UNIVERSIDADE ESTADUAL DO OESTE DO PARANÁ – *CAMPUS* DE FRANCISCO BELTRÃO, CENTRO DE CIÊNCIAS DA SAÚDE, PROGRAMA DE PÓS-GRADUAÇÃO *STRICTO SENSU* EM CIÊNCIAS APLICADAS À SAÚDE – NÍVEL MESTRADO

TANIA MARIA PAZIN MARQUES SILVA

ESTUDO CASO-CONTROLE PARA IDENTIFICAR FATORES DE RISCO ASSOCIADOS À SOROLOGIA ANTI-HCV REAGENTE EM HOMENS PRESOS EM PENITENCIÁRIAS DO ESTADO DO PARANÁ, BRASIL

FRANCISCO BELTRÃO – PR
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DISSERTAÇÃO apresentada ao Programa de Pós-graduação *Stricto Sensu* em Ciências Aplicadas à Saúde, nível Mestrado, do Centro de Ciências da Saúde, da Universidade Estadual do Oeste do Paraná, como requisito parcial para obtenção do título de Mestre em Ciências Aplicadas à Saúde.

Área de concentração: Fisiopatologia das doenças transmissíveis e não transmissíveis.

Orientadora: Dra. Lirane Elize Defante Ferreto de Almeida

FRANCISCO BELTRÃO – PR
MARÇO/2019

Ficha de identificação da obra elaborada através do Formulário de Geração Automática do Sistema de Bibliotecas da Unioeste.

Silva, Tania Maria Pazin Marques
Estudo caso-controle para identificar fatores de risco associados à sorologia anti-HCV reagente em homens presos em penitenciárias do estado do PARANÁ, BRASIL / Tania Maria Pazin Marques Silva; orientador(a), Lirane Elize Defante Ferreto de Almeida, 2019.
71 f.

Dissertação (mestrado), Universidade Estadual do Oeste do Paraná, Campus de Francisco Beltrão, Centro de Ciências da Saúde, Programa de Pós-Graduação em Ciências Aplicadas à Saúde, 2019.

1. Doenças infectocontagiosas. 2. Presos. 3. Epidemiologia. 4. HCV. I. Almeida, Lirane Elize Defante Ferreto de. II. Título.

FOLHA DE APROVAÇÃO

TANIA MARIA PAZIN MARQUES SILVA

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Essa dissertação foi julgada adequada para obtenção do título de Mestre em Ciências Aplicadas à Saúde e aprovada em sua forma final pela Orientadora e pela Banca Examinadora.

BANCA EXAMINADORA

Orientadora: Profª. Dra. Lirane Elize Defante Ferreto de Almeida
UNIOESTE

Membro da banca: Prof. Dr.Danilo Rodrigues Pereira da Silva
UFS

Membro da banca: Profª. Dra. Leia Carolina Lúcio
UNIOESTE

FRANCISCO BELTRÃO, PR
Março/2019

AGRADECIMENTOS

Agradeço a minha orientadora, Lirane, pela disponibilidade, paciência e dedicação na realização deste trabalho.

Aos pesquisadores e a toda a equipe responsável pela coleta e pelo levantamento transversal dos dados que deram origem a este estudo, realizados entre maio de 2015 e dezembro de 2016, nas penitenciárias paranaenses.

Aos professores Carolina Panis e Geraldo Emílio Vicentini pelo apoio e colaboração na elaboração das figuras apresentadas neste trabalho e pelas diversas dicas e orientações.

Ao meu esposo Fabio e aos meus filhos, Nestor e Valentine, pela compreensão, apoio e incentivo. Sem vocês, eu não teria chegado até aqui.

DEDICATÓRIA

Dedico este trabalho a minha mãe, minha maior fã, torcedora fiel das minhas conquistas, responsável pela realização dos meus sonhos e que, infelizmente, não conseguiu vivenciar comigo mais esta vitória.

LISTA DE ILUSTRAÇÕES

LISTA DE ABREVIATURAS E SIGLAS

HCV – Vírus da Hepatice C

INFOPEN – Levantamento Nacional de Informações Penitenciárias

IST – Infecção Sexualmente Transmissível

GAG – Glicosaminoglicanas

LDLR – Receptor de Lipoproteína de Baixa Densidade (do inglês Low-Density Lipoprotein Receptor)

CLDN1 – Claudina-1

OCLN – Ocludina

EGFR – Receptor de Fator de Crescimento Epidérmico (do inglês Epidermal Growth Factor Receptor)

EphA2 – Receptor de Efrina A2 (do inglês Ephrintype-A receptor 2)

IRES – Internal Ribosome Entry Site

VLDL – Lipoproteína de Densidade Muito Baixa

TR – Teste Rápido

Anti-HCV – Anticorpos contra o Vírus da Hepatite C

UDIs – Usuários de Drogas Injetáveis

DST – Doença Sexualmente Transmissível

DEPEN – Departamento Penitenciário Estadual

CIA – Chemiluminescent Immunoassay

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Resumo

O sistema penitenciário brasileiro apresenta sérios problemas relacionados ao aumento do número de presos, entre eles a propagação do vírus da hepatite C (HCV). Acentua-se o controle do HCV, pelo fato da população encarcerada ser considerada um grupo de alto risco para as doenças transmissíveis devido às condições favoráveis encontradas na prisão para a disseminação dessas morbidades. O objetivo principal deste estudo foi identificar fatores associados à infecção pelo vírus da hepatite C entre homens presos do sistema penitenciário do Paraná, Brasil. Realizamos um estudo caso-controle de março a maio de 2018 em onze penitenciárias paranaenses. Participaram 27 casos e 54 controles pareados por pertencerem à mesma penitenciária; idade de três anos para mais ou para menos que o caso; tempo de encarceramento 5 anos para mais ou para menos que o caso.Os casos foram definidos como presidiário com sorologia reagente para HCV. Os controles foram selecionados de presidiários com marcador sorológico para HCV não reagente. As variáveis analisadas foram: raça, estado civil, escolaridade, ocupação, número de vezes preso, tempo de condenação, história DST, conhecimento sobre hepatite, transfusão sanguínea, uso tatuagem, *piercing*, drogas ilícitas, drogas injetáveis, uso de preservativos, bebida alcoólica, orientação sexual, relação homossexual e visita íntima. Análise univariada e modelo de regressão logística foram realizados para examinar os prováveis fatores de risco associados à infecção pelo vírus da hepatite C. A análise de regressão logística mostrou que as drogas ilícitas (odds ratio = 4.00; IC 95%, 1.06 – 15.08) e as drogas injetáveis (odds ratio = 4,00; IC 95%, 1.41-11,35) foram os principais fatores de risco para aquisição da infecção pelo vírus da hepatite C. Este é o primeiro estudo caso-controle em homens presos sob regime fechado das penitenciárias Paranaenses. Este estudo fornece evidências de que a infecção do HCV está associada ao uso de drogas por essa população.

Palavras-chave: Hepatite C, Fatores de risco, Prisioneiros.

CASE-CONTROL STUDY TO IDENTIFY RISK FEATURES ASSOCIATED WITH ANTI-HCV SEROLOGY REAGENT IN PRISONERS IN PRISONS IN THE STATE OF PARANÁ, BRAZIL

Abstract

The Brazilian prison system presents serious problems related to the increasing the number of prisoners and becomes more intense in the control of the hepatitis C virus (HCV). The control of HCV is highlighted due to the fact that the incarcerated population is considered a high risk group for contagious diseases because the favorable conditions found in prison for spreading these morbidities.The main purpose of this study was to identify features associated with hepatitis C infection among male prisoners in the prison system (correctional institutions) of Paraná, Brazil.We led a case-control study from March to May 2018.Twenty-seven cases and 54 matched controls participated as they belonged to the same penitentiary, age of 3 years more or less than the case;time of imprisonment of 5 years for more or less than the case of eleven penitentiaries of Paraná. The cases were defined as any prisoner with reactive serology for HCV. Controls were selected from male prisoners with serologic marker for non-reagent HCV. The variables analyzed were: race, marital status, schooling, occupation, number of times arrested, sentencing time, STD history, hepatitis knowledge, blood transfusion, tattooing, piercing, illicit drugs, injecting drugs, condom use, alcoholic beverage, sexual orientation, homosexual relationship and intimate visit. Univariate analysis and logistic regression model were performed to assess the likely risk factors for acquiring infection by hepatitis C virus. Logistic regression analysis showed that illicit drugs (odds ratio = 4.00, 95% CI, 1.06 - 15.08) and injectable drugs (odds ratio = 4.00; 95% confidence interval, 1.41-11.35) were the main risk factor for the acquisition of hepatitis C virus infection. This is the first case-control study reported with male prisoners in the closed prison system of Paraná, Brazil.This study provides evidence that HCV infection is associated with drug use by this population.

Keywords: Hepatitis C, Risk factor, Prisoners.

SUMÁRIO

1. INTRODUÇÃO GERAL

O vírus da Hepatite C (HCV) foi identificado por Choo e colaboradores, em 1989, nos Estados Unidos, e é o principal agente etiológico da hepatite crônica, anteriormente denominada hepatite não-A, não-B (WESTBROOK; DUSHEIKO, 2014). Compreende um vírus RNA (do inglês Ribonucleic Acid) de fita simples, pertencente à família *Flaviviridae* e ao gênero *Hepacivirus* (WANG, 2013;TAHERKHANI; FARSHADPOUR, 2015); e é formado por cerca de 9600 nucleotídeos (El-SHAMY, 2014). Apresenta uma região terminal 5' não-codificadora altamente conservada, composta por 324 a 340 nucleotídeos. Após a região 5', inicia-se uma região aberta de leitura que codifica uma proteína de pouco mais de 3000 aminoácidos. Quando clivada, dá origem às proteínas estruturais, que formam a partícula viral e as não-estruturais envolvidas na replicação viral. As proteínas estruturais do HCV são compostas pelas proteínas do "core", altamente conservadas, e por duas proteínas do envelope, E1 e E2. As não-estruturais compreendem sete proteínas (p7, NS2, NS3, NS4A, NS4B, NS5A, NS5B). Finalmente, segue-se a extremidade 3' não-codificadora (RICE, 2011; WANG, 2013; BRASIL, 2015).

