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Prevalence and Risk Factors Of Viral Hepatitis In Multitransfused Thalassemia Patients From A Tertiary Care Centre, Haryana: A Retrospective Study

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Abstract

Thalassemia is an autosomal recessive disorder characterized by reduced or absent amounts of hemoglobin that leads to severe form of anemia. Iron overload and transfusion-transmitted infections (TTIs) are considered to be the major drawbacks of this therapy and contribute to morbidity and mortality among patients. Globally, hepatitis prevalence rates in thalassemic patients vary between 0.3% to 5.7% for hepatitis B surface antigen (HBsAg)-positivity and 4.4% to 85.4% for anti-hepatitis C antibodies. Hence the present study is conducted to find out the prevalence of viral hepatitis in this subset of population at our Centre so as to access the current situation and evaluate the scope of upgrading the current pre transfusion screening procedures to eliminate the risk of acquiring viral hepatitis by multitransfusion. The present study is conducted to find out the prevalence of viral hepatitis in this subset of population at our center. The current study was performed on a total of 342 subjects of thalassemia major and intermedia which comprised of 228 (66.67%) males and 114 (33.33%) females (Table 1) .129 (37.72%) cases were found to be HCV reactive, 13 (3.8%) cases were found to be HBV reactive, of which 9 were coinfection with HCV.

Keywords: NIL

Introduction

Thalassemia is an autosomal recessive disorder characterized by reduced or absent amounts of hemoglobin that leads to severe form of anemia. Incidence rate is higher in Middle East, South East Asia, Burma and Indian subcontinent. Thalassemia are classified according to the globin that is affected, hence the names *alpha* and *beta* thalassemia. Beta thalassemia may be the most well-known type of thalassemia and is also called Cooley's anemia. Beta thalassemia major (TM) usually causes severe anemia that can occur within months after birth. If left untreated, severe anemia can result in insufficient growth and development, as well as other common physical complications that can lead to a dramatically decreased life-expectancy. Regular blood transfusion therapy remains the main line of treatment .Iron overload and transfusion-transmitted infections (TTIs) are considered to be the major drawbacks of this therapy and contribute to morbidity and mortality among patients. (1)

The probability of acquiring TTIs is related to the probability of being exposed to the infected units of blood which in turn depends on the prevalence of the donors in the population and the number of units transfused. Globally, hepatitis prevalence rates in thalassemic patients vary between 0.3% to 5.7% for hepatitis B surface antigen (HBsAg)-positivity and 4.4% to 85.4% for anti-hepatitis C antibodies [2]. In the context of TTIs, hepatitis C virus (HCV) alone has been described to be responsible for 80%-90% of the cases in thalassemic patients worldwide [3]. More

than 75% of these cases progressed towards chronic hepatitis and 20%-30% of the patients developed cirrhosis.

Accurate estimates of the risk of viral hepatitis in thalassemia population are essential for monitoring the safety of blood supply and evaluating the efficacy of the tests performed as screening procedures. The major concern is due to the prevalence of asymptomatic carriers and blood donations during the window period of Infections. Hence the present study is conducted to find out the prevalence of viral hepatitis in this subset of population at our centre so as to access the current situation and evaluate the scope of upgrading the current pre transfusion screening procedures to eliminate the risk of acquiring viral hepatitis by multitransfusion.

Aim And Objectives

Aim

To assess the prevalence of HBsAg and Anti HCV antibodies in thalassemic patients visiting our centre for supportive therapy.

Objectives

1 To assess the trend of viral hepatitis in thalassemic patients over two decades.

2. To determine the associated risk factors.

Study Design And Methodology

Retrospective observational analysis of prospectively maintained cohort was done over a period of three months from May 2019 to July 2019 in Dept. of Microbiology and Dept. of Paediatric. All consecutive known patients of beta thalassemia major and intermedia diagnosed and registered under thalassemia welfare clinic were included. Patients selected were multiple blood transfusion dependent recipients transfused at least ten units of blood, irrespective of their demographic or clinical category. They were receiving regular transfusion either from Govt. blood banks which are hospital based or private blood banks; in order to maintain the hemoglobin level above 9 g%. These blood banks were accredited by the State Blood Transfusion Council. Patients who were having incomplete records, who were tested positive for HBV and HCV before starting transfusion and who left to follow up were excluded from the study.

