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CYNTHIA BRAGA DA CUNHA

**"Vulnerabilidades entre homens que fazem sexo com
homens em uma coorte do Rio de Janeiro, Brasil:
Estudos sobre sexo anal desprotegido e sobre doenças
sexualmente transmissíveis"**

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CYNTHIA BRAGA DA CUNHA

Tese apresentada ao Curso de Pós-Graduação em Pesquisa Clínica em Doenças Infecciosas do Instituto de Pesquisa Clínica Evandro Chagas para obtenção do grau de Doutor

Orientadores: RUTH KHALILI FRIEDMAN

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CUNHA, CB. Rio de Janeiro, 2013. **Vulnerabilidades entre homens que fazem sexo com homens em uma coorte do Rio de Janeiro, Brasil: Estudos sobre sexo anal desprotegido e sobre doenças sexualmente transmissíveis.** Tese [Doutorado em Pesquisa Clínica em Doenças Infecciosas] – Instituto de Pesquisa Clínica Evandro Chagas.

Resumo do Artigo 1: Sexo anal desprotegido entre homens que fazem sexo com homens vivendo com HIV no Brasil: um estudo transversal no Rio de Janeiro

Introdução: Muitos países estão enfrentando epidemias de HIV concentradas em populações vulneráveis, incluindo a população de homens que fazem sexo com homens (HSH). Sexo anal desprotegido (UAI) é a principal via de transmissão do HIV neste grupo e a compreensão dos fatores associados a esta prática nas diferentes culturas existentes nesta população. Como esta prática se associa à transmissão do HIV, à reinfeção e ao desenvolvimento da resistência do HIV aos antirretrovirais, representa importantes implicações para a saúde pública. Dados sobre UAI na população brasileira de HSH são escassos. Este estudo tem como objetivo avaliar a prevalência e fatores associados a UAI entre os HSH infectados pelo HIV que tiveram relações sexuais com parceiros soronegativos ou com sorologia desconhecida do sexo masculino.

Métodos: Trata-se de um estudo transversal conduzido em uma coorte do Instituto de Pesquisa Clínica Evandro Chagas (IPEC/Fiocruz) Rio de Janeiro, Brasil. Os 155 HSH incluídos no estudo responderam a uma entrevista ACASI e forneceram amostras biológicas. Modelos lineares generalizados foram utilizados para identificar as variáveis associadas com UAI.

Resultados: No total, UAI com parceiro masculino com status sorológico para o HIV negativo ou desconhecido foi relatado por 40,6% (63/150) dos HSH. Abuso sexual ou violência doméstica na vida foi relatado por 35,9%, sendo mais frequente entre os HSH que relataram UAI do que entre aqueles que não o relataram ($P = 0,001$). O uso de estimulantes antes do sexo foi relatado por 20% do HSH, sendo um pouco maior entre aqueles que relataram UAI (27,0% vs 15,2%, $P = 0,072$). Sexo comercial foi frequente entre os HSH (48,4%). Após a modelagem multivariada, HSH com relato de abuso sexual ou violência doméstica na vida ($RC = 2,70$, IC 95%: 1,08-7,01), sexo comercial

(RC = 2,28, IC 95%: 1,04-5,10), parceiros sexuais masculinos ($p = 0,039$) e sexo anal exclusivamente receptivo (RC = 0,21, 95% IC:0,06-0,75) foram associados a UAI. Níveis de CD4, carga viral para o HIV e terapia anti-retroviral não foram associados com UAI.

Conclusões: A prevalência de UAI encontrada para os parceiros com status sorológico para o HIV negativo ou desconhecido aponta a necessidade de diferentes tipos de intervenções como ferramentas adicionais de prevenção para os HSH mais vulneráveis. Os principais fatores associados a UAI foram abuso sexual ou violência doméstica na vida, sexo comercial e número de parceiros sexuais masculinos. Este agrupamento de diferentes problemas comportamentais, sociais e de saúde nessa população reforça a necessidade de uma abordagem abrangente no tratamento e prevenção do HIV entre HSH.

Palavras-chave: Homens que fazem sexo com homens, HIV, sexo anal desprotegido, países emergentes.

Resumo do Artigo 2: *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and sífilis entre homens que fazem sexo com homens no Brasil

Introdução: Doenças sexualmente transmissíveis (DST) são frequentemente assintomáticas e aumentam a plausibilidade de transmitir e adquirir HIV. No Brasil, as diretrizes padronizadas para o diagnóstico e tratamento de DST são baseados em uma abordagem sindrômica. Os testes de amplificação de ácidos nucleicos (TAAN) tem sido recomendados como exames de rotina para DST em alguns países, especialmente para homens que fazem sexo com homens (HSH). Dados limitados são disponíveis sobre como melhor definir os grupos alvo para realizar os exames de rotina utilizando TAAN dentro desta população. O objetivo deste estudo foi avaliar a prevalência de infecção *Neisseria gonorrhoeae* (NG) / *Chlamydia trachomatis* (CT) retal ou uretral e sífilis, bem como os fatores associados com a ocorrência de pelo menos uma DST entre os HSH infectados e não infectados pelo HIV no Rio de Janeiro, Brasil.

Métodos: De Agosto 2010 a Junho 2012, 391 HSH foram incluídos na coorte de homens do Instituto Nacional de Infectologia Evandro Chagas (INI) – FIOCRUZ, e 292 HSH (HIV-positivos: 211 e HIV-negativos: 81) foram incluídos no estudo. Os TAAN foram realizados em swabs retais e urina para CT e NG. O teste rápido de reagina de plasma e o ensaio para microhemaglutinação para *Treponema pallidum* foram realizados para o diagnóstico de sífilis.

Resultados: A prevalência geral de DST foi de 20,0% (IC 95%: 15,7-25,1): 10% clamídia ano-rectal; sífilis 9,9%; gonorréia ano-rectal 2,5%; e clamídia uretral 2,2%; não foi detectado nenhum caso de gonorrhoeae uretral. A proporção de HSH HIV-positivos que tiveram pelo menos uma DST era quase duas vezes maior do que HSH HIV-negativos (22,6% vs. 13,2%, $P = 0,09$). A frequência de cada DST, exceto para NG ano-rectal (1,5% vs. 5.2%), foi maior entre os HIV-positivos do que entre os indivíduos HIV-negativos. Entre os 211 participantes assintomáticos, 17,5% ($n = 37$) foram identificadas como tendo pelo menos uma DST; 10,4% ($n = 22/211$) apresentaram resultado positivo para clamídia ano-rectal. Sessenta e cinco por cento dos HSH HIV-positivos eram assintomáticos no momento do diagnóstico de DST, enquanto que 100,0% do HSH HIV-negativos eram. Idade (RPA [Razão de Prevalência Ajustada] = 0,78; IC 95%: 0,60-1,00 para cada dez anos a mais) e um status sorológico HIV positivo

(RPA [Razão de Prevalência Ajustada] = 2,05; IC 95%: 1,03-4,08) foram significativamente associados com o diagnóstico de DST.

Conclusões: Observou-se uma alta taxa global de prevalência de DST, especialmente entre os HIV-positivos e em indivíduos mais jovens, e a maioria das DST eram assintomáticas. A triagem de DST utilizando TAAN entre os HSH assintomáticos é uma intervenção potencialmente custo-efetiva para a prevenção da infecção pelo HIV entre HSH.

Palavras-chave: Doenças sexualmente transmissíveis; Condições de recursos limitados; HIV; Prevenção; *Chlamydia trachomatis*; *Neisseria gonorrhoeae*; Técnicas de Amplificação de Ácido Nucleico; Brasil

CUNHA, CB. Rio de Janeiro, 2013. Vulnerabilities among men who have sex with men in a cohort of Rio de Janeiro, Brazil: Studies on unprotected anal intercourse and on sexually transmitted diseases. Tese [Doutorado em Pesquisa Clínica em Doenças Infecciosas] – Instituto de Pesquisa Clínica Evandro Chagas.

Artigo 1 “Unprotected sex among men who have sex with men living with HIV in Brazil: a cross-sectional study in Rio de Janeiro”

Abstract

Background: Many countries are facing concentrated HIV epidemics among vulnerable populations, including men who have sex with men (MSM). Unprotected anal intercourse (UAI) is the main HIV transmission route among them and its understanding in the different cultures and how it relates to HIV transmission, re-infection and development of HIV antiretroviral resistance has important public health implications. Data on UAI among Brazilian MSM are scarce. This study aims to evaluate the prevalence and associated factors of UAI among HIV-infected MSM who had sex with seronegative or male partners with an unknown serostatus.

Method: A cross-sectional study nested in a cohort was conducted in Rio de Janeiro, Brazil. The one hundred and fifty five MSM included in the study answered an ACASI interview and provided biological samples. Generalized linear models were used to identify variables associated with UAI.

Results: Overall, UAI with an HIV-negative or unknown serostatus male partner was reported by 40.6% (63/155) of MSM. Lifetime sexual abuse or domestic violence was reported by 35.9%, being more frequent among MSM who reported UAI compared to those who did not ($P=0.001$). Use of stimulants before sex was reported by 20% of the MSM, being slightly higher among those who reported UAI (27.0% vs. 15.2%; $P=0.072$). Commercial sex was frequent among all MSM (48.4%). After multivariate modeling, the report of sexual abuse or domestic violence (OR=2.70; 95%CI: 1.08-7.01), commercial sex (OR=2.28; 95%CI: 1.04- 5.10), the number of male sexual partners ($p=0.039$) and exclusively receptive anal intercourse (OR=0.21; 95%CI: 0.06-

0.75) remained associated with UAI. CD4 levels, HIV viral load and antiretroviral therapy were not associated with UAI.

Conclusion: The UAI prevalence found with negative or unknown HIV status partners points out that other interventions are needed as additional prevention tools to vulnerable MSM. The main factors associated with UAI were a lifetime history of violence, commercial sex and the number of male sexual partners. This clustering of different behavioral, health and social problems in this population reinforce the need of a comprehensive approach on treating and preventing HIV among MSM.

Key words: Men who have sex with Men, HIV/AIDS, Unprotected anal intercourse, Low and middle income countries.

Artigo 2 “*Chlamydia trachomatis*, *Neisseria gonorrhoeae* and syphilis among men who have sex with men in Brazil”

Abstract

Background: Sexually transmitted diseases (STD) are frequently asymptomatic and increase the likelihood of transmitting and acquiring HIV. In Brazil, the guidelines for STDs diagnosis and treatment are based on the syndromic approach. Nucleic acid amplification tests (NAAT) has been recommended as routine STDs screening in some countries, especially for men who have sex with men (MSM). Limited data are available about how to best define target groups for routine screening by NAATs within this population. We aimed to assessed the prevalence of rectal and urethral *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) infections and syphilis, and the factors associated with having at least one STD among HIV-infected and uninfected MSM in Rio de Janeiro, Brazil.

Methods: From August 2010 to June 2012, 391 MSM were enrolled into the Evandro Chagas National Institute of Infectious Diseases-INI-Fiocruz cohort, and 292 MSM (HIV-infected:211 and HIV-uninfected:81) were included in this study. NAATs were performed on the rectal swabs and urine for CT and NG. The rapid plasma reagin test and microhemagglutination assay for *Treponema pallidum* were performed for syphilis diagnosis.

Results: The overall prevalence of STD was 20.0% (95%CI:15.7-25.1): 10% anorectal chlamydia; syphilis 9.9%; anorectal gonorrhoeae 2.5%; and urethral chlamydia 2.2%; no case of urethral gonorrhoeae was detected. The proportion of HIV-positive MSM who had at least one STD was nearly two times that of HIV-negative MSM (22.6% vs 13.2%; $P = 0.09$). The frequency of each STD, except for anorectal NG (1.5% vs.5.2%), was higher among HIV-positive than HIV-negative individuals. Among the 211 asymptomatic participants, 17.5% ($n = 37$) were identified as having at least one STD; 10.4% ($n = 22/211$) tested positive for anorectal chlamydia. Sixty five percent of HIV-positive MSM were asymptomatic at the time of the STD diagnosis, while 100.0% of the HIV-negative MSM. Age (APR = 0.78; 95%CI:0.60-1.00 for each additional ten years) and a positive-HIV serostatus (APR = 2.05; 95%CI:1.03-4.08) were significantly associated with STD diagnosis.

Conclusion: An overall high STD-prevalence rate was observed, especially among HIV-infected and in younger individuals, and the majority of STDs were asymptomatic. STD screening using NAATs among asymptomatic MSM is a potentially cost-effective intervention for the prevention of HIV infection among MSM.

Keywords: Sexually transmitted diseases; Resource limited settings; HIV prevention; Rectal clamydia; Rectal gonohrea; Nucleic acid amplification tests (NAAT), Brazil

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LISTA DE SIGLAS E ABREVIATURAS

ACASI	Audio Computer Assisted Interview
AIDS	Síndrome da Imunodeficiência Adquirida
ARV	Antirretrovirais
CDC	Centro de Controle e Prevenção de Doenças
CT	<i>Chlamydia trachomatis</i>
DST	Doença Sexualmente Transmissível
ELISA	Ensaio Imunoenzimático
cART	Tratamento Antirretroviral Combinado
HIV	Vírus da Imunodeficiência Humana
HSH	Homens que Fazem Sexo com Homens
IC	Intervalo de Confiança
IPEC/FIOCRUZ	Instituto de Pesquisa Clínica Evandro Chagas/Fundação Oswaldo Cruz
INI/FIOCRUZ	Instituto Nacional de Infectologia Evandro Chagas/Fundação Oswaldo Cruz
NAAT	Teste de Amplificação de Ácidos Nucléicos
NG	<i>Neisseria gonorrhoeae</i>
OMS	Organização Mundial de Saúde
ONG	Organização Não-Governamental
RC	Razão de Chances
UAI	Prática Sexual Anal Desprotegida

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1 INTRODUÇÃO

Desde o início da epidemia de HIV/AIDS nos anos 1980, o Ministério da Saúde do Brasil, em parceria com algumas ONGs/AIDS, e em sintonia com o movimento das autoridades de saúde dos países mais desenvolvidos, identificou os homens que fazem sexo com homens (HSH) como uma das parcelas da população mais atingidas pela infecção e que, portanto, mais demandava políticas de prevenção e de assistência. O Brasil tornou-se um modelo de abordagem dessa epidemia entre os países em desenvolvimento. Entretanto, muitos países da América Latina, Caribe, África, Ásia Central e Europa do Leste levaram mais de duas décadas para identificarem a associação entre HIV/AIDS e HSH, assumindo que esse perfil da epidemia não se restringia aos países mais ricos. A demora em incluir os HSH como parcela da população vulnerável ao HIV nesses países esteve e ainda está bastante relacionada à invisibilidade social de tais pessoas, moralmente estigmatizadas, ou mesmo criminalizadas, por sua orientação sexual preferencial, o que levou à sua subnotificação pelas autoridades sanitárias. Em mais de 80 países, a homossexualidade leva a penas que variam de períodos de prisão a pena de morte. Assim, em diversos países, os HSH não têm acesso, ou têm acesso muito limitado aos serviços de prevenção, tratamento e assistência especializados em HIV/AIDS. (Beyrer et al., 2010)

Homens fazem sexo com homens num cotidiano de busca de prazer e de relações humanas que, evidentemente, não se conduzem por prescrições dos profissionais da área da saúde. A prevenção da infecção por HIV/AIDS e das demais doenças sexualmente transmissíveis (DST), portanto, nem sempre está no escopo das atitudes e práticas sexuais entre os HSH, embora possa representar uma preocupação na conformação de seus relacionamentos.