Uma característica importante do HCV é sua heterogeneidade genética, que determina a caracterização de diversos genótipos do vírus, com diferentes subtipos. O HCV foi classificado em sete genótipos e mais de 70 diferentes subtipos (SMITH et al*.,* 2014; MESSINA et al*.,* 2015; TAHERKHANI; FARSHADPOUR, 2015). Os diferentes genótipos do vírus HCV resultam do acúmulo de mutações, que ocorrem na evolução do vírus, e podem influenciar alguns aspectos relativos à infecção como persistência da infecção, reinfecção, ausência de imunidade e aspectos relativos à distribuição geográfica, patogenia e resposta ao tratamento (El-SHAMY, 2014). Os sete genótipos possuem uma variabilidade de 30% a 35% entre si, e são nomeados por números de 1 a 7. Cada genótipo pode ser dividido em subtipos, que são identificados por letras (a, b, c, e assim sucessivamente). Existem 67 subtipos confirmados e 20 subtipos prováveis, que diferem entre si entre 15% a 25% de suas sequências nucleotídicas (SMITH et al., 2014; MESSINA et al*.,* 2015).

Essa diversidade genética desempenha um papel vital na capacidade do HCV de estabelecer infecção persistente e de evadir as várias pressões seletivas exercidas por respostas imunes e terapias antivirais (El-SHAMY, 2014; SMITH et al., 2014). A eficácia do tratamento contra o HCV depende do genótipo. Indivíduos infectados com o genótipo 1 respondem melhor à terapia com interferon-α, ribavirina e com os inibidores de protease do que aqueles infectados com os genótipos 2 ou 3 (El-SHAMY, 2014).

A transmissão do HCV ocorre principalmente por via parenteral (BRETAÑA, 2015). A transfusão de sangue contaminado com vírus da hepatite C foi um dos principais meios de transmissão do HCV até 1993, antes da introdução dos testes de triagem em doadores de sangue e hemoderivados (THURSZ; FONTANET, 2014).

São consideradas populações de risco aumentado para a infecção pelo HCV por via parenteral: indivíduos que receberam transfusão de sangue e/ou hemoderivados antes de 1993; pessoas que faziam ou fazem uso de drogas injetáveis, principalmente opiáceos, como a cocaína, em comparação a outras drogas injetáveis, como anabolizantes e complexos vitamínicos, inaláveis (cocaína) ou pipadas (crack), e que compartilham os equipamentos de uso; pessoas com tatuagem e *piercings*; pacientes de diálise ou que apresentem outras formas de exposição percutânea (por exemplo, consultórios odontológicos, clínicas de podologia, salões de beleza etc., que não obedecem às normas de biossegurança) (SNOW, 2014; WESTBROOK; DUSHEIKO, 2014; BRETAÑA, 2015; BRASIL, 2015).

As pessoas que injetam drogas ilícitas com agulhas não esterilizadas estão no maior grupo de risco de infecção por HCV (PEREIRA et al.2013;SNOW, 2014). Os usuários de drogas injetáveis mais antigos têm uma prevalência muito maior (aproximadamente 70% a 90%) da infecção pelo HCV, atribuível ao compartilhamento de agulhas durante a década de 1970 e 1980, antes de uma maior compreensão dos riscos de transmissão e da implementação de estratégias educacionais públicas (SNOW, 2014; TERRAULT, 2013).

Nos países desenvolvidos, a maioria das novas infecções por HCV são relatadas em usuários de drogas injetáveis. Os levantamentos mais recentes de UDIs(Usuários de drogas injetáveis ativos) nos Estados Unidos indicam que

aproximadamente um terço de usuários jovens (de 18 a 30 anos) estão infectados pelo HCV (TERRAULT, 2013).

A transmissão sexual é pouco frequente – menos de 1% em parceiros estáveis e ocorre, principalmente, a partir de relações sexuais com múltiplos parceiros e homossexuais masculinos, com prática sexual de risco (sem uso de preservativo), sendo que a coexistência de alguma das Infecções Sexualmente Transmissíveis (IST), inclusive o vírus da imunodeficiência humana, constitui um significativo facilitador dessa transmissão (WESTBROOK; DUSHEIKO, 2014; BRASIL, 2015). A transmissão sexual de HCV entre os casais heterossexuais monogâmicos é um evento infrequente. A prevalência máxima de infecção por HCV entre parceiros sexuais de indivíduos com infecção crônica por HCV foi de apenas 1,2%; e a incidência máxima de transmissão de HCV por sexo foi de 0,07% por ano ou aproximadamente um por 190.000 contatos sexuais (TERRAULT, 2013).

A transmissão vertical é rara quando comparada à hepatite B. Entretanto, já se demonstrou que gestantes com carga viral do HCV elevada ou coinfectadas pelo HIV apresentam maior risco de transmissão da doença para os recém-nascidos (WESTBROOK; DUSHEIKO, 2014). O risco de transmissão de HCV de mães infectadas para bebês varia de 4 a 7% quando a mãe é virêmica e quando está coinfectada com HIV este risco é duas a quatro vezes maior (THURSZ; FONTANET, 2014).

A hepatite C pode evoluir para doença aguda ou crônica. A doença aguda é clinicamente leve e tipicamente não reconhecida. Cerca de 20 a 30% dos infectados apresentam, na fase aguda, sintomas da doença, que pode manifestar-se por queixas inespecíficas, como: letargia; mal-estar geral; febre; problemas de concentração; queixas gastrointestinais, como perda de apetite, náusea; e intolerância ao álcool. Muitas vezes, os sintomas não são claros, podendo se assemelhar aos de uma gripe ou de outras infecções virais (WESTBROOK; DUSHEIKO, 2014; BRASIL, 2015). Sintomas mais específicos do vírus da hepatite C podem ser encontrados em uma minoria de indivíduos: icterícia, em um terço dos pacientes; urina escura; anorexia; aversão ao tabagismo entre fumantes; e pode ocorrer desconforto abdominal. As descobertas físicas são mínimas, e, portanto, o vírus é diagnosticado com pouca frequência,

particularmente naqueles que progridem para a hepatite crônica (WESTBROOK; DUSHEIKO, 2014).

Quando a infecção aguda pelo HCV persiste por mais de seis meses, o que é comum em cerca de 80% dos casos, caracteriza-se como crônica. A cronicidade é a principal complicação da hepatite C aguda, geralmente caracterizada por aminotransferases de soro aumentadas, podendo levar à fibrose e à cirrose. Cerca de 20% dos infectados cronicamente pelo HCV podem evoluir para cirrose hepática e cerca de 1% a 5% para câncer de fígado. O restante evolui de forma mais lenta e talvez nunca desenvolva hepatopatia grave (WESTBROOK; DUSHEIKO, 2014; BRASIL, 2015).

A hepatite crônica é a principal causa de doença hepática em estágio final, carcinoma hepatocelular e mortes relacionadas ao fígado. É importante destacar que a infecção pelo HCV já é a maior responsável pela cirrose e pelos transplantes hepáticos no mundo ocidental (WESTBROOK; DUSHEIKO, 2014; BRASIL, 2015).

O diagnóstico da hepatite C é baseado na detecção dos marcadores presentes no soro ou plasma da pessoa infectada, por meio de imunoensaios, e/ou da detecção do ácido nucleico viral, empregando técnicas de biologia molecular. O constante avanço tecnológico na área de diagnóstico permitiu o desenvolvimento de técnicas avançadas de imunoensaios, incluindo o de fluxo lateral, que são atualmente empregadas na fabricação de testes rápidos (TR) (HEIAT; RANJBAR; ALAVIAN, 2014).

O Anti-HCVé um anticorpo contra o HCV e é o marcador de triagem para a hepatite C. Indica contato prévio com o vírus, mas não define se a infecção é aguda, crônica ou se já foi curada. O diagnóstico de infecção aguda só pode ser feito com a viragem sorológica documentada, isto é, paciente inicialmente anti-HCV negativo que converte, tornando-se anti-HCV positivo e HCV-RNA positivo, detectado por técnica de biologia molecular. A infecção crônica deve ser confirmada pela pesquisa de HCV-RNA. O HCV-RNA é o primeiro marcador a aparecer entre uma a duas semanas após a infecção. É utilizado para confirmar a infecção em casos crônicos, monitorar a resposta ao tratamento e confirmar resultados sorológicos indeterminados, em especial, em pacientes imunossuprimidos (HEIAT; RANJBAR; ALAVIAN, 2014; BRASIL, 2015).

O tratamento da hepatite C depende do tipo do vírus (genótipo) e do comprometimento do fígado (fibrose) (WESTBROOK; DUSHEIKO, 2014; BRASIL, 2015). Nos últimos anos, no Brasil e em todo o mundo, com a disponibilidade das novas drogas antivirais de ação direta, e o uso dessas drogas em combinação, houve uma evolução considerável no tratamento da hepatite C. Para o uso racional desse arsenal terapêutico, deve-se seguir as diretrizes e os protocolos atualizados e além das orientações sobre triagem e cuidados, deve-se, também, seguir as recomendações sobre o uso destes medicamentos, especificamente, das combinações que dependem do genótipo viral e outros fatores clínicos (GLOBAL HEPATITIS REPORT,2017).

Globalmente, estima-se que o HCV infecte 180 milhões de pessoas, o que representa cerca de 3% da população mundial (WANG, 2013; EL-SHAMY, 2014). Também cerca de 110 milhões de pessoas no mundo são anti-HCV positivos, dos quais cerca de 80 milhões estão com infecção viral pelo HCV (EASTERBROOK et al.,2017). Em 2015, 71 milhões de pessoas viviam com infecção crônica pelo HCV, representando 1% da população global (GLOBAL HEPATITIS REPORT, 2017).

A infecção por HCV é distribuída de forma desigual no mundo, e há variações na prevalência entre países e entre regiões de um mesmo país (GLOBAL HEPATITIS REPORT, 2017). As regiões do mediterrâneo oriental e europeu registraram, em 2015, prevalências de 2,3% e 1,5% respectivamente. Na região das Américas, encontrou-se registro de prevalência de 0,7%; na Europa e nos Estados Unidos a prevalência varia entre 0,2% e 3%; podendo chegar a 5% no Egito e em outros países do continente africano (SILVA et al*.,* 2012).No Irã, a prevalência da infecção pelo HCV na população geral é menor do que a dos países vizinhos, como Afeganistão (1,1%), Turquia (1% -2,1%), Paquistão (4,7%), Iraque (7,1%) e Catar (6,3%) (TAHERKHANI; FARSHADPOUR, 2015).

