



Research Article

Differential Rheology Among ABO Blood Group System In Nigerians

O.I. Ajayi* O.O. Ekakitie**, O.C. Okpalaugo*

Departments of Physiology, *University of Benin, Benin city and **Federal University Ndufu-Alike Ikwo, Abakiliki, Nigeria

Keywords:

Hemorheology,
Deformability, Plasma
Viscosity, Transit time,
antigenic biochemistry

ABSTRACT

Background: ABO blood groups have been reported to have rheological significance and association with different disease conditions. The non-O blood groups (A, B, and AB) have shown more susceptibility to arterial and venous thrombotic diseases with no rheological delineation. The determinants of these blood groups are based on the presence or absence of the inherited antigenic substances on the erythrocyte membrane which are responsible for the alterations in membrane and cytoskeletal properties that could affect the rheology of blood. This study was therefore aimed at ascertaining how the varying membrane biochemical antigenic architecture affects the erythrocyte's rheological properties and that of the whole blood. **Methods:** A total of 138 young healthy subjects were studied; they comprised 40, 38, 50 and 10 subjects divided into blood groups (A, B, and O and AB) respectively. Hemorheological parameters such as Relative plasma viscosity (RPV), Hematocrit (HCT), Plasma Fibrinogen concentration (PFC), White blood cell count (WBC), Red blood cell count (RBC), Platelet count, Hemoglobin concentration (Hb) and Erythrocyte deformability (ED) were analyzed. The transit time model (the higher the transit time, the lesser the deformability) was used in analyzing RBC deformability. **Results:** We observed that blood group AB had significantly higher values of PFC, RPV and Platelet counts but significantly lower transit time ($p < 0.05$, respectively) when compared with other blood groups. The transit times were in the order of B>A>O>AB ($p < 0.05$, respectively). **Conclusion:** In conclusion, blood group AB seems to have a positive advantage of better RBC deformability despite its comparatively high RPV. This shows that hemorheological variations exists amongst the ABO blood groups and the red cell antigenic biochemistry may be a determinant of their membrane mechanical properties. Also, a slight increase in Plasma Fibrinogen Concentration seems to have a significantly profound effect on plasma viscosity and indeed RBC deformability via transit times.

© Copyright 2015 African Association of Physiological Sciences -ISSN: 2315-9987; e-ISSN: 2449-108X All rights reserved

INTRODUCTION

The rheological property of blood can be evident in its viscosity which is affected by packed cell volume, plasma viscosity, red cell aggregation and red cell deformability with plasma viscosity primarily depending on the concentration of plasma proteins especially, fibrinogen (Lewis, 2002). Deformability is

an intrinsic cellular property of erythrocytes determined by geometric and material properties of the cell membrane (Chien, 1987). The fluidity of blood is thus determined by the rheological properties of the plasma and cellular phases and by the volume fraction (hematocrit) of the cellular phase (Oguz and Herbert, 2003). In humans, Red blood cells (RBCs) are the most prevalent types of cells in blood and are the major determinants of the flow property of the whole blood which is increasingly sensitive to hematocrit alterations (Chien, 1975; Cokelet, 1987; Gunasekaran and Mehmet, 2003).

The RBC membrane includes the lipid bilayer and its associated proteins with an underlying cytoskeleton (Aleksander and Paul, 2005). RBC membrane variability which is concurrent with the ABO blood group system is effectuated by the presence or absence

Address for correspondence:

E-mail: olutayo.ajayi@uniben.edu

Tel: +2348037112749

TABLE 1: Some hemorheological parameters (Means \pm SEM) measured in the different ABO blood groups.

