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Prevalence, incidence and associated factors for HBV infection among male and female prisoners in Central Brazil: A multicenter study

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ABSTRACT

Background: Prison populations are at high risk for hepatitis B virus (HBV) infection. The aim of this study was to assess the prevalence, incidence, HBV associated factors and circulating genotypes/subtypes.
Methods: A total of 3,368 prisoners from 12 closed prisons were randomly recruited for a cross-sectional study. In addition, a cohort study was conducted 12 months later and included 1,656 individuals. Participants underwent an interview and blood collection for the detection of HBV serological markers and HBV-DNA phylogenetic analysis.
Results: HBV exposure (anti-HBc+) was 9.8% (95% CI: 8.8-10.8); 11.2% were female and 9.6% were male. HBsAg+ was 0.6%. Only 31.4% of the participants had HBV vaccination-like profile (anti-HBs+ alone; 30.4% male vs. 36.8% female; p = 0.004). Most individuals were susceptible to HBV (60.2% female vs. 52.2% male, p = 0.001). HBV isolates were classified as genotypes A (45.4%), D (27.3%) and F (27.3%). In males, HBV exposure was associated with increased age. Male prisoners had more evidence of HCV/HBV co-infection (10.7%) than females (3.4%) and the frequency of Treponema pallidum infection among prisoners who had been exposed to HBV was higher in female prisoners when compared with male (39.7% vs. 19.1%). The incidence of HBV was 0.18/100 person-years (95% CI: 0.12%–0.25%).
Conclusions: Our results indicate a high prevalence of HBV exposure in prisoners. Despite the low incidence of this infection, the occurrence of new cases indicates the need to implement preventive measures.

1. Introduction

Worldwide, it is estimated that over 257 million people are at risk of liver cirrhosis and hepatocellular carcinoma due to chronic hepatitis B virus (HBV) infection (WHO, 2017). In Brazil, approximately 17,000 new cases are reported annually, evidencing the impact of this disease on public health (Brasil, 2018). HBV infection is still a challenge to public health services and requires specific prevention actions, particularly focusing on key populations, such as prisoners (WHO, 2017).

Brazil has the third largest prison population in the world, with 682,901 people in penal institutions. The state of Mato Grosso do Sul (MS) has the highest rate of incarceration, where 18,688 share a space planned for 7,731 people (ICPS, 2014). In this setting, most imprisonments are due to drug-related crimes, since MS borders the two biggest marijuana and cocaine producers - Paraguay and Bolivia, respectively (CNM, 2016).

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Prison populations are at high risk of blood and sexually transmitted infections (STIs) due to illicit drug use, sharing of tattooing/piercing needles, unprotected homosexual activities while incarcerated and restricted access to healthcare and other prevention measures (Abiona, 2010). HBV infection is a major concern in a prison population with a global incidence estimate of 0.8%-3.8% per 100 person-years (py)(Gétaz et al., 2018; Gough et al., 2010; Khan et al., 2005; Weinbaum et al., 2003).

Despite that transmission events are greatly increased in prisons, HBV and other infectious diseases can be spread not only in this setting, but also outside. Since most people in prison return to the community after the incarceration time, information on disease prevalence, incidence and chain of transmission can improve health care services and guide future interventions (Sosmanj et al., 2011). If on one hand, the prison setting represents a challenge in HBV control, on the other hand, it provides an opportunity for treatment and prevention of new infections within and outside the prison environment (Hunt and Saab, 2009).

This multicenter study discussed the prevalence, within-prison incidence and associated factors with HBV infection among male and female prisoners in the Central region of Brazil.

2. Materials and Methods

2.1. Study population

Based on the information from the State Agency of the Administration of Prisons, at the time of data collection there were 9,913 inmates in 21 closed penal institutions that comprise the total closed subset. First, a multicenter cross-sectional study was conducted in 12 prisons, with 7,221 inmates, located in Campo Grande, Corumbá, Dourados, Ponta Porã and Três Lagoas, the five largest cities in the state. A total of 3,368 prisoners, from 12 of the 21 high security prisons of the state of Mato Grosso do Sul, Central Brazil, were randomly recruited between December 2013 and January 2014. The sample size was calculated based on the expected 2% prevalence of HIV with a variation of 1%, power of 80% and alpha-type error of 5%. We added 20% more individuals (total, 3,771 prisoners) to account for anticipated loss due to refusal to participate (Puga et al., 2017). Proportional stratified sampling was performed using each prison as a unit of randomization. At the time of data collection, inmates were ordered numerically in ascending order from the lists provided by the prison administrators, and a list of random numbers was generated using the Epi-Info 6.04 software (Atlanta, GA, USA). Eligibility criteria were 18 years of age or older, being an inmate in a closed prison system, be able to consent for themselves, suitable to be interviewed by a researcher alone (no risk markers).

In addition, one year after the first investigation, a prospective of a cohort study was conducted from December 2014 to January 2015 to estimate the incidence rate of HBV infection. The inclusion criteria were (i) to not leave prisons (for any reason) during this period; (ii) accepting to be interviewed regarding pre-defined risk-factors associated with reinfection; and (iii) being susceptible to HBV infection (HBsAg negative and/or total anti-HBc negative) or had no HBV vaccination-like profile (anti-HBs alone negative) in the cross-section survey conducted one year before(Puga et al., 2017).

Incidence of infection was defined as the average number of new infections (cohort study) in baseline seronegative subjects per 100 person-years (py) of follow-up. After being invited to participate in the research study, a member of the study staff explained the study aims and procedures, highlighting that their participation was voluntary and confidential. The voluntary participants signed written informed consent and separately, answered a questionnaire regarding socioeconomic and demographic characteristics, previous incarcerations, as well as individual risk behaviors for HBV infections and other sexually transmitted infections (STIs). Blood samples were collected and samples aliquots were stored at -20 °C for further serological and molecular analysis.