Donors of blood and blood products used for transfusion were screened at our institute by using standard donor screening procedures. Serological screening had been done for malaria, Syphilis, HIV, HBV and HCV infection by enzyme linked immunosorbentassay (ELISA). The status of HBsAg and Anti HCV in thalassemia patients is routinely being evaluated every three months at our institute or earlier if presenting with correlating clinical features on follow up. About five ml of whole blood sample is obtained just before packed red blood cells transfusion. It was subsequently allowed to clot and centrifuge for serum preparation for laboratory markers assessment. HBV status was detected by Merilisa HBsAg (direct solid phase microwell enzyme immunoassay, ELISA for the detection of HBsAg in human serum or plasma).HCV status was detected by Merilisa HCV (sandwich format microplate enzyme immunoassay for the detection of antibodies to Hepatitis C virus).The procedure was performed according to manufacturer's instruction.

Information regarding serostatus of the patients was retrieved from their case test results maintained at the Dept. of Microbiology while the patient details were taken from the standard case record database maintained at Dept. of Paediatrics. Patients with seropositivity for HBsAg or Anti HCV were considered cases and compared with patients of Thalassemia receiving transfusion and not developing hepatitis. Complete social and demographic details including age, gender, address, age of thalassemia diagnosis, no of transfusions received, years of receiving transfusion and blood group of the patients noted during their registration were evaluated. Serum investigation like Alanine aminotransferase (ALT), Aspartate aminotransferase(AST), Serum bilirubin, serum protein performed and noted at three months interval were also analyzed.

Since this is a retrospective data, data is represented as mean ± S.D. Categorical data has been analysed using chi-square/Fisher's exact test, whichever was applicable. The continuous data is seen by using student t test or Mann Whitney test whichever was applicable. Further univariate and multivariate logistic regression is applied to find out the risk factors associated with the cases. An appropriate analysis was carried out at the time of data analysis

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(Kaplan-Meier etc). P value ≤ 0.05 was considered significant.

Results

The current study was performed on a total of 342 subjects of thalassemia major and intermedia which comprised of 228 (66.67%) males and 114 (33.33%) females (Table 1) .129 (37.72%) cases were found to be HCV reactive, 13 (3.8%) cases were found to be HBV reactive, of which 9 were coinfection with HCV. The trend of incidence of HBV and HCV in multi transfused thalassemia population over a decade is shown in Figure 1 and Figure 2.The overall incidence of HBV and HCV reactive cases over 9 years show a significant decline .Prevalence of thalassemia with HCV is 40.10%.A significant decline in positive patients has been seen from around 99 cases to few cases. Prevalence of thalassemia with HBV is 4.01%, steep decline from 8 patients to zero patients in the current year was seen.

The mean age of the population was six and half years and age group of 0-10 years (Table 4) reported maximum no of subjects as well as cases of viral hepatitis. B positive blood group was the predominant blood group amongst the study population, HCV reactive cases and HBV reactive cases i.e.138 (40.4%), 40 (36.2%) ,6 (4.34%) (Table 2).Majority of patients of thalassemia only group received blood transfusions received till date in the range of 100-150 while patients who developed hepatitis had reported transfusions in frequency of >450 (Table 3) which was found to be statistically significant.

The results of the characteristics of patients with HBV and HCV infection are summarized in Table 5 and Table 6.A number of risk factors associated with HBV and HCV infection were compared between the HBV, HCV reactive Thalassemic and the control population. The mean age, total serum bilirubin, mean SGPT, mean SGOT levels were higher in HBV reactive cases while male/female ratio and no of patients receiving transfusion > 450 were higher in Thalassemia only population. The associations were not statistically significant. On comparing the parameters between HCV reactive and non reactive thalassemia patients, mean age, mean total serum bilirubin, mean SGOT levels and no of cases receiving transfusions >400 were the parameters significantly higher in HCV reactive cases as compared to non-reactive cases.

Table 1-Distribution of study population and cases according to the sex

	Thalassemia only	Thalassemia with hepatitis	HBV Reactive	HCV reactive
Male	228	99	7	92
Female	114	43	6	37
Total	342	132	13	129

Table 2-Distribution of study population and cases according to the blood group

Blood Group	Study population	HCV reactive	HBV reactive
A+	50	17	2
A-	7	1	1
B+	138	50	6
B-	14	9	0
AB+	27	14	1
AB-	4	1	0

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O+	88	30	3
O-	14	7	0
Total	342	129	13

Table 3 Distribution of study population and cases according to the no of blood transfusion received.