No Brasil, um estudo sobre a distribuição da epidemia, no período de 2002 a 2006, segundo a população das cidades (Grangeiro et al., 2010) concluiu que esta se mantém concentrada nas grandes cidades, e dentro de contextos que favorecem o aumento da taxa de infecção em determinados grupos. Tais contextos, essencialmente urbanos, permitem que, a partir das relações sociais e das práticas individuais, se visualizem panoramas de vulnerabilidade, como a intolerância e a violência sexual contra os HSH, com importante papel nas reais possibilidades de novas infecções. Da mesma forma, o uso de drogas e as relações homossexuais e bissexuais continuam a ser relevantes na epidemia; esses grupos apontam para os maiores riscos de infecção e tendem a crescer nas cidades analisadas. A redução no compartilhamento de seringas para uso de drogas não se refletiu na prevenção da

transmissão sexual, e o incremento do uso de outras drogas, como o crack, implica num maior risco de infecção. A epidemia no Brasil continua a ocorrer em áreas de maior nível de desenvolvimento humano, portanto, o chamado ‘empobrecimento da epidemia’ está ainda associado às características dos grandes centros: diferenças sociais e bolsões de pobreza. (Grangeiro, 2010)

1.1 HSH e relações anais desprotegidas

No período que seguiu o início da epidemia de HIV, nos Estados Unidos, houve reduções dramáticas nas práticas sexuais anais desprotegidas (UAI) entre HSH, tanto pelo hábito do uso de preservativos (Jin *et al.*, 2009) quanto pela abstinência sexual (Di Pietro, 2006).

A abstinência sexual, por sua vez, pode ter diferentes conceitos, que variam entre a ausência de contato sexual e a ausência de penetração; nenhuma dessas práticas é definitiva, já que todos podem se envolver em novas relações (Di Pietro, 2006). Nos Estados Unidos, o número de casos novos de AIDS entre os HSH só declinou de fato após o advento da cART (Tratamento Antirretroviral Combinado), em 1996, apesar da disseminação dessas práticas de sexo mais seguro. Mesmo assim, em 2004, um inquérito epidemiológico realizado pelo CDC (Centro de Controle e Prevenção de Doenças) em cinco cidades norte-americanas, revelou a vulnerabilidade dos HSH, pois entre 1767 HSH com uma média de 32 anos de idade, a taxa geral de infecção foi de 25%; entre os negros, que somam estigmas sociais, a taxa de infecção chegou a 46%, dos quais 67% não conheciam seu status sorológico (Di Pietro, 2006). Por outro lado, Cairns (2013) indica que gays negros relatam significativamente menos relações sexuais desprotegidas do que gays brancos, independentemente do status sorológico para o HIV. Dentre os homens com HIV, 56% dos negros e 68% dos brancos relataram sexo desprotegido ao menos uma vez em 2011; dentre os HIV-negativo e não testados, o sexo desprotegido ocorreu em, respectivamente, 49% e 58%, com taxas ainda mais altas (62%) nos homens HIV-negativo de origem hispânica. (Cairns, 2013)

Segundo Frost et al. (2008), uma parte da literatura especializada na prevenção do HIV se deteve em identificar práticas sexuais de risco e de redução de risco, desconsiderando, de alguma forma, questões mais profundas e mais amplas, como o desejo de estabelecer conexões íntimas com outras pessoas, o que pode estar fortemente associado à UAI. Para alguns homens, o preservativo representa uma barreira para a satisfação e para a intimidade

sexual, seja para encontros eventuais, namoros e relacionamentos duradouros. (Frost et al., 2008)

Uma meta-análise conduzida por Crepaz et al. (2009), a partir de trinta estudos norte-americanos relacionados a fatores preditores para UAI entre HSH soropositivos para o HIV no período de 2000 a 2007, revelou que a prevalência de UAI foi muito mais relevante quando o(s) outro(s) parceiro(s) eram soropositivos (30%) do que quando eram desconhecidos (16%) ou negativos (13%). Esses autores perceberam também que fatores como o uso de antirretrovirais, assim como a observação de carga viral indetectável e a adesão à medicação maior do que 90% não foram fatores associados à UAI. (Crepaz et al., 2009)

No Brasil, há alguns estudos sobre sexo desprotegido envolvendo os HSH. Um deles foi conduzido em cidades importantes de dez estados (Rocha et al., 2013), com 3.449 participantes HSH, infectados ou não pelo HIV no período de 2008 a 2009. Nesse estudo, a maioria dos fatores associados a essa prática foi bastante semelhante à literatura internacional, apesar de os autores não terem discriminado os dados com base no status sorológico para o HIV, o que prejudica possíveis inferências sobre a relação entre comportamento sexual e transmissão do HIV. No que diz respeito aos fatores comuns entre este e o nosso trabalho, temos que a prevalência geral da infecção pelo HIV foi de 14,2%, variando entre 5,2% (Recife) e 23,7% (Brasília); a prevalência geral de relações sexuais desprotegidas receptivas nos seis últimos meses foi de 36,5%, variando entre 24,4% em Itajaí e 40,1% em Curitiba. A maioria dos HSH (57,5%) tinha mais de 25 anos, se auto-identificavam como não-brancos; a escolaridade maior que 12 anos variou entre 65,2% em Belo Horizonte e 8,4% em Santos; a maioria era de solteiros ou de HSH que viviam sozinhos (84,5%) e 10,8% viviam com um parceiro masculino. O uso de álcool por, no mínimo, duas vezes por semana foi relatado por 63,6% dos participantes, enquanto 43,5% relatou uso de alguma droga ilícita. A maioria dos participantes (77,4%) referiram mais de um parceiro sexual nos seis últimos meses, enquanto 57% relataram parceria estável, 69,3%, parceria casual e 31,8%, parceria comercial. Observe-se que entre os que referiram parceria estável, 69,1% também tiveram sexo com parceiros casuais e/ou comerciais. (Rocha et al., 2013)

Ainda nesse estudo (Rocha et al., 2013), as suas identidades sexuais foram relatadas como homossexuais/HSH/gay por 64% e como bissexuais como 26,5%. Aproximadamente metade dos participantes nunca haviam sido testados para o HIV. O sexo anal receptivo desprotegido também foi associado com o tipo de parceiros sexuais (28,7% entre HSH com

apenas parceiros casuais/comerciais, 40,1 % misturavam parceiros estáveis aos casuais/comerciais, e 50,8 % entre parceiros unicamente estáveis). Os HSH que relataram relações sexuais apenas com parceiros masculinos foram os que mais frequentemente se envolveram em relações anais receptivas desprotegidas. (Rocha et al., 2013)

Em outro estudo brasileiro, conduzido na Bahia (Brignol, 2008) avaliaram-se a prática do sexo oral e anal sem o uso do preservativo masculino como importante fator para a infecção pelo HIV e outras DST na população dos HSH e travestis. Trata-se de um recorte do “Projeto Convida”, inquérito sobre conhecimentos, atitudes, comportamentos e práticas de risco para a infecção pelo HIV entre HSH na cidade de Salvador, em 2003. A população do estudo foi de HSH e travestis residentes na cidade de Salvador e região metropolitana que responderam ao questionário e que frequentaram o que a autora chamou de “cena gay” desta cidade. A prática do sexo anal e oral desprotegido foi de 48,5% e 68,6% respectivamente. A associação entre os diferentes grupos dos HSH e travestis e a prática do sexo anal desprotegido foi estatisticamente significativa para o grupo dos que se sentem em médio risco de contrair HIV (RC [Razão de Chances]=2,31; IC95%=1,68-3,19), os que se sentem em alto risco de contrair HIV (RC=1,56; IC95%=1,09-2,24), os que não responderam a percepção de risco (RC=3,20; IC95%=1,05-9,77) quando comparados aos que se sentem em pouco risco de contrair HIV; os ativos e passivos que gostam de todos os tipos de prática e parceria homossexual (RC=1,67; IC95%=1,07-2,61) quando comparados aos que não tem preferência por tipo de prática ou parceria; os persuadidos/cuidadosos ao sexo desprotegido (RC=1,48; IC95%=1,16-1,89), os persuasivos e persuadidos a prática do sexo anal sem proteção (RC=6,75; IC95%=4,38-10,40) quando comparados aos que praticam sexo anal com proteção. As práticas sexuais desprotegidas são frequentes na população dos HSH e travestis da cidade de Salvador, e os HSH parecem mais vulneráveis a estas práticas sexuais do que as travestis. (Brignol, 2008)

Se, por um lado, os homens que fazem sexo anal desprotegido e relatam algum comportamento para redução de risco têm chances três vezes maiores de se infectarem com o HIV do que os que não praticam sexo anal desprotegido, por outro, eles têm possibilidades menores de se infectarem do que aqueles que não utilizam qualquer prática de redução de risco. (Jin et al., 2009) É importante destacar, também, que a eficácia do tratamento antirretroviral vem se mostrando tão alta quanto a utilização do preservativo para a redução das chances de transmissão do HIV. (Wilson et al., 2008)

Alguns estudos se dedicam a entender as razões que levam as pessoas a realizarem sexo desprotegido, colocando-se diante da possibilidade de adquirir infecções sexualmente transmissíveis e de transmiti-las a seus parceiros sexuais. Assim, identificou-se a associação entre história de abuso sexual infantil e inúmeras dificuldades de lidar com suas questões pessoais, que vão se refletir em problemas como práticas sexuais desprotegidas, abuso de drogas e de álcool, depressão, prostituição e múltiplas parcerias sexuais (Sikkema *et al.*, 2009; Mimiaga *et al.*, 2009). Um desses estudos – com o objetivo de identificar as variáveis preditivas de relações sexuais desprotegidas nos quatro meses anteriores - foi conduzido por Sikkema *et al.* (2009) nos Estados Unidos, no período de 2002 a 2004, com 256 adultos (mulheres e HSH) infectados pelo HIV que relataram abuso sexual na infância.

Neste estudo, o abuso sexual foi definido como qualquer tipo de toque de natureza sexual indesejada, realizado por um adulto ou por alguém ao menos 5 anos mais velho que o participante; o abuso sexual infantil ocorreu quando a pessoa tinha 12 anos ou menos, e o adolescente, entre 13 e 17 anos. A grande maioria dessas pessoas (90%) experimentou, na infância ou na adolescência, abuso sexual vaginal ou anal com penetração; 87% foram abusados repetidas vezes, ao longo de suas vidas e, em média, tiveram dois molestadores. Os autores observaram que, entre essas pessoas infectadas pelo HIV, o sexo desprotegido foi associado significativamente ao uso de drogas e a dificuldades comportamentais de origem traumática entre mulheres e HSH, além de menor busca espiritual entre os HSH. Da mesma forma, a maioria dessas pessoas (69%) relatou atividades sexuais nos quatro últimos meses; os HSH tiveram significativamente mais parceiros e maior probabilidade de se envolverem em qualquer tipo de sexo desprotegido e em sexo desprotegido anal/vaginal com parceiros HIV-negativos ou com status sorológico desconhecido. (Sikkema *et al.*, 2009)

Nos Estados Unidos, o estudo EXPLORE foi o primeiro estudo a demonstrar uma relação preditiva entre a história de abuso sexual na infância e índices maiores de infecção por HIV entre os HSH não infectados. Foi um ensaio de intervenção comportamental conduzido durante quatro anos em seis cidades no período de , com 4244 participantes incluídos na abordagem inicial. O abuso infantil foi definido como “ter tido uma experiência sexual antes dos 13 anos de idade com alguém ao menos 5 anos mais velho” e/ou “ter tido uma experiência sexual entre os 13 e os 17 anos com alguém que fosse ao menos 10 anos mais velho”. Dentre esses participantes, 1686 (39,7%) relataram história de abuso sexual na infância, o que

aumenta as possibilidades de que essas pessoas se envolvam em relações anais desprotegidas e em relações anais desprotegidas sorodiscordantes. (Mimiaga *et al.*, 2009)

Esse estudo observou que a história de abuso sexual na infância era mais provável entre os HSH hispânicos ou negros, com menor escolaridade, desempregados e mais pobres. Os HSH que sofreram abuso sexual na infância também tinham maiores possibilidades de desenvolver depressão, de usar álcool e drogas ilícitas, além de serem menos eficientes na adoção de práticas sexuais mais seguras, de serem menos habilidosos a respeito das suas formas de comunicação sobre sexo mais seguro, e de possuírem normas sexuais menos seguras. (Mimiaga *et al.*, 2009)

Algumas tentativas de redução da transmissão do HIV durante o sexo anal desprotegido entre os HSH são descritas em alguns estudos. Entre os extremos das práticas de risco deliberado – barebacking – e a abstinência sexual, várias atitudes e comportamentos sexuais entre os HSH que se envolvem em relações sexuais anais desprotegidas concorrem de forma mais ou menos efetiva para evitar ou reduzir as possibilidades da infecção pelo HIV, segundo vários autores e diferentes coortes. A maioria dos autores concorda que as práticas de ‘serosorting’ (seleção por sorologia para HIV) podem ser úteis e preventivas, na perspectiva dos HSH HIV-negativo, assim como a ‘posição estratégica’ (insertiva ou receptiva) (Parsons *et al.*, 2005), o coito interrompido (Jin *et al.*, 2009) e a ‘segurança negociada’ (Kippax *et al.*, 1997). Além disso, entre os homens HIV-positivo, existem ‘abordagens de redução de danos’, que são um tipo útil de ‘serosorting’. (Crepaz *et al.*, 2009; Jin *et al.*, 2010)

