

HIGH PREVALENCE OF ALPHAHERPES VIRUS 2 (HSV-2)
POSITIVITY IN PRISONS FROM MIDWEST BRAZIL: A CROSS-
SECTIONAL STUDY

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Abstract

Herpes virus 2 (HSV-2) is the main cause of genital herpes, one of the most prevalent sexually transmitted infections (STIs) in the world. STIs are major public health problems in prisons because of the behaviors of prisoners and the presence of other factors that increase the risk of transmission. The present study aimed to estimate the prevalence and risk factors associated with HSV-2 infection at 12 prisons in Mato Grosso of Sul, Brazil. We tested 872 serum samples (732 from males, 140 from females) for anti-HSV-2 IgG, and tested the positive samples (n = 184) for anti-HSV-2 IgM. Anti-HSV-2 IgG positivity (n = 85, 43.1%, 95% CI = 34.6 to 40.4). The prevalence of HSV-2 positivity was much greater than reported in the general population of Brazil and in other prison populations worldwide. There was a greater risk of HSV-2 positivity in prisoners who were older, female, unmarried, HIV positive, positive for other STIs, not previously incarcerated, in the same cell with more than 26 individuals, and in those who reported having had genital discharge in the past month, having had a homosexual relationship in recent months, and not using or occasionally not using condoms during sexual intercourse. Further analysis of prisoners with active HSV-2 infections (anti-HSV-2 IgM positivity) indicated that unmarried status and the presence of 26 or more prisoners in the same cell increased the risk for active HSV-2 infection. This study provides important data on HSV-2 seroprevalence in the prison population of Brazil, and identified risk factors associated with HSV-2 infection. These data provide important information needed to implement procedures that better prevent and control of STIs in prison populations.

Keywords

Human herpes virus, seroprevalence, prisoners, epidemiology, Brazil

2 Background

3 Individuals living in precarious environments such as prisons, which are typically
4 characterized by poverty, conflict, discrimination, and apathy, often have poor health [1].
5 In particular, prisoners have a high risk for infectious diseases. Moreover, the
6 confinement and conditions in prisons make it difficult for these individuals to access
7 integrated and effective health care services [2]. Individuals in prisons throughout the
8 world have increased risk for many health problems. When convicted, prisoners in
9 precarious prisons, police stations, houses of detention/correction, and similar institutions
10 are typically exposed to environments with poor sanitary conditions, and they are
11 confined and in close proximity to others with infectious diseases. A recent study
12 described the prison environment as a site with great concentration and amplification of
13 situations and risk factors that facilitate the spread of infections [3]. Many factors favor
14 the spread of infectious diseases among prisoners, such as their idleness, overcrowding,
15 stress caused by incarceration and disruption of social and family ties, poor sanitary
16 conditions, physical abuse, dependence on licit and illicit toxic substances (alcohol and
17 tobacco), handmade tattoos, sharing of piercing-sharps, gestation without prenatal care,
18 and social marginalization [4] [5].

19 Brazil has the third-largest overall prison population in the world, according to
20 data of the Ministry of Justice. In 2019, there were 729.949 Brazilians in jail [6].

21 The Human alphaherpesvirus 2 (HSV-2) is primarily responsible for genital
22 herpes, and is widely distributed worldwide [7]. In addition, this virus is efficiently
23 transmitted, has rapid replication, and can remain latent in the sensory nerves for long
24 periods [8]. There are many symptoms of HSV-2 infections, including oropharyngeal,
25 cutaneous, and genital diseases, and encephalitis [9]. The initial infection usually

26 manifests as an ulcerative lesion in the genitalia, and is more common in adolescents and
27 sexually active adults [10];[11]; [12]. After an acute primary infection, the virus often
28 remains latent in the sensory ganglia, and may spontaneously re-activate depending on
29 the immune status and genetic predispositions of the patient. Reactivation may lead to
30 recurrent lesions or genital herpes, with manifestations ranging from asymptomatic viral
31 excretions to painful symptomatic blisters [13]; [14]; [15].

32 The World Health Organization (WHO) estimated that 417 million people aged
33 15 to 49 years have HSV-2 infections [16]. There is no compulsory notification for HSV-
34 2 infections, so data on the prevalence and incidence in Brazil are limited. Researchers
35 believe there is a high rate of HSV infection in Brazil, even though most individuals are
36 asymptomatic. The health ministry estimated that more than 90% of Brazilians have
37 antibodies against HSV-1 and/or HSV-2, even though the majority have never presented
38 with symptoms [17]. Some behaviors may increase the risk of HSV-2 infection, and these
39 are the same factors that increase the risk of sexually transmitted infections (STI) in
40 general populations: unprotected sexual activity, sexual intercourse with many
41 homosexual or heterosexual partners, sexual violence, unprotected sex between inmates,
42 and intimate visits with prisoners [2]. Given the lack of prevention policies regarding
43 HSV-2 infection in Brazilian prisons, the aim of this study was to estimate the
44 seroprevalence and predictive factors of HSV-2 infection among prisoners from 12
45 prisons in Midwest Brazil.

46 **Methods**

47 **Ethics**

48 This study was approved by the Education and Training Unit of the Federal
49 University of Grande Dourados (CE/UFGD) CAAE 05598912.0.0000.5160 opinion
50 191.877 and the State Agency of Administration of the Penitentiary System/MS
51 (Agepen/MS). The participants were approached and asked to sign an informed consent
52 form (ICF) which explained the purpose of the study. Emphasis was placed on the
53 confidentiality of each individual's identity and personal information by explaining that
54 only the team of researchers would have access to the information, and that all data would
55 be used exclusively for research purposes.

