

**CARLOS EDUARDO FERREIRA**

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**SINTOMAS DA MENOPAUSA EM MULHERES  
INFECTADAS PELO HIV: PREVALÊNCIA E  
FATORES ASSOCIADOS**

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**Tese de Doutorado**

**ORIENTADOR: Prof. Dr. AARÃO MENDES PINTO NETO**

**Unicamp  
2006**

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Tese de Doutorado apresentada à Pós-Graduação da Faculdade de Ciências Médicas da Universidade Estadual de Campinas para obtenção do Título de Doutor em Tocoginecologia, área de Tocoginecologia

**ORIENTADOR: Prof. Dr. AARÃO MENDES PINTO NETO**

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## **BANCA EXAMINADORA DA TESE DE DOUTORADO**

**Aluno: CARLOS EDUARDO FERREIRA**

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**Orientador: Prof. Dr. AARÃO MENDES PINTO NETO**

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### **Membros:**

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**Curso de Pós-Graduação em Tocoginecologia da Faculdade  
de Ciências Médicas da Universidade Estadual de Campinas**

**Data: 31/07/2006**

## ***Dedico este trabalho...***

*As mulheres com HIV.  
Que este trabalho possa, de alguma forma,  
qualificar a assistência de saúde prestada a vocês.*

*A minha esposa e companheira Daniela, meus filhos Thiago e Pedro.  
Vocês são as principais razões de minha vida.*

*Aos meus pais.  
Apoiadores e incentivadores em tudo na minha vida.*

*Aos amigos,  
que torceram por mim e acreditaram neste trabalho.*

# Agradecimentos

---

*Ao Professor Aarão pela imensa colaboração neste degrau de minha vida profissional.  
Amigo na maior parte e “Professor orientador” nos momentos de necessidades.*

*Ao amigo Délio Conde. Sua contribuição foi inestimável para esse trabalho. Meu sincero agradecimento.*

*À minha sempre amiga Sueli Chaves. O tempo se encarrega de nos mostrar o valor da amizade verdadeira. Sueli, mais uma vez, muito obrigado!!!*

*À Sirlei, pela paciência e carinho que sempre teve comigo.*

*À Margarete por sempre estar presente e me “lembrar” dos prazos...*

*Ao companheiro Jarbas Magalhães pelas orientações especializadas referente ao tema.*

*Vanda, bibliotecária, pela contribuição com os artigos.*

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# **Símbolos, Siglas e Abreviaturas**

<b>CD4</b>	Linfócitos T de defesa
<b>DST</b>	Doença Sexualmente Transmissível
<b>CAISM</b>	Centro de Atenção Integral à Saúde da Mulher
<b>HAART</b>	<i>Highly Active Antiretroviral Therapy</i> (Terapia antiretroviral altamente potente)
<b>IMC</b>	Índice de Massa Corpórea ( $\text{Kg}/\text{m}^2$ )
<b>SAE</b>	Ambulatório de Especialidades da Secretaria de Saúde de São José do Rio Preto
<b>UBS</b>	Unidade Básica de Saúde
<b>Unicamp</b>	Universidade Estadual de Campinas

# Resumo

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**Objetivo:** o objetivo deste estudo foi avaliar as características sócio-demográficas, a prevalência de sintomas da menopausa na mulher HIV positiva e fatores associados a tais sintomas comparando com grupo controle. Foram analisados: características dessa população (idade, raça, escolaridade, autopercepção de saúde, status menopausal, estado civil, paridade, tabagismo, uso de drogas, uso de antiretrovirais, índices de CD4, índice de massa corpórea, aposentadoria e comportamento de risco para DST), a prevalência de sintomas da menopausa (Vasomotores, psicológicos, sexuais, genito-urinários, palpitações, artralguas e insônia) e fatores associados com tais sintomas. Foi realizado um estudo corte transversal de mulheres no climatério divididas em 96 mulheres HIV positivas e 155 mulheres HIV negativas. Os critérios de inclusão foram: ter 40 anos ou mais e ser brasileira. O critério de exclusão usado foi o uso de Terapia de Reposição Hormonal há menos de seis meses. A prevalência dos sintomas foi estudada nas variáveis de controle e nas demais variáveis dependentes através do teste de qui-quadrado. A prevalência de um ou mais sintomas foi avaliada multivariadamente através de medidas repetidas pela técnica de GEE - estimação de equação generalizada e calculado o valor do Odds Ratio ajustado pelas variáveis de

controle. O nível de significância assumido foi de 5% e o software utilizado para análise foi o SAS versão 9.01. **Resultados:** A média de idade das mulheres com HIV e sem HIV foi de  $48,9 \pm 7,4$  e de  $51 \pm 8,7$  anos, respectivamente. Os sintomas psicológicos foram as queixas mais comuns seguido de vasomotor. Mulheres com idade entre 45 e 54 anos (OR:1,51;IC95%:1,19-2,75), rebendo aposentadoria (OR:1,94;IC95%:1,29-2,93), com HIV (OR:2,24; IC95%:1,36-3,68), com três ou mais filhos (OR:2,24; IC95%:1,17-4,27) e que referiram auto-percepção do estado de saúde como não muito boa/péssima (OR: 2,03;IC95%: 1,34-3,08) apresentaram maior chance de referir sintomas. Entre mulheres com HIV, a chance de referir sintomas foi menor para aquelas com idade maior ou igual a 55 anos (OR:0,10;IC95%:0,01-0,67). Receber aposentadoria aumentou a chance de referir sintomas (OR:2,43;IC95%:1,07-5,52). **Conclusão:** A prevalência de sintomas menopausais foi elevada em mulheres com HIV. A idade, receber aposentadoria, infecção pelo HIV, escolaridade, paridade, IMC, auto-percepção do estado de saúde foram associados ao risco de referir sintomas nas mulheres em geral. Entre as HIV positivas, a idade e recebimento de aposentadoria se associaram a tais sintomas.

# Summary

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**Objective:** the aim of this study was to evaluate sociodemographic characteristics, the prevalence of menopause symptoms and its associated factors in HIV-infected women, in comparison to a control group. The following factors were analyzed: population characteristics (age, race, school education, self-perception of health, menopausal status, marital status, parity, smoking, drug use, antiretroviral use, CD4 indexes, body mass index, receipt of public benefits and risk behavior for STD), the prevalence of menopause symptoms (vasomotor, psychological, sexual, genitourinary, palpitations, arthralgias and insomnia) and factors associated with these symptoms. A cross-sectional study of climacteric women was conducted, divided into 96 HIV-positive and 155 HIV-negative women. Inclusion criteria were: age 40 years or older and being Brazilian. Exclusion criteria were: Hormone Replacement Therapy within the past six months. The prevalence of symptoms in the control variables and in the remaining dependent variables was studied by the chi-square test. The prevalence of one or more symptoms was multivariately assessed by repeated measures using the GEE technique—generalized estimating equation models—and calculation of the adjusted Odds Ratio value by the control variables. The assumed significance level was 5% and SAS version 9.01 was the software

used for analysis was. **Results:** the mean age of HIV-infected and HIV-uninfected women was  $48.9 \pm 7.4$  and  $51 \pm 8.7$  years, respectively. Psychological symptoms were the most common complaints followed by vasomotor symptoms. The odds of reporting symptoms were higher in women aged between 45 and 54 years (OR: 1.51; 95%CI: 1.19-2.75) who received public benefits (OR: 1.94; 95%CI:1.29-2.93), had HIV (OR: 2.24; 95%CI: 1.36-3.68), had three or more children (OR: 2.24; 95%CI: 1.17-4.27) and had a fair/poor perception of their physical health(OR: 2.03; 95%CI:1.34-3.08). Among HIV-infected women, the odds of reporting symptoms were lower for those aged 55 or older (OR: 0.10; 95%CI: 0.01-0.67) and for those with two or more partners in the past year (OR: 0.32; 95%CI: 0.11-1.00). Receipt of public benefits increased the odds of reporting symptoms (OR: 2.43; 95%CI: 1.07-5.52). **Conclusion:** The prevalence of menopause symptoms was high in HIV-infected women. Age, receipt of public benefits, HIV infection, school education, parity and self-perception of health status were associated with the risk of reporting symptoms in women in general. Among the HIV-positive women, age, number of sexual partners in the past year and receipt of public benefits were associated with such symptoms.

# 1. Introdução

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O envelhecimento da população mundial é um processo relativamente recente na história da humanidade (Acevedo, 1998). Esse fenômeno mundial trouxe consigo um novo conceito: a expectativa do envelhecimento (Fries e Crapo, 1990).

No século XVII, apenas 28% das mulheres alcançavam a menopausa e 5% delas ultrapassavam os 75 anos. Hoje, em países desenvolvidos, 95% das mulheres vivem até a menopausa e 50% delas chegam aos 75 anos. A previsão para 2030 é que um bilhão e duzentos milhões de mulheres tenham mais de 50 anos. Atualmente, aproximadamente 9% da população mundial são de mulheres acima de 50 anos (Acevedo, 1998).