Na prática da ‘posição estratégica’, o homem HIV-negativo tem apenas um papel insertivo (Jin *et al.*, 2009); esse fenômeno tem sido cada vez mais relatado quando os HSH se envolvem em relações anais desprotegidas sorodiscordantes a fim de reduzirem seu risco. (Jin *et al.*, 2010) No coito interrompido, o homem HIV-negativo só se envolve numa relação anal desprotegida receptiva se não ocorrer ejaculação no interior do reto. (Jin *et al.*, 2009). Os homens que praticam a ‘segurança negociada’ acreditam que dispensar os preservativos pode ser uma atitude segura sob determinadas situações: se os parceiros sexuais estão num relacionamento estável, se ambos são HIV-negativo e conhecem o status HIV-negativo do parceiro, e tenham chegado a um acordo inequívoco sobre a natureza de suas práticas sexuais fora desse relacionamento. (Kippax *et al.*, 1997)

1.2. Clamídia, gonorreia e sífilis entre HSH

As DST são consideradas como um dos problemas de saúde pública mais comuns em todo o mundo. Em ambos os sexos, tornam o organismo mais vulnerável a outras infecções, além de terem relação com a mortalidade materna e infantil. Sabe-se que, num nível mundial, as principais infecções bacterianas sexualmente transmissíveis são causadas por *Chlamydia trachomatis* (CT) e por *Neisseria gonorreae* (NG) (Dudareva-Vizule *et al.*, 2013). No Brasil, as estimativas da Organização Mundial de Saúde (OMS) de infecções de transmissão sexual na população sexualmente ativa, independentemente de gênero ou orientação sexual, a cada ano, são: 937.000 casos de sífilis, 1.541.800 casos de gonorreia e 1.967.200 casos de clamídia. (www.aids.gov.br)

Num estudo realizado em seis capitais brasileiras no ano de 2005, a prevalência de gonorreia entre homens que procuraram clínicas de DST que referiram relações heterossexuais foi de 17,2% (110/639); a dos bissexuais, 24,6% (14/57); e a dos que tiveram relações exclusivamente homossexuais foi de 30,6% (15/49), existindo diferença estatisticamente significativa ($P=0,030$) quando se comparam os três grupos entre si, estimando-se risco duas vezes maior de infecção para os que referiram relações homossexuais quando comparados com os heterossexuais ($RC=2,12$; $IC95\%=1,06-4,20$). Também se estimou um risco de infecção gonocócica acrescido para os HSH quando comparados com os heterossexuais ($RC=1,81$; $IC95\%=1,10-2,98$). Em relação à infecção por clamídia, sua prevalência nos homens heterossexuais foi 12,6% (81/641); nos bissexuais, 14,0% (8/57) e nos que tiveram relações exclusivamente homossexuais, 18,0% (9/50); mas não houve diferença estatisticamente significativa quando se comparou os três grupos entre si ($p=0,540$), não se observando maior vulnerabilidade associada a uma determinada prática sexual. A prevalência de sífilis nos que relataram relações heterossexuais foi de 3,5% (24/683); nos que informaram relações homossexuais, 1,9% (1/29) e nos bissexuais, 6,1% (4/63), e ao se compararem os três grupos não se observam entre eles diferenças estatisticamente significativas ($p=0,450$). (Ministério da Saúde, 2005) Tal discrepância entre esses resultados e outros obtidos na literatura especializada deve estar relacionada a algumas questões do desenho deste estudo do Ministério da Saúde: os HSH não foram a população alvo, a avaliação em clínicas especializadas em DST não contemplou os assintomáticos, e a avaliação da presença de clamídia e de gonorreia se restringiu ao exame da urina.

Logo após o início da epidemia de HIV/AIDS, a prevalência de DSTs entre HSH declinou nos Estados Unidos, mas no final da década de 1990 surgem relatos de aumento do

número de casos de gonorreia retal e de sífilis neste país. (Mimiaga *et al.*, 2009) Nesse mesmo sentido, a incidência de proctite por clamídia e outras síndromes gastrintestinais sexualmente transmitidas, como sífilis e gonorreia, muito frequentes nos anos 1970 e 1980, foi reduzida, possivelmente devido ao uso de preservativos, e aumentou entre os HSH a partir do final dos anos 1990 em muitas cidades dos Estados Unidos e na Europa. (Singh e Marazzo, 2013)

No Brasil, um estudo (Ribeiro *et al.*, 2012) descreveu a prevalência de sífilis por região geográfica e a frequência de comportamentos e sintomas relacionados às DST entre 35460 conscritos com média de idade de 18 anos incluídos no estudo no ano de 2007. Os conscritos se submeteram a um teste treponêmico (ELISA) e responderam a um questionário comportamental e sócio-demográfico; 26417 (74,5%) já haviam tido relações sexuais com penetração. Cento e quarenta e sete resultados foram positivos (0,55%) e a prevalência por região geográfica foi de 0,85% no Norte, 0,82% no Nordeste, 0,34% no Sudeste, 0,26% no Sul e 0,49% no Centro-Oeste. O estudo mostrou a associação entre ter tido sífilis e ter 17 anos, ter escolaridade menor ou igual a 8 anos, viver nas regiões Norte e Nordeste, ser HSH, ter história prévia de DST e de úlceras genitais. Não houve resultados positivos entre os que não relataram relações sexuais. Os autores concluem sobre a importância de se aproveitar o período do alistamento militar para considerar novas estratégias de acesso e de aconselhamento desta população, permitindo, assim a implementação de uma política de cuidados de saúde mais apropriada. (Ribeiro *et al.*, 2012)

A transmissão das DST, segundo Singh e Marazzo (2013), é facilitada pelo grande número de parceiros sexuais, por práticas sexuais específicas – como intercurso anal e anilingus – e pelo fato de que a infecção pode ser provocada por um inóculo pequeno. Alguns autores (Repiso *et al.*, 2010), por estimarem também que o recente ressurgimento da sífilis em uma unidade de saúde de Málaga, Espanha, se devesse ao comportamento sexual, descreveram, em 2007 e 2008, a incidência desta doença em uma clínica e investigaram sua relação com os hábitos sexuais dos HSH. No período de dois anos, foram registrados 26 casos novos de sífilis, dos quais 19 eram sífilis precoce. Oito pacientes estavam coinfectados com HIV e 15 eram HSH; havia um grupo controle de 65 HSH sem sífilis. Os HSH com sífilis tiveram maior número de parceiros sexuais: RC 3,98 (IC95%=0,90-17,46) para a categoria “2 a 5 parceiros sexuais”; RC 3,22 (IC95%= 0,84-12,43) para a categoria “mais de 5 parceiros sexuais” quando comparados à categoria menos que 2 parceiros sexuais. O uso inconsistente de preservativos também foi significativamente mais comum entre os HSH com sífilis do que

os sem sífilis (RC 3,96; IC95%=1,15–13,61). Dessa forma, os autores concluem sobre a importância de programas públicos de prevenção da sífilis que considerem os HSH como público alvo prioritário. (Repiso *et al.*, 2010)

Na costa do Quênia, antes do início de um pequeno estudo para profilaxia pré-exposição ao HIV-1, foram triados 43 voluntários HIV-negativo de uma coorte de HSH com práticas de risco, para avaliar a presença de CT e de NG através de NAAT (Teste de Amplificação de Ácidos Nucléicos). A média de idade foi de 27 anos; nenhum dos voluntários relatou descarga uretral, mas um tinha disúria e outro, dor retal. Desse total, 11 (26%) HSH tiveram infecção por clamídia (excluído o linfogranuloma venéreo), gonorreia ou ambas; seis homens tiveram infecção uretral (5 por CT e 1 por NG) e cinco tiveram infecção retal (uma por CT, duas por NG e duas coinfeções). (Sanders *et al.*, 2010)

Na Alemanha, em 2012, foi conduzido um estudo em 22 sites que atendiam DST, com a finalidade de analisar fatores associados à presença de clamídia e gonorreia na faringe e no reto de 2247 HSH com mediana de idade de 34 anos, além de uma subamostra de 685 participantes que foram testados para infecção uretral. A prevalência de clamídia foi 1,5% nas amostras da faringe e 8,0% nas amostras retais, enquanto que para a gonorreia foi 5,5% e 4,6%, respectivamente. É importante que se observe que 90,8% dessas infecções permaneceriam indetectadas se apenas fossem testados os indivíduos sintomáticos, pois os sintomas faringianos foram relatados em apenas 5,1%, e os retais, em 11,9% das infecções. A infecção retal foi significativamente mais frequente quando os homens relataram múltiplos parceiros (2–5 parceiros: RC=1,85 / 6–10 parceiros: RC=2,10 / >11 parceiros: RC=2,95), quando tinham diagnóstico de HIV (RC=1,60) e prática anal receptiva sem preservativos (RC=1,54). A probabilidade de infecção faringiana também foi maior nos homens que relataram múltiplos parceiros (6–10 parceiros: RC=2,88 / >11, RC=4,96) e nos que tinham diagnóstico de HIV (RC=1,78). Na subamostra dos 685 participantes que foram testados para infecção uretral, 5,0% (IC95%=3,3%-6,6%) foram positivos. Foi detectada coinfeção por clamídia e gonorreia faringiana, retal e uretral em 0,3%, 1,0% e 0,3% das respectivas amostras. Setenta e cinco por cento das infecções por clamídia eram exclusivamente retais; as infecções por gonorreia foram 30% exclusivamente retais, 38% exclusivamente faringianas e 20% retais e faringianas concomitantemente. Se tivesse sido realizado somente um teste retal isolado, apenas 67% (64/96) das infecções seriam reveladas; um teste faringiano isolado revelaria 35% (34/96), e um teste uretral/urina revelaria 24% (23/96) das infecções. Por outro

lado, a associação de exame retal e faringiano revelaria 89% (85/96) das infecções prevalentes (Dudareva-Vizule *et al.*, 2013).

Os resultados encontrados por Dudareva-Vizule *et al.* (2013) assemelham-se a vários estudos, assim como aos de Kent *et al.* (2005) em duas clínicas em São Francisco no ano de 2003, onde também foi observado um grande número de infecções retais assintomáticas – 85,0% -, o que reforça a importância de se realizar uma triagem de rotina das DST para os HSH. Nesse estudo, a prevalência de clamídia e de gonorreia retal foi de 7,9 e 6,9, respectivamente; a uretral foi, respectivamente, de 5,2 e 6,0; a faringiana foi de 1,4 e 9,2, respectivamente. Os autores indicam que 53,0% das infecções por clamídia e 64,0% das gonorreias foram encontradas em sítios não uretrais e que, portanto, passariam despercebidas e não seriam tratadas caso fosse realizada apenas uma triagem uretral. O mesmo aconteceria com mais de 70,0% das infecções por clamídia se os HSH só fossem submetidos a exames para gonorreia. (Kent *et al.*, 2005)

Há um acordo entre praticamente todos os autores sobre a escassez de dados relativos à presença de DST em HSH e sobre a subestimação dessas infecções – a maioria assintomática - o que dificulta a elaboração de manuais de rastreamento para essa população. Entretanto, ao contrário da observação de Singh & Marazzo (2013), de Repiso *et al.* (2010), de Sanders *et al.* (2010) e de Kent *et al.* (2005), num estudo realizado por Cook *et al.* (2002) no ano de 1998 notaram que as infecções por clamídia e gonorreia (método PCR) foram incomuns entre os HSH de duas clínicas de Pittsburgh, nos Estados Unidos, mesmo entre aqueles com múltiplos parceiros ou entre os infectados pelo HIV. Para se ter uma ideia, de 566 HSH assintomáticos, brancos, de meia idade e envolvidos em sexo com múltiplos parceiros, a clamídia uretral foi detectada em um único indivíduo, e a anal, em apenas dois; não houve nenhum caso de gonorreia e, dentre os HSH soropositivos para o HIV, nenhum teve qualquer dessas infecções. Trata-se de um estudo cujo objetivo foi determinar a prevalência de infecções uretrais causadas por CT e NG em uma grande população de HSH a fim de acessar a viabilidade de uma triagem retal dessa população. Suas informações pretenderam colocar em questão as recomendações de triagem de todos os HSH com base em seu comportamento sexual individual ou na situação sorológica para o HIV. Tal incidência tão baixa, por se diferenciar da maior parte da literatura especializada, pode contribuir para instigar os pesquisadores interessados sobre a importância de se entenderem as diversas características comportamentais e sócio demográficas de suas populações de estudo.

O presente estudo divide-se em dois artigos. O primeiro é uma análise dos fatores relacionados às relações anais desprotegidas e o segundo, uma análise dos fatores relacionados às DST (não HIV/AIDS) da coorte de HSH do INI/Fiocruz (Instituto Nacional de Infectologia Evandro Chagas/Fundação Oswaldo Cruz). Consideramos, para este trabalho, as infecções causadas por CT e por NG retal e uretral, e sífilis.

2 OBJETIVOS

Artigo 1 “Unprotected sex among men who have sex with men living with HIV in Brazil: a cross-sectional study in Rio de Janeiro”: Avaliar a prevalência e fatores associados de sexo anal desprotegido entre HSH infectados pelo HIV e que tiveram relações sexuais com parceiros do sexo masculino soronegativos ou com sorologia desconhecida para o HIV.

Artigo 2 “*Chlamydia trachomatis*, *Neisseria gonorrhoeae* and Syphilis among men who have sex with men in Brazil”: Estimar a prevalência de sífilis e das infecções uretral e retal por NG e CT entre HSH; estudar as diferenças nas prevalências de cada DST de acordo com HIV e avaliar os marcadores de risco associados a ter pelo menos uma DST entre os HSH.

3 ARTIGOS

3.1 Artigo 1

Unprotected sex among men who have sex with men living with HIV in Brazil: a cross-sectional study in Rio de Janeiro

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Abstract

Background: Many countries are facing concentrated HIV epidemics among vulnerable populations, including men who have sex with men (MSM). Unprotected anal intercourse (UAI) is the main HIV transmission route among them and its understanding in the different cultures and how it relates to HIV transmission, re-infection and development of HIV antiretroviral resistance has important public health implications. Data on UAI among Brazilian MSM are scarce. This study aims to evaluate the prevalence and associated factors of UAI among HIV-infected MSM who had sex with seronegative or male partners with an unknown serostatus.

Method: A cross-sectional study nested in a cohort was conducted in Rio de Janeiro, Brazil. The one hundred and fifty five MSM included in the study answered an ACASI interview and provided biological samples. Generalized linear models were used to identify variables associated with UAI.

