1.1 Introduction

Screening of blood is mandatory for transfusion transmitted diseases and is routinely done in the blood banks. As blood is the major source of transmission of hepatitis B (HBV), hepatitis C (HCV), human immunodeficiency virus (HIV) & many other diseases. The hazards can be minimized by effective donor selection and screening.

Blood transfusion is a life-saving measure in various medical and surgical emergencies. Transfusion medicine, apart from being important for the medical treatment of individual, also has great public health importance (Giri PA, et al, 2012 Jan)

Blood transfusion has been and continues to be a possible source of disease transmission. A myriad of agents can potentially be transmitted through blood transfusions, including bacteria, viruses, and parasites Mudassar Zia, MD; (Emmanuel C Besa, Jun 2012)

Despite progress made in the prevention of transfusion-transmitted infections (TTIs) over the last few years, they continue to be a problem in many parts of the world, particularly in multitransfused patients. (El-Faramawy AA, et al, 2012).

Failures of blood screening due to low test quality or poor laboratory technique increase the risk of transfusion-transmitted infections. (Mourant AE, et al, 2013).

Mourant et al. concluded that the differences in frequencies of blood Groups A and B are the result of random genetic drift and founder effects as well as of natural selection, arising from differences in fitness between the various blood groups. (Davis. J. Anstee. 2010 June).

ABO blood group has been previously found to be associated with the risk of several malignancies, including gastric cancer, pancreatic cancer, epithelial ovarian and skin cancer. Interaction of micro-organisms and RBC membrane is probably because of antigenic similarity, adherence through specific receptors or modulation of antibody response. (Surabhi Tyagi and Alok Tyagi. 2013 Sep).

Every year more than 90 million units of blood are collected worldwide. (World Health Organization, 2008).

Each transfusion carries a risk of transmitting blood-borne pathogens, including mainly human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV) and syphilis. To improve blood transfusion safety, the World Health Organization (WHO) recommends an integrated strategy including establishment of well-organized blood transfusion services, prioritization of blood donation from voluntary non-remunerated donors, screening of donated
blood for at least the four major transfusion-transmissible infections (TTI) with quality-assured assays, rational use of blood and implementation of effective quality control systems. (World Health Organization, Aide-mémoire, 2002).

Nevertheless, particularly in low-resource countries, a significant proportion of donated blood remains unsafe as it is either not screened for all major TTIs or not in a quality-controlled manner. (World Health Organization, 2008, Jayaraman S, et al, 2010).

Africa faces the highest transfusion needs in the world, but also the highest prevalence of blood-borne pathogens and the weakest transfusion programs. (Tagny CT, et al, 2008).

Most blood banks in Africa are small, hospital-based and relying on an important proportion of replacement donors, in contrast with western transfusion units organized with large pools of voluntary donors. (Field SP, Allain JP, 2007).

In such settings with limited capacity and low throughput, WHO accepts the use of rapid and simple serological assays for TTI screening, provided that they are quality-assured, locally validated and quality-controlled. Rapid test-based screening protocols tend to be used increasingly in African blood banks. (Allain JP, Lee H, 2005).

Although safety of such a strategy has been recently challenged in an international quality control survey. (Laperche S, et al, 2009).

For some experts, rapid testing has also the advantage of immediate counseling of infected candidates and referral to appropriate care, although this is not the primary objective of transfusion medicine. (Allain JP, et al, 2009).

Candidate blood donors underwent a first screening by the national questionnaire, and non-deferred candidates were then routinely screened for HIV, HBV and syphilis by means of rapid or simple assays. HIV testing was performed with internationally quality-assured assays, while HBV and syphilis infections were usually screened by a variety of brands.
1.2 Rationale:
ABO and Rh grouping has been previously found to be associated with risk malignancy including gastric cancer, pancreatic cancer, epithelial ovarian and skin cancer.
As blood is the major source of transmission of hepatitis B (HBV), hepatitis C (HCV), human immunodeficiency virus (HIV) & many other diseases. The hazards can be minimized by effective donor selection and screening.
So these research conduct to act as predictive factor for association of blood group system and these mortal diseases for both donor and patient in our country and for whole different population worldwide.
1.3 Objective:

1. General objective:
   - To determine the correlation of transfusion transmitted Diseases with Rh type and ABO Blood Group System.

2. Specific objective:
   - To identify blood group of donors.
   - To determine the seroprevalence of HIV, HBV, HCV and syphilis infections in blood donors.
   - To correlate between blood group and transfusion-transmitted infection.
2. Literature review

2.1 ABO blood group system

ABO blood group antigens present on red blood cells and IgM antibodies present in the serum

The ABO blood group system is the most important blood type system (or blood group system) in human blood transfusion. The associated anti-A and anti-B antibodies are usually IgM antibodies, which are produced in the first years of life by sensitization to environmental substances, such as food, bacteria, and viruses. ABO blood types are also present in some other animals, for example rodents and apes, such as chimpanzees, bonobos, and gorillas. (Maton, et al, 1993).

