Major Article

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Clinical and epidemiological profile of female blood donors with positive serology for viral hepatitis B

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ABSTRACT

Introduction: Since women are frequently the minority among blood donors worldwide, studies evaluating this population usually reflect male features. We assessed the features of female blood donors with positive serology for HBV and compared them with those of men. **Methods:** The study comprised consecutive blood donors referred to a specialized liver disease center to be evaluated due to HBsAg- and/or anti-HBc-positive tests. **Results:** The study encompassed 1,273 individuals, 219 (17.2%) of whom were referred due to positive HBsAg test and 1,054 (82.8%) due to reactive anti-HBc test. Subjects' mean age was 36.8±10.9 years, and 28.7% were women. Female blood donors referred for positive HBsAg screening tests demonstrated higher prevalence of healthcare workers (9.3% vs 2.5%) and lower prevalence of sexual risk behaviors (15.1% vs 41.1%) and alcohol abuse (1.9% vs 19.8%) compared to men. Women had lower ALT (0.6 vs 0.8×ULN), AST (0.6 vs 0.8×ULN), direct bilirubin (0.2 vs 0.3mg/dL), and alkaline phosphatase (0.5 vs 0.6×ULN) levels and higher platelet count (223,380±50,293 vs 195,020±53,060/mm^3). Women also had a higher prevalence of false-positive results (29.6% vs 17.0%). No differences were observed with respect to liver biopsies. Female blood donors referenced for reactive anti-HBc screening tests presented similar clinical, epidemiological, and biochemical characteristics to those reported for positive HBsAg screening tests and similarly had a higher prevalence of false-reactive results. **Conclusions:** Compared to men, female blood donors with positive HBsAg and/or anti-HBc screening tests demonstrated higher prevalence of professional risk and false-positive results and reduced alteration of liver chemistry.

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

INTRODUCTION

Post-transfusion hepatitis (PTH) was first reported by Beeson in 1943[1]. PTH viral etiology had been suspected, and an Australian group identified an antigen in the serum of an indigenous individual during a study on multitransfused individuals with leukemia[2]. Subsequently, Gocke et al.[3] reported the presence of the Australia antigen in blood donors with PTH[3]. Among patients who received blood that tested positive for the Australia antigen, 74% developed hepatitis or antibodies against this antigen. In addition, 25% of PTH cases could be avoided if hepatitis B surface antigen (HBsAg) screening was implemented in blood banks[4]. In the early 1940s, the viral particle had not been identified yet, so it had not been confirmed that the Australia antigen belonged to a hepatitis virus. Thus, the United States of America recommended the investigation of this antigen in donors and the disposal of positive-tested units[5]. In 1971, the HBsAg test was introduced as a screening procedure for American blood donors and mandated as federal law in 1972[6]. The early detection methods had low sensitivity (hemagglutination or immunodiffusion), and post-transfusion hepatitis B continued to occur. Third-generation tests (radioimmunoassay or enzyme immunoassay) were implemented in 1975, and from this year on, the incidence of post-transfusion hepatitis B significantly decreased[6].

Some hypotheses have been proposed to explain the continuous hepatitis B transmission by transfusion even after the introduction of the HBsAg screening in blood donors, including errors in blood tests, hepatitis B virus (HBV) transmission by means other than transfusion, infected donors during the acute hepatitis B incubation period, and chronic HBV carrier donors with low HBsAg levels. HBsAg mutants can also be

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transfusion-transmitted since they are not generally identified during HBsAg screening. As the last hypothesis is the most likely, it was assumed that the use of an antibody against hepatitis B core antigen (anti-HBc) to screen blood donors could minimize PTH infection in countries with intermediate or high HBV prevalence[6]. Nevertheless, many countries with low HBV transmission prevalence (such as Canada) did not implement anti-HBc screening for various reasons[7]. Since 1993, HBsAg, anti-HBc, anti-HCV, and alanine aminotransferase (ALT) tests have been mandatory in Brazilian blood banks. Thus, the residual risk of PTH infection significantly decreased in the country[8]. Currently, the estimated residual risk of HBV transmission by transfusion varies from 1:30,821 to 1:62,482, depending on the applied method[9].