Results: Overall, UAI with an HIV-negative or unknown serostatus male partner was reported by 40.6% (63/155) of MSM. Lifetime sexual abuse or domestic violence was reported by 35.9%, being more frequent among MSM who reported UAI compared to those who did not ($P=0.001$). Use of stimulants before sex was reported by 20% of the MSM, being slightly higher among those who reported UAI (27.0% vs. 15.2%; $P=0.072$). Commercial sex was frequent among all MSM (48.4%). After multivariate modeling, the report of sexual abuse or domestic violence (OR=2.70; 95%CI: 1.08-7.01), commercial sex (OR=2.28; 95%CI: 1.04- 5.10), the number of male sexual partners ($p=0.039$) and exclusively receptive anal intercourse (OR=0.21; 95%CI: 0.06-0.75) remained associated with UAI. CD4 levels, HIV viral load and antiretroviral therapy were not associated with UAI.

Conclusion: The UAI prevalence found with negative or unknown HIV status partners points out that other interventions are needed as additional prevention tools to vulnerable MSM. The main factors associated with UAI were a lifetime history of violence, commercial sex and the number of male sexual partners. This clustering of different behavioral, health and social problems in this population reinforce the need of a comprehensive approach on treating and preventing HIV among MSM.

Key words: Men who have sex with Men, HIV/AIDS, Unprotected anal intercourse, Low and middle income countries.

Background

Men who have sex with men (MSM) remain a vulnerable population for HIV infection across the world [1]. In Brazil, HIV prevalence among the general population is below 0.6% [2]. However, in the largest study conducted in the country, HIV prevalence among MSM ranged from 9.1% to 16% [3]. Soon after the onset of the HIV epidemic, there were reductions in transmission among MSM due to the expansion of condom use [4] or even sexual abstinence [5,6]. Although condoms represent an effective barrier against sexual transmission, since the mid-1990s the proportion of men reporting unsafe sex – including “barebacking”, i.e. unprotected anal intercourse (UAI) in a risk context [7] – seems to have increased [8-11].

UAI is the main HIV transmission route among MSM [12]. Studies designed to increase the understanding about this sexual practice in the different cultures and how it relates to HIV transmission, re-infection and development of HIV antiretroviral resistance may have important public health implications. A meta-analysis from studies conducted in the US estimated an overall UAI prevalence among HIV-infected MSM at 43% (CI 95% 37-48) [12], with lower frequencies when sexual partners were of unknown (30%) or negative (16%) serostatus [12]. These differences may be related to the “sexual harm-reduction” approaches, such as serosorting (the use of the partners’ HIV serostatus - actual or presumed - as a guidance to make decisions when having UAI), strategic positioning (selectively engage in receptive UAI rather than insertive UAI) and negotiated safety (as agreements between steady couples related to sex with casual partners).[13-16].

Data on UAI prevalence and associated factors among Brazilian MSM are scarce, which limits the effectiveness of public policies designed to decrease HIV infection in this population. In a study conducted with over 3,000 HIV-positive and negative Brazilian MSM, UAI prevalence was 36.5%, and the associated factors reported were in accordance with the international literature [17]. However, the authors did not disaggregate data according to HIV serostatus, precluding inferences about attitudes and behaviors associated to HIV transmission.

Behavioral and contextual factors, specifically a higher number of sexual partners[18-20], a history of domestic or sexual violence[21,22], alcohol and illicit drug use, particularly stimulants[23-27], have been associated with UAI among MSM in the international literature. Given the importance of combined anti-retroviral therapy (cART) in the treatment and

prevention of HIV infection [28], researchers have also investigated the potential impact of its use, and consequential undetectable viral loads, on UAI reporting. Even though some results showed an increase in UAI among individuals with known undetectable viral load (UVL)[29] or with the belief that UVL decreases transmission[30], most evidence suggest that there is no association between UAI and UVL/cART use[31-34].

Considering the sustained high incidence rate of HIV among MSM and the lack of information on UAI among HIV-infected South American MSM, this paper aims to study the prevalence and associated factors of UAI among HIV-infected MSM in Brazil.

Methods

A cross-sectional analysis, nested within a cohort study was conducted at Instituto de Pesquisa Clinica Evandro Chagas (IPEC/FIOCRUZ), Rio de Janeiro, Brazil. A convenience sample of HIV–infected and non-infected high risk MSM older than 18 years was enrolled since 2010. Briefly, the cohort was designed to evaluate the prevalence and incidence of anal HPV infection and intraepithelial anal lesions. Participants were considered to be MSM if they had a male sexual partner(s) in the past 12 months, regardless of having a female partner(s).

Participants

The study population for the present analysis was a subset of HIV-infected MSM enrolled in the parent cohort, who reported having had anal intercourse with men at risk for HIV infection (HIV negative or with an unknown HIV serostatus) within the past 3 months.

Two hundred ninety four HIV-infected MSM were enrolled into the IPEC/FIOCRUZ men’s cohort from August 2, 2010 to June 30, 2012. Of these 294 MSM, a total 190 MSM were excluded from this analysis for the following reasons: 85/294 (28.9%) reported no male sexual partner/no anal intercourse in the past 3 months; 34/294 (11.6%) reported anal intercourse exclusively with an HIV-infected male partner; and 20/294 (6.8%) had missing data for anal intercourse data (Figure 1). Final sample was comprised by 155 HIV-infected MSM.

Measures

The outcome was defined as UAI with at least one man of unknown or negative HIV status in the 3 months preceding the interview.

Demographic variables were collected at enrollment visit and included: age, self-reported skin color (white and non-white) and schooling (years of formal education).

Data on behavior variables were collected during the enrollment visit via Audio Computer Assisted Interview (ACASI), which included the following:

- *Number of male partners* within the last 12 months (“During the past 12 months, how many men and how many transvestite/transsexual/transgender(s) did you have sex with?”);
- *Anal intercourse practices in the past 3 months* was measured through the following questions: a-“In the past 3 months, how many HIV-negative male partners did you have insertive anal sex with?”; b-“In the past 3 months, how many male partners, with an unknown HIV-serostatus, did you have insertive anal sex with?”; c- “In the past 3 months, how many HIV-negative male partners did you have receptive anal sex with?”; d-“In the past 3 months, how many male partners, with an unknown HIV-serostatus, did you have receptive anal sex with?”. The questions above were used to select the study population and were also used to formulate the variable “Anal intercourse practices” and its subcategories of **only insertive**, **only receptive** or **both**.
- *Unprotected anal intercourse in the past 3 months* was measured by the following questions: a- “In the past 3 months, how many HIV-negative male partners did you have insertive anal sex with, without using condoms?”; b- “In the past 3 months, how many HIV-unknown male partners did you have insertive anal sex with, without using condoms?”; c- “In the past 3 months, how many HIV-negative male partners did you have receptive anal sex with, without using condoms?”; d- “In the past 3 months, how many male partners, with an unknown HIV-serostatus, did you have receptive anal sex with, without using condoms?”.
- *Alcohol use, either before or during sex*, within the past 3 months was measured by the question “In the past 3 months, were you drunk or high before or during sex?”;

- *Stimulant use, either before or during sex*, within the past 3 months was measured by the question “In the past 3 months, did you use either inhaled or intravenous illicit drugs before or during sex?”; *Lifetime injection drug use* was measured by the question “Have you ever used intravenous illicit drugs in your life?”; however, due to limited observations, this response was not evaluated in the models.
- *Commercial sex within the past 3 months* was defined as the exchange of sex for money/other favors and/or the looking for prostitutes: “In the past 3 months, did you have sex for money, drugs or other favors?” and “In the past 3 months, did you look for prostitutes?”.
- *A lifetime history of sexual abuse or violence was determined based on a composite measure of the responses to the following 2 questions*: “Did you ever suffer domestic violence in your life?” and “Did you ever suffer sexual abuse in your life?”;

The Clinical and laboratory variables included the following:

- *Time since HIV diagnosis* was defined as the time since the first HIV-positive serology result until the date of the interview; results were presented using the median (interquartile range).
- *Combined antiretroviral therapy (cART)* was defined as the date of issuance of the initial prescription for combined antiretroviral treatment until the date of the interview. Individuals who have a cART prescription were classified as receiving cART.
- *CD4⁺ T cell count (cells/mm³)* was defined as the available result closest to the date of the interview. The specimens to measure CD4⁺ T cell count were obtained within a window period of 6 months before and up to 3 months the interview. Data was presented as median and interquartile range.
- *HIV viral load (copies/IU)*. Specimens were collected on the day of the interview and results were classified as either undetectable (less than 400 copies/IU) or detectable (equal to/higher than 400 copies/IU).

All biological analyses were performed at the IPEC Laboratories, which successfully participates in the College of American Pathologists (CAP) External Quality Assurance (EQA) proficiency testing panels and is certified by the Division of AIDS’ Virology Quality Assurance (VQA) program for quantitative and qualitative HIV assays.

Statistical analysis

Descriptive analysis and proportions of men who reported UAI in the past 3 months were presented. Chi-square tests and Fisher exact tests were used for categorical variables, and Student t test were used for continuous variables. Generalized linear models with logit link and binomial distribution [35] were used to identify independent variables associated with UAI in the past 3 months in the study population. Age (years) and the number of male partners in the last 12 months were modeled as restricted cubic splines with three knots [36].

After univariate analysis, observations with missing information on any selected variable were excluded. Covariates with p values <0.10 were selected, assessed for multi-collinearity using generalized colinearity diagnostics (GVIF) and entered in the initial multivariate model. Based on prior information concerning the effect of age in HIV incidence[37], we forced *a priori* the variable age as a continuous variable into the multivariate models. Covariates with the highest p values in the analysis of deviance (analogous to the likelihood ratio test) were sequentially removed. Variables with statistical significance at 5% ($p < 0.05$) and those that were not considered a confounder (e.g., when removed, a change equal to or higher than 10% in the odds ratio of any other variable of the model was observed) remained in the final model [38]. The Akaike Information Criterion (AIC) was also used for model selection. The Le Cessie-van Houwelingen-Copas-Hosmer test was used to evaluate the goodness-of-fit of the final model [39]. The predictive ability was evaluated using the Area Under the ROC Curve (AUC). Overdispersion was verified as well as the analysis of the residuals (Pearson and deviance residuals and Leverage or Cook's distances). The software R 3.0.2 was used to generate all analyses[40].

Ethics

The study was approved by the IPEC-FIOCRUZ IRB (CAE 0044.0.009.000-09) and all study participants signed an informed consent form prior to enrollment into the cohort.

Results

One hundred and fifty five MSM who reported anal sex with either an HIV-negative partner or a male partner with an unknown HIV-serostatus within the past 3 months were included. Overall, UAI with an HIV-negative or unknown HIV-serostatus male partner was reported by 40.6% (63/155) of MSM: 7.9% were exclusively with an HIV-negative partner, 76.2% were

exclusively with a partner with unknown HIV-serostatus and 15.9% with both, as shown in Table 1.

Table 2 describes the sociodemographic, behavioral, clinical and laboratorial characteristics of the study participants by UAI. Median age was 38 years, 53.6% were self-identified as white and 84.2% had more than 8 years of formal education. No significant differences at $p < 0.10$ level were observed in chance of UAI and skin color ($P = 0.799$) and years of education ($P = 0.882$). The median number of male sexual partners in the 12 months prior to the interview was 6.0; it was higher among those who reported UAI (Median=10; $P = 0.038$). Having only a single partner during the 12 months prior to the interview was reported by 12.4%.

Lifetime sexual abuse or domestic violence was reported by 35.9% and was significantly greater among MSM who reported UAI compared to those who did not ($p = 0.001$). Although 36.8% of MSM reported to be “high” from alcohol use before/during sex in the past 3 months, this was not statistically different from those who reported UAI and those who did not report UAI ($P = 0.337$). Stimulant usage before/during sex in the past 3 months was reported by 20.0% of the MSM, being slightly higher among those who reported UAI when compared to the group who did not. (27.0% vs. 15.2%; $P = 0.072$). Only 4 study participants (2.6%) reported injecting drug use during their lifetime.

Commercial sex in the past 3 months was frequent among all MSM (48.4%) and positively associated with UAI ($P = 0.001$). 58.1% participants reported both insertive and receptive sexual practices, while an exclusively insertive sexual practice was reported only by 16.1%. UAI was less frequently reported in exclusively receptive MSM (11.1%) when compared to those with exclusively insertive (17.5%) or with both insertive and receptive sexual practices (71.4%). ($P = 0.002$).

The median time since HIV diagnosis was 72.0 months and this was not associated with UAI ($P = 0.866$). Almost 82% of MSM were receiving cART at the time of the interview; this was associated with a lower likelihood of UAI ($P = 0.044$). Median CD4 count was higher among MSM who had UAI compared to those who did not report UAI, although no significance was observed at 10% ($P = 0.116$). Roughly half of the participants had an undetectable HIV viral load; this was not associated to a higher likelihood of having UAI ($P = 0.846$).

Multi-collinearity was not observed among significant variables ($P < 0.10$) and age after univariate analysis, which were entered in the initial multivariate model. In the final multivariate model (Table 3 and Figure 2), reporting sexual abuse or domestic violence (OR=2.70; 95%CI: 1.08-7.01) and having commercial sex within the past 3 months (OR=2.28; 95%CI: 1.04- 5.10) were positively associated with UAI, whereas the practice of exclusively receptive anal intercourse (OR=0.21; 95%CI: 0.06-0.75) was negatively associated with UAI. The shape of the association between the number of male partners in the past 12 months and UAI (modeled as the restricted cubic spline with 3 knots: 1.0, 6.0, 35.0) showed that the chance of UAI for each additional male partner increased quickly among participants who reported up to 20 partners and slowly among those who reported more than 20 (p -value = 0.039). Stimulants use before or during sex and receiving cART remained as confounder variables in the final multivariate model. Despite not having a statistically significant impact on UAI, the shape of association for age (years modeled as the restricted cubic spline with 3 knots: 26.1, 38.5, 51.0) is rather flat, though there is a low chance of UAI at the age extremes (p -value=0.301). There was no overdispersion in the model and the goodness-of-fit as well as the residual analysis were satisfactory.

Discussion

Most HIV -infected from our study have reported that they did not know their partner's serostatus, which is in accordance with prior data from Latin America [41]. The frequency of UAI with either negative or unknown HIV status partners was higher (40%) than that described in a meta-analysis conducted with HIV positive MSM from the U.S. (26%)[12]. Therefore, the risk of transmission, as well as re-infection and other sexually transmitted disease (STD) acquisition is increased among this population. Brazilian efforts on prevention, especially promoting condoms use and providing freely cART, have been very efficient in the control of HIV epidemics among general population [2]. However, they were not enough to control HIV transmission among MSM, a population presenting 10.5% HIV point prevalence. [42]. Thus, the UAI prevalence data presented in this study indicate that other effective interventions, such as Post-exposure prophylaxis (PEP) and pre-exposure prophylaxis (PrEP) [43-45], are needed as additional prevention tools to vulnerable MSM.