No Brasil, a expectativa de vida das mulheres ao nascer é de 72,6 anos. Vinte e quatro por cento das mulheres paulistas têm 45 anos ou mais (Brasil, 2002). A proporção de mulheres idosas (60 anos ou mais) no Brasil é de 9,3% e no estado de São Paulo é 9,9% (IBGE, 2000). A evolução das pirâmides etárias da população de 1980 para 2000 permite destacar importantes alterações na dinâmica demográfica expressa por proporções menores de crianças, maior de

população em idade ativa e crescente de idosos (IBGE, 2000). Conseqüentemente, existe, então, um grande número de mulheres na pós-menopausa que necessita ou necessitará de atenção à sua saúde (Acevedo, 1998).

Eventualmente, o climatério pode ser assintomático (Utian e Boggs, 1999), no entanto, normalmente, se caracteriza por sintomas psicológicos (nervosismo, cefaléia, depressão, irritabilidade, insônia), sintomas vasomotores (fogachos, tontura, sudorese, palpitação), sintomas urogenitais (incontinência urinária, vagina seca, dispareunia) e sintomas sexuais (diminuição da libido) (Kupperman et al., 1953; Utian, 1987; Maclennan, 1991).

A queda estrogênica associa-se, também, ao maior risco de doenças coronarianas (praticamente o dobro) e conseqüentemente a elevação da mortalidade por doenças cardiovasculares (Stampfer et al., 1991). O hipoestrogenismo é responsável pela diminuição da densidade mineral óssea com conseqüente aumento no risco de osteoporose e fraturas ósseas de coluna, quadril e punhos (Munk-Jensen et al., 1988).

Além do mais, a menopausa representa um marco psicológico e cultural que é o final da vida reprodutiva. É um importante marcador biológico do processo de envelhecimento, principalmente em culturas como a nossa onde a beleza e a juventude são hipervalorizadas (Avis et al., 1997).

Além disso, as mulheres menopausadas convivem com o perigo da infecção do HIV. Dados recentes do Ministério da Saúde mostram que 90% das transmissões do vírus entre as mulheres são por relações sexuais heterossexual

e os números de novas mulheres com o vírus são de oito mil mulheres / ano (Brasil, 2003). Em 1984 a doença atingia 18,9 homens para cada uma mulher e em 2004 atingiu 1,5 homens para cada uma mulher (Dourado et al., 2006).

A epidemia de HIV Aids no Brasil que até 1990 atingia principalmente áreas metropolitanas de São Paulo e Rio de Janeiro, acometendo principalmente indivíduos masculinos com alto nível socioeconômico e pertencendo às categorias de transmissão homossexual-bissexuais além de casos portadores de hemofilia ou em receptores de sangue. A partir desta data constatou-se uma transição no perfil epidemiológico resultando na heteressexualização, feminização, pauperização e interiorização da doença (Castilho e Chequer, 1997; Castilho et al., 2000; Rodrigues-Junior e Castilho, 2004). Devido ao uso de antiretrovirais altamente potentes (HAART), a taxa de mortalidade diminuiu drasticamente e, conseqüentemente, as mulheres com HIV/Aids estão atingindo a menopausa (Sellers e Angerame, 2002; Pallela et al., 2003). No Brasil, a sobrevida de pacientes com Aids até 1995 era de 18 meses após o diagnóstico, passando para 56 meses após o uso disseminado e gratuito dos antiretrovirais em 1996 (Ministério da Saúde, Plano estratégico Programa nacional DST/AIDS 2005).

A incidência de casos de AIDS em indivíduos com idade avançada, nos últimos anos, deve-se provavelmente ao aumento da sobrevida e ao tempo que os portadores do HIV ficam assintomáticos (Brasil, 2004a; b). Soma-se a esses fatores, um maior número de mulheres infectadas pelo HIV que hoje fazem Terapia de Reposição Hormonal com melhora da sexualidade. Além disso, houve o advento de drogas para impotência masculina, muito usadas por uma

população de homens que se encontra em faixa etária que, tradicionalmente, pouco usam o condon masculino e/ou praticam sexo seguro. Segundo dados da Pesquisa de Conhecimento, Atitudes e Práticas na População Brasileira de 15 a 54 anos (PCAP-BR, 2004), dirigida à avaliação de desempenho do programa brasileiro de AIDS, oitenta e sete por cento de indivíduos entre 40 e 54 anos tiveram vida sexual ativa no último ano das quais apenas 41,5% usaram preservativos regularmente com parceiros eventuais e 16,2% usaram quando tinham parceiros fixo (PCAP-BR, 2004).

O fato de não haver risco de gravidez parece ser importante fator desestimulador do uso de preservativos. Sabe-se também que a mulher menopausada tem maior risco potencial de contaminação por DST devido às mudanças fisiológicas que ocorrem naturalmente como parte de envelhecimento. Mucosas vaginais atroficas, com aumento da friabilidade de tecido cervical, associada à diminuição geral da imunidade celular e humoral, fazem com que mulheres menopausadas sejam mais susceptíveis à DST, particularmente o HIV (São Paulo, 2004). Somam-se a isso, mulheres que se submeteram à laqueadura tubárea são aquelas cujos parceiros usam menos condons constituindo-se em grupo mais propenso em adquirir HIV/AIDS (Magalhães et al., 2002).

Em 2002, o número de mulheres soropositivas com 40 anos ou mais notificadas era 16.770, ou seja, 20,3% do total de infectadas (Brasil, 2002). Em 2004, o número de diagnóstico positivo em mulheres com 40 anos ou mais foi de 3.930 (32% do total de diagnóstico em mulheres) no Brasil (Brasil, 2004b).

Mundialmente, mais de 10% da população contaminada tem 50 anos ou mais. Nos Estados Unidos, historicamente, pessoas de idade avançada sempre ignoraram os programas de prevenção para HIV/AIDS. Reconhecendo o risco de infecção e envelhecimento da epidemia, novas estratégias de saúde para a mulher menopausada foram implementadas. As mulheres de maior risco são aquelas com atividade sexual sem condom, usuárias de drogas e álcool, que receberam transfusão de sangue antes de 1985, com antecedentes de DST, com diagnósticos suspeitos de doenças de Alzheimer, de Parkinson, de Acidente Vascular Cerebral (são doenças próprias da idade que podem mascarar o diagnóstico de AIDS devido a semelhança de sinais e sintomas) e doenças respiratórias. Para estas, preconiza-se o aconselhamento para teste de HIV, permitindo orientações de prevenção e tratamento precoce (Merson et al., 2000; Sellers e Angerame, 2002; Willians e Donnelly, 2002; Wilson, 2003).

Estudo norte americano recente sugere que as mulheres menopausadas HIV positivas são mais sintomáticas que as não infectadas, porém aquelas que apresentam doença avançada com contagem de CD4 baixa apresentam menos sintomas. Neste estudo, o sintoma mais freqüente relatado foi a depressão (Miller et al., 2005).

O diagnóstico da AIDS em pacientes com faixa etária mais elevada é difícil e tardio já que, naturalmente, durante o envelhecimento há sobreposições de doenças crônico-degenerativas e os profissionais não estão habituados a considerar a AIDS como um diagnóstico provável (Rossin et al., 2001).

A resposta imunológica do indivíduo com idade avançada ao tratamento com os antiretrovirais (HAART) é semelhante a de pacientes jovens. É importante, porém, diagnóstico precoce, pois a população idosa apresenta sintomatologia mais severa (Tumbarello et al., 2003). Estudos relatam que a mulher HIV positiva tem maiores chances de precocidade da menopausa (Schoenbaum et al, 2005). Parece também que as pacientes HIV positivas com contagens baixas de CD4, apresentam maior chance de falência ovariana precoce (Clark et al., 2001). Talvez, uma das explicações seja a hiperprolactinemia e hipogonadismo hipogonadotrófico causado pelos antiretrovirais de alta potência (Santoro et al., 2005). Além disso, o tratamento com antiretrovirais tende a piorar o perfil lipídico desta população (Dubé et al., 2002; Hirsch e Battegay, 2003; Hui, 2003). A menopausa precoce, a infecção pelo HIV e uso de HAART parecem aumentar ainda mais os potenciais riscos de dislipidemia, resistência insulínica e osteoporose (Schoenbaum et al., 2005).

Em relação a osteoporose, já se sabe que é uma complicação metabólica da infecção pelo HIV e de seu tratamento. Os antigos antiretrovirais aceleravam ainda mais a perda óssea nas pacientes no climatério. Arnsten et al estudaram mulheres com 40 anos ou mais, HIV positivas e relataram, para mulheres brancas, perda óssea mais acentuada em relação as HIV negativas independente do uso de antiretrovirais (Arnsten et al., 2006).

