European Journal of
Health Sciences
(EJHS)

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European Journal of Health Sciences
ISSN 2520-4645 (online)
Vol.9, Issue 1, No 1, pp 1 - 11, 2023

www.ajpojournals.org

Blood Group System: Clinical Insight and Relevance in Medical Practice

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Article History

Submitted 12.03.23; Revised Version Received 09.04.23; Accepted 19.04.23

Abstract

Purpose: Thirty three blood group systems have recently received recognition from the International Society of Blood Transfusion. Numerous types of antigens have been found on the red cell membranes in addition to the ABO and Rhesus systems. One of the few significant tests that the anesthesiologist orders during the perioperative period is blood grouping and cross matching. To avoid difficulties associated with transfusions, it is crucial to have a thorough awareness of the blood group system, their clinical importance, typing and cross-matching tests and current implications. To explore the various blood group systems, their clinical significance, and their relevance in medical practice, including transfusion medicine, prenatal care and genetic testing

Methodology: Relevant databases such as PubMed, Google Scholar and Scopus to search for literature related to blood group system were used for this study. Search strategy including keywords related to barium studies, cross-sectional imaging and low resource economies. This may include terms such as blood group system, ABO blood group, clinical significance, medical practice. Search terms in combination with Boolean operators (AND, OR, NOT) are used to retrieve relevant articles.

Findings: Undoubtedly blood group systems is highly relevant in medical practice so as to prevent haemolytic transfusion reaction and alloimmunization of individual blood which can result to death of infants and other individuals. As beneficial as blood transfusion is blood group system of the donor and recipient must be identified to make the blood transfusion process safe. Blood group systems also gives clinical insights in medical practice which make disease diagnosis and treatment easier to approach.

Recommendations: Health care providers should be trained to properly identify and type blood samples and blood banks should have appropriate quality control measures in place to ensure the accuracy of blood typing and cross matching. Healthcare providers involved in organ transplantation should be familiar with the blood group compatibility guidelines and communicate effectively with blood banks to ensure the availability of compatible donor organs.

Keywords: *Blood Group, Antigen, Transfusion, Rhesus*

1.0 INTRODUCTION

Simply put, a blood group is any variation or polymorphism present in the blood. On the other hand, the term "blood group" is typically only used to describe red cell surface antigens or blood cell surface antigens in general. Human red cell membrane proteins, glycoproteins, and glycolipids show hereditary variations (Daniels, 2013). Some of the many functions that these proteins perform include membrane transporters (Diego, Kidd), adhesion and receptor molecules (Duffy, Lutheran), complement-regulating glycoproteins (Cromer, Knops), enzymes (Yt, Kell, Dombrock), structural elements (Diego, Gerbich), and glycocalyx components (MNS). Blood group antigens, which are polymorphic antigens present in the red cell membrane and may cause an immune reaction in individuals, are found there (Romphruk et al. , 2019). To detect these changes, alloantibodies, which form either "naturally" as a result of immunisation by pervasive environmental antigens or as a result of alloimmunization by human red blood cells, which are typically introduced through blood transfusion or pregnancy, are used. Although other techniques, such DNA sequence analysis, can be used to identify variation in red cell surface proteins, such variants cannot be referred to as blood groups until they are characterized by an antibody(Daniels, 2013).

Blood grouping is still employed as a trustworthy investigative tool in developing nations even though Deoxyribonucleic acid (DNA) techniques have mostly superseded it in forensic laboratories around the world. Blood grouping is also done for paternity testing, transplant medicine, transfusion medicine, and other medical purposes(Kanchan *et al.*, 2015).

According to legend, Karl Landsteiner made the discovery of the ABO blood group system in 1900. He conducted extensive research on serology, leading to the identification of crucial blood types like the O, A, and B types, compatibility testing, and subsequent transfusion procedures. His discovery earned him the Noble Prize in 1930. His impressive legacy includes more than 346 publications, according to his obituary. Later, Jan Jansky in Poland described the four sorts of human blood groupings(Mitra *et al.*, 2014).