Parameters	BLOOD GROUP			
	A	B	O	AB
PFC (g/l)	2.36 \pm 0.14	2.49 \pm 0.20	2.38 \pm 0.12	3.22 \pm 0.2
WBC count ($10^3/\mu\text{l}$)	4.72 \pm 0.27	5.34 \pm 0.45	4.95 \pm 0.29	5.3 \pm 0.54
RBC count ($10^6/\mu\text{l}$)	4.58 \pm 0.15	4.70 \pm 0.13	4.52 \pm 0.15	4.53 \pm 0.40
HgB conc. (g/dl)	12.54 \pm 0.37	12.94 \pm 0.37	12.84 \pm 0.44	11.56 \pm 0.93
HCT (%)	38.51 \pm 0.97	38.6 \pm 1.15	37.85 \pm 1.26	36.32 \pm 3.30

of specific antigenic markers on the red cell membrane specifically on the Band 3 proteins which is the most abundant integral protein of the RBC membrane upon which the ABO typifications are anchored (Fakuda and Fakuda, 1981; Cartron, 2008). The ABO antigen is a carbohydrate based structure which are expressed on the surface of red cells specifically on the band 3 and Glycophorins (Cartron, 2008). Band 3 comprises of 25% of the total membrane and has a structural and transporter role; it supports a number of RBC antigens and is important for maintaining the flexibility of RBCs. It also has a role in anion exchange as it exchanges Cl^- for HCO_3^- , thus removing CO_2 from tissues (Embury *et al.*, 1984).

Experimental evidence so far has not shown decisive copula between ABO red cell varying membrane properties and its rheological significance; however, previous studies have established alterations in hemorheological parameters under pathological conditions (Mohandas and Gallagher, 2008; Parthasarathi and Lipowsky, 1999.). Case-control studies have also implicated the non-O (A, B and AB) blood groups to be independently associated with venous thromboembolism (VTE) (Jenkins and O'Donnell, 2006 and Ohira *et al.*, 2007). In furtherance to these reports, this study was designed to ascertain if hemorheological disparity exist amongst the different ABO blood groups as it may provide possible explanation for prior findings especially in ABO differential disposition to some cardiovascular diseases.

METHODS

Subjects:

The A total number of 138 subjects were randomly selected and enrolled for this study. They were normal healthy individuals with ages between 18-40 years. They comprised of 40, 38, 50 and 10 subjects divided into blood groups (A, B, and O and AB) respectively.

Specimen collection:

Ten milliliters (10ml) of blood was collected from cubital vein and divided appropriately into 0.5ml of 3.8% sodium citrate in a plastic containers and Ethylene Diamine Tetra acetic acid (EDTA) plastic containers. The blood collected into sodium citrate plastic tube was centrifuged immediately and the plasma separated and stored into stopper tubes and used within 3 hours of collection for plasma fibrinogen concentration (PFC). The EDTA blood sample was used for red cell deformability, RPV, HCT, PFC, WBC count, RBC count, Platelet count and Hb concentration.

Laboratory Analysis:

RBC Deformability: The Transit time model. The EDTA blood samples were spun to separate plasma from whole blood. HCT was adjusted to 30% with saline – this is to equate the population of red cells in each group and sample. Their transit times (sec/ml) through tiny pores ($5.0\mu\text{m}$) were recorded as a function of erythrocyte deformability.

PFC was analyzed using the Gravimetric Assay Method (Mackie and Machin, 1989). RPV was determined using the Method of Reid and Ugwu, (1987) while automated Hema-Analyzer was used to estimate HCT, WBC count, RBC count, Platelet count and Hb concentration.

RESULTS

There were no statistically significant differences observed between WBC count, RBC count Hb concentration and HCT ($P > 0.05$, respectively) while PFC exhibited a significant increase ($P < 0.05$) in Blood group AB compared to other blood groups. Fig. 1 compares the RBC deformability of the different blood groups. Transit time (a measure of RBC deformability) for blood group B was significantly higher ($P < 0.05$) when compared with blood group O and AB but no

significant difference was observed when the transit time for A and B where compared ($P>0.05$).