Transfusion Group based on no of transfusions received till date	Thalassemia only patients	HCV Reactive	HBV Reactive
0-50	59	5	2
50-100	1	1	1
100-150	84	11	1
150-200	1	13	1
250-300	22	18	0
300-350	11	8	1
350-400	1	15	2
400-450	21	8	0
>450	0	41	4
Total	200	129	13

Table 4

AGE GROUP(yr)	No of thalassemia only patients	HBV Reactive	HCV Reactive
0-10	85	13	121
10-20	19	0	3
20-30	4	1	3
30-40	1	0	1
HBV		**Chi-square=10.466** **p-value=0.0149 (S)**	**Chi-square=7.981** **p-value=0.046 (S)**

Table 5 Comparison of variables between HBV reactive and non reactive cases

Variable	HBV Reactive	HBV Non Reactive	P value
Sex Male/Female	1.12	11.04	0.317

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Mean Age	8.2	6.1	0.41
Mean Total serum bilirubin <1.2 >1.2	1.71(0.99) 6 7	1.44(1.88) 201 128	0.614 0.11
SGPT Mean <40 >40	102.38(54.57) 2 11	98.86(230.31) 98 231	0.956 0.093
SGOT Mean <56 >56	105.23(71.07) 2 11	89.50 (225.25) 100 229	0.802 0.246
Total Serum protein(mean) <1 >1	7.45(0.77) 0 13	8.58(19.50) 2 327	0.835 0.778
No of cases receiving transfusion>400	2	50	0.919

Table 6 Comparison of variables between HCV reactive and non reactive cases.

Variable	HCV Reactive	HCV Non Reactive	P value
Sex Male/Female	2.486	1.76	0.156
Mean Age	9.4	8.26	1.48
Total serum bilirubin	2.11(2.80)	1.063(0.619)	<0.001
Mean			

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<1.2				
>1.2	56	151	<0.000	
	73	62		
SGOT	140.78(350.67)	59.40(45.26)	<0.001	
Mean				
<40	16	86		
>40	113	127	0.012	
SGPT	157.52(354.79)	63.56(53.805)	0.68	
Mean				
<56	19	81	0.263	
>56	110	132		
Total Serum protein(mean)	9.39(28.510)	8.02(9.86)	0.599	
No of cases received >400 transfusions till date	33	19	<0.001	

Figure 1-Line diagram showing the trends of Hepatitis B positive cases over a decade

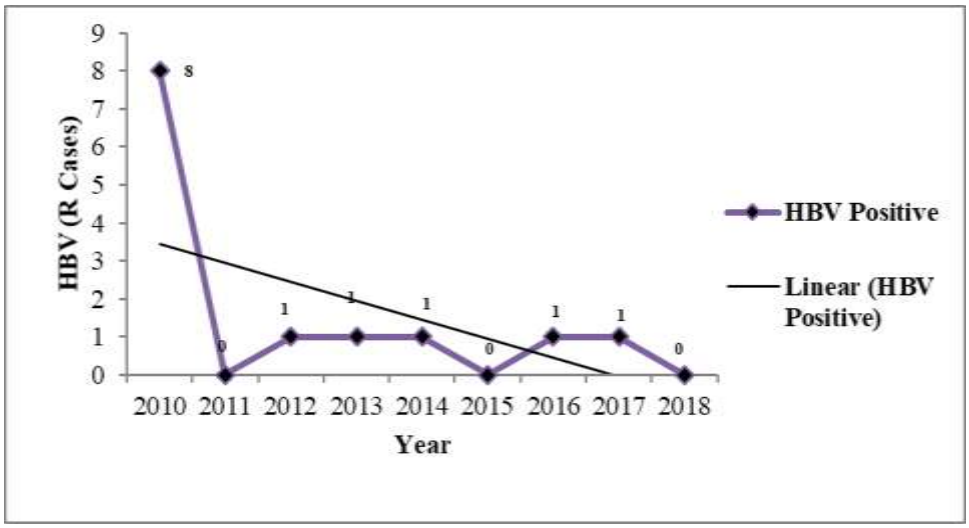

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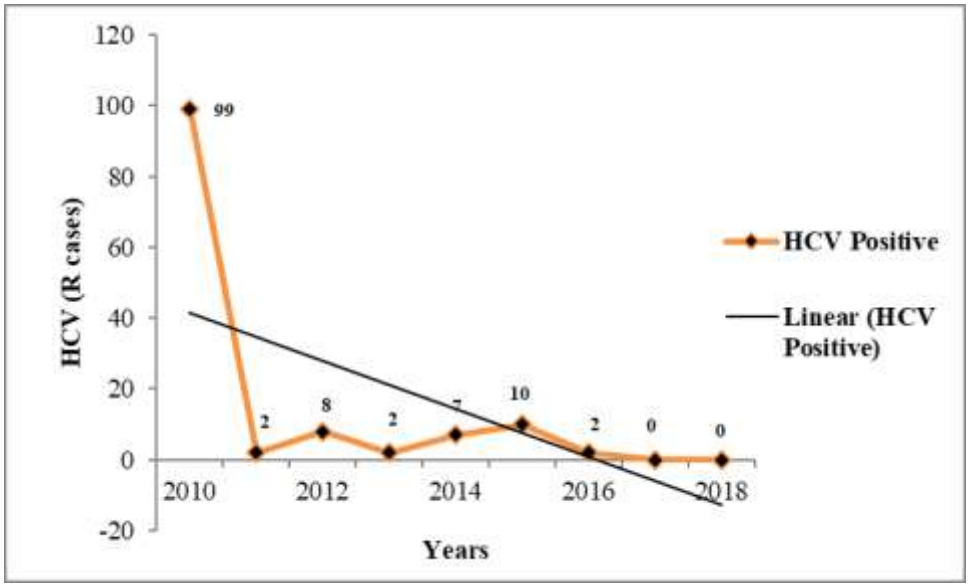
Fig 2 Line Diagram showing trends of Hepatitis C positive cases over a decade from 2010 to 2018