Segundo estudo da distribuição global da HCV, realizado em 2013, referente ao ano de 2005, identificou-se como regiões com alta prevalência (>3.5%): a Ásia Central e Oriental e o Norte de África/Oriente Médio. Como regiões com prevalência moderada (1.5%-3.5%): Sul e Sudeste Asiático, Andino, Central e Sul da América Latina, Austrália, Caribe, Oceania, Europa Central, Oriental e Ocidental e África subsaariana. Regiões com baixa prevalência (<1.5%): Ásia Pacífico, América Latina tropical (Brasil) e América do Norte (MOHD

HANAFIAH et al., 2013). No Brasil, conforme estudo realizado em adultos e adolescentes de todas as macro-regiões do país, registrou-se uma prevalência de 1,3% (PEREIRA et al., 2013).

O vírus da hepatite C exibe alta diversidade genética do HCV, caracterizada por variações regionais na prevalência de genótipos, e representa um desafio para o desenvolvimento melhorado de vacinas e tratamentos pan-genotípicos, ou seja, tratamentos que levem em consideração estas variações e a região do mundo. Para tanto, tendências globais na prevalência do genótipo do HCV devem ser consideradas (MESSINA, 2015).

O genótipo de HCV 1 é o mais prevalente em todo o mundo, que inclui 83,4 milhões de casos (46,2% de todos os casos de HCV), cerca de um terço dos quais estão no Leste Asiático. O genótipo 3 é o segundo mais prevalente globalmente (54,3 milhões, 30,1%). Os genótipos 2, 4 e 6 são responsáveis por um total 22,8% de todos os casos; o genótipo 5 compreende ao restante <1%. Enquanto os genótipos 1 e 3 dominam na maioria dos países independentemente do *status* econômico, as maiores proporções dos genótipos 4 e 5 estão em países de baixa renda (MESSINA, 2015).No Brasil, podem ser encontrados os genótipos 1, 2, 3, 4 e 5. As frequências gerais são de 64,9% para o genótipo 1; 4,6% para o genótipo 2; 30,2% para o genótipo 3; 0,2% para o genótipo 4; e 0,1% para o genótipo 5 (BRASIL, 2015).

As prevalências e as fontes de contaminação da hepatite C variam de acordo com a localização geográfica, os grupos populacionais e os fatores de risco (MAGRI et al., 2015; SEQUERA et al., 2015). A população prisional é um grupo vulnerável a esta infecção, devido a sua vulnerabilidade social e as condições das penitenciárias que favorecem a transmissão. Sugere-se, também, que o próprio encarceramento pode ampliar o risco de infecção (MAGRI et al., 2015; BEHZADIFAR et al., 2018). Este excesso de risco pode ser explicado por várias causas; algumas devido aos problemas estruturais e logísticos das prisões e outros aos problemas habituais ou comportamentos adquiridos durante a reclusão (SEQUERA et al., 2015; BEHZADIFAR et al., 2018).

Em junho de 2016, segundo o INFOPEN (2017), a população prisional brasileira ultrapassou, pela primeira vez na história, a marca de 700 mil pessoas privadas de liberdade, o que representa um aumento da ordem de 707% em relação ao total registrado no início da década de 1990. Com isso, o Brasil ocupa

a 4ª colocação mundial em relação a taxa de população prisional (PUGA et al., 2017; BRASIL, 2017). O estado de São Paulo concentra 33,1% de toda a população prisional do país, com 240.061 pessoas privadas de liberdade; seguido pelo estado de Minas Gerais, com 68.364 presos. O estado do Paraná apresenta-se na terceira colocação em número de pessoas privadas de liberdade, com 51.700 presos (BRASIL, 2017). Essa super população, somada às condições de confinamento e a fatores comportamentais, é considerada de alto risco para adquirir várias doenças, principalmente as doenças infecciosas, como as hepatites virais (PUGA et al., 2017; SOUSA, 2013).

Estima-se que aproximadamente 15,1% de 10,2 milhões de indivíduos encarcerados estejam vivendo com HCV (DOLAN et al., 2016). Em comparação com outros estudos internacionais, essa taxa é menor do que a prevalência relatada entre prisioneiros na Itália, de 22,4% (BRANDOLINI et al., 2013); na Indonésia, de 34,1% (PRASETYO, 2013); em Azerbaijan, de 38,2% (AZBEL et al.,2015); e na Austrália, de 47,4% (SNOW et al., 2015); e, maior do que a verificada na França, de 4,8% (SEMAILLE, 2013); em Colatina-Brasil, de 1%(FALQUETTO et al., 2013); e nos Estados Unidos da América, de 10,1% (ALVAREZ et al., 2014).

O que se tem observado mundialmente é uma variação da prevalência do anti-HCV na população encarcerada, conforme mostra revisão sistemática de Zampino e seus colaboradores (2015), com variação entre 3,1% e 38% entre os vários países estudados. A prevalência da infecção pelo vírus da hepatite C (HCV) em encarcerados é 10 vezes maior do que a da população em geral, e 40% dos portadores crônicos de hepatites virais já foram encarcerados (SEQUERA et al., 2015).

No Brasil, revisão sistemática de Magri et al. (2015) e de Rosa et al. (2012), apontaram variação da hepatite C de 1% a 41% e 3,1% a 14,8%, respectivamente. Essa variação se explica devido a vários fatores, como localização geográfica da prisão, idade, penas de prisão anteriores, prevalência do uso de drogas intravenosas e ainda diferenças na qualidade dos serviços públicos de saúde, disponibilizado a essa população, além de hábitos, e taxas de comportamentos de alto risco nas diferentes regiões geográficas (DOLAN, et al., 2010; POMPILIO, et al., 2011; ZAMPINO, et al., 2015; TAHERKHANI; FARSHADPOUR, 2015).

A contaminação no sistema prisional pelo vírus da hepatite C tem sido associada à troca de sangue traumático, a tatuagens, ao uso de drogas injetáveis, e à atividade sexual (GOIS et al., 2012; MOHAMED et al., 2013; ALVAREZ et al., 2014; SNOW, 2014; WENGER et al., 2014; MAGRI et al.,2015; PUGA et al., 2017;BEHZADIFAR et al., 2018; MORADI et al., 2018). As condições de confinamento somadas aos fatores adicionais (compartilhamento de material usado para o consumo de drogas, para tatuagens, *piercings* e lâminas de barbear, além da esterilização inadequada ou reutilização de instrumentos médicos ou odontológicos) e a deficiência na assistência à saúde, também aumentam a vulnerabilidade das pessoas ao HIV/AIDS e outras infecções sexualmente transmissíveis (MOHAMED et al., 2013;RAMENAZI et al., 2014; BRASIL, 2015; MAGRI et al., 2015; BELAUNZARÁN-ZAMUDIO et al., 2017; AISYAH et al., 2018).

Essa população é considerada de alto risco, uma vez que, está mais vulnerável à transmissão parenteral, por ser formada, em grande parte, por usuários de drogas que injetam drogas ilícitas com agulhas não esterilizadas. A história de uso de drogas é bastante elevada dentro da prisão, correlacionada diretamente com o vício, que é anterior ao aprisionamento (GOIS et al., 2012; SNOW, 2014; PUGA et al., 2017).

Um estudo realizado na Escócia mostrou uma prevalência geral de infecção por HCV de 19% em uma população de 4.904 presos. Destes, 53% em presos com histórico de uso de drogas injetáveis e 3% naqueles sem histórico de uso (ZAMPINO et al., 2015). Há diferença significativa na exposição ao HCV entre os presos do sexo masculino e sexo feminino. Vários estudos relatam a prevalência do anti-HCV na população encarcerada do sexo masculino (ROSA et al., 2012; ROUX et al., 2014; MAGRI et al., 2015). No estudo de Pugaet al. (2017), verificou-se maior prevalência do anti-HCV na população encarcerada do sexo masculino (2,7%) do que no sexo feminino (0,6 %). Em outro estudo de metanálise, os internos do sexo masculino e os usuários de drogas injetáveis apresentaram uma probabilidade 24 vezes maior de serem positivos para o HCV do que os usuários de drogas não injetáveis (PUGA et al., 2017).

Alvarez et al. (2014) verificaram que os reclusos com infecção por HCV eram significativamente mais propensos a relatar uma história de de uso de drogas injetáveis, atividade sexual com usuários de drogas injetáveis e

diagnóstico de HIV (ALVAREZ et al., 2014). Isso faz com que a taxa de prevalência de coinfecção HCV/HIV seja bastante elevada entre os presos do sexo masculino, provavelmente devido à similaridade nas vias de transmissão dessas infecções. É comum os presos se envolverem em várias atividades que são consideradas fatores de risco para a coinfecção HCV/HIV, incluindo comportamentos sexuais de alto risco, compartilhamento de agulhas/seringas, vários tipos de instrumentos para tatuagens e uso de drogas (PUGA et al., 2017).

Em revisão sistemática sobre a saúde penitenciária, os estudos apontaram as condições precárias de confinamento (a desnutrição, a superlotação das celas, a marginalização social, a dependência de drogas ilícitas e o baixo nível socioeconômico) como fatores que facilitam a elevada disseminação de doenças e agravos, destacando-se tuberculose, hepatite B e C, HIV e outras IST (GOIS et al., 2012).

E ainda, em relação ao tempo de encarceramento, Puga et al. (2017) em estudo de coorte de 1656 presos da região Centro-Oeste do Brasil, encontraram associação entre a exposição ao HCV e um período de encarceramento maior que 48 meses, e também observaram novos casos de infecção pelo HCV. Portanto, quanto mais longo for o encarceramento, maior o risco de adquirir novas infecções devido ao uso inconsistente do preservativo ou à partilha de agulhas e seringas contaminadas. Além disso, o diagnóstico deficiente e a falta de conhecimento sobre a transmissão do HCV ou tratamento médico podem influenciar o risco de HCV (PUGA et al., 2017).

