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HEPATITIS C VIRUS INFECTION IN BETA THALASSEMIA MAJOR PATIENTS UNDERGOING REPEATED BLOOD TRANSFUSION – A STUDY IN SUBDIVISION LEVEL BLOOD BANK CATERING RURAL WEST BENGAL,INDIA.

Pathology

KEYWORDS: Thalassemia major, Hepatitis C virus, blood transfusion.

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ABSTRACT

Conservative management of beta thalassemia major patients with repeated blood transfusion is the cornerstone of therapy. But this bears a significant risk of transfusion transmitted infections (TTIS) including Hepatitis C virus (HCV)-hepatitis. Strict donor selection criteria and good performance of TTI laboratory of blood bank are the two key factors in prevention of HCV infection in thalassemia. The present study was conducted in a subdivision(Health District) level blood bank of rural West Bengal to evaluate seropositivity for iatrogenic HCV infections in thalassemia patients. Seropositivity were 1.75% and 2.08% in the age group of 1-5 years and 6-10 years respectively. The result necessitates all measures to implement "safe blood transfusion protocol" to its maximum.

Hepatitis C virus (HCV) is recognized as the cause of almost all parenterally acquired cases of what was previously known as non-A, non-B hepatitis[1,2]. The virus has not been isolated but was cloned in 1988 using recombinant DNA technology[2]. HCV is a single standard RNA virus, classified as a separate genotypes within flavivirus family[2]. It has six major genotypes and numerous subtypes and quasi species, which may permit it to escape host clinically surveillance[2].

Acute hepatitis C is clinically indistinguishable from other viral hepatitis. Incubation period varies from 2 to 24 weeks (average 7 to 9 weeks)[2]. The clinical illness with insidious onset of jaundice and malaise appears mild compared to hepatitis B and may even be asymptomatic. Only 25% cases are icteric. Persistent Hepatitis C infection develops in 85% of patients after the onset of acute hepatitis C. Chronic infection with hepatitis C virus trends to persist in 50-70% of infected individuals[2,7]. These chronically infected individuals are at a considerable higher risk (10-20%) of developing chronic liver disease, cirrhosis and hepatocellular carcinoma(HCC)[2,7].

Effective therapy to prevent the progression of HCV infection to cirrhosis liver failure or HCC is not yet available for majority of patients[7,8].

The incidence of HCV infection worldwide is not well known, but from the review of published prevalence studies. WHO estimates that 3% of the world population is infected with HCV and around 170 million individuals are chronic carriers at risk of developing liver cirrhosis and liver carcinoma[3]. In many countries, particular population subgroups such as so called voluntary blood donors, have a very high prevalence of HCV infection specially in the developing world[3,4,5].Risk categorization study shows that they are basically professional donors in disguise of voluntary donors and many of them are drug abusers and leader of unsafe life. In the USA, an estimated 4 million people have contracted in the disease, 4 times more than HIV infection4. Approximately 3-4 million new acute infections and about 54000 deaths occur every year all over the world[4,5]. It has also became a leading reason for liver transplantation from another point of view[5]. The annual incidence of HCV infection in South East Asian countries is largely unknown, primarily because over 50% of the infectious cases are asymptomatic. In addition, many symptomatic acute HCV cases are not laboratory confirmed[6]. In India HCV antibodies have been found in 2% of voluntary blood donors[6]. Testing of blood samples from hepatocellular carcinoma cases have shown that 42% of patients in India had markers of HCV infection. A high prevalence of HCV markers have also been detected in patients with chronic liver disease[6].

In India, screening for HCV has been made mandatory for all blood bank from July 1, 1997[6].

Major prevention problem persists in the developing countries. Many of them cannot afford the anti HCV blood test kits and often there are short supply of kits in blood banks. Regarding private blood bank datas are not easily accessible. Responsibility of drug control department is not also properly executed sometimes due to meager staff pattern. On the other side there is always a chance of use of contaminated equipment's for injections and other medical / dental procedure.

With this background knowledge we have planned our study to look into the prevalence of HCV seropositivity amongst thalassemia major patients who are undergoing repeated blood transfusion as a part of their conservative management protocol. We have selected this group of patient population as the are high risk of having TTIS.

Materials and Method: Beta thalassemia major patients registered in the blood bank of a subdivision hospital(Health district) were studies over a period of five years from December 2010 to December 2015. It came to a cohort of 124 patients who got regular blood transfusion from the blood bank. Sporadic dropout were excluded from result calculation.

This cohort of 124 patients were studies after dividing them three groups e.g. Age gr. 1-5yrs, Age gr. 6-10years and age gr. 11-15 years.

To be included in the study, patient had to meet following criteria(Inclusion criteria):

1. HPLC confirmed Beta thalassemia major patients
2. Patients were registered with blood bank of SD hospital for moderate transfusion regimen treatment that aimed at maintaining pre transfusion hemoglobin level at 9 ± 0.5gm/dl
3. Blood transfusion carried out at the hospital by providing packed cell at the rate of 10-15ml/kg body weight of the child.
4. Mostly patients were transfused once in every four weeks with an aim of maintaining pretransfusion Hb level at 9 ±0.5gm/dl
5. All the patients were screened for HIV, HCV, HBV at the time of registration in the study and thereafter periodically every six months.