A população de pacientes HIV positivas continua crescendo devido a novos casos e também devido ao controle da doença principalmente a partir de 1996, quando o Ministério da Saúde instituiu acesso irrestrito e gratuito aos antiretrovirais e o advento de drogas antiretrovirais de alta potência (HAART) com

conseqüente aumento da sobrevida. Existe também, como discutido anteriormente, um aumento da contaminação de mulheres em idade avançada. Não conhecemos suas características adequadamente e nem sabemos como conduzi-las em relação a sintomas climatéricos, a presença de patologias como a osteoporose, doenças cardiovasculares e alterações metabólicas. Além disso, literatura até a atualidade é pobre em relação a tópicos específicos como, por exemplo, a reposição hormonal nessas mulheres: qual paciente realmente necessitará? Quando iniciar e até quando continuar? Qual a melhor via de administração? Assunto amplamente discutido e dominado para menopausadas HIV negativas. Porém, para essa nova população, trata-se de um assunto obscuro. Necessita-se também de uma política de Saúde Pública para aconselhamento desta população a respeito do HIV e identificação de indivíduos contaminados nessa faixa etária.

Justificou-se este estudo para podermos entender melhor essa nova população e oferecer meios para que ela possa ter uma melhor qualidade de vida.

## 2. Objetivos

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### 2.1. Objetivo geral

Avaliar a prevalência e os fatores associados aos sintomas menopausais em mulheres com HIV.

### 2.2. Objetivos específicos

- Comparar as características das mulheres infectadas pelo HIV e as não infectadas.
- Avaliar a prevalência de sintomas da menopausa de acordo com as características das mulheres.
- Verificar os fatores associados com os sintomas da menopausa na população geral do estudo.
- Verificar os fatores associados com os sintomas da menopausa nas mulheres infectadas pelo HIV.

## 3. Publicação

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----- Original Message -----

**Sent:** Tuesday, July 11, 2006 9:27 AM

**Subject:** En:GE3457

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Dear Dr. Conde,

Please consider that we have received your manuscript entitled "Menopause Symptoms in Women Infected with HIV: Prevalence and Associated Factors". It has been numbered as GE3457. Please refer to this number in all future correspondence.

The review process will begin as of now. You will be notified as soon as the Editor takes a decision regarding the suitability of your manuscript for publication in Gynecological Endocrinology. Thank you for your contribution.

Sincerely,

Dr. M.R. Parisen Toldin

Editorial assistant to Prof. A.R.Genazzani

Gynecological Endocrinology

----- Original Message -----

**From:** [Délío Conde](#)

**To:** [Gynecological Endocrinology](#)

**Sent:** Monday, July 10, 2006 6:54 PM

**Subject:** Menopause Symptoms in Women Infected with HIV: Prevalence and Associated Factors

Dear Prof. Genazzani,

We are sending the manuscript entitled "Menopause Symptoms in Women Infected with HIV: Prevalence and Associated Factors" for examination by the editorial board of the Gynecological Endocrinology, the official journal of the International Society of Gynecological Endocrinology and further publication in the original article section.

We are also attaching a copy of the article and a covering letter.

Thank you for your attention.

Sincerely,

Délío Marques Conde, MD

Department of Gynecology and Obstetrics

Universidade Federal de Goiás, Brazil



# **Menopause Symptoms in Women Infected with HIV: Prevalence and Associated Factors**

**Short-title:** Menopause Symptoms in Women Infected with HIV

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**Keywords:** Menopause, HIV, AIDS, Menopause symptoms

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## Abstract

**Objective:** To evaluate the prevalence and factors associated with menopause symptoms in HIV-infected women. **Methods:** A cross-sectional study of two groups of women was conducted: 96 with HIV and 155 without HIV. Women aged 40 years or older, non-users of hormone therapy in the last six months and native Brazilians were included. The prevalence of menopause symptoms was calculated according to the studied variables. Symptoms were grouped into six categories: vasomotor, psychological, genitourinary, weight gain, palpitations and insomnia. The generalized estimating equation model was applied to identify the factors associated with menopause symptoms in all women and only for HIV-infected women. **Results:** The mean age of women with and without HIV was  $48.9 \pm 7.4$  and  $51 \pm 8.7$  years, respectively. The median age at menopause for HIV-infected women was 47.5 years. Menopause symptoms were more frequent in HIV-infected women, highlighting psychological and vasomotor symptoms. HIV infection was associated with menopause symptoms (odds ratio [OR]:1.65,  $p=0.03$ ), as well as age ranging from 45 to 54 years (OR: 1.77,  $p=0.01$ ), higher parity (OR: 2.38,  $p=0.01$ ) and self-perception of health as fair/poor (OR: 2.07,  $p<0.01$ ). Among HIV-infected women, the likelihood of presenting symptoms decreased in those aged 55 or older (OR: 0.16,  $p=0.03$ ), and increased in retired women (OR: 2.61,  $p=0.02$ ). **Conclusion:** Menopause symptoms were common in HIV-infected women. HIV infection was independently associated with menopause symptoms, whereas age and being retired were associated with the occurrence of these symptoms in HIV-infected women.

## Introduction

Currently, it is estimated that there are 1.6 million people living with the human immunodeficiency virus (HIV) in Latin America. More than a third of these cases were registered in Brazil [1], which maintains an elevated incidence rate, particularly due to the increasing number of cases among women [2]. In Brazil, there was notification of 12,300 women with HIV in 2004, 30% of these women aged between 40 and 60 years [2].

Since the advent of highly active antiretroviral therapy (HAART) with free and universal access to these medications, there has been a decrease in mortality due to HIV. Furthermore, early diagnosis of the infection and prophylaxis against opportunistic infections have contributed to increase survival [3]. Thus, more women are living longer after the diagnosis of HIV infection.

Considering that the median age at menopause was reported to be between 46 [4] and 50 years [5] for HIV-infected women, the diagnosis of infection and use of antiretroviral therapy may coincide with the menopausal transition. In the menopausal transition, the occurrence of vasomotor, psychological and sexual symptoms may compromise quality of life [6,7], which may be aggravated by the diagnosis of HIV infection, contributing towards a worse quality of life in these women.

The relationship between HIV and estrogen is controversial. In animal studies, some authors have observed that the use of topical estrogen protected against viral infection, possibly stimulating proliferation of the vaginal epithelium [8]. On the contrary, it has been reported that estrogen may stimulate HIV replication [9], consequently compromising the prognosis. However, the impact

of HIV on menopause [5] and the risks and benefits associated with hormone therapy remain little known.

Previous studies have reported several repercussions of estrogen deficiencies in HIV-infected women. The prevalence of hot flashes and vaginal dryness in postmenopausal women with HIV was reported as 86.7% and 53.3%, respectively [5]. HIV-infected women with advanced disease may report less menopause symptoms [10]. Some authors have reported an association between menopause symptoms and illicit drug use [5,11], and between these symptoms and postmenopausal status [5]. In addition to symptoms commonly associated with estrogen deficiency, a higher prevalence of depression was described among HIV-infected women than among those uninfected with the virus [12].

Sociocultural and racial/ethnic factors may influence the perception and experience of menopause symptoms [13]. Considering the influence of these factors and lack of studies on the topic, the present study was conducted to investigate the prevalence of menopause symptoms and its associated factors in women living with HIV.

## **Methods**

### **Sample size**

Calculation of sample size was based on the prevalence of 90% [10] of at least one menopause symptom, using a statistical ponderance technique by generalized estimating equation models with repeated measures.

Assuming a sample error of 3.75% (expected prevalence between 86.25% and 93.75%) and a significance level of 5%, an estimate of at least 246 women was made for the sample size, subdivided into HIV-infected and HIV-uninfected women.

### **Subjects**

From June 2005 to May 2006, a cross-sectional study was conducted, including HIV-infected and HIV-uninfected women. Included were women aged 40 years or older, Brazilian and non-users of hormone therapy in the past six months. Women uninfected with HIV were selected among those seeking primary care clinics in the city of São José do Rio Preto, Brazil. Participants infected with HIV were selected among women attending a specialized public service in the same city. In general, users of this service are women of low income who spontaneously seek medical care or are referred for specialized evaluation. During outpatient consultation, women who met the inclusion criteria were consecutively invited to participate in the study. With their consent, these women underwent an interview in the same health unit, immediately following outpatient consultation. Interviews were administered by previously trained health professionals.

Sequentially, 102 HIV-infected women and 160 HIV-uninfected women were invited. Six HIV-infected and five HIV-uninfected women refused to participate in the study, allegedly due to lack of time. Thus, 96 HIV-infected and 155 HIV-uninfected women were included. The HIV-infected women in the study had been previously diagnosed with HIV infection by a reactive enzyme-linked immunosorbent assay (ELISA) and a positive Western blot assay. Participants who were considered HIV-uninfected did not undergo these tests. Institutional Review Board approval was obtained for the study and all women signed an informed consent form.

