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Original Research Article

Correlation of Transfusion Transmitted Infection, Liver Function Test and Serum Ferritin with Multiple Blood Transfused Thalassemic Patients at Tertiary Health Care Centre

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Abstract

Background: Thalassemia is one of the major hemoglobinopathies among the population all around the world. Beta thalassemia major results in severe anemia which needs regular repeated blood transfusion, which leads to iron over load in the body which damages the liver, kidney and other. HIV, Hepatitis B and Hepatitis C are common among multiple blood transfusion patients. So to know the severity of the patient, we retrospectively & prospectively correlated transfusion transmitted infection, liver function test and serum ferritin with multiple blood transfused thalassemic patients. *Methods:* Total 200 subjects were studied. We examined all patients who are clinically and Hematological suspicion of thalassemia and patients diagnosed to have halassemia based on High Performance Liquid Chromatography (HPLC) over a period of 2 years 3 months. The patients groups were evaluated according to the clinicohematological presentation and HPLC study. *Results:* Mean value of serum ferritin in thalassemia major group was found to be significantly increased (4103.21 ± 2786.9 ng/ml). In thalassemia major group, out of 78 cases 4 cases found reactive for HBV and 9 cases found reactive for HCV. *Conclusion:* There is significantly higher seroprevalence of both hepatitis B and C markers was observed among the multi-transfused thalassaemic children. Blood screening has significantly reduced the risk of transfusion related hepatitis B and C. However, the risk is still there. So, the health care providers who are involved in the management and blood transfusion of thalassaemic patients should be more aware of this problem.

Keywords: Performance Liquid Chromatography (HPLC); Beta Thalassemia; Serum Ferritin; Transfusion Transmitted Infection (TTI).

Introduction

Thalassemia is one of the major hemoglobinopathies among the population all around the world. It is a single gene hereditary hemoglobin disorder in human. It has been reported that now a day's approximately 1 out of 14 peoples are carrier of different sub types of thalassemia. Each year about 400000 infant born are with serious hemoglobinopathies and carrier frequency is about 270 million [1].

Beta thalassemia major results in severe anemia which needs regular repeated blood transfusion, which lead to iron overload in the body. Iron overload also damages the liver and kidney secondary to iron deposition in these organs. Following iron chelator over dose acute renal failure or hemolysis occurs which leads to bilirubin production which ultimately metabolized in liver for excretion. In beta thalassemia major clinical jaundice with history of chronic blood transfusion may lead to cirrhosis and hepatomegaly related to significant extramedullary haematopoisis [2,3]. Among the blood transfusion hazards, blood borne viruses which include HIV, Hepatitis B and Hepatitis C virus which may lead to chronic hepatitis, liver cirrhosis and heptocellular carcinoma [4,5]. The management of the iron overload in these patients requires the administration of iron chelator continuously and evaluation of serum ferritin level at regular interval. Serum ferritin is most commonly employed test, as it is simple, cost effective and readily available [6,7].

Materials and Methods

The present study is observational prospective study in which a total of 200 clinically and haematologically suspected cases of thalassemia during the period of May 2015 to August 2017 were selected.

All the patients (OPD and Indoor) who are clinically and Hematological suspicion of thalassemia. Patients presented with previous history of blood transfusion. All patients diagnosed to have thalassemia based on High Performance Liquid Chromatography (HPLC) along with family members of these patients were taken as inclusion criteria.

After consent was taken, 2 ml of venous blood is collected in EDTA bulb and 2 ml in two plain bulbs with all aseptic precautions. Complete blood count performed by using Cellenium three part cell coulter and LFT, KFT were performed by semi automated biochemistry analyzer. Tests for HIV, HBV, HCV, are done by ELISA and serum ferritin by fully automated analyzer.

Samples were run on HPLC machine Bio-Rad variant-II and hemoglobin graph was obtained and diagnosis of thalassemia was confirmed using values of different hemoglobin fractions and retention times.

Maternal/Paternal consanguineous marriage among family members is noted and Family studies of cases was carried out wherever possible, to confirm the diagnosis as family study is effective for centers which do not have facility for genetic analysis. Mother, father, siblings, son and daughter of patient were studied.

Results

In the present study, total 200 suspected cases of Thalassemia were studied by HPLC in Department of Pathology in Tertiary Care Hospital from May 2015 to August 2017.

Total 200 subjects were studied, out of which 150 cases were diagnosed as cases of thalassemia based on HPLC values and remaining 50 subjects show normal pattern by HPLC. These 50 cases were taken as normal control group.

