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Original Research Article

Seroprevalence of Parvovirus B19 in Multiple Transfused Patients

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Abstract

Background: Human parvovirus B19 virus is one of the recently found agent in transfusion transmitted diseases. Multitransfused patients are at increased risk of parvovirus B19 infection because virus easily escapes inactivation methods and donor units are not routinely screened for B19. There are only few studies suggesting this globally and in Asia. Hence, the aim of this study is to find the prevalence of B19 infection among multi-transfused patients. *Materials and methods:* One hundred and seventy-three multi-transfused patients of different age, gender and diseases with history of multiple transfusion were considered. Assessment of parvovirus B19 specific IgM antibodies in the serum were done by Enzyme-linked immunosorbent assay (ELISA) using B19 VPI and VP2 recombinant and purified antigens. *Results:* 52 (30%) out of 173 multitransfused patients tested positive for anti-B19 IgM antibodies. Age of the multitransfused patient are from 08 months to 80 years and B19 infection arehighest in less than one to ten year age group with highest prevalence among thalassemia patients (23%). 1/1 HIV positive and 20/50 anti-HCV positive multitransfused patients are found in co-infection with Anti-B19 IgM. *Conclusions:* Anti-B19 IgM seropositivity is detected in high rates among multitransfused patients. Several measures must be implemented to prevent iatrogenic and nosocomial transmissions including blood donor screening, especially blood given to hematological disorders patients. Data from this study also support the B19 vaccine introduction that primarily protect multitransfused patients against that infection.

Keywords: B19; Blood transfusion; Parvovirus; Multitransfused.

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Introduction

Human parvovirus B19 is a newly emerging non-enveloped DNA virus discovered by Australian virologist in London. Parvovirus B19 belongs to the genus. Erythrovirus of the family Parvoviridae.[1–5] It causes erythema infectiosum or fifth disease in children, aplastic crisis, reticulocytopenia and

cessation of erythropoiesis of the bone marrow.[6,7] It is transmitted via respiratory route, blood and its blood products and from mother to child through transplacental route.[6,7] B19 is a thermostable virus and escapes the currently applied viral inactivation methods. Therefore, the issues on safety of blood and blood products were raised.[1–5] B19 infected patients usually develop mild flu like illness and also many times an infected person may be asymptomatic. Patient develops a protective antibody and lifelong immunity once he is attacked by this viral infection.[8] This disease is very commonly found these days and 40–60% adults are found IgG antibody positive.[9] Parvovirus B19 infects erythropoetic cells in the bone marrow which causes transient anemia and this can be clinically significant in hemoglobinopathies and haematological stress conditions.[10]

It was observed that there is low frequency of active B19 in donors and if the disease persists it is of mild clinical course, So infection does not create major problems in transfusion recipients though it can cause serious illness in multiple transfused patients like hemoglobinopathies, haemodialysis etc.[10] There are very few report on B19 infection in Indian subcontinent. Recently, a study by Choudhary N. et al.[11] showed that parvovirus B19 infection in blood donors is 39.9% which may increase morbidity in multiple transfused or immune-compromised patients.[11] There was evidence that as age advances, the prevalence of infection rises. It is high in blood donors with poor standard of living, poor socioeconomic status, low educational level, overcrowding and with poor housing conditions.

In a study of 90 multi-transfused beta-thalassemia major patients, anti-B19 IgM antibodies were detected in 37 (41.1%).[12] Mean age of the thalassemia patient was eight years (range 2–18 years) and B19 infection was highest in the six-to-ten year range.

Currently, there is no any mandatory test done for screening of blood donor to detect parvovirus B19. Furthermore, B19 has been found to be transmitted by transfusion of blood or its components.[13–15] Few studies have shown antibodies to B19 in thalassemia major patients and its transmission is from South East Asia. Hence, the present study was undertaken to find the seroprevalence of B19 by detecting recent transmission/infection as evidenced by IgM antibodies in multiple transfused patients from Central India. Additionally multi-transfused patients were also screened for HBsAg, human immunodeficiency virus (HIV) antibodies, and hepatitis C virus (HCV) antibodies, to find coinfections with B19.

Materials and Methods

A Prospective study was carried out in one and a half years, in the Pathology Department of RD Gardi Medical College in India. A total of 173 multi-transfused patients were enrolled in the study; all of them have a history of transfusion of a total of at least ten units of allogenic blood or blood components. Patients who had been transfused less than 10 units of blood as a part of their management were not included in this study.

