Prevention of Transfusion Transmitted Malaria in an Endemic area– A Challenge for Blood Banks

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Background:

Malaria is one of several blood borne infections that are transmitted through transfusion of blood. The disease is caused by Plasmodia, of which two species vivax and falciparum are prevalent in Pakistan. Transmission of this parasite through blood transfusion is important as only a small number of infected red cells from donor can lead to malaria in the recipient. Moreover, the diagnosis is often missed and unexpected in a patient who is otherwise critically sick. This may be life threatening in extreme cases, especially if the species is Plasmodium falciparum.

The first case of transfusion malaria was reported in 1911. Since then increasing number of cases have been reported world wide. The risk of acquiring malaria through transfusion is dependent on incidence and prevalence of the disease at a particular area. In countries like USA and Canada, where malaria is not endemic the incidence is as very low. The annual incidence reported by US Center for Disease Control (CDC) is only 1 -3 cases per year. However, in endemic countries like ours, the rate of transmission may be as high as 50 cases per million blood donation. We do not know the actual prevalence of transfusion transmitted malaria in Pakistan. The incidence was reported to be nil by Rahman M et al in 2003 from Punjab. However, this appears to be an underestimation of overall burden of transfusion malaria that can be measured only through a comprehensive national surveillance program.

In a country like ours where malaria is endemic, there is a need of screening every donor through proper laboratory tests to alleviate the chances of post transfusion malaria.

Laboratory screening for Transfusion-transmitted Malaria

National Institute of Health (NIH) consensus conference in 1995 requires that every donor blood should be screened for various infections including HIV, Hepatitis B and C, malaria and syphilis. However, there is no suitable test yet available for screening malaria in the donors. The different diagnostic tests available for malaria include examination of peripheral smear, QBC, various serological tests including PCR. However, all of these tests have their limitations in terms of specificity, sensitivity and cost effectiveness. Hence, it the challenge for a blood bank to properly screen the donated blood for malaria by a test which should be simple, sensitive, fast and at the same time economically feasible also.

Various strategies for Screening Malaria:

1. Donor history: A report prepared by WHO in 1998 stated that the most effective way of screening donors is to take proper history of malaria or fever that could be due to malaria. Donor selection criteria should be designed to exclude potentially infectious individuals from donating red cells. However, the infected donor may have a very low parasitemia; he may not have a clinical history of recent past or present history of febrile illness. Thus, there are good chances that he may pass out through donor screening process. Further more, the acquired immunity in adults in malaria endemic areas may result in low grade parasitemia without symptoms. Such carriers can also be difficult to identify on history basis alone.

Federal Drug Administration (FDA) and American Association of Blood Bank (AABB) had set the following criteria for donors who have traveled to or lived in an endemic area:

1. Travelers may donate blood 6 months after returning from endemic areas provided they are free of symptoms and have not taken anti-malarial drugs.
2. Persons with past history of malaria should be deferred for 3 years after becoming asymptomatic.
3. People who had been on chemoprophylaxis can donate blood after 3 years of stopping their therapy.
4. Immigrants or visitors from endemic area can be accepted as donors 3 years after departure if they are asymptomatic.
5. Proven carriers of malaria or persons who had malaria due to P malariae are excluded permanently from donating blood.

The 3 years limit has been established because infection with the relapsing forms of malaria (Plasmodium vivax and Plasmodium ovale) rarely persist for more than 3 years after a naturally acquired infection. Infection with Plasmodium falciparum usually has clinical malaria with in 3 months but may show asymptomatic infection for a year or more. Plasmodium malariae may remain undetected in blood for several years.

However, these deferral policies are not practical for endemic areas as exclusion would include nearly all the donors.
Furthermore, it is not always possible to obtain accurate travel and immigration history. Some cases of transfusion transmitted malaria would always occur because of occasional asymptomatic persistence of malarial parasites.

2. Examination of Peripheral film:

The gold standard for malaria diagnosis is peripheral film examination. However, this is very labor intensive and skill effective. The reason is that the asymptomatic blood donors have very low levels of parasite count and sensitivity of peripheral film microscopy declines in parallel with the density of malarial parasites in the blood. Thus, microscopy of blood films involving a large numbers of blood donors on daily basis seem to be impractical.

3. QBC:

It is another method of identifying the malarial parasites in the peripheral blood. It involves staining of the centrifuged and compressed layer of red cell layer with acridine orange and its examination under UV light source. It is fast and more sensitive than smear examination and can detect parasites even less than 100/ul. However the test is non specific and stains nucleic acid from all cell types and therefore technically demanding. The major disadvantage is that it requires costly equipment and consumables.

4. Automated analyzers:

Some hematology cell counters detect parasites by giving abnormal signals that are produced by hemozoin in white cells. Hemozoin is the pigment produced by the parasites as a breakdown product of hemoglobin present in host red cells. As the red cells rupture, they release hemozoin which is engulfed by phagocytic cells like neutrophils and monocytes. Initial studies have shown good results in terms of sensitivity and specificity. But its value in donor screening is yet to be evaluated as parasitemia and production of hemozoin is lower in them.

5. Rapid diagnostic tests:

Immunochromatographic tests are based on the detection of parasite antigens from the peripheral blood using either monoclonal or polyclonal antibodies against the parasite antigen targets. Currently these tests capture histidine rich protein II, a pan malaria aldolase and parasite specific lactate dehydrogenase. The rapid diagnostic tests are simple, user friendly not requiring skilled technologists and equipment.

These tests usually have a sensitivity of 35-97% for P falciparum and 2-97% for P vivax or non-falciparum species. There is also a possibility of false positive and false negative results with these tests. The sensitivity of these tests is considerably less at low levels of parasitemia and non immune individuals.

These assays may serve as a promising test for screening our donors. But there is a need to develop the devices so that they may have high acceptable sensitivity and an affordable cost.

6. ELISA:

It is an interesting alternative for the screening of blood donors. It is automated with fast through put and compatible with other transfusion screening procedures. However, the test lacks sensitivity as the low levels of antibodies cannot be detected by this method. A study done recently demonstrated that combined detection of antigens and antibodies may represent a sensitive strategy for the testing of blood donors. More trials are required before ELISA can be accepted as a valuable option for this purpose.

7. PCR:

The major advantages of using a PCR based technique are its high sensitivity as it can detect parasites as low as 5 or less per µl of blood and identification of species. Rubio et al in 1999 found semi nested PCR to be very useful for screening donors at risk who were immigrants in Spain. However, the test may be positive after successful treatment of malaria as PCR can detect DNA from non viable parasites also. Hence, PCR testing in endemic areas will result in false positive results with too much loss of donated blood. The other associated problems are its prolonged time frame and cost in-effectiveness. The cost of screening through PCR was estimated to be $3,972,624 per case of malaria averted.

Although PCR technique is very promising for the screening of malaria, but still it can not be considered as a method of choice for our purpose. The future advances in PCR technique may help to overcome the problems of cost and timings.

Conclusions:

Transfusion associated malaria is often severe and fatal. The detection of infected donor is difficult in endemic areas due to the lack of suitable screening test. Deferral of donors based on history is not practical for endemic areas. Blood smear staining techniques show poor results due to the low parasite concentration in many asymptomatic blood donors. Antibody detection test is not helpful because of universal presence of the antibodies in healthy donors in malaria endemic areas. Malarial antigen test seem to be promising but more costly. PCR technique, although is the most sensitive test is not economically feasible and impractical also because of its prolonged duration.

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It is highly amenable that sensitive tests which are simple, fast, cost effective should be introduced for malaria screening in blood donors.

References: