Archives of Hematology and Blood Diseases ISSN: 2639-3581

Volume 2, Issue 2, 2019, PP: 21-26



### Is Screening of Blood Donors for G6PD Deficiency and Hemoglobinopathies a Necessity for Transfusion Medicine in India?

**R S Balgir** 

Scientist F/Deputy Director (Senior Grade) & Head, Division of Human Genetics, Regional Medical Research Centre (Indian Council of Medical Research), Chandrasekharpur, Bhubaneswar, Odisha, India. *balgirrs@yahoo.co.in* 

\*Corresponding Author: Dr. Ranbir S Balgir, Scientist F/Deputy Director (Senior Grade) & Head, Division of Human Genetics, Regional Medical Research Centre, Chandrasekharpur, Bhubaneswar, Odisha, India.

#### Abstract

Blood is a highly essential and valuable life saving human tissue. It plays a major role in the supply of oxygen and nutrients to different body parts and subsequently in the collection and transport of gaseous wastes from the body. A blood donor is a person who donates blood to a relative, friend or unknown patient as a voluntary/nonremunerated or remunerated donor, and renders an important human service to the society. The blood of donors is rigorously screened for infection or contamination such as hepatitis, malaria, HIV, and ABO or Rhesus blood group compatibility, etc. prior to transfusion, but no test is being performed for the detection of  $\beta$ -thalassemia, hemoglobin disorders or glucose-6-phosphate dehydrogenase (G6PD) enzyme deficiency in India. This study was designed to find the magnitude of hemoglobin disorders,  $\beta$ -thalassemia, and G6PD deficiency among 208 randomly selected blood donors aged 18 to 45 years in a Blood Bank at a tertiary hospital in eastern coast of southern Odisha. The prevalence of hemolytic disorders such as  $\beta$ -thalassemia trait and G6PD deficiency was observed to be 3.9% in each case, among the blood donors of coastal Odisha. These findings are consistent with those hereditary studies conducted elsewhere. Both these genetic disorders cause severe hemolytic anemia in malaria endemic region of Odisha. Screening of blood donors for hemoglobin disorders including  $\beta$ -thalassemia, sickle cell disease, and G6PD deficiency should be introduced urgently along with other screening criteria in Blood Banks and should be made mandatory prior to blood transfusion in India and in tropical and subtropical countries of the world. This will act as a safe measure and reduce risky complications among recipient patients to mitigate the sufferings of needy persons in India and elsewhere.

**Keywords:** Blood donor screening, Transfusion medicine, Hemoglobin disorders, G6PD Deficiency, Hemolytic anemia, Coastal Odisha, India.

### **INTRODUCTION**

Blood is an essential component of our body. It is a connective tissue fluid that plays a major role in transport of oxygen and nutrients to various parts such as tissues, organs, and systems of the body. It is impossible for a person to survive without blood. A blood donor is a person who donates blood to Blood Bank as a relative of a patient or friend as nonremunerated donor or as remunerated donor, or as a voluntary donor and renders an important service to the needy society. Therefore, blood is a highly essential for life saving, and valuable human tissue. According to WHO Report [1], the blood donors are classified into three groups: a). Family or replacement low risk donors, are those who supply the blood to a patient from within the family or the community. They are not paid donors, but sometimes may be given money or some other form of payment by the patient or by the relatives. This form of donation is advantageous because they meet the need of blood in emergency and they could become voluntary donors after realizing the importance of blood donation. b).

Paid commercial or professional donors who receive money or other rewards in exchange. c). Voluntary or non-remunerated donor who donates blood, plasma or other blood components at its own free will and receives no payment for it.

The donated blood of these donors is rigorously screened for any sort of infection or contamination such as hepatitis, malaria, HIV, and ABO or Rhesus compatibility, etc. but to the best of our knowledge, no test is performed for the detection of hemoglobinopathies (including  $\beta$ -thalassemias) in India or elsewhere in tropical and subtropical countries of the world where malaria and hemoglobin disorders are rampantly prevalent. This unscreened blood (for hemoglobinopathies) sometimes with β-thalassemia or sickle cell disease or trait, when transfused to a normal patient is no way advantageous because nearly half of the donated blood of such subjects contains the abnormal hemoglobin, β-thalassemia, or glucose-6phosphate dehydrogenase (G6PD) enzyme deficiency containing cells. The life span of such donated red blood cells is reduced from the normal range (90-120 days) and the hemolysis occurs rapidly.