Participants were interviewed about the following sociodemographic characteristics: age, race/ethnicity, level of education, body mass index (BMI), smoking habit, receipt of public benefits, marital status and parity. Menopausal status was categorized as: premenopausal, perimenopausal, postmenopausal and surgical menopause. Premenopausal was defined as regular menstruation with no change in bleeding pattern over the past 12 months; perimenopausal when there was a report of amenorrhea for at least three months in the past year; postmenopausal was cessation of menstruation in the past 12 months. Surgical menopause was defined as cessation of menstruation due to hysterectomy and/or bilateral oophorectomy.

Age at first sexual intercourse and number of sexual partners in the past year were investigated. Among HIV-related factors, illicit drug use in the past five years was investigated (intravenous drugs, crack, cocaine, heroine, marijuana), CD4 cell count (cells/mm<sup>3</sup>) measured by flow cytometry and use of HAART for at least three months. HAART was defined according to current guidelines [14]. Self-perception of health status was categorized as: excellent, good, fair, or poor.

The occurrence of menopause symptoms in the two weeks prior to inclusion in the study was investigated. Symptoms were grouped into six categories: vasomotor (hot flashes, dizziness, night sweats), psychological (irritability, depression, mood lability, decreased interest in sex and loss of concentration), genitourinary (urinary incontinence, dyspareunia, vaginal dryness), weight gain, palpitations and insomnia, according to the methodology used in a previous study [10].

### **Statistical analysis**

Results were presented as median, means and standard deviations (SD) or as absolute and relative frequencies, according to the type of variable. The Chi-square test and the Fisher's exact test were used to evaluate the association among sociodemographic variables, menopausal status, sexual behavior, drug use and HIV infection, or the Wilcoxon test was used for variables expressed in continuous values.

The prevalence of menopause symptoms was evaluated in each of the variables by percentages and by the Chi-square or Fisher's exact test. The symptoms were: vasomotor, psychological, genitourinary, weight gain, palpitations and insomnia.

Generalized estimating equation (GEE) models were used to study the factors associated with groups of menopause symptoms, which were treated with repeated measures, according to the methodology used in a previous study [10]. Each group of symptoms was treated as a repeat measure and the SAS GENMOD program was used to measure the factors associated with these

symptoms and their effect. Psychological symptom was not included as an outcome variable, because its prevalence was higher than 90% in most factors studied, making mathematical convergence of the statistical model difficult. A model was constructed for all participants and another model was built only for HIV-infected women.

For statistical analysis, SAS program version 9.01 (SAS Institute, Cary, NC) was used. The level of significance adopted was 5%.

## Results

The mean ( $\pm$ SD) age was  $48.9\pm 7.4$  years in HIV-infected women and  $51.0\pm 8.7$  years in HIV-uninfected women. The median age of HIV-infected women at menopause was 47.5 years. Considering all women, mean BMI was  $26.0\pm 5.4$  Kg/m<sup>2</sup> and age at first sexual intercourse was  $18.0\pm 3.6$  years. The mean use of HAART was  $5.5\pm 3.7$  years.

It was observed that the majority of women were perimenopausal and postmenopausal, a larger proportion of HIV-infected women were non-white ( $p=0.01$ ), drug users ( $p<0.01$ ), received public benefits ( $p<0.01$ ), had a low level of school education ( $p=0.01$ ) and had no partner ( $p<0.01$ ). Other characteristics are displayed in Table 1.

The prevalence of menopause symptoms, according to sociodemographic characteristics, HIV status, CD4 cell count, use of HAART and other variables are demonstrated in Table 2. It was observed that psychological and vasomotor symptoms were the most frequent complaints in HIV-infected women, being reported by 97.9% and 78.1% of these women, respectively. Vasomotor, psychological, and genitourinary symptoms and insomnia were more prevalent in HIV-infected women (all respective  $p$  values lower than 0.05), while weight gain was more frequent in HIV-uninfected women ( $p=0.03$ ). No difference was observed in the prevalence of palpitations. The occurrence of vasomotor, psychological and genitourinary symptoms was significantly higher in women with a fair/poor perception of their physical health (all respective  $p$  values equal to 0.01). Genital symptoms were more frequent in women with higher parity ( $p<0.01$ ).

In the total sample of women, factors independently associated with menopause symptoms were: age between 45 and 54 years (odds ratio [OR]:1.77,  $p=0.01$ ), receipt of public benefits (OR: 2.00,  $p<0.01$ ), HIV infection (OR: 1.65,  $p=0.03$ ), having three or more children (OR: 2.38,  $p=0.01$ ) and self-perception of health as fair/poor (OR: 2.07,  $p<0.01$ ) (Table 3).

The GEE model applied only to HIV-infected women showed that receipt of public benefits was associated with menopause symptoms (OR: 2.61,  $p=0.02$ ), while age 55 years or older decreased the odds of reporting these symptoms (OR: 0.16,  $p=0.03$ ) (Table 4).

## **Discussion**

In this study of Brazilian women, we investigated the prevalence and factors associated with menopause symptoms in HIV-infected women. The women assessed were users of the public health service, belonged to a lower social strata and had attained a low level of education. In Brazil, the tendency to pauperize HIV infection is a concern, since a high number of cases occur on the outskirts of urban centers and among the underprivileged segments of the population [15].

It was observed that HIV infection was independently associated with menopause symptoms. A significant association of such symptoms with age and receipt of public benefits was also seen. In the total population studied, the number of children and self-perception of health were associated with the presence of symptoms. HIV-infected women were 65% more likely to report symptoms than HIV-uninfected women, consistent with the description of other authors [4,10]. A previous study conducted in the United States also showed greater odds of reporting symptoms in HIV-infected women, although in a lower proportion (24%) [10].

CD4 cell count did not influence the report of menopause symptoms. CD4 cell count is a marker of immune status in HIV infection, which may be associated with changes in hormone levels, menstrual cycle and menopause symptoms [10,16-18]. Other authors have shown an association between CD4 cell count and menopause symptoms [10,18], i. e. the less advanced the immunosuppressive effects of HIV, the more frequent the occurrence of symptoms. It is possible that women with advanced disease have specific

symptoms related to HIV infection or opportunistic infections, whose severity may minimize the impact of menopause symptoms. However, studies with larger samples to investigate these findings are warranted.

Schoenbaum et al. [4] described a relationship between lower CD4 cell count ( $<200$  cells/mm<sup>3</sup>) and early onset of menopause. In the present case study, the median age at menopause in HIV-infected women was 47.5 years. In line with our results, Cejtin et al. [19] and Clark et al. [18], assessing HIV-infected women described the median age at menopause as 47.7 and 47 years, respectively. However, Fantry et al. [5] observed a median age of 50 years at menopause in these women. It is worth highlighting that in a population-based study conducted in Brazil, it was observed that the mean age at menopause was 51.2 years [20]. The differences observed may be partly attributed to diversity of the studied populations, which may be associated with different levels of sex hormones [16,21].

In the present study, the most frequent symptom was psychological, with a higher prevalence in HIV-infected women. Miller et al. [10] reported a similar prevalence of psychological symptoms, while Fantry et al. [5] reported a prevalence of irritability in 74.8% of HIV-infected women. Applying specific instruments, Morrison et al. [12] reported a significant difference in the prevalence of major depressive disorder among HIV-infected (19.4%) and HIV-uninfected (4.8%) women. In a previous study of women presumed to be seronegative for HIV and aged between 45 and 60 years, the prevalence of psychological symptoms was 82% and not related to menopausal status [22], as observed in the current case study and also described among HIV-infected women [18].

It is important to remember that these women experience two conditions that may contribute to a higher prevalence of psychological symptoms: menopausal transition and HIV infection. Depressive symptoms increase during the menopausal transition [23]. A methodological difficulty encountered in studies of depression conducted in case studies with known medical illness is to differentiate depressive from disease-related symptoms [12,24].

The prevalence of vasomotor and genitourinary symptoms, weight gain, palpitations and insomnia in HIV-infected women was high and similar to that reported in a North American study [10]. It was also similar to that observed among Brazilian women of the general population [22]. Menopause symptoms may negatively influence quality of life [7], particularly vasomotor symptoms, represented mainly by hot flashes, whose etiology and mechanisms are still unknown [25]. Approximately 40% to 70% of women in the menopausal transition have vasomotor symptoms, and many of them seek medical care to treat these symptoms [26,27]. Although estrogen deficiency seems to be the main cause of vasomotor symptoms, their prevalence and intensity vary according to the sociocultural characteristics and health status of the population.

It is worth keeping in mind that there was no association between race/ethnicity and menopause symptoms in the present study, consistent with that described by other authors [5,10]. However, data from the Study of Women's Health Across the Nation (SWAN) demonstrated that there were differences in the prevalence of symptoms according to race/ethnicity [28]. A possible explanation is related to intense miscegenation in Brazil making it

difficult to evaluate the influence of race/ethnicity on the report and experience of menopause symptoms [7].

