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ORIGINAL ARTICLE

Transfusion transmissible malaria: seroprevalence of malaria parasitemia in blood donors in Garhwal region of Uttarakhand, India

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ABSTRACT

Background and Objectives: Malaria was the first ever reported case of transfusion transmitted infection (TTI). Transfusion transmissible malaria (TTM) can result in febrile transfusion reaction in the recipient. TTM can be fatal if the blood transfusion recipient is from vulnerable population i.e. pregnant women or young children. Therefore, the present study was done to estimate the seroprevalence of malaria parasitemia among blood donors in Garhwal region.

Materials and Methods: Study subjects were healthy blood donors who had passed the screening criteria for blood donation. Donors with a history of malaria were temporarily deferred for 3 months following full recovery. Screening of the donated blood units for malaria parasite was done using immunochromatography based rapid diagnostic test. Thin smear examination was performed for malaria parasite species identification.

Results: A total of 1984 blood donations were screened for TTI. The seroprevalence of HBV, HCV HIV and syphilis was 0.3% (n=6), 0.25% (n=5), 0% (n=0) and 0% (n=0) respectively. The seroprevalence of malaria parasite was 0.05% (n=1). *Plasmodium vivax* was identified upon thin smear examination. The donor reactive for malaria parasite was a replacement donor and gave no recent history of fever or any past history of malaria.

Conclusion: Meticulous donor screening combined with rapid diagnostic tests for malaria parasite is the most practical strategy to prevent TTM in Garhwal region of India.

Keywords: Blood transfusion; Blood donor; Malaria

INTRODUCTION

The primary aim of blood center is to provide blood that is safe for transfusion (1). Despite rapid advancement in the field of transfusion medicine, blood transfusion carries an inherent risk of transfusion transmitted infections (TTIs) (2). As per the Drugs and Cosmetics Act 1940, Government of India, the donated blood must be tested for human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), syphilis and malaria.

Malaria, caused by intracellular protozoan parasite

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Plasmodium, is a major public health problem in India (3). Malaria is an endemic disease in India, however, the degree of endemicityis highly variable in different parts of India (4).

Malaria parasite can survive at 4°C, therefore both whole blood and packed red blood cell can result in transfusion transmitted malaria (TTM) (5). Malaria parasite has shown to be present in blood stored at 4°C even after 28 days of storage (6). There are very few case reports published in the literature discussing TTM (7-9). TTM is an aspect of concern especially if the blood transfusion recipient is from vulnerable population i.e. pregnant women or young children, as it can be fatal in these patients (5).

Most of the reported cases of TTM are due to *P. falciparum, P. vivax* and *P. malariae* (10). *P. falciparum* and *P. vivax* can persist for 1 year and 3 year respectively in an asymptomatic carrier state (11). An important characteristic of TTM is that the pre-erythrocyctic phase of malaria parasite infection, seen in case of natural infection is omitted in case of TTM. Therefore, the immune system of the host gets less time to respond to the infection, which can result in higher rate of complications and more fatality (12). The infective dose of TTM is very small and as few as 10 infected RBCs can result in TTM (13).

To prevent TTM, blood transfusion services use two types of strategies: (i) donor deferral; (ii) testing of donated blood. The strategies used are different for endemic and non-endemic countries. Moreover, the time period of donor deferral, whether temporary or permanent donor deferral and the type of screening test varies from one country to another (14).

Therefore, the present study was planned to estimate the seroprevalence of malaria parasitemia in blood donors in the Himalayan region of Uttarakhand, India.

MATERIALS AND METHODS

Study design, population and procedure. The present study was a cross sectional study conducted in the blood center of a tertiary care teaching hospital in a hilly region of Northern India from 1st January 2021 till 31st December 2021. Participants were the healthy blood donors who donated the blood in the hospital blood center or the blood donation camps during the study period. Pre-donation screening of all individuals was done as per the criteria given in the Drugs and Cosmetics (Second Amendment) Rules, 2020 issued by the Government of India (15). Individuals with history of malaria were deferred for 3 months following full recovery. Blood sample for TTI testing was obtained using venipuncture technique (16), in EDTA vacutainers. Rapid diagnostic test (Abbott Malaria Ag Pf/Pv) for detection of malaria parasite was performed using manufacturer's instructions and microscopic examination was conducted on antigen positive samples to identify the species.

Definition of blood donors. Voluntary donors: Blood donors who donated blood on their own free will, Replacement donors: Blood donors who are relatives or friends of the patient and donated blood in lieu for the blood requirement of the patient.

Ethical considerations. The study was based as per the ethical guidelines given in the "Declaration of Helsinki" and was conducted after obtaining ethical clearance from the Institute's ethical clearance committee.

Statistical analysis. The data generated was entered electronically and analyzed using the Statistical Package for Social Sciences (SPSS) software version 20(IBM Corp., US). Frequency and percentage were calculated for representation of the continuous variables.The categorical data was expressed in frequency and chi-square test was used for comparison of proportions. Statistical tests were performed at a significance level of 0.05.