Studies evaluating blood donors typically reflect the features of male subjects, since women are typically the minority in this population[10] [11] [12]. The current study sought to assess clinical, epidemiological, biochemical, and serological features of female blood donors positive for HBV and to compare their results with those of male donors as well as to define whether this female population had liver disease.

METHODS

Sample features

The current retrospective cross-sectional study included consecutive blood donors referred to the Hepatitis Outpatient Clinic at São Paulo Hospital between September 1997 and August 2006. Subjects referred due to positive HCV serology and/or elevated ALT levels were excluded from the study, as well as those who had insufficient clinical and laboratory data in their medical records.

Data collection

Information about all subjects referred to the aforementioned institution was reviewed. Clinical, epidemiological, biochemical, serological, and histological data were collected from standardized medical records. The following clinical variables were analyzed: sex; age; probable HBV infection route, including professional risk (healthcare professional), sexual risk (multiple sexual partners, defined as three or more sexual partners within 6 months, prior sexually transmitted disease, and men who have sex with men), parenteral risk (characterized by parenteral drug use with syringe sharing [illegal intravenous drugs or the so-called *energetic* substances] or blood product transfusions), vertical risk (virus carrier mother), and horizontal risk (household contact with HBV carriers); body mass index (BMI); and ethanol abuse, defined as alcohol consumption greater than 20g per day in women and 30g in men[13]. ALT, aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), direct bilirubin (DB), prothrombin activity (PA), and platelets were evaluated as laboratory variables.

Laboratory analyses

Alanine aminotransferase and aspartate aminotransferase were analyzed by an automated kinetic method using Hitachi 917 equipment and Boehringer Mannheim® reagents at temperatures between 27°C and 37°C. The ALT reference values were up to 41U/L for men and 31U/L for women. Normal AST values were up to 38U/L for men and 32U/L for women. ALP and GGT were also analyzed by automated kinetic method, with temperatures between 27°C and 37°C. The ALP reference value was up to 250U/L for both sexes. For GGT, the reference values were up to 30U/L for men and 24 U/L for women. DB was determined by direct colorimetric Jendrassik-Grof Method, with normal values up to 0.4mg/dL. Albumin was obtained by colorimetric method (bromocresol), with the normal value equal to or greater than 3.4g/dL. PA was quickly analyzed by a modified method, and values between 70% and 100% were considered normal. The blood platelet counts were performed by an automated system (ABX Pentra), with normal values between 150,000 and 500,000/mm^3. Biochemical analyses were performed at the Central Laboratory of the Hospital São Paulo. The results used in the ALT, AST, ALP, and GGT analyses were expressed in multiples of the upper limit of normal (ULN) according to sex. The other variables were expressed in absolute values.

HBsAg, anti-HBc, immunoglobulin M (IgM) anti-HBc, antibody against hepatitis B surface antigen (anti-HBs), hepatitis B "e" antigen (HBeAg), and antibody against hepatitis B "e" antigen (anti-HBe) were tested by microparticle enzyme immunoassays (MEIA; Imx®, Abbott Laboratories, North Chicago, IL, USA) whenever required. Anti-HBs levels greater than 10mUI/mL were considered reactive, and values above 100mIU/mL, after one vaccine dose, were considered indicative of an anamnestic response in individuals with reactive anti-HBc tests[14]. The tests were performed according to the manufacturers' specifications, and the results were expressed as positive, reactive, inconclusive, non-reactive, or negative (in absolute value form), depending on the case.

Histological analysis

Liver biopsy was indicated for HBsAg chronic carriers positive for HBeAg test and/or with elevated ALT[15]. The same pathologist analyzed all liver biopsy slides. The national classification for chronic hepatitis was used to assess structural changes, portal inflammatory infiltrate, and periportal and lobular necroinflammatory activity. Individuals were evaluated based on the presence of 1) significant periportal inflammatory activity, defined by the presence of moderate piecemeal necrosis (few-to-numerous areas in a few portal tracts or small outbreaks in many portal tracts) or piecemeal necrosis in large areas of many portal tracts, and 2) significant fibrosis, characterized by the presence of portal-portal and/or central-portal fibrous bridges or cirrhosis.