Table 1: Group wise distribution Cases

Group	Diagnosis	No of Cases
A	Beta Thalassemia Major (BTM)	78 (39%)
B	Beta Thalassemia Minor (BTT)	65 (32.5%)
C	Sickel cell-Beta Thalassemia (SBT)	7 (3.5%)
D	Normal	50 (25%)
Total		200

Table 2: Socio-demographic features of cases among all groups in present study (n=150)

	Age wise distribution			
Age (Yrs)	Gr–A (n=78) BTM	Gr–B (n=65) BTT	Gr –C (n=7) SBT	Total
0-10	61 40.67%	23 15.33%	5 3.33%	89 59.33%
11-20	17 11.33%	9 6%	2 1.33%	28 18.66%
21-30	0	20 13.33%	0	20 13.33%
31-40	0	8 5.33%	0	8 5.33%
41-50	0	5 3.33%	0	5 3.33%

Sex wise distribution				
Male	52 66.66%	38 58.46%	4 57.14%	94 62.66%
Female	26 33.33%	27 41.53%	3 42.85%	56 37.33%

Maximum study subjects belonged to 0 to 10 years of age. 62.66% of the subjects were Male and 37.33% were female with M: F ratio 1.6:1. Muslims (38%) was the most common ethnic background among all the groups followed by Buddhism (30.66%) then Hindu (28%).

Table 3: Mean Hematological Parameters of cases among all Groups in present study

Parameters	Group-A (BTM)	Group-B (BTT)	Group-C (SBT)
Hb (gm %)	7.29	10.13	11.2
RBC (million/ mm3)	3.38	4.17	4.35
MCV (fl)	72.01	80.83	75.42
MCH (pg)	22.86	24.09	24.42
MCHC (gm/dl)	29.19	29.61	30.57

- Highest hemoglobin (11.2 gm%), RBC (4.35 million/mm^3), MCV (80.83 fl), MCHC (30.57 gm/dl) was found in Group C and lowest hemoglobin (7.29 gm%), RBC (3.38 million/ mm^3), MCH (22.86 pg), MCHC (29.19 gm/dl) was found in Beta Thalassemia major. Highest MCV (80.83 fl) was found in Beta Thalassemia trait i.e. Group B and lowest MCV (72.01 fl) was found in Beta Thalassemia major.
- Highest hemoglobin (11.2 gm%) was found in Sickle cell Beta Thalassemia i.e. Group C and lowest hemoglobin (7.29 gm%) was found in Beta Thalassemia major.
- Highest RBC (4.35 million/mm^3) was found in Sickle cell Beta Thalassemia i.e. Group C and lowest RBC (3.38 million/mm^3) was found in Beta Thalassemia major.
- Highest MCV (80.83 fl) was found in Beta Thalassemia trait and lowest MCV (72.01 fl) was found in Beta Thalassemia major.
- Highest MCH (24.42 pg) was found in Sickle cell Beta Thalassemia and lowest MCH (22.86 pg) was found in Beta Thalassemia major.
- Highest MCHC (30.57 gm/dl) was found in Sickle cell Beta Thalassemia and lowest MCHC (29.19 gm/dl) was found in Beta Thalassemia major.

Table 4: Average values of LFT & KFT of cases among all groups

Parameters		Gr–A (BTM)	Gr–B (BTT)	Gr–C (SBT)
LFT	SGOT (IU/L)	51.04 ± 28.85	25.23 ± 4.96	18.85 ± 6.96
	SGPT (IU/L)	53.60 ± 35.03	28.49 ± 5.28	22.85 ± 1.86
	S.Bilirubin (mg/dl)	1.27 ± 0.75	0.68 ± 0.19	0.71 ± 0.26
KFT	Blood Urea (mg/dl)	25.54 ± 8.39	20.89 ± 5.20	19.28 ± 5.12
	S.Creatinine (mg/dl)	0.51 ± 0.21	0.54 ± 0.22	0.45 ± 0.19
	S. Ferritin (ng/ml)	4103.21 ± 2786.9	44.62 ± 24.51	-

In the present study mean ± SD values of LFT and KFT parameters of all groups were found to be within normal range.

Mean ± SD value of serum ferritin in Group A were found to be significantly increased (4103.21 ± 2786.9 ng/ml) which may be due to irregular chelation therapy.

History of consanguineous marriage

Out of 150 cases, 49 cases are having History of Consanguinity in family. 28 (57.14%) cases of group A i.e. Beta Thalassemia Major, 20 (40.81%) cases of group B i.e. Beta Thalassemia Minor and 1 (2.04%) case of group C i.e. Sickel cell Beta Thalassemia. Most of the Consanguinity in family was from Muslim community which may be due to variation in geographical distribution.

Frequency of blood transfusion

Beta thalassemia major patients require frequent blood transfusion as a part of therapy. Among all thalassemia major group, mean frequency of blood transfusion were found 25 days and 20 day's for age 0 to 10 yrs and 11 to 20 yrs respectively. Most of cases were transfused at interval of 3-4 weeks. None of the cases from other groups had received any blood transfusion.