The study protocol, informed consent, and questionnaire were approved by the Ethics Committee of the Universidade Federal da Grande Dourados, under protocol number 191.877, CAAE 05598912.00000.5160.

2.2. Serological tests

All serum samples were tested for the presence of HBV serological markers (HBsAg, anti-HBs and total anti-HBc), HIV (anti-HIV-1/2) and hepatitis C (anti-HCV) infections by using enzyme-linked immunosorbent assay (ELISA, DiaSorin S.p.A). The HBsAg positive samples were submitted to anti-HBc IgM, HBeAg and anti-HBe detection (Biokit S.A., Bioelisa, Spain). The HCV positivity was considered in individuals who were positive for anti-HCV by enzyme-linked immunosorbent assay (ELISA–Murex Diagnostics, UK) and confirmed by “line immunoassay” (INNO-LIA III HCV Ab, Innogenetics, Belgic). Positive samples were submitted to detection of HCV RNA by Real Time HCV assay (qPCR) (Abbott RealTime HCV®) described by Puga et al., 2017(Puga et al., 2017). The anti-HIV-1/2 was determined using enzyme immunosorbent assay and confirmed by Western Blot assay as described by Sgarbi et al., 2015(Sgarbi et al., 2015). The prevalence of lifetime syphilis was determined using a treponemal test (ELISA; ICE*Syphilis, DiaSorin, Saluggia, Italy). Active syphilis was defined as VDRL titers $\geq$1:8 confirmed by a treponemal test as recommended by the Brazilian Ministry of Health and described by Correa et al., 2017(Correa et al., 2017).

For the analysis of the HBV vaccination-like profile, the schedule was considered complete for those who received the three doses of the hepatitis B vaccine. This information was collected verbally, because of the unavailability of vaccine cards in the prisons investigated.

2.3. Molecular analysis

Nucleic acid was extracted from all HBsAg positive (with or without total anti-HBc) sera using the robotic Roche MagNA Pure LC system (software version 3.0.11) and the MagNA Pure isolation kit (Roche, Applied Sciences, Indianapolis, IN) according to manufacturer's instructions. The partial S-gene (441 bp) was amplified by nested-PCR performed with Perfecta SYBR FastMix chemistry (Quanta BioSciences, Gaithersburg, MD). The first round of amplification was carried out with sense primer HBV_S1F CTA GGA CCC CTG CTC GTG TT and antisense primers HBV_S1R TCG AAC CAC TGA ACA AAT GGC ACT. The second round of amplification was performed with sense primer HBV_SNF GTT GAC AAG AAT CCT CAC AAT ACC and antisense primer HBV_SNR GGC TGA GGC CCA CTC CCA TA, as previously described (Forbi et al., 2010).

Amplicons derived from the nested PCR were sequenced using their respective nested primers and BigDye v3.1 sequencing kit (Applied Biosystems) by an automated sequencer (ABI 3130xl, Applied Biosystems, Foster City, CA). Sequencing PCR involved 25 cycles, each cycle consisting of 96 °C for 10 s, 50 °C for 5 s and 60 °C for 4 min. Sequences were analyzed using the SeqMan and MegAlign programs of the Lasergene DNA and protein software version 13.0 (DNASTAR Inc., Madison, WI). HBV genotypes were classified based on the S-gene sequence by comparing each sequence with published reference sequences from GenBank. Neighbor-joining tree was built using the Mega program version 6.0(Tamura et al., 2013).

2.4. Data analysis

The prevalence rates of hepatitis B infection and vaccination status were calculated with 95% confidence interval (95% CI). Frequencies of HBV exposure (any HBV marker: HBsAg positive; HBsAg/anti-HBc positive; anti-HBc alone positive; anti-HBc/anti-HBs positive), HBV vaccination-like profile (anti-HBs alone), and susceptibility are reported overall and by selected covariates. Chi-square and Fisher's exact test were initially used to determine the relationship between the dependent variable (total anti-HBc or isolated anti-HBs) and each independent variable, estimating the odds ratio in univariate analysis. Variables with a p-value of 0.20 or less on univariate were included in a stepwise logistic regression model and p-value of less of 0.05 was considered significant. Analyses were performed using the SPSS v. 22 for Windows, SPSS Inc., Chicago IL, USA. Package v.11. Sensitivity, specificity and positive predictive value (PPV) were calculated to verify the reliability of self-report HBV vaccination status. Serologic test results (anti-HBs alone) were used as "gold standard" indicators of hepatitis B vaccination-like profile. Ives–Gibbons correlation coefficient calculation (Ives and Gibbons, 1967) was performed to verify the agreement between HBV self-report vaccination and the number of individuals with the correspondent serological profile (anti-HBs alone). All prisoners (864 males and 191 females) with serological HBV vaccination-like profile (isolated anti-HBs ≥ 10mIU/mL) were excluded to HBV risk factors analysis.

3. Results

Of 3,771 eligible prisoners, 3,368 (89.3%) provided blood tests and completed the questionnaire. The study included 2,848 (84.6%) male and 520 (15.4%) female prisoners. Socio-demographic characteristics, sexual behaviors and substance use of the study population are presented in Table 1. Differences between male and female prisoners were noted for almost all variables, highlighting the importance of analyzing them separately, as described by Puga et al., 2017(Puga et al., 2017).