Diagnostic resolution

Subjects were investigated according to the main reason for their referral. Blood donors presenting positive or indeterminate screening tests for HBsAg and/or anti-HBc had their serology test repeated. Individuals who did not return to confirm serology were considered lost to follow-up. Individuals with repeated negative serology were considered to have false-positive

screening results. Those with repeated reactive serology were considered to have true positive results. Individuals with true positive HBsAg results were investigated for HBeAg profile. Subjects showing aminotransferase values greater than 10×ULN and reactive anti-HBc IgM test were defined as having *acute hepatitis B*.

Individuals with true positive anti-HBc results were tested for anti-HBs. Those with confirmed reactive anti-HBc and anti-HBs serology were defined as *naturally immune to HBV*. Subjects with confirmed reactive anti-HBc test and non-reactive anti-HBs were defined as having an *isolated anti-HBc* profile. Individuals with other diagnoses were defined as *other*.

Statistical analysis

Numerical variables with normal distribution were expressed as mean and standard deviation and compared using Student's *t*-test. Numerical variables with abnormal distribution were expressed as median and compared using the Mann-Whitney test. Qualitative variables were represented by frequency (%) and analyzed by chi-squared test or Fisher's exact test, as appropriate. P values lower than 0.05 were considered statistically significant.

Bivariate analysis was performed to identify features that differed between sexes. All tests were performed using Statistical Package for Social Sciences software, version 17.0 (SPSS Statistics, Chicago, Illinois, USA).

Ethical considerations

The study protocol met the 1975 Helsinki Declaration ethical guidelines and was approved by our institutional review board (0704/04).

RESULTS

General sample analysis

Throughout the study period, 2,315 donors were assisted in the Hepatitis Outpatient Clinic. They had been referred from blood banks due to abnormal liver test results. Seventy-one subjects were excluded due to insufficient data in their medical records. In addition, 320 donors had been referred due to elevated ALT levels, and 651 (29%) due to reactive or inconclusive anti-HCV test. The study comprised 1,273 individuals, 219 (17.2%) of whom had been referred due to positive or inconclusive HBsAg tests, and 1,054 (82.8%) due to reactive or inconclusive anti-HBc tests.

Donors referred due to positive or inconclusive HBsAg serology

Among the 219 donors with positive or inconclusive HBsAg serology, the mean age and standard deviation were 34.4 ± 10.8 years, and 54 (24.7%) were women. Approximately one-third of these 219 (34.7%) subjects reported sexual risk behavior for HBV transmission. Clinical, epidemiological, and laboratory variables as well as the comparative analysis according to sex are shown in **Table 1**.

The comparison between sexes revealed that women had a lower ratio of positive HBsAg and reactive anti-HBc tests at the time of referral (81.5% vs 93.3%; p = 0.010 and 72.2% vs 84.2%; p = 0.049). However, there was no difference between sexes on repeat testing for these serological markers in the Hepatitis Outpatient Clinic **(Table 2)**. HBe status was tested in 120 subjects among the 146 chronic HBV carriers, of whom 14 (11%) tested positive for HBeAg and 106 (89%) were negative. The prevalence of HBeAg did not significantly differ between sexes (3.2% vs 13.5%; p = 0.185).

Of the 14 subjects with positive HBeAg serology, eight underwent biopsies, of whom two individuals showed liver reaction. None of the six individuals with chronic hepatitis had cirrhosis. Eight of the 106 subjects with negative HBeAg serology underwent biopsies due to elevated ALT. Five of these 106 subjects had chronic hepatitis, and one had cirrhosis. Of the 16 subjects who underwent liver biopsy, one was excluded from the analysis due to insufficient material. When the remaining 15 subjects were compared according to sex, men and women did not significantly differ regarding the presence of significant fibrosis (100.0% vs 23.4%; p = 0.095) or significant inflammatory periportal activity (50.0% vs 38.5%; p = 1,000).

The final diagnosis distribution and comparative analysis between sexes are shown in **Table 1**. Of the 146 individuals with confirmed HBsAg positivity, two had acute hepatitis B, and 144 were chronic HBV carriers.

Donors who were referred due to reactive or inconclusive anti-HBc serology

Of the 1,054 donors with reactive or inconclusive anti-HBc serology, 340 (32.3%) were women. The mean age and standard deviation were 38.5 ± 11.0 years. More than one-fourth of the sample (28.6%) reported sexual risk behavior for HBV transmission, and only nine (0.9%) subjects reported that their mothers were HBV carriers. Subjects' clinical, epidemiological, and biochemical features as well as the comparative analysis according to sex are detailed in **Table 3**.