Study Objective

To explore the various blood group systems, their clinical significance, and their relevance in medical practice, including transfusion medicine, prenatal care and genetic testing

2.0 METHODOLOGY

Relevant databases such as PubMed, Google Scholar and Scopus to search for literature related to blood group system were used for this study. Search strategy including keywords related to barium studies, cross-sectional imaging and low resource economies. This may include terms such as blood group system, ABO blood group, clinical significance, medical practice. Search terms in combination with Boolean operators (AND, OR, NOT) are used to retrieve relevant articles.

Inclusion Criteria

- Studies that investigate the relationship between blood group and disease susceptibility
- Studies that examine the prevalence and distribution of different blood groups in different populations
- Peer reviewed articles that provides a comprehensive overview of the current state of knowledge on blood group systems and their clinical implications

Exclusion Criteria

- Articles that discuss the use of blood groups for non-medical purposes (e.g. forensics, anthropology)
- Studies that are not published in peer reviewed journals

Blood Group System

One or more antigens are involved in blood group systems, and these antigens are controlled by either a single gene locus or a complex of two or more extremely closely related homologous genes that recombine very infrequently. A list of all currently recognized blood group systems has been defined by the International Society of Blood Transfusion. The 349 red cell antigens that make up the 43 currently recognized blood group systems are determined genetically by 48 genes. The first 10 chronologically arranged blood groups are discussed below together with the newly defined "Er blood system":

ABO System

The four primary groups of the ABO system are A, AB, B, and O, and they are identified by the presence or lack of A and B antigens. Three allelic genes, A, B, and O, located on the long arm of chromosome 9q, regulate the production of these antigens. This ABO system is highly important in transplantation and transfusion services(Apecu *et al.*, 2016). There are 2 variations of the blood group A which includes A1 and A2 the variation is as a result of The A1 and A2 phenotypes having different carbohydrate branching structures and have different amounts of the A antigen on the RBCs (A1 has more than A2). 20% of group A members are A2, and 80% of group A members are A1(Fayyaz *et al.*, 2014).

These antibodies (anti-A and anti-B) are frequently "naturally occurring" antibodies made in response to contact with non-self A and/or B antigens, which are frequently present in food and microorganisms, especially the gut microbiota. Antibodies in this system (i. e. beginning in the first few months of life, anti-A and anti-B) are produced. Anti-A and anti-B, frequently of the IgM isotype, are present in the blood of almost all healthy individuals who lack the appropriate antigen; IgG anti-A and anti-B are frequently found in group O individuals. H antigen is the precursor substrate for A and B antigens. Rare are the "Bombay" (O) phenotypic RBCs, which lack the H antigen and subsequently the A and B antigens. These RBCs were initially discovered in Bombay, India. Clinically, Bombay individuals can develop powerful anti-H with the same hemolytic potential as anti-A and anti-B, and they can only accept RBC transfusions from other Bombay individuals(Fayyaz *et al.*, 2014).

MNS System

Only the Rh blood group system is more intricate than the MNS blood group system in terms of complexity. Although hemolytic illness in fetuses and newborns has been caused by antibodies to low- and high-prevalence MNS antigens, many alloantibodies to MNS antigens are typically not clinically significant. On glycophorin A (GPA), glycophorin B (GPB), or hybrids produced by single nucleotide substitution, uneven crossing over, or gene conversion between the glycophorin genes, the MNS antigens are present. According to Reid (2009), the antibodies in the MNS system are fully developed at birth. At the moment, it has 50 antigens (Castilho, 2020; ISBT, 2022).

PIPK System

The antigens of the P1PK blood group system are transported on glycosphingolipids. Three antigens have now been detected in the system: P1, Pk, and NOR. Pk and NOR were characterized in 1951 and 1982, respectively, and Landsteiner and Levine discovered the P1 antigen in 1927. Similar to the ABO system, sera from people lacking the necessary antigen may contain inborn antibodies of the immunoglobulin (Ig) M or IgG class that are focused on the missing carbohydrate groups. Anti-P1 is typically a weak and cold-reactive antibody unrelated to HTR or hemolytic illness of the fetus and infant, whereas Pk antibodies can cause hemolytic transfusion reaction (HTR) and anti-NOR is thought to be a polyagglutinin (Hellberg et al., 2013).

