ORIGINAL RESEARCH PAPER
Volume - 9 | Issue - 6 | June - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

REGULAR VISUAL INSPECTION OF PLASMA & PLATELETS REVEALING UNCONJUGATED HYPERBILIRUBINEMIA IN HEALTHY VOLUNTARY BLOOD DONORS- WHETHER TO TRANSFUSE OR DISCARD?

Pathology

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ABSTRACT

Background: The study was done to ascertain prevalence of unconjugated hyperbiliribnemia in asymptomatic healthy blood donors and review the literature about feasibility of utilizing blood components from those donors. **Materials & Methods:** This retrospective study was done for a period of 3 years. A total of 23,501 blood units were collected and all the units were subjected to mandatory transfusion transmitted screening. All the plasma and platelet concentrate bags which were icteric on visual inspection were subjected tonbiochemical investigations to rule out other causes of hyperbilirubinemia. **Results:** Among 23,501 units collected, 69 units (0.29 %) were icteric on visual inspection. All these units had unconjugated hyperbilirubinemia and tested negative for transfusion transmissible infections. **Conclusion:** As there are no studies to document the safety of the recipients receiving such abnormal colored plasma as well as to document the hazards in its transfusion, the question arises whether to transfuse such units or not. Majority of blood donors, whose plasma and platelets icteric, are aymptomatic. High colored plasma particularly unconjugated hyperbilirubinemia might suggest Gilbert's syndrome or any underlying occult hepatitis infection. Proper guidelines are to be framed about the use and discarding of blood components in these donors.

KEYWORDS

Icterus, Blood component, donation.

INTRODUCTION:

Bilirubin is the end product of heme breakdown. Majority (80%) originates from the degradation of erythrocyte hemoglobin in the reticuloendothelial system; the rest 20% is derived from inefficient erythropoiesis in bone marrow and degradation of other heme proteins (1). An elevated level of bilirubin in blood is termed as hyperbilirubinemia. Normal serum bilirubin concentration ranges from 0.1 - 1.2 mg/dl, most of which is unconjugated (0.1 to 1.0 mg/dl). A bilirubin level of less than 2 mg/dl is generally not accompanied by visible jaundice (2). Jaundice is manifested when equilibrium between bilirubin production and excretion is disturbed. It is clinically evident when the serum bilirubin levels rise above 2.5 mg/dl (3).

Bilirubin, a yellow-orange bile pigment, is the catabolic product of heme metabolism. Approximately 85 percent of the heme moiety comes from the hemoglobin degradation of red blood cells, while the remaining derives from the ineffective erythropoiesis and the breakdown of other hemoproteins such as cytochromes, myoglobin, and catalast. The microsomal heme oxygenase enzyme of the reticuloendothelial system converts heme to biliverdin, which in turn is reduced to unconjugated bilirubin by a second enzyme biliverdin reductase. In liver hepatocytes, unconjugated bilirubin gets conjugated with one or two molecules of glucuronic acid by the enzyme UDP-glucuronosyltransferase (4).Therefore, unconjugated hyper bilirubinemia can result from dysfunction of any of these conjugation steps- Increased bilirubin production, impaired bilirubin uptakeand impaired bilirubin conjugation (5).

Donated blood shows high colored plasma and platelets with mild increase in unconjugated bilirubin level in asymptomatic donors. No guidelines exist, as to whether such blood bags can be issued to patients or should be discarded. This study has been done to find the prevalence of mild hyperbilirubinemia in seronegative healthy donors in our tertiary care teaching hospital in North Karnataka.

MATERIALS AND METHODS:

This retrospective study was carried out in voluntary blood donors who donated whole blood in the department of Transfusion Medicine at a tertiary care teaching hospital in Northern Karnataka from 1st January 2017 to 30th December 2019. The whole blood was collected only from those voluntary donors who were found fit as per standard questionnaire, including medication history, physical examination, and investigations as per Directorate General of Health Services and National AIDS Control Organisation guidelines. Blood (450 mL) collected was separated into various components such as packed red blood cells, fresh frozen plasma, platelet concentrate, cryoprecipitate, as per departmental standard operating procedure.