Most prisoners (54.1% females and 55.3% males) were under 30 years old, reported less than ten years of schooling (67.6% females and 73.8% males) and were prisoners in the capital of MS state. Differently from the female prisoners, male prisoners had more previous incarceration (62.4% vs 40.7%; $p < 0.001$), illicit drug use history (54.8% vs 38.5%; $p < 0.001$), self-reported active tuberculosis (6.6% vs 3.1%; $p = 0.002$), hepatitis C virus (HCV) exposure (2.7%

Table 1
Hepatitis B virus exposure, HBV vaccination-like profile, and susceptibility by demographic, behavioral, and clinical characteristics among prisoners in Central Brazil.

	Female				Male			
	Total no. (%)	HBV exposed and active HBV infection no.[a] (%)	HBV vaccination-like profile no.[b] (%)	Susceptible no.[c] (%)	*Total no. (%)*	HBV exposed and active HBV infection no.[a] (%)	HBV vaccination-like profile no.[b] (%)	Susceptible no.[c] (%)
Total	520	58 (11.2)	191 (36.7)	271 (52.1)	2.848	272 (9.6)	864 (30.3)	1.712 (60.1)
Age (years)								
≤30	279 (54.1)	20 (35.1)	141 (74.2)	118 (43.9)	1559 (55.3)	58 (21.9)	645 (75.3)	856 (50.5)
31-40	145 (28.1)	16 (28.1)	31 (16.3)	98 (36.4)	776 (27.5)	77 (29.1)	147 (17.1)	552 (32.5)
41-50	65 (12.6)	16 (28.1)	12 (6.3)	37 (13.8)	337 (12.0)	79 (29.8)	47 (5.5)	211 (12.4)
>50	27 (5.2)	05 (8.7)	06 (3.2)	16 (5.9)	146 (5.2)	51 (19.2)	18 (2.1)	77 (4.5)
Missing	04	01	01	02	30	07	07	16
Education (years)								
>12	14 (2.8)	02 (3.7)	02 (1.1)	10 (3.7)	66 (2.4)	09 (3.5)	15 (1.8)	42 (2.5)
10-12	149 (29.6)	11 (20.4)	59 (32.2)	79 (29.6)	653 (23.8)	51 (19.8)	224 (26.8)	378 (22.9)
≤9	341 (67.6)	41 (75.9)	122 (66.7)	178 (66.7)	2027 (73.8)	198 (76.7)	598 (71.4)	1231 (74.6)
Missing	16	04	08	04	102	14	27	61
City of imprisonment								
Dourados	-	-	-	-	535 (18.8)	51 (18.8)	215 (24.9)	269 (15.7)
Campo Grande	269 (51.7)	24 (41.4)	106 (55.5)	139 (51.3)	1520 (53.4)	132 (48.5)	448 (51.9)	940 (54.9)
Três Lagoas	77 (14.8)	16 (27.6)	32 (16.7)	29 (10.7)	283 (9.9)	23 (8.4)	92 (10.6)	168 (9.8)
Corumbá	81 (15.6)	08 (13.8)	16 (8.4)	57 (21.0)	260 (9.1)	31 (11.4)	25 (2.9)	204 (11.9)
Ponta Porã	93 (17.9)	10 (17.2)	37 (19.4)	46 (17.0)	250 (8.8)	35 (12.9)	84 (9.7)	131 (7.7)
Previous incarceration								
No	308 (59.3)	29 (50.0)	107 (56.0)	172 (63.7)	1065 (37.6)	99 (36.7)	333 (38.6)	633 (37.3)
Yes	211 (40.7)	29 (50.0)	84 (44.0)	98 (36.3)	1764 (62.4)	171 (63.3)	529 (61.4)	1.064 (62.7)
Missing	01			01	19	02	02	15
Drug history								
No	318 (61.5)	40 (69.0)	99 (51.8)	179 (66.8)	1.267 (45.2)	151 (56.3)	348 (40.8)	768 (45.6)
Yes	199 (38.5)	18 (31.0)	92 (48.2)	89 (33.2)	1.539 (54.8)	117 (43.7)	504 (59.2)	918 (54.4)
Missing	03			03	42	04	12	26
History of STI(s)								
No	451 (88.6)	48 (85.7)	164 (88.2)	239 (89.5)	2.345 (87.2)	197 (75.8)	740 (90.5)	1.408 (87.3)

Table 1 (*Continued*)

	Female				Male			
	Total no. (%)	HBV exposed and active HBV infection no.[a] (%)	HBV vaccination-like profile no.[b] (%)	Susceptible no.[c] (%)	*Total no. (%)*	HBV exposed and active HBV infection no.[a] (%)	HBV vaccination-like profile no.[b] (%)	Susceptible no.[c] (%)
Yes	58 (11.4)	08 (14.3)	22 (11.8)	28 (10.5)	345 (12.8)	63 (24.2)	78 (9.5)	204 (12.7)
Missing	11	02	05	04	158	12	46	100
Number of sexual partners (last 5 y)								
≤1	452 (86.9)	50 (86.2)	158 (82.7)	244 (90.0)	1.943 (68.2)	195 (71.7)	555 (64.2)	1.193 (69.7)
2-5	52 (10.0)	04 (6.9)	26 (13.6)	22 (8.1)	701 (24.6)	58 (21.3)	236 (27.3)	407 (23.8)
>5	16 (3.1)	04 (6.9)	07 (3.7)	05 (1.9)	204 (7.2)	19 (7.0)	73 (8.5)	112 (6.5)
Self-reported HBV vaccination								
Not vaccinated	196 (39.0)	22 (39.3)	55 (30.6)	119 (44.7)	1.445 (55.5)	149 (57.5)	359 (45.1)	937 (60.5)
Vaccinated	306 (61.0)	34 (60.7)	125 (69.4)	147 (55.3)	1.160 (44.5)	110 (42.5)	437 (54.9)	613 (39.5)
Missing	18	02	11	05	243	13	68	162
Self-reported active tuberculosis								
No	498 (96.9)	53 (93.0)	182 (97.3)	263 (97.4)	2.542 (93.4)	230 (88.5)	786 (94.9)	1.526 (93.4)
Yes	16 (3.1)	04 (7.0)	05 (2.7)	07 (2.6)	179 (6.6)	30 (11.5)	42 (5.1)	107 (6.6)
Missing	06	01	04	01	127	12	36	79
Anti-HCV positive								
No	517 (99.4)	56 (96.6)	191 (100.0)	270 (99.6)	2.771 (97.3)	243 (89.3)	852 (98.6)	1.676 (97.9)
Yes	03 (0.6)	02 (3.4)	-	01 (0.4)	77 (2.7)	29 (10.7)	12 (1.4)	36 (2.1)
Anti-HIV positive								
No	510 (98.1)	55 (94.8)	190 (99.5)	265 (97.8)	2.803 (98.4)	266 (97.8)	853 (98.7)	1.684 (98.4)
Yes	10 (1.9)	03 (5.2)	01 (0.5)	06 (2.2)	45 (1.6)	06 (2.2)	11 (1.3)	28 (1.6)
Anti-*T. pallidum* positive								
No	432 (83.1)	35 (60.3)	164 (85.9)	233 (86.0)	2.576 (90.4)	220 (80.9)	809 (93.6)	1.547 (90.4)
Yes	88 (16.9)	23 (39.7)	27 (14.1)	38 (14.0)	272 (9.6)	52 (19.1)	55 (6.4)	165 (9.6)