2.1.1 Genetics:

A and B are co-dominant, giving the AB phenotype. Blood groups are inherited from both parents. The ABO blood type is controlled by a single gene (the ABO gene) with three types of alleles inferred from classical genetics: i, IA, and IB. The gene encodes a glycosyltransferase—that is, an enzyme that modifies the carbohydrate content of the red blood cell antigens. The gene is located on the long arm of the ninth chromosome (9q34).

The IA allele gives type A, IB gives type B, and i gives type O. As both IA and IB are dominant over i, only ii people have type O blood. Individuals with IAi or IBi have type A blood, and individuals with IBIB or IBi have type B. IAIB people have both phenotypes, because A and B express a special dominance relationship: co-dominance, which means that type A and B parents can have an AB child. A couple with type A and type B can also have a type O child if they are both heterozygous (IBi, IAi) The cis-AB phenotype has a single enzyme that creates both A and B antigens. The resulting red blood cells do not usually express A or B antigen at the same level that would be expected on common group A or B red blood cells, which can help solve the problem of an apparently genetically impossible blood group. (Australian Red Cross Blood Service. October 2013).

Historically, ABO blood tests were used in parental testing, but in 1957 only 50% of American men falsely accused were able to use them as evidence against paternity. Stanford.

Occasionally, the blood types of children are not consistent with expectations—for example, a type O child can be born to an AB parent—due to rare situations, such as Bombay phenotype and cis AB. (The Owen Foundation. July 2008).

2.1.2 History of discoveries of the blood types:
The ABO blood group system is widely credited to have been discovered by the Austrian scientist Karl Landsteiner, who identified the O, A, and B blood types in 1900. (von Decastello A, Sturli A, 1902).

Landsteiner originally described the O blood type as type "C", and in parts of Europe it is rendered as "0" (zero), signifying the lack of A or B antigen. Landsteiner was awarded the Nobel Prize in Physiology or Medicine in 1930 for his work. Alfred von Decastello and Adriano Sturli discovered the fourth type, AB, in 1902. (Janský J, 1907).

Ukraine marine uniform imprint, showing the wearer's blood type as "B (III) Rh+".

Due to inadequate communication at the time, it was subsequently found that the Czech serologist Jan Janský had independently pioneered the classification of human blood into four groups. (Erb IH, May 1940).

But Landsteiner's independent discovery had been accepted by the scientific world while Janský remained in relative obscurity. Janský's nomenclature is, however, still used in Russia and states of the former USSR, in which blood types O, A, B, and AB are respectively designated I, II, III, and IV. (Moss WL, 1910).

The designation A and B with reference to blood groups was proposed by Ludwik Hirschfeld. Ludwik Hirschfeld and E. von Dungern discovered the heritability of ABO blood groups in 1910–11. Felix Bernstein demonstrating the correct blood group inheritance pattern of multiple alleles at one locus in 1924. (Morgan, et al, 1969).

Watkins and Morgan, in England, discovered that the ABO epitopes were conferred by sugars, to be specific, N-acetylgalactosamine for the A-type and galactose for the B-type. (Watkins, W. M, 1980).

After much published literature claiming that the ABH substances were all attached to glycosphingolipids. (Finne et al, 1978)


that contains ABH substances attached and represent the majority of the antigens. (Järnefelt, et al, 1978).

The main glycoprotein carrying the ABH antigens were identified to be the Band 3 and Band 4.5 proteins and glycophorin. (Yamamoto, et al, 1990).
Later, Yamamoto's group showed the precise glycosyl transferase set that confers the A, B and O epitopes. (Benjamin A, 2008).

2.1.3 Antigens of Blood groups:
Student blood test. Three drops of blood are mixed with anti-B (left) and anti-A (right) serum. Agglutination on the right side indicates blood type A. The central principle of the ABO system is that antigens – in this instance, sugars physically exposed on the exterior of red blood cells – differ between individuals, who have immunological tolerance only toward what occurs in their own bodies. As a result, many humans express isoantibodies – antibodies against isoantigens, natural components present in the bodies of other members of the same species but not themselves. Isoantibodies may be present against the A and/or B antigens in people who do not themselves have the same antigens in their own blood. These antibodies act as haemagglutinins, which cause blood cells to clump and break apart if they carry the foreign antigens. This harsh response, though an adaptive reaction useful against infection, can cause death when large amounts of such cells are encountered after a blood transfusion, a circumstance not encountered in natural selection prior to modern history. Because A and B antigens are chemically modified from a precursor form that is also present in type O individuals, people with type A and B antigens can accept blood from type O individuals.
Anti-A and anti-B antibodies (called isohaemagglutinins), which are not present in the newborn, appear in the first years of life. Anti-A and anti-B antibodies are usually IgM type, which are not able to pass through the placenta to the fetal blood circulation. O-type individuals can produce IgG-type ABO antibodies.
The precursor to the ABO blood group antigens, present in people of all common blood types, is called the H antigen. Individuals with the rare Bombay phenotype (hh) do not express antigen H on their red blood cells. As the H antigen serves as a precursor for producing A and B antigens, the absence of the H antigen means that the individuals also lack A or B antigens as well (similar to O blood group). However, unlike O group, the H antigen is absent, hence the individuals produce isoantibodies to antigen H as well as to both A and B antigens. If they receive blood from someone with O blood group, the anti-H antibodies will bind to the H antigen on the red blood cells ('RBC') of the donor blood and destroy the RBCs by complement-mediated lysis. Therefore, people with Bombay phenotype can receive blood only from other hh donors (although they can donate as though they were type O). Some individuals with the blood group
A1 may also be able to produce anti-H antibodies due to the complete conversion of all the H antigen to A1 antigen.