Apesar de existir uma compreensão do cenário que envolve a transmissão de doenças infecciosas nos presídios, ainda são escassos os estudos epidemiológicos voltados para essa população, principalmente no Brasil. Recentemente, em uma revisão sistemática conduzida por Magri (2015) sobre a prevalência da hepatite C em encarcerados do Brasil, em que se selecionaram estudos de 1989 a 2014, verificou-se que nenhum dos estudos relacionados foi conduzido no estado do Paraná, que apresenta a terceira maior população carcerária do Brasil. O crescimento desenfreado e exponencial do número de presos somado às condições precárias e aos baixos investimentos em segurança pública nos conduz a um estudo que permitirá conhecer a realidade dessa região em relação à disseminação do vírus da hepatite C, traçar um perfil do encarcerado, dos possíveis fatores de risco relacionados, contribuir para

elaboração de protocolos de monitoramento da doença e implantação de projetos de orientação sobre as infecções sexualmente transmissíveis, na qual se encontra a hepatite C.

2. OBJETIVOS

2.1 Geral

Identificar fatores de risco associados à sorologia Anti-HCV reagente em presidiários sob regime fechado do estado do Paraná, Brasil.

2.2 Específicos

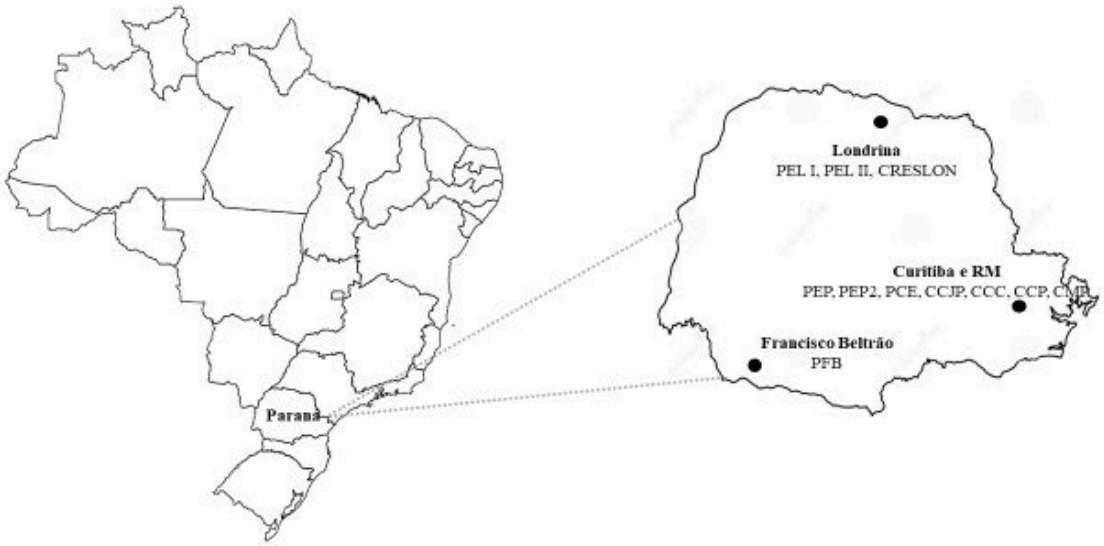
a) Caracterizar a amostra de indivíduos que participaram da pesquisa com e sem a presença do marcador sorológico anti-HCV.

b) Levantar possíveis fatores de risco associados ao marcador sorológico anti-HCV reagente em homens presos sob regime fechado, no estado do Paraná, Brasil.

3. METODOLOGIA

O presente estudo faz parte de um levantamento transversal realizado entre maio de 2015 e dezembro de 2016 em onze penitenciárias paranaenses, intitulado *Prevalência de HIV e Hepatite B e C na população carcerária das penitenciárias do estado do Paraná*. Com base nas informações do Departamento Penitenciário do Paraná (DEPEN, PR), no momento do estudo, havia cerca de 19.000 presos em 23 instituições penais fechadas masculinas. Onze das 23 prisões fechadas de alta segurança de seis cidades do estado (Francisco Beltrão, Londrina, Curitiba, São José dos Pinhais, Pinhais e Piraquara) foram incluídas (Figura 1). As penitenciárias foram escolhidas por estarem localizadas em uma cidade pequena, com menos de 100 mil habitantes; uma de médio porte, com até 600 mil habitantes; e uma de grande porte (Curitiba e região metropolitana), com mais de 2 milhões de habitantes. No sistema penal fechado o preso permanece todos os dias na unidade prisional sob supervisão.

Figura 1 – Localização geográfica das Penitenciárias incluídas no estudo Paraná-Brasil.



Legenda: PEL – Penitenciária Estadual de Londrina, CRESLON – Centro de Reintegração Social de Londrina, PEP – Penitenciária Estadual de Piraquara, PCE – Penitenciária Central do Estado, CCJP – Casa de Custódia de São José dos Pinhais, CCC – Casa de Custódia de Curitiba, CCP – Casa de Custódia de Piraquara, CMP – Complexo Médico Penal, PFB – Penitenciária Estadual de Francisco Beltrão, RM – Região Metropolitana de Curitiba.

O tamanho da amostra foi calculado com base na prevalência esperada de 50% de HCV, com variação de 1%, poder de 80% e erro tipo alfa de 3%. A população do estudo foi de 8.142 presos (757 em Francisco Beltrão, 1876 em Londrina e 5509 em Curitiba e região metropolitana), o tamanho da amostra foi de 954 presos. Adicionamos, aproximadamente, 25% de indivíduos para contabilizar a perda antecipada devido à recusa em participar, totalizando 1192 presos. A distribuição da amostra entre as penitenciárias foi proporcional ao número de presos de cada penitenciária, sendo 120 em Francisco Beltrão, 278 em Londrina, 794 em Curitiba e região metropolitana). A amostragem estratificada proporcional foi realizada usando cada prisão como uma unidade de randomização. Ao total foram entrevistados 1.132 presos devido 60 perdas ou recusas (5%).

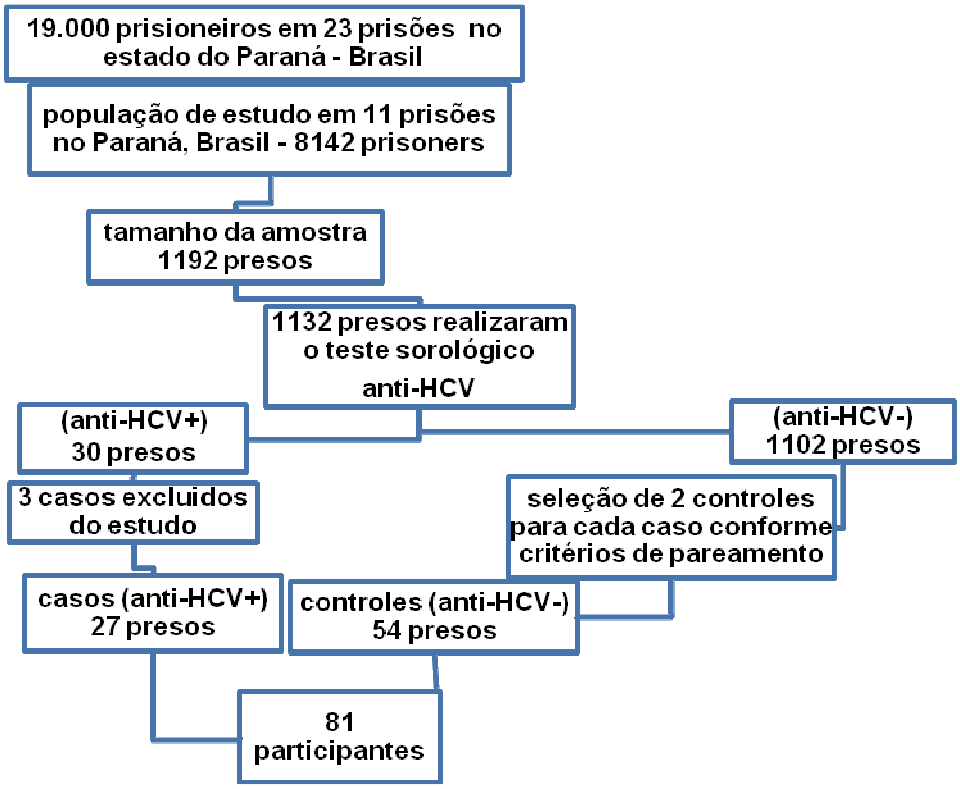
A coleta de dados foi realizada por meio do instrumento de coleta (apêndice) e, no dia da coleta de dados, os prisioneiros foram organizados numericamente em ordem crescente a partir das listas fornecidas pela prisão, e uma lista de números aleatórios foi gerada usando o *software Microsoft Excel®,* 2007. Para ser elegível para participar, os pacientes tinham que: (a) ter 18 anos ou mais (b) estar sob custódia (c) capaz de consentir para si (d) adequado para ser entrevistado apenas por um pesquisador (sem marcadores de risco) (e) capaz de entender o português falado. Este estudo foi realizado com a aprovação do Comitê de Ética em Pesquisa da Universidade Estadual do Oeste do Paraná, sob número 810.574. Todos os participantes elegíveis forneceram consentimento informado por escrito antes da participação. A participação no estudo foi voluntária e nenhuma compensação foi fornecida. O tratamento oferecido aos indivíduos que não participaram do estudo foi o mesmo dado aos participantes.

Para investigação da prevalência do anti-HCVem amostras de soro, foi utilizado o teste enzimático quimioluminescente de 3ª geração (conhecido como CIA, do inglês *enhancedchemiluminescenceimmunoassay*), no equipamento Vitros 5600. A análise e a interpretação dos resultados foram realizadas conforme instruções do fabricante.

A partir dos dados e resultados deste levantamento transversal, realizamos o estudo de caso-controle, no período março a maio de 2018, para investigar os fatores de risco associados ao marcador sorológico para hepatite C, em homens presos do regime fechado do sistema penitenciário do Paraná, Brasil. Os casos

foram definidos como presos com sorologia reagente para HCV. Controles foram selecionados dos presos com marcador sorológico para HCV não reagente. Foram identificados, no primeiro estudo, 30 homens presos com sorologia reagente para HCV, porém, participaram 27 casos e 54 controles pareados por pertencerem à mesma penitenciária, com idade de três anos para mais ou para menos que o caso; tempo de encarceramento de 5 anos para mais ou para menos que o caso de oito penitenciárias paranaenses. Do total de casos, três foram excluídos por não ser possível parear conforme os critérios estabelecidos, totalizando uma população de estudo de 81 presos. O fluxograma de recrutamento encontra-se representado esquematicamente na Figura 2.