[a] Defined as ever infected with HBV according to positive hepatitis B core antibody.
[b] Defined as positive (≥10 mIU/mL) hepatitis B surface antibody in combination with negative hepatitis B core antibody and hepatitis B surface antigen.
[c] Defined as negative hepatitis B core antibody, negative hepatitis B surface antibody, and negative hepatitis B surface antigen. HBV: hepatitis B virus; STI: sexually transmitted infections; HIV: human immunodeficiency virus; HCV: hepatitis C virus.

vs. 0.6%; $p < 0.001$) and lifetime syphilis infection (16.9% vs. 9.6%; $p < 0.001$). In addition, male prisoners had higher rates of HCV/HBV co-infection than females (10.7% vs. 3.4%; $p < 0.001$). On the other hand, it was observed that 5.2% of females who had been exposed to HBV tested positive to HIV, compared with 2.2% of male prisoners (Table 1).

3.1. HBV Infection

Serological evidence of past or present HBV infection (HBsAg and/or anti-HBc-positive) was 9.8% (95% CI: 8.8 to 10.8), varying from 9.6% (95% CI: 8.8 to 10.8) among male prisoners to 11.2% (95% CI: 8.4 to 13.9) among female prisoners. The prevalence of HBV carriers (HBsAg positive) was 0.6%, with no difference between male and female prisoners (0.6% vs 0.8%; $p > 0.05$). Of 3.368 prisoners, the serological evidence of previous HBV vaccination (isolate anti-HBs positive ≥ 10mIU/mL) was 31.4%, (30.4% males vs. 36.8% females; $p = 0.004$). Most of the study population tested negative for all HBV serologic markers and was susceptible to HBV infection (58.9%) with differences in susceptibility between male and female prisioners (60.2% vs. 52.2%, $p = 0.001$) (Table 2).

HBV DNA was detected in 12/17 (70.6%) HBsAg-positive samples. Genotypes A (A1 33.3%; A2 8.3%), D (D2 8.3%; D3 16.7%) and F (F4 16.7%; F2 8.3%) were identified in 45.4%, 27.3% and 27.3% of HBV DNA positive samples, respectively.

After multivariable analysis, age over 30 years, self-reported active tuberculosis and HCV exposure were associated with HBV exposure among male prisoners. Among total anti-HBc positive female prisoners, lifetime syphilis infection was more than three times higher than among anti-HBc negative female prisoners (Table 3).

During the cohort study period (2015-2016), of 1,983 prisoners susceptible for HBV infection, 1,656 were continuously incarcerated and provided written informed consent and venipuncture to the HBV incidence survey. All serial samples were confirmed to be from the same individuals, all of whom tested negative for all HBV serological markers at baseline. Among them, 3 new cases of HBV infection were detected, and the incidence rate was 0.18/100 person-years (95% CI = 0.12%–0.25%). The presence of HBV DNA was detected in 1 out of 3 HBsAg positive samples. All HBV incidence cases were females and the mean age was 33.3 years. Two of them were incarcerated in Corumbá and one in Três Lagoas prisons. Risk

Table 2
Prevalence of hepatitis B virus serological markers among prisoners in Central Brazil (N = 3.368).

Category	Serological marker	All Prisoners		Male		Female		p-value
		(N = 3,368) n (%)	(N = 2,848) 95% CI[a]	(N = 520) n (%)	95% CI[a]	n (%)	95% CI[a]	
HBV exposure								
	Alone HBsAg	03 (0.1)	0.1–0.1	02 (0.1)	0.0–0.1	01 (0.2)	0.1–0.3	0.391
	HBsAg/Anti-HBc	15 (0.5)	0.2–0.7	12 (0.5)	0.2–0.7	03 (0.6)	0.4–0.8	0.425
	Anti-HBc alone	39 (1.2)	0.8–1.5	37 (1.3)	0.9–1.7	02 (0.4)	0.2–0.6	0.073
	Anti-HBc/Anti- HBs	273 (8.1)	7.2–9.0	221 (7.8)	6.8–8.7	52 (10.0)	7.4–12.6	0.086
	Any HBV marker	330 (9.8)	8.8–10.8	272 (9.6)	8.5–10.6	58 (11.2)	8.4–13.9	0.295
HBV vaccination-like profile	**Alone anti-HBs**	1055 (31.4)	29.8–32.9	864 (30.4)	28.6–32.0	191 (36.8)	32.6–40.9	**0.004**
Not exposed, susceptible	**No marker**	1983 (58.9)	57.2–60.5	1712 (60.2)	58.3–61.9	271 (52.2)	47.8–56.4	**0.001**

[a] Confidence Interval; IFisher's Exact Test. HBV: hepatitis B virus; HBsAg: HBV surface antigen; anti-HBc: hepatitis B core antibodies; anti-HBs: hepatitis B surface antibody.

