

Circumcision as a Risk Factor for Urethritis in Racial Groups

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Abstract: A retrospective population-based case-control study of sexually transmitted urethritis was conducted at a large military base over a 21-month period. During the study, 9,514 patients were seen for sexually transmitted disease. The analysis was restricted to active duty males and showed that Blacks had 14.8 times the incidence rate of gonococcal urethritis (GCU) and 4.7 times the rate of nongonococcal urethritis (NGU) compared to Whites. There were

slightly fewer cases of NGU than GCU. A case-control study of active duty soldiers showed that both Black and White circumcised subjects were 1.65 times as likely to have NGU as uncircumcised subjects (95% CI: 1.37–2.00). However, circumcision was not associated with an increased incidence of GCU. (*Am J Public Health* 1987; 77:452–454.)

Introduction

Gonococcal urethritis (GCU) is the most commonly occurring reportable communicable disease in the US,¹ with over a million cases reported annually. Non-gonococcal urethritis (NGU) secondary to *Chlamydia trachomatis*, *Ureaplasma urealyticum*, and other agents is not a reportable disease in many states. However, the incidence is estimated to be twice that of GCU.^{2–5} Population based incidence studies,^{6,7} cohort studies,^{8–10} and clinic-based studies¹¹ have all shown that GCU occurs two to 10 times more frequently in the Black population, whereas the NGU rates are about the same or slightly higher among Whites. Risk factors shown to be associated with the acquisition of GCU and NGU include unmarried status, multiple sexual partners, low socioeconomic status, and a history of previous sexually transmitted urethritis (STU). However, when all of these factors are controlled for, the rate of GCU remains higher in Blacks.^{3–5}

The data are sparse regarding the importance of the prepuce in the acquisition of STU. Parker, *et al*,¹² in their case-control study of 1,350 men attending a public health clinic in Perth, Australia showed that the uncircumcised men were twice as likely as circumcised men to have GCU. There was no association with NGU. However, confounding by number of sexual partners, marital status, and use of condoms was not controlled for in that clinic-based study.

The prepuce may provide a physical or immunological barrier against infection or an excellent milieu for infectious agents to grow and multiply.¹² This prompted us to investigate the possibility that the elevated risk of STU found in Blacks was due to the influence of the prepuce, since circumcision is more prevalent in the White population.

In order to test the hypotheses that circumcision is associated with the risk of acquiring GCU or NGU a retrospective, population-based case-control study was conducted at a large US military post.

Methods

Study Site

The study was conducted at a US military post with a history of high rates of sexually transmitted disease (STD) in active duty members, dependents, and the local civilian community.¹³ Regulations at the post, enforced with good success for a period of four years, included a strict policy of

referring all STD cases to the Epidemiologic Disease Clinic (EDC). In addition to STDs, the EDC is used for all those diseases of epidemiologic importance, and all reportable communicable disease; it serves a population averaging 48,472 on active duty and 101,791 eligible dependents.

Case and Control Definitions

Persons seen by a military physician on the post with signs or symptoms consistent with any STD and persons eligible for care at the military hospital who presented to the local county health department with signs or symptoms consistent with any STD were referred without treatment to the EDC. Only those active duty members and dependents who elected to seek care from and pay a private physician were missed from the STD surveillance.

Criteria for inclusion in the study population as a case included: presentation to the EDC during the period of the study January 1, 1983 to September 30, 1984; granting of informed consent (there were no refusals); completion of a standardized history and physical and laboratory examination; active duty male; receiving the diagnosis of GCU or NGU according to Centers for Disease Control criteria.¹⁴

Criteria for inclusion in the study population as a control were similar except that the patients presented with a history of recent sexual contact, and were worried about having a STD, yet after examination were found to be without signs and symptoms consistent with any STD and their urethral smear gram stains and modified Thayer-Martin cultures were negative.

Procedures

Every subject entering the EDC during the study period had a standardized history by a STD technician including sociodemographic information, time since last exposure, and use of condom. This was followed by a contact tracing interview and a standardized genitourinary physical examination. For this study, circumcision was defined as the objective surgical absence of a prepuce.