Hemoglobinopathies or hemoglobin disorders are the monogenic disorders of blood, posing a major genetic and public health problem, and most commonly encountered in Southeast Asia and in the Indian subcontinent [2]. Of the several abnormal hemoglobins so far identified [3], there are three abnormal variants sickle cell (Hb S), hemoglobin E (Hb E) and hemoglobin D (Hb D), which are predominantly prevalent in India. There are regional variations for these structurally variants of hemoglobin; the cumulative allele frequency for these variants in different parts of India has been found to be 5.35% [4]. The average allele frequency of sickle cell and hemoglobin D has been observed to be 4.3% and 0.86%, respectively with hemoglobin E constituting 10.9% in North Eastern region of India [4]. The sickle cell disease is wide spread in tribal as well as nontribal communities especially in the Central-Eastern India. With a prevalence range of 3-17%, the  $\beta$ -thalassemia is prevalent throughout India [3]. Therefore, hemoglobinopathies are a huge genetic burden and pose a major public health care challenge in India.

In view of the above scenario of blood donations and high prevalence of hemoglobinopathies including  $\beta$ -thalassemia [5,6] and G6PD deficiency [7,8] in India,

this study was designed with an objective to find the magnitude of prevalence of hemoglobinopathies and G6PD enzyme deficiency among the blood donors at a Blood Bank in a tertiary hospital in Eastern coast of Odisha, India.

### **MATERIALS AND METHODS**

For the present study, blood samples were collected from blood donors attending the Red Cross Blood Bank of MKCG Medical College and Hospital, Berhampur, Odisha and were analysed for screening of hemoglobinopathies and glucose-6-phosphate dehydrogenase (G6PD) enzyme deficiency at the Department of Human Genetics, Regional Medical Research Centre, Bhubaneswar (Odisha) during the period from May to October 2004. A total of 208 randomly selected blood donors aged between 18-45 years were included in study. They were both replacement and voluntary healthy blood donors. Blood Donor Selection criteria were used as prescribed in WHO guidelines[1] and physical examinations were done by a medical doctor.

A portion (2-3ml) of donated blood was collected in EDTA containing vials and transported under wet ice cold conditions to Human Genetics Laboratory at Bhubaneswarforscreeningofhemoglobinopathies and  $\beta$ -thalassemia syndrome. Laboratory investigations were carried out following the standard procedures after cross checking for quality control from time to time. Hematological parameters were studied by using an automated Blood Cell Counter (Model-MS4, Melet Schloesing Laboratories, Cergy-Pontoise Cedex, France).

The sickling test was performed by using 2% freshly prepared sodium metabisulphite solution as reducing agent for the presence or absence of sickle cell hemoglobin [9]. The routine hemoglobin lysate electrophoresis was carried out on cellulose acetate membrane (CAM) in Tris-EDTA-Borate buffer at pH 8.9 and quantification of A<sub>2</sub> fraction of adult hemoglobin was done by elution method [9,10]. The value more than 3.5% of A<sub>2</sub> fraction of adult hemoglobin was taken as cut off point for determining the  $\beta$ -thalassemia trait. Those individuals having the very high hemoglobin A<sub>2</sub> value, i.e. more than 10% were suspected to have Hb A<sub>2</sub> plus Hb E; and the test was confirmed by the investigations of other family members. Estimation of fetal hemoglobin was done according to technique described by Weatherall [10].

The diagnosis of sickle cell- $\beta$ -thalassemia was based on the findings of hemoglobin (Hb) A, F, S and A<sub>2</sub> on electrophoresis under alkaline pH, elevated HbA<sub>2</sub> levels (>3.5%). All the doubtful cases were further subjected to hemoglobin variant analysis for detecting any discrepancy (made for Bio-Rad Diagnostics, Hercules California, USA).