Table 3
Factors associated with hepatitis B virus exposure among male and female prisoners in Central Brazil*

	HBV exposure N (%)	OR (95% CI)	*p*-value	Male aOR† (95% CI)	*p*-value	HBV Exposure N (%)	OR (95% CI)	*p*-value	Female aOR† (95% CI)	*p*-value
Age (years)										
≤30	58/914 (6.3)	1				20/138 (14.5)	1			
31-40	77/629 (12.2)	2.05 (1.44-2.94)	<**0.001**			16/114 (14.0)	0.96 (0.47-1.95)	0.918		
41-50	79/290 (27.2)	5.52 (3.81-8.00)	<**0.001**			16/53 (30.2)	2.55 (1.20-5.42)	**0.013**	1.22 (0.87-1.72)	0.230
>50	51/128 (39.8)	9.77 (6.27-15.2)	<**0.001**	1.99 (1.69-2.33)	<**0.001**	5/21 (23.8)	1.84 (0.60-5.59)	0.275		
Education (years)										
>12	9/51 (17.6)	1				2/12 (16.7)	1			
10-12	51/429 (11.9)	0.63 (0.29-1.37)	0.240			11/90 (12.2)	0.73 (0.14-5.22)	0.649		
≤9	198/1429 (13.9)	0.75 (0.36-1.56)	0.443			41/219 (18.7)	1.12 (0.24-5.45)	1.000		
City of imprisonment										
Corumbá	31/235 (13.2)	1				8/65 (12.3)	1			
TrêsLagoas	23/191 (12.0)	0.90 (0.50-1.60)	0.723			16/45 (35.6)	3.93 (1.50-10.25)	**0.004**	1.14 (0.88-1.49)	0.311
Ponta Porã	35/166 (21.1)	1.75 (1.03-2.99)	**0.036**	1.02 (0.91-1.16)	0.644	10/56 (17.9)	1.54 (0.56-4.24)	0.392		
Dourados	51/320 (15.9)	1.24 (0.77-2.02)	0.368			-				
Campo Grande	132/1072 (12.3)	0.92 (0.60-1.40)	0.712			24/163 (14.7)	1.23 (0.52-2.90)	0.635		
Previous incarceration										
No	99/732 (13.5)	1				29/201 (14.4)	1			
Yes	171/1235 (13.8)	1.02 (0.78-1.34)	0.841			29/127 (22.8)	1.75 (0.99-3.10)	**0.052**	1.39 (0.73-2.62)	0.307
Drug history										
No	151/919 (16.4)	1				40/219 (18.3)	1			
Yes	117/1035 (11.3)	0.64 (0.50-0.84)	**0.001**	0.92 (0.68-1.25)	0.629	18/107 (16.8)	0.90 (0.49-1.66)	0.749		
History of STI(s)										
No	197/1605 (12.3)	1				48/287 (16.7)	1			
Yes	63/267 (23.6)	2.20 (1.60-3.03)	<**0.001**	1.23 (0.85-1.80)	0.261	8/36 (22.2)	1.42 (0.61-3.31)	0.411		
Number of sexual Partners in the last five years										
≤1	195/1388 (14.0)	1				50/294 (17.0)	1			
2-5	58/465 (12.5)	0.87 (0.63-1.19)	0.392			04/26 (15.4)	0.90 (0.35-2.30)	1.000		
>5	19/131 (14.5)	1.03 (0.62-1.72)	0.886			04/09 (44.4)	2.61 (1.20-5.66)	**0.057**	1.64 (0.87-3.09)	0.120
Self-reported hepatitis B vaccination										
Not vaccinated	149/1086 (13.7)	1				22/141 (15.6)	1			
Vaccinated	110/723 (15.2)	1.12 (0.86-1.47)	0.374			34/181 (18.8)	1.25 (0.69-2.25)	0.455		
Self-reported active tuberculosis										
No	230/1756 (13.1)	1				53/316 (16.8)	1			

Table 3 (*Continued*)

	HBV exposure N (%)	OR (95% CI)	*p*-value	Male aOR† (95% CI)	*p*-value	HBV Exposure N (%)	OR (95% CI)	*p*-value	Female aOR† (95% CI)	*p*-value
Yes	30/137 (21.9)	1.86 (1.21-2.85)	**0.004**	1.64 (1.01-2.65)	**0.043**	04/11 (36.4)	2.83 (0.80-10.03)	0.092	1.89 (0.48-7.45)	0.361
Anti-HCV positive										
No	243/1919 (12.7)	1				56/326 (17.2)	1			
Yes	29/65 (44.6)	5.55 (3.34-9.22)	<**0.001**	2.38 (1.31-1.77)	**0.004**	02/03 (66.7)	9.64 (0.85-108.18)	**0.025**	8.54 (0.59-123.51)	0.116
Anti-HIV positive										
No	266/1950 (13.6)	1				55/320 (17.2)	1			
Yes	06/34 (17.6)	1.35 (0.55-3.30)	0.501			03/09 (33.3)	2.40 (0.58-9.92)	0.210		
Anti-*T. pallidum* positive										
No	220/1767 (12.5)	1				35/268 (13.1)	1			
Yes	52/217 (24.0)	2.21 (1.57-3.12)	<**0.001**	1.18 (0.78-1.80)	0.429	23/61 (37.7)	4.02 (2.15-7.55)	**0.000**	3.31 (1.67-6.56)	**0.001**

§Statistically significant (P ≤ 0.05). HBV: hepatitis B virus; OR: odds ratio; CI: confidence interval; aOR: adjusted OR; STI: sexually transmitted infections; HIV: human immunodeficiency virus; HCV: hepatitis C virus.

