

NAVAL HEALTH RESEARCH CENTER

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TRANSMITTED INFECTIONS IN A MALE
U.S. NAVY POPULATION***

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PREVALENCE OF CIRCUMCISION AND ITS ASSOCIATION WITH HIV AND
SEXUALLY TRANSMITTED INFECTIONS IN A MALE U.S. NAVY POPULATION

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Abstract

Objectives: To determine circumcision prevalence and its association with HIV and STI in a male United States military population.

Design: Case-control study of HIV-infected U.S. military personnel (n = 232) from 7 military medical centers and male U.S. Navy controls (n = 516) from an aircraft carrier.

Methods: Cases and controls completed similar self-administered HIV behavioral risk surveys. Case circumcision status was abstracted from medical charts while control status was reported on the survey. Cases and controls were frequency matched on age. Multiple logistic regressions were constructed separately to evaluate the role of circumcision in the acquisition of HIV and STI.

Results: Cases (84.9%) and controls (81.8%) reported similar proportions of circumcision. Prevalence of circumcision among United States-born men was higher (85.0%) than those born elsewhere (58.1%). After adjustment for demographic and behavioral risk factors, lack of circumcision was not found to be a risk factor for HIV (OR = 0.9; 95% CI, 0.51–1.7) or STI (OR = 1.08; 95% CI, 0.52–2.26). The odds of HIV infection were 2.6 higher for irregular condom users, 5 times higher for those reporting STI, 6.2 times higher for those reporting anal sex, 2.8–3.2 times higher for those with 2–7+ partners, nearly 3 times higher for Blacks, and 3.5 times higher for men who were single or divorced/separated.

Conclusions: Although known HIV risk factors were found to be associated with HIV in this military population, there was no significant association with male circumcision. Randomized clinical trials currently underway should shed more light on this pressing topic.

Keywords: HIV, risk factors, male circumcision, sexually transmitted infection, military, sex behavior

Introduction

With an estimated 5 million new infections, 3 million deaths, and 40 million prevalent infections in 2003, reducing the incidence of HIV infection remains a critical, worldwide goal. In recent years, several studies conducted among sub-Saharan African male populations report circumcision to be associated with reduced risk of HIV infection [1–5]. Compelling evidence from studies conducted among sub-Saharan African populations of circumcision's protective effect against HIV acquisition, is now considered substantial enough that many are advocating for male circumcision as one component of a comprehensive HIV prevention package [5,6].

Whether circumcision of male infants should be recommended as a method of HIV prevention in developed countries such as the United States remains the subject of heated controversy. Thus far, the majority of studies investigating the association of circumcision and HIV have been conducted among Sub-Saharan African populations, which differ substantially from developed nations in terms of HIV risk factors, sexual practices, and medical care availability.

Ulcerative sexually transmitted infections (STIs), such as genital herpes, syphilis, and chancroid, known risk factors for HIV infection [2,7–11], are more prevalent among sub-Saharan African populations, the same populations with low levels of circumcision. This may be a major source of residual confounding in the HIV–circumcision association.

Relatively few studies have been conducted in the United States or other developed nations investigating the association between circumcision status and STI acquisition, and, to our knowledge, none have been of large enough scale to report any

significant finding regarding an association with HIV acquisition. With respect to STI acquisition, these studies have yielded inconsistent results, with several showing a protective effect of circumcision [11–13] while others found an increased risk for STIs among circumcised males [14].

In addition to STI acquisition, several studies among western populations have shown circumcision to have a strong protective effect against urinary tract infections (UTIs) among male infants [15–17] and penile cancer in middle-aged and older men [18–20]. However, there is still controversy surrounding the practice of male circumcision, as opponents argue that the medical benefits do not outweigh the risks, and that the neonatal procedure causes unnecessary pain, reduced penile sensitivity, and violates the human rights of the unconsenting child [14,21–23]. This case-control study describes the prevalence and demographic determinants of circumcision in a U.S. military population and the association of circumcision and HIV/STI acquisition.

Methods

Study population

HIV seropositive case participants in this case-control study were male, active-duty U.S. personnel from all branches of the military recruited from 7 military medical referral centers throughout the United States as a part of a larger case-series study. Enrollment and study procedures are described elsewhere [24,25]. All cases had documented HIV seroconversion and completed a self-administered behavioral risk factor questionnaire.