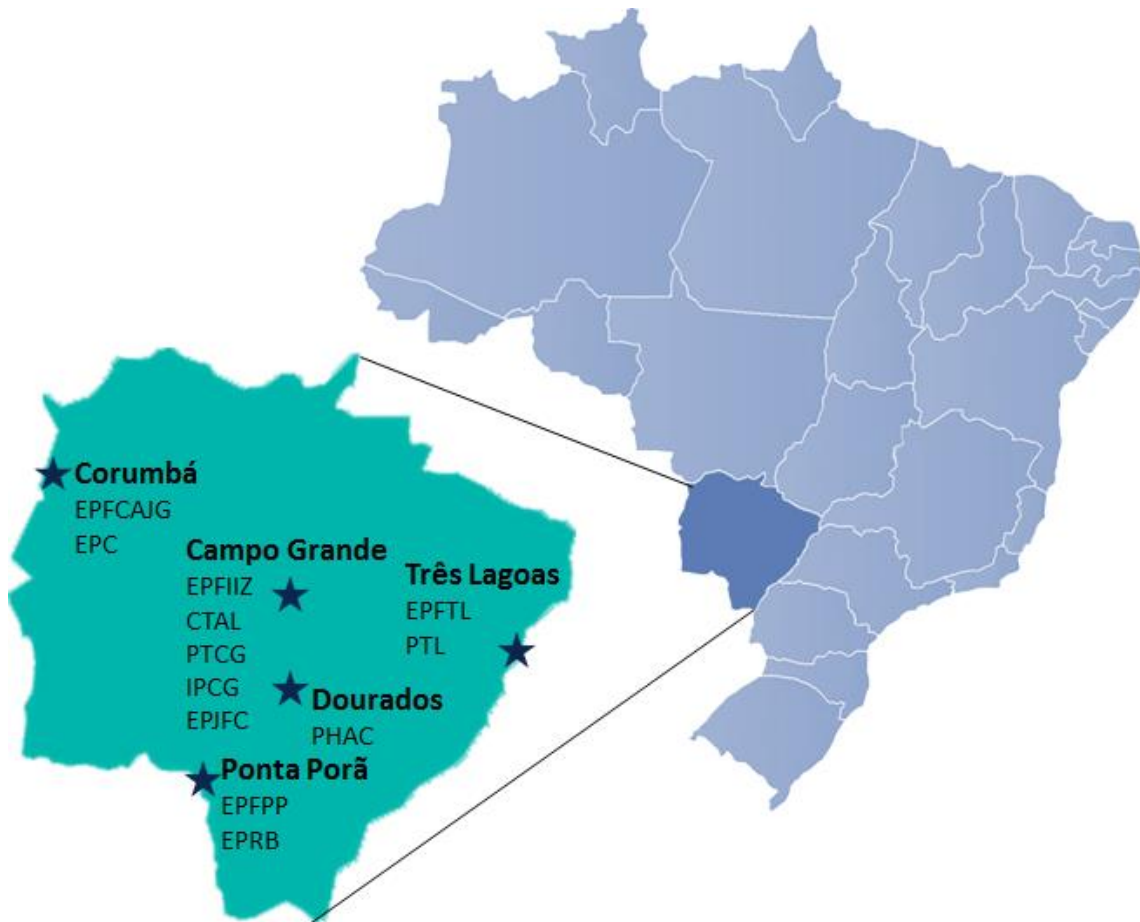
56 **Study participants and procedures**

57 This was a multicenter, retrospective, descriptive study, which analyzed
58 observations of primary data and laboratory test results. The study was conducted from
59 March 2013 to March 2014 in 12 prisons (4 for females and 8 for males) from Mato
60 Grosso do Sul, Brazil (Figure 1).

61 The directors of each penal establishment were contacted to obtain authorization
62 for the team of investigators and for evaluation of logistical needs. Subjects were included
63 if they signed the ICF, authorized the use of samples for research, and provided answers
64 to a questionnaire about certain general factors (age, sex, education, knowledge about
65 sexually transmitted infections, and socioeconomic and behavioral factors that were used
66 to identify risk factors.

67

68 **Figure 1:** Locations of the 12 study prisons in the state of Mato Grosso do Sul, Brazil
 69 (adapted from Puga *et al*, 2017).



70

Abbreviations: EPFCAJG, women's penal establishment Carlos Alberto Jonas Giordano; EPFTL, women's penal establishment Três Lagoas; EPFPP, women's penal establishment Ponta Porã; EPFIIZE, women's penal establishment Irmã Irma Zorzi; EPC, penal establishment de Corumbá; PTL, penal establishment Três Lagoas; EPRB, penal establishment Ricardo Brandão; CTAL, Centro de Triagem Anozio Lima; PTCG, penal establishment de Campo Grande; IPCG, penal establishment Campo Grande; EPJFC, penal establishment Jair Ferreira de Carvalho; PHAC, penal establishment Harry Amorim Costa.

71

72 A team of trained health professionals performed the interviews, which were
73 conducted while the prisoners were sunbathing. The interviewers always maintained a
74 safe distance from the interviewees to guarantee the physical integrity of interviewers of
75 the participants. The study subjects were told that participation was voluntary, and they
76 had a right to refuse without any threat of reprisal.

