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Prostate-specific antigen test in Brazilian indigenous: a cross-sectional study

Rastreamento do antígeno prostático específico em indígenas brasileiros: um estudo transversal

Detección de antígeno prostático específico en indígenas brasileños: un estudio transversal

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Abstract
We estimated the prevalence of screening for prostate cancer in indigenous people in Brazil. We also studied how ethnicity, age, social conditions, lifestyle, and history of sexually transmitted infections are associated with altered prostate-specific antigen (PSA) values. This is a cross-sectional study with indigenous people, ≥ 40 years old, from Dourados reserve, Mato Grosso do Sul, Brazil. The patients underwent total PSA and rapid tests for syphilis, HIV, and hepatitis B and C. PSA values were compared with sociodemographic conditions, presence of urological symptoms, clinical data on sexually transmitted infections, lifestyle, and family history of cancer. Out of the 498 men invited to participate in the study, 31.53% (157/498) were ≥ 40 years old and were included. The mean (±SD) age was 54.75 (±11.23) years, and 78.3% (123/157; 95% CI: 0.71–0.84) of the population never underwent any preventive examination for prostate cancer. The mean PSA value was 0.081 ng/mL for the 157 participants, and 4.4% (7/157) had > 2.5 ng/mL and 1.9% (3/157) had values ≥ 4 ng/mL. Rapid tests for STIs showed that 5.73% (9/157) of the participants had syphilis and 0.64% (1/157) had HIV, and Hepatitis B and C virus infection. The results showed that most indigenous people ≥ 40 years never underwent any preventive examination for prostate cancer, and 4.4% had an altered PSA exam result. Future studies should assess the factors that hinder adherence to prostate cancer screening, as well as the existence of a pathophysiological correlation between the occurrence of prostate cancer and STIs.
Keywords: Prostatic neoplasm; Prostate-specific antigen; Sexually transmitted diseases; Early detection of cancer.

Resumo
Estimar a prevalência do rastreamento do câncer de próstata nos povos indígenas brasileiros. Avaliar como etnia, idade, condições sociais, estilo de vida e história de infecções sexualmente transmissíveis estão associados aos valores alterados do antígeno prostático específico (PSA). Este é um estudo transversal com povos indígenas, ≥ 40 anos, da reserva de Dourados, Mato Grosso do Sul, Brasil. Os pacientes foram submetidos ao exame de PSA total e testes rápidos para sífilis, vírus da imunodeficiência humana (HIV) e hepatite B e C. Os valores do PSA foram comparados com as condições sociodemográficas e outros fatores de risco. Dos 498 homens, 31,53% (157/498) tinham ≥ 40 anos. A idade média foi de 54,75 (DP ±11,23) anos e 78,3% (123/157; IC 95%: 0,71-0,84) da população nunca havia sido submetida ao rastreamento para o câncer de próstata. O valor médio do PSA foi de 0,081 ng/mL para os 157 participantes, e 4,4% (7/157) tinham > 2,5 ng/mL e 1,9% (3/157) tinham valores ≥ 4 ng/mL. Os testes rápidos para

infecções sexualmente transmissíveis (ISTs) mostraram que 5,73% (9/157) dos participantes tinham sífilis e 0,64% (1/157) tinha HIV. Ademais, 0,64% (1/157) tinha infecção pelos vírus da Hepatite B e C. Os resultados mostraram que a maioria dos povos indígenas ≥ 40 anos nunca foi submetida a exame preventivo para o câncer de próstata e 4,4% tiveram um resultado alterado no exame de PSA. Estudos futuros devem avaliar os fatores que dificultam a adesão ao rastreamento para o câncer de próstata, bem como a existência de correlação fisiopatológica entre a ocorrência de câncer de próstata e ISTs.
Palavras-chave: Câncer de próstata; Antígeno prostático específico; Infecções sexualmente transmissíveis; Detecção precoce de câncer.

