

Original Article

Frequency of Hepatitis B and C in Patients with Sickle Cell Disease- Experience at Tertiary care Hospital

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ABSTRACT

Objectives: To determine the frequency of hepatitis B and C in patients with Sickle Cell Disease (SCD).

Study Design: Cross-sectional study

Place and Duration: Department of Internal Medicine, King Salman Armed Forces Hospital, Kingdom of Saudi Arabia.

Material and Methods: Total 47 patients of either gender with age more than 15 years who were diagnosed cases of SCD were recruited. The diagnosis of SCD was established by cellulose acetate electrophoresis with citrate agar electrophoresis. The diagnosis of hepatitis B and C was established by measuring hepatitis b surface antigen (HBsAg) and Anti-HCV antibodies through 3rd generation Enzyme Linked Immunosorbent Assay (ELISA). Patients were excluded who could have hepatitis due to other reasons.

Results: Six (n=6) patients were excluded who could have hepatitis due to other reasons. Data of remaining 41 patients was analyzed with mean age of 24.27 years \pm 4.29 SD. There were 28 males and 13 females with male to female ratio 2.15. Frequency of hepatitis B was found to be 7.32 % (n = 3), while frequency of hepatitis C was found to be 12.2 % (n=5) in our study.

Conclusion: A significant percentage of SCD patients were having hepatitis B and C. Blood transfusion protocol and their safety should be improved. Early detection of hepatitis B/C in transfused SCD patients is also essential. Further large-scale studies are needed taking number of blood transfusions as a variable in the study.

Key words: Sickle cell disease, Hepatitis B, Hepatitis C, Blood Transfusion

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Introduction

The major risk factor for developing hepatitis B and C in patients with sickle cell disease (SCD) is receiving multiple blood transfusions. The main idea was to estimate the burden of hepatitis B and C in patients with SCD in urban population of Saudi Arabia.

Sickle cell disease (SCD) is an inherited disorder due to homozygosity for the abnormal hemoglobin, hemoglobin S (HbS) that is poorly soluble when deoxygenated.¹ The polymerization of deoxy HbS is essential to vaso-

occlusive phenomena. Fetal hemoglobin (HbF) is a major modulator of polymerization in that the higher the HbF levels, the more benign the clinical and hematologic features of sickle cell anemia.² Subsequent changes in red cell membrane structure and function, disordered cell volume control, and increased adherence to vascular endothelium also play an important role.³ The prevalence of SCD in Saudi Arabia varies significantly in different parts of the country showing eastern region dominance with a prevalence of

145 per 10,000, followed by the southern region with a prevalence of 24 per 10,000, western region 12 per 10,000, and central region with 6 per 10,000. No cases were found in the northern regions.^{4,5,6} The major risk factor for liver disease in patients with SCD is receiving multiple blood transfusions, which is associated with infection (hepatitis B and C) and excessive iron stores^{7,8,9} The prevalence of chronic viral hepatitis is increased in patients with SCD compared with the general population. In addition, patients with SCD may be more susceptible to developing severe disease when acutely infected.¹⁰ The prevalence of chronic hepatitis B infection in sickle cell anemia patients is low in large scale studies from the United States (0 to 3.3 percent seropositivity for HBsAg), reflecting the low prevalence of infection in the general population.¹¹ In parts of the world with a high prevalence of hepatitis B, higher rates of chronic hepatitis B exist in individuals with SCD compared with the general population. Antibodies against hepatitis C virus have been detected in 10 to 20 percent of patients with SCD.^{12,13} The risk of infection is increased in patients who have received multiple transfusions. The rationale was to crudely measure the burden of hepatitis B and C in patients with SCD in urban population of Saudi Arabia in order to give further inputs towards devising safe blood transfusion strategy as well as early detection of hepatitis B/C among those patients. This will help in preventing infection transmission and early referral to gastroenterology for further management of these patients.