Regarding the diagnostic assessment performed in the blood bank, 932 (88.4%) individuals had reactive anti-HBc screening tests, whereas 122 (11.6%) had inconclusive tests. Viral serology tests were repeated at the hepatitis outpatient clinic, and two subjects had reactive HCV results. One of these two individuals was lost to follow-up, and the other had positive hepatitis C virus-ribonucleic acid (HCV-RNA) confirmed but did not return for the liver biopsy. When the HBsAg test was repeated, three (0.3%) subjects tested positive for HBsAg and were treated as chronic HBV carriers. When the anti-HBc test was repeated, 184 (17.5%) individuals had non-reactive results. However, 21 (11.4%) of these 184 subjects had anti-HBs reactive serology, suggesting that the framework had favorably evolved by the time the anti-HBc test was repeated, and these individuals were naturally immune to HBV. Therefore, 163 (15.5%) individuals received a *false-reactive* diagnosis in the screening test. Reactive results in the anti-HBs antibody reactivity test were observed in 583 (55.3%) subjects, and they were also classified as naturally immune to HBV.

TABLE 1 - Clinical characteristics and final diagnosis of 219 blood donors with positive HBsAg, according to sex.

Characteristics	Number	Total	Sex		p
			female	male	
			n = 54 (24.7%)	n = 165 (75.3%)	
Age (years)*	219	34.4 ± 10.8 (33.0)	32.9 ± 10.1 (31.0)	34.9 ± 11.0 (34.0)	0.224[t]
BMI (kg/m²)*	181	25.66 ± 4.5 (24.5)	25.6 ± 4.8 (23.8)	25.7 ± 4.5 (24.8)	0.564[MW]
Professional risk	217	9 (4.1%)	5/54 (9.3%)	4/163 (2.5%)	0.044[F]
Sexual risk	216	75 (34.7%)	8/53 (15.1%)	67/163 (41.1%)	0.001[χ2]
IDU	217	4 (1.8%)	1/53 (1.9%)	3/164 (1.8%)	1.000[F]
Transfusion	217	14 (6.5%)	4/53 (7.5%)	10164 (6.1%)	0.749[F]
Vertical risk	217	1 (0.5%)	1/53 (1.9%)	0/164 (0.0%)	0.244[F]
Horizontal risk	217	14 (6.5%)	5/53 (9.4%)	9/164 (5.5%)	0.338[F]
Alcohol abuse	214	33 (15.4%)	1/52 (1.9%)	32/162 (19.8%)	0.002[χ2]
Biochemistry					
ALT (×ULN)*	180	1.1 2.7 (0.7)	0.7 ± 0.3 (0.6)	1.3 ± 3.1 (0.8)	0.016[MW]
AST (×ULN)*	175	0.9 1.5 (0.7)	0.7 ± 1.2 (0.6)	1.3 ± 1.8 (0.8)	0.013[MW]
DB (mg/dL)*	145	0.4 ± 0.9 (0.3)	0.2 ± 0.1 (0.2)	0.5 ± 1.1 (0.3)	0.004[MW]
ALP (×ULN)*	149	0.7 0.3 (0.6)	0.6 ± 0.3 (0.5)	0.7 ± 0.3 (0.6)	0.024[MW]
GGT (×ULN)*	159	0.9 1.0 (0.7)	0.8 ± 0.6 (0.7)	1.0 ± 1.1 (0.7)	0.768[MW]
platelets (/mm³)*	113	203,050 ± 53.627 (200,000)	223,380 ± 50.293 (215,000)	195,020 ± 53.060 (190,000)	0.011[t]
PA (%)*	114	90.2 ± 11.7 (94.7)	91.3 ± 10.5 (94.7)	89.8 ± 12.3 (95.0)	0.762[MW]
albumin (g/dL)*	101	5.3 ± 9.4 (4.3)	4.2 ± 0.5 (4.2)	5.6 ± 10.7 (4.4)	0.111[MW]
Final diagnosis					
lost to follow-up	219	27 (12.3%)	5 (9.3%)	22 (13.3%)	0.429[χ2]
false-positive HBsAg	219	44 (20.1%)	16 (29.6%)	28 (17.0%)	0.044[χ2]
chronic HBsAg carrier	219	146 (66.7%)	33 (61.1%)	113 (68.5%)	0.318[χ2]
acute hepatitis B	219	2 (0.9%)	0 (0.0%)	2 (1.3%)	1,000[F]