Resumen

Estimamos la prevalencia de detección de cáncer de próstata en pueblos indígenas en Brasil. También estudiamos cómo el origen étnico, la edad, las condiciones sociales, el estilo de vida y la historia de las infecciones de transmisión sexual se asocian con valores alterados de antígeno de prostato específicos de próstata (PSA). Este es un estudio transversal con personas indígenas, ≥ 40 años, de la reserva de Dourados, Mato Grosso do Sul, Brasil. Los pacientes se sometieron a lo PSA total y pruebas rápidas para la sífilis, el VIH y los valores de hepatitis B y C. Lo PSA se compararon con las condiciones sociodemográficas, la presencia de síntomas urológicos, datos clínicos sobre infecciones de transmisión sexual, estilo de vida y antecedentes familiares de cáncer. De los 498 hombres invitados a participar en el estudio, el 31.53% (157/498) tenían ≥ 40 años. La edad media (± DE) fue de 54.75 (± 11.23) años, y el 78.3% (123/157; IC del 95%: 0.71–0.84) de la población nunca había se sometió a ningún examen preventivo para el cáncer de próstata. El valor medio de PSA fue de 0.081 ng/ml para los 157 participantes, y el 4.4% (7/157) tenía> 2.5 ng/ml y 1.9% (3/157) tenían valores ≥ 4 ng/ml. Las pruebas rápidas para las ITS mostraron que 5.73% 9/157) de los participantes tenían sífilis y 0.64% (1/157) tenían VIH e infección por el virus de la hepatitis B y C. Los resultados mostraron que la mayoría de las personas indígenas ≥ 40 años nunca se sometieron a ningún examen preventivo para el cáncer de próstata, y el 4.4% tuvo un resultado alterado del examen de PSA. Los estudios futuros deben evaluar los factores que dificultan el cribado del cáncer de próstata, así como la existencia de una correlación fisiopatológica entre la aparición del cáncer de próstata y las ITS.
Palabras clave: Neoplasia prostática; Antígeno Prostático Específico; Enfermedades de transmisión sexual; Detección precoz del cáncer.

1. Introduction

Prostate cancer (PCa) is the most common nonmelanoma cancer in men worldwide. It is the second most cause of mortality behind only lung cancer, with 15,576 deaths in Brazil in 2018, corresponding to 13.3% of cancer deaths (INCA, 2019). Data on the early detection of PCa are limited in Brazil. Low access to specialized health services and lack of recommendation from the Ministry of Health on systematic screening for prostate-specific antigen (PSA) contribute to underreporting and data scarcity.

PSA screening significantly increases early diagnosis and therefore leads to a decreased mortality by PCa (Pinsky et al., 2017). Although there are differences in the performance of PSA screening, many studies have estimated the prevalence of PCa and evaluated the factors associated with high PSA values, contributing to actions for preventing and controlling PCa. The main factors associated with performing PSA screening are age, visits to the general practitioner, treatment for benign prostatic hyperplasia, marital status, and socioeconomic level. (Spencer et al., 20172006; Nair-Shalliker et al., 20172018). Age, race, family history, obesity, and lifestyle habits such as smoking, alcohol consumption, and a high-fat diet are the strong risk factors associated with PCa (Pernar et al., 20172018). In addition, socioeconomic factors, sexual activity, and sexually transmitted infections (STIs) can influence the likelihood of developing PCa. Gonorrhea, human papillomavirus (HPV), and syphilis are the main STIs related to PCa (Lian et al., 20172015; Sutcliffe et al. 2006).

PSA values and PCa incidence rates vary significantly according to race and ethnicity. Genetic and environmental influence on the incidence of PCa among Caucasians, Alaska natives, and Native Americans have robust evidence (White et al., 20172014). However, in Brazil, there are few studies on the specific risk factors for PCa in indigenous people. In addition, there are no specific PSA values for which biopsy would be indicated for this population. Thus, we assessed the factors related to access to the examination of PSA in the male population of the largest peri-urban indigenous reserve in Brazil, located in

Dourados, Mato Grosso do Sul. We also evaluated if ethnicity, age, social conditions, lifestyle, and history of STIs are associated with altered PSA values.

2. Methodology

Population characterization

Mato Grosso do Sul is a state in the Midwest region that has the second largest indigenous population in Brazil, with 73,181 indigenous people. Guarani-kaiowá, Terena, and Guarani-Nhandeva are the main ethnic groups, and they represent 96% of the state's population. Dourados has the largest Brazilian peri-urban reserve, with a health base pole that serves approximately 15,186 indigenous people (SIASI, 2013). Out of those, 13,094 live in Bororó and Jaguapirú villages, of which 1,309 are men between 29 and 49 years, and 422 are > 50 years (IBGE, 2010).