Control participants from a general Navy aircraft carrier population completed similar questionnaires. Controls were assumed to be HIV seronegative. U.S. Department

of Defense policy stipulates that all military personnel undergo predeployment HIV screening and test negative.

Case and control participants had to meet two criteria for inclusion in this study. First, their circumcision status had to be available. Case circumcision status was abstracted from previously collected medical data, with 51.2% (294/574) having this information available. The control population was limited to those who answered the circumcision question (yes/no) on the self-administered survey (93.3%; 859/ 921). Second, using a combination of survey questions, cases and controls had to be categorized as having had sex during their reporting time frame (286 cases and 801 controls).

Case participants reported behaviors occurring within their seroconversion window (SCW), the time between the last negative and first positive HIV test. To reduce variability in the length of the SCW, and recall bias, only cases with a SCW of 3 or less years (median = 1 year) were included (n = 234). Providing comparable reporting time frames controls were asked to report their behaviors within last 12 months.

The Institutional Review Boards of participating institutions approved both studies; all participants provided informed consent.

Data collection

Case participants' data collection occurred between February 1997 and June 2001. Demographic characteristics, sexual risk behaviors, and STI history were assessed. Circumcision status for cases was abstracted from medical records obtained during the case study.

The control survey was conducted in April 2002 during a “safety stand-down,” a period of time when all personnel at a military command engage in safety training rather than performing their regular jobs. Controls were administered a questionnaire comparable to that of the cases, with the deletion of questions not applicable for an HIV-seronegative population, and the addition of questions regarding circumcision status, HIV testing, and supplemental condom use questions.

Demographic characteristics, including age, ethnicity, country, and state of birth (U.S.-born), marital status, education, and rank were collected. HIV risk behaviors, including number of sexual partners, engaging in anal or group sex, geographic location of sex (U.S. or foreign), STI history, and condom use during vaginal, anal, and oral sex were collected.

Statistical analysis

Since cases were significantly older than controls, and age was thought to be associated with both HIV risk and prevalence of circumcision, frequency matching on age was performed. Eight strata were created with matching ratios varying from 1:1 to 1:4 depending upon the number of available controls. The final sample comprised 232 cases and 516 frequency matched controls.

Comparisons of demographics and sexual risk behavior by case status were performed using analysis of variance (ANOVA) and chi-square tests. Circumcision prevalence was compared using chi-square tests.

Unconditional logistic regression was used to examine the effect of circumcision on HIV infection after adjustment for demographic, and sexual behavior risk variables. Accounting for age frequency matching, 7 dummy variables were created and included in

all models. For model building purposes, all demographic and sexual risk behavior variables univariately associated with HIV were initially included in the models. The final logistic regressions included variables that remained significantly ($p \leq .05$) associated with HIV status. Likewise, multivariate logistic regression models were used to examine the independent association between circumcision status and STI history.

Potential participation biases were examined through demographic comparisons of men with (participants) and without (nonparticipants) circumcision status available using ANOVA and chi-square tests. All statistical analyses were performed using SAS (Release 9.0, SAS Institute, Inc., Cary, NC, 2002).

Results

Among the cases, availability of circumcision status differed greatly by participation site ($p < 0.001$). However, after adjusting for site, there were no significant demographic differences between cases who had ($n = 294$; 51.2%) and did not have ($n = 280$; 48.8%) their circumcision status available. Furthermore, among the controls, no demographic differences were found between those who reported their circumcision status ($n = 859$; 93.3%) and who did not ($n = 62$; 6.7%).

The proportion of circumcised men did not significantly differ between cases (84.9%) and controls (81.8%). Case participants were more likely to be Black, single or divorced, and have some college or a bachelor's degree or higher, and be of E4-E6 military ranks than the controls (Table 1).

The prevalence of circumcision among this U.S. military population was particularly high (more than 85%) for birth-years 1945-1964 and 1970-1979, with a decline during 1965-1969 (77.1%) and the 1980s (74.2%) (Table 2). Prevalence of

circumcision differed dramatically by ethnicity, with the highest prevalence among whites (92.4%) and the lowest among Hispanics (44.1%). There was a significantly higher proportion of circumcised men among those born in the United States (85.0%) as compared with men born in other countries (58.1%). There were some regional differences, with the highest prevalence of circumcision among men born in the Midwest (90.2%) and Northeast (86.8%), followed by the West (85.0%) and the South (82.0%).