The lifetime history of violence or sexual abuse increased the chances of UAI by almost 3 times. This outcome is particularly concerning seeing that the frequency of UAI for the study population was 40.6%, with greater than half of the men who had UAI reporting previous

violence or sexual abuse. Increasing evidence supports the associations of both childhood sexual abuse and intimate partner violence with sexual risk behavior in MSM. An intervention trial [21] aimed to reduce risk behavior in MSM in six American cities found a 39.7% point prevalence of reported child sexual abuse, which was associated with a 1.24 (95% CI: 1.12 to 1.36) increased chance of UAI. Similarly, a positive association was found between intimate partner violence and UAI, depression, and substance abuse among 814 MSM from Chicago[46]. Less is known on these issues in middle-income countries [47] and there are still methodological problems to be solved regarding definitions and study design [48], but results found here point to an important and under evaluated threat to health among this population.

Commercial sex within the past 3 months also increased the likelihood of UAI in MSM. In our study, this variable included both MSM who received money in exchange for sex and/or looked for sexual partners on the streets. Because commercial sex is illegal in many countries, accurately assessing frequency of commercial sex is difficult. As a result, the research data on the association of commercial sex with UAI may be underreported and its association with UAI may be therefore difficult to measure. In a sample of MSM who paid for sex in Pakistan, almost 60% of them reported that their last intercourse event was unprotected [49]; however, more than 80% of interviewed MSM from India reported to have used condoms during their last paid intercourse with other men[50].

Results are also contradictory on the risk of HIV infection among MSM who exchanged sex for money. A meta-analysis from studies conducted in China found no difference in the HIV infection risk for "money-boys" compared to other MSM [51]. However, in a small recent study, including 463 Chinese MSM from the general population, commercial sex increased the chance of HIV infection by 4 times (95% 1.19-13.69)[52]. Even less is known about commercial sex among HIV-infected MSM, including possible cultural differences related to stigma and discrimination that may play a factor in the ability to negotiate the use of safe sex practices. As a result, additional research is still necessary on this topic.

Most MSM (57%) reported both insertive and receptive anal intercourse during the last 3 months, which is in accordance with the international literature [53,54]. MSM who reported having only receptive anal intercourse reported less UAI compared to those who only had insertive sex. These findings may be related to an increased awareness with one's own health and an intention to protect themselves from super-infection and STD. These data also raise questions about serosorting and strategic positioning as risk reduction practices among

Brazilian MSM. Further studies are necessary to evaluate these practices and risk reduction strategies adopted by HIV-positive MSM and their impact on HIV transmission.

The chance of UAI was associated with the number of male sexual partners within the past 12 months ($P=0.039$). However, we could observe that for MSM who had more than 20 male sexual partners, the odds of UAI for each additional partner did not increase as quickly when compared to participants who reported up to 20 partners.

In accordance with the recent literature, viral load and cART use [55,12] were not associated with UAI in this study. In contrast to the available literature, our findings indicated that being a younger age and being “high” from alcohol use or recreational stimulant use before/during sex were not associated with UAI. However, these findings must be interpreted with caution and the lack of statistical significance may be associated with the small size of our study population. Alcohol and stimulant consumption may be used to increase sexual performance [56], but intoxication decreases risk perception of HIV transmission [57]. Studies conducted with HIV-infected MSM have found a positive association between sexual risk behavior and the excessive consumption of alcoholic beverages [58,30].

Lastly, it is important to highlight that subjects who reported UAI also reported a higher number of sexual partners, a higher frequency of lifetime history of violence, and had a higher frequency of alcohol and stimulant use before/during sex than MSM who had no UAI. Different theories have been proposed to explain the clustering of different health problems/risky behaviors within the same populations. Dr. Merrill Singer, for example, has proposed the concept of syndemics [59], meaning different problems act synergistically in the worsening of health. Several authors have studied the concept of internalized homophobia as a predictor of risky behavior and psychological issues among MSM[60-62]. These theories are far from disentangling the multiple components related to risky behavior, and there is a debate on their real impact on health [63], but they certainly reinforce the need for a comprehensive approach on treating and preventing HIV among MSM.

As our sample is not probabilistic - and results may not be generalized to a broader population - further research is needed. Nevertheless, our results offer insight on factors associated with unprotected sexual practices among HIV-infected MSM in Brazil. As a limitation, the study was not specifically designed to evaluate intimate partner violence, sexual abuse or other kinds of violence, and as a result the measures were not standardized accordingly. However,

given the large prevalence of these factors, those findings indicate a pressing need for studies to support targeted interventions for Brazilian MSM.

Conclusions

Most MSM included in the present study were not aware of their partner's HIV serostatus. The high prevalence of UAI with HIV negative or with unknown HIV status male partners indicates that additional prevention strategies are urgently needed for this population. The factors associated with UAI in our study included a lifetime history of violence or sexual abuse, commercial sex and the number of male sexual partners in the past 12 months. The clustering of different health, behavioral, and social problems among these MSM reinforces the need for a comprehensive approach towards treatment and prevention of HIV in this population.

Competing Interests

The authors declare no competing interests.

Authors' contributions

CBC participated in the design of the study, performed the statistical analysis and wrote the first draft of the manuscript. All authors contributed to the design of the study, writing and revising the manuscript and all authors approved the final version.

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Figure 1. Study population and outcome. IPEC/Fiocruz, 2010-2012.

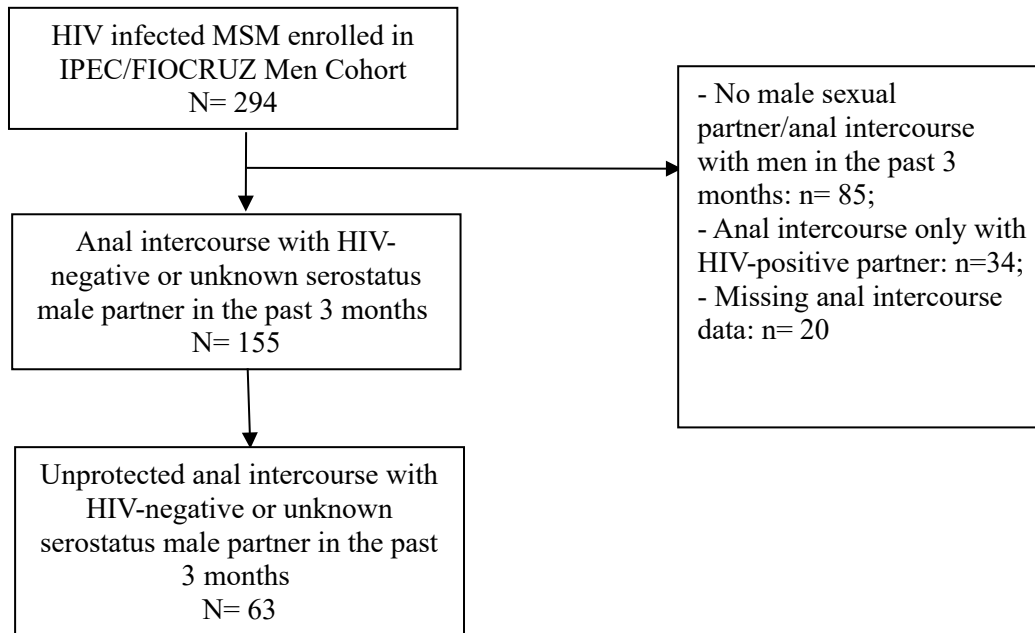
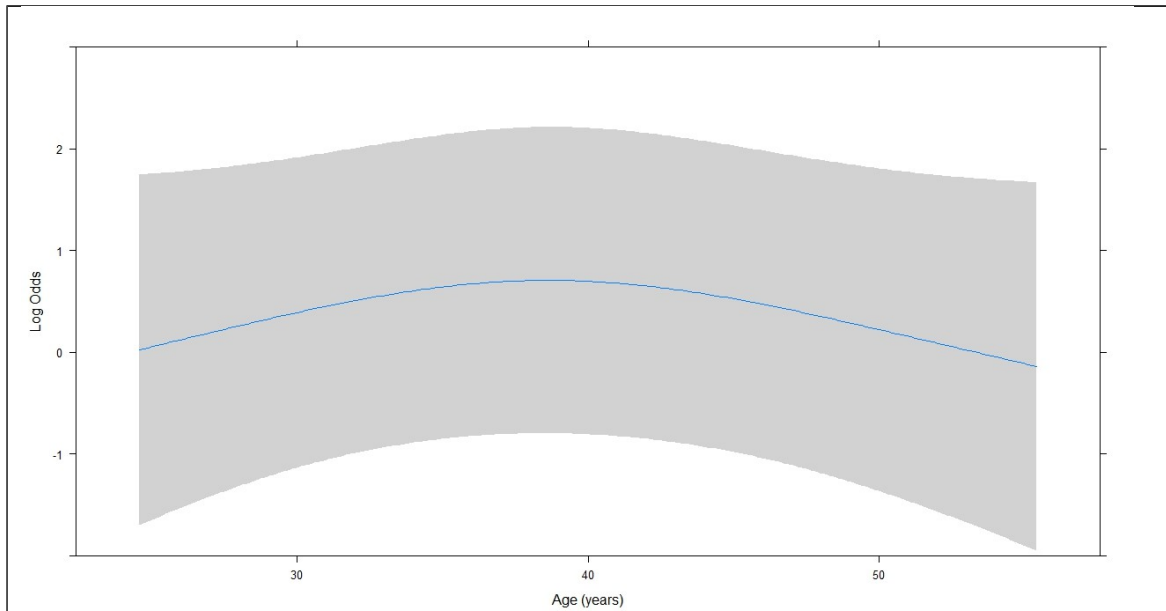
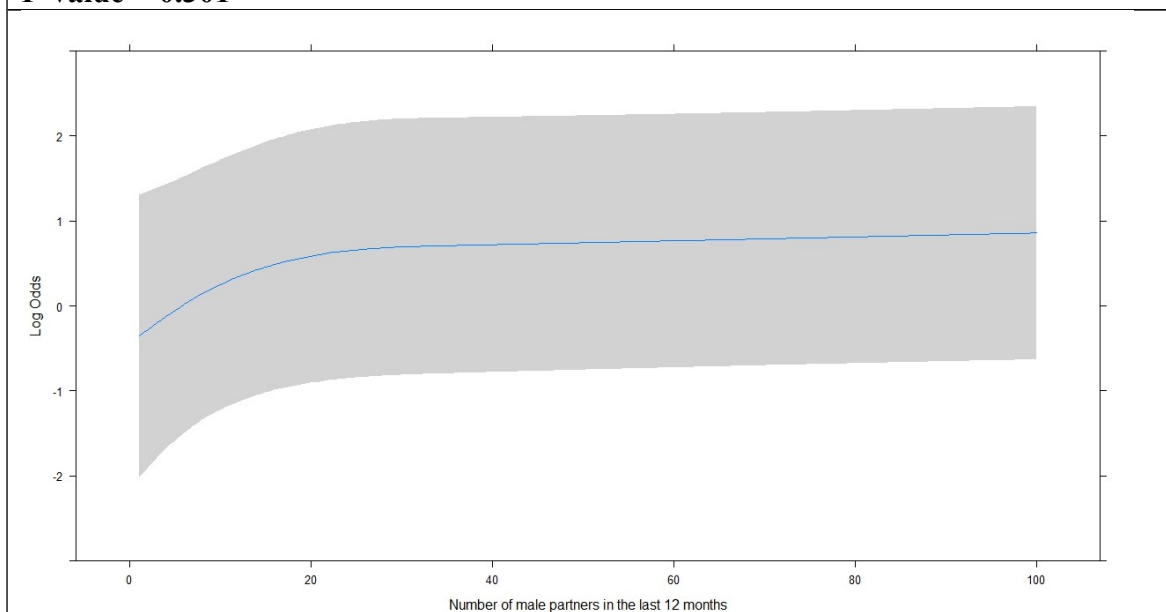


Figure 2. Restricted cubic spline analysis of the functional form of the association between age (years) and number of male partners in the last 12 months and the unprotected anal intercourse in the final model, IPEC/Fiocruz, 2010-2012.



P-value = 0.301



P-value = 0.039

Table 1. Unprotected anal intercourse according to partner(s) HIV-serostatus. IPEC/Fiocruz, 2010-2012.

HIV partner serostatus	Unprotected anal intercourse within the past 3 months					
	No		Yes		Total	
	N	%	N	%	N	%
Only HIV-negative	23	25.0	5	7.9	28	18.1
Only unknown HIV	57	62.0	48	76.2	105	67.7
Both	12	13.0	10	15.9	22	14.2
Total	92	100.0	63	100.0	155	100.0

Table 2. Characteristics of UAI with an HIV negative/unknown serostatus partner within last 3 months (N= 155). IPEC/FIOCRUZ, 2010-2012.

Characteristics	Unprotected anal intercourse			P-value*
	No 92(%)	Yes 63(%)	Total 155(%)	
Age**	40.5 (31.5-48.0)	37.0 (32.0-43.0)	38 (32.0-45.0)	0.107
White	48 (52.7)	34 (54.8)	82 (53.6)	0.799
Years of education				0.882
< 4	5 (5.6)	2 (3.2)	7 (4.6)	
4 a 8	10 (11.1)	7 (11.3)	17 (11.2)	
> 8	75 (83.3)	53 (85.5)	128 (84.2)	
No of male partners last 12 months**	5.0 (2.0-10.0)	10.0 (3.0-30.0)	6.0 (3.0-15.0)	0.038
Lifetime sexual abuse or violence	23 (25.0)	32 (52.5)	55 (35,9)	0.001
Alcohol use before sex last 3 months	31 (33.7)	26 (41.3)	57 (36,8)	0.337
Stimulant use before sex last 3 months	14 (15.2)	17 (27.0)	31 (20.0)	0.072
Commercial sex last 3 months	34 (37.0)	41 (65.1)	75 (48.4)	0.001
Anal intercourse with men last 3 months				0.002
Only insertive	14 (15.2)	11 (17.5)	25 (16.1)	
Only receptive	33 (35.9)	7 (11.1)	40 (25.8)	
Both	45 (48.9)	45 (71.4)	90 (58,1)	
Months since HIV diagnosis**	70.7 (33.3-162.4)	75.0 (44.1-134.5)	72.0 (33.8-148.8)	0.866
Receiving cART	80 (87.0)	46 (74.2)	126 (81.8)	0.044
CD4 count (cels/mm ³)**	541.5 (381.0-759.0)	647.0 (414.0-927.0)	581.0 (393.0-837.0)	0.116
Undetectable viral load	47 (51.6)	28 (50.0)	75 (51.0)	0.846

* Chi-square test or Fisher's exact test were applied for categorical variables. Student t test was used for continuous variables.

