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Article/Artigo

Clinical and epidemiological profile of blood donors with positive serology for viral hepatitis in southern Brazil

Perfil clínico e epidemiológico de doadores de sangue com sorologias positivas para hepatites virais no sul do Brasil

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ABSTRACT

Introduction: Positive serological tests for hepatitis viruses B and C at blood banks are an important reason for blood deferral. Additionally, high residual risk for transfusing hepatitis-contaminated blood has been estimated in southern Brazil. This study aimed to identify risk factors for positive serological tests for viral hepatitis (VH) in blood donors (BD). **Methods:** A case-control study included consecutive BD with positive serology for VH, between 2008 and 2009. Cases and controls (BD with negative serology for VH) were paired 1:1 by sex and donation date. Assessment of clinical and epidemiological characteristics related to viral hepatitis was conducted. **Results:** Among 1,282 blood donors (641 cases and 641 controls), those with positive serology for viral hepatitis had higher mean age (p<0.001); higher proportion of replacement donation (p<0.001); first donation (p<0.001); and interviewer deferment (p=0.037), compared to controls. Furthermore, donors with positive tests were less regular donors (p<0.001), had less previous history of rejection (p=0.003) and showed lower hematocrit median before donation (p=0.019). Multivariate analysis demonstrated that age (OR=1.056, 95%CI 1.042-1.069, p<0.001), replacement donation (OR=1.545, 95%CI 1.171-2.038, p=0.002) and first donation (OR=9.931, 95%CI 7.486-13.173, p<0.001) were independently associated with positivity of serological tests for viral hepatitis. **Conclusions:** Specific characteristics of blood donors were associated with positive serology for viral hepatitis. These peculiarities should be taken into account when assessing candidates for blood donation.

Keywords: Blood donors. HBsAg. Anti-HBc. Anti-HCV.

RESUMO

Introdução: Testes sorológicos positivos para os vírus de hepatites B e C nos bancos de sangue são importante causa de descarte de bolsas de sangue. Além disso, estima-se um alto risco residual de transfundir sangue contaminado com vírus de hepatite no sul do Brasil. Este estudo objetiva identificar fatores de risco para sorologias positivas para hepatites virais (HV) em doadores de sangue (DS). **Métodos:** Estudo caso-controle que incluiu, consecutivamente, DS com sorologias positivas para HV entre 2008 e 2009. Casos e controles (DS com sorologias negativas para HV) foram pareados 1:1 de acordo com gênero e data da doação. **Resultados:** Entre 1.282 doadores de sangue incluídos (641 casos e 641 controles), aqueles positivos para HV, quando comparados aos controles, apresentaram maior média de idade (p<0,001), maior proporção de doações direcionadas (p<0,001), primeira doação (p<0,001) e recusa pelo entrevistador (p=0,037). Outrossim, doadores positivos eram, com menos frequência, doadores regulares de sangue (p<0,001), apresentavam menos história prévia de rejeição na doação (p=0,003) e evidenciaram menor mediana de hematócrito (p=0,019). Análise multivariada demonstrou que idade (OR=1,056; IC95% 1,042-1,069; p<0,001), doação direcionada (OR=1,545; IC95% 1,171-2,038; p=0,002) e primeira doação (OR=9,931; IC95% 7,486-13,173; p<0,001) foram independentemente associadas a testes positivos para HV. **Conclusões:** Características específicas de DS foram associadas com sorologias positivas para HV. Estas peculiaridades devem ser levadas em consideração na avaliação de candidatos a doação de sangue.

Palavras-chaves: Doadores de sangue. HBsAg. Anti-HBc. Anti-HCV.

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INTRODUCTION

Chronic viral hepatitis B and hepatitis C are currently disseminated worldwide, with about 350 million infected and 170 million carriers, respectively[1,2]. Although hepatitis B has other forms of transmission, such as sexual and vertical transmission, both have efficient parenteral transmission in common, especially by blood transfusion and due to intravenous drug use[1,2].