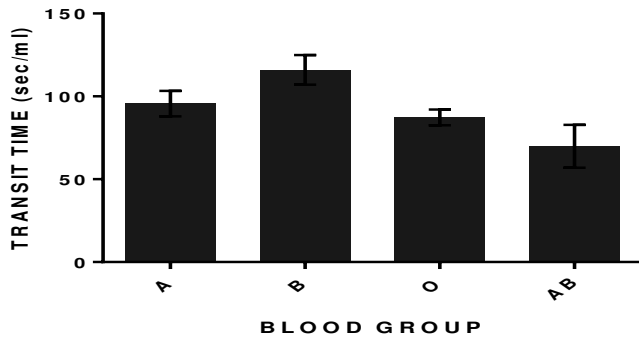


Fig. 1
RBC deformability (Means ± SEM) in different blood groups

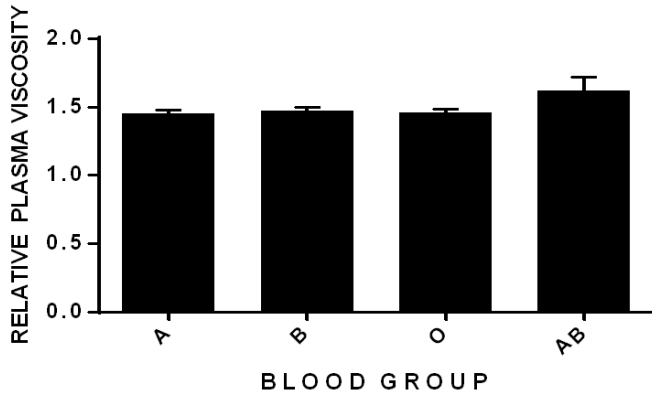


Fig. 2
Relative plasma viscosity (Means ± SEM) in different blood groups

The relative plasma viscosity for the different blood groups are presented in Fig.1. RPV for blood group AB was significantly higher ($P<0.05$) when compared with other blood groups.

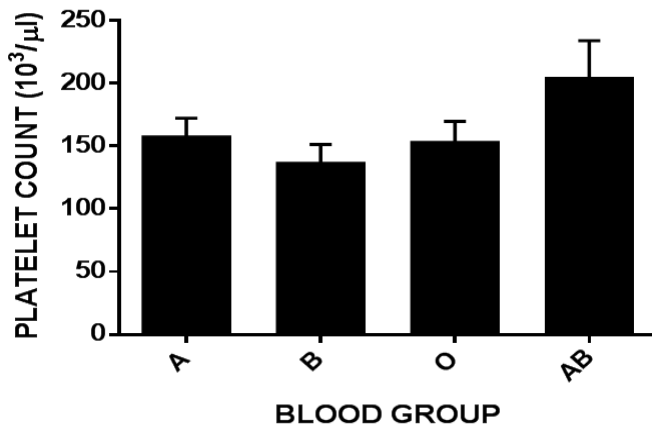


Fig. 3
Platelet count (Mean ± SEM) for the different blood groups

Fig. 3 compares the Platelet count (Mean ± SEM) for the different blood groups. The platelet count was significantly higher in blood group AB when compared with blood group B ($P<0.05$). No significant difference was observed when compared with other blood groups ($P>0.05$).

DISCUSSION

The role of under-membrane structure in regulating erythrocyte shape and deformability have been well reported and the flow properties of blood suspension are influenced by both red blood cell deformation and aggregation. In investigating hemorheological variations amongst the different ABO blood groups, emphasis was on the RBC deformability, as rigidified forms of erythrocytes has been postulated to produce abnormal cell-endothelial interaction, blocking capillary blood flow and inhibiting capillary exchange at important areas resulting in abnormal microcirculation and acute organ dysfunction (Oguz and Herbert, 2003).

In this study, we have demonstrated significantly higher transit time in blood group B ($P<0.05$, respectively) than blood groups O and AB. There was no significant differences ($P>0.05$) observed between A and B. The transit times recorded were in the order of $B>A>O>>AB$. This indicates a faster deformability function of Group AB compared with the rest. The exact mechanism behind this observed difference is not fully understood. It is plausible however, to relate the viscoelastic nature and membrane properties of the B red cells which contains D-galactose (with a molecular weight of 186.156), with this observation; both theoretical and experimental evidences are suggestive of a critical role for the spectrin-based skeletal network in determining membrane elasticity, the precise structural basis of the effect remains uncertain (Walensky *et al.*, 2003; Bennett, 1989; Bennett and Baines, 2001; Mohandas and An, 2006). The binding of spectrin to various membrane complexes play a key role in regulating membrane mechanical function (Manno *et al.*, 2002; An *et al.*, 2005).