Rhesus System

ABO is the most significant system, followed by the Rhesus system. The Rh-system currently has 50 defined blood type antigens, only five of which are important. RBC surface Rh factor or immunogenic D-antigen may or may not be present in an individual. As a result, the status is either Rh-positive (D-antigen present) or Rh-negative (D-antigen absent). Contrary to the ABO system, individuals with D-negative RBCs usually do not have anti-Rh antibodies in their blood unless their circulatory systems have been exposed to D-positive RBCs. The immunoglobulin G composition of these immunological antibodies allows them to cross the placenta. When pregnant Rh-negative women who have given birth to Rh-positive children receive anti-D Ig prophylaxis against the Rh vaccine(Mitra *et al.,* 2014).

Lutheran System

Twenty antigens that are identified by antibodies that are typically clinically benign make up the Lutheran blood group system. On chromosome 19, the 15 exon BCAM gene, originally known as LU, is located. The immunoglobulin superfamily's Lutheran glycoproteins, which are found in vascular endothelia, bind isoforms of laminin with five chains. These molecules are part of the extracellular matrix(Daniels, 2013).

Kell System

The Kell blood group system has 35 antigens allocated to it, making it exceedingly polymorphic. The kell glycoprotein expression is not essential for erythrocyte function. Due to hemolytic illness in the fetus and infant, the first alloantibody was found in 1946. (HDFN). The antigen was given the name "Kell" after the woman whose serum contained the antibodies. The maternal antibody responded with the duo's firstborn child's RBCs as well as paternal and newborn RBCs(Denomme, 2015).

Lewis System

Out of the six antigens in the Lewis blood group system, Le(a) and Le(b) are the two that are most important. Rather than being made by red blood cells, plasma delivers Le(a) and Le(b) into the membrane of the red cell. associated with tissue ABH antigen production.(International society of blood transfusion (ISBT, 2022).

Duffy System

In addition to having highly immunogenic glycoprotein antigens on their surfaces, red blood cells (RBC), vascular endothelial cells, alveolar epithelial cells, collecting tubules in the kidney, and

Purkinje cells in the brain also have these on their surfaces. The entire Duffy blood group system is made up of these antigens. The first blood group system to be discovered on chromosome 1 through cytogenetic research was the Duffy blood group system. The FYA and FYB genes, which result in the major antigens Fya and Fyb, respectively, in Duffy blood type systems. Blood transfusion responses and hemolytic illness in fetuses and newborns are linked to antibodies against the Duffy blood group antigens(Killeen, 2022).

Kidd System

The Kidd blood group system was discovered in 1951 and consists of three high-incidence antigens: Jka, Jkb, and two antagonistic antigens, Jka and Jkb. All people, with the exception of those who have the extremely unusual Kidd-null trait, express the Jk3 antigen. Thus, there are four possible Kidd phenotypes: Jk(a b), Jk(a b), and Jk(a b). The Kidd antigen-carrying glycoprotein, which transports urea on both erythrocytes and endothelial cells of the renal vasa recta, is a 43-kDa, 389-amino acid protein with 10 membrane-spanning domains. The HUT11/UT-B/JK (SLC14A1) gene, which is located on chromosome 18q12-q21, generates this glycoprotein. (Lawicki *et al.*, 2017).

Diego System

In the current Diego blood group system (DI), there are 22 antigens. Three antigens have a high prevalence, compared to 19 antigens with a low prevalence. The Diego blood group antigens are carried by the erythroid band 3 protein anion exchanger 1 (AE1), which is produced by a single gene called SLC4A1 (solute carrier family 4, anion exchanger, member 1) (Figueroa, 2013).