Sr No	Author	No of subjects	Place	Year	Journal	HBV Positivity	HCV positivity
1	Banerjee D et al [4]	200	East zone	1990	Indian J Med Res	22.1	-
2	Choudhary N et al[5]	39	Kolkata	1993 1994 1995	Indian J Med Res	17.9 35.9 69.2	23 30.7 35.9
3	Ghosh K et al [6]	400	West India	2000	Indian J med Res	6	23.9
4	Jaiswal SP [7]	104	Indore	2001	Hepatol Res	56%	21%
5	Singh H [8]	70	Luckhnow	2003	Vox Sanguinis	5.7	20
6	Khakhar V et al[9]	90		2006	Indian J Pathol Microbiol	6.6	-
7	Vidija P et al [10]	200	Jamnagar	2010	Indian J Hematol blood Transfusion	2%	2%
8	Jagdish et al [11]	237	Rajkot	2015	Journal Of Applied Hematology	1.26%	-

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Sr No	Author	No of subjects	Place	Year	Journal	HBV Positivity	HCV positivity
1	Ahmed [12] Kamel Mansour	200	Egypt	2012	Hematol Oncol stem cell Ther	29.0%	40.5%
2	Saqib H Ansari [2]	160	Pakistan	2012	Journal of the College of Physicians and Surgeons Pakistan	1.25%	13.1%
3	Ghufranud Din eta al [13]	95	Pakistan	2014	Asian Pac J Trop Med	3%	49%
4	ZeZe Th Atwa et al [14]	121	Egypt	2016	Journal of Infection and Public health	5%	20%
6	Maysam Yousefi[15]	152	Iran	2016	Int J Infect	-	8.5%
5	Tyng-Yuan Jang et al[16]	140	Taiwan	2017	PLOS ONE	6.4%	45.7%

Discussion

In the present study the Seroprevalence of HBV was 3.8% and HCV 37.72% .This is in concordance to various national and international studies published in which the HBV prevalence ranges from 1.26% to 56% and HCV prevalence ranges from 2% to 49%. The less prevalence of HBV can be attributed to the incorporation of HBV vaccine in the universal immunization programme. In India, mandatory screening for HCV was introduced in 2002 which had led to dramatic decrease in seroprevalence of HCV in post screening era to <1% compared to 1-1.9% in the pre screening era. The high prevalence of HCV seropositivity in our study can be attributed to patients receiving intermittent transfusions at peripheral non standardized centres, HCV infected blood collected during window period and presence of immune variant strains. The present study had maximum subjects and cases as males. This can be due to the higher number of parents bringing their male children for medical attention as compared to the female ones. Maximum viral hepatitis cases had received blood transfusions>450 as compared to subjects who received it in the range of 100-150. Every unit of blood transfused is associated with 1 % chances of transfusion transmitted infections. The prevalence rate of seropositivity increases with the number of transfusions units. Although the mean age of cases was higher as compared to subjects for both HBV and HCV, the association was not significant. In the present study, mean age , mean total serum bilirubin , mean SGOT levels and no of cases receiving transfusions >400 were the parameters significantly higher in HCV reactive cases as compared to non reactive cases. The findings have also been similarly reported by Maysam et al and Ghosh et al. Higher age reflects higher no of transfusions received. [15,6]Table 1 and 2 reflect the various studies done in India and internationally

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which illustrate the prevalence rates at various centres.

In conclusion, we have shown a high frequency of hepatitis C infection in a cohort of thalassemic patients undergoing regular transfusion. It is apparent that late diagnosis and frequent transfusion in peripheral centers contribute to HBV and HCV infection in these patients. However, efforts should be made to identify the real reasons for the reported higher prevalence of HCV in the current study, which might include comparison of ELISA kits of different manufacturers, rigid implementation of quality control measures while testing and use of more specific and sensitive testing for HCV. Furthermore the use of nucleic acid testing or equivalent to that like core related antigen testing should be advocated for testing missing cases at blood bank during window period.

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