Production of the H antigen, or its deficiency in the Bombay phenotype, is controlled at the H locus on chromosome 19. The H locus is not the same gene as the ABO locus, but it is epistatic to the ABO locus, providing the substrate for the A and B alleles to modify. Fareed, et al., 2014.

The H locus contains three exons that span more than 5 kb of genomic DNA, and encodes the fucosyltransferase that produces the H antigen on RBCs. The H antigen is a carbohydrate sequence with carbohydrates linked mainly to protein (with a minor fraction attached to ceramide moiety). It consists of a chain of β-D-galactose, β-D-N-acetylgalactosamine, β-D-galactose, and 2-linked, α-L-fucose, the chain being attached to the protein or ceramide.

The ABO locus, which is located on chromosome 9, contains seven exons that span more than 18 kb of genomic DNA. Exon 7 is the largest and contains most of the coding sequence. The ABO locus has three main allelic forms: A, B, and O. The A allele encodes a glycosyltransferase that bonds α-N-acetylgalactosamine to the D-galactose end of the H antigen, producing the A antigen. The B allele encodes a glycosyltransferase that bonds α-D-galactose to the D-galactose end of the H antigen, creating the B antigen.

In the case of the O allele, when compared to the A allele, exon 6 lacks one nucleotide (guanine), which results in a loss of enzymatic activity. This difference, which occurs at position 261, causes a frame shift that result in the premature termination of the translation and, thus, degradation of the mRNA. This results in the H antigen remaining unchanged in the case of O groups.

The majority of the ABO antigens are expressed on the ends of long polylactosamine chains attached mainly to band 3 protein, the anion exchange protein of the RBC membrane, and a minority of the epitopes are expressed on neutral glycosphingolipid.

2.1.4 Role of ABO antigens in transfusion medicine:

For a blood donor and recipient to be ABO-compatible for a transfusion, the recipient must not be able to produce Anti-A or Anti-B antibodies that correspond to the A or B antigens on the surface of the donor's red blood cells (since the red blood cells are isolated from whole blood before transfusion, it is unimportant whether the donor blood has antibodies in its plasma). If the antibodies of the recipient's blood and the antigens on the donor's red blood cells do correspond,
the donor blood is rejected. On rejection, the recipient may experience Acute hemolytic transfusion reaction.

In addition to the ABO system, the Rh blood group system can affect transfusion compatibility. An individual is either positive or negative for the Rh factor; this is denoted by a '+’ or ‘−’ after their ABO type. Blood that is Rh-negative can be transfused into a person who is Rh-positive, but an Rh-negative individual can create antibodies for Rh-positive RBCs. Because of this, the AB+ blood type is referred to as the "universal recipient", as it possesses neither Anti-B nor Anti-A antibodies in its plasma, and can receive both Rh-positive and Rh-negative blood. Similarly, the O− blood type is called the "universal donor"; since its red blood cells have no A or B antigens and are Rh-negative, no other blood type will reject it.

Identification of ABO and Rh gene frequencies among human populations has various benefits in transfusion medicine, transplantation and disease risk. (Liu, QP, et al, 2007).

2.1.5 Alteration of ABO antigens for transfusion:
In April 2007, an international team of researchers announced in the journal Nature Biotechnology an inexpensive and efficient way to convert types A, B, and AB blood into type O. BBC.

This is done by using glycosidase enzymes from specific bacteria to strip the blood group antigens from red blood cells. The removal of A and B antigens still does not address the problem of the Rhesus blood group antigen on the blood cells of Rhesus positive individuals, and so blood from Rhesus negative donors must be used. Patient trials will be conducted before the method can be relied on in live situations.

Another approach to the blood antigen problem is the manufacture of artificial blood, which could act as a substitute in emergencies. (Yazer M, et al, 2006).

2.1.6 Distribution and evolutionary history:
The distribution of the blood groups A, B, O and AB varies across the world according to the population. There are also variations in blood type distribution within human subpopulations. In the UK, the distribution of blood type frequencies through the population still shows some correlation to the distribution of placenames and to the successive invasions and migrations including Vikings, Danes, Saxons, Celts, and Normans who contributed the morphemes to the placenames and the genes to the population. (Cserti CM, Dzik WH, 2007).
The two common O alleles, O01 and O02, share their first 261 nucleotides with the group A allele A01. (Calafell, et al, 2008).