The first reports of hepatitis following a blood transfusion occurred in 1943[3], but only in 1965 the Australia antigen was related to post-transfusion hepatitis in blood recipients[4]. In 1971, a detection test for hepatitis B surface antigen (HBsAg) was introduced for screening of blood donors[5] and after 1986, alanine aminotransferase (ALT) and hepatitis B core antigen (anti-HBc) tests were included in several countries in the routine testing of donors[6]. Following these measures, posttransfusion hepatitis rates decreased dramatically to 2% to 3%[4]. With the identification of hepatitis C virus (HCV)[7], studies showed that this agent was responsible for 90% of parenterally acquired hepatitis and at least 50% of sporadic non-A, non-B hepatitis[4,8]. Since the implementation of blood donor screening for anti-HCV, in the early 1990s, the incidence of posttransfusion hepatitis C has diminished markedly[9].

Despite blood donor screening performed through interviews by health professionals, the prevalence of positive serology for hepatitis B and hepatitis C viruses varies depending on the region studied. In England, the prevalence of viral hepatitis infection in blood donors is low and decreasing: 0.39:100,000 donations for hepatitis B virus (HBV) and 0.17:100,000 donations for HCV[10]. These rates are much lower than those reported in the United States (1:63,000 HBV; 1:103,000 HCV) and France (1:112,000 HBV; 1:217,000 HCV)[11,12]. In Brazil, the prevalence rates of viral hepatitis in blood banks is not negligible: 0.3%-1.5% forHBsAg, 3.7%-11.1% for anti-HBc and 0.9%-2.6% for anti-HCV[13,14]. In southern Brazil, the residual risk for transfusing

HBsAg contaminated blood decreased almost three-fold during the decade from 1990 to 2000, but a more recent study shows that it still remains very high, at 1:2,077, with a corresponding incidence of 3:1,000 person/year. Similarly, although residual risk for hepatitis C was reduced by more than 30-fold in the late 1990s, compared with earlier periods, the risk of 1:13,721 and corresponding incidence of 0.5:1,000 person/year are still very high compared to developed countries[15]. In fact, up to 40% of blood donors with anti-HCV reactive serology have a history of previous parenteral exposure[16], which suggests that many donors omit information in the initial screening.

Due to the high prevalence rate of viral hepatitis in Brazil and the noteworthy risk of acquiring viral hepatitis following the transfusion of blood products, this study aimed to identify clinical characteristics of blood donors in a blood center in the southern region of Brazil, with positive tests for viral hepatitis, and compare these to individuals with negative serology in order to contribute to the blood bank screening process.

METHODS

Patients

This cross-sectional study was conducted at the Hematology and Hemotherapy Centre of Santa Catarina (HEMOSC), Criciuma, SC, southern Brazil. Criciuma is an industrial centre with about 190,000 inhabitants and is located in the southern State of Santa Catarina. Consecutive blood donors with positive serology for viral hepatitis who donated blood between January 2008 and December 2009 were included. Individuals with incomplete data were excluded. When a blood donor presented repeated donations, only the first donation was included. Individuals with positive or indeterminate serology were paired with individuals with negative serology according to sex and donation date.

Methods

Demographics, laboratory and other clinical variables were extracted from blood bank records. Patients were evaluated according to positive serological tests for viral hepatitis. Positive serology for viral hepatitis was defined as follows: HBsAg positive or indeterminate, anti-HBc reactive or indeterminate and anti-HCV reactive or indeterminate.