Sample collection and preparation

Five milliliters of blood was drawn from each subject after obtaining informed consent and added into clot activator vacutainer. After clotting, blood samples in the vacutainer were centrifuged at 3000 rpm for 10 min and the resulting sera were collected into aliquot tubes for serological analysis of B19 IgM antibodies. The serum samples were used immediately or stored at –20°C until tested.

Quantitative determination of IgM antibodies against parvovirus B19 by in vitro diagnostic Enzyme-linked immunosorbent assay technique, using one of the commercially available ELISA kits (NovaLisa B19 IgM) manufactured by NOVA TEC, Germany, with test sensitivity 98.77% and specificity 99.65%. Sera were tested at 1: 100 dilutions, incorporating a set of negative and positive control sera. Optical densities (O.D.) were read at 450 nm with a reference filter of 620 nm in an ELISA reader. Index values more than or equal to 11 NTU were taken as positive for anti-B19 IgM antibodies. Furthermore, the samples were also screened for HBsAg, anti-HIV, and anti-HCV, using commercial ELISA kits, to find the coexisting infections in the study group.

Statistical methods

A computerized analysis of the data were carried out using SPSS program version 16.

Results

The age of the multi-transfused patients were from 08 months to 80 years, out of which 73 (42%) patients were in the age groupof <1–10 years, 28 (16%) were in the age group of 11–20 years, 12 (6.9%) patients were in the age group of 21–30 years, 11(6.3%) were in the 31–40 year age group, 15 (8.6%) were in the 41–50 year age group and 34 patients belongs to more than 50 years age group respectively. Out of

173 patients, 94 were thalassemia major patients, 51 hemodialysis, 07 sickle cell diseases, 06 hemato-oncology, 03 from acute blood loss and 12 belong to others category tested by ELISA. Anti-B19 IgM antibodies were detected in 39 (41.4%) thalassemia patients, 10 (19.6%) haemodialysis patients, 1 (14%) sickle cell disease patient and 2 from others. None of the patients were seropositive for B19 antibody from hemato-oncology and acute blood loss category.

Predominance of male patients were observed in this randomized group among 173 multitransfused patients 115 (63.5%) were males and 58 (34%) were females. According to gender, 58% (30 of 52) males and 42% (22 of 52) females were positive for anti-B19 IgM antibodies. The prevalence of IgM antibodies was 27, 41, 0, 20, 27, and 19% in males and 54, 67, 33, 0, 0 and 15% in females of age groups 0–10, 11–20, 21–30, 31–40, 41–50, and >50 years, respectively. The anti-B19 IgM antibody positivity in the age groups shown in Table 1. Coexistence of B19 infection along with human immunodeficiency virus (HIV) are seen in one and with HCV in 20 multiple transfused patients.

Discussion

Multitransfused patients who require very frequent transfusions are more prone to acquire transfusion transmitted infections like parvovirus B19. In the present study, the range of patient is from 8 months to 80 years of age. The possibility of acquiring transfusion-transmitted diseases is related to the possibility of being exposed to the infected units of blood,[2] which depends on the prevalence of asymptomatic and mutant forms of viremic blood donors in the population and the number of units transfused.[3] So, the high-risk of transfusion transmitted diseases can be appreciated. The mutant form of viruses are not easily detected by our routine ELISA techniques. The present study in multiple transfused patients shows a high prevalence of IgM (30%) antibodies. Very few of the cross-sectional studies were reported from India and only one study and a case report has dealt with the problem of parvovirus B19 infection and its transmission in thalassemia patients.[12] Globally, only few studies and case reports have showed the concern of parvovirus B19 infection in thalassemia patients. One of the studies done on 60 thalassemia major patients by Siritantikorn et al.[16] from Thailand, in which he found anti-B19 IgG in 38% and anti-B19 IgM in only 4% of these positive anti-parvovirus B19 IgG patients, and gave the conclusion that acute and chronic persistent parvovirus B19 infection was found in the thalassemic patients from Thailand. Conflicting to findings of present study, blood transfusion had a major role in elevating the prevalence of parvovirus B19 infection in multiple transfused patients. A case report in 22-year-old female thalessemic major patient with aplastic crisis, followed by transitory heart failure after one week and acute tricuspid incompetence by Zanella et al.[15] found B19 transmission due to single-donor transfusion, the patient's serum contained both anti-B19 IgM antibodies and B19 DNA in the acute phase by polymerase chain reaction and was found present up to four months after diagnosis. The serum samples collected at the time of donation from one of the donors before the appearance of clinical symptoms was found with B19 IgM antibodies and anti-B19 DNA. There is scarcity of reports of the problem of Parvovirus B19 transmission was found because of prolonged multiple transfusions, by estimating the results obtained from hemophilia patients, who are dependent on multiple transfusions with plasma-derived products lifelong, mainly coagulation factors which are made from large pools of donors, and are the embodiment examples of patients at risk for developing blood-borne infections. In USA a study was conducted among haemophilia patients and parvovirus B19 infection was seen in 97% of the population.[3] Eighty-nine percent of this disease is found commonly in the United Kingdom by Williams et al.[17] In the present study no significant relations of age and gender was found in multiple