* HBV-vaccinated individuals were excluded.

† Adjusted for variables with a *p*-value of 0.20 or less on univariate analysis.

behaviors found in 2 out of 3 new HBV cases included history of non-injecting drug use (non-IDU), tattooing inside the prison, previous imprisonment, homosexual contact, history of irregular condom use and sharing cutting instruments.

3.2. Hepatitis B Immunization

Of the 520 female prisoners, 306 (58.8%) self-reported receiving HBV vaccine, nevertheless only 125 (40.8%) had a serological HBV vaccination-like profile (isolate anti-HBs ≥10mIU/mL). Moreover, 11.1% (34/306) had evidence of previous HBV infection, and 48.0% (147/306) were still susceptible to HBV infection. Never receiving a dose of HBV vaccine was reported by 39.0% of female and 55.5% of male prisoners (p < 0.001). Among 2,848 male prisoners, 1,160 (40.7%) self-reported receiving HBV vaccine. However, only 437 (37.7%) had HBV vaccination-like profile, 9.5% (110/1,160) had evidence of past infection, and 52.8% (613/1,160) were still susceptible to HBV infection (Table 1). Of note, a moderate agreement (r3,107 = 0.17) between self-reported HBV vaccination and the number of persons with isolated anti-HBs was found using calculation of Ives–Gibbons correlation coefficient. This finding is supported by poor sensitivity (0.58), specificity (0.58) and positive predictive value (0.38) of the self-reported answers. After multivariate analysis, age under 30 years, city of imprisonment and self-reported hepatitis B vaccination were independently associated with HBV

Table 4
Factors associated with hepatitis B vaccination-like profile among female prisoners in Central Brazil.

	HBV Vaccination-like profile N (%)	OR (95% CI)	*P* value	Male aOR (95% CI)	*P* value	HBV Vaccination-like profile N (%)	OR (95% CI)	*P* value	Female aOR (95% CI)	*P* value
Age (years)										
>50	18/95 (18.9)	1				6/22 (27.3)	1			
41-50	47/258 (18.2)	0.95 (0.52-1.74)	0.875			12/49 (24.5)	0.86 (0.27-2.70)	0.803		
31-40	147/699 (21.0)	1.13 (0.66-1.96)	0.639			31/129 (24.0)	0.84 (0.30-2.34)	0.744		
≤30	645/1501 (43.0)	3.22 (1.91-5.43)	<**0.001**	1.96 (1.69-2.28)	<**0.001**	141/259 (54.4)	3.18 (1.20-8.40)	**0.014**	2.11 (1.57-2.85)	<**0.001**
Education (years)										
<9	598/1829 (32.7)	1				122/300 (40.7)	1			
10-12	224/602 (37.2)	1.21 (1.00-1.47)	**0.042**	1.04 (0.86-1.26)	0.662	59/138 (42.8)	1.08 (0.72-1.63)	0.680		
>12	15/57 (26.3)	0.73 (0.40-1.33)	0.311			2/12 (16.7)	0.29 (0.06-1.35)	0.096	0.87 (0.59-1.30)	0.521
City of imprisonment										
Corumbá	25/229 (10.9)	1				16/73 (21.9)	1			
Campo Grande	448/1388 (32.3)	3.88 (2.52-5.98)	<**0.001**			106/245 (43.3)	2.71 (1.47-4.99)	<**0.001**		
TrêsLagoas	92/260 (35.4)	4.46 (2.74-7.27)	<**0.001**			32/61 (52.5)	3.93 (1.86-8.30)	<**0.001**	1.39 (1.10-1.75)	**0.005**
Ponta Porã	84/215 (39.1)	5.23 (3.18-8.60)	<**0.001**			37/83 (44.6)	2.86 (1.41-5.79)	**0.003**		
Dourados	215/484 (44.4)	6.52 (4.14-10.25)	<**0.001**	1.27 (1.18-1.37)	<**0.001**					

Table 4 (*Continued*)