Exclusion criteria: Patients who had been transfused less than 10 units of blood as a part of their management in our hospital blood bank were excluded from our study.

Study of history and clinical features:A patient information proforma was prepared and filled up in blood bank for every patient. Age at diagnosis, Laboratory reference number for HPLC result, frequency of transfusion, history of jaundice, hepatosplenomegally, awareness of TTIs, records of TTIs screening of blood bank, results of regular screening for TTIs were taken in the patient information proforma.

Tests for HCV antibodies: About 3 ml of blood collected by a vacutenure. serum separated and stored at -20^{0}c till the test for HCV antibodies was performed in a batch. Tests were performed in duplicate for each patient .Tests were performed in batches of atleast 10 cases, every time also running two negative and two positive controls, each in duplicate .A third generation ELISA kit was used for identification of HCV antibodies.

Results:
The result of the present study has been tabulated.

Table 1:Requirement of blood by the thalassemia patients

Age in years	No of cases	Average body weight(kg)	Average blood required ml/kg/year
1-5 yrs	57	13.8	110.0
6-10 yrs	48	20.3	150.0
11-15 yrs	19	31.5	180.0

Table 2: Serology status of HCV infection in thalassemia patients undergoing repeated blood transfusion

Age in years	No of cases	Number of patients becoming seropositive treatment period
1-5 yrs	57	01 (1.75%)
6-10 yrs	48	01 (2.08%)
11-15 yrs	19	Nil

Table 3: comparison of present study with some previous published studies.

Country	Year of publication	Number of patients studied	HCV seropositivity(%)	Referrence number
India	1992	54	11.1	8
India	1993	72	16.7	2
India	2002	50	30	9
Bangladesh	2003	259	12.5	10
Pakistan	2004	60	35	1
Iran	2001	466	15.7	11

Discussion: Regular interval blood transfusion is mandatory for all the thalassemia major patients and it is the cornerstone of conservative management. It seems logical that a lower end point target hemoglobin will ensure a very rational use of blood[1].

The moderate transfusion regimen of 2005 as recommended by Thalassemia International Federation is utilized in our study group with an aim of maintaince of pre transfusion hemoglobin to 9±0.5gm/dl(Table-1)[1,2].

In our blood bank we provided ABO, Rh matched coombs cross matched blood to the patients. However we could not use leucocyte filters for financial constraints.

Transfusion transmissable infection (TTI) screening for all blood units collected in voluntary donation camps and in house collection arena was formidable with our blood bank. Both internal audit and external quality control with random sample survey of true seropositive and seronegative of our blood units in referral centre medical college proved our strong performance status.

However as per literature reviews, multiple transfusion patients are always at a risk of developing TTI including HIV, HBV and HCV[7,8].

In our study with our protocol of TTI testing we have found that in the age group of 1-5yrs, one case became positive for HCV and that constitutes only 1.75% of all the cases of that particular age group(Table-2).

Again in the age group of 6-10 years one patient became seropositive for HCV and that contributed 2.08% of total cases of that age group(Table-2).

We have compared the results of present study with the results of different other studies from our country in different years[2,8,9] and also with the study results published from Bangladesh[10],Iran[11] and Pakisthan[1].(Table-3)

We tried to trace the donor units used in those particular cases but our regular TTI screerning records showed no defect in our process of issuing donor unit of blood.

However a number of other features are also important in transfusion of TTI in thalassemia patients. One important factor is the use and reuse of disposable by unscrupulous elements in the society.

But more important is the riddle of serology in diagnosis of hepatitis C infection. All the Government sector blood bank are still not equipped with detection of HCV-RNA in voluntarily donated blood units, which is the gold standard in establishing a diagnosis of hepatitis C. With all available resources, detection of anti HCV with contemporary Immunoassay is our mode of diagnosis. But this antibody may never become detectable in 5-10% of patients with acute hepatitis C and levels of anti HCV may become undetectable after recovery from acute hepatitis C. Furthermore Non specificity can confound immunoassays for anti HCV, specially in persons with a low prior probability of infections such as voluntary blood donors. Testing for HCV RNA can be used in such settings to distinguish between true positive and false positive cases.

Conclusion: In India, screening of all donated blood units for HCV have been made mandatory in all blood banks from July 1, 1997. But to further reduce the incidence of TTI in patients getting multiple blood transfusion (e.g. thalassemia), health education is of prime importance. All the blood bank should follow donor selection criteria strictly. A serious considerations should be given to history of jaundice and drug addiction in donors. While selecting donors preference must be given to the repeat voluntary donors and young donors without past history of jaundice. Blood camps should be arranged by thalassemia management units in institution of higher studies eg,colleges and universitiesThe thalassemic patients should be encouraged to stick to one thalassemia management centre and blood bank for personalized treatment. Although it is understandable that provision of blood may not be that prompt in every visit. The voluntary blood donor service when augmented, can tremendously improve upon the "safe blood transfusion". So to conclude, in our setup serious attempts have to be made to ensure a safe blood transfusion, so as to cut down the prevalence of HCV hepatitis in multiply transfused thalassemic patients.

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