However, unlike the group A allele, a guanosine base is subsequently deleted. A premature stop codon results from this frame-shift mutation. This variant is found worldwide, and likely predates human migration from Africa. The O01 allele is considered to predate the O02 allele.

Some evolutionary biologists theorize that the $I^A$ allele evolved earliest, followed by $O$ (by the deletion of a single nucleotide, shifting the reading frame) and then $I^B$. This chronology accounts for the percentage of people worldwide with each blood type. It is consistent with the accepted patterns of early population movements and varying prevalent blood types in different parts of the world: for instance, B is very common in populations of Asian descent, but rare in ones of Western European descent. Another theory states that there are four main lineages of the ABO gene and that mutations creating type O have occurred at least three times in humans.[33] From oldest to youngest, these lineages comprise the following alleles: $A101/A201/O09$, $B101$, $O02$ and $O01$. The continued presence of the O alleles is hypothesized to be the result of balancing selection.( Chemistry and Materials Science, 2005).

Both theories contradict the previously held theory that type O blood evolved earliest.

2.2 Disease risks:

Compared to O group individuals, non-O group (A, AB, and B) individuals have a 14% reduced risk of squamous cell carcinoma and 4% reduced risk of basal cell carcinoma. Wolpin, et al, 2010. Conversely, type O blood is associated with a reduced risk of pancreatic cancer. (Amundadottir, et al, 2009).


Gastric cancer has reported to be more common in blood group A and least in group O. (Glass, et al, 1985).

According to Glass, Holmgren, et al., those in the O blood group have an increased risk of infection with cholera, and those O-group individuals who are infected have more severe infections. The mechanisms behind this association with cholera are currently unclear in the literature. (American Red Cross, 2007).

2.2.1 Viral Hepatitis:

Before the late 1970’s, the risk of transmitting hepatitis by transfusion was very high because of blood collection from prisoners and paid donors and the lack of sensitive serological tests.
Between 1965 and 1972, approximately 1 in 60 units of blood transmitted hepatitis. The change to an all-volunteer blood supply and the introduction of a third generation test for HBsAg in the mid 1970’s led to a marked reduction in transfusion transmitted hepatitis B infection. The risk decreased even further with the implementation of ALT and anti-HBc tests in 1987 and 1988 as surrogate markers for hepatitis C. Nucleic acid testing for Hepatitis B virus was introduced in 2009. Today the risk of transmitting hepatitis B is estimated to be 1 case per 352,000 units and the window period has been reduced to 5-8 days. In the late 1970’s, approximately 10% of patients who were transfused with multiple units of red cells became infected with hepatitis C. The introduction of more stringent donor eligibility criteria and both serological and nucleic acid tests hepatitis C virus antibody and RNA has reduced the risk of transmission to about 1 infection per 2,000,000 units transfused. The natural history of transfusion acquired HCV is similar to that of HCV acquired through other modes of transmission. Approximately 50% of patients will develop chronic elevations of liver enzymes and 10% of these will develop cirrhosis.

2.2.2 HIV-1:
The risk of transmitting HIV-1 by transfusion has almost been completely eliminated over the past 25 years. The risk has decreased from 1 case per 100 transfused units in 1983 to 1 case per 2 million today. The risk declined dramatically with the identification and deferral of donors with high-risk behaviour in 1983 and the introduction of HIV-1 antibody testing in 1985. In late 1995, blood banks began to test donors for p24 antigen to identify donors in the window period of an early infection who did not have detectable antibody. P24 antigen testing decreased the window period from 22 to 16 days. In late 1999, blood banks introduced nucleic acid testing for HIV-1 RNA to further reduce the possibility that a unit collected during the window period might be transfused. The window period is now estimated to be 11 days.

HIV-2:
HIV-2 also causes AIDS and can be transmitted by blood. The FDA licensed the first combination test kit for detecting antibodies to HIV-1 and HIV-2 on September 25, 1992. All blood centers were required to implement this combination test by June 1993. Very few cases of HIV-2 have been detected in the United States. The risk of transmitting HIV-2 by blood Transfusion is very small.
2.2.3 Syphilis:
Syphilis is also a systemic disease caused by Treponema palladium which can be spread by sexual contact, blood transfusion and via vertical transmission. The World Health Organization (WHO) estimates that 12 million new cases of syphilis occur each year. Despite the fact that *T. pallidum* cannot survive in properly stored blood and the inescapable cost implications of syphilis testing of blood donors particularly in resource-poor settings, it must be noted that the emphasis of blood transfusion should be on two fundamental objectives – safety and protection of human lives. “Syphilis screening of donated blood, no matter what the incidence is in the donor population, has been considered to have value as a „lifestyle“ indicator, as individuals exposed to syphilis may also have been exposed to other sexually transmitted diseases”(14). Several studies have assessed the association of blood groups with blood-borne infections but based on different sample sizes, test methodology, covered age, social risk factors, and geographic conditions, results have been different.