Figura 2 – Fluxograma do recrutamento do primeiro estudo e processo de triagem dos casos e controles.



Fonte: Elaborado pela autora.

Após a seleção dos casos e controles foram testadas as variáveis: raça/cor, estado civil, escolaridade, ocupação quando foi preso, número de vezes no sistema prisional, tempo de condenação, história de DST, conhecimento sobre hepatite, transfusão sanguínea, uso tatuagem, uso *piercing*, uso drogas ilícitas,

uso drogas injetáveis, uso de preservativos, uso bebida alcoólica, orientação sexual, relação homossexual e visita íntima. Um número de identificação anônimo foi utilizado para cruzar as informações contidas nos questionários.

Todo o processamento e análises foram realizados no programa SPSS 24.0. Frequências absolutas (n) e relativas (%) foram utilizadas para a descrição das características amostrais. A comparação entre casos e controles foi realizada por meio do teste de Qui-quadrado, com correção de continuidade. As variáveis que apresentaram $p < 0,20$ nessa análise foram inseridas no modelo de regressão logística binária para a identificação de fatores de risco independentes para a infecção pelo HCV, sendo considerados com significância estatística os valores que apresentaram um $p<0,05$.

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5. ARTIGO CIENTÍFICO

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Original article

Characteristics associated with anti-HCV serological markers in prisoners in the state of Paraná, Brazil: A case-control study

ABSTRACT

Background: The prison system in Paraná, Brazil, is experiencing serious problems related to the increasing number of prisoners.Control of hepatitis C virus (HCV) has become more intense because the incarcerated population is considered a high-risk group for contagious diseases due to the favorable conditions found in prisons for the spread of these morbidities. The objective of this study was to identify features associated with hepatitis C infection among male prisoners in the prison system (correctional institutions) of Paraná state, Brazil.

Methods: This was a case-control study (27 cases and 54 controls) of men incarcerated in eleven penitentiaries in Paraná, Brazil. Information was obtained through a questionnaire in a cross-sectional epidemiological survey on HCV infection during the period from May 2015 to December 2016. Eligible men were recruited after testing positive for anti-HCV antibodies. The cases and controls were selected based on serological resultsfrom enzyme-linked immunosorbent assays and were matched by age, location of the penitentiary and time in prison. Logistic regression analysis was used to identify risk factors.

Results: The logistic regression analysis showed that the main significant risk factor for the acquisition of HCV infection was the use of injectable drugs (OR= 4.00; $IC_{95\%}$:1.41-11.35; p: <0.001).

Conclusions: This study provides evidence that HCV infection is associated with drug use by this population. This information is pivotal for tailoring prevention programs and guiding specific socioeducational measures that aim to reduce or prevent HCV transmission within the prison setting.

Keywords: Hepatitis C. Risk factor. Prisoners.

Introduction

Infection with type C viral hepatitis (HCV) is common among the prison population. It is also thought that incarceration itself may increase the risk of infection.[1,2]This increased risk can be explained by several causes,some associated with the prisons' structural and logistic problems and others withcommon problems or behaviors acquired during seclusion.[2,3] It is estimated that approximately 15.1% of the 10.2 million incarcerated individuals are living with HCV.[4] This rate is lower than the prevalence reported among prisoners in

international studies, including studies in Italy (22.4%)[5], Indonesia (34.1%)[6] and Azerbaijan (38.2%).[7]

What has been observed worldwide is a variation in anti-HCV prevalence in the incarcerated population, ranging from 1% in a study carried out in Colatina, Brazil,[8]to 47.4% in a study carried out in Australia.[9] A systematic review byMagri and his collaborators indicated a variation in hepatitis C prevalence from 1% to 41% in Brazil.[1] This variation is associated withdifferences in geographical prison location, age, previous prison sentences, intravenous drug use, and even the quality of public health services available to the population, as well as withthe different habits and high-risk behaviors in different geographic regions.[10-13]

Contamination by hepatitis C virus in prisons has been linked to trauma-induced blood exposure, tattooing, intravenous drug use, and sexual activity.[1,2,9,14-19] Confinement plus additional factors (sharing of material used for drug use, tattoos, piercings and razor blades in addition to inadequate sterilization or reuse of medical or dental instruments) and deficiencies in health care also increase the vulnerability of prisoners to HIV/AIDS and other sexually transmitted infections.[1, 15, 20-23]

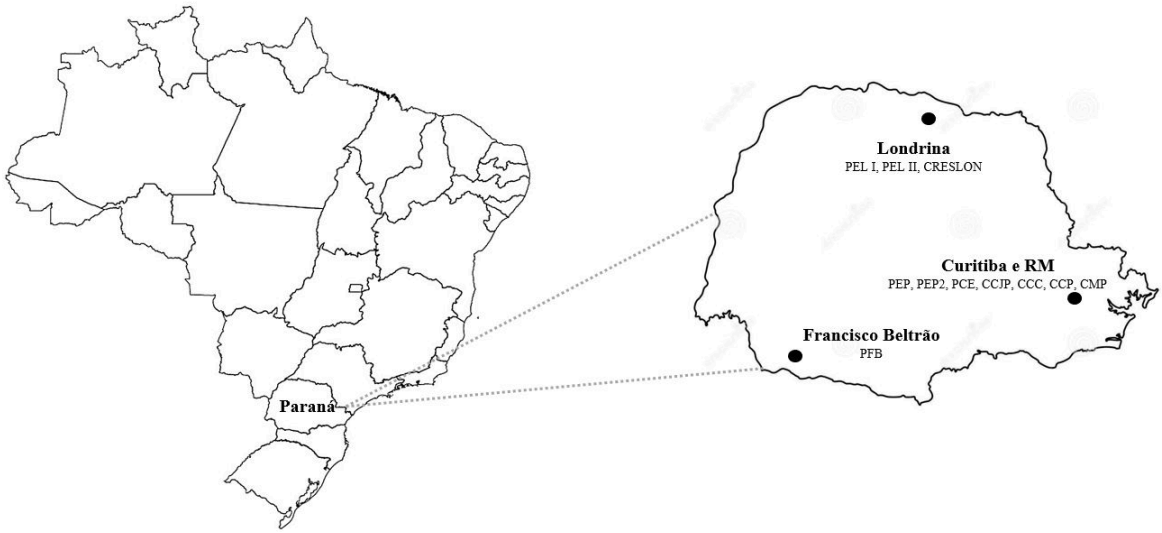
Although there is some understanding of the scenarios that lead to the transmission of infectious diseases in prisons, epidemiological studies are still scarce for this population, especially in Brazil.Recently, a systematic review of studies from 1989 to 2014 conducted by Magri and collaborators on the prevalence of hepatitis C in prisoners in Brazilconfirmed that none of the related studies had been conducted in the state of Paraná, Brazil.[1] This study aimed to analyze the factors associated with hepatitis C infection among inmates of the Paraná prison system.

Materials and methods

This study is part of a cross-sectional survey carried out from May 2015 to December 2016 in 11 penitentiaries in Paraná state titled “Prevalence of HIV and Hepatitis B and C in the prison population in prisons in the state of Paraná.” Based on information from the Penitentiary Department of Paraná (DEPEN, PR) at the time of the study, there were approximately 19,000 prisoners in 23 closed male prisons. Eleven of the 23 high-security closed prisons in six cities of the state

(Francisco Beltrão, Londrina, Curitiba, São José dos Pinhais, Pinhais, and Piraquara) were included (Fig. 1). Our criteria for selecting the participating cities considered both the size of the cities as well as the presence of penitentiaries in closed regime. Three cities - all located in the state of Paraná - were then selected to took part in the study (Francisco Beltrão, a small-sized city, with a population of up to 100 thousand inhabitants; Londrina, a relatively large city, but with a population smaller than a million inhabitants; and Curitiba, a large city formed by more than a million inhabitants).[24] In the closed-regime systems, inmates remain under daily supervision within the prison limits.

Fig. 1 – Geographic locations of the penitentiaries included in the study in Paraná, Brazil.



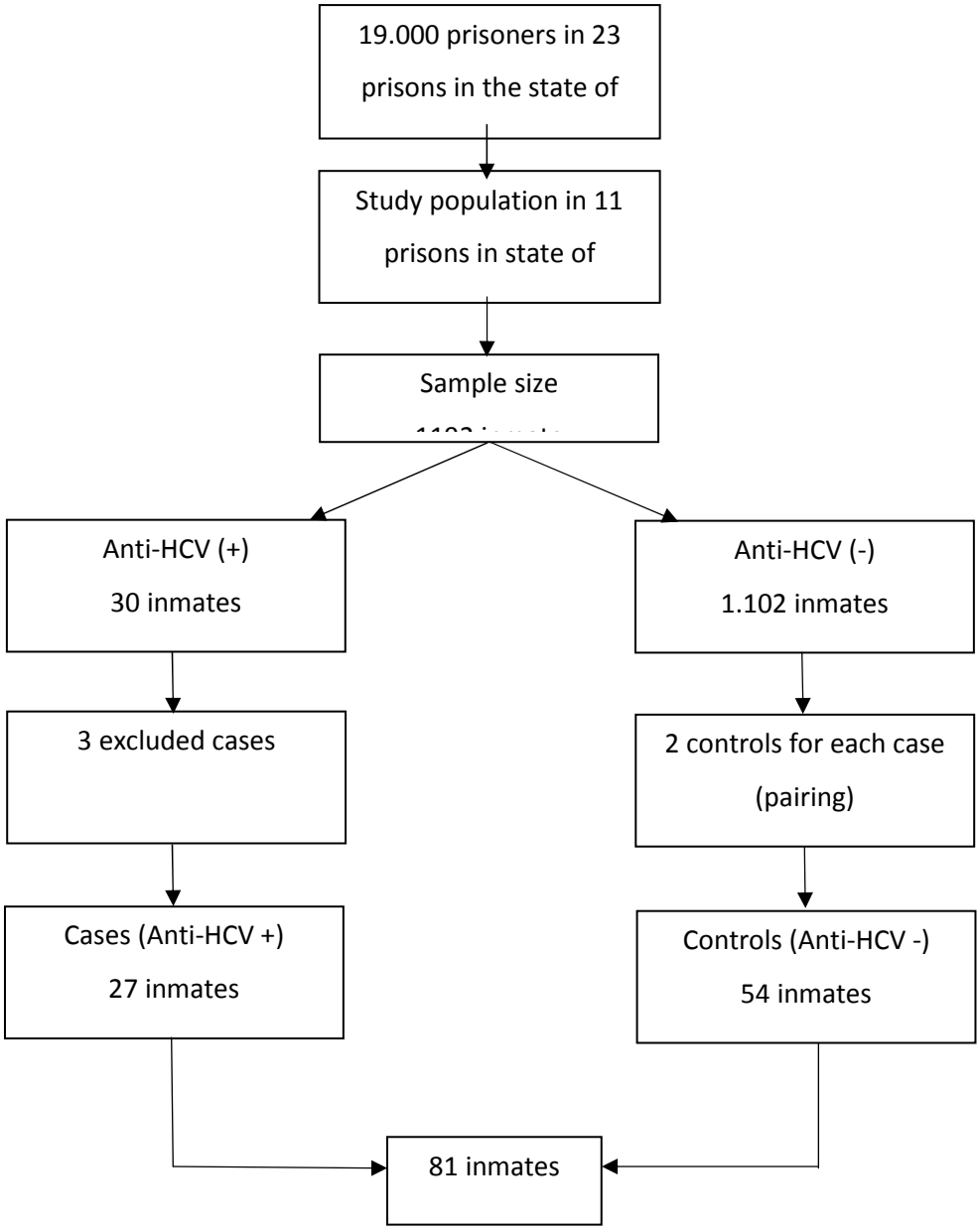
Legend: PEL - State Penitentiary of Londrina, CRESLON - Social Reintegration Center of Londrina, PEP - State Penitentiary of Piraquara, PCE - Central State Penitentiary, CCJP - House of Custody of São José dos Pinhais, CCC - House of Custody of Curitiba , CCP - House of Custody of Piraquara, CMP - Criminal Medical Complex, PFB - State Penitentiary of Francisco Beltrão, RM - Metropolitan Region of Curitiba.