77 A simple random probability sampling form was used, so that participants were
78 likely to be representative of the overall population, thus ensuring the internal validity of
79 the study. The collected serum samples were sent to the Oswaldo Cruz Foundation, Rio
80 de Janeiro, to be tested for HSV-2.

81 The number of subjects (N) was determined as: $N = z^2 \times p \times (1 - p)/e^2$. Where z
82 is the confidence level based on a standard normal distribution (1.96 for 95%), p is the
83 expected prevalence (0.113 in the general population, because no data were available for
84 the study population), and e is the maximum acceptable error in the estimate (0.05).

85 A total of 872 serum samples were examined (732 males and 140 females) from
86 different age groups. All randomly selected individuals were arrested in a closed
87 regime, over 18 years-old, and provided informed consent. The exclusion criteria were:
88 volunteering to participate without initially being screened, being pregnant, having a
89 mental illness, and being unable to respond to the questionnaire for any reason.

90 **HSV-2 tests**

91 Serum samples were tested for anti-HSV-2 IgM and anti-HSV-2 IgG using an
92 enzyme-linked immunosorbent assay type-specific glycoprotein C2 gG2 (Euroimmun
93 commercial kit, Luebeck, Germany). The test protocol was followed according to the
94 instructions of the manufacturers, using internal positive and negative controls that were
95 part of the assay kit.

96 **Data analysis**

97 The questionnaire data were entered into a database. Inferential statistics using
98 Pearson's χ^2 analyses were calculated, and all variables that were significant at the
99 univariate level ($p < 0.05$) were entered into unadjusted and adjusted logistic regression
100 models to predict the ORs and 95% CIs for associations with the dependent variable (anti-
101 HSV-2 IgG and anti-HSV-2 IgM positivity). Analyses were performed using the RStudio
102 Desktop statistical package.

103 **Results**

104 *Characteristics of the study population*

105 Analysis of the sociodemographic characteristics of the participating prisoners
106 (Table 1) indicated that a majority were male (84%), had fewer than 4 years of education
107 (66.7%), were married (60%), and were not users of injection drugs (84%). Most
108 participants (82%) worked before incarceration, and 65% of women and 94.6% of men
109 said they were not injectable drug users (IDUs). The average incarceration time was 17
110 months, and most participants were previously in jail. Analysis of the sexual histories of
111 the participants indicated that 94.1% were heterosexual, but 11.6% reported having a
112 previous homosexual relationship. In addition, 34.3% reported using condoms only
113 sometimes or never during intercourse.

114 The overall HSV-2 prevalence was 43.1% (95% CI: 34.6 to 40.4), and the
115 prevalence was greater in females than males (68%, 95% CI: 8.4 to 10.7 vs. 37%, 95%
116 CI: 2.54 to 3.07). The HSV-2 females-to-male prevalence ratio was 4.2 (95% CI: 2.5 to
117 7.1, $p < 0.001$; Table 1). Moreover, the prevalence of HSV-2 positivity was greater in
118 females than males of all ages, except for those who were 62 years-old or more (Figure
119 2).

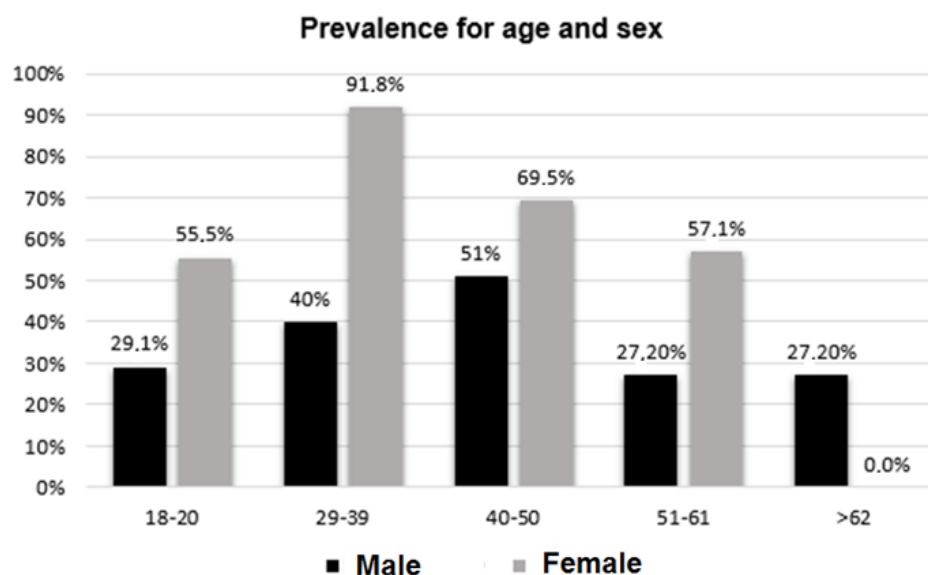
Table 1: Association of HSV-2 positivity with sociodemographic characteristics, risk factors, and prison variables among male and female prisoners at baseline (n = 872).