Case and control participants differed significantly with respect to sexual risk characteristics (Table 3). A higher proportion of cases did not use condoms regularly (91.0%), had sex in either a foreign country or both a foreign country and the United States (27.6%), reported anal sex (72.8%), group sex (29.5%), had more sexual partners (almost 75% had 3 or more partners), and had higher prevalence of STIs (22.8%), as compared with controls.

In multivariate logistic regression analysis (Table 4), lack of circumcision was not found to be associated with HIV (OR = 0.90; 95% CI, 0.51–1.70) after controlling for significant demographic and sexual risk covariates. These data confirmed an association between HIV and inconsistent condom use (OR = 2.60; 95% CI, 1.36–4.98), recent history of STI (OR = 5.04; 95% CI, 2.46, 10.32), and anal sex (OR = 6.24; 95% CI, 3.98–9.78). Having multiple sexual partners was also associated with increased risk of being HIV positive, with OR = 2.83 (95% CI, 1.21–6.59) for those with two partners, OR = 3.88 (95% CI, 1.98–7.63) for men with 3-6 sexual partners, and OR = 3.24 (95% CI, 1.60–6.58) for those who had 7 or more sexual partners. Demographic characteristics associated with HIV-infection included Black ethnicity (OR = 2.97; 95% CI, 1.81–4.87),

single marital status (OR = 3.51; 95% CI, 1.85–6.63), and being divorced/separated (OR = 3.53; 95% CI, 1.62–7.70).

No statistically significant association was found between circumcision status and history of STI either univariately or multivariately (data not shown). For the entire group, odds of having a history of STIs among uncircumcised men were not different from those for circumcised men (OR = 1.08; 95% CI, 0.52–2.26) after adjusting for age, ethnicity, marital status, history of anal sex, and condom use. Similarly, no associations were observed when the circumcision–STI association was examined separately among HIV cases and controls.

Discussion

This case-control study of the role of circumcision status in HIV acquisition among a U.S. military population provides evidence that lack of male circumcision is not a risk factor for HIV or STI acquisition in this population, with no significant association found either univariately or after adjustment for demographic and sexual risk factors. In fact, the direction of the association indicated lack of circumcision to be protective for HIV infection, although without statistical significance. Known HIV risk factors, including: having multiple partners, inconsistent condom use, history of STI, anal sex, and demographic characteristics of Black ethnicity and single or divorced marital status, were strongly associated with HIV status in this population.

During the past 20 years in the United States, overall rates of male circumcision have declined; in part due to changes in attitudes, and in part due to changes in the country's ethnic distribution. Caucasians have the highest prevalence of circumcision in the United States, whereas Hispanics and Blacks report significantly lower rates.

Differences in changes by ethnicity and geography are evident, with the West experiencing the most dramatic decline, from 64% to 37% [26], attributed largely to the increasing Hispanic population. However, circumcision rates have increased in the Midwest and South, and among Blacks [12,14]. Given the heavy burden of HIV among U.S. Black and Hispanic populations, and the lower rates of circumcision among these racial/ethnic groups [26], it was anticipated that an association between circumcision and HIV would be found, hence a possible means to reduce the burden of HIV/AIDS in these communities. The findings of this study indicate that it is unlikely that lack of circumcision is contributing to the ethnic disparity in HIV rates in the United States.

The few case-control studies conducted among high-risk populations in Africa showed mixed results for circumcision as a risk factor for HIV [27–29]. This study's findings of no significant association between circumcision status and both HIV and STI contradict a number of studies, finding an association, conducted principally among African populations [30,31]. However, one case-control study of a general population in Senegal [32] also found a protective effect for lack of circumcision on HIV status.

Studies of HIV or STI and circumcision status conducted in developed nations have yielded contradictory findings [12,13,33]. Results from cross-sectional and cohort analyses of the project RESPECT study group, U.S. sexually transmitted disease clinic-based populations, showed slightly elevated risk for gonorrhea and syphilis among uncircumcised men, while there was essentially no risk difference found for chlamydial infection. Biological and mechanical mechanisms for increasing risk through microabrasion and the inherent infectiousness of the organisms may explain these findings.