The G6PD enzyme deficiency was detected using dichlorophenol indophenol dve (DCIP) as described

by Bernstein [11], and subsequently confirmed by those of Beutler and coworkers [12].

### RESULTS

Out of 208 blood donors who were screened for hemoglobinopathies and  $\beta$ -thalassemias in the coastal belt of Odisha state, the majority (28.8%) of them (Table 1) were young people (21-25 years age group), followed by 26-30 years age group (23.1%), and between 36-45 years (19.2%).

Age in years	No.	Percentage
18-20	16	7.7
21-25	60	28.8
26-30	48	23.1
31-35	28	13.5
36-40	40	19.2
41-45	16	7.7
Total	208	100.0

**Table 1.** Distribution of blood donors in different age groups.

The caste-wise distribution of these blood donors showed that the majority belonged to general castes (42.3%), followed by the other backward castes (36.5%), and scheduled castes (13.5%). The frequency of blood donors in scheduled tribes was very low **Table 2**. Distribution of blood donors in different castes

(7.7%) (Table 2). This shows a general trend that the tribals are very scared of and reluctant to donate their blood for fear of weakness or perhaps the evil spirit may adversely affect their health.

**Table 2.** Distribution of blood donors in different caste groups.

Caste Groups	No.	Percentage
General castes	88	42.3
Scheduled Castes	28	13.5
Scheduled Tribes	16	7.7
Other Backward Castes	76	36.5
Total	208	100.0

Regarding prevalence of hereditary hemolytic disorders among the blood donors of coastal Odisha,  $\beta$ -thalassemia trait and G6PD deficiency was observed to be 3.9%, respectively in each category, in coastal

Odisha (Table 3). More than 90% of the total blood donors were normal healthy persons. Both these genetic disorders cause hemolytic anemia in malaria endemic region of Odisha.

Table 3. Distribution of	of blood donors in	relation to h	hemoglobinopathie	s and G6PD deficiency.

Hemoglobinopathies/Diagnosis	No.	Percentage
Normal	192	92.2
β-thalassemia trait	8	3.9
G6PD Deficiency	8	3.9

The hematological picture of the blood donors including the carriers of  $\beta$ -thalassemia major and G6PD deficiency in coastal Odisha is presented in

Table 4. The red cell indices also showed the normal status of the blood donors in Odisha as was apparently expected.

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Hematological Indices	Normal (N=192)		β-Thalassemia Trait (N=8)		G6PD Deficiency (N=8)	
	Mean	SD	Mean	SD	Mean	SD
Hb (g/dl)	13.28	1.90	12.45	2.05	13.05	4.03
RBC (x10 <sup>3</sup> /µl)	5.25	1.11	6.10	0.42	5.26	1.36
MCV (fl)	85.36	5.27	67.45	6.43	87.95	3.32
MCH (pg)	27.24	3.75	20.20	2.12	27.30	4.38
MCHC (g/dl)	32.81	2.25	30.00	0.28	32.30	0.00
Hb A <sub>2</sub> (%)	1.90	0.47	5.10	0.56	1.60	0.42
Hb F (%)	0.50	0.22	0.50	0.14	0.60	0.14

Table 4. Comparison of hematological indices between normal and disease group blood donors.

SD= Standard Deviation

### **DISCUSSION**

It is surprising to know that out of 208 blood donors screened for hemoglobinopathies including β-thalassemia and G6PD deficiency at Red Cross Blood Bank of MKCG Medical College and Hospital, Berhampurduring May to October 2004, the prevalence of both β-thalassemia trait and G6PD deficiency each was recorded to be 3.9% which was moderately high and may cause clinical complications among blood recipients. None of the cases were found to have either sickle cell anemia or sickle cell-β-thalassemia although these disorders are commonly encountered in coastal Odisha state [5, 6, 8]. Blood donors are not screened either for hemoglobinopathies or G6PD deficiency before taking the blood which may lead to complications and exaggerations to the recipient. It becomes very important in those localities or regions where the high prevalence of hemoglobin disorders and G6PD deficiency exist [5, 6, 8]. If the blood of a person having abnormal hemoglobin, β-thalassemia trait or G6PD deficiency is transfused to a normal person, the life span of the red blood corpuscles (RBC) being short (less than 120 days), leads again to anemia with the result the very purpose of blood transfusion is being defeated. This shows the importance and necessity of donor blood screening for hemoglobinopathies and G6PD deficiency before collecting and transfusing the blood to the recipient patient.