Variable	N (%)	Missing	OR (95% CI)	P value
HSV-2 positivity	375 (43.1)			
Sex				
Male	732 (83.9)		1	
Female	140 (16.1)		4.2 (2.5-7.1)	<0.001
Sociodemographics				
Age, years, mean±SD	32.04 ±10.09		1.9 (1.1-3.3)	0.02
Schooling, less than 4 years	584 (66.7)		0.4 (0.2-0.8)	0.05
Marital status				
Married	525 (60.2)		1	
Not married	347 (39.7)		1.9 (1.5-2.5)	0.04
Drug history				
Non-IDU	731 (83.8)	3	1	0.04
IDU	7(0.8)	2	0.9 (0.6-1.2)	0.3
Sexual history				
<i>Sexual preference</i>		4		
Heterosexual	845 (97)		1	0.12
Homosexual	23 (2.6)		1.2 (0.7-2.0)	0.10
<i>Previous homosexual intercourse</i>	69 (7.9)		1.3 (0.2-5.7)	0.20
<i>Condom use</i>		1		
Always	296 (33.9)		1	
Sometimes/never	565 (64.7)		1.9 (1.2-2.9)	0.02
Other Risky behaviors				
<i>History of STI(s)</i>				
No	767 (87.9)		1	
Yes	103 (12)	5	4.9 (1.7-13.5)	<0.001
HIV status				
Negative	863 (98.9)		1	
Positive	9 (1)		2.3 (1.4-3.8)	<0.001
<i>Presence of genital discharge*</i>				
No	785 (90)		1	
Yes	87 (9.9)		1.6 (0.9-1.8)	0.09
Prison history				
<i>Previous incarceration</i>				
No	372 (42.6)		1	
Yes	493 (56.5)	7	1.2 (1.1-1.7)	0.03
<i>Time in prison, months, mean±SD</i>	17 ± 24			
<i>Number of individuals in lockup</i>	142 (16.2)			
< 26			1	
26-50			2.3 (1.2-5.2)	<0.001
Penal institution**				0.8
EPFCAJG	26 (2.9)			
EPFTL	18 (2)			

EPFPP	22 (2.5)
EPFIIZ	74 (8.5)
EPC	87 (10)
PTL	72 (8.2)
EPRB	78 (8.9)
CTAL	34 (3.9)
PTCG	159 (18.2)
IPCG	83 (9.5)
EPJFC	87 (10)
PHAC	132 (15)

Here and below: Significant p values are in bold; IDU- injecting drug user, STI: sexually transmitted infection; *Presence of genital discharge in the last month; **See abbreviations in Figure 1.

Figure 2: Prevalence of HSV-2 positivity* among male and female prisoners in different age groups.



*Here and below: Presence of anti-HSV-2 IgG.

120 *Multivariable analysis*

121 The multivariable model (Table 2), adjusted, indicated significant and
 122 independent associations of HSV-2 positivity with female sex, age older than 18 to 29
 123 years, unmarried status, history of an STI, no previous incarceration, being incarcerated
 124 with more than 26 others, presence of genital discharge, previous homosexual intercourse,

125 HIV-positivity, and no use/occasional use of condoms during sexual intercourse ($p < 0.01$
 126 for all comparisons).

Table 2: Multivariate analysis of factors associated with HSV-2 positivity*.

Variable	HSV-2 positivity (n=376)			p-value
	n (%)	Prevalence (%)	aOR (95% CI)	
Sex				
Male	732 (83.9)	280 (32.1)	1	
Female	140 (16.1)	96 (11)	3.4 (2.3- 5.0)	<0.001
Age group (years)				
18-29			1	
29-39	301 (34.5)	141 (16.1)	1.8 (1.2-2.8)	0.001
40-50	123 (14.1)	67 (7.6)	2,7 (1.6-4.6)	<0.001
51-61	39 (4.4)	23 (28)	2.6 (1.1-6.0)	0.02
Marital status				
Married			1	
Not married	347 (39.7)	137 (15.7)	1.8 (1.1-3.1)	0.02
History of STI(s)				
No			1	
Yes	19 (2.1)	11 (1.2)	4.9 (1.7-13.5)	0.002
Previous incarceration				
Yes			1	
No	373 (42.7)	163 (18.6)	1.5 (1.1-2.1)	0.01
Number of individuals in lockup				
<26			1	
26-50	142 (16.2)	54 (6.1)	1.8 (1.2-2.7)	<0.001
Genital discharge**				
No			1	
Yes	87 (9.9)	53 (6)	4.8 (2.5-6.6)	<0.001
Previously homosexual intercourse				
No			1	
Yes	69 (7.9)	25 (2.8)	1.9 (1.1-3.3)	0.01
HIV status				
Negative			1	
Positive	9 (1)	6 (0.6)	5.4 (3.1-9.8)	0.01
Condom use				
Always			1	
Sometimes/never	242 (27.7)	117 (13.4)	1.9 (1.2-2.9)	0.001

*presence of anti-HSV-2 IgG

127 We further analyzed patients with active HSV-2 infections, based on anti-HSV-2
 128 IgM positivity (Table 3). The results of this multivariable analysis which adjusted for the
 129 same factors in Table 2 indicated that non-married status (aOR=2.6, 95% CI = 1.03 to

130 6.5) and the presence of 26 or more prisoners in the same cell (aOR = 2.9, 95% CI = 1.2
131 to 7.2) were significantly associated with active HSV-2 infection.

Table 3: Multivariable analysis of factors associated with the presence of active HSV-2 infection* (n = 85) among those who were positive for anti-HSV-2 IgG (n = 184).

Variable	aOR (95% CI)	p-value
Marital status		
Married	1	
Not married	2.6 (1.03-6.5)	0.01
Number of individuals in lockup		
<26	1	
26-50	2.9 (1.2-7.2)	0.01

*presence of anti-HSV-2 IgM.

132 Discussion

133 The present study is the first epidemiological study of the seroprevalence of
134 HSV-2 in prisoners at penal establishments of Brazil.