Assessment of clinical and epidemiological variables included: age (in years); sex; marital status (married/stable union, single, separated, divorced, widowed); ethnicity (white or nonwhite skin color); education (in years); alcoholism, defined as daily intake of alcohol exceeding 30g for men and 20g for women; previous exposure to acupuncture; homosexual relationships; previous use of injectable drugs; type of donation, spontaneous or replacement; first donation; regular donation, at least twice a year; previous deferral; *test-seeking* donation, where the blood donor declares their intention to perform blood tests (viral hepatitis, HIV or other); interviewer deferment, decision by the interviewer refusing the donated blood; donor self-exclusion, the donor's decision following the interview; body mass index, defined as weight/height^2; systemic hypertension, defined as systolic blood pressure ≥140mmHg and/or diastolic blood pressure ≥ 90mmHg; capillary hematocrit, obtained by finger prick; and simultaneous HIV-positive test results.

Statistical analysis

Continuous variables were compared using the Student *t* test or the Mann-Whitney U test when appropriate. Categorical variables were compared using the χ^2 test or Fisher exact test. A p value of less than 0.05 was considered statistically significant. Bivariate and regression analysis were used to identify variables independently associated with the presence of positive serology for viral hepatitis. All tests were two-tailed and performed using the Statistical Package for Social Science software, version 15.0 (SPSS, Chicago, IL, USA).

Ethical considerations

The study protocol conformed to the ethical guidelines of the revised Helsinki Declaration (2000) and was approved by the local Research Ethics Committee, under no. 09.410.4.01.III.

RESULTS

From January 2008 to December2009, 32,000 individuals donated blood at the HEMOSC. Among these, 693 individuals fulfilling the entry criteria were considered eligible. After excluding 52 patients with insufficient clinical data and/or repeated donations, 641 blood donors with positive serology for viral hepatitis were included in the analysis (**Figure 1**). As determined, 641 blood donors with negative serology were paired according to sex and date of donation

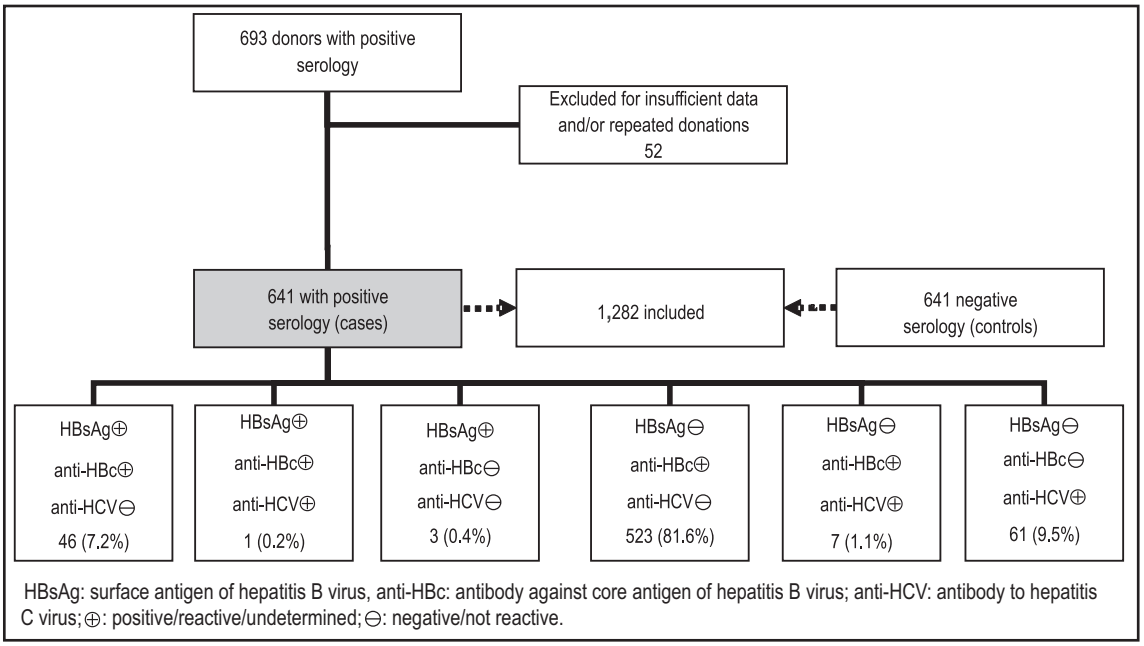

FIGURE 1 - Flow diagram of the potential candidates for participation in the study and seropositivity for viral hepatitis.

as controls, such that a total of 1,282 individuals were included in the study. Of the 641 donors with positive serology, fifty (7.8%) blood donors tested positive for HBsAg, 577 (90%) blood donors tested reactive for anti-HBc and 69 (10.8%) tested reactive for anti-HCV.