Number of Reactive cases for TTI

Beta thalassemia major patients require frequent blood transfusion as a part of therapy. So majority of TTI found in Group A i.e. thalassemia major, out of 78 cases 4 cases found reactive for HBV and 9 cases found reactive for HCV and none of the cases was reactive for HIV. All the cases from Group B and Group C were non reactive for HBV, HCV and HIV.

Discussion

In the present study out of the total 200 subjects, 78 cases were of Beta Thal Major, 65 cases of Beta Thal Trait, 7 cases of sickle – beta Thalassemia and 50 members were normal.

The average age of presentation of beta Thal Major was 7.34 yrs. The average age of presentation of Beta Thal Trait was 20.24 yrs. The average age of presentation of sickle–beta Thalassemia was 10.83 yrs. Out of 150 cases; 94 (62.66%) were male and 56 (37.33%) were female with M: F ratio 1.6:1. Hence Study groups show male predominance.

Vidja, Prakash J., et al. [8] (2011) reported 200 cases of thalssemia major there were 130 males and 70 females and M: F ratio was 1.85:1 with male predominance.

Faruqi Amna, Syed Tousif Ahmed, and Farah Ahmed [7] (2014) in demographic study of thalssemia major found that male predominance. Kumar S et al. [9] (2017) they studied hematological profile of 211 children with congenital hemolytic anemia and reported that there were 59 cases of thalssemia major of which 38 (64.4%) were male and 21 (35.6%) females, M: F ratio 1.8:1, they also reported 30 cases of thalssemia trait which includes 17 (56.6%) male and 13 (43.4%) females, M:F ratio 1.3:1. Study showed male predominance.

Relevant Hematological Parameters

All the cases in studies were presented with sever anemia with reduced RBC, MCV, MCH and MCHC. In present study maen Hb 7.29 gm%, mean RBC 3.38 million/mm^3, mean MCV 72.01fl, mean MCH 22.86 pg and mean MCHC 29.19 gm/dl. Presentation of cases depends upon duration from last blood transfusion and severity of disease (Table 5).

Cases were presented with mild anaemia, normal RBC, reduced MCV, MCH, and MCHC. In present study mean Hb 10.13 gm%, mean RBC 4.17 million/mm^3, mean MCV 80.83 fl, mean MCH 24.09 pg and mean MCHC 29.61 gm/dl (Table 6).

All the cases in the studies were presented with mild to moderate anemia and reduced MCV & MCH.

In present study mean Hb 11.2 gm%, mean RBC 4.35 million/mm^3, mean MCV 75.42 fl, mean MCH 24.42 pg and mean MCHC 30.57 gm/dl (Table 7).

Table 5: Relevant mean Hematological Parameters in Group A (BTM)

Studies	Hb g/dl	RBC Million /mm^3	MCV fl	MCH pg	MCHC g/dl
Rao, Seema, et al. [10] (2010)	5.4	2.4	74.9	23.3	31.1
Faruqi, Amna et al. [7] (2014)	7.9	2.9	79.3	26.9	33.9
Karim, Md Fazlul, et al. [11] (2016)	7.2	-	70	23.8	34.1
Pravin M. Meshram et al. [12] (2017)	4.1	2.31	59	16	27.1
Present study	7.3	3.38	72.01	22.86	29.19

Table 6: Relevant mean Hematological Parameters in Group B (BTT)

Studies	Hb g/dl	RBC million/mm^3	MCV fl	MCH pg	MCHC g/dl
Rao, Seema, et al. [10] (2010)	10.3	5.06	68.6		28.3
Shrivastav, et al. [13] (2013)	10.4	5.38	62.1		30.3
Pravin M. Meshram et al. [12] (2017)	10.1	5.06	66.2		30.0
Present study	10.13	4.17	80.83		29.61

Table 7: Relevant mean Hematological Parameters in Group C (SBT)

Studies	Hb g/dl	RBC million/mm^3	MCV fl	MCH pg	MCHC g/dl
Rao, Seema, et al. [10] (2010)	7.6	3.49	75.2	21.8	29.2
Mukherjee, et al. [14] (2010)	8.99	3.89	68.30	22.76	29.2
Shrivastav, et al. [13] (2013)	7.91	3.62	70.28	22.5	32.1
Pravin M. Meshram et al. [12] (2017)	6.56	2.79	75.5	23.4	31.1
Present study	11.2	4.35	75.42	24.42	30.57

Average values of LFT & KFT

In the present study mean ± SD values of LFT and KFT parameters of all groups were found to be within normal range.