2.3 Blood Type and Cancer:
Although there are probably over a thousand publications on the associations of blood groups and disease, many are based totally on statistical analyses. Most of the earlier studies have been controversial, because they were small studies and/or had inadequate controls and/or had been analyzed incorrectly. Nevertheless, it is difficult to argue with the general pattern that emerges from the large body of statistical data on malignancy, coagulation, and infection. Some of the findings on microbe receptors, and the association with important immune proteins, are most convincing and suggest that blood group antigens do play an important biological role: A role that is often completely unrelated to the red blood cell. It can be said at the outset, that cancers in general tend to be associated with group A, and slightly less strongly with group B. With that, let's look at some trends among selected cancers with regard to blood type.

**Breast Cancer:**
Breast cancer is the most common cancer among women. And while the mortality rates are falling slightly for some sub-populations of women, it is still a potentially lethal adversary. Standard treatment can vary but procedures such as lumpectomy surgery (removal of the tumor and some surrounding tissue), mastectomy (removal of the whole breast), chemotherapy, radiation, and hormone-blocking therapy are the norm with any combination of the above strategies potentially employed. Mammograms have been a major push within medicine as a
means of early detection; however, many of my patients have actually discovered there tumors on self-examination of breast tissue, so I cannot overemphasize this self-help procedure (especially for A's and AB's as we will see). While many risk factors are associated with the development of breast cancer, it is seldom mentioned that blood type has an influence on susceptibility and outcomes. In fact, some researchers have even gone so far as to say that "blood groups were shown to possess a predictive value independent of other known prognostic factors" when discussing breast cancer. Other researchers have actually suggested that a degree of the susceptibility to breast cancer, from a gene perspective, might be a result of a breast cancer-susceptibility locus linked to the ABO locus located on band q34 of chromosome 9. (Costantini M, et al., 1990).

My observation has been that blood type A women have a generalized tendency to worse outcomes and a more rapid progression with this cancer. Research indicates that blood type A women are over-represented among breast cancer patients, and that this trend occurs even among women thought to be at low risk for cancer. One of the most significant risk factors for a rapidly progressing breast cancer is also blood type A, and blood type A women have been observed to have poorer outcomes once they are diagnosed with breast cancer. In complete opposition to this blood type A tendencies, we find blood type O. Blood type O infers a slight degree of resistance against breast cancer, and even among patients, blood type 0 showed a significantly lower risk of death. Type AB's fall nearer to A's, having a slight increase in susceptibility and a more dramatic trend towards recurrence and shorter survival times. Blood type B generally acts a bit more like blood type O, imparting a degree of reduced susceptibility or reduced risk. This is particularly evident among women who do not have a family history of breast cancer. However, there are two areas to consider if you are a blood type B woman. If you have had a family member with breast cancer, the protection normally associated with being a B women goes out the window, and you need to be more aware of the possibility of breast cancer. Also, if you are a B women and currently have or have had breast cancer, statistically speaking, your odds of a recurrence of breast cancer tend to be higher. Part of the reason for this is that you tend to survive the original cancer, but nevertheless, you might want to consider some of the long-term immune building and anti-cancer strategies we will discuss. (Mourali N, et al., 1980)

Breast cancer shows a weaker association with being a non-secretor.
Female Reproductive Cancer:
As a general rule, gynecological tumors occur more frequently and are associated with worse prognosis in blood type A women. As examples, endometrial cancer occurs more frequently in Type A, ovarian cancer occurs more frequently in A's and AB's. For both of these cancers blood type A is associated with worse 5- and 10-year survival. Conversely, the best survival rate is seen among blood type O women, followed by B women. Type B women are also the least likely to have an ovarian tumor that is malignant. With regard to cervical cancer, analysis also shows a strong trend towards higher frequency of cancer and poor outcomes among A women, a slight trend towards increased risk for B’s, and a better 5-year survival among 0 blood phenotype. (Marinaccio M, et al 1995).

Key point:
* Type O associated with better 5-year survival for cervical cancer.
* Type O associated with better 5- and 10-year survival for endometrial cancer.
* Type O and B associated with better 5-year survival for ovarian cancer.

Similar to other cancers we will mention, ovarian cancer is characterized by a loss of blood type antigens. Uterine endometrial cancers often have an opposite presentation. Normal endometrial tissue does not contain ABO antigens; however, over 20% of endometrial cancers have detectable A, B or H antigens. An increased rate of expression of Lewis group antigens, particularly Lewis(b) antigen, is also observed in endometrial cancers compared with its expression in normal endometria. (Metoki R, et al, 1989).

Bladder Cancer:
Bladder cancer appears to be an exception to the generalized observation of A's and cancer aggressiveness. In a study by Llopis et al, the researchers noticed that blood group O had a tendency to increased aggressiveness, higher tumor grade, and more relapses. Surprisingly, blood type A individuals generally were less likely to have aggressive cancer and were somewhat protected against relapses of bladder cancer. Srinivas et al observed a similar trend. They found that among 141 patients with bladder cancer, individuals with blood group A had lower grade tumors and lower mortality rates. Blood type O's generally had higher grade tumors and higher mortality rates. Other researchers have also observed similar trends, such as the blood type O

Blood Type O is associated with higher grade, larger, more aggressive bladder cancer. They tend to have the greatest tendency to advanced disease, more relapses, and higher mortality rates. Blood type A is actually protective for this type of cancer. Blood type AB inherits the A tendency for protection, while blood type B’s fall closer to O with regard to this cancer.
tendency to higher grade tumors, larger tumors, progression to advanced disease, and increased rates of mortality (especially after 8 years). (Llopis B, et al, 1990).