Er System

This is the five antigen blood group system that was recently discovered. The five human red blood cell surface antigens (Era, Erb, Er3, Er4, and Er5) that make up the Er blood group system are Era, Erb, Er3, Er4, and Er5. Era and Er3 both have incidences that are higher than 99 percent of the total human population, while Erb has an incidence that is less than 0.01 percent. Er4 and Er5 are extremely prevalent in the general population. The expression of the Er blood group antigens is regulated by the gene PIEZO1. In 1982 and 1988, respectively, Era and Erb were first found. Er was upgraded to a blood group in 2022 after being acknowledged as a blood group collection by the International Society of Blood Transfusion in 1990 (Anome, 2022; Raul et al., 2013).

The creation of an altered protein on the cell surface of these people was caused by particular modification found by scientists in the gene encoding the Piezo1 protein. These scientists established Er as a new blood group system by using DNA sequencing and gene editing methods to demonstrate that Piezo1 is the carrier for these locations (Seattle Times, 2022). Red blood cells use piezo proteins, which are mechanosensory proteins to detect pressure. Only a few hundred copies of the protein are found in each cell's membrane. This study really emphasizes the relevance of lowly expressed proteins for transfusion therapy as well as their potential for antigenicity (Seattle Times, 2022).

Relevance of Blood Group Systems in Medical Practice

Blood transfusions are one of the most crucial elements of contemporary medicine, and they involve determining the blood types of the parties involved. Blood transfusions are necessary for many major surgical procedures, including the care of trauma patients, obstetric care with significant bleeding during childbirth, and the treatment of numerous medical conditions,

particularly hematological diseases (Jerslid *et al.* , 2008). The ABO and Rhesus blood group systems are the most clinically significant blood type systems from the perspectives of hemolytic disease of the fetus and newborn (HDFN) and hemolytic transfusion reaction (HTR). Additional clinically useful blood group systems include those of Kell, Duffy, Kidd, MNS, Diegos, and others. (Erhabor *et al.,* 2021). Therefore the relevance of blood group systems is seen in ensuring compatibility of the donor and the recipient. Furthermore, the presence or absence of specific proteins on the surface of the red blood cells determines the blood type of a person. A blood type mismatch during a transfusion can result in alloimmunization or the production of antibodies against the foreign blood group

Compatibility Testing

The use of compatibility testing helps to avoid alloimmunization and hemolytic transfusion responses when a recipient receives a transfusion of a donor's blood. Sensitization by a foreign antigen and subsequent exposure to the same antigen, respectively, result in alloimmunization and hemolytic transfusion responses(Erhabor *et al.,* 2021; Haryani *et al.,* 2017). The compatibility testing includes: ABO and Rhesus blood typing, antibody screening meant for the detection of unexpected antibodies and cross matching(Obeta *et al.,* 2020).

ABO and Rhesus Blood Typing

ABO incompatibility, which results in complement-mediated intravascular hemolysis, is the most lethal of all transfusion-related reactions. Therefore, accurate blood grouping or typing is crucial. Before transfusion, ABO typing is done by checking serum for the A and B antibodies and RBCs for the A and B antigens(Obeta *et al.,* 2020). Rh typing is the next phase, and not more than 15% of the population is Rh-negative(Erhabor *et al.,* 2021).

Cross Matching

This procedure uses red blood cells from the donor and serum from the recipient. It aids in establishing whether blood compatibility between the donor and receiver exists. It is crucial because it aids in the detection of anomalies in the ABO blood grouping and abnormal antibodies. It comes in two varieties: major/full (which uses patient serum and donor cells) and minor/emergency (which uses patient cells and donor serum)(Erhabor *et al.,* 2021).

Antibody Screening

A safe blood transfusion for the recipient is also ensured by doing this. In order to identify the existence of unexpected antibodies, recipient serum and, in certain situations, donor serum are combined with commercially manufactured and readily available red cells that contain all the antigens(Mitra *et al.,* 2014).