Materials and Methods

It was a cross-sectional study and was carried out at department of Internal Medicine, King Salman Armed Forces Hospital, Kingdom of Saudi Arabia. Data was collected for 6 months, from November 2013 to April 2014. Study design was approved by the hospital ethical committee. All patients diagnosed with SCD in their childhood presenting to emergency and/or admitted as inpatient were included in the study. Records were verified in detail and diagnosis of SCD was confirmed where combination of cellulose acetate electrophoresis with citrate agar electrophoresis was used. The diagnosis of hepatitis B and C was established by measuring HBsAg and Anti HCV through 3rd generation Enzyme Linked Immunosorbent Assay (ELISA). Patients who were positive for HBsAg or Anti HCV were referred to gastroenterology department for further management. Total 47 patients of either gender with age more than 15

years who were diagnosed cases of SCD were recruited after fully informed, understood and voluntarily written consents. Patients were excluded who had history of Homo/Hetero Sexual contact, tooth extraction, major Surgery and IV-drug abuse.

Results

Total 47 patients were recruited as per our inclusion criteria. Six (n=6) patients were excluded who could have hepatitis due to other reasons like homo/hetero sexual contact, tooth extraction, major surgery and drug abuse. Data of remaining 41 patients was analyzed. There were 28 males and 13 females with male to female ratio 2.15. Demographic data of study population is presented in table I. Frequency of hepatitis B was found to be 7.32 % (n = 3), while frequency of hepatitis C was found to be 12.2 % (n=5) in our study.

Table I: Demography of the study population

	Number	Mean Age \pm SD (years)
Male	28 (68.3 %)	24.89 \pm 4.58
Females	13 (31.7%)	22.92 \pm 3.53
Total	41 (100%)	24.27 \pm 4.29

Discussion

The overall incidence of liver disease in patients with SCD has not been well established, however, liver can be affected by a number of complications due to the disease itself and its treatment.^{14,15} In addition to the vascular complications from the sickling process, patients with SCD have often received multiple transfusions, placing them at higher risk for viral hepatitis, iron overload, and the development of pigment gallstones, all of which may contribute to the development of liver disease. It is unclear whether cirrhosis was due to the sickle cell anemia itself or to concurrent liver disease acquired as a consequence of multiple transfusions, leading to excessive iron overload and/or chronic hepatitis B or C infection.^{16,17} Frequency of hepatitis B was found to be 7.32 % (n = 3), while frequency of Hepatitis C was found to be 12.2 % (n=5) in this study. The results are concordant with already published data. In order to propose strategies to improve blood safety in sickle cell disease in Mali, Diarra AB¹⁸ conducted a prospective study of 133 patients with sickle cell anemia recruited at the sickle cell disease

research and control center of Bamako from November 2010 to October 2011. Prevalence of viral infections observed at the time of enrolment of patients in the study was 3% and 1% respectively for HBV and HCV. Three cases of seroconversion after blood transfusion were detected, including one for HIV, one for HBV and one another for HCV in sickle cell anemia patients. All these patients had received blood from occasional donors. Le Turdu-Chicot C¹⁹ retrospectively studied the prevalence of anti-HIV-1 and 2, anti-HTLV-I, anti-Hepatitis B and C viruses (HBV and HCV) antibodies, anti-HBV vaccinal coverage, transfused patients and alloimmunizations frequencies among adult sickle cell patients attending the sickle cell center (SCC) of Guadeloupe. Among the studied samples (n = 331) all patients with anti-HCV (n = 9, 2.7%) positive serology had transfusion history. Five patients (1.5%) had an active hepatitis B. Vaccination against HBV efficiently protected 247 patients (74.4%) and 57 had post-hepatitis B antibodies. Hasan MF²⁰ in his study detected antibody to HCV in 10/99 patients (10.10%) with sickle cell disease. Seven of 30 patients (23.33%) who received more than 10 U of packed red blood cells were positive for HCV antibody. Only 3/38 (7.9%) patients with less than 10 U of packed red blood cells in the past were positive for HCV antibody. None of the patients who never received blood transfusion were positive for HCV. Vichinsky EP²¹ reviewed blood component therapy and its risks for sickle cell patients. They found that transfusion acquired infections have shown a marked decrease but still present a major risk. Viral hepatitis transmission is currently low, but at least 10% of adult sickle cell patients are hepatitis C positive, and they often have liver damage. Namasopo SO²² determined the prevalence of HCV infection and determined whether blood transfusion increases risk among 244 SCD patients. 65% had a history of blood transfusion. Among the transfused, five (3.2 %) patients were HCV positive. Among patients with no history of transfusion, one patient (1.1 %) was HCV positive. Risk of HCV was higher among the transfused OR 2.7(CI 0.31-24). Patients who received more than two units were more likely to be HCV positive (p=0.03). Hassan M²³ determined the prevalence of hepatitis C virus antibodies in 150 SCD patients from the Howard University Hospital Center for sickle cell disease between year 1983 and 2001. Antibodies to HCV were detected in 53 patients (35.3%). Thirty nine of 77 patients (51%) who received more than 10 units of