135 Our results have several important implications for public health. First, the
136 overall prevalence of HSV-2 infection was 43.1%, almost four-times higher than the
137 global prevalence (11.3%;[16, 18], and also higher than the prevalence in the general
138 population of Brazil (about 30%; [19]. The prevalence of HSV-2 infection in this study
139 was also higher than reported in previous studies of prisoners elsewhere in the world. For
140 example, the seroprevalence was 20.5% at prisons in northern Italy, 21.3% at prisons in
141 southern Italy [20], 19.9% in a cross-sectional regional level study of prisons in Portugal
142 [21], and 14.5% at prisons in Nigeria [22].

143 The higher prevalence of HSV-2 infection in Brazil may be due to the
144 ineffectiveness of its prison organization, in which incarceration can directly and
145 indirectly cause adverse health effects [3].

146 We also found that the estimated prevalence of HSV-2 infection was greater in
147 female (68%) than male (37%) prisoners. Statistical analysis indicated the prevalence was

148 3.4-fold greater in women (95% CI = 2.3 to 5.0). A similar study in Australia [23] also
149 reported that women had a higher seroprevalence rate for HSV-2 than men. This may be
150 because the signs and symptoms in women occur in the vaginal mucosa, and therefore
151 tend to be less visible [24, 25]; [26]. In addition, the sexual transmission of herpes from
152 men to women is much more efficient than the transmission from women to men [12, 27,
153 28]. Furthermore, HSV-2 can be transmitted to the fetus during pregnancy and delivery
154 [24, 25].

155 Our results indicated that the risk for HSV-2 increased with age (age 29 to 39
156 years: aOR = 1.8, 95% CI = 1.2 to 2.8; age 40 to 50 years: aOR = 2.7, 95% CI = 1.6 to
157 4.6; age 51 to 61 years: aOR = 2.6, 95% CI = 1.1 to 6.0). This may be because those who
158 are older simply have more years during which they could possibly be exposed.

159 Our results indicated that prisoners who already had another STI had a nearly 5-
160 fold increased risk of HSV-2 positivity (95% CI = 1.7 to 13.5). A cohort study of prisoners
161 in Nigeria reported the risk of HSV-2 positivity was 30-fold higher for those with another
162 STI (95% CI = 11.3 to 82.3) [22]. A study of prisoners in the United States reported that
163 those with HSV-2 infections had an up to 3-fold increased risk of other transmissible
164 STIs, including HIV [29]; this study also found that HIV seropositivity was associated
165 with a 5-fold increased risk for HSV-2 infection (95% CI = 3.1 to 9.8). A 2017 study by
166 our group found that the prevalence of HSV-2 in HIV-positive pregnant women was 3-
167 fold greater than the prevalence of HIV-negative pregnant women [30].

168 The present study also showed that prisoners who were not previously
169 incarcerated had an increased risk of HSV-2 positivity relative to those who were
170 previously incarcerated (aOR = 1.5, 95% CI = 1.1 to 2.1) and that the presence of 26 or
171 more other prisoners in the same cell increased the risk of HSV-2 positivity (aOR = 1.8,
172 95% CI = 1.2 to 2.7). None of our study participants reported apparent lesions from HSV-

173 2 infections, however the presence of genital discharge in the last month increased the
174 risk for HSV-2 positivity, even though HSV-2 infection is typically characterized by no
175 apparent signs or symptoms. The most common symptoms of infection are vaginal
176 discharge and/or discomfort during sexual relations [31].

177 Although our prisoners reported a low frequency of homosexual intercourse
178 (7.9%), individuals who did have homosexual intercourse had an increased risk of HSV-
179 2 positivity (aOR = 1.9, 95% CI = 1.1 to 3.3). Many previous studies have examined
180 HSV-2 in populations of men who have sex with men. The results indicated a high
181 prevalence in this population, thus demonstrating the importance of implementing
182 prevention programs that target these high-risk groups [32]; [33]; [34]; [35].

183 The presence of anti-HSV-2 IgM was detected in 46% of prisoners who were
184 anti-HSV-2 IgG-positive. However, the presence of this IgM does not necessarily suggest
185 a primary infection, because reactivation of a latent infection may lead to anti-HSV-2
186 IgM positivity [36]. We also found that the presence of more prisoners in the same cell
187 (<26 vs. 26 to 50) is associated with an increased risk of active HSV-2 infection (aOR =
188 2.9, 95% CI = 1.2 to 7.2). This is likely because overcrowding increases contact among
189 prisoners, and is also associated with more intimate contact and worse hygiene.

190 Conflict in the prison environment can adversely impact the health of prisoners,
191 and ultimately impact society at large by contributing to the spread of multiple STIs. This
192 is because there is significant mobility into and out of prisons, with about 30 million
193 people transiting each year worldwide there is also great mobility within individual
194 prisons, due to transfers among different units, and the return of former prisoners who
195 committed subsequent crimes [37]. Thus, the high rate of HSV-2 infection at prisons in
196 Brazil may have a significant economic impact on Brazilian society at large. Appropriate

197 interventions are necessary because the cost of prevention is much lower than the cost of
198 treatment [38, 39].

199 This study had some limitations. First, the reported associations rely upon the
200 veracity and memory of the study participants', especially regarding risky behaviors.

201

202 **Conclusions**

203 This could lead to biases in the relationships of different study variables with
204 HSV-2 infection. Moreover, the rarity of previous studies on this topic and of data on
205 HSV-2 in prison populations worldwide make it difficult to compare our results with
206 those of prisoners in other geographic areas. This emphasizes the urgent need for more
207 studies of STIs in prison populations.