** Median (IQR)

Table 3. Factors associated with unprotected anal intercourse among MSM who have sex with an HIV negative/unknown serostatus partner within the last 3 months (N= 152)*, IPEC/Fiocruz, 2010-2012. *****

Characteristics* **	Adjusted OR (CI 95%)	P-value
Lifetime sexual abuse or violence	2.70 (1.08 - 7.01)	0.034
Stimulant use before sex last 3 months	1.48 (0.57 - 3.83)	0.418
Commercial sex last 3 months	2.28 (1.04 - 5.10)	0.040
Anal intercourse last 3 months		1
Only Insertive		
Only receptive	0.21 (0.06 - 0.75)	0.018
Receptive and insertive	0.75 (0.25 - 2.22)	0.603
Receiving cART	0.52 (0.18 - 1.47)	0.218

Le Cessie-van Houwelingen-Copas-Hosmer test (P-value): 0.723; AUC: 0.795

* Three MSM were excluded from initial multivariate model due to missing data in at least one covariate.

**Age was forced *a priori* the variable age into the multivariate models; Number of male partners, Stimulant use before sex, and currently receiving cART was a confounder and remained in the final multivariate model.

*** Age (years) and Number of male partners within the last 12 months were modeled as restricted cubic spline with three knots (coefficients not shown).

3.2 Artigo 2

***Chlamydia trachomatis*, *Neisseria gonorrhoeae* and syphilis among men who have sex with men in Brazil**

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Abstract

Background: Sexually transmitted diseases (STD) are frequently asymptomatic and increase the likelihood of transmitting and acquiring HIV. In Brazil, the guidelines for STDs diagnosis and treatment are based on the syndromic approach. Nucleic acid amplification tests (NAAT) has been recommended as routine STDs screening in some countries, especially for men who have sex with men (MSM). Limited data are available about how to best define target groups for routine screening by NAATs within this population. We aimed to assessed the prevalence of rectal and urethral *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) infections and syphilis, and the factors associated with having at least one STD among HIV-infected and uninfected MSM in Rio de Janeiro, Brazil.

Methods: From August 2010 to June 2012, 391 MSM were enrolled into the Evandro Chagas National Institute of Infectious Diseases-INI-Fiocruz cohort, and 292 MSM (HIV-infected:211 and HIV-uninfected:81) were included in this study. NAATs were performed on the rectal swabs and urine for CT and NG. The rapid plasma reagin test and microhemagglutination assay for *Treponema pallidum* were performed for syphilis diagnosis.

Results: The overall prevalence of STD was 20.0% (95%CI:15.7-25.1): 10% anorectal chlamydia; syphilis 9.9%; anorectal gonorrhoeae 2.5%; and urethral chlamydia 2.2%; no case of urethral gonorrhoeae was detected. The proportion of HIV-positive MSM who had at least one STD was nearly two times that of HIV-negative MSM (22.6% vs 13.2%; $P = 0.09$). The frequency of each STD, except for anorectal NG (1.5% vs.5.2%), was higher among HIV-positive than HIV-negative individuals. Among the 211 asymptomatic participants, 17.5% ($n = 37$) were identified as having at least one STD; 10.4% ($n = 22/211$) tested positive for anorectal chlamydia. Sixty five percent of HIV-positive MSM were asymptomatic at the time of the STD diagnosis, while 100.0% of the HIV-negative MSM. Age (APR = 0.78; 95%CI:0.60-1.00 for each additional ten years) and a positive-HIV serostatus (APR = 2.05; 95%CI:1.03-4.08) were significantly associated with STD diagnosis.

Conclusion: An overall high STD-prevalence rate was observed, especially among HIV-infected and in younger individuals, and the majority of STDs were asymptomatic. STD screening using NAATs among asymptomatic MSM is a potentially cost-effective intervention for the prevention of HIV infection among MSM.

Keywords: Sexually transmitted diseases; Resource limited settings; HIV prevention; Rectal clamydia; Rectal gonohrea; Nucleic acid amplification tests (NAAT), Brazil

Background

In developed settings, the prevalence of sexually transmitted diseases (STDs) among gay and other men who have sex with men (MSM) has been on an upward trend since the late 1990s [1]. In low- and middle-income countries STDs are a significant burden to the health care system [2], further fueled by a lack of systematic surveillance and population-based studies of STD prevalence. In South America, including Brazil, the proportion of new HIV infections is on the rise in young gay and other MSM [3], making this population particularly vulnerable to other sexually transmitted diseases (STDs) [4].

There are several factors, such as the number of sexual partners [5], inconsistent condom use [6] and HIV infection [7] that are associated with increased prevalence of STDs among MSM. Individuals infected with HIV are more susceptible to other STDs because they are immunocompromised and less capable of mounting a protective response against sexually transmitted pathogens [8,9]. STDs are frequently asymptomatic, therefore, increasing the likelihood of transmitting and acquiring HIV [10].

Because targeted groups within this population are not well defined or studied, routine STD screening should be recommended for all MSM [11]. In Brazil, STD clinical management relies mostly on the syndromic approach, as molecular STD diagnosis is not routinely available in the Public Health System [12].

This study aimed to assess the prevalence of rectal and urethral CT and *Neisseria gonorrhoeae* (NG) infections and syphilis, as well as to describe the factors associated with a positive diagnosis of at least one STD among HIV-infected and uninfected MSM at a referral center for MSM health in Rio de Janeiro, Brazil.

Materials and Methods

A cross-sectional analysis, nested within a cohort study was conducted at Evandro Chagas National Institute of Infectious Diseases-INI-Fiocruz (formerly known as the Evandro Chagas Clinical Research Institute-IPEC), Rio de Janeiro, Brazil. The parent cohort study was designed to evaluate the prevalence and incidence of anal HPV infection and intraepithelial anal lesions among HIV infected and uninfected men [13]. In summary, men were recruited by trained staff either while in the clinic waiting room or by phone. Inclusion criteria for the parent cohort study were: being aged 18 years or

older, not having anal cancer or related treatments (surgery, radiotherapy, and chemotherapy) and a willingness to sign the informed consent form. The exclusion criteria were: the use of immunomodulators agents, such as prednisone (dosage > 10 mg/day), interleukin or interferon. HIV positive men were already under care at the INI HIV Clinic, and HIV negative men attending the clinic for HIV prevention services. At the enrollment visit, information on demographic, sexual behavior, substance use as well as history of prior STDs were collected using Audio Computer Assisted Interview (ACASI) and specimens for STD diagnostic testing were collected. The study population for the present analysis were men who have sex with men (MSM), herein defined as men that reported having at least 1 male sexual partner within the past 12 months (regardless of having female partners).

From August 2, 2010 to June 30, 2012, 391 MSM were enrolled into the parent cohort study. Of these, 72 (18.4%) were excluded for not having a male sexual partner(s) within the last 12 months, and 27 (6.9%) were excluded because of missing information regarding their sexual partners within the past 12 months (Fig.1). In total, 292 MSM were included in this analysis. To determine the prevalence for each specific STD, we considered all participants who had available results for each of the STDs under evaluation, thus explaining the different denominators. The outcome “Having one or more STD at study entry” was defined as having a positive testing for at least one of the following STDs: CT (rectal, urethral, or urine), NG (rectal, urethral, or urine) or syphilis, at the study baseline visit. If a participant tested positive for at least one of the STDs under evaluation, regardless of having missing data on other STD tests, his data contributed to the analysis of the outcome “Having one or more STD at study entry”. Thus, 275 men were included in the analysis of the associated factors of having at least one STD (Fig.1).

STD diagnosis

Rectal CT and NG infection were diagnosed using APTIMA Combo 2 assay (Gen-Probe/Hologic San Diego, CA). Testing was processed at the Johns Hopkins STD Laboratory, in Baltimore, Maryland, USA. All indeterminate results for rectal CT/NG were repeated using the same tests on the same sample. If the repeated test was conclusive, the results were reported accordingly. If remained indeterminate, the result was reported as negative. Urethral CT and NG infection were diagnosed using urine samples on the Abbott RealTime platform and the NG/CT Amplification Reagent Kit

(Abbott Molecular, Des Plaines, IL); these samples were processed at the INI-Fiocruz Laboratories.

The rapid plasma reagin (RPR) test was performed for syphilis screening; positive results were confirmed using a microhemagglutination assay for *Treponema pallidum* (MHA-TP). Titers equal to or higher than 1/8 and a positive MHA-TP constituted a syphilis diagnosis. HIV infection was diagnosed according to the Brazilian HIV diagnosis algorithm (www.aids.gov.br). HIV-negative participants were tested at the baseline visit and also at each follow-up visit. Both the INI-Fiocruz Laboratories and the Johns Hopkins University STD Research Laboratory successfully participate in the College of American Pathologists (CAP) External Quality Assurance (EQA) proficiency testing panels for all relevant testing associated with this study.

Measures

STD-related symptoms included urethral/anal discharge, anal or genital nodules, anal or genital ulcers, spontaneous anal pain, tenesmus and anal pruritus. Individuals were considered symptomatic when at least one of the above-referenced symptoms was reported.

Demographic variables included age, self-reported skin color (further classified as white or non-white) and schooling (years of formal education).

The *number of male and female sexual partners* within the last 12 months was determined using the following questions: “During the past 12 months, how many men and how many transvestite/transsexual/transgender(s) did you have sex with?” and “During the past 12 months, how many women did you have sex with?” The latter question was categorized as “none” or “at least one female partner”.

Stable partner in the past 3 months was defined as “Yes” if the participant considered at least one sexual partner within the last 3 months to be a stable partner (husband, wife, boyfriend or girlfriend).

HIV-positive male sexual partner in the past 3 months was determined using the following questions: a) “In the past 3 months, how many HIV-positive male partners did you have insertive anal sex with?” and b) “In the past 3 months, how many HIV-positive male partners did you have receptive anal sex with?”.

Each study participant provided information, if known, on the HIV serostatus of his sexual partners. Independent HIV testing was not performed on the partners. *Alcohol and stimulant use before or during sex* were determined using the following questions: “In the past 3 months, were you drunk or high before or during sex?” and “In the past 3 months, did you use either inhaled or intravenous illicit drugs before or during sex?” [14].

Commercial sex within the past 3 months was defined as the exchange of sex for money/other favors and/or seeking commercial sex workers. This was determined using the following questions: “In the past 3 months, did you have sex for money, drugs or other favors?” and “In the past 3 months, did you look for commercial sex workers?”.

Anal sexual practices with male partners during the past 3 months were evaluated using the following questions: a) “In the past 3 months, how many HIV-negative male partners did you have insertive anal sex with?”; b) “In the past 3 months, how many male partners, with an unknown HIV-serostatus did you have insertive anal sex with?”; c) “In the past 3 months, how many HIV-negative male partners did you have receptive anal sex with?”; and d) “In the past 3 months, how many male partners, with an unknown HIV-serostatus did you have receptive anal sex with?” The answers were categorized as ‘only insertive’, ‘only receptive’ or ‘both’.

Unprotected anal intercourse during the past 3 months was defined as any positive answer to the following questions: “In the past 3 months how many: a) HIV-negative male partners did you have insertive anal sex with, without using condoms? b) male partners, with an unknown HIV-serostatus did you have insertive anal sex with, without using condoms? c) HIV-negative male partners did you have receptive anal sex with, without using condoms? and d) male partners, with an unknown HIV-serostatus, did you have receptive anal sex with, without using condoms?”.

Statistical analysis

For those with results available we have described the overall prevalence of CT, NG and syphilis. These results are sorted out based on HIV status. The overall prevalence for *having one or more STD at study entry*’ outcome and the confidence interval for the proportion [15] were calculated and are also presented sorted to HIV status using Chi-square test for comparison. Generalized linear models using logarithmic linkage and Poisson distribution with robust variance were used to estimate the prevalence ratio

between selected variables and the outcome [16]. Age, schooling, skin color, number of male sexual partners within the previous 12 months, having female partners, having a stable partner, having an HIV-positive sexual partner, having been high from alcohol and having used stimulants before/during sex, reporting commercial sex, position during anal sex, unprotected anal sex with male partner (s) in the last 3 months and HIV status were evaluated in the univariate analysis. Variables that were associated with an STD according to the univariate analysis ($P < 0.25$) were entered into the initial multivariate model. Multi-collinearity was tested using generalized colinearity diagnostics (GVIF). Variables were kept in the final multivariate model if (a) the P value < 0.05 or (b) it was a confounder, e.g., when removed, a change equal or higher than 10% in the prevalence ratio of any other variable of the model was observed [17]. We forced the variable age (a priori) into the multivariate models. The STATA/SE 10.1 software was used to perform the analysis.

Ethics

The study was approved by the IPEC-FIOCRUZ IRB (CAAE 0044.0.009.000-09); all study participants signed an informed consent prior to cohort enrollment.

Results

Overall 292 participants were included in this analysis, 211 HIV-infected and 81 HIV-uninfected. The HIV-infected participants were significantly older than the HIV-uninfected [median (IQR): 39.0 (31.0–46.0) vs 33.0 (27.0–40.0); $P = 0.000$], more frequently self-reported as white (53.4% vs 27.5%; $P < 0.0001$), had a lower number of male sexual partners within the previous 12 months [median (IQR): 5.0 (2.0–10.0) vs 10.0 (4.0–20.0); $P = 0.002$], and had less unprotected receptive or insertive anal sex with other men during the past 3 months (35.6% vs 50.7%; $P = 0.027$) Overall, 8.3% ($n = 24/289$) of participants were circumcised (7.5% HIV-infected and 8.6% HIV-uninfected; $P = 0.759$). The median time since HIV diagnosis was 75.8 (41.2–162.4) months; 77% ($n = 161/209$) of the HIV-infected participants were using cART at study entry; the median CD4 cell count (IQR) was 555.0 (375.0–789.5) cells/mm³ with 7.8% ($n = 15/192$) having less than 200 cells/mm³; 37.1% (75/202) had a detectable HIV viral load. All study participants consented to STD screening including the genital swabbing procedures.