The reduced deformability in Group B and the efficiency of blood group AB could therefore be due to the influence of the biochemical composition and property (composed of a terminal D-Galactose and N-acetyl Galactosamine) of the AB antigen on the functionality of the Band 3 proteins and its complex adjoining relation to spectrin. It is interesting therefore to note that, decreased deformability in group B indicates a reduced ability for oxygen delivery and when coupled with the efficiency of antigen A in group AB produced a seemingly synergistic efficacy as observed in improved deformability and the ultimate increase in tissue oxygen delivery

We also recorded an increase in relative plasma Viscosity in blood group AB with a concomitant increase in PFC when compared with other blood groups, the relative lower transit time appears a compensatory mechanism for better oxygen delivery. The literature richly supported the theory that plasma viscosity is mainly dependent on PFC and an increase in its concentration is proportionate to an increase in plasma viscosity (Lowe, 1988; Oguz and Herbert, 2003; Ajayi *et al.*, 2007; Imoru and Emeribe, 2008), this is also evident in this study.

There were no significant differences in the values of WBC and red cell indices within the ABO blood groups. Our values for the red cell indices white blood cells and platelets however, were in line with those of Saathoff *et al.*, (2008) and Benedict *et al.*, (2012). Thus emphasizing the fact that Sub-Saharan Africa has a lower reference range for Hematological parameters when compared with those obtainable in the western world. De Maeyer and Adiels-Tegman (1985), adduced the prevalence of parasitic infections such as malaria, malnutrition and helminthes infestations in this region to the low red cell indices.

Another interesting observation in this study is the significantly higher platelet counts ($P < 0.05$, respectively) in blood group AB compared with other blood groups. This proves a likelihood of higher risk of clotting disorders especially thrombosis in AB than other blood groups. Several recent studies indicated increased risk of thrombosis by an association between the AB alleles of the ABO blood group (Magaly *et al.*, 2009). Taiwo *et al.*, (2012) suggested a positive correlation between platelet count and fibrinogen concentration. The non-O (A, B and AB) blood type is the most important risk factor for venous thromboembolism (blood clots in veins), making up 20% of attributable risk for the condition (CMAJ, 2013).

In Conclusion, this study has shown that hemorheological variations exist amongst the ABO blood groups. Blood group AB possess better red cell deformability despite its high RPV, PFC and platelet counts. It seems therefore that the improved deformability may be compensatory to prevailing factors of platelet activation in normal situations. Biochemical properties of the red cell antigens could therefore be a determinant of their membrane mechanical properties and rheology of the whole blood.

ACKNOWLEDGEMENTS:

The authors sincerely thank all staff of the department of physiology, University of Benin. Our profound gratitude also goes to Mr. Osakwe, Jane, Evans and Chidi who worked with us to ensure smooth completion of this work.