Study design and sample size

This cross-sectional study analyzed, from September 2017 to January 2020, indigenous men aged over 40 years, who lived in Bororó and Jaguapirú villages. The estimated sample size was calculated based on the population of 1,730 men over 29 years of age described in the last census (IBGE, 2010). The methodological procedures of this cross-sectional study are available in other studies (Medronho et al., 20172008; Santiago et al., 20172013). The prevalence of PCa used was 4% (Faria et al. 2010), with a 95% confidence interval and a 3% margin of error, resulting in a sample of 150 men, and 20% more individuals were added to account for the loss due to refusal to participate.

Data and blood collection

Each participant underwent an interview, in which a standardized questionnaire was used. The interviews were conducted in Portuguese, and when necessary, the participation of indigenous language interpreters was used. The following variables were obtained during the interview: age, marital status, educational background, drug use, sexual and STI history, blood transfusion performed for PSA screening at some point in life, ethnicity, village, income, presence of urological symptoms (dysuria, weak jet, nocturia, hematuria), smoking, alcohol consumption, high-fat diet, and family history of cancer. After appropriate antisepsis, a 10 mL sample of the peripheral venous blood was obtained using a vacuum tube system, and it was then processed to obtain the serum and stored at −20 °C for serological assays.

PSA screening

PSA values were determined by using the chemiluminescent immunoassay technique with paramagnetic particles (Beckman Coulter UniCel DxI 800 Access Immunoassay System). The study participants were classified into those with values greater than 2.5 ng/mL or less than 2.5 ng/mL; participants with values > 2.5 ng/mL were referred to a urologist for further tests. The PSA values were adjusted according to age, with the following values being considered: > 2.5 ng/mL (age between 40 and 49 years); > 3.5 ng/mL (age between 50 and 59 years); > 4.5 ng/mL (age between 60 and 69 years); and > 6.5 ng/mL (age over 70 years). All participants with altered results in PSA screening were referred to a urologist and complementary exams.

Rapid tests for STIs

To determine the serological profile for STIs, rapid tests were used. For HIV 1 and 2, a Rapid Check HIV 1–2™ (Federal University of Espírito Santo, Vitória, Brazil) and Biomanguinhos HIV ½™ (Bio-Manguinhos, Oswaldo Cruz

Foundation, Rio de Janeiro, Brazil) were used. Alere Determine ^{Syphilis} TP rapid test was used for syphilis diagnosis, Alere Vikia™ HBsAg for hepatitis B, and Alere Vikia™ HCV for hepatitis C. All participants received the results of their serological tests individually, and an infectious diseases physician specializing in infectious diseases prescribed appropriate treatment to those with positive tests. All new cases of STIs identified in the study were reported to the Notifiable Disease database (Sistema de Informação de Agravos de Notificação, SINAN).

Statistical analysis

Questionnaire-based data and biological testing results were recorded, double-checked for quality control, and entered into Research Electronic Data Capture (REDCap), which is an online database. Data were analyzed using SPSS version 22.0 (IBM, Armonk, New York, United States). Descriptive statistics were performed, and the results were presented in proportions (%) for categorical variables. Non-normally distributed numerical variables were compared using the Mann-Whitney test (2 groups) or Kruskal-Wallis (≥ 3 groups). The Spearman correlation test was used to compare the age and PSA values. Values with $p < 0.05$ were considered statistically significant.