The blood is screened for HIV, hepatitis, malaria, ABO and Rhesus blood group compatibility, etc. as per WHO guidelines [1]. However, it is not screened for hemoglobinopathies or G6PD deficiency neither in the state of Odisha nor in India or elsewhere in the world. Several studies have shown the blood donors suffering from various genetic disorders as carrier or trait form [13, 14]. These abnormalities may be sickle cell trait [15] or  $\beta$ -thalassemia minor [16, 17] or G6PD deficiency [18] among the blood donors. Fabritius and coworkers [14] showed sickle cell trait (7.75%), Madan and coworkers [18] recorded G6PD deficiency (1.3%), and Jain [16] presented  $\beta$ -thalassemia trait (2.35%) and Meena and coworkers [17] reported (1.58%) among the blood donors. The findings of the present study (Table 3) are consistent with the above mentioned studies. Thus, it is concluded that donors' blood should be screened for at least above mentioned hemolytic disorders in India where they are highly prevalent prior to the blood transfusion.

It is a pity that on certain situations/occasions the blood bank authorities in India in some cases ask to donate the blood for replacement to the carrier parents or siblings (who share defective genes) of the β-thalassemia major or homozygous sickle cell disease patients and who frequently require blood transfusions. This is not justifiable because the parents of all full blown cases of either β-thalassemia major or homozygous sickle cell disease are the carriers of defective genes, that is, they do have the defective blood with shorter or limited span of RBCs life. Therefore, it is not advisable to insist the carrier parents/siblings to donate the blood for replacement them-selves unless there is an acute shortage of blood or emergency situation; however, they may be requested to bring either healthy friends or other relatives for donation of blood for replacement either as voluntary donor or as donor on payment basis. This will serve the purpose of the blood bank as well as at the same time serve the requirement of the needy patients.

It should be remembered that the hemoglobinopathies including  $\beta$ -thalassemia and G6PD deficiency have probably evolved in the world to counter the menace of Plasmodium falciparum malaria in highly endemic geo-ecological regions of the world including India [19]. The indiscriminate use of anti-malarial drugs against malaria can cause acute hemolytic anemia, even fatal also in patients suffering from G6PD deficiency [19, 20]. Thus, a caution for use of antimalarial drugs in patients suffering from hemoglobinopathies including  $\beta$ -thalassemia and G6PD deficiency is advisable.

It is suggested that screening of blood donors for hemoglobinopathies including  $\beta$ -thalassemia, sickle cell disease, and G6PD deficiency should be introduced along with other screening criteria of the Blood Bank and should be made mandatory prior to blood transfusion especially among the  $\beta$ -thalassemia major or homozygous sickle cell disease patients in India. This will also reduce or mitigate the sufferings of affected needy patients in the vulnerable at risk communities in India.

### **CONCLUSIONS**

Screening for hemoglobinopathies including  $\beta$ -thalassemia, sickle cell disease, and G6PD deficiency of blood donors should be introduced in the screening protocol of Blood Banks and should be made mandatory prior to blood transfusion in India. This will reduce complications risk among the recipient patients and help mitigate the sufferings of needy persons in India.

### **ACKNOWLEDGEMENTS**

Author is grateful to Dr. V. M. Katoch, Secretary, Department of Health Research, Government of India and Director General, Indian Council of Medical Research, New Delhi for providing the necessary research facilities and the subjects for their kind cooperation. Thanks are also due to Mr. R. K. Mishra, Laboratory Technician for laboratory support during the study.

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**Citation: R S Balgir.** Is Screening of Blood Donors for G6PD Deficiency and Hemoglobinopathies a Necessity for Transfusion Medicine in India?. Archives of Hematology and Blood Diseases. 2019; 2(2): 21-26.

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