Using the GEE model to evaluate factors related to menopause symptoms, including HIV-infected and HIV-uninfected women, it was observed that women aged between 45 and 54 years were more likely to report symptoms, possibly because climacteric symptoms tend to be more intense in this age range. The intensity of symptoms increases in the menopausal transition and postmenopause, and women attribute their symptoms to a variety of factors [29]. In general, the menopausal transition begins with menstrual irregularities and ends with cessation of menses. Although it was previously believed that a progressive decrease in hormone production occurred, menopausal transition is characterized as the fluctuation in reproductive hormones and presence of symptomatology [30].

We also noted increased symptoms among retired women, probably because these women exerted less physical activity or had withdrawn from work due to their condition, and we observed that the HIV-positive population had more symptoms. Women who practiced regular physical activity tended to have less menopause-related symptoms such as depression, hot flashes, irritability and headache [31-33]. Furthermore, it was confirmed that women who perceived their health as fair/poor also had more symptoms, consistent with a previous report [10]. It is well-known that women attribute their symptoms to a variety of conditions, highlighting a change in health status, e.g. being HIV-positive, lack of information, stress, among others.

In the present cohort, an association between parity and menopause symptoms was observed that did not persist when we exclusively assessed HIV-

infected women. Genitourinary symptoms were more frequent in women with higher parity. In a different cultural context, a study of Italian HIV-negative women was conducted in outpatient menopause clinics, observing an association between higher parity and urine leakage [32], consistent with that observed by other authors [31] and also the present study.

When we assessed the factors associated with menopause symptoms exclusively among HIV-infected women, it was observed that only age and receipt of public benefits were associated with the presence of these symptoms. In women aged 55 years or older, the odds of presenting symptoms decreased significantly. This confirms the report by other authors that older women present less symptoms [33,34]. Perhaps this was due to the fact that these women adapted to low estrogen levels or had other more important issues, and menopause symptoms were of secondary consideration. It is well-known that menopause symptoms do not exist in a significant percentage of women [28]. As observed in the general study population, receipt of public benefits also significantly increased the prevalence of symptoms in HIV-positive women, implying that a negative social impact is associated with this condition.

Data of the current study should be interpreted taking a few limitations into account. It is a cross-sectional study that precludes the establishment of causal inferences. We only assessed the presence and not the intensity of menopause symptoms. Another limitation is that the group of women considered uninfected with HIV did not undergo laboratory tests.

It is possible that this was the first study in Latin America to assess menopause symptoms in HIV-infected women. We identified HIV infection as a

factor independently associated with menopause symptoms. In addition, age and receipt of public benefits were factors associated with the presence of symptoms among HIV-infected women. Prospective studies should be able to determine the actual influence of HIV infection on the experience of menopause, as well as the impact of hormonal or alternative therapies for the relief of menopause symptoms in this population. The long-term relationship between HIV infection, bone density and cardiovascular disease in women going through the menopausal transition should be the target of future investigation. Furthermore, it is worth emphasizing the need to develop public health strategies for the early diagnosis of HIV infection during the menopausal transition, because of the increasing number of diagnoses in this phase of a woman's life.

## References

1. The Joint United Nations Programme on HIV/AIDS [Internet]. 2006 Report on the global AIDS epidemic [cited 2006 Jul 4]. Available from: [http://data.unaids.org/pub/GlobalReport/2006/2006\\_GR-ExecutiveSummary\\_en.pdf](http://data.unaids.org/pub/GlobalReport/2006/2006_GR-ExecutiveSummary_en.pdf)
2. Brazilian Health Ministry [Internet]. AIDS/STD Epidemiologic Bulletin 2005 [cited 2006 Jul 4]. Available from: <http://www.aids.gov.br>
3. Hacker MA, Petersen ML, Enriquez M, Bastos FI. Highly active antiretroviral therapy in Brazil: the challenge of universal access in a context of social inequality. *Rev Panam Salud Publica* 2004;16:78-83.
4. Schoenbaum EE, Hartel D, Lo Y, Howard AA, Floris-Moore M, Arnsten JH, Santoro N. HIV infection, drug use, and onset of natural menopause. *Clin Infect Dis* 2005;41:1517-1524.
5. Fantry LE, Zhan M, Taylor GH, Sill AM, Flaws JA. Age of menopause and menopausal symptoms in HIV-infected women. *AIDS Patient Care STDS* 2005;19:703-711.
6. Blümel JE, Castelo-Branco C, Binfa L, et al. Quality of life after the menopause: a population study. *Maturitas* 2000;34:17-23.
7. Conde DM, Pinto-Neto AM, Santos-Sa D, Costa-Paiva L, Martinez EZ. Factors associated with quality of life in a cohort of postmenopausal women. *Gynecol Endocrinol* 2006; (*In press*).
8. Smith SM, Mefford M, Sodora D, et al. Topical estrogen protects against SIV vaginal transmission without evidence of systemic effect. *AIDS* 2004;18:1637-1643.

9. Katagiri D, Hayashi H, Victoriano AF, Okamoto T, Onozaki K. Estrogen stimulates transcription of human immunodeficiency virus type 1 (HIV-1). *Int Immunopharmacol* 2006;6:170-181.
10. Miller SA, Santoro N, Lo Y, Howard AA, Arnsten JH, Floris-Moore M, Moskaleva G, Schoenbaum EE. Menopause symptoms in HIV-infected and drug-using women. *Menopause* 2005;12:348-356.
11. Ferri CP, Dunn J, Gossop M, Laranjeira R. Factors associated with adverse reactions to cocaine among a sample of long-term, high-dose users in Sao Paulo, Brazil. *Addict Behav* 2004;29:365-374.
12. Morrison MF, Petitto JM, Ten Have T, Gettes DR, Chiappini MS, Weber AL, Brinker-Spence P, Bauer RM, Douglas SD, Evans DL. Depressive and anxiety disorders in women with HIV infection. *Am J Psychiatry* 2002;159:789-796.
13. Avis NE, Stellato R, Crawford S, Bromberger J, Ganz P, Cain V, Kagawa-Singer M. Is there a menopausal syndrome? Menopausal status and symptoms across racial/ethnic groups. *Soc Sci Med* 2001;52:345-356.
14. U.S. Department of Health and Human Services/Henry J. Kaiser Family Foundation [Internet]. Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents [cited 2006 Jul 4]. Available from: [http://www.aidsinfo.nih.gov/ContentFiles/HIVandItsTreatment\\_cbrochure\\_en.pdf](http://www.aidsinfo.nih.gov/ContentFiles/HIVandItsTreatment_cbrochure_en.pdf)
15. Takahashi RF, Shima H, SOUZA M. Women and AIDS: profile of an infected population and its social implications. *Rev Lat Am Enfermagem* 1998;6:59-65.
16. Cofrancesco J, Shah N, Ghanem KG, Dobs AS, Klein RS, Mayer K, Schuman P, Vlahov D, Rompalo AM. The effects of illicit drug use and HIV infection on sex hormone levels in women. *Gynecol Endocrinol* 2006;22:244-251.

17. Harlow SD, Schuman P, Cohen M, Ohmit SE, Cu-Uvin S, Lin X, Anastos K, Burns D, Greenblatt R, Minkoff H, Muderspach L, Rompalo A, Warren D, Young MA, Klein RS. Effect of HIV infection on menstrual cycle length. *J Acquir Immune Defic Syndr* 2000;24:68-75.
18. Clark RA, Cohn SE, Jarek C, Craven KS, Lyons C, Jacobson M, Kamemoto L. Perimenopausal symptomatology among HIV-infected women at least 40 years of age. *J Acquir Immune Defic Syndr* 2000;23:99-100.
19. Cejtin HE, Kim S, Taylor RN, Watts DH, Minkoff HL, Massad LS, Preston-Martin S, Anastos K, Cejtin HE. Menopause in HIV in women in the Women's Interagency HIV Study (WIHS) [Abstract WePeD6504]. Presented at XV International AIDS Conference. Bangkok, 2004.
20. Pedro AO, Pinto Neto AM, Paiva LH, Osis MJ, Hardy E. Age at natural menopause among Brazilian women: results from a population-based survey. *Cad Saude Publica* 2003;19:17-25.
21. Randolph JF Jr, Sowers M, Bondarenko IV, Harlow SD, Luborsky JL, Little RJ. Change in estradiol and follicle-stimulating hormone across the early menopausal transition: effects of ethnicity and age. *J Clin Endocrinol Metab* 2004;89:1555-1561.
22. Pedro AO, Pinto-Neto AM, Costa-Paiva LH, Osis MJ, Hardy EE. Climacteric syndrome: a population-based study in Campinas, SP, Brazil. *Rev Saude Publica* 2003; 37:735-742.
23. Freeman EW, Sammel MD, Liu L, Gracia CR, Nelson DB, Hollander L. Hormones and menopausal status as predictors of depression in women in transition to menopause. *Arch Gen Psychiatry* 2004;61:62-70.