REFERENCES

- Adnot S, Raffestin B, Eddahibi S, Braquet P, Chabrier PE (1991). Loss of endothelium-dependent relaxant activity in the pulmonary circulation of rats exposed to chronic hypoxia. *J Clin Invest.* 87: 155-162
- Alpert MA, Concannon MD, Mukerji B, Mukerji V (1994). Primary pulmonary hypertension. Pharmacotherapy of chronic pulmonary arterial hypertension: value and limitations. Part I: *Angiology.* 45: 667-676
- Boe J, Simonsson BG (1980). Adrenergic receptors and sympathetic agents in isolated human pulmonary arteries. *Eur J Respir Dis.* 61: 195-202
- Cederqvist B, Wiklund NP, Persson MG, Gustafsson LE (1991). Modulation of neuroeffector transmission in the guinea pig pulmonary artery by endogenous nitric oxide. *Neurosci Lett.* 127: 67-69
- Cheng W, Oike M, Hirakawa M, Ohnaka K, Koyama T, Ito Y. (2005). Excess l-arginine restores endothelium-dependent relaxation impaired by monocrotaline pyrrole. *Toxicol Appl Pharmacol.* 207: 187-194
- Cho YJ, Han JY, Lee SG, Jeon BT, Choi WS, Hwang YS, Roh GS, Lee JD (2009). Temporal changes of angiotensin and Tie2 expression in rat lungs after monocrotaline-induced pulmonary hypertension. *Comp Med.* 59: 350-356
- Colucci WS, Holman BL, Wynne J, Carabello B, Malacoff R, Grossman W, Braunwald E (1981). Improved right ventricular function and reduced pulmonary vascular resistance during prazosin therapy of congestive heart failure. *Am J Med.* 71: 75-80
- Dinh-Xuan AT, Higenbottam TW, Clelland CA, Pepke-Zaba J, Cremona G, Butt AY, Large SR, Wells FC, Wallwork J (1991). Impairment of endothelium-dependent pulmonary-artery relaxation in chronic obstructive lung disease. *N Engl J Med.* 324: 1539-1547
- Faber JE, Szymeczek CL, Cotecchia S, Thomas SA, Tanoue A, Tsujimoto G, Zhang H (2007). Alpha1-adrenoceptor-dependent vascular hypertrophy and remodeling in murine hypoxic pulmonary hypertension. *Am J Physiol* 292: H 2316-H 2323
- Faber JE, Szymeczek CL, Salvi SS, Zhang H (2006). Enhanced alpha1-adrenergic trophic activity in pulmonary artery of hypoxic pulmonary hypertensive rats. *Am J Physiol.* 291: H2272-H2281
- Haneda T, Nakajima T, Shirato K, Onodera S, Takishima T (1983). Effects of oxygen breathing on pulmonary vascular input impedance in patients with pulmonary hypertension. *Chest.* 83: 520-527.
- Inoue M, Watanabe K, Mori C, Tanaka O (1994). The effect of bunazosin on monocrotaline-induced pulmonary hypertension in rats. *Acta Paediatr Jpn.* 36: 133-138