The sample size was calculated based on the expected prevalence of 50% HCV with 1% variation, a power of 80%, and 3% alpha error.The study population included8,142 inmates, and the sample size was 954 inmates.We added approximately 25% more individuals (total: 1,192 inmates) to account for anticipated loss due to participation refusal.Proportional stratified sampling was

performed using each prison as a randomization unit.A total of 1,132 prisoners were interviewed, with 60 losses or refusals (5%).On the day of data collection, the prisoners were sorted numerically in ascending order from the lists provided by the prison, and a list of random numbers was generated using the software *MicrosoftExcel*® 2007. To be classified, patients had to be (a) 18 years of age or older, (b) in custody, (c) able to consent for themselves, (d) able to be interviewed only by a researcher (without risk markers) and (e) able to understand spoken Portuguese.This study was carried out with the approval of the research Ethics Committee of the State University of West Paranáunder approval number 810.574. Alleligible participants provided informed written consent prior to participation. Their participation in the study was voluntary, and no compensation was provided.The treatment offered to the individuals who did not take part in the study was the same as that given to the participants. Prisoners identified as HCV-positive received medical assistance.To investigate the prevalence of anti-HCV antibodies, we used a 3rd generation chemiluminescent enzyme test (Architect® anti-HCV assay – Germany) in serum samples onai4000 instrument (Architect System, United States of America [USA]). The test results were analyzed according to the manufacturer's instructions.

Based on the results of this intersectional survey, we performed case-control studiesduring the period from March to May 2018 to investigate the risk factors associated with the serological marker for hepatitis C in men incarcerated in the closed regime of the penitentiary system of Paraná, Brazil.In the first study, 30 prisoners with reactive serology for HCV were identified.These included 27 cases and 54 control subjectsthat belonged to the same penitentiary, were within three years of age of the cases and had atime of imprisonment within 5 years of that of the casesin eight penitentiaries of Paraná.Of the total cases, three were excluded because it was not possible to match them according to the established criteria, producing a total study population of 81 prisoners. A case was defined as any inmate with reactive serology for HCV.Controls were selected from among prisoners withserologic markers for non-reactive HCV.A flowchart of the recruitment strategy is shownin Fig. 2.

Fig.2 – Recruiting flowchart of the first study and screening process of cases and controls.



After case and control selection, the following information was obtained: race/color, marital status, schooling, occupation when incarcerated, number of times in the prison system, conviction time, STD history, knowledge of hepatitis B and C transmission routes, blood transfusion history, tattoo history, piercing history, illicit drug use, injectable drug use, condom use, alcoholic beverage use, sexual orientation, homosexual relationship history, and intimate visit history. Anonymous identification numberswere used to cross-reference the information contained in the questionnaires.

All processing and analysis steps were performed with the Statistical Package for Social Science, version 24.0 (SPSS Inc., Chicago, IL, USA) program. Absolute (n) and relative (%) frequencies are used to describe the sample features. Initial comparisons between groups were performed by factorial ANOVA (groups vs penitentiaries). Comparisons between cases and controls for categorical variables were performed using chi-square tests with continuity correction.The variables that presented p <0.20 in this analysis were inserted into a binary logistic regression model to identify independent risk factors for HCV infection, with values that presented a p <0.05 being considered statistically significant.

Results

The cases (n=27) were selected concomitantly with the controls (n=54) from the survey database "Prevalence of HIV and Hepatitis B and C in the prison population of the Paraná State Penitentiaries", which identified a prevalence of positive serology of 2.7% ($IC_{95\%}$ 1.9 – 3.8). The selected patients from the control group and the case group were statistically similar for all paired variables: penitentiary, age, and time of imprisonment (Table 1).

Table 1 – Description of the paired variables of the cases (27) and controls (54) according to the penal unit, average age, and prison time in the State Prisons of Paraná

	Sample N		Average age		**Average prison time**	
Penitentiary	Case	Control	Case	Control	Case	Control
PFB	01	02	32*	31,00±1.14	9*	7±0.00
PEL I	02	04	45.50±2.12	45.25±2.63	4.50±2.12	5.00±3.74
PEL II	04	08	45.25±11.53	44.63±10.24	3.50±2.08	3.75±2.60
PEC	07	14	42.29±8.14	42.21±7.89	4.71±2.69	5.36±3.93
PEP II	05	10	32.60±9.81	33.10±8.60	1.80±1.92	2.00±2.40
CCC	03	06	39.33±3.78	38.17±3.43	1.67±2.08	2.00±1.26
CCP	03	06	30.67±9.02	30.67±8.07	0.33±0.57	0.16±0.40
CMP	02	04	39.50±0.71	44.50±11.03	0.50±0.71	0.75±1.50
Total	27	54	38.96±9,10	39.13±9.26	14.25±14.06	15.11±12,63

*Just one subject. Effects of ANOVA information for case vs control: age ($F = 0.017$; $p = 0.896$) and prisiontime ($F = 0.001$; $p = 0.999$).

Table 2 shows the general characteristics of the two groups. The participants' mean age was 39 years, and positive serology was predominantly found among individuals over 30 years of age. It was observed that although the differences were not statistically significant, the cases had a higher prevalence of unemployment, had been in the prison system more often, reported greater knowledge about hepatitis, and had a higher prevalence of blood transfusions, illicit drug use, and homosexual relationships than the controls.However, the only variable that presented statistical significance was injectable drug use; the cases presented a prevalence of use almost three times higher than that of the controls.

Table 2 – **Socio demographic characteristics, risk factors, prison variables and HCV infection among male prisoners of the penitentiaries of the state of Paraná, Brazil (n = 81).**

	Cases (n = 27)		**Control (n = 54)**		**p-value**
	n	**%**	**n**	**%**	
Skin color					
White	13	48.1	29	53.7	0.814
Other	14	51.9	25	46.3	
Marital state					
Married/cohabiting	11	40.7	28	51.9	0.479
Single/divorced	16	59.3	26	48.1	
Education					
Incomplete elementary school	14	51.9	27	50.0	0.875
Complete elementary education	13	48.1	27	50.0	
Were employed					
Yes	9	33.3	26	48.1	0.303
No	18	66.7	28	51.9	
Number of times in the prison system					
Up to 2 times	5	18.5	19	35.2	**0.197**
More than 2 times	22	81.5	35	64.5	
Conviction time					
Up to 12 years	15	55.6	26	48.1	0.694
More than 12 years	12	44.4	28	51.9	
DST history					
Yes	11	40.7	26	48.1	0.693
No	16	59.3	28	51.9	
Knowledge about hepatitis					
Yes	14	51.9	20	37.0	0.301
No	13	48.1	34	63.0	
Blood transfusion					
Yes	7	25.9	8	14.8	0.363
No	20	74.1	46	85.2	
Tattooing					
Yes	19	70.4	32	59.3	0.464

No	8	29.6	22	40.7	
Piercing					
Yes	5	18.5	12	22.2	0.923
No	22	81.5	42	77.8	
Illicit drugs use					
Yes	24	88.9	36	66.7	**0.060**
No	3	11.1	18	33.3	
Injecting drug use					
Yes	12	44.4	9	16.7	**0.016**
No	15	55.6	45	83.3	
Condoms use					
Yes	14	51.9	32	59.3	0.418
No	4	14.8	9	16.7	
Do not know	9	33.3	13	24.1	
Alcohol consumption					
Yes	24	88.9	49	90.7	0.794
No	3	11.1	5	9.3	
Sexual orientation					
Heterosexual	25	92.6	47	87.0	0.708
Other	2	7.4	7	13.0	
Homosexual relationship					
Yes	5	18.5	3	5.6	**0.148**
No	22	81.5	51	94.4	
Intimate visit					
Yes	7	25.9	19	35.2	0.556
No	20	74.1	35	64.8	

Note: STD = sexually transmitted diseases, Fr =frequency

The main variables (table 2) were included in the logistic regression model ($p< 0.20$) to identify independent risk factors for hepatitis C (table 3) it was observed that two of the four variables presented statistical significance: illicit drug use and injectable drug use. When these variables were included together in the model, collinearity was observed between them (those who used illicit drugs were the same individuals who used injecting drugs); thus, construction of a multiple regression model was not possible.However, given the result of the initial analysis and the narrow OR confidence interval, injecting drug use is the main risk factor for hepatitis C infection in prisoners.