Among the 1,282 individuals, the mean age was 36.5 ± 11.0 years-old, 68% were men, and 99% were white. Sixty-six percent of blood donors were either married or had a stable union and 55% had more than eight years of schooling.

When individuals with positive serology for viral hepatitis were compared with controls **(Table 1)**, they presented higher mean age (38.3 ± 11.0 vs 34.7 ± 10.7 years-old; p<0.001); higher proportion of replacement donation (41.8% vs 27.1%; p<0.001); first donation (69.5% vs 23.2%; p<0.001); and interviewer deferment (3.6% vs 1.7%; p=0.037). Donors with positive tests for viral hepatitis were seldom regular donors (3.6% vs 45.2%; p<0.001), less frequently had more than eight years of schooling (44.8% vs 64.4%, p<0.001), had a history of previous refusal (10.2% vs 15.8%; p=0.003), and showed lower hematocrit values before blood donation (42.0 vs 43.0g/dL; p=0.019).

TABLE 1 - Distribution of clinical and epidemiological variables of 1,282 blood donors, according to the positivity of serological tests for viral hepatitis, Criciuma, Brazil, 2008-2009.

		Serological tests for viral hepatitis		
	Total	positive	negative	
Clinical variables	n = 1,282	n = 641	n = 641	P‡
Age (years)*	36.5 ± 11.0 (37.0)	38.3 ± 11.0 (39.0)	34.7 ±10.7 (34.0)	< 0.001
Male (%)	68.2	68.2	68.2	1,000
Caucasian (%)	99.2	99.1	99.4	0.525
Married/stable union (%)	65.6	68.1	63.2	0.065
Education > 8 years (%)	54.7	44.8	64.4	< 0.001
Alcohol abuse (%)	0.9	0.9	0.8	0.762
Acupuncture (%)	0.2	0.3	0.2	0.625
Homosexual intercourse (%)	0.5	0.8	0.3	0.452
IVD (%)	1.0	1.4	0.6	0.163
Replacement donation (%)	34.5	41.8	27.1	< 0.001
First donation (%)	46.4	69.5	23.2	< 0.001
Regular donation (%)	24.4	3.6	45.2	< 0.001
Previous deferral (%)	13.0	10.2	15.8	0.003
Partner blood donor (%)	1.5	1.1	1.9	0.249
Test seeking (%)	0.4	0.6	0.2	0.218
Advice for deferral (%)	2.7	3.6	1.7	0.037
Donor self-exclusion (%)	0.5	0.9	0.2	0.124
Pre-donation Ht (%)*	42.6 ± 3.4 (42.0)	42.5 ± 3.1 (42.0)	42.8 ± 3.6 (43.0)	0.019
Anti-HIV ⊕ (%)	0.5	0.8	0.2	0.218

IVD: intravenous drug, Ht: hematocrit, HIV: human immunodeficiency virus.

* Mean ± standard deviation and median, ‡ Student's *t* test, Mann-Whitney, χ^2or Fisher's exact test, when appropriate for comparison between groups, ⊕: positive/reactive/undetermined.

The variables *regular donation* and *previous deferral* were not included in the multivariate analysis, since they presented very similar information to the *first donation*.

Multivariate analysis **(Table 2)** showed that age (OR=1,056, 95%CI 1.042 to 1.069; p<0.001), replacement donation (OR=1.545, 95%CI 1.171 to 2.038, p=0.002) and first donation (OR=9.931; 95%CI 7.486 to 13.173; p<0.001) were independently associated with positive serological tests for viral hepatitis.

