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## Implications of Hyperbilirubinaemia among Apparently Healthy Blood Donors in Benin City, Nigeria

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### ABSTRACT

The ultimate goal of blood transfusion service is to provide qualitative, safe and adequate blood and blood products to recipients. Transfusion of hyperbilirubinized blood may be detrimental in clinical practice during exchange blood transfusion. This is particularly implicative when blood with poor morphological and biochemical constituents are transfused to neonates and critically ill patients. To determine the incidence and possible implications of hyperbilirubinaemia among blood donors in Benin City, Nigeria, blood samples were collected from 100 Transfusion-Transmissible Infections (TTI) seronegative commercial donors and 20 TTI voluntary donors. These blood samples were analyzed for serum bilirubin (unconjugated and total) concentrations, Packed Cell Volume (PCV) and hemoglobin concentration using the Evelyn's, Mally's, microhaematocrit and cyanometheamoglobin methods, respectively. Out of the 120 blood donors, 8 (6.67%) of the commercial donors had a total bilirubin greater than 1 mg dL<sup>-1</sup> (hyperbilirubinaemic) while none of the voluntary donors had total bilirubin values >1 mg dL<sup>-1</sup>. The Mean SEM serum unconjugated bilirubin, total bilirubin, PCV and hemoglobin of the commercial donors were 0.35±0.02 and 0.50±0.03 mg dL<sup>-1</sup>, 36.4±0.45% and 11.5±2.38 g L<sup>-1</sup>, respectively while the levels in control subjects were 0.05±0.01 and 0.09±0.02 mg dL<sup>-1</sup>, 44±0.64% and 13.2±2.54. Serum bilirubin was significantly higher ( $p = 0.00062$ ) while the PCV and hemoglobin concentration were lower ( $p = 0.00145$  and  $p = 0.00125$ , respectively) in commercial blood donors when compared with voluntary blood donors. Based on our findings, screening of blood for bilirubin level before transfusion is not needful, however serum bilirubin screening of blood to be transfused to neonates and critically ill patients should be considered.

**Key words:** Blood transfusion, asymptomatic jaundice, bilirubin, gilbert's diseases

### INTRODUCTION

The demand for blood and blood products for transfusion in Nigeria is high due to frequent road traffic accidents, blood loss during surgery, blood loss during child delivery (labour) and high incidence of anemia. Blood transfusion is generally an intravenous process of receiving blood products into recipient's/patient's circulation system. Blood product transfusions are indicative in several medical conditions to replace lost components of blood. Despite several researches to provide alternatives to blood transfusion, no perfect alternative has been found (Nwogoh *et al.*, 2011).

In view of this, the goal of any blood transfusion service is to provide qualitative, safe and adequate blood to recipients/patients (Federal Ministry of Health, 2005). There are enormous challenges that impede achieving these goals, these included cases of transfusion transmissible infections, unavailability of voluntary donors, blood products with poor qualities due to morphological and biochemical alterations. Despite these, serious efforts have been made by government, donor agencies and voluntary organizations towards ameliorating these problems (Nwogoh *et al.*, 2011). Blood donations received in hospital services come from three major sources, viz; voluntary, family-replacement and commercial sources (Nwogoh *et al.*, 2011).

A voluntary blood donor is a well-meaning member of the society who donates his or her blood without any inducement for use by a recipient not known to him or her, they are also called voluntary non-remunerated blood donor (Federal Ministry of Health, 2005). A replacement blood donor is a family member or relative of a patient, donating a unit of blood to be used for a specific patient (WHO., 2010; Bates and Hassall, 2010).

A commercial blood donor offers a unit of blood for a fee paid by a contracted hospital vendor. It is a well-established fact that the safest source of blood comes from a voluntary (non-remunerated) donor but because voluntary blood donated to most hospitals in developing nations are grossly inadequate, commercial donation becomes the only available alternative (Van der Poel *et al.*, 2002).

