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Original Research Article

Enhancing blood safety: the utility of NS-1 antigen capture ELISA for detecting acute dengue infections among blood donors during peak transmission periods and the potential to curtail dengue spread

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ABSTRACT

Background: Dengue fever is a viral disease transmitted by mosquitoes and affects millions of people worldwide. It can also be transmitted through blood transfusions, particularly during peak transmission periods.
Methods: This was a cross sectional study which was conducted over a two-month period (June 2022 to July 2022) at a tertiary hospital blood bank. A total of 180 nonrepetitive serum samples were collected from voluntary blood donors and analyzed using the dengue NS-1 Ag Microlisa ELISA kit.
Results: Among the 180 samples two samples tested positive for the dengue virus NS-1 antigen using the NS-1 antigen capture ELISA, indicating a prevalence of acute dengue virus infection among blood donors during the peak transmission period of 1.2% (2/180).
Conclusions: The use of NS-1 antigen testing was shown to be useful for dengue virus detection. Routine screening of blood donors for dengue virus is not universally implemented in many countries, partly due to the lack of sensitive and specific screening tests. However, the use of serological tests, such as ELISA for dengue antibodies or NS-1 antigen, can effectively detect dengue virus in blood donors. Interventions made during peak transmission periods can help in curtailing the spread of dengue infections.

Keywords: Dengue fever, Transfusion transmission, Screening

INTRODUCTION

Dengue fever is a debilitating mosquito-borne viral disease that affects millions of people every year, particularly in tropical and subtropical regions. According to the world health organization (WHO), about 390 million dengue infections occur worldwide each year, with 96 million resulting in illness. There are four distinct serotypes of dengue virus (DENV 1-4), which can cause a spectrum of clinical illnesses ranging from mild fever to severe and potentially fatal forms of the disease. Infection with one serotype does not provide immunity against the other serotypes, and sequential infections put individuals at greater risk for developing severe dengue. Therefore, individuals can experience multiple dengue infections, which can lead to severe complications, such as dengue hemorrhagic fever and dengue shock syndrome.[1]

In addition to being transmitted through mosquito bites, the dengue virus can also be transmitted through blood transfusions. The transmission of the dengue virus through blood transfusion has been documented in several countries, including Singapore, Taiwan, and Brazil. In a study conducted in Brazil, researchers found that up to 4.4% of blood donors during a dengue outbreak were positive for the dengue virus.[2] The risk of transfusion-transmitted dengue is particularly high during peak

transmission periods, such as the monsoon season in many endemic regions.[3]

The NS-1 antigen is an early diagnostic marker of dengue virus infection that can be detected within the first few days of infection.[4] The use of NS-1 antigen testing in conjunction with traditional serology testing has been shown to increase the sensitivity of dengue virus detection, particularly during the early stages of infection when viral load is high and antibody production has not yet occurred.[5]

According to the ministry of health and family welfare, dengue cases in the year 2022 in Karnataka were around 7317 cases with 4 deaths. The total number of cases in the year 2022 in India was around 110473 cases.[6] Karnataka alone contributed to around 6.6% of the total caseload.[7]

In this study, the use of the NS-1 antigen capture ELISA allowed the detection of acute dengue infections among blood donors, which could potentially prevent the transmission of the virus through blood transfusion. The use of this method is particularly important during peak transmission periods when the risk of dengue virus transmission through blood transfusion is high.

However, routine screening of blood donors for dengue virus is not universally implemented in many countries, including those with endemic dengue transmission. However, several studies have shown that the use of serological tests, such as enzyme-linked immunosorbent assays (ELISAs) for dengue antibodies or NS1 antigen, can effectively detect dengue virus in blood donors. Hence, the screening of asymptomatic blood donors will help in curtailing at least the transfusion-related spread of Dengue infections. Interventions made during the peak transmission periods will also additionally help in bringing down the caseload. Hence this study aims in detecting NS-1 antigen detection among voluntary blood donors in our blood bank.

METHODS

This prospective cross-sectional study was carried out over a 2-month period (June 2022 to July 2022), which corresponded to the peak transmission period for dengue fever. A total of 180 non-consecutive serum samples were collected from voluntary blood donors at the KR hospital blood bank in Mysore, following ethical clearance. The samples were analyzed using the dengue NS-1 Ag Microlisa (J. Mitra PVT LTD) ELISA kit as per the manufacturer's instructions.

Four ml of venous blood was drawn from each donor using sterile vacutainer tubes without anticoagulant (red top tubes). The tubes were subjected to centrifugation at 3000 rpm for 15 minutes, and the serum obtained was used for NS1 antigen testing of the dengue virus. The serum samples were stored at -20°C until analysis. Commercial NS-1 antigen capture enzyme-linked immunosorbent assays (ELISA) (dengue NS1 Ag Microlisa (J. Mitra PVT LTD) was employed for the analysis of serum samples.