All bags were mandatorily screened for HIV, HBsAg, HCV, malaria and syphilis. The detection of p24 antigen, anti-HIV-1&2 antibodies, hepatitis B surface antigen (HBsAg), anti-HCV antibodies and antigens was performed using the Genscreen ULTRA HIV Ag-Ab, MONOLISA HBsAg Ultra and Monolisa HCV Ag-Ab ULTRA (Bio-Rad, Marnes-la- Coquette, France) by 4 th generation ELISA .Infectious disease testing by enhanced chemiluminescence method is done using VitrosEciQ (Ortho Clinical Diagnostics, Johnson & Johnson, USA), syphilis by (Tulip Diagnostic) VDRL-Rapid Plasma Reagin (RPR) CARBOGEN and for malaria by SD Bio Standard diagnostic Bioline M P—Ag-PF/Pan.

Plasma bags were observed visually for any abnormalities such as suspended particles and yellowish discoloration before storing them for freezing. Platelet concentrates were visually examined for swirling and discoloration. All plasma and platelet concentrate showing icteric discoloration were included in the study. All these units which were included in the study were subjected to biochemical investigations to detect hyperbilirubinemia. Three milliliters of plasma samples were collected from plasma bag segments in bulbs, and transported (in dark closed box) to biochemistry laboratory for estimation of total and direct serum bilirubin. Biochemical tests were done on (Hitachi-902) automated analyzer and (Bio System-350) semi-automated analyzer. Biochemical investigations revealing total bilirubin of more than 1 mg /dl is taken into consideration. After data collection, data entry was done in Microsoft Excel sheet. Qualitative data were analyzed with the help of frequency and percentage table.

RESULTS:

A total of 23,501 units were collected during the study period. Among those units, 69 units(0.29%) were found to be icteric. The hyperbilirubinemia was predominantly unconjugated. None of these donors had clinical jaundice or history of jaundice. None of the donors gave history of transfusion, hepatitis like illness, or exposure to hepatotoxic drugs or intake of ayurvedic drugs.

Table1: Total icteric units and levels of unconjugated bilirubin

Unconjugated bilirubin (mg/dl)	No of Donors (n =69)	Percentage (%)
1-1.5	16	23.1
1.5-2	28	40.5
2-2.5	15	21.7
2.5-3	03	4.3
3-3.5	04	5.7
3.5-4	01	1.4
4-4.5	01	1.4
4.5-5	00	0
More than 5	01	1.4

Table2: Age group distribution of donors whose component is icteric

Age group of donors (in years)	Number(n =69)	Percentage (%)
19-20	10	14.4
20-25	23	33.3
25-30	09	13
30-35	16	23.1
35-40	07	10.1
More than 40	04	5.7

Out of 69 units of unconjugated hyperbilirubinemia, 28(40.5%) units had bilirubin between 1.5 to 2 mg/dl,16(23.1%) units had bilirubin between 1 to 1.5, mg/dl,15(21.7%) units had bilirubin between 2 to 2.5, mg/dl and1(1.4%) units had bilirubin more than 5 mg/dl(Table1).

Age of the donors ranged from 18 to 60 years. Twenty three (33.3%) donor units were in the age group of 20-25 years, 16 (23.1%) donors were in the age group of 30-35 years, 10 (14.4%) donors were in the age group of 19-20 years (Table2).

All units were from male donors only. All 69 units were negative for TTI screening. As per our study the prevalence of unconjugated hyperbilirubinemia in asymptomatic healthy donors in our population is 0.29 %

DISCUSSION:

Blood transfusion service has tremendous significance in clinical practice, its ultimate goal is to provide qualitative, safe and adequate blood to recipients/patients. Surprisingly, little information is available in regards to incidence of hyperbilirubinaemia in apparently healthy blood donors and its possible implications in blood recipients.
All the voluntary donors included in our study were healthy and questionnaires were asked as per the rules and regulations. There was no recent history of drug intake was present. No past history of episodes of jaundice was present. No family history of recurrent episodes of jaundice or any known hemolytic disorders could be elicited. On clinical examination also, donors were non-icteric. All 69 units were negative for HIV, hepatitis B and C, malaria, and syphilis.