An analysis of data from the 2000 British National Survey of Sexual Attitudes and Lifestyles (Natsal), found an overall circumcision rate of 15.8% with no statistically significant difference in cumulative STI incidence by circumcision status [34]. Although the British population has relatively low rates of circumcision, and the United States has moderately high rates, the British population's circumcision rates likewise differ by ethnicity and country of origin. However, the associations were opposite those seen in the United States, with ethnic minority men in Britain more likely to report circumcision, as were men born outside the country. Considering “developed” countries as monolithic in terms of the role of circumcision in STI and HIV risk may be misleading. Nonetheless, there are similarities in sanitary conditions and relative access to healthcare.

Differences in the various study findings may be due to uncontrolled confounding by religion [35,36], hygiene practices, restrictive social rules limiting partners outside of marriage, or differences in sexual practices and risk behaviors [7,37,38], rather than circumcision, per se. Basic health and sanitation conditions, as well as access to healthcare in the United States, are generally better and more comprehensive than in many African nations, which can greatly influence the role of circumcision, or lack thereof, in HIV transmission.

In our study, while there were differences in the method of circumcision reporting between cases and controls, and differences in the rates of available circumcision status, no differences in demographics were seen after adjustment for participation location. Site-specific history-taking practices, and differences in clinical report forms account for reporting differences, not biases, with respect to patient characteristics. Some reporting bias could be present due to differences in clinician versus self-report data, although the

direction of the bias is unclear [39]. The rates of circumcision found among the cases (85%) and controls (81%) are quite similar to the rates reported by the Centers for Disease Control and Prevention [26].

As discrepant evidence regarding the role of male circumcision in HIV/STI transmission has surfaced and societal perceptions of circumcision have changed, the policy of the American Academy of Pediatrics (AAP) regarding routine neonatal circumcision in the United States was reassessed. In 1999, the AAP Task Force on Circumcision issued a policy statement recognizing the existing scientific evidence demonstrating medical benefits of neonatal circumcision, and yet concluded that the data remain insufficient to recommend routine neonatal circumcision; thus leaving the decision up to parents with the guidance of their pediatrician.[20]

This study adds weight to the evidence that lack of circumcision is not a risk factor for HIV in the general population of a developed country. Although known HIV risk factors such as inconsistent condom use, history of STI, multiple partners, and anal sex were found to be associated with HIV in this military population, there was no significant association with male circumcision. Randomized clinical trials currently underway should shed more light on this pressing topic.

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Table 1. Comparison of demographic characteristics by HIV status

	Total	Cases	Controls	
Demographic characteristics	n = 748	n = 232	n = 516	<i>P</i> value*
	%	%	%	
Ethnicity				
Black	28.9	44.4	21.9	< 0.001
White	47.7	40.5	51.0	
Hispanics	11.2	6.9	13.2	
Other	12.2	8.2	14.0	
Marital Status				
Single	49.3	60.8	44.2	< 0.001
Married, living apart	10.6	6.0	12.6	
Married, living together	29.4	12.9	36.8	
Divorced or separated	10.7	20.3	6.4	
Education				
High school or less	41.8	32.8	45.9	0.033
Some college	46.1	53.7	42.8	
Bachelor's degree or higher	12.0	13.6	11.4	
Rank				
E1-E3	24.5	18.7	27.0	0.236
E4-E6	60.6	69.0	56.9	
E7-E9	6.5	4.6	7.3	
O1-O5	8.4	7.8	8.7	
Circumcision status				
Circumcised	82.8	84.9	81.8	0.334
Uncircumcised	17.3	15.1	18.2	

*Adjusted for frequency matching on age.

Table 2. Prevalence of male circumcision by year of birth, ethnicity, and place of birth among a general U.S. military population (n =748)

Characteristic	n	(%)	<i>P</i> value*
Year of birth			
1945-1959	33	(89.5)	--**
1960-1964	72	(86.8)	
1965-1969	91	(77.1)	
1970-1974	132	(88.6)	
1975-1979	167	(84.8)	
≥ 1980	109	(74.2)	
Ethnicity			
African American	175	(81.0)	< 0.001
White	330	(92.4)	
Hispanics	37	(44.1)	
Other	77	(84.6)	
Country of birth			
USA	583	(85.0)	0.015
Other	36	(58.1)	
Region of birth (US)			
Northeast	72	(86.8)	0.005
Midwest	83	(90.2)	
South	182	(82.0)	
West	85	(85.0)	

*Adjusted for frequency matching on age.