RESULTS

A total of 1984 blood donations were done from 1st January 2021 to 31st December 2021. Out of these 1447 (72.93%) were voluntary donors and 579 (29.18%) were replacement donors. Out of the total of 1984 donors, 12 blood donors were positive for various transfusion transmitted infections. The seroprevalence of TTI was more among voluntary donors as compared to replacement donors (0.2% (n=3) vs 1.55% (n=9); $p<0.05$)) (Table 1). The seroprevalence of various TTIs among blood donors is shown in Table 1. Among the reactive donors, HBsAg was seen in six donors (0.3%), anti-HCV was seen in five donors (0.25%), malaria parasite was seen in one donor (0.05%), HIV or syphilis was not seen in any of the

Table 1. Seroprevalence of malaria parasitemia in blood donors in India

Study	Prevalence of malaria	Method of testing
Dubey et al. (5)	0.09%	RDT
Bahadur et al. (18)	0.03%	RDT
Negiet al. (19)	0.002%	RDT
Pallaviet al. (20)	0.00%	RDT
Fernandeset al. (21)	0.01%	RDT
Rawatet al. (22)	0.06%	RDT
Present study	0.05%	RDT

RDT- Rapid diagnostic test

donors. All 12 donors were of age less than 40 years, among these seven (58.33%) donors were in the age group 18-30 years, while five (41.66%) donors were in the age group of 31-40 years. Blood group of the donor reactive for malaria parasite was O positive. *Plasmodium vivax* species was identified upon thin smear examination. The donor reactive for malaria parasite was a replacement donor and had no recent history of fever, nor any history of past malaria infection.

DISCUSSION

Testing of blood for malaria parasite is mandatory as per Drugs and Cosmetics Act 1940, Government of India. Transfusion transmitted malaria was the first ever report case of transmission of an infection through blood transfusion (14). In the current scenario, blood centers are less concerned about transfusion transmitted malaria as compared to other TTI. In the present study, the prevalence of malaria among blood donors was 0.05% which correlates with the low annual parasite incidence (API) of less than 1 in this region, resulting in the categorization of this Himalayan state in Category I under the National Vector Borne Disease Control Programme (NVBDCP) (17). In various studies done in different parts of India, the prevalence of malaria among blood donors range from 0% to 0.09% as shown in Table 1 (5, 18-22).

In the present study, 100% of the donors reactive for the malaria parasite (n=1), were replacement donor. This finding is similar to the results from other studies in which, 100% of the donors found reactive for malaria parasite were replacement donors (19, 22). This is due to the fact that unlike voluntary blood donors, who donate blood with their free will, replacement donors, donate blood under pressure for their friends/ relatives and are therefore likely to conceal history which might result in the deferral for blood donation (23).

Serological tests for malaria can be broadly divided into two types: (i) antigen detection tests; (ii) antibody detection tests. Therefore, another important question is whether to use antigen or antibody based test for ensuring blood safety in India. As already discussed, the prevalence of malaria among blood donors range from 0% to 0.09% in various Indian studies. In the current study, the prevalence rate was 0.05%. Few studies in India have also assessed the malaria antibody prevalence in Indian blood donors in which it ranged from 12.39% to 17.4% (5, 24).

Furthermore, the utility of antibody screening for many endemic diseases is marred by issues in differentiating recent and past infections (25). In a study by Kyabayize et al. the mean duration of antigen positivity was till 32 days after complete anti-malaria treatment (26). Therefore, if a donor is temporarily deferred, he will most likely give a negative result malaria antigen test after three months of complete treatment, whereas antibody test will be positive in such individual. Therefore, in view of the high malaria antibody prevalence, use of antibody based test in India or other endemic countries will result in unnecessary wastage of blood.

At the same time it should remembered that as little as 0.00004 parasite/µL can result in TTM, which is well below the detection limit of the commonly employed diagnostic tests such as smear microscopy (detection limit of 10-50/µL) and RDT (detection limit50-100/µL) (5). Although there are no specific guidelines, but the malaria screening policies have to be made depending upon the local seroprevalence of malaria. Based on the above discussion, antigen based screening tests are better suited in endemic countries like India, compared to antibody detection based serological tests.

Commonly available light microscopy based tests for detecting malaria use thick smear and thin smear for diagnosis. These tests are classically considered gold standard for malaria diagnosis (27), owing to their high reliability viz. lower detection limit (higher sensitivity) as well as higher specificity, compared to antigen based RDT tests. They are also capable of identifying the species causing infection. The high dependency on the observer's skill performing

microscopy reduces this advantage to some extent though. Moreover, RDTs detect antigen, instead of the whole parasite, providing them with additional advantage over microscopy (28).

RDTs have their own set of challenges, with both false positives as well as false negatives. False negatives can occur especially in case of infections with *P. falciparum*, due to mutations in the *hrp2/hrp3* gene mutation/ deletion (29). False positive RDTs are generally seen in conditions such as Rheumatoid arthritis (RA factor positive patients) (30), circulating HRP-2 antigen after successful treatment (31), African trypanosomiasis (32), schistosomiasis and *Salmonella* Typhi infection. False positive *P. falciparum* RDT test can be seen in patients suffering from Leishmaniasis (33). The RDT test kit used in the present study had a sensitivity of 95.5% (P.v) to 99.7% (P.f), and a specificity of 99.5%.

In the present study, *P. vivax* species was identified upon microscopy. Malaria in India can mainly be attributed to 2 species, *P. falciparum* and *P. vivax* (34), out of which *P. falciparum* is the dominant species responsible for majority (55-60%) of the infections (35). A total of 45 fatalities due to TTM have been reported in literature (36). A majority of these fatalities (11/45) were attributed to *P. falciparum* (11). Lastly, locally transmitted malaria case in the US has raised concerns of changing epidemiology of malaria in view of climate change that can cause changes in the habitat of the vector (36). Therefore, TTM should be taken seriously in blood centers to ensure blood safety.

CONCLUSION

In view of the current seroprevalence rate of malaria parasite, meticulous donor screening combined with rapid diagnostic tests for malaria parasite is the most practical strategy to prevent TTM in Garhwal region of Uttarakhand, India. Blood transfusion services must take appropriate measures depending upon seroprevalence of malaria in the region to prevent TTM.

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