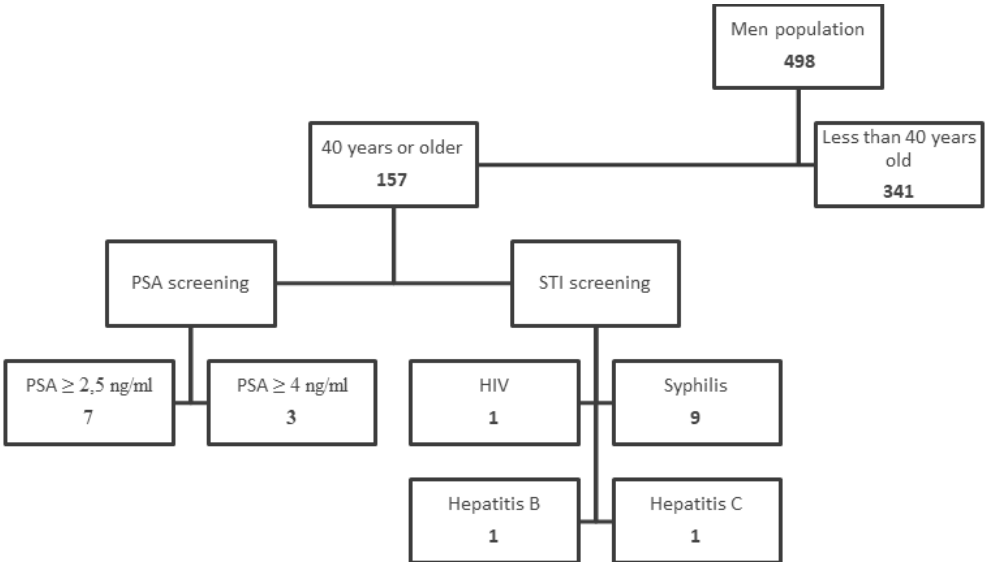
Ethical approval

This study complied with the requirements from the Research Ethics Committee of the Universidade Federal de Grande Dourados (UFGD) and from the National Research Ethics Council (number 2.000.496, April 5, 2017). All eligible individuals provided written informed consent before participating in the study. The serological test results were reported directly to the patients by an infectious disease physician and were referred for specialized treatment.

3. Results

Out of the 498 males invited to participate in the study, 157 (31.53%) were > 40 years old and agreed to participate (Figure 1). The mean (± standard deviation, SD) age was 54.75 (±11.23) years, ranging from 40 to 91 years, and the median age was 52 years.

Figure 1 - Flow chart for study design, screening process, and number of cases detected for prostate-specific antigen (PSA) and sexually transmitted infection (STI) in indigenous people from Dourados (MS), Brazil.



*HIV = human immunodeficiency virus. Source: Authors.

Among the participants, most were between 40 and 49 years old (40.7%; 64/157), belonging to the Guarani-Kaiowá ethnic group (67.5%; 106/157), residents of the Bororó Village (54.1%; 85/157), with a married partner (78.3%; 123/157), who had < 4 years of schooling (63%, 99/157) and family income between 1 and 2 minimum wages (45.2%, 71/157). In addition, 78.3% (123/157; 95% confidence interval, CI: 0.71–0.84) of the population surveyed had never undergone any preventive examination for PCa (Table 1).

Table 1 - Prevalence of failure to perform preventive exams for prostate cancer, according to socioeconomic and demographic in indigenous Brazilian population (n = 157).

Variables	Not Screened (%not screend/total)[1]	Not Screened Prevalence[2] (CI 95%)	Prevalence ratio (CI 95%)
Age Groups (years)			
40-49	58 (90.06%)	0.37 (0.29-0.45)	1
50-59	34 (73.91%)	0.22 (0.15-0.29)	0.59 (0.42-0.75)
60-69	21 (67.75%)	0.13 (0.08-0.20)	0.35 (0.20-0.52)
>70	10 (62.50%)	0.06 (0.03-0.11)	0.16 (0.06-0.32)
Ethnicity			
Guarani-kaiwá	87 (82.08%)	0.55 (0.47-0.63)	1
Terena	22 (68.75%)	0.14 (0.09-0.20)	0.25 (0.14-0.39)
Other ethnical groups	16 (76.20%)	0.10 (0.06-0.16)	0.18 (0.09-0.31)
Village			
Bororó	71 (83.53%)	0.45 (0.37-0.53)	1
Jaguapirú	52 (72.23%)	0.33 (0.26-0.41)	0.73 (0,58-0.85)
Water distribution			
Yes	112 (77.25%)	0.71 (0.64-0.78)	1
No	11 (91.67%)	0.07 (0.04-0.12)	0.09 (0.04-0.19)
Type of housing			
Brick	92 (76.67%)	0.59 (0.50-0.66)	1
Wood/ Daub /Shack /Tarp	31 (83.79%)	0.20 (0.14-0.27)	0.34 (0.22-0.47)
Marital status			
Single/separated	95 (77.24%)	0.61 (0.52-0.68)	1
Married	28 (82.36%)	0.18 (0.12-0.25)	0.30 (0.19-0.42)
Education (years)			
0-4	81 (81.82%)	0.52 (0.43-0.60)	1
Over 4	42 (72.41%)	0.27 (0.20-0.34)	0.52 (0.38-0.66)
Means of communication			
Yes	119 (78.29%)	0.76 (0.68-0.82)	1
No	4 (80%)	0.03 (0.01-0.06)	0.04 (0.01-0.11)
Religion			
Yes	98 (77.17%)	0.62 (0.54-0.70)	1
No	25 (84.40%)	0.16 (0.11-0.23)	0.26 (0.16- 0.39)
Income/ Family Unit (min. wages)			
Up to 2	111 (79.80%)	0.71 (0.63-0.78)	1
Over 3	12 (66.67%)	0.08 (0.04-0.13)	0.11 (0.4-0.21)
Government Benefit			
No	91 (83.50%)	0.58 (0.50-0.66)	1