HBsAg: hepatitis B surface antigen; **BMI:** body mass index; **IDU:** intravenous drug use; **ALT:** alanine aminotransferase; **ULN:** times the upper limit of normal; **AST:** aspartate aminotransferase; **DB:** direct bilirubin; **ALP:** alkaline phosphatase; **GGT:** gamma glutamyl transferase; **PA:** prothrombin activity; **[t]**Student's t test; **[MW]**Mann-Whitney test; **[F]**Fisher's exact test; **[χ2]**chi-squared test. *Mean ± standard deviation (median).

TABLE 2 - Distribution of 219 blood donors with HBsAg-positive or inconclusive serology, according to repeated HBsAg and anti-HBc positivity and comparison according to sex.

Serology	Number	Total	Sex		p
			female	male	
Positive HBsAg BB	219	198 (90.4%)	44/54 (81.5%)	154/165 (93.3%)	0.010[χ2]
Reactive anti-HBc BB	219	178 (81.3%)	39/54 (72.2%)	139/165 (84.2%)	0.049[χ2]
Repeated positive HBsAg	192	148 (77.1%)	33/49 (67.3%)	115/143 (80.4%)	0.060[χ2]
Repeated reactive anti-HBc	161	130 (80.7%)	31/39 (79.5%)	99/122 (81.1%)	0.819[χ2]

HBsAg: hepatitis B surface antigen; **anti-HBc:** antibody against hepatitis B core antigen**; BB:** blood bank; **[χ2]**chi-squared test; repeated: serology repeated at the hepatitis outpatient clinic.

TABLE 3 - Clinical characteristics and final diagnosis of 1,054 blood donors with anti-HBc reactive or inconclusive, according to sex.

Characteristics	Number	Total	Sex		P
			female	male	
			n = 340 (32.3%)	n = 714 (67.7%)	
Age (years)*	1,041	38.5 ± 11.0 (39.0)	38.8 ± 10.9 (39.0)	38.3 ± 11.1 (38.0)	0.807[t]
BMI (kg/m²)*	780	25.9 ± 3.8 (25.6)	25.9 ± 4.0 (25.6)	25.8 ± 3.7 (25.6)	0.723[t]
Professional risk	1,040	45 (4.3%)	32/337 (9.5%)	13/703 (1.8%)	< 0.001[χ2]
Sexual risk	1,033	295 (28.6%)	32/331 (9.7%)	263702 (37.5%)	< 0.001[χ2]
IDU	1,033	9 (0.9%)	3/332 (0.9%)	6/701 (0.9%)	1,000[F]
Transfusion	1,033	67 (6.7%)	25/332 (7.5%)	42/701 (6.0%)	0.348[χ2]
Vertical Risk	1,017	9 (0.9%)	4/327 (1.2%)	5/690 (0.7%)	0.480[F]
Horizontal risk	1,018	40 (3.9%)	14/327 (4.3%)	26/691 (3.8%)	0.691[χ2]
Alcohol abuse	1,006	149 (14.8%)	9/327 (2.8%)	140/679 (20.6%)	< 0.001[χ2]
Biochemistry					
ALT (ULN)*	389	0.8 ± 0.5 (0.7)	0.7 ± 0.5 (0.6)	0.8 ± 0.5 (0.7)	0.003[MW]
AST (×ULN)*	379	0.7 0.4 (0.7)	0.7 ± 0.3 (0.7)	0.8 ± 0.5 (0.7)	0.165[MW]
DB (mg/dL)*	204	0.3 ± 0.2 (0.3)	0.2 ± 0.1 (0.2)	0.3 ± 0.2 (0.3)	< 0.001[MW]
ALP (×ULN)*	255	0.6 0.3 (0.6)	0.6 ± 0.2 (0.6)	0.6 ± 0.3 (0.6)	0.301[MW]
GGT (×ULN)*	274	1.2 1.3 (0.8)	1.0 ± 1.0 (0.7)	1.3 ± 1.4 (0.9)	0.006[MW]
platelets (/mm³)*	177	225,330 ± 57,334 (224,000)	243,940 ± 53,952 (237,000)	218,200 ± 57,189 (216,500)	0.002[MW]
PA (%)*	127	94.2 ± 8.7 (100.0)	96.1 ± 7.4 (100.0)	93.4 ± 9.2 (100.0)	0.125[t]
albumin (g/dL)*	124	4.5 ± 0.4 (4.5)	4.5 ± 0.3 (4.5)	4.5 ± 0.5 (4.6)	0.604[t]
Final diagnosis					
lost follow-up	1,054	116 (11.0%)	31 (9.1%)	85 (11.9%)	0.177[χ2]
false-positive anti-HBc test	1,054	163 (15.5%)	66 (19.4%)	97 (13.6%)	0.014[χ2]
natural immunity to HBV	1,054	604 (57.3%)	198 (58.2%)	406 (56.9%)	0.674[F]
isolated anti-HBc	1,054	166 (15.7%)	45 (13.2%)	121 (16.9%)	0.122[χ2]
others	1,054	5 (0.5%)	0 (0.0%)	5 (100.0%)	0.182[F]