24. Perkins DO, Leserman J, Stern RA, Baum SF, Liao D, Golden RN, Evans DL. Somatic symptoms and HIV infection: relationship to depressive symptoms and indicators of HIV disease. *Am J Psychiatry* 1995;152:1776-1781.
25. Kronenberg F. Hot flashes: epidemiology and physiology. *Ann N Y Acad Sci* 1990; 592:52-86.
26. Pedro AO, Pinto-Neto AM, Costa-Paiva L, Osis MJ, Hardy E. Climacteric women seeking medical care, Brazil. *Rev Saude Publica* 2002;36:484-90.
27. Schwingl PJ, Hulka BS, Harlow SD. Risk factors for menopausal hot flashes. *Obstet Gynecol* 1994;84:29-34.
28. Sherman S. Natural history of menopause studies and related efforts at the National Institute on Aging, NIH. In Schneider HPG, Naftolin F, editors. *Climacteric medicine - Where do we go?* 1 ed. London: Taylor & Francis; 2005. p. 16-26.
29. Woods NF, Mitchell ES. Symptoms during the perimenopause: prevalence, severity, trajectory, and significance in women's lives. *Am J Med* 2005; 118(12 Suppl 2):14-24.
30. Santoro N. The menopausal transition. *Am J Med* 2005; 118 (Suppl 2):8-13.
31. Gold EB, Sternfeld B, Kelsey JL, Brown C, Mouton C, Reame N, Salamone L, Stellato R. Relation of demographic and lifestyle factors to symptoms in a multi-racial/ethnic population of women 40-55 years of age. *Am J Epidemiol* 2000;152:463-473.
32. Progetto Menopausa Italia Study Group. Factors associated with climacteric symptoms in women around menopause attending menopause clinics in Italy. *Maturitas* 2005;52:181-189.

33. Guthrie JR, Dennerstein L, Taffe JR, Lehert P, Burger HG. Hot flushes during the menopause transition: a longitudinal study in Australian-born women. *Menopause* 2005;12:460-467.
34. Li C, Samsioe G, Borgfeldt C, Lidfeldt J, Agardh CD, Nerbrand C. Menopause-related symptoms: what are the background factors? A prospective population-based cohort study of Swedish women (The Women's Health in Lund Area study). *Am J Obstet Gynecol* 2003;189:1646-53.

Table 1 – Characteristics of women according to HIV status (N=251)

Characteristics	HIV-infected (n=96)		HIV-uninfected (n=155)		p-value*
	n	%	n	%	
<b>Age (yr)</b>					<b>0.12</b>
40-44	31	32.3	33	21.4	
45-54	45	46.9	77	50.0	
≥55	20	20.8	44	28.6	
<b>Menopausal status</b>					<b>0.61</b>
Premenopausal	18	18.8	31	22.1	
Perimenopausal	25	26.0	37	26.4	
Postmenopausal	37	38.5	43	30.7	
Surgical menopause	16	16.7	29	20.7	
<b>Race</b>					<b>0.01</b>
White	54	56.8	104	72.7	
Non White	41	43.2	39	27.3	
<b>Education (yr)</b>					<b>0.01</b>
Illiterate	8	8.3	8	5.2	
1-3	30	31.3	27	17.5	
4-7	35	36.5	50	32.5	
≥8	23	24.0	69	44.8	
<b>Receipt of public benefits</b>					<b>&lt;0.01</b>
Yes	48	50.0	37	24.0	
No	48	50.0	117	76.0	
<b>Marital status</b>					<b>&lt;0.01</b>
Without partner	71	74.0	55	36.4	
With partner	25	26.0	96	63.6	
<b>Parity</b>					<b>0.61</b>
Nullipara	7	7.4	10	6.7	
1-2	41	43.2	74	49.7	
≥3	47	49.5	65	43.6	
<b>Drug use</b>					<b>&lt;0.01</b>
Yes	11	11.5	0	0	
No	85	88.5	155	100.0	
<b>Smoking habit</b>					<b>0.01</b>
Smokes	37	38.5	30	19.4	
Never smoked/No longer smokes	59	61.5	125	80.6	
<b>Body mass index (kg/m<sup>2</sup>)</b>					<b>&lt;0.01</b>
≤26	44	74.6	61	43.9	
>26	15	25.4	78	56.1	
<b>Perception of health</b>					<b>0.26</b>
Excellent/good	65	67.7	113	74.3	
Fair/poor	31	32.3	39	25.7	
<b>Age at 1<sup>st</sup> sexual intercourse (yr)</b>					<b>0.01</b>
≤18	71	74.0	81	53.3	
>18	25	26.0	71	46.7	
<b>Number of sexual partners in the past year</b>					<b>0.28</b>
0-1	79	87.8	138	92.0	
≥2	11	12.2	12	8.0	
<b>CD4 count (cells/mm<sup>3</sup>)</b>					
≥501	32	37.6			
201-500	43	50.6			
≤200	10	11.8			
<b>Highly active antiretroviral therapy</b>					
Yes	77	81.1			
No	18	18.9			

\*Chi-square test.

Table 2 – Prevalence of menopause symptoms according to characteristics of the studied population (N=251)

Characteristics	n	Psychologica					Insomnia (n=244)
		Vasomotor (n=235)	I (n=240)	Genitourinary (n=241)	Weight gain (n=245)	Palpitations (n=243)	
<b>Age (yr)</b>							
40-44	67	62.5	89.2	53.2	53.8	41.9	50.0
45-54	122	70.2	88.8	60.0	56.7	44.9	56.3
≥55	64	66.1	93.5	84.1	53.2	48.4	58.1
<b>Menopausal Status</b>							
Premenopausal	49	53.3	87.2	55.6	54.2	43.8	44.9
Perimenopausal	62	78.3	88.3	54.4	58.3	44.3	58.3
Postmenopausal	81	66.7	92.2	77.2	54.4	43.6	60.3
Surgical menopause	46	67.4	91.3	64.4	54.5	50.0	51.1
<b>Race</b>							
White	160	99.0	66.0	66.7	54.2	42.6	54.8
Non-white	81	52.0	70.3	60.8	52.6	48.7	58.4
<b>Education (yr)</b>							
Illiterate	36	58.3	92.9	71.4	43.8	43.8	56.3
1-3	58	64.3	90.9	75.0	47.3	51.8	57.1
4-7	86	75.3	95.2	75.6	57.1	44.6	59.5
≥8	93	62.8	85.2	48.9	60.7	40.9	48.9
<b>Receipt of public benefits</b>							
Yes	85	72.2	92.7	80.0	59.0	51.2	64.6
No	168	65.2	89.8	58.0	53.4	41.9	50.3
<b>Marital Status</b>							
Without Partner	128	71.2	92.1	63.6	53.2	46.4	63.8
With Partner	122	64.2	87.6	66.4	57.6	42.7	44.0
<b>Parity</b>							
Nullipara	18	53.3	86.7	33.3	56.3	40.0	62.5
1-2	115	64.2	90.0	55.6	61.9	43.8	52.7
≥3	114	72.4	91.8	79.8	47.7	48.2	56.4
<b>HIV status*</b>							
Infected	96	78.1	97.9	73.0	46.9	52.1	66.7
Uninfected	155	59.7	86.1	60.4	61.1	40.8	47.3
<b>CD4 count (cells/mm<sup>3</sup>)</b>							
≥501	31	78.1	93.8	63.3	40.6	56.3	65.6
201-500	43	72.1	100.0	81.6	44.2	48.8	65.1
≤200	10	90.0	100.0	70.0	50.0	70.0	80.0
<b>Highly active antiretroviral therapy</b>							
Yes	77	80.5	98.7	72.6	45.5	55.8	68.8
No	18	66.7	94.4	73.3	50.0	38.9	55.6
<b>Drug use</b>							
Yes	11	72.7	100.0	70.0	45.5	45.5	72.7
No	240	67.0	90.4	64.9	56.0	45.3	54.1
<b>Smoking</b>							
Currently	67	71.2	94.0	53.8	56.7	53.7	62.7
Never smoked/No longer smokes	184	65.7	89.6	69.4	55.1	42.0	52.0
<b>Body mass index (kg/m<sup>2</sup>)</b>							
≤26	105	69.0	92.2	68.6	45.2	43.7	59.6
>26	93	70.2	88.5	59.3	75.6	44.9	50.0
<b>Perception of health</b>							
Excellent/good	178	61.9	87.7	58.2	55.7	36.3	52.0
Fair/poor	70	80.0	98.5	83.3	54.3	67.1	62.9
<b>Age at 1<sup>st</sup> sexual intercourse (yr)</b>							
≤18	152	69.9	92.5	69.2	55.6	50.3	56.3
>18	96	62.2	87.9	59.3	54.8	37.0	52.7
<b>Number of partners in the past year</b>							
0-1	217	65.2	90.0	65.5	56.7	43.4	52.6
≥2	23	81.0	95.2	63.6	38.1	47.6	68.2

\*For HIV-infected women: vasomotor, n=75; psychological: 94; genitourinary, n=65; weight gain, n=45; palpitations, n=50; insomnia, n=64.