In 1997, the World Health Organization (WHO) set a goal of achieving 100% voluntary donation by the year 2020. As at year 2010, only 57 of 126 countries surveyed had established this standard, regrettably many African nations were not part of the successful ones (WHO., 2011). Many countries are making significant improvement towards achieving the 100% voluntary donor blood procurement but not so much has been achieved in Nigeria. Sadly, only 5% of voluntary donation has been achieved in some major donor centers in Nigeria. The main sources of blood donations in Nigeria are from commercial (remunerated) blood donors, these blood have been found to be generally inferior in terms of safety and qualities when compared to voluntarily donated blood (Agboola *et al.*, 2010).

Commercial blood donation account for 95.3% compared to 4.7% from replacement and volunteer donors in Benin City, Nigeria, this obviously places recipients/patients in some forms of potential health risks (Nwogoh *et al.*, 2011). There exist a general policy of blood screening before utilization, this involves laboratory testing/screening for transfusion transmissible viral pathogens in order to ensure only safe blood are transfused to recipients, these pathogens include Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) and syphilis. This screening may not assure 100% safety to some recipients, particularly neonates who needed exchange blood transfusion. It has been established that some donors might have asymptomatic hyperbilirubinaemia that are not secondary to any of the routine screened transfusion transmission infections (O'Shea *et al.*, 2010). However, laboratory testing for bilirubin is not part of the requirements during pre-donation screening; it may prove useful to some categories of patients who hitherto had poor or immature liver metabolic turn-over.

Blood donated by someone who is hyperbilirubinaemic alters the quality of blood in the recipient's circulatory system. Transfusion insufficient efficacy of any given unit of blood product can result to mild to serious acquired hyperbilirubinemia in neonates and patients on intensive care, thus aggravating some hematological and biochemical status of these recipients (Zubair, 2010). In view of this, we sought to determine the serum bilirubin concentrations of safe blood donors attending a major blood banking facility in Benin City, Nigeria, in order to determine

and compare serum bilirubin concentrations of commercial and voluntary donors. The significance of this study is to determine the need to conduct serum bilirubin testing alongside other screening tests as part of requirements for blood donation during exchange blood transfusion.

## **MATERIALS AND METHODS**

**Study area:** This was a prospective cross sectional study carried out at Benin City. Benin City is located in Edo state of the south-south geographical region of Nigeria.

**Scope of the study:** This study consisted of hundred transfusion-transmissible infection seronegative and consented commercial blood donors who presented for donation at Luli laboratory. Luli laboratory is the main blood products supplier to major public and private hospitals in Benin City, Nigeria. More so, a control group of 20 consented voluntary donors that presented in the University of Benin Teaching Hospital were recruited for this study. Subjects who had prior history of jaundice or family history of hyperbilirubinaemia, diabetic, hypertensive, those less than 20 years and greater than 50 years were excluded from the study.

**Sample collection and preparation:** Samples were collected between February, 2013 and April 2014. Five milliliter of blood was collected aseptically using new sterile syringes. Two milliliter was gently and carefully dispensed into Ethylene Diamine Tetra-amine Acid (EDTA) container while the remaining 3 mL was dispensed into plain vacutainer tubes. The tubes were then appropriately labelled with participants' study number. Sera from these blood samples in plain tubes were separated by allowing the blood to clot at room temperature and centrifuged at 2500 rpm for 10 min. The EDTA anticoagulated whole blood and sera were then separated using clean Pasteur pipettes, transferred into serum containers and stored at 4°C until laboratory analysis. All samples collected were analyzed within 6 h of collection.

**Ethical clearance and informed consent:** This study was conducted in accordance with the Declaration of Helsinki and the protocol was approved by the ethical research committees of Luli laboratory services and University of Benin Teaching Hospital, Benin city, Nigeria. All the subjects gave their written consent to voluntarily participate in the study. All data were analyzed anonymously throughout the study.

## **Laboratory procedures**

**Parameters analyzed included:** Haematocrit by microhaematocrit centrifuge method, hemoglobin estimation by cyanometheamoglobin method and conjugated bilirubin/total bilirubin by Evelyn and Malloys methods, respectively.

**Statistical analysis:** All data collected were analyzed using SPSS version 19 and the Mean±standard error of mean (SE) was derived and student t-test for unpaired means was evaluated to compare the mean of the test group and the control group. Pearson correlation coefficient was also derived between measured variables to access the relationship between. A two sided  $p < 0.05$  at 95% Confidence Interval (CI) was considered statistically significant for t-test to determine the statistical association between the groups.