Yes	34 (68%)	0.22 (0.15-0.29)	0.38 (0.26-0.52)
Employment status			
Employed	66 (77.65%)	0.42 (0.34-0.50)	1
Unemployed	57 (79.17%)	0.36 (0.29-0.44)	0.86 (0.71-0.95)
STI			
Syphilis	6 (66.67%)	0.04 (0.01-0.08)	1
HIV	1 (100%)	0.01 (0.00-0.04)	0.25 (0.00-0.81)
Hepatitis B	1 (100%)	0.01 (0.00-0.04)	0.25 (0.00-0.81)
Hepatitis C	1 (100%)	0.01 (0.00-0.04)	0.25 (0.00-0.81)

[1]patients not screened / total number of individuals. in the subgroup.
[2]Patients not screened/ total number of individuals of patients in the study.
CI = confidence interval; STI = sexually transmitted infection; HIV = human immunodeficiency virus. Source: Authors.

The mean PSA value was 0.081 ng/mL, and 4.4% (7/157) of the participants showed values > 2.5 ng/mL and 1.9% (3/157) had values ≥ 4 ng/mL. The PSA values were high in only 1.9% (3/157) of the participants with ages between 60 and 69 years; no other age group had the PSA value corrected by age. The Spearman correlation test showed a positive and moderate correlation between age and PSA ($\rho = 0.375$; $P > 0.001$*). Patients with altered PSA values did not agree to undergo the follow-up proposed with a digital rectal examination and biopsy.

Frequencies of each risk factors present in individuals with normal PSA values < 2.5 ng/mL and altered values > 2.5 ng/mL are shown in Table 2.

Table 2 - Distribution of indigenous people according to risk factors for prostate cancer for normal and altered prostate-specific antigen (PSA) values.

Variables	N (%)	PSA < 2,5 ng/ml	PSA > 2,5 ng/ml
Age Groups (years)			
40-49	64	64	0
40-59	46	44	2
60-69	31	27	4
>70	16	15	1
Ethnicity			
Guarani-kaiwá	106	100	6
Terena	32	31	1
Other ethnical groups	21	21	0
Prostate test			
Any test	34	34	0
Digital rectal examination	11	11	0
PSA	22	22	0
Biopsy	0	0	0
Ultrasound	3	3	0
Lower Urinary Tract Symptoms			
Any Symptoms	28	24	4
Dysuria	19	16	3
Dysfunctional bladder	4	4	0
Nocturia	3	2	1
Hematuria	2	2	0

Other risk factors			
Familiar history of cancer	19	18	1
High-fat diet	46	43	3
Alcohol use over the last year	68	65	3
Smoking	28	26	2
Former smokers	106	100	6
STI			
Positive test for STI	30	30	0
HIV	1	1	0
Syphilis	9	9	0
Hepatitis B	1	1	0
Hepatitis C	1	1	0
STI symptoms			
Chancre	5	4	1
Urethral discharge	4	4	0
Genital warts	6	6	0
Behavioral characteristics			
Marital status			
Single/separated	34	31	3
Married	123	119	4
Illicit drug use			
Yes	4	4	0
No	153	146	7
Shared sharp objects			
Yes	13	13	0
No	144	137	7
Sexual partners in the last year			
< one	141	135	6
> two	16	15	1
Condom use			
Always	10	9	1
Sometimes or never	147	141	6
History of STIs			
Yes	11	11	0
No	146	139	7

STI = sexually transmitted infection; HIV = human immunodeficiency virus. Source: Authors.

The Kruskal-Wallis test showed no effect of ethnic groups on the PSA value [X^2 (2) = 0.406; P > 0.05). The PSA value distribution was not the same for Jaguapirú and Bororó villagers (U = 2488; P < 0.05; P = 0.044*). There was no difference between PSA values and STI history (U = 854; p > 0.05) or syphilis (U = 749; P > 0.05). The Mann-Whitney U test revealed that the distribution of PSA values was the same among the patients with presence or absence of lower urinary tract symptoms (U = 451; P > 0.05); family history of cancer (U = 1208; P > 0.05), lipid-rich diet (U = 2801; P > 0.05), previous year's alcohol consumption (U = 2835; P > 0.05), and smoking (U = 1868; P > 0.05). Rapid tests showed a prevalence of 7.64% (9/157) for syphilis and 0.64% (1/157) for HIV and Hepatitis B and C virus infection.