**Lung Cancer:**

Lung Cancer is and has been one of the leading causes of cancer deaths in the U.S. It is expected that about 180,000 new cases will be diagnosed within the U.S. this year, and of these, about 160,000 people will die. While the incidence of lung cancer has been declining in men since the 1980s, it is still rising in women. The most well known risk factor for lung cancer is cigarette smoking (which has been linked to 85 to 90 percent of all cases). Other well known risk factors include exposure in the workplace to certain substances including asbestos and some organic chemicals, radiation exposure especially in smokers, and even second hand environmental tobacco.

Because of the close associated of lung cancer with cigarette smoking, we would expect this strong risk factor to possibly overwhelm any blood type differences. However, we still see a higher number of A's and a lower number of O's with lung cancer. This trend is even greater among individuals younger than 50 (where it is especially high). This suggests that smoking, which increases risk for lung cancer with each decade of exposure, somewhat mutes the blood type connection in a population which has had many decades of smoking history, but still cannot camouflage the blood type A connection to lung cancer. (Roots I, et al, 1988).

**Colon Cancer:**

Colorectal cancer is among the most frequent cancers in the United States, with an estimated 133,000 new cases predicted (94,000 for colon and 39,000 for rectum). About 55,000 deaths from colorectal cancer are expected this year.

Some of the most common risk factors include a family history of colorectal cancer; polyps or inflammatory bowel disease. Other risk factors can include physical inactivity, exposure to certain chemicals and a high-fat or low-fiber diet.

Colon cancer is actually one of the relatively few diseases with a significant association to an individual's Rh blood type. Although Rh+ and Rh- individuals are about equally likely to have colon cancer, Rh- individuals are more likely to have a localized disease, while Rh+ individuals are more likely to have metastatic disease. This suggests that Rh+ patients with colorectal cancer are less protected against tumour spread than Rh- patients, especially with regard to regional lymph node metastases. (Halvorsen TB, 1986).
Early studies showed an association of cancers of the large intestine with blood type A. However, this association is weaker than that found with stomach cancer. Perhaps the largest link to blood type and colon cancer is found with respect to the appearance or disappearance of blood type antigens. It is commonly recognized that altered blood group antigen expression is a hallmark of malignancy in this form of cancer. During the progression to malignancy of colonic cancer cells, the blood group antigens A, B, H, and Le(b), which are normally expressed only in the proximal colon, can be re-expressed in distal colon cancers or deleted in proximal colon cancers. An individual can also actually even express an antigen which is incompatible with the individual's blood type (so a blood type B could express an A antigen). Because of this phenomenon, of colon cancer cells altering of the surface structure, some researchers have suggested that specific lectins (such as amaranth lectin) might provide a useful tool for early detection of colon cancer (in fact they might also be potentially useful therapeutically as well). The lectins that have been discussed to date have been specific for blood type A. This is in order to take advantage of the changed structural glycoconjugates which tend to have a more A-like alteration (though this would be to an extent influenced by primary ABO type, secretor status, and Lewis phenotype). (Laferte S, et al. 1995)
3. Material and Methods

3.1 Study setting and design:
This cross-sectional study was conducted at the National Administration of Blood Transfusion Service in Khartoum State apparently healthy donors from different age groups and from different localities were screened. It was study executed by the regular blood bank staff. All consecutive candidate blood donors, either voluntary or replacement, were invited to participate and after signing the informed consent, enrolled. The study complied with the STROBE recommendations for reporting on cross-sectional diagnostic studies and with the STARD guidelines for comparisons between diagnostic tests.
Ethical clearance is done.

3.2 Data collection:
The outcome variable was the serological report of the individual whether positive or negative or any TTIs.

3.3 Sample Collection and Lab Testing: Rapid test screening and confirmatory procedures For this study, and by analogy to the quality assurance process for drugs, we considered as “quality assured” diagnostic tests.

3.3.1 HIV testing:
Presence of HIV-1 and HIV-2 antibodies was screened with the quality-assured rapid test Determine HIV-1/2, which has a reported sensitivity of 100% and specificity of 99.4% [17]. For study purposes and in accordance with national algorithms for diagnostic HIV testing, blood found positive was thereafter tested for confirmation with another quality-assured rapid test Uni-Gold HIV-1/2 (Trinity Biotech, Dublin, Ireland) which is 100% sensitive and specific on whole blood. Both rapid tests are in the WHO bulk procurement 2010 list for HIV test kits. Reported HIV seroprevalence corresponds to the proportion of cases tested positive with both tests.