Table 3 – Independent hepatitis C predictors in men arrested in the penitentiary system in Paraná by multivariate logistc regression analyses.

	OR_{br} (IC 95%)	**p**
Number of times in the prison system		
Up to 2 times	1	
More than 2 times	2.39 (0.78 – 7.32)	0.128
Illicit drugs use		

Yes	4.00 (1.06 – 15.08)	0.041
No	1	
Injecting drug use*		
Yes	4.00 (1.41 – 11.35)	**<0.001**
No	1	
Homosexual relation		
Yes	3.86 (0.85 – 17.60)	0.081
No	1	

Note:* Main variable in the final model.

Discussion

There have been few studies in Brazilian male prisons that estimate the risk factors for hepatitis C infection.[1] Most of the studies conducted on this disease have aimed to determine the prevalence of the virus.[12] Therefore, among the advantages of this study, we highlight the case-control design with representation of prisoners in eleven closed-regime male penitentiaries in the state of Paraná. It is worth mentioning that this is the first study in the state of a social nature that shows a clear view of the prevalence of HCV and the risk factors related to exposure to HCV among prisoners.

The prison population is considered to be at high risk for acquiring infectious diseases[1,25] because prisoners are confined and present risky behavioral factors such as low education levels[25], irregular and infrequent use of condoms, multiple sexual partners, sex under the influence of alcohol and drugs[26-28], and little use of preventive measures.[1] These risk factors and behaviors can precede arrest and frequently continue during incarceration.[18,29]

Prisoners with a history of previous incarcerations have had a greater opportunity to acquire HCV infection than those who have not previously been incarcerated.[1,18] Several studies have revealed that a previous history of incarceration is related to frequent exposure to high-risk activities such as unsafe lifestyles, risky sexual behaviors, exposure to sharps for tattooing, and sharing of needles, syringes and other paraphernalia for illicit drug use.[1,12,18,25]

Recently, Stone et al. published a systematic review and meta-analysis of 41 studies on this subject. It has been identified that both recent and past incarceration contribute to an increased risk of HCV acquisition ranging from 62% to 21%.[30] In the present study, previous incarceration was significantly associated

with HCV infection in the univariate analysis. However, this factor was not considered an independent predictor of viral infection, suggesting that there must be other factors that confound the relationship between these two variables.[29]

Studies have identified that homosexual relationships offer a greater chance of HCV infection than heterosexual relationships; in our study, in the final model, this association was not confirmed. [28, 32]It is believed that this association may be related to risk behaviors rather than to homosexuality itself, according to Santos and collaborators.[33]

We identified an effect of illicit drug use as a factor associated with HCV exposure. These findings have also been identified in other studies worldwide and in Brazil. [18, 25,29,32] Despite the significance of illicit drug use in univariate analysis in the final model, only the injecting drug use variable was associated with positive serology for HCV, since it was identified that those who used illicit drugs were the same individuals who used injecting drugs (collinearity). In our study, the odds of contracting hepatitis Cwere 4 times higher formen who used injecting drugs(OR = 4.00; $IC_{95\%:}$ 1-11.12) than for prisoners in the same prison system who did not use this type of drug. Injecting drug-using prisoners and males in a meta-analysis study were 24 times more likely to be HCV-positive than non-injecting drug users. [26]

Worldwide, there is a continuing epidemic of hepatitis C virus infection among young white adults who use injecting drugs and are below 30 years of age with a history of previous or simultaneous opiate consumption.[33-34]HCV infection prevalence is 10 to 15 times higher in people who inject drugs, with higher rates among new injectors. A quarter of injecting drug users will be infected within two years after starting.In addition, HCV is approximately 10 times more infectious than HIV, and injecting drug use increases the risk by 3% to10% compared to 0.3% for HIV contamination.Furthermore, the virus remains infective in liquid and syringes and on inanimate surfaces for weeks.[35-37]

The relationship between illicit drug use, HCV infection and imprisonment is very close, as injecting drug users (IDUs) are the individuals with the highest rates of incarceration dueto involvement in illicit activities, and they use drugs through crime to finance their addictions.[38]A recent meta-analysis of six published studies on the incidence of HCV in prisoners reported that the risk of HCV infection was

eight times higher in injecting drug-using prisoners than in injecting drug-usingnonprisoners.[30]

In a cohort of 735 Australian prisoners with a history of injecting drug use that were followed for more than 14 years, 55.1% of prisonerswere found to have some history of HCV, and 47.4% of those tested in the prison were seropositive for HCV.In this study, drug injection in prison was found to be strongly associated with HCV seropositivity by Snow and collaborators.[9] Roux and collaborators also reported injecting drug use in 99% of cases in their survey of sociodemographic and behavioral characteristics of participants tested for HCV infection in a prison population in southwestern France. [39]

In Latin America and the Caribbean, 11.3% of prisoners who carry HIV and hepatitis C use injecting drugs, and in Brazil, the prevalence is approximately 9.2%.[40]In Brazilian studies, there are reports of syringe sharing for drug use in 32.5% of prisoners.The use of illicit drugs is common in prison environments, and even when the use of only inhaled illicit drugs has been reported, high frequency of use ends up being a bridge to injectable drug use.[41]Pereira and collaborators, in their study on populations from 26 Brazilian states and the Federal District, showed with a multivariate model that the use of injectable drugs (OR = 6.65; $IC_{95\%}$: 2.47 – 17.91) and the use of inhaled drugs (OR = 2.59; $IC_{95\%}$: 1.34 – 5.81) are predictive factors for HCV infection.[41]

The epidemiological impact of various risk factors for acquiring HCV infection has been investigated in a number of studies on prison populations, and in the results, the use of injecting drugs has beenfound to be the main risk factor associated with HCV infection in prison populations.[9,10,30,37]Although such risk behavior is strictly prohibited in prisons around the world, almost half of illicit drug users continue to use such substances after arrest.In addition, the difficulty in obtaining sterile injecting equipment in prison results in widespread sharing of infected equipment and increased risk of HCV transmission.[12]

It should be clarified that the use of injecting drugs is also a risk factor outside the prison environment.In developed countries, most new HCV infections are reported in injecting drug users. The most recent surveys of active IDUs in the United States indicate that approximately one third of young users (ages 18-30) are infected with HCV. [42]

The seroprevalence of HCV observed in this study was 2.7%,which is higher than that in the range of 0.7% and 1.38% reported among people aged 10-69 years.[41,43-44]The seroprevalence of HCV in this study was slightly higher than that found in a study by Puga and others[18] among men in penitentiaries in the state of Mato Grosso do Sul (2.4%) and different from those in studies performed on prisoners in São Paulo (8.7%) and in Minas Gerais (6.34%).[24,45] The prevalence of HCV infection among prisoners in Paraná was lower than that found in studies in Australia (29%), England (24.2%), Italy (22.4%), Ghana (18.7%), Iran (7.4%), and Lebanon (3.4%).[46-48]

The presence of hepatitis C virus can manifest as an acute infection, with development of symptoms in 20% to 30% of cases, or as a chronic infection that can result in liver fibrosis, cirrhosis, or hepatocellular carcinoma in 70% or 80% of cases.[33-34]The possibility of infection without apparent symptoms makes it difficult to diagnose infection early and, consequently, postpones the treatment of chronic patients.This situation of delayed diagnosis is frequent within the prison system since the infrastructure and health services in the system to care for the prisoner are poor, when they exist.[48]There is also an absence of educational campaigns and guidance for the practice of safe sex, sexual transmission among men who have sex with other men (HSH) is higher in the prison environment than in the outside environment, reaching rates of 8,6%. In relation to the HIV-positive prisioners the only report having anal sex before imprisonment came from Israel with fee 6.5% in between HSH.[49]

Educational campaigns and guidelines for the practice of safe sex among the prison population would be useful for reducing the prevalence rates of HCV and other sexually transmissible diseases.The lack of healthybehavior is related to the low effectiveness of the medical teams in prison environments, which hinders medical care, since prisons are environmentscharacterized by conditions of insecurity and fear. [50]

This study has limitationsbecause some behavioral risks may have been underreported by the research participants due to fact that vulnerability can leadto discrimination and stigmatization. Such underreporting could have contributed to underestimation of the potential risk factors associated with HCV exposure.

In conclusion, we observed injectable drug useto be the main risk factor for hepatitis C infection in men incarcerated in the penitentiary system in state of

Paraná, Brazil.The increased risk was associated with a high frequency of risky behavior before and during incarceration, especially for injecting drug users.These results suggest an urgent need for effective prevention programming, education, prison strategies, and programs adapted to local contexts as well as new direct-acting antiviral drugs, treatment strategies, and therapies.

Serological testing for screening and monitoring of IDUs and treatment of drug abuse and addiction among prisoners in needin the prison system would make it possible to evaluate the success of harm reduction strategies (needle/syringe sharing programs for injecting drugs and tattoos).Finally, studies using phylogenetic analysis will also enhance understanding of the routes of HCV transmission in this population.

Acknowledgements

This research was funded by the Ministry of Health and the State University of Western Paraná (UNIOESTE) under agreement 797322/2013.

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6. APÊNDICES

INSTRUMENTO DE COLETA

DATA ___/___/___ No. QUEST. ___ ___ ___ ___

1) NASCIMENTO ___/___/___ IDADE ____

2) ESTADO CIVIL _____ 1. Casado 2. Solteiro 3. Amasiado 4. Viúvo 5.Divorc./separ.

3) FILHOS _____

4) LOCAL NASC. _____ 1. Francisco Beltrão 2. Londrina 3. Curitiba 4. Outra cidade do Estado do Paraná 5. Outro Estado 6. Outro país

5) LOCAL RESID. ____ 1. Francisco Beltrão 2. Londrina 3. Curitiba 4. Outra cidade do Estado do Paraná 5. Outro Estado 6. Outro país

6) ESCOLARIDADE ____ 1. Nenhuma; 2. Fund.Inc; 3.Fund.Com.; 4.Médio Inc.; 5. Médio.Com; 6.Sup.Inc.; 7.Sup.Com.