Table 3 – Factors associated with menopause symptoms of HIV-infected and HIV-uninfected women, based on generalized estimating equation model, excluding psychological symptom (N=251)

<b>Characteristics</b>	<b>Adjusted OR*</b>	<b>95% CI</b>	<b>p-value</b>
<b>Age (yr)</b>			
33-44	1.00		
45-54	1.77	1.18-2.66	0.01
≥55	1.24	0.67-2.29	0.49
<b>Receipt of public benefits</b>			
No	1.00		
Yes	2.00	1.35-2.95	<0.01
<b>HIV status</b>			
Uninfected	1.00		
Infected	1.65	1.06-2.55	0.03
<b>Parity</b>			
Nullipara	1.00		
1-2	1.84	0.97-3.48	0.06
≥3	2.38	1.26-4.50	0.01
<b>Perception of health</b>			
Excellent/good	1.00		
Fair/poor	2.07	1.40-3.05	<0.01

\*Adjusted for age, menopausal status, race, years of education, HIV status, receipt of public benefits, marital status, parity, smoking habit, body mass index, perception of health, age at 1st sexual intercourse, number of sexual partners in the past year.

Table 4 – Factors associated with menopause symptoms of HIV-infected women, according to generalized estimating equation model, excluding psychological symptom (N=96)

<b>Characteristics</b>	<b>Adjusted OR*</b>	<b>95% CI</b>	<b>p-value</b>
<b>Age (yr)</b>			
33-44	1.00		
45-54	0.88	0.34-2.30	0.80
≥55	0.16	0.03-0.83	0.03
<b>Receipt of public benefits</b>			
No	1.00		
Yes	2.61	1.20-5.69	0.02

\*Adjusted for age, menopausal status, race, years of education, receipt of public benefits, marital status, parity, use of highly active antiretroviral therapy, CD4 cell count, drug use, smoking habit, body mass index, self-perception of health, age at first sexual intercourse, number of sexual partners in the past year.

## 4. Conclusões

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- As mulheres do estudo eram semelhantes em relação a status menopausal, idade, paridade, número de parceiros sexuais no último ano e auto-classificação de saúde. As mulheres HIV positivas tinham menor nível de escolaridade, apresentavam maior porcentagem de não brancas, uma maior taxa de mulheres que recebiam aposentadoria, eram mais magras, a maioria vivia sem companheiro, referiram maior uso de drogas e tabagismo, iniciaram atividade sexual mais precocemente e praticavam sexo anal mais frequentemente que as mulheres HIV negativas.
- Os sintomas mais comuns encontrados foram os psicológicos seguidos dos vasomotores.
- As mulheres do estudo tinham maior chance de apresentar sintomas de menopausa quando tinham idade entre 45 e 55 anos, recebiam aposentadoria do estado, eram HIV positivas, tinham três filhos ou mais e auto-classificação de saúde não muito boa/péssima.
- As mulheres HIV positivas tinham menor chance de apresentar sintomas se tivessem 55 anos ou mais. Receber aposentadoria do estado aumentou a chance dessas mulheres apresentarem sintomas.

## 5. Referências Bibliográficas

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Acevedo PL. Envejecimiento poblacional y menopausia en Latinoamerica. In: Campos OG, Urzua EA, Castro PC. **Menopausia y longevidad: perspectiva clinica y epidemiologica en Latinoamerica**. Ediciones Sociedad Chilena de Climaterio. Santiago de Chile, Editora. Bywaters, 1998. p.49-72.

Arnsten JH, Freeman R, Howard A, Floris-Moore M, Santoro N, Schoenbaum EE. Human immunodeficiency virus infection and bone mineral density in middle-aged women. *Clin Infect Dis* 2006; 42:1014-20.

Avis NE, Crawford SL, Mckinglay SM. Psychosocial, behavioral, and health factors related to menopause symptomatology. *Womens Health* 1997; 3:103-20.

Brasil. Ministério da Saúde. **Boletim epidemiológico** – AIDS e DST – Ano XVI – Nº 01 14<sup>a</sup> a 52<sup>a</sup> Semanas Epidemiológicas – abril a dezembro de 2002.

Brasil. Ministério da Saúde. **Boletim epidemiológico** – AIDS e DST – Ano XVII nº01 – 01<sup>a</sup> à 52<sup>a</sup> Semanas epidemiológicas janeiro a dezembro de 2003.

Brasil. Ministério da Saúde. **Boletim epidemiológico** – AIDS e DST – Ano XVIII – Nº 01 – 01<sup>a</sup> – 26<sup>a</sup> Semanas Epidemiológicas, janeiro a Junho de 2004a.

Brasil. Ministério da Saúde. **Boletim epidemiológico**. C.R.T. – DST/AIDS - SP. C.V.E. Ano XXIII – N° 1 outubro 2004b.

Brasil. Ministério da Saúde. **Boletim epidemiológico** – AIDS e DST –Ano II – N° 01 – 01<sup>a</sup> – 26<sup>a</sup> Semanas Epidemiológicas, janeiro a Junho de 2005.

Brasil. Ministério da Saúde. **Plano Estratégico**. Programa Nacional de DST e Aids. Março de 2005.

Castilho EA, Chequer P. A epidemia da aids no Brasil. In A epidemia de aids no Brasil: situação e tendências. Coordenação Nacional de DST e Aids, Brasília, Ministério da Saúde, p9-12, 1997.

Castilho EA Chequer P Szwarcwald CL. A Aids no Brasil. In: Rouquayrol E, Almeida N (eds). Epidemiologia e Saúde. Editora Médica e científica, Rio de Janeiro. Coordenação Nacional de DST e Aids. Boletim epidemiológico. Ministério da Saúde, Brasil, XIII, 2000.

Clark RA, Mulligan K, Stamen Vic E, Chang B, Watts H, Andersen J, et al. Frequency of anovulation and early menopause among women enrolled in selected adult AIDS clinical trials group studies. **J Infect Dis**. 2001; 184:1325-7.

Dourado I, Veras mA, Barreira D, Brito AM. Aids epidemic trends after te introduction of antiretroviral therapy in Brazil. **Rev Saude Publica** 2006; 40(suppl):9-17.

Dube MP, Qian D, Edmondson-Melancon H, Sattler FR, Goodwin D, Martinez C, et al. Prospective, intensive study of metabolic changes associated with 48 weeks of amprenavir-based antiretroviral therapy. **Clin Infect Dis** 2002; 35:475-81.

Fries JF, Crapo LM. The rectangularization of life. In: Byyny RL, Speroff L. **A clinical guide for the care of older women**. Baltimore, Willians & Wilkins, 1990. p.1-28.

Hirsch HH, Battegay M. HIV-infection, HAART (highly-active antiretroviral therapy) and hyperlipidemia. *Dtsch Med Wochenschr* 2003; 128:1051-4.

Hui DY. Effects of HIV protease inhibitor therapy on lipid metabolism. *Prog Lipid Res* 2003; 42:81-92.

IBGE. Instituto Brasileiro de Geografia e Estatística – IBGE. Censo Demográfico 2000. Características gerais da população. Censo demogr., Rio de Janeiro, p. 1-178, 2000

Kupperman HS, Blatt MHG, Wiesbader H, Filler W. Comparative clinical evaluation of estrogenic preparations by the menopausal and amenorrheal indices. *J Clin Endoc Metab* 1953; 13:688-803.

Magalhães J, Amaral E, Giraldo PC, Simões JA. HIV infection in women: impact on contraception. *Contraception* 2002; 66:87-91.

MacLennan AH. Hormone replacement therapy and the menopause –Australian Menopause Society. *Med J Aust* 1991; 155:43-4.

Merson MH, Dayton JM, O'Reilly K. Effectiveness of HIV prevention interventions in developing countries. *AIDS* 2000;14(Suppl 2):S68-84.

Miller SA, Santoro N, Lo Y, Howard AA, Arnsten JH, Floris-Moore M, Moskaleva G, Schoenbaum EE. Menopause symptoms in HIV-infected and drug-using women. *Menopause* 2005;12:348-56.

Munk-Jensen N, Nielsen SP, Obel EB, Eriksen PB. Reversal of postmenopausal vertebral bone loss by oestrogen and progestogen: a double blind placebo controlled study. *Br Med J* 1988; 296:1150-2.

Palella FJ Jr, Deloria-Knoll M, Chmiel JS, Moorman AC, Wood KC, Greenberg AE, et al. HIV Outpatient Study Investigators. Survival benefit of initiating antiretroviral therapy in HIV-infected persons in different CD4+ cell strata. ***Ann Intern Med*** 2003;138:620-6.

PCAP-BR, 2004 – Pesquisa de Conhecimento, Atitudes e Práticas na População Brasileira de 15 a 54 anos, 2004.