208 The results of our study indicate there is an urgent need to implement effective
209 health education strategies in Brazilian prisons. In particular, there is a need to improve
210 preventive measures, provide appropriate care for individuals with STIs, and reduce the
211 conditions of overcrowding, high stress, and exposure to illicit drugs. Serological
212 screening at the time of confinement may be a simple but effective intervention.

Abbreviations

HSV-2- Herpes virus 2;

STIs- Sexually transmitted infections;

IgG- Immunoglobulin of glycoprotein G;

IgM- Immunoglobulin of glycoprotein M;

HIV- human immunodeficiency virus;

WHO- World Health Organization;

CE- Ethics Committee (initials in Portuguese);

UFGD- Federal University of Grande Dourados (initials in Portuguese);

CAAE- Presentation certificate for Ethical Appreciation (initials in Portuguese);

MS- Mato Grosso of Sul;

Agepen- State Agency of Administration of the Penitentiary System (initials in Portuguese);

ICF- informed consent form;

EPFCAJG, women's penal establishment Carlos Alberto Jonas Giordano;

EPFTL, women's penal establishment Três Lagoas;

EPFPP- women's penal establishment Ponta Porã;

EPFIIZE- women's penal establishment Irmã Irma Zorzi;

EPC- penal establishment de Corumba; PTL, penal establishment Três Lagoas;

EPRB- penal establishment Ricardo Brandão;

CTAL- Centro de Triagem Anozio Lima;

PTCG- penal establishment de Campo Grande;

IPCG- penal establishment Campo Grande;

EPJFC- penal establishment Jair Ferreira de Carvalho;

PHAC- penal establishment Harry Amorim Costa;

pValue- Probability of obtaining the observed results of a test;

ORs- An odds ratio is a statistic that quantifies the strength of the association between two events;

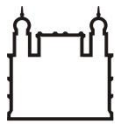
IDU- injecting drug user;

SD- Standard deviation (SD) measures the amount of variability, or dispersion, for a subject set of data from the mean;

aOR- Odds Ratio adjusted by logistic regression;

CI- Confidence interval;

Declarations



Ministério da Saúde

FIOCRUZ

Fundação Oswaldo Cruz

17th January, 2020

Ethics approval and consent to participate

Dear Editor for BMC Infectious Diseases,

Please find enclosed our manuscript entitled “HIGH PREVALENCE OF ALPHAHERPES VIRUS 2 (HSV-2) POSITIVITY IN PRISONS FROM MIDWEST BRAZIL: A CROSS-SECTIONAL STUDY”

This study was approved by the Education and Training Unit of the Federal University of Grande Dourados (CE/UFGD) CAAE number: 05598912.0.0000.5160 opinion 191.877 in 26th January, 2013 and the State Agency of Administration of the Penitentiary System/MS (Agepen/MS). The participants were approached and asked to sign an informed consent form (ICF) which explained the purpose of the study. Emphasis was placed on the confidentiality of each individual’s identity and personal information by explaining that only the team of researchers would have access to the information, and that all data would be used exclusively for research purposes.

These documents are below for consultation.

Sincerely yours,

Vanessa de Paula, Ph.D.



17th January, 2020

Availability of data and materials

Dear Editor for BMC Infectious Diseases,

Please find enclosed our manuscript entitled “HIGH PREVALENCE OF ALPHAHERPES VIRUS 2 (HSV-2) POSITIVITY IN PRISONS FROM MIDWEST BRAZIL: A CROSS-SECTIONAL STUDY” by Nathália Alves Araujo de Almeida, Lyana Rodrigues Pinto Lima, Marco Antonio Moreira Puga, Ana Rita Coimbra Motta de Castro, Marco Aurelio Horta and Vanessa Salete de Paula. This study has a population with disabilities and difficult access and therefore releases research data from research is not applicable, however the data that support the findings of this study are available from [Puga *et al*, 2017] but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of [Julio Croda, Director of the Communicable Disease Surveillance Department at the Ministry of Health's Health Surveillance Secretariat and Ana Rita Coimbra Motta de Castro, public health researcher responsible for collection].

I'm sorry I can't share the data, we sincerely hope our manuscript is acceptable for publication and look forward to your reply.

Sincerely yours,

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Competing interests

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I declare for due purposes that this publication does not contain financial and / or non-financial interests.

I am available for further additional clarification.

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Declaration of Funding

Dear Editor for BMC Infectious Diseases,

Please find enclosed our manuscript entitled “HIGH PREVALENCE OF ALPHAHERPES VIRUS 2 (HSV-2) POSITIVITY IN PRISONS FROM MIDWEST BRAZIL: A CROSS-SECTIONAL STUDY”

I declare that for the development of the research we have public funding from CNPQ (Scientific and Technological Development) and CAPES (Higher Education Personnel Improvement Coordination) Ministry of Health and Ministry of Education in Brazil. These investments range from the payment of the professionals involved to the purchase of inputs for laboratory tests.

I am available for further additional clarification.

Sincerely yours,

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Authors' contributions

Dear Editor for BMC Infectious Diseases,

Please find enclosed our manuscript entitled “HIGH PREVALENCE OF ALPHAHERPES VIRUS 2 (HSV-2) POSITIVITY IN PRISONS FROM MIDWEST BRAZIL: A CROSS-SECTIONAL STUDY” All authors of the manuscript worked for the work to be successfully completed, below is the role of each author.