STD prevalence

Table 1 shows the prevalence of STD, both overall and individual, stratified by HIV status. The most frequently diagnosed STDs were rectal Chlamydia (10.0%) and Syphilis (9.9%), while urethral Chlamydia (2.2%) and Rectal Gonorrhea (2.5%) were less commonly reported. Among MSM who participated in the analysis of associated factors to have at least one STD, 199 and 76 were HIV-infected and uninfected MSM, respectively. A total of 20.0% (95%CI: 15.7–25.1) had at least one STD, not including HIV infection. The proportion of HIV-positive MSM who had at least one STD (N = 45/199) was nearly 1.7 times that found for the HIV-negative MSM (N = 10/76) (22.6% vs 13.2% $P = 0.09$). A single STD was detected in 14.7% (n = 43) participants and 4.1% (n = 12) were diagnosed with two STDs. The frequency of each STD, except for anorectal NG, was higher among HIV-positive than HIV-negative individuals.

STD symptoms

Information on STD symptoms was available for 263 participants, with 211 (80.2%) being asymptomatic and 52 (19.8%) reported having symptoms (Table 2). Anorectal symptoms were reported by 10.9% of participants, with rectal discharge (3.4%), anal nodules (4.1%), and anal ulcers (5.2%) being the most frequently reported symptoms. Of the 32 participants with anorectal CT or NG infection, 9.4% had anorectal symptoms; 1.5% and 2.3% of the participants reported having genital ulcers or nodules, respectively. No urethral discharge was reported. Among MSM with syphilis, 13% presented rectal or genital ulcers.

Among the 211 asymptomatic participants, 17.5% (n = 37) were identified as having at least one STD: rectal gonorrhea in 2.8%, urethral chlamydia in 1.5%, rectal chlamydia in 10.4%, and syphilis in 5.7%. 65% of the HIV-infected MSM and 100% of the HIV negative MSM were asymptomatic at the time of the STD diagnosis.

Participants' characteristics according to STD diagnosis

The characteristics of these participants are described in Table 3 and are sorted by STD infection status. For those participants with at least one STD (n = 55), the median age was 35.0 years (IQR 29.0–42.0); approximately 20% had less than eleven years of schooling; 53.7% self-reported to be non-white. The median number of male sexual partners in the last 12 months was 8.0 (IQR 3.0–27.0). Within the last 3 months before

entering the study, 32.7% participants had an HIV-positive partner; 20.8% used stimulants before or during sex; 46.3% practiced commercial sex, and almost 60% reported both insertive and receptive anal sex. Almost half of the HIV-infected MSM diagnosed with an STD had a detectable plasma HIV viral load.

Factors associated with STD diagnosis

In the univariate analysis, besides age and HIV serostatus, some sexual risk behaviors were found to be associated with high STD prevalence. For each 10 male sexual partners in the past 12 months, a 1% increase in STD prevalence was observed (NAPRs = 1.01; 95% CI: 1.00–1.02). MSM who reported having HIV-positive male sexual partners during the 3 months prior to cohort enrollment had a higher STD prevalence as opposed to those who reported no such partners (NAPRs = 1.46; 95% CI: 0.88–2.42). Stimulant use before or during sex in the 3 months prior to cohort enrollment (NAPRs = 1.52; 95% CI: 0.86–2.70) was also associated to a high STD prevalence in the univariate analysis.

In the final multivariate model, age (APR = 0.78; 95% CI: 0.60–1.00 for each additional ten years) and HIV infection (APR = 2.05; 95% CI: 1.03–4.08) remained significantly associated with any STD diagnosis (Table 4).

Discussion

A high STD prevalence rate was observed among the MSM enrolled in this study, particularly anorectal CT (10%) and syphilis (9.9%). Because of its potential for facilitating HIV acquisition and transmission, the high prevalence of anorectal CT infection may be a contributing factor to the ongoing HIV epidemic in MSM in our setting. In order to confirm this hypothesis, additional representative, population-based MSM studies are needed.

Our findings are consistent with other reports [18], showing that most anorectal chlamydial and gonococcal infections as well as syphilis were asymptomatic. Our data emphasize the need to educate MSM, particularly those who are HIV infected, on the topic of STD awareness. Asymptomatic STDs are especially concerning because as the untreated infections persist, the risk of contracting and transmitting HIV increases [19]. Additionally, in the absence of symptoms, the infected individual is not prompted to seek health services or adjust his risk practices [20]. We believe that these data are the first to describe the prevalence of anorectal CT and NG in MSM in Brazil. Our findings

illustrate the urgent need to implement STD screening to MSM [11,21], as they remain the most affected by the HIV epidemic in our country [3].

As seen in other studies, when compared to HIV-negative men, HIV-positive men were more often diagnosed with STD (22.6% vs 13.2%) [22–25]. We observed that the HIV-infected MSM in our study had a high prevalence of anorectal CT and syphilis as seen in other settings [26,27]. The discrepancy between sexual behavior and STD prevalence may be explained by the fact that HIV-positive individuals enrolled in our study were engaged in care and had a median follow-up period of 6.5 years (IQR: 3.4–13.5), therefore receiving positive prevention counselling that might have influenced their sexual risk behavior. Moreover, as STD molecular screening is not standard of care in Brazil, and diagnosis is only done using the syndromic approach, it may be the case that the higher prevalence among the HIV positive MSM was driven by infections acquired prior to their linkage to care, that may have remained undiagnosed and thus, untreated.

In our study, only two variables were associated with an increased risk of a STD diagnosis in the multivariate analysis, younger age and HIV co-infection. Several studies have also found that younger age is associated with an increased risk for a STD diagnosis [7,28,29]. This finding is of paramount importance because 40% of new HIV diagnoses in Brazil are among the very young MSM aged 15–24 years [3]. Our study showed that for every additional ten years of age, the prevalence of having at least one STD decreased by 22%. These results may contribute to the development of recommendations for targeted routine STD screenings for MSM in our setting.

Potential explanations for the lack of an association with well-accepted variables, such as the number of sexual partners, stimulant use before or during sex in the past 3 months and unprotected sex, are the different methods and measures used across the different studies and the limited sample size. Another explanation may be related to our definition of STD, which combined different STDs into a composite endpoint. For example, different factors may be predictive of syphilis, urethral CT and rectal NG.

Although progress has been made in increasing HIV prevention and treatment services in resource-limited settings, major hurdles remain for the diagnosis of other STDs. As a result the information on CT and GC infection is likely to be grossly underestimated. Because many STDs are asymptomatic, the current clinical standard of relying on sexually active persons to self-detect STD symptoms is an inadequate triage method [30]. Although it is well recognized that routine STD testing for MSM should be

incorporated into the Brazilian clinical guidelines, the high cost burden to implement such testing makes it an unattainable goal. More epidemiological, coupled with cost effectiveness studies are urgently needed to better define targeted MSM groups for screening. Our results show that younger MSM and those living with HIV/AIDS are important targets for STD screening. The striking benefit of cART in preventing HIV transmission among heterosexual and MSM serodiscordant couples [29,30] has paved the way and triggered the expansion of utilizing cART for prevention. Hence, STD co-infections in HIV-infected populations may have significant implications on the expected outcomes of the HIV Test and Treat policy, which was recently adopted by the Brazilian Ministry of Health [31].

Our study has several limitations. First, regardless of HIV serostatus, all participants were under care at our institution. As a result they may have received HIV prevention counseling and may have received STD treatment, prior to enrollment into the parent cohort study, leading to an underestimation of our STD prevalence rate. In addition, although we have used CASI to collect sexual behavior data, we cannot exclude that underreporting of risky sexual risk behavior in HIV-infected MSM was related to social desirability bias. We enrolled a convenience sample at a single site, and data may not be generalizable to MSM in Brazil. In addition, the small sample size precluded the analysis of factors associated with individual STDs.

Conclusions

In summary, our findings showing a high STD prevalence rate, especially the high proportion of asymptomatic GC and CT infections support the CDC recommendation to offering periodic CT and GC NAAT testing to MSM in developing countries [11]. It poses a challenge to the Brazilian health system that offers only syndromic management of STD irrespective of the population. [32]. Lack of diagnosis of asymptomatic GC and CT infections in a context of an epidemic mostly driven by MSM may compromise the impact of the current test-and-treat strategy on the control of the HIV epidemic in Brazil. Routine GC and CT NAAT testing targeting asymptomatic MSM may be proven to be cost-effective and should be explored in Brazil [33].

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Competing interests

The authors declare that they have no competing interests.

Authors' contributions

CBC: participated in the design of the study, performed the statistical analysis and wrote the first draft of the manuscript. RKF; RBB; CG; MRCG; BHS; SWC; LC; JRC; CY; VGV and BG: contributed to the design of the study, writing and revising the manuscript. All authors read and approved the final manuscript.

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Figure 1. Study population- INI/Fiocruz, 2010–2012

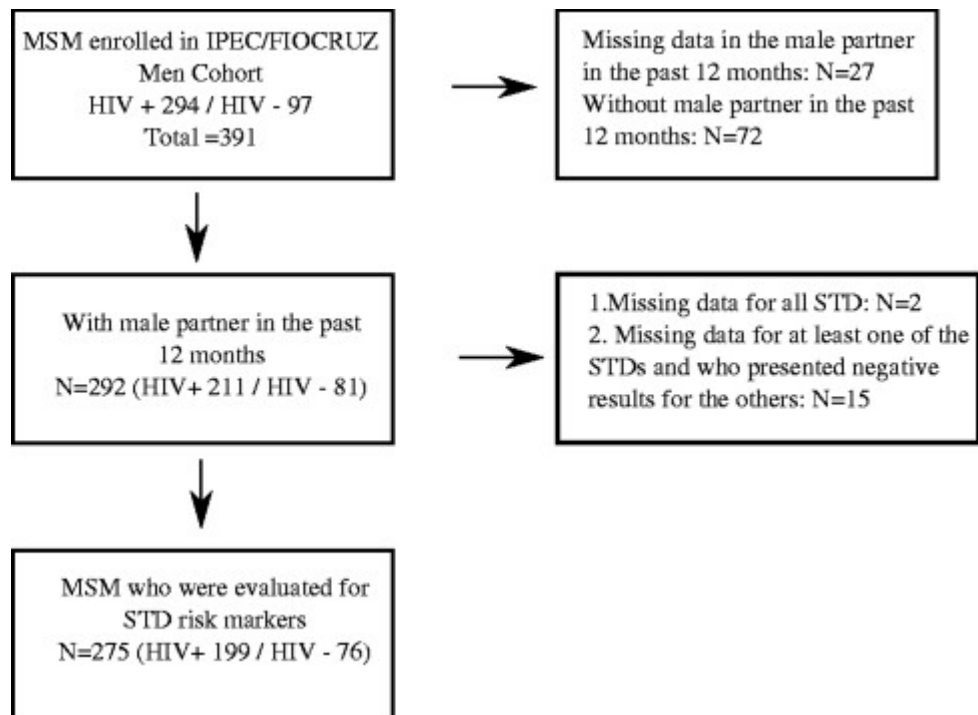


Table 1. Prevalence of Sexually Transmitted Diseases among Men who have Sex with Men. INI/FIOCRUZ, 2010-2012.

	Gonorrhea		Chlamydia		Syphilis	At least one
	Urethral	Rectal	Urethral	Rectal		STD
	(N = 273) ^a	(N = 279) ^a	(N = 273) ^a	(N = 279) ^a	(N = 284) ^a	(N = 275) ^b
N (%)	-	7 (2.5)	6 (2.2)	28 (10.0)	28 (9.9)	55 (20.0)
HIV serostatus. N (%)						
Positive	-	3 (1.5)	6 (3.0)	24 (11.9)	22 (10.8)	45 (16.4)
Negative	-	4 (5.2)	-	4 (5.2)	6 (7.5)	10 (3.6)

^a Different denominators are explained by availability of results for each STD evaluated.

^b Participants who tested positive for at least one STD, regardless of having missing information for other STD, were included and considered as an event. HIV-infected MSM = 199; HIV-uninfected MSM = 76

^c Number of HIV-infected MSM according to the availability of results for each STD: urethral NG = 197; anorectal NG = 202; urethral CT = 197; anorectal CT = 202; Syphilis = 204; At least one STD = 199

^d Number of HIV-uninfected MSM according to availability of results for each STD: urethral NG = 76; anorectal NG = 77; urethral CT = 76; anorectal CT = 77; Syphilis = 80; At least one STD = 76

Table 2. Proportion of at least one STD^a among symptomatic^b and asymptomatic MSM, INI/Fiocruz, Rio de Janeiro, Brazil

At least one STD	Symptomatic^b, n (%)	Asymptomatic, n (%)
Yes	15 (28.8)	37 (17.5)
No	37 (71.2)	174 (82.5)
Total	52 (100.0)	211 (100.0)

^a At Least One STD = Chlamydia/Gonococcal urethral and/or anal infection or Syphilis

^b Symptomatic = report of urethral/anal discharge, anal or genital nodule, anal or genital ulcer, spontaneous anal pain, tenesmus and, anal pruritis

Table 3. Characteristics of MSM according to sexually transmitted disease. INI/FIOCRUZ, Rio de Janeiro, Brazil

Characteristics	Sexually Transmitted Disease – N(%)		
	No	Yes	Total N = 275
Age ¹	38.0 (30.0-46.0)	35.0 (29.0-42.0)	38.0 (30.0-45.0)
Less than 11 years of schooling	50 (23.1)	12 (22.2)	62 (23.0)
Skin color – Non White	117 (53.7)	29 (53.7)	146 (53.7)
No. of male sexual partners in the last 12 months ¹	5.0 (2.0-14.0)	8.0 (3.0-27.0)	5.0 (2.0-15.0)
Had a female sexual partner in the last 12 months	23 (10.5)	7 (12.7)	30 (10.9)
Had a stable partner in the last 3 months	100 (46.9)	25 (47.2)	125 (47.0)
HIV-positive male sexual partner in the last 3 months	48 (23.1)	17 (32.7)	65 (25.0)
High from alcohol use before/during sex in the last 3 months	120 (56.3)	29 (54.7)	149 (56.0)
Stimulant use before/during sex in the last 3 months	28 (13.1)	11 (20.8)	39 (14.7)
Commercial sex in the last 3 months	86 (40.4)	25 (46.3)	111 (41.6)
Anal intercourse with men in the last 3 months			
Only insertive	34 (16.3)	8 (15.4)	42 (16.2)
Only receptive	43 (20.7)	5 (9.6)	48 (18.5)
Both	101 (48.6)	30 (57.7)	131 (50.4)
None sexual partner	30 (14.4)	9 (17.3)	39 (15.0)
Unprotected anal sex with men in the last 3 months	80 (38.5)	23 (44.2)	103 (39.6)
HIV infected	154 (70.0)	45 (81.8)	199 (72.4)
Time since HIV diagnosis, months (N = 185)			
Median (IQR)	75.4 (40.3-163.8)	85.4 (42.0-161.9)	78.5 (41.2-162.4)
<12	6 (4.1)	1 (2.6)	7 (3.8)
12-36	28 (19.2)	8 (20.5)	36 (19.5)
>36	112 (76.7)	30 (76.9)	142 (76.8)
Currently receiving cART (N = 197)	122 (80.3)	33 (73.3)	155 (78.7)
Current CD4 (N = 183)			
Median (IQR)	542.0 (359.0-781.0)	597.5 (425.0-803.0)	554.0 (376.0-781.0)
<200	11 (7.7)	3 (7.5)	14 (7.7)
200-350	23 (16.1)	4 (10.0)	27 (14.8)
>350	109 (76.2)	33 (82.5)	142 (77.6)
Total	143 (100.0)	40 (100.0)	183 (100.0)
HIV viral load (N = 193)			
Indetectable	99 (65.6)	23 (54.8)	122 (63.2)
Detectable	52 (34.4)	19 (45.2)	71 (36.8)
Total	151 (100.0)	42 (100.0)	193 (100.0)