Saral, Nishtha, et al. [15] (2015) found the activities of the liver enzymes in serum (ALT, AST) were significantly higher in β-thalassemic patients as compared to controls, the values were 36.56 ± 22.05U/L in ALT and 40 ± 23.41U/L in AST. They also observed the value of serum bilirubin level as 0.95 ± 0.62 mg/dl.

Karim, Md Fazlul, et al. [11] (2016) studied Liver function test in 54 cases of Beta-thalassemia major patients and found AST and ALT levels as 74.8 ± 21.7 IU/L & 85.5 ± 26.8 U/L respectively. Also found serum creatinine level as 0.4 ± 0.2 mg/dl.

Voskaridou, E., et al. [16] (2006) reported mean serum creatinine as 0.78 ± 0.35 mg/dl and did not mention about blood urea for Sickle Beta Thalassemia.

Average values of serum Ferritin

In the present study mean ± SD value of serum ferritin in Group A were found to be significantly increased (4103.21 ± 2786.9 ng/ml) which may due to irregular chelation therapy. Whereas serum ferritin of all cases in Group B was not performed, however mean found 44.62 ± 24.51 ng/ml in some cases of Group B who were tested. Serum ferritin was not performed in any cases of Group C (sickle Beta Thalassemia).

Bhagat, Sonali S., et al. [17] (2013) found Serum Ferritin level as 3869.4 ± 996.06 (ng/ml) before supplementation of antioxidants and 3703.27 ± 546.3 (ng/ml) in Beta thalassaemia major patients which was a non significant decrease in the levels of serum ferritin. Asif, Mahmood, et al. [18] (2014) found the average values for serum ferritin as 4777.04 ± 13 (ng/ml) for 90 cases of thalassemic patients.

Singh, Dr. Suby et al. [19] (2016) studied 100 cases of thalassaemia major and thalassaemia minor, they observed that majority (28%) of the patients had serum ferritin value between 2001 ng/ml - 3000 ng/ml. The mean and S.D. was observed to be 4160 + 2426 ng/ml.

Blood transfusion

In present study, most of the cases of thalassemia major were transfused at an interval of 3-4 weeks.

Other groups were not transfused because cases were having mild anemia and most of them presented without any complaint.

Mahyar, Abolfazl, et al. [20] (2010) found the minimum and maximum interval between two blood transfusions as 10 and 30 days respectively, with a mean interval of 21.07 ± 5.81 days in beta thalassemia major cases.

Bejaoui, Mohamed, and Naouel Guirat [21] (2013) stated most of the patients of thalassemia major 325/391(83.1%) were transfused at intervals of 3-4 weeks; 51 patients (13%) were transfused at an interval of 5-8 weeks and 15 patients (3.8%) poorly controlled were transfused only in an emergency situation.

Number of Reactive cases for HBV, HCV & HIV:

Beta thalassemia major patients require frequent blood transfusion as a part of therapy. So majority of TTI found in Group A i.e. thalassemia major, In present study out of 78 cases 4 (2.66%) cases found reactive for HBV and 9 (6%) cases found reactive for HCV and none of the cases was reactive for HIV.

Vidja, Prakash J., et al. [8] (2011) observed out of 200 multiple blood transfused beta thalassaemia patients 7% (14/200) patients were infected with TTI. The seroreactivity for HIV was 3% (06/200), the seroreactivity for HBV was 2% (04/200) and the seroreactivity for HCV was 2% (04/200).

Modi D, Rathod GB, Delwadia KN, Goswami HM [22] (2016) tested 93 thalassemic children for anti HIV, HBsAg and anti HCV. They observed that the out of 93 chidren 4 (4.3%) were seropositive for HIV, 4 (4.3%) were seropositive for HBsAg and 19 (20.4%) were seropositive for HCV.

Mittal, Kundan, Pankaj Abrol, and Jaivinder Yadav [23]. (2017) observed the incidence of transfusion transmitted infections increases with increase in number of transfusions. They found 38.5% patients of 10-100 transfusion group, 55% of 201-300 transfusion group, 48% of 30-400 transfusion group and 66.6% of more than 400 transfusion groups to be seropositive for various viral markers. They found 75 patients were reactive for HCV, 5 patients were found positive for HBV. No patient was found reactive for HIV.

Conclusion

With increase number of transfusion chances of transfusion transmitted infections increases, also derangement of LFT, KFT and serum ferritin had been observed in many studies, so laboratory tests like CBC, bilirubin, tranaminase and serum ferritin should be checked prior to regular blood transfusion

Incidence of HIV positivity has decreased due to mandatory screening of all blood bags. Window period can be decreased by using improved diagnostic technology. Donor awareness programme and providing a good questionnaire before blood donation can lead to self-exclusion of high risk donors. Purely voluntary donors are ideal for donation.

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