- Ajayi O.I, Famodu A.A and Oviasu E. (2007). Fibrinogen: a marker of cardiovascular disorders in Nigerians. *Turkish journal of Hematology* **24(1)**:18-22.
- Aleksander S.P. and Paul C.J. (2005): microcirculation and Hemorheology *Annu. Rev. Fluid Mech.* **37**:43–69.
- An X., Debnath G., Guo X., Liu S., Lux S.E., Baines A., Gratzner W. and Mohandas N. (2005): Identification and functional characterization of protein 4.1R and actin-binding sites in erythrocyte beta spectrin: regulation of the interactions by phosphatidylinositol-4,5-bisphosphate. *Biochemistry.* **44**:10681-10688.
- Benedict N., Augustina A.O. and Nosakhare B.G. (2012): Blood Donation in Nigeria: Standard of the Donated Blood. *J Lab Physicians.* **4**: 94-7.
- Bennett V. (1989): The spectrin-actin junction of erythrocyte membrane skeletons. *Biochim Biophys Acta.* **988**:107-121.
- Bennett V. and Baines A.J. (2001): Spectrin and ankyrin-based pathways: metazoan inventions for integrating cells into tissues. *Physiol Rev.* **81**: 1353-1392.
- Canadian Medical Association Journal (2013). AB blood type strong risk factor for venous blood clots. <http://www.sciencedaily.com/releases/2013/02/13>. Accessed. 10/06/2015.
- Cartron J.P. (2008): Blood group antigens structure and function: Recent advances. *Hematology Education: The Education Program for the Annual Congress of the European Hematology Association* **2**:158-174.
- Chien S. (1975): Biophysical behavior of red cells in suspension. In: Surgenor DM, ed. *Red Blood Cell*, Vol. 3. New York: Academic Press: 1031–1133
- Chien S (1987). Red cell deformability and its relevance to blood flow. *Annual Review of Physiology* **49**:177–192
- Cokelet G.R. (1987): Rheology and tube flow of blood. In: Skalak R, Chien S, eds. *Handbook of Engineering*. New York: Mc- Graw-Hill; 14. 1–14.17
- De Maeyer E. and Adiels-Tegman M. (1985): The prevalence of anaemia in the world. *World Health Stat Q* **38**:302-16.
- Embury S.H., Clark M.R., Monroy G. and Mohandas N. (1984): Concurrent sickle cell anemia and alpha-thalassemia. Effect on pathological properties of sickle erythrocytes. *J Clin Invest.* **73**:116-123.
- Fukuda M. and Fukuda M.N. (1981): Changes in red cell surface glycoproteins and carbohydrate structures during the development and differentiation of human erythroid cells. *J Supramol Struct.* **17**: 324.
- Gunasekaran S. and Mehmet M. (2003): *Cheese rheology and texture*, CRC Press, ISBN 1-58716-021-8.
- Imoru M. and Emeribe A. O. (2008): Hemorheologic profiles in apparently healthy pregnant women in Calabar, *Nigeria African Journal of Biotechnology.* **7(24)**: 4354-4358.
- Jenkins P.V. and O'Donnell J.S. (2006): ABO blood group determines plasma von Willebrand factor levels: a biologic function after all? *Transfusion.* **46(10)**:1836-44.
- Lewis S.M. (2002): Miscellaneous tests. In: Lewis S.M., Bain B.J., Bates I. (Eds), *Dacie and Lewis Practical Hematology*. London: Churchill Livingstone. 9: 527-542.
- Lowe G.D. (1988): Rheology of paraproteinemias and leukemias. In: Lowe GDO, ed. *Clinical Blood Rheology.* **2**: 67–88
- Mackie I.J. and Machin S.J. (1989): *Laboratory Haematology: An Account of Laboratory Techniques* (ed. by I. Chanarin), Churchill Livingstone, Edinburgh. Pp. 279–280.
- Magaly B. P. L, Aldemir B., Júlia F. C., Fátima C. B. M, Washington B., Raul A. M. and José A. R. L. (2009). Increased risk of venous thrombosis by AB alleles of the ABO blood group and Factor V Leiden in a Brazilian population. *Genet Mol Biol* **32(2)**: 264–267.
- Manno S., Takakuwa Y. and Mohandas N. (2002): Identification of a functional role for lipid asymmetry in biological membranes: Phosphatidylserine-skeletal protein interactions modulate membrane stability. *Proc Natl Acad Sci U S A.* **99**:1943-1948.
- Mohandas N. and An X. (2006): New insights into function of red cell membrane proteins and their interaction with spectrin-based membrane skeleton. *Transfus Clin Biol.* **13**:29-30.
- Mohandas N. and Gallagher P.G. (2008): Red cell membrane: past, present, and future. *Blood.* **112**: 3939-3948.
- Oguz K.B., and Herbert J.M. (2003) *Blood Rheology and Hemodynamics Seminars in Thrombosis and Hemostasis.* **29**; 5.
- Ohira T., Cushman M., Tsai M.Y., Zhang Y., Heckbert S.R., Zakai N.A., Rosamond W.D. and Folsom A.R. (2007): ABO blood group, other risk factors and incidence of venous thromboembolism: the Longitudinal Investigation of Thromboembolism Etiology (LITE). *J Thromb Haemost.* **5(7)**:1455-61.
- Parthasarathi K, Lipowsky H.H. (1999): Capillary recruitment in response to tissue hypoxia and its dependence on red blood cell deformability. *Am. J. Physiol.* **277**: 2145-2157.
- Reid H.L. and Ugwu A.C. (1987). A simple technique for rapid determination of plasma viscosity. *Nig. J. Physiol.* **3**:45-48.

- Robert E. and Marx D.D.S. (2001): Platelet-Rich Plasma (PRP): What Is PRP and What Is Not PRP? *Implant Dentistry*; **10**: 4.
- Saathoff E., Schneider P., Kleinfeldt V., Geis S., Haule D., Maboko L., Samky E., de Souza M., Robb M. and Hoelscher M. (2008): Laboratory reference values for healthy adults from southern Tanzania. *Trop Med Intern Health*. **13**:612-25.
- Taiwo, O.O., Nsa, N.B., Oyewole, O.S., Olufemi, O. and Aderemi, A.O. (2012). Evaluation of Hemorheological Parameters in Cigarette Smokers in Western Nigeria. *Greener Journal of Medical Sciences*. **2 (6)**; 146-151.
- Walensky L.D., Mohandas N., Lux S.E. (2003): In: Handin R.I., Lux S.E., Stossel T.P. eds. *Blood, Principles and Practice of Hematology* (2nd edition). Philadelphia, PA: Lippincott Williams & Wilkins; 1726-1744.