Risk Factors For Incident Neisseria Gonorrhoeae In A Prospective Cohort Of Kenyan Female Sex Workers

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Abstract

299 sex workers in Nairobi, Kenya were followed a median of 14 months (IQR: 6-24 months) until acquisition of GC infection or censoring. At the initial visit and subsequent visits every two months, cervical samples were collected for GC and CT testing by PCR. At baseline, 18 (6%) of the 299 women had prevalent GC infection. Thirty-one incident cases of GC were detected over 345 years of observation, giving an incidence of 9.0 GC infections per 100 women-years. After controlling for age, HIV-serostatus and significant univariate variables, incident CT infection (Adjusted (A)HR = 5.9, 95% CI 2.2-15.8), and clinical findings of cervicitis (AHR = 3.1, 95% CI 1.1-8.6) remained independent risk markers for incident GC. In addition, the temporality of the relationship between the pathogens suggests a possible direct role of CT increasing the risk of GC.

Research location: Kariobangi Nairobi City Council Clinic under Kenyatta National Hospital

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INTRODUCTION

Neisseria gonorrhoeae, the second most common sexually transmitted bacterial infection with a global incidence of 62 million cases per year[1], is an etiologic agent of pelvic inflammatory disease and has been associated with an increased risk of HIV-1 infection[2]. Multiple studies have focused on female sex workers (FSWs) as a high risk group for acquisition and transmission of sexually transmitted infections (STIs)[2,3,4,5], and serving as a core group in the transmission of HIV and STIs in sub-Saharan Africa[3]. However, there are limited data that indicate risk factors for incident N. gonorrhoeae infection (GC) and interaction with other STIs[6]. Given the lack of a protective anamnestic response to GC[7], discovering sociodemographic and behavioral correlates of incident infection are important to develop efficient disease control strategies.

METHODS

A 299 member closed longitudinal cohort of female sex workers was assembled as part of an STI epidemiology and immunobiology study[8] in May 2000 at the Kariobangi Nairobi City Council Clinic in Nairobi, Kenya. The study protocol underwent ethical review and approval at the relevant institutions. At the initial visit women were counseled on the risks involved with their current occupation and encouraged to find another profession. The women were treated for any current bacterial STI, directed on harm reduction, and provided free condoms. To join the cohort, written informed consent was necessary as well as the collection of demographic characteristics and a clinical history. A general physical and pelvic examination were included at the initial visit. Cervical specimens acquired during examination were tested for Neisseria gonorrhoeae and Chlamydia trachomatis by molecular detection. Blood was taken for syphilis and HIV-1 serology as well as CD4+ and CD8+ lymphocyte counts.

Each participant was asked to return to the clinic every two months for follow up. At each successive visit, clinical and behavioral histories were determined since the time of the previous visit. Women were examined for N. gonorrhoeae and C. trachomatis infection. Every six months, blood was drawn and tested for HIV and syphilis serology as well as CD4 and CD8 lymphocyte counts. After every visit, women

were asked to come back four days later to receive the results of the tests. If positive for N. gonorrhoeae or C. trachomatis, the woman would receive a one-time dose 500 mg of ciprofloxacin or a 7 day regimen of two daily doses of doxycycline 100 mg.

Molecular detection of N. gonorrhoeae and C. trachomatis was performed by polymerase chain reaction (PCR) assay (Amplicor, Roche Diagnostic System, Inc., Somerville, NJ). Sera for HIV serology examination was performed using a synthetic enzyme immunoassay (ELISA, Detect HIV-1, Biochem ImmunoSystems, Inc., Montreal, Canada). If the serological exam was positive, a second confirmatory exam was performed (Recombigen, Cambridge Biotech LTD, Ireland). Serologic screening for syphilis was done using Rapid Plasma Reagin (Bento-Dickinson, Baltimore, MD) and Treponema pallidum hemagglutination assay (TPHA, Biotech Laboratories, UK).

RESULTS

Demographic and clinical characteristics were assessed at enrollment. Subjects were followed for a median of 14 months (IQR 6 – 24 months). Thirty participants were diagnosed with 31 GC infections over 345 women-years of observation giving an incidence of 9.0 infections per 100 women-years. Cox regression analysis was used to calculate hazard ratios (Table 1).

Figure 1

Table 1: Baseline data and univariate analysis of the association between incidence and demographic characteristic, and clinical and laboratory findings for 299 sex workers enrolled in a cohort in Nairobi, Kenya.