	Male					Female				
	HBV Vaccination-like profile N (%)	OR (95% CI)	*P* value	aOR (95% CI)	*P* value	HBV Vaccination-like profile N (%)	OR (95% CI)	*P* value	aOR (95% CI)	*P* value
Previous incarceration										
No	333/966 (34.5)	1				107/279 (38.4)	1			
Yes	529/1593 (33.2)	0.94 (0.79-1.19)	0.512			84/182 (46.2)	1.37 (0.94-2.01)	**0.096**	1.54 (1.00-2.39)	**0.049**
Drug history										
No	348/1116 (31.2)	1				99/278 (35.6)	1			
Yes	504/1422 (35.4)	1.21 (1.02-1.43)	**0.024**	1.06 (0.87-1.29)	0.560	92/181 (50.8)	1.86 (1.27-2.73)	**0.001**	1.37 (0.89-2.11)	0.147
History of STI(s)										
No	740/2148 (34.5)	1				164/403 (40.7)	1			
Yes	78/282 (27.7)	0.72 (0.55-0.95)	**0.023**	1.01 (0.73-1.41)	0.894	22/50 (44.0)	1.14 (0.63-2.07)	0.654		
Self-reported hepatitis B vaccination										
Not vaccinated	359/1296 (27.7)	1				55/174 (31.6)	1			
Vaccinated	437/1050 (41.6)	1.86 (1.56-2.21)	<**0.001**	1.88 (1.55-2.29)	<**0.001**	125/272 (46.0)	1.84 (1.23-2.74)	**0.003**	1.56 (1.01-2.40)	**0.042**
Self-reported active tuberculosis										
No	786/2312 (34.0)	1				182/445 (40.9)	1			
Yes	42/149 (28.2)	0.76 (0.52-1.10)	0.146	1.12 (0.73-1.71)	0.598	05/12 (41.7)	1.03 (0.32-3.30)	0.957		
Anti-HCV positive										
No	852/2528 (33.7)	1				191/461 (41.4)	1			
Yes	12/48 (25.0)	0.65 (0.33-1.26)	0.206			0/01	0.58 (0.54-0.63)	0.401		
Anti-HIV positive										
No	853/2537 (33.6)	1				190/455 (41.8)	1			
Yes	11/39 (28.2)	0.77 (0.38-1.56)	0.477			01/07 (14.3)	0.23 (0.02-1.94)	0.143	0.25 (0.02-2.39)	0.233
Anti-*T. pallidum* positive										
No	809/2356 (34.3)	1				164/397 (41.3)	1			
Yes	55/220 (25.0)	0.63 (0.46-0.87)	**0.005**	0.91 (0.63-1.33)	0.650	27/65 (41.5)	1.00 (0.59-1.71)	0.972		

* HBV-exposed individuals were excluded. †Adjusted for variables with a *p*-value of 0.20 or less on univariate analysis. § Statistically significant ($P \leq 0.05$). HBV: hepatitis B virus; OR: odds ratio; CI: confidence interval; aOR: adjusted OR; STI: sexually transmitted infections; HIV: human immunodeficiency virus; HCV: hepatitis C virus.

vaccination-like profile response among male prisoners. Among female participants, age under 30 years, city of imprisonment, previous incarceration and self-reported hepatitis B vaccination were independently associated with HBV vaccination-like profile (Table 4).

4. Discussion

To our knowledge, this is the first cross-sectional/cohort multicenter study of prevalence, incidence and associated factors of HBV infection in the male and female prison population in Brazil. These epidemiological data may provide important information to elucidate the role the correctional setting plays in risk of HBV infection and information for developing hepatitis B prevention strategies.

The serological evidence of past and present HBV infection (9.8%; 95% CI: 8.8 to 10.8) found in this study was approximately three times higher than in the first-time blood donors (3.04%) from the same region and was twice as high as the prevalence found in a large population-based study conducted in the Central region of Brazil (4.3; IC 95% 3.7-4.9)(Pereira et al., 2009; Brazil, 2010; Lindenberg et al., 2013). This high prevalence of HBV exposure is in agreement with similar studies done on prisoners in different parts of the world, suggesting that prisoners still have a greater vulnerability to HBV acquisition (Verneuil et al., 2009; Adjei et al., 2008; Solomon et al., 2004).

This reported prevalence is similar to other studies conducted in prisoners in Brazil, such as among prisoners with active tuberculosis in Campo Grande, MS (10.2%)(Iglecias et al., 2016) and in incarcerated youth from Salvador, Bahia (11.1%)(Fialho et al., 2008), and lower than in female prisoners in Goiânia, Goiás (18.9%) (Barros et al., 2013), São Paulo, SP (21%)(Maerrawi and Carvalho, 2015), Ribeirão Preto, SP (19.5%)(Coelho et al., 2009), Munhuaçu, Minas Gerais (17.5%)(Catalan-Soares et al., 2000) and Campo Grande, MS (17.9%)(Stief et al., 2010).

When compared to international studies, the prevalence of HBV exposure found in our study was higher than that found in Iran (7.4%)(Nokhodian et al., 2012) and lower than the prevalence observed in Switzerland (32.4%)(Gétaz et al., 2018), Australia (21.7%)(Reekie et al., 2014), Spain (30.4%)(Hoya et al., 2011) and

Italy (52.7%)(Babudieri et al., 2005). Although these regions were also classified as low endemic areas, these different rates might be explained by the low frequency of injecting drugs among our studied population (1%).

The prevalence of active hepatitis B infection observed in this study (0.6%) is in accordance with the prevalence of HBV infection found in this low endemic area (Lindenberg et al., 2013; Souto, 2016; Paoli et al., 2018). Despite the fact that differences between male and female prisoners were observed for most high-risk variables, no difference was found in the prevalence of past and/or present HBV infection.

Moreover, most participants were still susceptible to HBV infection (58.9%), with different rates between male and female prisoners. These data suggest lower vaccination coverage than desired, especially among prisoners aged > 30 years. Immunization programs started in the infant population in the 1989s and gradually covered the older age groups (Brasil, 2013). Although HBV vaccine has been used in Brazil in the last 20 years, these young adults were born prior to the implementation of the national immunization strategy. The application of HBV vaccine in this high-risk group should be implemented as a priority of the national immunization program.

The classic HBV vaccination schedule (3 doses at 0, 1 and 6 months) might not be applicable to all prisoners as they either might be released anytime during this 6-month period or might develop HBV infection due to high-risk behaviors before achieving proper anti-HBs seroprotection levels. Currently different accelerated vaccination schemes have been proposed for HBV vaccination, including a 0, 1 and 2 months or 0, 1 and 3 weeks vaccination regimen (Asli et al., 2011; Das et al., 2019). For this population highly vulnerable to HBV infection, results suggest that a reduced course of hepatitis B vaccination schedule will likely be advantageous because those prisoners will rarely complete the traditional schedule (Asli et al., 2011).