## **RESULTS**

A total of 120 participants were recruited into this study. Their Blood samples' Packed Cell Volume (PCV), hemoglobin, unconjugated and total bilirubin were determined.

Table 1: Total and unconjugated bilirubin levels, PCV and hemoglobin concentration of participants

Donors	Total Bilirubin (mg dL <sup>-1</sup> )	Unconjugated bilirubin		PCV (%)	Hemoglobin (g L <sup>-1</sup> )
		(mg dL <sup>-1</sup> )			
Commercial	0.50±0.03	0.28±0.02		36.44±0.45	11.5±2.38
Voluntary	0.09±0.02	0.05±0.01		44.00±0.64	13.2±2.54
p-value	0.00062	0.00084		0.00145	0.00125

PCV: Packed cell volume, All values were expressed with Mean±SEM

Table 2: Pearson correlation coefficients of PCV and bilirubin in both the test and control participants

Parameters	Test		Control	
	p-value	r-value	p-value	r-value
PCV vs total bilirubin	0.8408	-0.35	0.5714	-0.135
PCV vs unconjugated	0.9869	-0.32	0.5255	-0.126

PCV: Packed cell volume

Table 3: Pearson correlation coefficients of hemoglobin and bilirubin in both test and control participants

Parameters	Test		Control	
	p-value	r-value	p-value	r-value
Hemoglobin vs. total bilirubin	0.943	-0.07	0.644	-0.110
Hemoglobin vs. unconjugated bilirubin	0.443	-0.78	0.193	-0.304

Out of the 120 blood donors, 8 (6.67%) of the commercial donors had a total bilirubin greater than 1 mg dL<sup>-1</sup> (hyperbilirubinaemic) while none of the voluntary donors had total bilirubin values <1 mg dL<sup>-1</sup>. The Mean±SEM serum unconjugated bilirubin, total bilirubin, PCV and hemoglobin of the commercial donors were 0.35±0.02 and 0.50±0.03 mg dL<sup>-1</sup>, 36.4±0.45% and 11.5±2.38 g L<sup>-1</sup>, respectively while the levels in control subjects were 0.05±0.01 and 0.09±0.02 mg dL<sup>-1</sup>, 44±0.64% and 13.2±2.54 (Table 1). Serum bilirubin was significantly higher (p = 0.00062) while the PCV and hemoglobin concentration were lower (p = 0.00145 and p = 0.00125, respectively) in commercial blood donors when compared with voluntary blood donors (Table 1). There was insignificant negative correlation between serum total bilirubin concentrations and Packed Cell Volume (PCV) in the commercial blood donors and voluntary blood donors groups (p = 0.8408; r = -0.35 and p = 0.5714; r = -0.135, respectively). There was insignificant negative correlation between serum unconjugated bilirubin concentrations and Packed Cell Volume (PCV) in the commercial blood donors and voluntary blood donors (p = 0.9869; r = -0.32 and p = 0.5255; r = -0.126, respectively) (Table 2). Likewise, there was insignificant negative correlation between hemoglobin concentrations and serum total bilirubin concentration in the commercial blood donors and voluntary blood donors (p = 0.943; r = -0.07 and p = 0.443, r = -0.78, respectively) (Table 3). There was insignificant negative correlation between hemoglobin concentrations and serum unconjugated bilirubin concentration in the commercial blood donors and voluntary blood donors (p = 0.644; r = -0.110 and p = 0.193; r = -0.304, respectively) (Table 3).

## 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.

Out of the 120 donors studied, only 8 (6.67%) had a total serum bilirubin concentration greater than 1 mg dL<sup>-1</sup>, they were from commercial blood donors. The increase in serum bilirubin was due to the increase in unconjugated bilirubin which conforms to the study carried out by Arora *et al.*

(2009) and Naiman *et al.* (1996). The study revealed that serum unconjugated bilirubin concentration was significantly high among normal blood donors. Asymptomatic jaundice can be exacerbated following prolonged fasting, surgery and excessive alcohol consumption (Namasivayam *et al.*, 2013).

