Etiological analyses of marked neonatal hyperbilirubinemia in a single institution in Taiwan. Chang Gung Med J. 2012;35(2):148-54.
16. Mariani M, Barcellini W, Vercellati C, Marcello AP, Fermo E, Pedotti P, et al. Clinical and hematologic features of 300 patients affected by hereditary spherocytosis grouped according to the type of the membrane protein defect. Haematologica. 2008;93(9):1310-7.
17. Miraglia del Giudice E, Perrotta S, Nobili B, Pinto L, Cutillo L, Iolascon A. Coexistence of hereditary spherocytosis (HS) due to band 3 deficiency and beta-thalassaemia trait: partial correction of HS phenotype. Br J Haematol. 1993;85(3):553-7.