Male and female prisoners were engaged in a range of parenteral (sharp objects sharing, history of non-IDU) and sexual (irregular condom use and history of STIs) risk behaviors which expose them to HBV infection (Babudieri et al., 2005). These behaviors, acquired out of prison, might continue after incarceration. Compared to women, male prisoners had a higher frequency of previous incarceration, mean of incarceration sentence length, history of non-IDU, self-reported active tuberculosis, hepatitis C virus exposure and lifetime syphilis infection. A study conducted in Finnish prisoners (Viitanen et al., 2011) also observed that a shorter cumulative time in prison and being a first-time prisoner were more common for female compared to male prisoners.

The risk of HBV infection among male prisoners increased with age. This is in line with many epidemiological studies conducted in different group populations which observed that HBV infection is strongly associated with increased age(Stief et al., 2010; Souto, 2016; Paoli et al., 2018; Belaunzaran-Zamudio et al., 2017). The presence of genotypes A, D and F in this study was in accordance with data reported in other populations and in the Midwest region of Brazil (Mello et al., 2007; Lago et al., 2019; Lampe et al., 2017).

In previous studies conducted by our group, a high prevalence of HCV exposure (2.4%), HIV (1.6%) and Treponema pallidum (10.7%) infections were observed among prisoners with positivity for HBV infection (Puga et al., 2017; Sgarbi et al., 2015; Correa et al., 2017). In addition, male prisoners had more evidence of HCV/HBV co-infection (10.7%) than female (3.4%). The similarity in the transmission routes of these infections may explain the high frequency of these co-infections (Babudieri et al., 2005).

Self-reported history of active tuberculosis (TB) was associated with HBV exposure among male prisoners. The prevalence of active TB in the jail system is an important public health problem worldwide. Previous studies have reported that TB rates among Brazilian prisoners are more than 20 times higher than in the general population (Carbone et al., 2015). In a study conducted in prisoners with active tuberculosis, in the same region, Iglecias et al. (2016) observed a similar prevalence of HBV exposure of 10.2% (95%CI 6.2–14.2)(Iglecias et al., 2016). These similar prevalence rates in different populations (prisoners with and without active tuberculosis) may suggest that TB remains a persistent problem in the prison environment regardless of the clinical TB status of the prisoners.

An association between lifetime syphilis and a higher prevalence of exposure of HBV was only found among female prisoners. This key population might engage in high-risk sexual practices that may predispose them to acquiring STI infections while incarcerated (homosexual practices, inconsistent condom use), but they often have these same risk factors prior to being in the prison system. Studies in Mexico identified that condom use in Mexican prisons or elsewhere is scarce and little detailed (Fialho et al., 2008; Belaunzaran-Zamudio et al., 2017). It is important to note that, despite the occurrence of high-risk behaviors, Brazilian incarcerated persons have restricted access to free condoms, a vital harm reduction measure.

Moreover, the information on self-reported hepatitis B vaccination has low concordance with HBV vaccination-like profile results, although this was a protecting factor associated with serological evidence of HBV vaccination. The self-reported history of HBV vaccination would appear to be unreliable; use of this information could lead to misclassification and underestimation of the number of prisoners who need to receive the hepatitis B vaccine.

Self-reporting and recall-bias are some of the limitations of this cross-sectional study. Once some HBV vaccinated individuals lose detectable levels of anti-HBs over time, the frequency of susceptibility might be overestimated. In addition, we had insufficient numbers of new events of hepatitis B to examine associated factors for HBV infection during the cohort study. Despite these limitations, this study represents very well the male and female prisoner population of Central Brazil since we used a large sample size. Despite the elapsed time since our sampling, our study still reflects the current scenario once no mass hepatitis B vaccination campaigns or other preventive measures have been implemented in the prison population, to our knowledge. Moreover, due to the lack of current studies on the prevalence and incidence of HBV in Brazilian prisoners, our study may provide valuable information to close the gaps in HBV control public policies. The opportunity to conduct gender comparison and incidence estimation and to investigate risk factors associated with HBV infection may improve the development of effective prevention and health care services.

Despite low incidence rates of HBV infection among prisoners (0.18/100 person-years) compared with incidence rates found in other low prevalence countries (2.7/100 person-years), these new cases detected inside prisons are a reflection of high-risk activities and a lack of prevention programs and reinforce the urgent need for general prevention efforts. During incarceration, new infections may be acquired due to overcrowding, insufficient infection control and absence of harm reduction efforts. Despite this, prisoners are excellent subjects for routine screening, hepatitis B vaccination and treatment in order to break this chain of transmission (Kazi et al., 2010; Moradi et al., 2018).

5. Conclusions

In conclusion, the results of the present study indicate that individual and collective prevention measures such as health education actions, periodic serological screening, strategies to increase HBV vaccination coverage, harm reduction programs and

follow-up of HBV positive individuals are necessary for prevention and control of HBV infection in populations of prisoners.

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Conflicts of Interest

The authors declare no conflict of interest.

Author Contributions

Conceptualization, GRR, MAP, JC and ARCMC; methodology, GRR, MAP, LMB, TST, SMSW, GAC.; validation, BVL, ARCMC, MAP and JC; formal analysis, LMB, SMVLO, VOLC, MAP, MAP; investigation, TST, SFB, SMSW; GAC; SS resources, JC, ARCMC.; data curation, SMVLO, VOLC, SFB, RTSY.; writing—original draft preparation, GRR, BVL, ARCMC.; writing—review and editing, GRR, BVL, ARCMC.; visualization, SS, RTSY.; supervision, JC, ARCMC.; project administration, LMB, ARCMC.; funding acquisition, JC, SMVLO, ARCMC.

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