All subjects had a urethral smear gram stain and a modified Thayer-Martin plate inoculated and incubated in 5 per cent carbon dioxide incubator. *Neisseria gonorrhoeae* was identified and confirmed by standard technique. Those subjects with a urethral smear positive for gram negative intracellular diplococci (GNID) and/or modified Thayer-Martin culture positive for *Neisseria gonorrhoeae* were diagnosed as GCU.^{14,15} Those subjects with a urethral smear negative for GNID and four or more polymorphonuclear leukocytes per oil immersion field (PMNs/HPF), and a modified Thayer-Martin culture negative for *Neisseria gonorrhoeae* were diagnosed as NGU.^{14,15}

Centers for Disease Control Guidelines¹⁴ were used to treat all cases of GCU. Those subjects with GCU who had

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TABLE 1—Case and Control Demographic Comparison

Demographics	Control (N = 553)	Non-Gonococcal Urethritis (N = 2543) %	Gonococcal Urethritis (N = 2982) %
Race			
White	29.0	33.0	14.0
Black	65.0	60.0	81.0
Other Ethnic Group	6.0	7.0	5.0
Rank			
Junior Enlisted	25.5	28.4	31.2
Junior Non-Commissioned Officer	51.3	56.2	58.8
Senior Non-Commissioned Officer	21.6	12.3	9.3
Commissioned Officers	1.5	3.1	0.7
Education			
Non-High School Graduate	4.4	4.9	5.2
High School Graduate	73.9	73.2	80.3
Some College	21.7	21.9	14.5

post-gonococcal urethritis (four or more PMNs/HPF in the absence of GNID, with a negative modified Thayer-Martin urethral culture test-of-cure) after adequate treatment were given the additional diagnosis of NGU.

Over 97 per cent of the infections were treated initially with one antibiotic. In this way, mixed GCU/NGU infections were more likely to be identified and coded. A subject with GCU who was diagnosed after treatment as having post-gonococcal urethritis secondary to NGU was coded as one incident case of GCU and NGU. If a subject returned to the EDC at any time after a successful course of treatment with an interval without symptoms, he was treated as a new incident case.

Data Analysis

The data were input into a Vax 11/700 mini-computer and checked for accuracy and coding errors. Only active duty males with complete information were included in this analysis. The data set was analyzed using the Statistical Analysis System (SAS) for cross-tabulations. The PLR program on the BMDP statistical package was used to perform non-stepwise multiple logistic regression on the data set. Mantel-Haenszel summary odds ratio¹⁶⁻¹⁸ were performed on the data set.

Results

During the 21 months of the study, there were 9,514 STD subjects seen in the EDC. Eighty-four per cent were male, 67 per cent Black, 27 per cent White, and 6 per cent other ethnic groups. Eighty-six per cent were active duty members and 14 per cent were military dependents. During the study the active duty male population averaged 45,250 resulting in 950,250 persons/months of observation.

In Table 1, the race, rank, and educational parameters of the control population and two case populations for the two individual case-control studies being evaluated are shown. The proportion of Blacks in the GCU population was markedly higher than that of the control group, and the proportion of GCU cases with "some college" was somewhat lower than the control group.

There were 3,057 cases of GCU of which 2,982 were in active duty males with a resultant incidence density of 3.13/1000 person-months for the active duty population. There were 2,653 cases of NGU of which 2,543 were in active

TABLE 2—Multiple Logistic Regression Analysis of Gonococcal Urethritis by Circumcision and Other Covariates

Variable	Odds Ratio	(95% CI)
Circumcision		
Circumcised versus Uncircumcised	0.88	(0.71-1.09)
Race		
Black vs White	1.20	(1.11-1.32)
Other vs White	1.00	(0.87-1.16)
Sexual Partners		
2-3 vs 0-1	1.09	(0.96-1.22)
4+ vs 0-1	1.27	(1.05-1.54)
Marital Status		
Married vs Unmarried	0.74	(0.59-0.93)
Education		
High-school graduate vs Non-graduate	0.76	(0.59-0.99)
Age (years)	0.98	(0.96-1.01)

TABLE 3—Multiple Logistic Regression Analysis of Non-Gonococcal Urethritis by Circumcision and Other Covariates

Variable	Odds Ratio	(95% CI)
Circumcision		
Circumcised vs Uncircumcised	1.65	(1.37-2.00)
Race		
Black vs White	1.01	(0.90-1.14)
Other vs White	0.81	(0.64-1.01)
Sexual Partners		
2+ vs 0-1	0.93	(0.83-1.04)
Marital Status		
Married vs Unmarried	0.95	(0.76-1.19)
Education		
High-school graduate vs Non-graduate	0.97	(0.88-1.06)
Age (years)	0.98	(0.92-1.04)

duty males with a resultant incidence density of 2.68/1000 persons-months for the active duty population.