7) Qual sua cor ____ 1. Preta 2. Parda 3. Branca 4. Amarela 5. Indígena

8) Tem um profissão definida ____ 1. Sim; 2. Não; 3. Não sabe

9) Exercia a profissão antes de ser preso ____ 1. Sim; 2. Não; 3. Não sabe

10) No momento em que foi preso, você estava empregado ____ 1. Sim; 2. Não; 3. Não sabe

11) É a primeira vez que passa no sistema prisional ____ 1. Sim; 2. Não; 3. Não sabe

12) Quantas vezes já foi preso ____

13) Sua pena atual é de quanto tempo ____ anos ____ meses

14) Há quanto tempo está preso nesta condenação ____ anos ____ meses

15) VOCÊ JÁ FOI DETIDO QUANDO MENOR DE IDADE ____ 1. Sim; 2. Não; 3. Não sabe

16) JÁ INTERNOU EM REFORMATÓRIO ____ 1. Sim; 2. Não; 3. Não sabe

17) Já teve alguma vez na vida uma DST ____ 1. Sim; 2. Não; 3. Não sabe

18) Se sim, qual tipo que foi 1. Verruga 2. Corrimento pelo pênis 3. Ferida

19) CIRCUNCIDADO ____ 1. Sim; 2. Não; 3. Não sabe

20) TEM TATUAGEM ____ 1. Sim; 2. Não; 3. Não sabe

21) SE SIM, JÁ FEZ ALGUMA TATUAGEM NA PRISÃO? _____1. Sim; 2. Não; 3. Não sabe

22) JÁ COLOCOU ALGUMA VEZ PIERCING ____ 1. Sim; 2. Não 3. Não sabe

23) Se sim, alguma vez colocou piercing quando estava na prisão 1. Sim; 2. Não 3. Não sabe

24) Na prisão, já compartilhou alguma vez com os colegas objetos de uso pessoal como ____ 1. Sim; 2. Não 3. Não sabe

25) Se sim, quais foram estes objetos ____ 1. Escova de dentes 2. Lâminas de barbear, 3. Cortadores de unhas, 4. Giletes, 5. Tesouras, 6. Outros

26) Você sabe como pega o HIV ____ 1. Sim; 2. Não

27) JÁ FEZ TESTE DE ANTI-HIV ____ 1. Não; 2. Uma vez; 3. Mais de uma vez; 4. Não sabe

28) RESULTADO ____ 1. Positivo; 2. Negativo; 3. Não sabe; 4. Não se aplica

29) Você já teve hepatite alguma vez ____ 1. Sim; 2. Não 3. Não sabe

30) Você sabe como pega hepatite ____ 1. Sim; 2. Não

31) Já tomou vacina para hepatite B ____ 1. Nunca 2. Tomou uma dose 3. Tomou duas doses 4. Tomou três doses.

32) Se sim, tomou alguma dose na prisão ____ 1. Sim; 2. Não 3. Não sabe

33) Desde que você chegou aqui, a prisão já fez alguma campanha de prevenção de DST, Aids e hepatites. ____ 1. Sim; 2. Não 3. Não sabe

34) Você gostaria de participar de alguma campanha preventiva____ 1. Sim; 2. Não 3. Não sabe

35) Você gostaria de saber informações sobre alguma doença ____ 1. Sim; 2. Não 3. Não sabe

36) TRANSFUSÃO SANGUINEA ____ 1. Não; 2. Uma vez; 3. Mais de uma vez; 4. Não sabe

37) JÁ FEZ SEXO COM USUARIO DE DROGAS ____ 1. Sim; 2. Não 3. Não sabe

38) Já usou drogas ilícitas alguma vez na vida ____ 1. Sim; 2. Não; 3. Não sabe

39) Se sim, com que idade usou a primeira vez ____

40) Se sim, atualmente na prisão usa alguma droga ilícita ____ 1. Sim; 2. Não; 3. Não sabe

41) Já usou drogas ilícitas injetáveis alguma vez na vida ____ 1. Sim; 2. Não; 3. Não sabe

42) Se sim, com que idade usou a primeira vez ____

43) Se sim, já compartilhou a mesma agulha/seringa com outras pessoas em grupo __ 1. Sim; 2. Não; 3. Não sabe

44) Se sim, atualmente na prisão usa alguma droga ilícita injetável ___ 1. Sim; 2. Não; 3. Não sabe

45) Se sim, já compartilhou a mesma agulha/seringa com colegas na prisão __ 1. Sim; 2. Não; 3. Não sabe

46) Compartilhar agulhas e seringas traz alguma doença ____ 1. Sim; 2. Não; 3. Não sabe

47) Se sim, quais doenças são causadas por compartilhar agulhas e seringas _____

48) ORIENTAÇÃO SEXUAL ____ 1. Heterossex.; 2. Homossex.; 3. Bissex.; 4. Travesti.; 5. Desconhecido

49) Já teve relação sexual com homem alguma vez na vida ____ 1. Sim; 2. Não; 3. Não sabe

50) Já teve relação sexual com algum colega na prisão ____ 1. Sim; 2. Não; 3. Não sabe

51) Que tipo de relação sexual tem com o colega ____ 1. Ativo; 2. Pas.; 3. Ativo/pas.; 4. Só oral; 5. Só masturb.; 6. Não sabe

52) Se sim, usa preservativo quando tem relação com o colega de prisão ____ 1. Sim; 2. Não; 3. Não sabe

53) VISITA INTIMA ____ 1. Sim; 2. Não

54) USO DE PRESERVATIVO NA VISITA INTIMA ____ 1. Sempre; 2. Às vezes; 3. Nunca; 4. Não se aplica

55) Se não usa, qual o motivo ____ 1. Porque não tem 2. Porque não gosta 3. Porque é com seu (ua) parceiro (a) fixo (a)

56) A prisão distribui preservativo ____ 1. Sim; 2. Não; 3. Não sabe

57) USO DE TABACO ____ 1. Sim; 2. Não; 3. Não sabe

58) Já tomou bebida alcoólica alguma vez ____ 1. Sim; 2. Não; 3. Não sabe

59) Se sim, com que idade tomou a primeira vez ____

60) Se sim, atualmente na prisão toma bebida alcoólica ____ 1. Sim; 2. Não; 3. Não sabe

61) NOS ÚLTIMOS 30 DIAS VOCÊ FOI VACINADO COM A VACINA DA GRIPE (INFLUENZA H1N1): ___ 1 Sim 2 ___Não

Resultados de exames para hepatite B e hepatite C

HBsAg ____ 1. Reagente; 2. Não reagente; 3. Indeterminado
Anti-HBs ____ 1. Reagente; 2. Não reagente; 3. Indeterminado
Anti-HBc total ____ 1. Reagente; 2. Não reagente; 3. Indeterminado
Anti-HCV ____ 1. Reagente; 2. Não reagente; 3. Indeterminado

Resultados de exames sorológico de HIV
1ª. amostra - Anticorpos e/ou antígenos do HIV – Etapa I _____ 1.Reagente 2. Não reagente 3. Indeterminado
2ª. amostra - Anticorpos e/ou antígenos do HIV – Etapa II_____ 1.Reagente 2. Não reagente 3. Indeterminado

Sorologia para sífilis
Amostra _____ para sífilis 1.Reagente 2. Não reagente 3. Indeterminado

7. ANEXOS

7.1 Parecer do Comitê de Ética em Pesquisa

UNIVERSIDADE ESTADUAL DO OESTE DO PARANÁ/

Plataforma Brasil

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: PREVALÊNCIA DE HIV E HEPATITE B E C NA POPULAÇÃO CARCERÁRIA DAS PENITENCIÁRIAS DO ESTADO DO PARANÁ

Pesquisador: Lirane Elize Defante Ferreto de Almeida

Área Temática:

Versão: 2

CAAE: 33349314.9.0000.0107

Instituição Proponente: UNIVERSIDADE ESTADUAL DO OESTE DO PARANA

Patrocinador Principal: Secretaria de Vigilância em Saúde
Universidade Estadual do Oeste do Paraná/ UNIOESTE

DADOS DO PARECER

Número do Parecer: 810.574

Data da Relatoria: 25/09/2014

Apresentação do Projeto:

Projeto de pesquisa bem apresentado e de relevância para o estado do Paraná.

Objetivo da Pesquisa:

Claros e concisos.

Avaliação dos Riscos e Benefícios:

A avaliação de risco e benefícios foi realizada dentro de parâmetros éticos condizentes com a metodologia de pesquisa proposta.

Comentários e Considerações sobre a Pesquisa:

Foram feitas as considerações indicadas em parecer anterior.

Considerações sobre os Termos de apresentação obrigatória:

Foram adequados conforme indicação.

Recomendações:

Sem recomendações.

Conclusões ou Pendências e Lista de Inadequações:

Aprovado.

Endereço: UNIVERSITARIA
Bairro: UNIVERSITARIO **CEP:** 85.819-110
UF: PR **Município:** CASCAVEL
Telefone: (45)3220-3272 **E-mail:** cep.prppg@unioeste.br

7.2 Normas da revista

THE BRAZILIAN JOURNAL OF INFECTIOUS DISEASES

Official publication of the Brazilian Society of Infectious Diseases

AUTHOR INFORMATION PACK

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ISSN: 1413-8670

DESCRIPTION

The Brazilian Journal of Infectious Diseases is the official publication of the Brazilian Society of Infectious Diseases (SBI). It aims to publish relevant articles in the broadest sense on all aspects of microbiology, infectious diseases and immune response to infectious agents.

The *BJID* is a bimonthly publication and one of the most influential journals in its field in Brazil and Latin America with a high impact factor, since its inception it has garnered a growing share of the publishing market.

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Introduction

The Brazilian Journal of Infectious Diseases is the official publication of the Brazilian Society of Infectious Diseases (SBI). It aims to publish relevant articles in the broadest sense on all aspects of microbiology, infectious diseases and immune response to infectious agents. The BJID is a bimonthly publication and one of the most influential journals in its field in Brazil and Latin America with a high impact factor, since its inception it has garnered a growing share of the publishing market.

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Book chapter
Taylor DM, Personnet J. Epidemiology and natural history of Helicobacter pylori infection. In: Blaser MJ, Smith PD, Ravdin J eds. Infections of the gastrointestinal tract. New York: Raven Press, 1994.

Book
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Abstract
Blatt SP, Butzin CA, Lucey DR, Melcher GP, Hendrix CR. Anergy status and CD4 CD29 memory T-cells predict progression to AIDS (abstract PoB 3480). In: Program and abstracts: VIII International Conference on AIDS (Amsterdam). Amsterdam: CONGREX Holland, 1992.

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