3.3.2 HBV testing:
Hepatitis B surface antigen (HBsAg) testing was performed with the rapid test Healthease. However, since this test lacked independent quality assurance data, another rapid test, Determine HBsAg (Abbott Laboratories, Illinois, USA), from the WHO bulk procurement 2010 list, was supplied by ITM and run in parallel during the study (reported sensitivity: 100%; specificity:
99.4% . Antibodies Sera were checked for the presence of hepatitis B surface antigen (HBsAg) using ELISA, Hepanostika HbsAg (Murex Biotech Ltd, Dartford, UK).

3.3.3 HCV testing:
HCV testing, not performed routinely in the provincial hospital, was added to the pre-donation serological screening during the study period. HCV antibodies were detected through the quality-assured rapid test., IgG antibodies to HCV were detected using an ELISA technique (Murex anti-HCV version 4.0) according to the manufacturer’s instructions.

3.3.4 Syphilis testing:
For the same reason as for HBV, syphilis was screened with 2 rapid plasma regain (RPR) card tests in parallel: one used routinely in the blood bank, the RPR test Ara- Gen (AraGen Biotech, Amman, Jordan), and the quality assured RPR test BD Macro-Vue RPR (Becton, Dickinson and Company, Maryland, USA) supplied by the ITM for this study. In case of discordant results, both tests were repeated.

3.3.5 ABO blood grouping and Rhesus (RH) typing:
ABO and Rh blood groups determinations were carried out on a slide using monoclonal blood grouping antisera; anti-A, anti-B, and anti-D.

3.4 Management of blood donations and candidate donors:
Blood reactive to any of the locally used or ITM-supplied screening tests was discarded. All donors found positive with any screening test were offered specific counseling about the need for further confirmatory workup and were informed when the confirmatory results were available (immediately for syphilis, several months later for HBV and HCV infections after workup in Maputo and Antwerp). Individuals with confirmed serological diagnosis of TTI were evaluated and managed according the current standard of care in Mozambique. Donors found with positive Determine HIV-1/2 but negative Uni-Gold HIV-1/2 (discordant results) were immediately retested and in case of persistent discordance were referred to the HIV counseling program where both tests were repeated within one month according to the national algorithm. Donors with confirmed HIV infection were immediately referred to the HIV care and treatment program.

3.5 Quality control of the laboratory results:
Internal quality controls were performed weekly. External quality control took place in the INS, where all sera with discordant rapid test results for HBsAg were analyzed with EIA (as already mentioned). The INS retested also 10% of the samples for which both HBsAg rapid tests had
given concordant results. All samples reactive to HCV rapid testing as well as 10% of the non-reactive samples were rechecked at the INS. External quality control of screening and confirmatory results was also performed for all four pathogens

3.6 Data Management and Statistical Analysis:

Data entry will be carried out by using Microsoft office excel worksheet and analyzed by percentage and comparison.
4.1 Results and Observations:
The seroprevalence rates of TTIs according to the various blood groups and Rh factor is given in Table:

<table>
<thead>
<tr>
<th>Blood group</th>
<th>Total donor</th>
<th>Anti- HIV</th>
<th>HBsAg</th>
<th>Anti-HCV</th>
<th>VDRL</th>
</tr>
</thead>
<tbody>
<tr>
<td>A positive</td>
<td>148</td>
<td>6</td>
<td>8</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>% (4.1%)</td>
<td>(5.4%)</td>
<td>(0.68%)</td>
<td>(1.4%)</td>
<td></td>
</tr>
<tr>
<td>A negative</td>
<td>10</td>
<td>1</td>
<td>2</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>% (10%)</td>
<td>(20%)</td>
<td>(10%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B positive</td>
<td>86</td>
<td>2</td>
<td>6</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>% (2.3%)</td>
<td>(6.9%)</td>
<td>(1.2%)</td>
<td>(2.3%)</td>
<td></td>
</tr>
<tr>
<td>B negative</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>% (25%)</td>
<td></td>
<td>(25%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O positive</td>
<td>211</td>
<td>7</td>
<td>20</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>% (3.3%)</td>
<td>(9.5%)</td>
<td>(1.4%)</td>
<td>(0.5%)</td>
<td></td>
</tr>
<tr>
<td>O negative</td>
<td>14</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>% (7.1%)</td>
<td>(7.1%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AB positive</td>
<td>21</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>% (4.8%)</td>
<td>(4.8%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AB negative</td>
<td>6</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>500</td>
<td>16</td>
<td>38</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>% (3.2%)</td>
<td>(7.6%)</td>
<td>(1.6%)</td>
<td>(1.2%)</td>
<td></td>
</tr>
</tbody>
</table>
5.1 Discussion:

Association between blood groups and diseases is not something new. Diseases like peptic ulcer, gastric carcinoma, erythroblastosis foetalis, coronary artery diseases and venous thromboembolism, neuroendocrine tumors in MEN type 1, have shown their association with various blood groups. Evidence collected by David J. Anstee showed that selection by infectious diseases at the level of the ABO and secretor genes is persuasive but for other blood group antigens, founder effects appear more likely to account for the distribution of blood group polymorphisms. (Anstee DJ, 2010 Jun).