Blacks had 4.7 times the rate of Whites for NGU and 14.8 times the White rate for GCU. The other ethnic groups were intermediate between Blacks and Whites for both diseases.

Circumcision Effects

Eighty-five per cent of the Whites, 34 per cent of the Blacks, and 33 per cent of the other ethnic groups were circumcised. Less than 1 per cent of both cases and controls reported using condoms. There was no association between GCU and circumcision in any of the three racial groups (Mantel-Haenszel summary odds ratio 0.90 (95 per cent CI 0.73, 1.11).

In order to control for a variety of factors potentially confounding such an association, a maximum likelihood estimate (MLE) logistic regression analysis was done using GCU as the dependent variable in the model. Table 2 shows the results of the analysis, odds ratio, and 95 per cent CI for each variable, after controlling for the other variables. GCU was not associated with circumcision in this analysis.

In contrast to GCU, circumcision was associated with an increased incidence of NGU in both Blacks and Whites. The Mantel-Haenszel summary odds ratio was 1.70 (95% CI 1.37, 2.10) (data available on request to authors).

In Table 3, the same logistic regression analysis was conducted using NGU as the dependent variable and the same independent variables. Only circumcision was associ-

ated with NGU in the model, with an odds ratio of 1.65 (95 per cent CI 1.37–2.00).

Discussion

Racial differences in STU incidence were higher than those previously reported.²⁻⁵ Some of this difference could reflect racial differences in seeking care from private physicians, but this is not felt to be important based on information provided by local private physicians, and by the representativeness of the ranks in the study population.

The incidence figures also indicate that NGU is occurring less frequently than GCU in this population in contrast to previously reported ratios of 2–2.5 NGU cases per GCU case in civilian populations.^{2,3} It is possible that the nature of this young, military population may account for the different ratio.

The control group was representative of members of the military post community who are sexually active and worried about having been in contact with a partner with STD but who have not acquired STU as shown by the closeness of the case and control populations in Table 1 with respect to all the variables except the presence or absence of diagnosed disease.

It is clear from Tables 2 and 3 that the racial differences almost disappear in this case-control analysis, after controlling for the other variables. This suggests that for both NGU and GCU there is no biologic mechanism accounting for the difference in rates among the races identified in the population-based incidence data.

The data in Table 2 re-emphasize the association of marital status, race, education, and number of sexual partners in the last month with the risk of acquiring GCU, as well as providing evidence for no association between circumcision and the risk of acquiring GCU.

For NGU, the results in Table 3 show that among this population of sexually active men, having a prepuce (being uncircumcised) was protective for acquiring NGU and there were no associations with the other variables and NGU.

Since the symptoms of NGU are often subtle, it is possible that uncircumcised men were more likely than circumcised men to overlook the presence of urethral discharge. On the other hand, the low proportion of NGU to GCU seen in this study population may reflect the fact that more symptomatic NGU cases were seen in this study.

The findings of this study are intriguing because circumcision is much less common in Black and other ethnic groups compared to Whites and one *a priori* hypothesis was that the presence of a prepuce may increase the risk of acquiring NGU and GCU independent of other factors. Wiswell *et al*¹⁹ found a protective effect of circumcision when looking at the rate of urinary tract infections in infant males, and Parker, *et*

*al*¹² found circumcision to be protective for GCU. However, the findings of this study suggest that the prepuce has a protective effect against the acquisition of NGU and that there is no association of circumcision with GCU.

Having a prepuce may be protective against NGU by effecting the physiologic milieu of the glans penis, by association with post-coital genital hygiene behavior, or by local immune defense mechanisms acting against the agent. Further basic research needs to be done to clarify these relations.

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