4. Discussion

In this study, the mean PSA value was 0.081 ng/mL, and 4.4% (7/157) of the indigenous people had PSA values > 2.5 ng/mL and 1.9% (3/157) had values ≥ 4 ng/mL. Similar results were described among the indigenous people of the Macuxi and Yanomani ethnic groups from Amazon, Brazil, with a median PSA value of 0.52 ng/mL and values > 2.5 ng/mL in 8.7% and ≥ 4 ng/mL in 5.8% of the participants (Lima Junior, 2015). Nevertheless, a study performed with no-indigenous Brazilians, with a median age of 60 years, obtained an average PSA level of 2.0 ng/mL (Mori et al., 2020). Our study showed that the indigenous population from Midwest of Brazil has a low prevalence of altered PSA tests when compared with the no-indigenous Brazilian populations (Lima Junior, 2015; Arruda et al., 2003). There is no consensus as to whether these differences in PSA observed in our study, levels stem from the genotypic diversity of populations or environmental factors, especially dietary habits, lifestyle, and access to healthcare services. In addition, we did not find statistically significant differences in PSA values among the Guarani-Kaiowá, Terena, and other ethnic groups evaluated.

In our study, only 21.7% (34/157) of indigenous people reported having undergone PSA screening before. In addition, low family income and low education level were associated with poor screening tests for PCa, similar to that reported in the United States (Spencer et al., 2006) and Australia (Nair-Shalliker et al., 2018). Population-based studies from Brazil and EUA showed a high rate of PSA screening, ranging from 24.5% to 70.9% (Mori et al., 2020; Amorim, 2011). Higher education presupposes greater knowledge of diseases, such as PCa, which could lead to a greater probability of carrying out screening, as well as maintaining other practices related to self-care (Nair-Shalliker et al., 2018). The Brazilian Ministry of Health and INCA do not recommend PSA screening in the public network, (Araújo et al., 2020) and the number of PSA screening is higher in private clinics than in public clinics (Nardi et al., 2012). This could be a factor that reflects the low screening of PSA in the studied population

We observed that PSA screening was more frequently done in the age group of ≥ 70 years. This may be due to the development of comorbidities that come with aging; thus, placing higher demand from the healthcare services regarding preventive testing (Nair-Shalliker et al., 2018; Lima et al. 2018; Santiago et al., 2013). In addition, PSA levels increase with age, similar to that reported in the general population (Pernar et al., 2018; Lima Junior et al., 2018) and the Macuxi ethnic population of the Amazon Forest region in Brazil (Lima Junior et al., 2018). The prejudice of the indigenous people with screening can justify the fact that none of the patients with altered PSA values agreed to undergo the follow-up proposed by this study, with a digital rectal examination and biopsy. This study, as well as others, showed a higher prevalence of screening tests for PCa in married men or men with a partner (Amorim, 2011; Santiago et al., 2013). This may have been attributed to the incentive that men would receive from their partners since self-care and disease prevention practices are more practiced among women (Lima et al. 2018).

A high prevalence of syphilis in the indigenous male population was identified. However, no association was observed between STI and altered PSA values when analyzed separately or together. The presence of syphilis chancre, urethral discharge, genital warts, or self-reported STI histories was also not associated with variation in PSA values in previous studies.

Our study has some limitations. Firstly, information about the performance of preventive tests for PCa was obtained through self-reporting; therefore, it is subject to memory and information bias. Secondly, the cross-sectional design of the research, in turn, limits the possibility of interpreting the associations found as derived from cause-effect relationships. Nevertheless, this is the first study that evaluated the prevalence of PSA in indigenous people from the largest peri-urban reserve in Brazil.

5. Conclusion

This study showed that the indigenous population has a low prevalence of altered PSA values. Furthermore, the poor adherence to prostate exams may be related to the low access to healthcare services and highlights that public screening policies may be effective in preventing PCa in socially vulnerable populations. In addition, was identified a high prevalence of syphilis in this population and future studies should assess whether there is any pathophysiological correlation between the incidence of prostate cancer and the occurrence of previous sexually transmitted infections.

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