anti-HBc: antibody against hepatitis B core antigen; **BMI:** body mass index; **IDU:** intravenous drug use; **ALT:** alanine aminotransferase; **ULN:** times the upper limit of normal; **AST:** aspartate aminotransferase; **DB:** direct bilirubin; **ALP:** alkaline phosphatase; **GGT:** gamma glutamyl transferase; **PA:** prothrombin activity; **HBV:** hepatitis B virus; [t]Student t test; [χ2]chi-squared test; [F]Fisher's exact test; [MW]Mann-Whitney test. *Mean ± standard deviation (median).

Taking the serological variables repeated at the hepatitis outpatient clinic into consideration, there was no difference between women and men in the prevalence of HBsAg (0.0% vs 0.9%; p = 0.556), the confirmation of the reactive anti-HBc test (68.2% vs 72.6%; p = 0.235), anti-HBs reactivity (53.1% vs 48.9%; p = 0.149), or anti-HCV reactivity (3.2% vs 1.5%, p = 0.535).

Of the 166 individuals with an *isolated anti-HBc* profile, 112 were referred for vaccination, as illustrated in **Figure 1**. Of the 82 subjects with isolated anti-HBc who received one dose of anti-HBV vaccine, 52 were subjected to anti-HBs antibody evaluation, of whom 33 (63.5%) showed reactive anti-HBs tests with levels above 100mIU/mL, indicating an anamnestic response to HBV. The 19 individuals who showed no anamnestic response were referred to finish the immunization program, but they did not return for anti-HBs serology reassessment. Thirty individuals received two or three doses of vaccine, and 24 (82.8%) of the 29 who underwent anti-HBs serology seroconverted. These subjects were discharged, and it was not possible to determine whether the immunity was acquired or was an anamnestic response to HBV. Of the 163 individuals with false-reactive anti-HBc test results, 32 received three doses of vaccine. The anti-HBs antibody was screened in 23 of these individuals, and it was reactive in 22 (95.7%).

Of the donors with an *isolated anti-HBc* profile, 54 were lost to follow-up before vaccination; 31 were vaccinated, but the presence of anti-HBs antibody was not assessed after vaccination; 33 had natural immunity to HBV corroborated by anamnestic response; and 24 responded to 2 or 3 doses of vaccine. The assessment of the final diagnosis and comparative analysis according sex are shown in **Table 3**.