TABLE 2 - Factors associated with positive serological tests for viral hepatitis among blood donors in Criciuma, Brazil, 2008-2009, by multivariate analysis.

Factors	*Odds ratio*	CI 95%	P
Age	1,056	1,042 - 1,069	< 0.001
Education ≤ 8 years	-	-	0.087
Replacement donation	1,545	1,171 - 2,038	0.002
First donation	9,931	7, 486 - 13,173	< 0.001
Interviewer advice for deferral	-	-	0.437
Pre-donation hematocrit	-	-	0.052

CI: confidence interval.

DISCUSSION

The proportions of viral hepatitis antigens/antibodies described in this study are similar to those previously reported in other regions of Brazil: anti-HBc (74-92%), HBsAg (6-16%) and anti-HCV (4-19%)[13,14,17-19]. In Campinas, among 29,833 blood donors evaluated, 1.5% were HBsAg-positive, 11% were anti-HBc-reactive and 2.6% were anti-HCV-reactive. In Rio de Janeiro, amongst 128,497 blood donor samples collected from 1998 to 2005, significant reductions in the overall prevalence of HBsAg (from 0.4 to 0.2%) and anti-HBc (from 6.1 to 2%) were observed. Similarly, a decline in anti-HCV prevalence rates was observed in Brazilian blood donors, from 1% in 1998 to 0.8% in 2004, with an increase in HCV prevalence to 1.1% in 2005[13]. In southern Brazil, Rosini et al evaluated 263,795 blood donor samples collected between 1999 and 2001 and also verified a significant reduction in the mean frequency of HBsAg and anti-HBc during the study period, from 1% to 0.6% and from 8.8% to 5.4%, respectively; however, the values varied considerably among the different regions[18]. In part, this reduction may be a reflection of systematic interviews with screening questionnaires and exclusion of donors reporting defined risk factors.

In this study, analysis verified that 81.6% of individuals presented reactive serology for anti-HBc and were HBsAg-negative. Several interpretations are possible regarding this finding. When anti-HBc is associated with HBsAg, it indicates carrier status for hepatitis B virus (HBV); when associated with anti-HBs, it characterizes the profile of immunity to HBV. Anti-HBs is not performed in blood blanks, so this outcome could not be evaluated. However, reactive anti-HBc in the absence of HBsAg and anti-HBs, is considered as *isolated anti-HBc*. The significance of the isolated anti-HBc presence remains uncertain. This finding may correspond to: false positive results; natural immunity, with loss of anti-HBs over time or failure of individuals to produce this antibody; immunological window period, during the resolution of acute infection, after becoming HBsAg-negative and before the rise of anti-HBs; or, finally, a chronic HBV carrier with low viral load and undetectable HBsAg[20].

Since individuals with positive serology for viral hepatitis in this study were paired for sex, no difference could be demonstrated

between those with positive and negative serology for viral hepatitis. However, it is known that men represent the majority of blood donors with reactive serology, with prevalence ranging from 76% to 84%[21-22].

The average age of 37 years-old is similar to that described by other authors, ranging between 34 and 41 years-old[23-24]. Higher mean age in this study was independently associated with seropositivity for viral hepatitis. The direct relation between age and prevalence of hepatitis has already been described in Brazil[25]. In Canada, positivity rates for HBV and HCV have decreased in number among donors aged under 30 and 45 years-old, respectively[26,27]. The decline in HBV infection among the younger population is expected due to vaccine immunization, which was included in the basic immunization program in Brazil in 1998. Regarding HCV, older donors could be more exposed to parenteral risk of transmission, since they have lived in a period where no preventive measures against hepatitis transmission were adopted; i.e., serological screening in blood banks, use of disposable material in invasive procedures, not sharing needles among users of intravenous drugs. Older individuals may present greater risk of sexual contamination through unprotected sex, since the use of condoms was largely stimulated only after the discovery of HIV in the 1980s. In addition, individuals aged between 20 and 30 years-old may be more conscious concerning prevention of sexual and parenteral transmission due to public health educational programs in the past two decades.