Statistical methods

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions.

Chi-square test or Fischer's exact test (for 2×2 tables only) was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation.

Inclusion criteria

All voluntary blood donors were included in study.

Exclusion criteria

Volunteers who had any symptoms of Fever or any other constitutional symptoms were not included in the study.

RESULTS

Among the 180 blood donors, the majority were males (82%). Maximum donors (54%) belonged to the age group of 20 years to 30 yrs. The age range of the blood transfusion donors was 20 to 57 years. The mean age of the donors was 32.33 years. The samples were evenly distributed during the months of June and July.

Out of the 180 samples tested, only 2 samples tested positive for the dengue virus NS-1 antigen using the NS-1 antigen capture ELISA. Therefore, the prevalence of acute dengue virus infection among blood donors during the peak transmission period was 1.2% (2/180). The NS-1 Antigen positivity was found among a 23 years old male and 35-year-old male donors respectively and was detected during the month of July.

DISCUSSION

Today, severe dengue affects most Asian and Latin American countries and has become a leading cause of hospitalization and death among children in these regions.[9] Dengue is emerging as a major public health problem in Karnataka.[10] Karnataka has recorded a 21 per cent rise in cases of dengue fever since 2020, according to statistics shared by the national vector borne disease control programme (NVBDCP).[6] DENV has one major consequence in the area of transfusion because the virus can be transmitted through blood and cause hemorrhagic outcomes in the recipients of blood components.[8] Since the donors are asymptomatic there are high chances of unknown transmission of Dengue during transfusion episodes.[10,11]

The present study was an attempt to establish the increasing rates of Dengue seropositivity among the asymptomatic blood donors in a tertiary hospital in Karnataka, a southern Indian state, to assess the risk of transfusion transmission during the peak transmission periods.

In our study prevalence of acute dengue virus infection by NS-1 antigen positivity was 1.2% (2/180) but a similar study done by Mangwana.et al for NS-I antigenemia among 1708 blood donors in a tertiary care centre in North India could not find any positive result among the donors.[13] Another study was conducted on 200 blood donors from Kerala by Raj et al demonstrated NS-1 positivity of 0.56% (1/200) more-closer to our study.[16]

However higher rates of seropositivity was also seen by El-Shemi et al who reported seropositivity of 5.3% for dengue NS1 antigen, 5.5% for dengue IgM antibody, and 38.9% for dengue IgG antibody among blood donors in Makkah, Saudi Arabia but in our study the seropositivity was only 1.2%, it can be attributed to the small sample size and shorter duration of the study.[17]

NS-1 can be detected in the blood of infected patients from the first day of symptoms and circulates at levels in the nanogram per ml to milligram per ml range during the acute phase of infection, and blood levels of NS1 correlate with peak viraemia and disease severity in secondary DENV infection. Several studies have suggested that NS1 is a key mediator of dengue pathogenesis.[14,15]

American association of blood banks committee recently included dengue, among other emerging infectious agents such as vCJD, hepatitis E virus, Chikungunya virus, and Babesia as high priority for increased monitoring in American blood supply.[18] Thus emphasizing the importance of routine screening of blood donors for the same. It is important that dengue should not be neglected in the screening panel at least in endemic areas.

However, newer developments such as pathogen inactivation systems convincingly help in the reduction of transfusion-transmitted infections which was successfully demonstrated by the use of the intercept technology for platelets during the Chikungunya outbreak in reunion Island in 2006 and the recent Zikavirus outbreak in the north and south America.[19] As the spectrum of pathogens transmitted by transfusion increases it is only plausible to adapt the pathogen inactivation systems rather than increasing the panel of screening tests as tried in developed countries. But in developing countries, the feasibility and acceptability in terms of practical aspects of these technologies are still questionable.

Limitation

The use of a single serological test in a limited sample size constraints the interpretation of the study, moreover additional confirmation with molecular methods were also not done.

CONCLUSION

Dengue infection must be proactively handled. Routine screening of blood donors for dengue is not cost-effective. But taking into consideration the increase in prevalence since 2020, recent seroprevalence study data, the danger that the infection itself poses if transfused to a diseased patient is the most important factor. So, it is extremely necessary to introduce the practice of routine screening in at least endemic and hyperendemic areas. The aim of this study itself was to accomplish this fact. However, it is only prudent to do further studies covering a broad geographical area and population to lay down a confirmed hypothesis showing that transfusion screening is necessary in endemic areas.

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