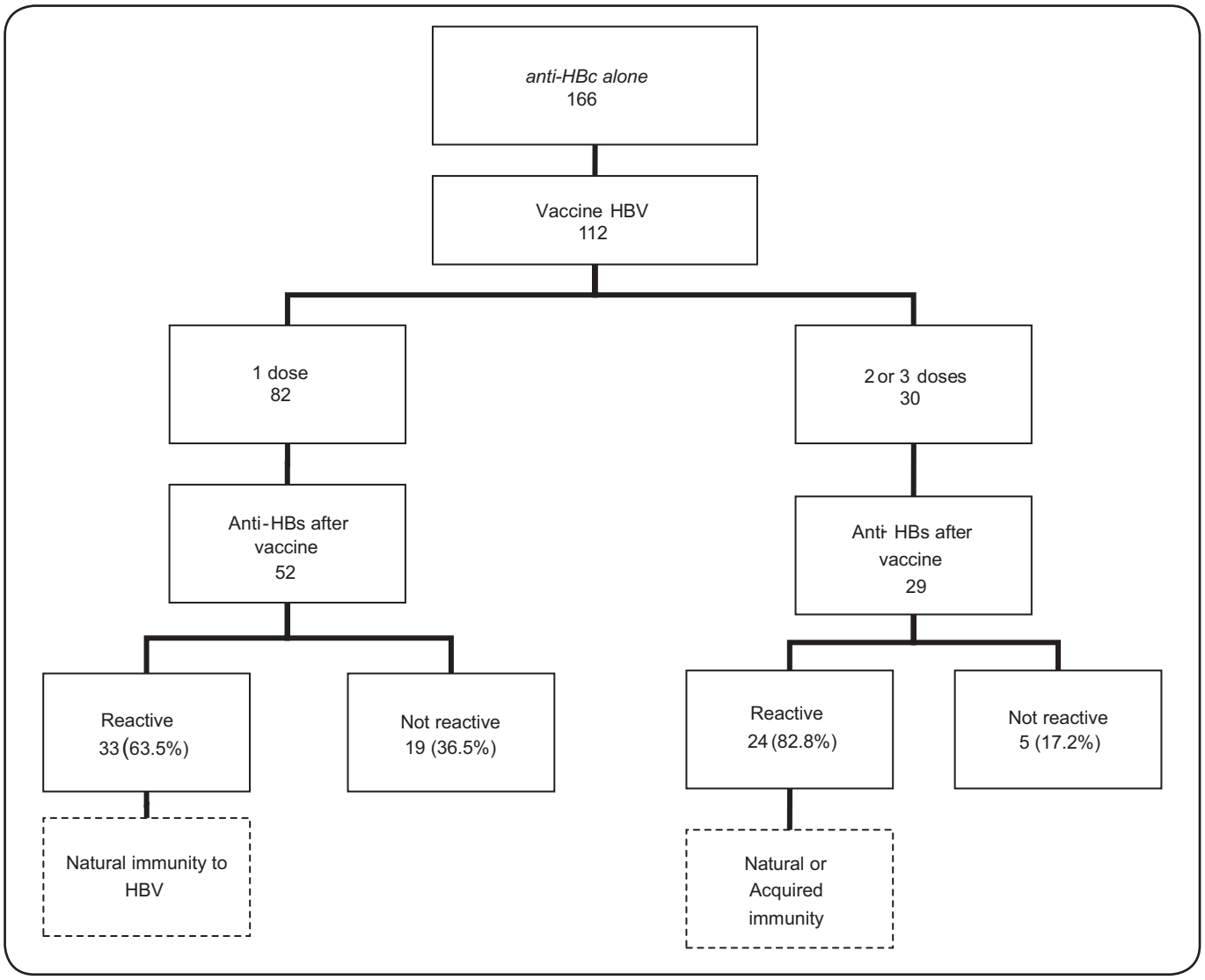

FIGURE 1 - Distribution of 166 blood donors with the *anti-HBc alone* profile confirmed by the hepatitis outpatient clinic, according to their response to vaccination. **Anti-HBc:** antibody against hepatitis B core antigen; **HBV:** hepatitis B virus; **anti-HBs:** antibody against hepatitis B surface antigen.

DISCUSSION

Among transfusion-transmitted infections, hepatitis B is considered an important public health problem. However, such transmission can be prevented by measures taken in blood banks, such as an interview to investigate risk factors as well as the evaluation of HBsAg and anti-HBc serology. The current study differs from previous research in that it evaluated the diagnostic evolution and final health condition of subjects rejected from blood donation and referred to specialized liver disease care services. In addition, this study identified clinical, epidemiological, and laboratory features that differ between sexes.

Studies involving donors at blood banks have reported similar prevalence rates among markers to those found in the current study. The anti-HBc hepatitis marker was observed frequently, whereas HBsAg was less frequent[10] [16] [17] [18]. The mean age between 34 and 39 years was similar to that described in the literature[19] [20] [21]. The current study found that 31% of the referred individuals were female, and this percentage is consistent with the findings of other studies, which reported a female prevalence from 2.1% to 47% among blood donors[16] [19] [22] [23] [24].