In Brazil, voluntary blood donation is insufficient to meet the demand for blood transfusion[28]. Campaigns to encourage blood donation stimulate not only the general population, including provision of transportation for employees of large companies, but also family members of patients who are receiving blood transfusion or are hospitalized[29]. Although remunerated donation is illegal in most countries, other rewards, such as free meals or tickets for entertainment do exist. More subtle rewards include offers of free tests, such as those for high blood pressure, cholesterol, glucose etc, which are beyond the mandatory donation screening for hemoglobin concentration and infection markers. The arguments against encouraging these donations include inadvertent recruitment of individuals with a lifestyle that puts blood recipients at higher risk, but some providers feel unable to sustain a sufficient blood supply without such encouragement[30,31]. Pereira et al[32] showed that replacement donors present 2.5-fold higher seropositivity for HBV, HCV and HIV than volunteer donors. In this study, observation revealed that individuals who make replacement donations have a higher proportion of seropositivity for viral hepatitis than those who make spontaneous donations. However, multivariate analysis showed that this variable alone does not predict seropositivity for viral hepatitis. An African study that compared 6,640 first-time volunteer and 4,360 replacement donors verified that the viral safety of both groups was similar overall. Surprisingly, the prevalence of HBsAg carrier status in first-time volunteer donors over the age 20 was significantly higher than in replacement donors by a wide margin (20.3 and 15.1%, respectively; $p<0.0001$)[33]. First time donors were three times more likely to test positive for hepatitis compared to controls, as shown in several studies[22,26,32,34]. It is likely that the first donation represents an important risk factor, because these individuals have never been tested for infectious diseases, different from regular donors, who have already undergone screening. There are people who seek blood donation for personal gains, such as a leave of absence from work, getting a free snack after donation, or having serological tests performed, which is described as *test-seeking* in the United States. Gonçalez et al demonstrated that among 1,600 Brazilian blood donors, 8.8% admitted HIV test-seeking motivation for donating blood. Although the numbers were low, test-seeking was associated with HBsAg and HCV positivity ($p=0.04$ and 0.06, respectively)[35].

Blood donation is a quick, inexpensive, simple and unstigmatized way to perform exams. Nevertheless, there is a global trend to reduce the rates of positivity for hepatitis among first-time donors[27,36], albeit less significant than among repeat donors[37]. However, the prevalence of hepatitis C has increased among first-time donors aged between 50 and 59 years-old[36]. Individuals who donate blood twice or more in one year are considered regular donors. In this study, a smaller proportion of this class of donors tested positive for hepatitis virus, probably because they had previously been subjected to serological tests for screening and because the motivation for donation, in most cases, was assumed to be altruistic.

A smaller number of individuals who studies continued after junior school had positive tests for viral hepatitis, but this finding was not significant in the multivariate analysis. An inverse relationship between schooling and positivity for hepatitis has already been described[32,34,36]. This factor may be related to less knowledge regarding ways to prevent sexual and parenteral transmission of hepatitis viruses.

Even though a higher proportion of individuals with positive serology for viral hepatitis presented lower hemoglobin levels compared to controls, this difference had no clinical significance. Despite reports of aplastic anemia in patients with HBV, anemia is not usually a sign of chronic hepatitis[38].

We acknowledge that the use of retrospectively collected data might have led to selection bias. However, this was unlikely to have occurred in this study because data were collected from standardized medical records by a single researcher, thus minimizing possible bias.

In conclusion, higher age at blood donation is associated with higher prevalence of positive tests for viral hepatitis; regular blood donors, who donate spontaneously, show a significantly lower risk of presenting positive serology for viral hepatitis. These peculiarities should be taken into consideration in campaigns for the dissemination of blood donation and assessment of prospective donors.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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