Table 1: Prevalence of anti-B19 IgM antibodies in multi-transfused patients according to age and gender

Age distribution groups (in years)	Sex Distribution			Positive (%) Anti-B19 IgM		
	Total	Male	Female	Total	Male	Female
<1–10	73	45	28	27	12 (27)	15 (54)
11–20	28	22	06	13	09 (41)	04 (67)
21–30	12	06	06	02	00 (0)	02 (33)
31–40	11	05	06	01	01 (20)	00 (0)
41–50	15	11	04	03	03 (27)	00 (0)
>50 years	34	21	13	06	04 (19)	02 (15)

Table 2: Prevalence of anti-B19 IgM antibodies in multitransfused patients according to disease category

Disease Category	Total	Positive (%) Anti-B19 IgM
Thalassemia	94	39 (41)
Haemodialysis	51	10 (20)
Sickle cell disease	07	01 (14)
Haemato-oncology	06	00 (00)
Acute blood loss	03	00 (00)
Others	12	02 (17)

Table 3: Transfusion-transmitted disease markers and anti-B19 IgM antibodies in multitransfused patients

Transfusion-transmitted diseases	Total (%)	Positive (%) Anti-B19 IgM
HBsAg	4/173 (2)	0/4 (0)
HIV	1/173 (0.6)	1/1 (100)
Anti-HCV	50/173 (29)	20/50 (40)

Table 4: Comparison of prevalence of anti-B19 antibodies from previous studies

Study	Place	Year	Sample Size	Prevalence of anti-B19 antibodies
Siritantikorn et al.[16]	Thailand	2007	60	04% (IgM)
Kishore J. et al.[12]	India (Lucknow)	2011	90	41.1% (IgM)
Present Study	India (Ujjain)	2019	173	30% (IgM)

transfused patients for the prevalence of parvovirus B19. A study from northern India there was found increase of HCV infection with increasing age.[18] A positive correlation was found in the present study between the number of units transfused and the prevalence of anti-B19 antibodies in multi-transfused patients, thalassemia patients are found in more frequent need of blood products than other category of multi-transfused patients. Table 2 shows the category wise, number of patients enrolled in the present study. Seventy thalassemia patients and Twenty hemophilia patients who received periodic transfusions of packed cells and components in a study from Eastern India were found to have an increased prevalence of transfusion transmitted disease (TTD) markers with increasing number of transfusions.[4] Overlapping of transfusion related infections like HCV, HIV and HBV in multiple transfused patients can be seen and there is possibility of the simultaneous infections can occur. Also parvovirus B19 co-infections were seen in twenty-one multi-transfused patients with HIV and anti-HCV positivity in the present study as shown in Table 3.

Only donors or donor units positive for anti-B19 IgG antibodies are noted safe, because the risk of parvovirus B19 transmission emerges when donors are either viremic which is parvovirus B19 DNA positive and the estimated range of incidence is from 1:30,000 to 1:3,000 of such a viremic donor has been estimated and is now 0.88%, depending on the sensitivity of the detection method used[19] or else has anti-B19 IgM antibodies. Current and determined infection in the donor are noted in parvovirus B19 IgM antibody-positive donor units. So, such types of donor units can be noted as potentially infective, as viremia may further persist, although there is a negligible chance of false positivity which cannot be completely eliminated. For the safety of blood supply, the blood supplying governing body should be careful to watch for new threats even after controlling transfusion-transmitted infections like, HIV, HBV and HCV. Recently, many new agents have contented the broad definition of emerging blood-transmitted infections, which includes parvovirus B19, dengue, and West Nile virus (WNV).[2] Although, we need serological monitoring for a longer duration, and also larger number of patients should be included to set up exact correlations. So, advancement of pathogen Inactivation is required to decrease the incidence of parvovirus B19 transmission and safety of the blood or its components. Lately, in Holland, nano-filtration of the factor IX concentrate has been tried, in patients who need lesser number of transfusions to eliminate the B19 parvovirus.[20] Morever, for appearing and re-appearing pathogens including Parvovirus B19, a multi-pathogen microarray technology has to be developed to bring the infectious disease risk to almost zero.

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