Rodrigues-Júnior AL, Castilho EA. A epidemia de Aids no Brasil, 1991 – 2000: descrição de espaço temporal. ***Rev Soc Med Tropical*** 2004; 37:312-7.

Rossin IR; Machado AA; Fatori A; Figueiredo JFC; Figueiredo LTM; Fonseca BAL; Moya MJ; Castro G; Martinez R. Perfil clínico-epidemiológico de indivíduos idosos com AIDS atendidos em um Hospital Universitário de Ribeirão Preto, Brasil. ***JBA*** 2001; 2: 13-18.

Santoro N, Arnsten JH, Buono D, Howard AA, Schoenbaum EE. Impact of street drug use, HIV infection, and highly active antiretroviral therapy on reproductive hormones in middle-aged women. ***J Womens Health*** 2005; 14:898-905.

São Paulo. Secretaria da Saúde. **O Climatério em Suas Mãos**. Manual para profissionais de Saúde. Prefeitura do Município de São Paulo, 2004.

Schoenbaum EA, Hartel D, Yungtai Lo, Howard A, Floris-Moore M, Arnsten JH, Santoro N. HIV infection, Drug use, and Onset of Natural Menopause. ***Clinical Infectious Disease*** 2005; 41:1517-24.

Sellers CR, Angerame MC. HIV/AIDS in older adults: a case study and discussion. ***AACN Clin Issues*** 2002;13:5-21.

Stampfer MJ, Colditz GA, Willett WC, Manson JE, Rosner B, Speizer FE, et al. Postmenopausal estrogen therapy and cardiovascular disease. Ten year follow-up from the nurses health study. ***New Engl J Med*** 1991; 25:756-62.

Tumbarello M, Rabagliati R, De Gaetano Donati K, Bertagnolio S, Tamburrini E, Tacconelli E. et al. Older HIV-positive patients in the era of highly active antiretroviral therapy: changing of a scenario. **AIDS** 2003; 17:128-31.

Utian, W.H. - Overview on menopause. **Am. J. Obstet, Gynecol.** 1987; 156:1280-3.

Utian W.H, Boggs PP. The North American Menopause Society 1998. Menopause Survey. Part I: Postmenopausal women's perceptions about menopause and midlife. **Menopause** 1999; 6:122-8.

Williams E, Donnelly J. Older Americans and AIDS: some guidelines for prevention. **Soc Work** 2002; 47:105-11.

Wilson MM. Menopause. **Clin Geriatr Med** 2003; 19:483-506.

## **6. Bibliografia de Normatizações**

França JL, Borges SM, Vasconcellos AC, Magalhães MHA. **Manual para normatização de publicações técnico-científicas**. 4<sup>a</sup> ed., Editora UFMG, Belo Horizonte, 1998. 213p.

Normas e procedimentos para publicação de dissertações e teses. Faculdade de Ciências Médicas, UNICAMP. Ed. SAD – Deliberação CCPG-001/98 (alterada 2005).

# 7. Anexos

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## 7.1. Anexo 1 – Ficha para coleta de dados

### O CLIMATÉRIO EM MULHERES HIV POSITIVAS

Data: \_\_\_\_/\_\_\_\_/\_\_\_\_

Número no estudo: [\_\_\_\_]

HIV+: [\_\_\_\_]

Número do prontuário: [\_\_\_\_]

HIV -: [\_\_\_\_]

UBS: \_\_\_\_\_

---

Data: \_\_\_\_/\_\_\_\_/\_\_\_\_

HIV+: [\_\_\_\_]

Número no estudo: [\_\_\_\_]

HIV-: [\_\_\_\_]

1- Idade: [\_\_\_\_!\_\_\_\_] anos completos

2- Raça: branca [1] não branca [2]

3- Qual o seu estado civil?

- [1] Solteira
- [2] Casada / amasiada
- [3] Separada/Divorciada
- [4] Viúva

4- Escolaridade: até que ano escolar a senhora freqüentou.

- [1] Nenhum
- [2] De 1 a 3 anos
- [3] De 4 a 7 anos
- [4] De 8 a 11 anos
- [5] De 12 ou mais

5- Aposentadoria: a senhora recebe aposentadoria do estado:

- [1] sim
- [2] não

6- Paridade:

- [1] nenhum
- [2] um
- [3] dois
- [4] três ou mais

7- Sintomas da menopausa (na época da coleta):

vasomotores

[1] Fogachos:	sim [1]	não [2]	2 semanas
[2] Tontura:	sim [1]	não [2]	2 semanas
[3] Sudorese noturna:	sim [1]	não [2]	2 semanas

Psicológicos

[4]: labilidade de humor:	sim [1]	não [2]	2 semanas
[5] Diminuição do interesse sexual:	sim [1]	não [2]	1 ano
[6] Perda de concentração:	sim [1]	não [2]	2 semanas
[7] Depressão:	sim [1]	não [2]	2 semanas
[8] Irritabilidade:	sim [1]	não [2]	2 semanas

Genito-urinário

[9] Incontinência urinária:	sim [1]	não [2]	2 semanas
[10] Secura vaginal:	sim [1]	não [2]	2 semanas
[11] Dispareunia (dor na relação sexual):	sim [1]	não [2]	2 semanas
[12] Ganho de peso:	sim [1]	não [2]	
[13] Palpitação:	sim [1]	não [2]	2 semanas
[14] Insônia:	sim [1]	não [2]	2 semanas

8 - em relação a sua menstruação no último ano:

- [1] Pré-menopausa: presença de fluxo regular sem mudança no padrão
- [2] *Perimenopausa precoce*: presença de sangramento regular nos últimos três meses mas com falhas no último ano.
- [3] *Perimenopausa tardia*: presença de ciclos regulares no último ano mas irregulares nos últimos 3 meses.
- [4] *Menopausa ou Pós-menopausa*: ausência de sangramento menstrual por período igual ou superior a 12 meses consecutivos. Qual a idade da última menstruação: \_\_\_\_\_ anos.
- [5] *Menopausa cirúrgica*: pacientes hysterectomizadas e/ou ooforectomizadas.

9- FSH: [1] inferior a 40 mUI/ml                      [2] igual ou superior a 40 mUI/ml                      [3] não tem

10- Exame físico

[1] Peso: [ ]Kg  
[2] Altura: [ ]cm  
[3] I.M.C: [ ]

11- Uso de antiretrovirais: sim [1] não [2] Há quanto tempo:

12- Contagem de células CD4 (células/mm<sup>3</sup>): classificados em:

[1]  $\geq 501$   
[2] 201 – 500  
[3]  $\leq 200$

13 - Tabagismo: a senhora fuma:

[1] sim  
[2] não  
[3] já fumou, mas parou há mais de 5 anos

14- Uso de drogas: a senhora usa ou usou alguma destas drogas nos últimos cinco anos:

[1] drogas injetáveis  
[2] crack  
[3] cocaína  
[4] heroína  
[5] maconha  
[6] nenhuma

15- De modo geral, com a Senhora Classifica sua saúde:

[1] excelente  
[2] boa  
[3] não muito boa  
[4] péssima

16- Idade da primeira relação sexual: \_\_\_\_ anos

17- Número de parceiros sexuais no último ano: \_\_\_\_ parceiros

18- Número de parceiros sexuais na vida toda: \_\_\_\_ parceiros

19- Tipos de relação sexual praticada (pode ser mais de um):

[1] Vaginal  
[2] Oral ativa  
[3] Oral passiva  
[4] Anal

## 7.2. Anexo 2 – Consentimento Pós-informação Oral

Prezada Senhora. estamos realizando uma pesquisa sobre menopausa em mulheres contaminadas ou não pelo HIV, com mulheres residentes na cidade de São José do Rio Preto, que tem o seguinte nome “O climatério em mulheres HIV +”. A pessoa responsável pela pesquisa é a Dr. Carlos Eduardo Ferreira, do Departamento de Ginecologia da UNICAMP e Médico ginecologista da Secretaria Municipal de Saúde e Higiene de São José do Rio Preto.

Gostaríamos de convidá-la a participar do estudo. Se aceitar este convite, sua participação consistirá em responder a um questionário que contém perguntas sobre a senhora relacionadas a diversos assuntos sobre a menopausa. O tempo aproximado para responder ao questionário é de 10 minutos.

Sua participação e opinião são muito importantes para nosso estudo. A Senhora tem a liberdade de aceitar ou recusar a participar do estudo, bem como a de não responder alguma (s) das perguntas do questionário, se assim desejar.

Asseguramos-lhe que o seu nome não aparecerá no questionário, que receberá apenas um número pelo qual será identificado. De igual modo, quando os resultados desta pesquisa forem divulgados, nunca será mencionado o nome de qualquer pessoa que tiver respondido o questionário. A Senhora aceita participar do estudo respondendo o questionário?

**Entrevistadora:** para todas as mulheres que aceitarem participar, aplicar o questionário.