When risk factors for contracting hepatitis B were assessed among blood donors who were referred due to positive or inconclusive HBsAg serology, a high rate of health professionals was observed among women. Women are known to comprise the majority (91%) of health professionals[25]. The risk of HBV nosocomial transmission is approximately 100 times higher than that of HIV[26]. Several cases of HBV transmission to healthcare professionals were reported in the 1990s, and it continues to occur[27] despite the compulsory vaccination of these professionals. In State of Goiás, 24% HBsAg prevalence

was observed among health professionals, and of the 75% with a vaccination history, 90% were immune[28]. In the present study, similar to a study conducted in the City of Rio de Janeiro (6% vs 12%)[24], sexual risk factors were much less prevalent in women than in men, possibly because women adopt a less promiscuous attitude and also tend to talk less about their sexual behavior.

In the current study, women demonstrated lower ALT, AST, direct bilirubin, and PA levels and higher platelet levels, which may indicate less significant liver disease. Similar to the present study, Hayashi et al.[29] evaluated 1,163 HBsAg carriers and also found lower rates of women presenting changes in liver tests (18% vs 7%, p = 0.001). Chronic hepatitis B progresses less aggressively in women, possibly due to estradiol. This compound proved to be a potent endogenous antioxidant that suppressed hepatic fibrosis in animal models. Furthermore, male individuals demonstrate a poorer response to the action of estrogens because they have fewer specific receptors to this hormone[29]. However, the current study found no difference in inflammatory activity and staging between sexes, possibly due to the small number of individuals who underwent liver biopsy. Most studies of hepatitis B in women have investigated hepatitis B behavior during pregnancy, and we found only one study on sex differences in hepatitis B characteristics. Hooshyar et al.[30] evaluated 82 patients with chronic hepatitis B and observed significantly lower liver stage scores in liver biopsy specimens from women than men. Furthermore, stages greater than 1 were not seen in women[30].

Approximately 20% of the individuals referred due to HBsAg were false positives. The highest rate of false-positive results was found among women. There are many reasons for false-positive results including local prevalence of HBV, technical issues, vaccination, and pregnancy. The prevalence of the disease is known to influence the specificity of diagnostic tests: in low-prevalence settings, even very good tests have poor positive predictive value[31]. HBsAg prevalence in Brazil is low, with reports ranging from 0.6% to 0.8%[18] [32]. The designation of borderline cases as positive would cause false-positive tests to avoid false-negative results, which may be more harmful than false positives[33]. Other possible causes include problems with equipment and vaccination against influenza or rabies, as well as the presence of heterophile antibodies[34]. Another known cause of false-positive results is immunization against hepatitis B. HBsAg may be detected right after vaccination, which is why it is recommended to avoid donating blood for up to 7 days after vaccination[35]. An additional well-recognized cause of false-positive results is pregnancy, where more than 50% of discrepant results are false positive[36].

The current study found that 15.5% of the subjects had false-reactive anti-HBc serology. This percentage is similar to that described by other authors[19]. However, as in the evaluation of HBsAg, the highest rate of false-reactive results was found among women. Several authors found low specificity of total anti-HBc tests when enzyme immunoassays were used[37] [38]. When the anti-HBc test was repeated, 17% of individuals were false reactive[39], but they could be identified as reactive again if the test was repeated[40]. Thus, in cases in which another donation is attempted, the blood may be discarded, resulting in loss to the donor and the blood bank. Therefore, donors presenting false-reactive anti-HBc results are not free to make further donations.

We acknowledge some limitations to our analysis. First, the use of retrospectively collected data might have led to selection bias. However, it was unlikely to have occurred in the current study, because all HBsAg and/or anti-HBc patients were consecutively included. Second, the relatively small number of women with positive serology for HBV also implies a possible selection bias, which could limit the ability to extend these findings to other populations. Nevertheless, the number of women included was sufficient for statistically meaningful results. Finally, it is conceivable that the high percentage of false-positive results may have influenced the clinical and laboratory profile of patients, since women with false-positive results would have normal laboratory results. Nonetheless, the present study aimed to describe and compare patients according to their initial serological profile. Taking into account that differences between sexes are rare in the literature, the present findings are undoubtedly valuable.

In conclusion, the current study found that female blood donors with positive HBsAg and/or anti-HBc screening tests presented higher prevalence of professional risk and false-positive results and reduced alteration of liver chemistry compared to men.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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