packed red blood cells were positive for HCV antibody, and only 14 of 61 patients (23%) who received less than 10 units of packed red blood cells transfusion were positive for HCV antibodies (P<0.001). None of the 12 patients who never received transfusion were positive for HCV antibody. They concluded that the prevalence of HCV antibody and iron overload is directly related to the number of blood transfusions in patients with sickle cell disease. Lesi OA²⁴ determined the frequency of antibodies to Hepatitis C virus, assessed the role of blood transfusion in transmission of infection and evaluated the clinical implication of anti-HCV seropositivity in 278 SCD patients. The overall anti-HCV prevalence was 5.0% (14/278). Anti-HCV was positive in 7% (5/76) of never transfused compared with 5% (9/202) of previously transfused sicklers, (p = 0.5). Ejiofor OS²⁵ conducted a study among 269 children with SCD attending the paediatrics sickle cell clinic at University of Nigeria Teaching Hospital (UNTH) Enugu, with 136 transfused SCD patients as subjects and 133 age and sex matched non-transfused SCD who served as controls. The results showed an HCV antibody prevalence of 6.6% among the transfused and 5.3% among the non-transfused (controls) SCA patients (P = 0.610). There was positive association between number of transfusions and HCV sero-positivity, such that those who had received 4 or more units of blood had a prevalence rate of more than 50% (P = 0.001). Remesar M²⁶ estimated the prevalence of HCV, HBV and HIV infection in a population of multi-transfused Argentinean patients in a multi center, cross sectional study of 504 patients from national referral institutions in Buenos Aires, who had received more than ten units of blood products in more than two occasions. Among them 35 (6.9%) patients had hemoglobinopathies. Overall prevalence rates of viral markers were: anti HCV antibody 9.3%, anti Hepatitis B core antibody (anti HBc) 4.8% and Hepatitis B surface Antigen (HBsAg) 0.20%. There was a significant statistical association (p < 10(-5), OR =78.8 [29.7-209.7]) between anti HCV antibodies and having been transfused before 1993, when screening blood donors for anti HCV antibodies became mandatory in their country.

Current evidence about hepatitis B/C infection in SCD patients highlights the need to optimize transfusion protocol and their safety in these patients. It may be improved by the introduction of latest technique for detecting the viral genome in the panel of screening tests and a policy of transfusions of blood units only

from regular blood donors. With improved screening techniques, the likelihood of acquiring new HCV and HBV infection with blood transfusion may be significantly reduced. As the current evidence highlights that the prevalence of hepatitis B/C infection in SCD patients is directly related to the number of blood transfusions, patients who get repeated transfusions should be screened for Hepatitis B and C for early diagnosis and early referral to gastroenterology for further management which could result in better outcome in these patients. One study found that in individuals with HCV infection and SCD, the use of standard doses of pegylated interferon and ribavirin was associated with outcomes that were similar to those that have been reported in patients with HCV alone.²⁷ Low-dose intradermal vaccination against hepatitis B is effective and immunogenic in sickle cell patients and may provide a more economical alternative for communities where the cost of vaccination is limiting.²⁸ We recommend effective screening policy for blood transfusions, periodic screening of SCD patients who are on multiple blood transfusions and further large scale studies taking number of blood transfusions as a variable in the study. We also recommend vaccination for HBV in SCD patients and early initiation of therapy for HCV positive SCD patients.

Conclusion

A significant percentage of SCD patients were having hepatitis B and C. Blood transfusion protocol and their safety should be improved by the introduction of latest technique for detecting the viral genome in the panel of screening tests and developing a policy of transfusions of blood units only from regular blood donors. Early detection of hepatitis B/C in transfused SCD patients is also essential. Further large scale studies are needed taking number of blood transfusions as a variable in the study.

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