NAAA- Responsible for the master's thesis defended in 2019, he performed all diagnostic tests and manuscript writing.

LRPL- Responsible for processing samples and assisting in diagnostic tests.

MAMP- Responsible for filling the entire database of participants.

AR- Study coordinator responsible for sample collection and data processing.

MH -Responsible for statistical analysis.

VSP- manager of the laboratory in which the research was conducted, responsible for writing and developing the study and the manuscript.

All authors have read and agree with the submission of the manuscript

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Acknowledgements

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I would like to thank the research PARTICIPANTS who voluntarily accepted contributed to this work.

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To all the DIRECTORS responsible for the criminal institutions that allowed the work to be carried out.

Sincerely

Vanessa de Paula, Ph.D.

References

1. Lynch JP, Lynch JP, Sabol WJ: **Prisoner Reentry in Perspective**. 2001.
2. Puga MA, Bandeira LM, Pompilio MA, Croda J, Rezende GR, Dorisbor LF, Tanaka TS, Cesar GA, Teles SA, Simionatto S *et al*: **Prevalence and Incidence of HCV Infection among Prisoners in Central Brazil**. *PLoS One* 2017, **12**(1):e0169195.
3. Minayo MC, Ribeiro AP: **Health conditions of prisoners in the state of Rio de Janeiro, Brazil**. *Cien Saude Colet* 2016, **21**(7):2031-2040.
4. Crofts N, Cooper G, Stewart T, Kiely P, Coghlan P, Hearne P, Hocking J: **Exposure to hepatitis A virus among blood donors, injecting drug users and prison entrants in Victoria**. *J Viral Hepat* 1997, **4**(5):333-338.
5. Levy M, Johnson CG, Kraa E: **Tonsillopharyngitis caused by foodborne group A streptococcus: a prison-based outbreak**. *Clin Infect Dis* 2003, **36**(2):175-182.
6. **World Prison Brief | an online database comprising information on prisons and the use of imprisonment around the world** [<http://www.prisonstudies.org/>]
7. Roizman B, Whitley RJ: **The nine ages of herpes simplex virus**. *Herpes* 2001, **8**(1):23-27.
8. Grinde B: **Herpesviruses: latency and reactivation – viral strategies and host response**. In: *J Oral Microbiol. Volume 5*, edn.; 2013.
9. Kimberlin DW: **Herpes simplex virus infections of the central nervous system**. *Semin Pediatr Infect Dis* 2003, **14**(2):83-89.
10. Schomogyi M, Wald A, Corey L: **Herpes simplex virus-2 infection. An emerging disease?** *Infect Dis Clin North Am* 1998, **12**(1):47-61.
11. Bettahi I, Zhang X, Afifi RE, BenMohamed L: **Protective immunity to genital herpes simplex virus type 1 and type 2 provided by self-adjuvanting lipopeptides that drive dendritic cell maturation and elicit a polarized Th1 immune response**. *Viral Immunol* 2006, **19**(2):220-236.
12. Xu F, Sternberg MR, Kottiri BJ, McQuillan GM, Lee FK, Nahmias AJ, Berman SM, Markowitz LE: **Trends in herpes simplex virus type 1 and type 2 seroprevalence in the United States**. *Jama* 2006, **296**(8):964-973.
13. Morrison LA: **Replication-defective virus vaccine-induced protection of mice from genital herpes simplex virus 2 requires CD4 T cells**. *Virology* 2008, **376**(1):205-210.
14. Vagvala SP, Thebeau LG, Wilson SR, Morrison LA: **Virus-encoded b7-2 costimulation molecules enhance the protective capacity of a replication-defective herpes simplex virus type 2 vaccine in immunocompetent mice**. *J Virol* 2009, **83**(2):953-960.
15. Chentoufi AA, Benmohamed L: **Mucosal herpes immunity and immunopathology to ocular and genital herpes simplex virus infections**. *Clin Dev Immunol* 2012, **2012**:149135.
16. Looker KJ, Margaret AS, May MT, Turner KM, Vickerman P, Gottlieb SL, Newman LM: **Global and Regional Estimates of Prevalent and Incident Herpes Simplex Virus Type 1 Infections in 2012**. *PLoS One* 2015, **10**(10):e0140765.
17. Penello AM, Campos, B.C., Simão, M.: **Herpes genital**. *J Bras Doenas Sex Transm* 2010, **22**(2):64-72.
18. Olsson J, Kok E, Adolfsson R, Lovheim H, Elgh F: **Herpes virus seroepidemiology in the adult Swedish population**. *Immun Ageing* 2017, **14**:10.
19. Clemens SA, Farhat CK: **Seroprevalence of herpes simplex 1-2 antibodies in Brazil**. *Rev Saude Publica* 2010, **44**(4):726-734.
20. Sarmati L, Babudieri S, Longo B, Starnini G, Carbonara S, Monarca R, Buonomini AR, Dori L, Rezza G, Andreoni M: **Human herpesvirus 8 and human herpesvirus 2 infections in prison population**. *J Med Virol* 2007, **79**(2):167-173.
21. Marques NM, Margalho R, Melo MJ, Cunha JG, Melico-Silvestre AA: **Seroepidemiological survey of transmissible infectious diseases in a portuguese prison establishment**. *Braz J Infect Dis* 2011, **15**(3):272-275.
22. Ibrahim A: **Seroepidemiology of Herpes Simplex Virus Type-2 (HSV-2) Among Incarcerated Population of Potiskum Medium Security Prison Potiskum Yobe State: Study of Prevalence and Associated Risk Factors**. *IntJCurrMicrobiolAppSci* 2015, **4**:632-637.
23. Simpson PL, Reekie J, Butler TG, Richters J, Yap L, Grant L, Richards A, Donovan B: **Factors Associated With Sexual Coercion in a Representative Sample of Men in Australian Prisons**. *Arch Sex Behav* 2016, **45**(5):1195-1205.
24. Brown ZA, Benedetti J, Ashley R, Burchett S, Selke S, Berry S, Vontver LA, Corey L: **Neonatal Herpes Simplex Virus Infection in Relation to Asymptomatic Maternal Infection at the Time of Labor**. <http://dxdoiorg/101056/NEJM199105023241804> 2010.