Unconjugated hyperbilirubinemia is defined by elevated unconjugated bilirubin with normal direct bilirubin. This may be explained by hemolytic anaemia with overproduction of bilirubin from damaged erythrocytes or Gilbert's syndrome whose predominant defect is most likely due to impaired uptake of unconjugated bilirubin into liver cells (Crawford and Gollan, 1993). Hyperbilirubinemia originates from reduced activities of the enzyme glucuronyltransferase which conjugates bilirubin and some other lipophilic molecules (Crawford and Gollan, 1993). Conjugation renders the bilirubin water-soluble, thereafter, it is excreted in bile into the duodenum. Since our subjects don't have prior history of jaundice or family history of hyperbilirubinaemia, it may be asserted that these donors had Gilbert's Syndrome. Gilbert's syndrome otherwise known as "Non-hemolytic jaundice", it is a benign abnormality of bilirubin metabolism that occurs in 7-10% of the population (Radu and Atsmon, 2001). This chronic disease is characterized by mild persistent unconjugated hyperbilirubinemia. The patient usually does not manifest this disease until after the second decade of life, they are usually asymptomatic and unaware of the disease until it is detected by routine laboratory testing for other reasons (O'Shea *et al.*, 2010). Patients who were hitherto not jaundiced but receive such hyperbilirubinaemic blood may develop secondary jaundice, increased bilirubin load and liver overload especially in neonates and critically ill patients (Maxwell and Wilson, 2006).

Findings from our study showed a significant lower PCV and hemoglobin concentration in commercial blood donors than the voluntary donors  $p = 0.00145$  and  $p = 0.00125$ , respectively. This is consistent with previous reports (Jeremiah and Koate, 2010; Adediran *et al.*, 2013; Erhabor *et al.*, 2013). This indicated that commercial (remunerated) donors were more prone to reduction in mean values of PCV, hemoglobin concentration and other red cells biochemical indices. There was insignificant negative correlation between serum total/unconjugated bilirubin concentrations and Packed Cell Volume (PCV) ( $p > 0.05$ ) in the two study groups. Likewise, there was insignificant negative correlation between serum total/unconjugated bilirubin concentrations and hemoglobin concentrations in the two groups ( $p > 0.05$ ). These findings are in consonance with those reported by Koul *et al.* (2006) in Kashmir valley of Indian subcontinent. The study investigated 1000 randomly selected blood donors for serum bilirubin levels, PCV and hemoglobin concentrations. From the study, it was shown that no statistical association existed between correlation of PCV and serum bilirubin, likewise hemoglobin concentration and serum bilirubin levels of voluntary and commercial blood donors.

In a blood bank study conducted in Mumbai, out of the 2734 donors, 25 donors had increased serum bilirubin with a mean level of  $2.19 \text{ mg dL}^{-1}$  which made up of 0.91% prevalence. In our study, the prevalence of hyperbilirubinaemia was 6.67% of the participants studied. We demonstrated a relatively high value could in comparison to previous studies, this could be attributable to sociocultural, feeding behaviors of our subjects and could also be due to the sample size differences between these studies. However, it is worthy to note that there is paucity of information in regards to previous similar studies (Arora *et al.*, 2009).

Based on findings from our study, it can be asserted that commercial blood donors are potential source of hyperbilirubinaemic blood than voluntary donors probably due to differences in their social lifestyles and frequencies in blood donation exercises in a year (Mahida *et al.*, 2008).

No pre-donation signs and symptoms could be used to track mild hyperbilirubinaemia and since the prevalence from our study was relatively high and considering that they were all commercial blood donors, screening of blood to be transfused to neonates and critically ill patients should be considered. However, serum bilirubin screening for recipients other than the aforementioned is not warranted. There is a need to enact policies that discourage commercial blood donation and encourage/sustain voluntary (non-remunerated) blood donors.

It's hereby recommended that more studies should be carried out on larger scale (cohort) in order to make better conclusion on the prevalence and socioeconomic factors that may predispose to hyperbilirubinaemia in Nigeria and other nations for the benefit of clinical utilities. There is need to enlighten healthcare workers on the significance of transfusing neonates and critically ill patients with hyperbilirubinaemic-free blood.

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