Missing data: STD = 5.8%, Years of schooling = 3.1%, Skin color = 2.1%, Female sexual partner in the last 12 months = 4.1%, Stable partner in the last 3 months = 3.4%, HIV-positive male sexual partner in the last 3 months = 5.8%, High from alcohol use before/during sex in the last 3 months = 3.4%, Stimulant use before or during sex in the last 3 months = 3.4%, Commercial sex in the last 3 months = 3.1%, Anal intercourse with men in the last 3 months = 5.8%, Unprotected anal sex with men in the last 3 months = 5.8%, Time since HIV diagnose = 7.0%, Currently receiving cART = 1.0%, Current CD4 = 8.0%, HIV viral load = 3.0%. ¹Median (IQR)

Table 4. Factors associated with sexually transmitted diseases diagnosis among MSM. INI/FIOCRUZ, Rio de Janeiro, Brazil

Characteristics	PR ^a (CI 95%)			
	NAPR ^b	P value	APR ^c	P value
Age (each ten years)	0.82 (0.64-1.05)	0.110 ^d	0.78 (0.60-1.00)	0.049
Less than 11 years of schooling	0.96 (0.54-1.71)	0.885	-	-
Skin color – Non White	1.00 (0.62-1.62)	0.996	-	-
No. of male sexual partners in the last 12 months (each ten partners)	1.01 (1.00-1.02)	0.095 ^d		
Had a female sexual partner in the last 12 months	1,19 (0,59-2,39)	0,623	-	-
Had a stable partner in the in the last 3 months	1.01 (0.62-1.63)	0.977	-	-
HIV-positive male sexual partner in the last 3 months	1.46 (0.88-2.42)	0.146 ^d	-	-
High from alcohol use before/during sex in the last 3 months	0.95 (0.58-1.54)	0.832	-	-
Stimulant use before/during sex in the last 3 months	1.52 (0.86-2.70)	0.148 ^d	-	-
Commercial sex in the last 3 months	1.21 (0.75-1.95)	0.431	-	-
Anal intercourse with men in the last 3 months (Ref: Only insertive)				
Only receptive	0.55 (0.19-1.55)	0.255	-	-
Both	1.20 (0.60-2.42)	0.606	-	-
None sexual partner	1.21 (0.52-2.83)	0.658	-	-
Unprotected anal sex with men in the last 3 months	1.21 (0.74-1.97)	0.447	-	-
HIV infected	1.72 (0.91-3.24)	0.094 ^d	2.05 (1.03-4.08)	0.040

^aPR= Prevalence Ratio

^bNAPR = Non-Adjusted Prevalence Ratio

^cAPR = Adjusted Prevalence Ratio; 260 participants were included in the multivariate models; 15/275 (5.4%) had missing data in at least one covariate.

^dVariables with P<0.25 in univariate analysis and were entered in the initial multivariate model.

4 CONCLUSÕES & RECOMENDAÇÕES

Como indicado na maior parte da bibliografia especializada no tema desta tese, nos últimos tempos houve elevações aparentes nas frequências das práticas de sexo anal desprotegido e das taxas de prevalência e de incidência das DST entre os HSH, possivelmente atribuídas às mais variadas percepções de vulnerabilidades entre essa população, muito relacionadas ao entendimento de que o HIV/AIDS é menos sério devido à disponibilidade do cART.

Os fatores associados ao sexo anal desprotegido encontrados neste trabalho apontam que a história de violência sexual ou doméstica, a prática de sexo comercial e o relato de intercurso anal desprotegido parecem estar relacionados. Acreditamos que a baixa auto-estima promovida por inúmeros preconceitos sobre uma ‘normalidade’ sexual leva os HSH e as travestis e transexuais a serem excluídos dos principais espaços de educação, de cultura e de saúde. Dessa forma, as relações sexuais desprotegidas e comerciais muitas vezes refletem falta de empoderamento e, conseqüentemente, dificuldade de reivindicação do uso do preservativo por essa parcela dos HSH. Por outro lado, a identificação de violência doméstica/sexual contra HSH e travestis vem sendo cada vez mais divulgada, e algumas ações afirmativas por parte das autoridades e da sociedade civil vêm reduzindo o estigma e promovendo a cidadania dessas populações, como o casamento entre pessoas do mesmo sexo, a utilização do nome social de travestis e transexuais nos cartões do SUS e a campanha de cadastro de travestis e transexuais no ensino médio da rede pública do Rio de Janeiro.

Dentro dessa perspectiva, percebemos a necessidade de que se difundam para os HSH aconselhamento sobre sexo mais seguro, nos moldes das variadas formas de prevenção que existem hoje para a abordagem da infecção pelo HIV: reforço das campanhas para o uso de preservativos, ‘serosorting’, ‘posição sexual estratégica’, coito interrompido, ‘segurança negociada’, profilaxia pré-exposição ao HIV de determinadas subpopulações de alta vulnerabilidade, profilaxia pós-exposição ao HIV e, mais recentemente, o tratamento imediato de todos os indivíduos que se descobrem soropositivos para o HIV.

A triagem clínica das DST entre os HSH – quaisquer que sejam seus parceiros: gays, mulheres, travestis e transexuais – é importantíssima devido à relevância das infecções assintomáticas, que, portanto, torna sua transmissão muito mais possível. Para isso, o CDC (2010) recomendou uma triagem de ao menos uma vez por ano: 1. sorologia para HIV em HSH HIV-negativo ou que não foram testados no ano anterior, 2. sorologia para sífilis (com teste confirmatório para avaliar sífilis não tratada, parcialmente tratada ou resposta sorológica lenta após um tratamento), 3. Teste para infecção uretral por NG e CT em homens que tiveram relações sexuais insertivas no ano anterior (o teste de urina usando NAAT é a abordagem preferida), 4. Teste para infecção retal por NG e CT em homens que tiveram relações anais receptivas no ano anterior (a abordagem preferida é NAAT de um swab retal) e 5. Teste para infecção faríngea para NG em homens que tiveram intercurso oral receptivo no ano anterior (NAAT é a abordagem preferida). O CDC (2010) não recomenda teste para infecção faríngea para CT.

Os estudos aqui analisados se originam de diversas formas de recrutamento e muitas vezes divergem sobre as características dos indivíduos mais expostos. O Brasil ainda não possui uma recomendação sistematizada sobre as populações que devam ser alvo de triagem sistemática para as DST. Particularmente as parcelas mais pobres da população de HSH – sua maioria - requerem um trabalho de implementação de políticas públicas específicas, a fim de que a saúde dos indivíduos mais vulneráveis seja abordada de uma forma geral, e especificamente, na prevenção, na detecção precoce e no tratamento do HIV/AIDS e das DST, nos moldes dos manuais de orientações para comunidades populares, do Ministério da Saúde (2008) e do CDC (2010).

Nos últimos anos, a implementação, no Brasil, de crescente número de clínicas comunitárias e clínicas de família vem dando acesso a um número cada vez maior de pessoas com chances de serem avaliadas quanto à presença de DST. Trata-se de espaços que podem favorecer diversos tipos de estudos, pois reúnem os papéis de educação para a saúde, prevenção de doenças e tratamento da população geral. Esses estudos seriam possíveis com um adequado treinamento ético e técnico de seus profissionais para uma escuta atenta e isenta de qualquer julgamento moralista, o que é um desafio para o sucesso da abordagem da população de HSH, gays, travestis e transexuais,

assintomáticos e sintomáticos (ainda hoje, grande parte dos indivíduos sintomáticos busca tratamento de DST em farmácias particulares) das áreas de ação dessas clínicas.

Em suma, este estudo nos permite concluir e recomendar:

- a-** HSH HIV-positivos continuam a se engajar em relações sexuais anais desprotegidas;
- b-** História de violência doméstica e de abuso sexual e a prática de sexo comercial, fatos que representam situação de vulnerabilidade social e possivelmente econômica, estiveram associados às práticas de relações sexuais anais desprotegidas entre HSH HIV-positivos;
- c-** O maior número de parceiros sexuais também esteve associado à prática de sexo anal desprotegido entre HSH HIV-positivos;
- d-** A prevalência de doenças sexualmente transmissíveis foi acessada em uma população de HSH HIV-positivos e HIV-negativos em acompanhamento em uma instituição especializada para prevenção e assistência ao HIV/AIDS. Ou seja, apesar de não avaliado, é possível que a grande maioria não apresentava queixas e sinais clínicos de DST. Na literatura, grande parte dos estudos de prevalência é proveniente de clínicas de atendimento especializado para DST;
- e-** A prevalência de DST estudadas foi mais frequente entre os HSH HIV-positivos e os mais jovens;
- f-** Este estudo nos faz refletir sobre a necessidade de delinear e incorporar no nosso sistema de saúde recomendações para avaliação sistemática e tratamento das DST em pessoas sintomáticas e assintomáticas, principalmente naquelas que se engajam em situações de risco e maior vulnerabilidade, com estabelecimento de um fluxo de referência e contra-referência para diagnóstico e tratamento.
- g-** A notificação compulsória das DST deve ser considerada para fins de melhor monitoramento destas doenças no País.

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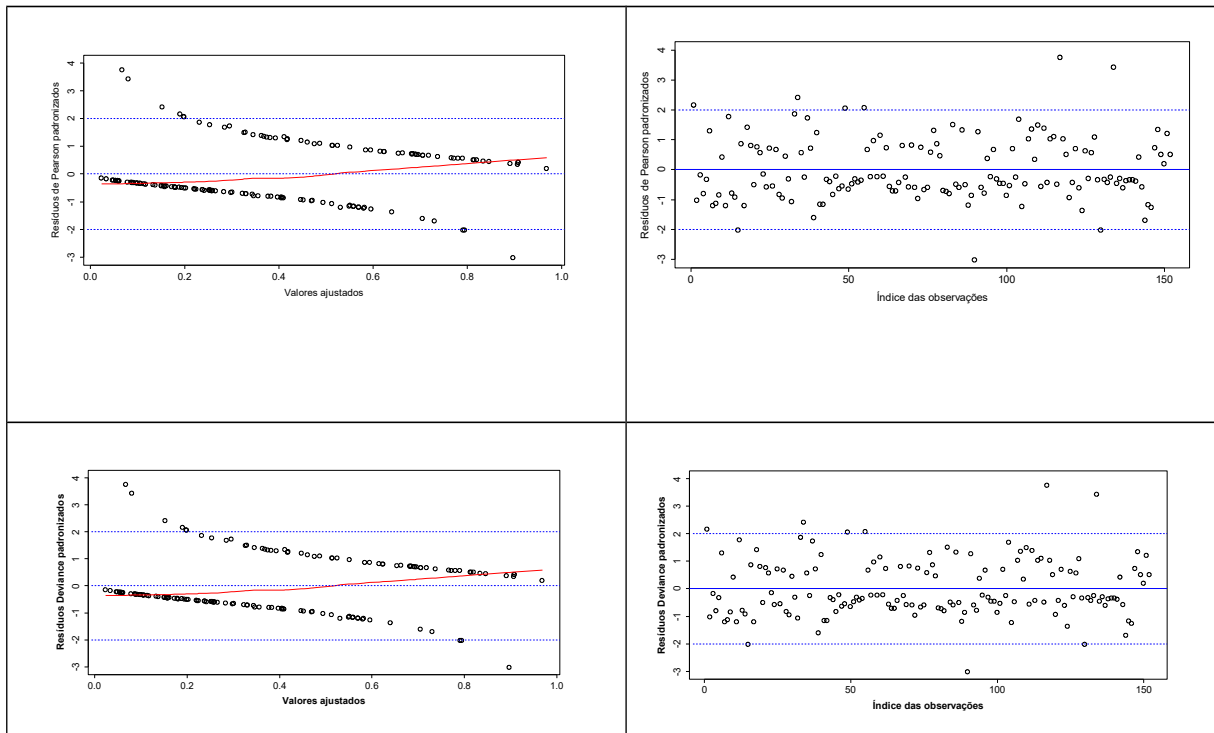
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ANEXO I. Análise de Resíduos

ARTIGO 1

Figura 1. Análise de pontos influenciáveis para o modelo final.



A figura 1 apresenta a análise gráfica realizada no modelo final estimado onde observou-se que:

- 3,9% dos homens (6/152) tinham Pontos de Alavanca (*Leverage*) (> 2) e destes 66,7% (9/6) tiveram sexo anal desprotegido;
- 2,6% dos homens (4/152) tinham Resíduos *Deviance* ($> |2|$) e destes 75,0% (3/4) tiveram sexo anal desprotegido;
- Nenhum apresentou Pontos de Alavanca (*Leverage*) (> 2) com Resíduos *Deviance* ($> |2|$) considerados como elevados e
- As Distâncias de Cook estimadas foram maiores que $4/n$ E maiores que duas vezes a média das distâncias em 7,2% (11/152) dos homens. Destes 11, 4 observações são de homens que tiveram sexo anal protegido e 7 são de homens que tiveram sexo anal desprotegido. Porém, as magnitudes estimadas das Distâncias de Cook foram muito baixas por serem próximas de zero, ou seja, mesmo refazendo a análise, ao excluir estas observações, os coeficientes estimados pelo modelo não iriam mudar substancialmente.

ARTIGO 2

Como foi utilizado o modelo linear generalizado com variância robusta, a estrutura de variância/covariância é diferente e os resíduos não são os mesmos de um modelo linear generalizado sem uso da variância robusta. Por esse motivo não foram feitos os gráficos dos resíduos. Porém, foi verificada a bondade do ajuste do modelo e o ajuste final foi considerado como adequado.