25. Hollier LM, Wendel GD: **Third trimester antiviral prophylaxis for preventing maternal genital herpes simplex virus (HSV) recurrences and neonatal infection.** 2017.
26. Kaul R, Nagelkerke NJ, Kimani J, Ngugi E, Bwayo JJ, Macdonald KS, Rebbaprgada A, Fonck K, Temmerman M, Ronald AR *et al*: **Prevalent herpes simplex virus type 2 infection is associated with altered vaginal flora and an increased susceptibility to multiple sexually transmitted infections.** *J Infect Dis* 2007, **196**(11):1692-1697.
27. Langenberg AG, Corey L, Ashley RL, Leong WP, Straus SE: **A prospective study of new infections with herpes simplex virus type 1 and type 2.** Chiron HSV Vaccine Study Group. *N Engl J Med* 1999, **341**(19):1432-1438.
28. Clemens SAC, Instituto de Pós-Graduação Médica Carlos Chagas RdJ, Brasil, Universidade Federal de São Paulo SP, Brasil, Farhat CK, Universidade Federal de São Paulo SP, Brasil: **Seroprevalence of herpes simplex 1-2 antibodies in Brazil.** *Rev Saúde Pública* 2010, **44**(4):726-734.
29. Altice FL, Marinovich A, Khoshnood K, Blankenship KM, Springer SA, Selwyn PA: **Correlates of HIV infection among incarcerated women: implications for improving detection of HIV infection.** *J Urban Health* 2005, **82**(2):312-326.
30. Lima LRP, Fernandes L, Villela DAM, Morgado MG, Pilotto JH, de Paula VS: **Co-infection of human herpesvirus type 2 (HHV-2) and human immunodeficiency virus (HIV) among pregnant women in Rio de Janeiro, Brazil.** *AIDS Care* 2018, **30**(3):378-382.
31. Groves MJ: **Genital Herpes: A Review.** *Am Fam Physician* 2016, **93**(11):928-934.
32. Rodrigues J, Grinsztejn B, Bastos FI, Velasque L, Luz PM, de Souza CT, Georg I, Pilotto JH, Veloso VG: **Seroprevalence and factors associated with herpes simplex virus type 2 among HIV-negative high-risk men who have sex with men from Rio de Janeiro, Brazil: a cross-sectional study.** *BMC Infect Dis* 2009, **9**:39.
33. Silva AdSd, Lima LRP, Perse AdS, Castro LS, Rezende GRd, Pires FR, Puga MAM, Bandeira LM, Tanaka TSO, Motta-Castro ARC *et al*: **Epidemiological evaluation of herpes simplex virus in men who have sex with men in Mato Grosso do Sul, Brazil.** 2015.
34. Thienkrua W, Todd CS, Chonwattana W, Wimonsate W, Chaikummao S, Varangrat A, Chitwarakorn A, van Griensven F, Holtz TH: **Incidence of and temporal relationships between HIV, herpes simplex II virus, and syphilis among men who have sex with men in Bangkok, Thailand: an observational cohort.** In: *BMC Infect Dis. Volume 16*, edn.; 2016.
35. Vergara-Ortega DN, Sevilla-Reyes EE, Herrera-Ortiz A, Torres-Ibarra L, Salmeron J, Lazcano-Ponce E, Sanchez-Aleman MA: **Real time PCR to evaluate HSV-2 shedding from anal and genital samples among men who have sex with men, living with HIV.** *J Med Virol* 2018, **90**(4):745-752.
36. Tada DG, Khandelwal N: **Serum HSV-1 and 2 IgM in Sexually Transmitted Diseases - More for Screening Less for Diagnosis: An Evaluation of Clinical Manifestation.** *J Glob Infect Dis* 2012, **4**(3):S1-4.
37. Zachariah R, Massaquoi M: **Cotrimoxazole prophylaxis for HIV-positive TB patients in developing countries.** - PubMed - NCBI. *Trop Doct* 2006, **36**(2):79-82.
38. Sousa KAAd, Universidade Federal do Piauí T, Brasil, Universidade Federal do Piauí T, Brasil, Araújo TMed, Universidade Federal do Piauí T, Brasil, Universidade Federal do Piauí T, Brasil, Teles SA, Universidade Federal de Goiás G, Brasil, Universidade Federal de Goiás G, Brasil, Rangel EML *et al*: **Factors associated with HIV prevalence in a prison population.** *Rev enferm USP* 2017, **51**.
39. Arruda AJCG de VDd, Silva CC da *et al*: **HEALTH WHILE A RIGHT OF PRISONERS AND THE PRISON SYSTEM SUB JUDICE ORIGINAL ARTICLE.** 2017.