Clinical Insight of Blood Group System in Medical Practice

Blood groups systems can give insight in medical practice based on their relationship with either disease predisposition or disease treatment. The haemostasis is significantly influenced by the ABO blood groups. Both factor VIII and von Willebrand factor plasma levels are significantly impacted by them. ABO glycol transferases, which function to control thrombosis, are thought to be the reason blood types A and AB are linked to an increased risk of myocardial infarction, ischemic stroke, and venous thromboembolism. Non-O groups (i.e A, AB, B) have a higher incidence of cerebral venous thrombosis(Ward *et al.,* 2020). By inhibiting rosette formation, group

O can provide protection from falciparum malaria. Vibrio cholerae strains had more severe infections when exposed to blood group O. (O1 El Tor and O139)(Erhabor *et al.,* 2021). The chemokine receptor known as the Duffy antigen is crucial to the inflammatory response. As a result, Duffy null individuals, who lack this antigen, may be at risk for HIV infection, particularly if neutropenia is present. It has been demonstrated that HIV interacts with other antigens, including those found in the Rh, Lutheran, and OK blood group systems. Pk antigen overexpression in cells makes them seem immune to HIV infection(Davison *et al.,* 2020). Blood type A women are more likely to develop neoplasms with poorer prognoses and severe disease progression. Greater than the existing percentage of female blood group A carriers in the female population, these women make up a sizeable share of breast cancer patients. Contrarily women with blood group O, appear to be somewhat "protected" from getting breast cancer, and their prognosis is typically better if they do. Women with blood groups AB and B have similar prognoses to those with blood groups A and O respectively, while women with blood groups B and O have comparable prognoses(Bezek *et al.,* 2021). Individuals with blood group A has been shown to be more predisposed to pancreatic cancer while those with blood group B are more predisposed to ovarian cancer(Mitra *et al.,* 2014). ABO, secretor and Lewis histo-blood group systems is associated with the digestive form of Chagas disease caused by *Trypanosoma cruzi* (Rubia *et al.,* 2016). Females with blood type A have reportedly been found to be more prone to COVID-19 infection (Fan et al., 2020). Group O may be associated with a decreased risk of SARS-CoV-2 infection, whereas group A may be associated with a higher risk of SARS-CoV-2 infection and severe illness.(Goel *et al.,* 2021).

Despite low amniotic bilirubin levels and low antibody titers, Kell alloantibodies during pregnancy have been shown to decrease erythropoiesis, which can lead to significant illness. It is believed that the infant's ongoing inhibition of erythropoiesis due to residual alloantibody is what causes late-onset anemia with reticulocytopenia(Denomme *et al.,* 2015). Kidd antigens are notorious for causing delayed hemolytic transfusion reactions because of the potent anamnestic response displayed by antibodies directed against them. (Lawicki *et al.,* 2017). As side effects of sickle cell disease and polycythemia vera, respectively, lutheran glycoproteins may potentially be involved in vascular occlusion and thrombotic events(Daniels, 2013). Women who have the uncommon phenotypes p, P1k, and P2k miscarry more frequently than other women(Hellberg *et al.,* 2013).

3.0 CONCLUSION AND RECOMMENDATIONS

Conclusion

Undoubtedly blood group systems is highly relevant in medical practice so as to prevent haemolytic transfusion reaction and alloimmunization of individual blood which can result to death of infants and other individuals. As beneficial as blood transfusion is blood group system of the donor and recipient must be identified to make the blood transfusion process safe. Blood group systems also gives clinical insights in medical practice which make disease diagnosis and treatment easier to approach.

Recommendation

- Health care providers should be trained to properly identify and type blood samples and blood banks should have appropriate quality control measures in place to ensure the accuracy of blood typing and cross matching

- Healthcare providers involved in organ transplantation should be familiar with the blood group compatibility guidelines and communicate effectively with blood banks to ensure the availability of compatible donor organs

Recommendation for Further Studies

Even though numerous practices have been done in this field, further research is still needed to be done due to new trends that are emerging daily

Recommendation for Practice

Regular training sessions should be provided to healthcare providers involved in blood typing and crossmatching to ensure that they are up-to-date with latest techniques and procedures

Conflict of interest: There was no competing interest

Funding: Nil

Acknowledgment: I want to appreciate Mr Ojo-Rowland Olawale and Mr Ogunlusi Pelumi for typing and collation of papers for this research

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