**Year of birth and age are highly collinear, therefore, adjustment for age is not performed.

Table 3. Comparison of sexual risk characteristics by status

	Total	Cases	Controls	
Sexual risk characteristics*	n = 748	n = 232	n = 516	<i>P</i> value**
	%	%	%	
Condom use (vaginal & anal sex)				
Always	15.1	9.1	17.8	0.009
Irregular	84.9	91.0	82.2	
Any STIs				
Yes	9.4	22.8	3.3	< 0.001
No	90.6	77.2	96.7	
Number partners				
1	33.8	10.8	44.2	< 0.001
2	9.1	8.2	9.5	
3-6	23.3	37.5	16.9	
7+	21.7	37.1	14.7	
Missing	12.2	6.5	14.7	
Anal sex				
Yes	39.4	72.8	24.4	< 0.001
No	60.6	27.2	75.6	
Group sex				
Yes	18.5	29.5	13.7	< 0.001
No	81.5	70.5	86.3	

Sex location				
US only	78.2	69.0	82.4	< 0.001
Foreign only or US & foreign	17.7	27.6	13.2	
Missing	4.1	3.5	4.5	

*Reported during seroconversion window for cases and past 12 months for controls.

**Comparison of cases and controls for each sexual risk characteristic after adjusting for frequency matching on age.

Note: STI, sexually transmitted infection.

Table 4. Multivariate logistic regression model of HIV and circumcision status association^a

Variable	OR	95% CI	<i>P</i> value
Circumcision status			
Circumcised	1.0*	--	0.816
Uncircumcised	0.90	0.51, 1.70	
Condom use (vaginal & anal sex) ^b			
Always	1.0*	--	0.004
Irregular	2.60	1.36, 4.98	
Any STIs			
No	1.0*	--	< 0.001
Yes	5.04	2.46, 10.32	
Number of partners			
1	1.0*	--	< 0.001
2	2.83	1.21, 6.59	
3-6	3.88	1.98, 7.63	
7+	3.24	1.60, 6.58	
Missing	1.04	0.43, 2.47	
Anal sex			
No	1.0*	--	< 0.001
Yes	6.24	3.98, 9.78	
Ethnicity			
White	1.0*	--	< 0.001
Black	2.97	1.81, 4.87	
Hispanic	0.82	0.36, 1.86	
Other	1.13	0.54, 2.38	

Marital Status

Married, living together	1.0*	--	< 0.001
Single	3.51	1.85, 6.63	
Married, living apart	0.86	0.37, 2.03	
Divorced or separated	3.53	1.62, 7.70	

^aOdds of being a case vs. a control adjusted for all variables in the table and age frequency matching categories.

*Reference category.

^bAll sexual risk behaviors were reported within last 12 months (for controls) or within seroconversion window (for cases).

Note: STI, sexually transmitted infection; OR, odds ratio; CI, confidence Interval

REPORT DOCUMENTATION PAGE

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6. AUTHORS Thomas, Anne G, PhD; Bakhireva, Ludmila N, MD, MPH; Brodine, Stephanie K, MD; Shaffer, Richard A, PhD.	
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13. SUPPLEMENTARY NOTES

14. ABSTRACT (maximum 200 words) Objectives: To determine circumcision prevalence and its association with HIV and STI in a male United States military population. Design: Case-control study of HIV-infected U.S. military personnel (n = 232) from 7 military medical centers and male U.S. Navy controls (n = 516) from an aircraft carrier. Methods: Cases and controls completed HIV risk surveys. Case circumcision status was abstracted from medical charts while control status was reported by survey. Multiple logistic regressions were constructed evaluating the role of circumcision in the acquisition of HIV and STI. Results: Cases (84.9%) and controls (81.8%) reported similar proportions of circumcision. Prevalence of circumcision among U.S.-born men was higher (85.0%) than those born elsewhere (58.1%). After adjustment for demographic and behavioral risk factors lack of circumcision was not found to be a risk factor for HIV (odds ratio [OR] = 0.9; 95% confidence interval [CI], 0.51–1.7) or STI (OR = 1.08; 95% CI, 0.52–2.26). Conclusions: Although known HIV risk factors were found to be associated with HIV in this military population, there was no significant association with male circumcision. Randomized clinical trials currently underway should shed more light on this pressing topic.

15. SUBJECT TERMS HIV, risk factors, male circumcision, sexually transmitted infection, military, sex behavior
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