The observations were anlysed for causes of hyperbilirubinemia. Various causes in these cases could be considered are Congenital hyperbilirubinemia, Drug-induced hemolysis, Hemolytic anemia, Primary liver pathology including the various causes of hepatitis. With regards to our study, with no history of hemolytic anemia, jaundice, no anaemia, icterus on clinical examination and high unconjugated bilirubin suggests towards Gilbert's syndrome (GS). This chronic disease is characterized by mild persistent unconjugated hyper bilirubinemia. The patient usually does not manifest this disease until after the second decade and is symptomless and unaware of disease until it is detected by routine laboratory testing for other reasons.GS is the most common hereditary cause of increased bilirubin, and is found in up to 5% of the population. The main symptom is otherwise harmless jaundice which does not require treatment; caused by elevated levels of unconjugated bilirubin in the bloodstream (6). Hence a significant number of our donors with hyperbilirubinemia might be cases of Gilbert's Syndrome. But, further investigations of liver enzymes, LDH has to be done before labeling as Gilbert's syndrome. J. L. Naimane et al. has argued that normal donor with Gilbert's syndrome can donate blood and components which can be utilized to even neonate without any harm (7).

A similar study by Koul et al. was conducted in Kashmir with 1000 randomly selected blood donors. Those with hyperbilirubinemia were further evaluated. Three percent of the blood donors had evidence of Gilbert's Syndrome whereas in our study the prevalence of hyperbilirubinemia in asymptomatic healthy donors was 0.29% only. Mean serum bilirubin levels in their study were 2.64 mg/dl (8). The mean serum bilirubin level in our study was 1.9 mg/dl. No other cause of jaundice could be identified upon investigation.

Arora et al conducted a similar study in Mumbai wherein 25 donors (0.91%) had increased serum bilirubin with a mean level of 2.19 mg dL (9). Jashnani et al. in their study found hyperbilurbinemia in approximately 1.5% of the blood units collected annually. They were in dilemma and felt that guidelines regarding cut off, issuing such units, and discarding of such units need urgent attention from central authorities (10). Amos et al reported that 6.67% of the commercial donors had a total bilirubin greater than 1 mg/dl (11).

A similar study was conducted by Kulkarni et al reported 61 units of icteric plasma out of 7030 donors. Out of these, 50 had Gilbert syndrome with serum bilirubin greater than 1.2 mg/dl and increased unconjugated fraction and all other hematological and biochemical parameters within normal limits.

Existing rules and regulations prohibit issue of blood and components if plasma is abnormal in color. In our blood bank, we are not willing to expose our recipients to any complication related to blood transfusion. As a result, we follow a policy of discarding icteric blood bags including all components when the serum bilirubin is more than 1 mg/dl .Other units which is icteric and when the serum bilirubin is within normal limits, we segregate those units and preserve for quality control and sterility studies and are not utilised for transfusion for the safety of the patient as there were no guidelines regarding usage of those units.

CONCLUSION:

To conclude, until evidence are available to confirm the safety of recipients receiving blood with abnormal colored plasma, we will continue to follow the above said policy. Regulatory agencies of the blood bank should decide whether screening tests of blood components should also include serum bilirubin levels. A reassessment of existing policies and regulations is warranted. It is also recommended that in subjects with no evidence of underlying disease the reason for discard can be classified as “idiopathic unconjugated hyperbilirubinemia” unless its hereditary nature can be documented by appropriate studies.

There is no financial support and sponsorship. There is no conflict of interest among the authors.

ACKNOWLEDGEMENT:

We thank Dr. Col U. S. Dinesh, Registrar,Shri Dharmasthala Manjunatheshwara University for his guidance and support.

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