The study was done on the samples of 500 apparently healthy human blood donors and it was found that “yes”, there does seem to be a preference of a particular infection to a particular blood group, Seroprevalence of HIV (10%), HCV (25%), HBsAg (20%) and syphilis (10%) was detected.

• The Rh NEGATIVE blood groups were found to be more prone to TTIs.
• More patients with blood Group A negative were found to be affected with HIV, HBsAg and VDRL while blood Group B negative was more common in patients affected by HCV.

In a study conducted in Karnataka, India. A. Banu reported that “O Rhesus positive” was the most prevalent blood group in both adult (40.13%) and paediatric (43.33%) HIV seropositives. (Banu A, Ahmed SM, Shastri S, 2011).

Omar and co-workers reported that seroprevalence of HBs Ag and HCVAb were found to be higher in donors who has blood group O and lowest in blood group AB donors, while the distribution of Rh in hepatitis infections was higher between Rh positive donors.

(Omar AAA, et al., 2012).

Kumar and associates reported that the highest prevalence of HIV and HBV infection were found in individuals with blood group O and Rh positive.

(Kumar MR, et al. 2013).

In an analysis for sero-prevalence of antibodies to HIV, HBV and syphilis and its relationship to blood group in healthy Nepalese males, Joshi and Ghimire showed a tendency of high affinity of those diseases in the subjects with O “positive” blood group. However, no real association of those infections was found with the blood group (HIV: X²=0.902, p=0.99; HBsAg: X²=1.212, p=0.99; RPR: X²=3.975, p=0.789).

(Joshi SK, 2003 Oct).
Not much study have been reported establishing relation between ABO and Rh blood group system. Sathe et al conducted a study in Aurangabad but reported that “There is no evidence of any association between sero-positivity for syphilis and ABO blood groups”.
The results of given study is not in agreement with other studies reported on association of Transfusion transmitted infection with ABO and Rh-system blood group. Most of similar studies have reported that blood group “O” and “Rhesus positive” is more prone to TTI. The probable reason may be that the sample size in given study is small as compared to other similar studies reported in the text.
5.2 Conclusion:
This study clearly shows that there is preference for negative blood groups by the TTIs and even the specificity of a particular infection to a particular blood group is noted.

5.3 Recommendation:
Other similar large scale studies are required to find out how can this association help us to improve our screening programmed? Can particular blood groups be categorized as high risk donors? Should they be given some extra attention while screening? Should such people be otherwise also advised in good faith to get their blood tested for TTIs even if they do not intend to donate? What about the list of second choice blood groups which are transfused considering them safer. How safe is to routinely transfusing them in other emergency conditions? What about the so called universally safe O negative, the exchange transfusions done in newborns in the window period.
Food for thought and follow up…. 
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Maresch C, Schluter PJ, Wilson AD, Sleigh A: Residual infectious disease


Mudassar Zia, MD:(2012) Chief Editor: Emmanuel C Besa,MDTransfusion-Transmitted Diseases.


Sudan University of Science and Technology
College of Graduated Studies
Questionnaire
Master Degree

TOPIC: The association of transfusion transmitted diseases and blood group of blood donors

Questions for definitive exclusion:
01 Do you have more than 65 years of age?
02 Do you have a disease without cure (chronic)?
03 Were you once suspected of being infected with HIV?
04 Did you have once hepatitis/jaundice?
05 Did you already have once a venereal disease?
06 Do you belong to a risk group for HIV infection (injection of drugs, sexual contacts without condom, traditional vaccines with blades used for different persons, several blood transfusions)?
Questions for temporary exclusion:

07 A person with HIV can not donate blood?
08 Were you refused before to donate blood?
09 Do you suffer from diseases of the cardiovascular system (e.g. pericardial pain)?
10 Do you suffer from diseases of the respiratory system (e.g., asthma)?
11 Do you suffer from diseases of the gastrointestinal system (e.g.; peptic ulcer)
12 Do you suffer from diseases of the central nervous system (e.g. epilepsy)?
13 Do you suffer from diseases of the muscular/skeletal system?
14 Do you suffer from diseases of the genital/urinary system?
15 Do you suffer from diseases of the endocrine system? (e.g. diabetes).
16 Do you suffer from diseases of the immune system? (e.g. allergy)
17 Do you have a blood disease? (e.g. hemophilia)?
18 Do you have a fever?
19 Are you pregnant /menstruating? (women)
20 Are you taking any medication?
21 Were you vaccinated in the last 4 weeks?
22 Were you operated in the last 6 months?

Physical examination:

23 Control if donor has infectious diseases
24 Do you have a blood pressure higher than 160/110 mmHg or lower than 120/80 mmHg?
25 Do you have a pulse higher than 120 beats per minute (bpm) or lower than 70 bpm?
26 Do you have a weight below 50 kg?
27 Do you have a hemoglobin level below 12.5 g/dl?
28 Others