	Overall (n=299)	No (n=228)^	Yes (n=30)^	HR (95% CI)
Age ≥ 25 years	88	72 (32%)	6 (20%)	0.55 (0.22, 1.3)
Years lived in Nairobi (mean ± SD)	14.2 ± 9.1	14.4 ± 8.9	12.7 ± 8.7	0.98 (0.93, 1.0)
Prostitution duration years (mean ± SD)	3.9 ± 3.1	4.0 ± 3.1	3.6 ± 3.1	0.96 (0.83, 1.1)
Average clients per week ≥ 8	11.7 ± 7.1	Δ	Δ	0.67 (0.31, 1.5)
Charge > 150 Kenyan shillings (~USD 2)	179 ± 147	103 (45%)	12 (40%)	0.83 (0.40, 1.7)
Age at menarche ≥ 15	14.6 ± 1.7	125/227 (55%)	17/29 (59%)	1.1 (0.53, 2.4)
Age at first intercourse ≥ 15	15.6 ± 1.9	169/224 (75%)	26/29 (90%)	2.7 (0.81, 8.9)
Single	205 (69%)	159/227 (70%)	19 (63%)	0.85 (0.40, 1.8)
Work at Bar vs. club, home, street, other	236 (79%)	186/227 (82%)	20 (67%)	0.45 (0.21, 0.97)
Regular condom use (≥ 75%)	123 (41%)	Δ	Δ	1.4 (0.59, 3.2)
Have a regular partner	162 (54%)	Δ	Δ	1.4 (0.67, 3.0)
Condom use ≥ 75% with regular partner	25 (16%)	Δ	Δ	1.9 (0.69, 5.4)
Current family planning method				
None	90 (30%)	Δ	Δ	1.3 (0.56, 2.9)
Combined oral contraceptives	74 (25%)	Δ	Δ	1.1 (0.45, 2.6)
Depomedroxyprogesterone	94 (31%)	Δ	Δ	0.60 (0.24, 1.5)
Currently douche	253 (85%)	190 (83%)	29 (97%)	5.2 (0.71, 38.6)
Douche more than once per day	173 (59%)	134/227 (59%)	18/29 (62%)	1.1 (0.51, 2.3)
Douche with water and soap	188 (63%)	134/227 (59%)	26 (87%)	3.8 (1.33, 10.9)
Have sex during menses	70 (24%)	55/225 (24%)	7/29 (24%)	0.94 (0.40, 2.2)
Have anal sex*	34/267 (13%)	25/205 (12%)	3/26 (11%)	0.81 (0.24, 2.7)
Smoke cigarettes	73 (24%)	53 (23%)	7 (23%)	0.93 (0.40, 2.2)
Ever drink alcohol	214 (72%)	161 (71%)	22 (73%)	1.2 (0.53, 2.7)
Use of antibiotics since enrollment	244 (82%)	217 (95%)	27 (90%)	0.97 (0.27, 3.4)
Use of antibiotics at current visit	-	Δ	Δ	0.52 (0.69, 3.4)
Clinical severity score > 0	65 (22%)	Δ	Δ	1.2 (0.43, 3.1)
Abdominal pelvic pain (any)	55 (18%)	Δ	Δ	0.49 (0.11, 2.1)
Abnormal vaginal discharge on exam	70 (23%)	Δ	Δ	0.97 (0.78, 5.0)
Cervicitis	28 (9%)	Δ	Δ	3.1 (1.2, 8.4)
Cervical friability	51 (17%)	Δ	Δ	2.1 (0.79, 5.7)
Health problems in past year at baseline		111 (49%)	10 (33%)	0.52 (0.24, 1.1)
Vaginal discharge	70 (23%)	62 (27%)	3 (10%)	0.30 (0.09, 0.98)
Painless genital ulcer	13 (4%)	12 (5%)	1 (3%)	0.63 (0.09, 4.7)
Severe abdominal pain	0	56 (25%)	6 (20%)	0.78 (0.32, 1.9)
Tuberculosis	3 (1%)	3 (1%)	0	0.00
Syphilis	23/296 (8%)	Δ	Δ	0.60 (0.08, 4.5)
HIV-1 seropositive	87/296 (29%)	Δ	Δ	1.4 (0.64, 3.0)
Among HIV+, WBC (mean ± SD)		Δ	Δ	0.76 (0.36, 1.6)
Among HIV+, CD4 < 300		Δ	Δ	1.2 (0.12, 11.2)
Among HIV+, CD8 < 800		Δ	Δ	5.7 (0.59, 55.4)
Prevalent *N. gonorrhoeae*	18 (6%)	-	-	-
Incident *C. trachomatis*	24 (8%)	Δ	Δ	7.3 (3.0, 17.8)
T. vaginalis since enrollment	22/185 (12%)	40/143 (28%)	7/19 (37%)	1.7 (0.67, 4.4)
Bacterial Vaginosis since enrollment	141/274 (51%)	177 (78%)	25 (83%)	1.9 (0.72, 5.0)
PID since enrollment	55 (18%)	100/227 (44%)	16 (53%)	1.8 (0.88, 3.8)

^ - 41 women never returned after baseline assessment: no diagnosis of incident GC infection could be made
* - 32 women refused to answer the query
Δ - Variables measured during follow-up changed over time.

In multivariate analysis, incident C. trachomatis infection (CT) (AHR = 5.9, 95% CI 2.2–15.8) and clinical cervicitis (AHR = 3.1, 95% CI 1.1–8.6) were associated with incident GC after adjusting for age, HIV-1 serostatus and significant univariate factors. Of the 30 participants infected with incident GC, nine (30%) were diagnosed with incident CT at some point during follow-up; the majority of those (5/9, 56%) were coinfected.

DISCUSSION

In a cohort of FSWs, incident infection with N. gonorrhoeae was independently associated with incident C. trachomatis infection and clinical cervicitis. Regular condom use and HIV-1 seropositivity were not associated with incident GC, but were kept in the model due to their potential

confounding effect. The majority of participants infected with both GC and CT during the study were coinfected. Reasons for association and coinfection include overlap of partnership networks and that one pathogen may influence the local immune response and therefore susceptibility to the other.

Centralized social venues (bars) have been strongly associated with the acquisition of N. gonorrhoeae [9]. In this cohort, 79% worked from bars. These venues provide a central site for commercial sex that may be frequented by repeat clients. Models indicate that denser networks, where clients have contact with multiple partners, maintain high endemic STI levels and increase the likelihood of infection[4]. The amount of unprotected sexual encounters between follow-up periods (mean = 23.5 ± 7.1) and the high transmissibility of N. gonorrhoeae and C. trachomatis may explain the rate of coinfection.

Our study is not equipped to determine the order of pathogenic infection. However, distinct mechanisms enable N. gonorrhoeae to increase host susceptibility to C. trachomatis due to repression of lymphocyte proliferation through receptor adhesion[10]. On the other hand, C. trachomatis can predispose the adaptive immune system to either a Th1 or Th2 response. A Th2 dominant response may impede clearance of N. gonorrhoeae due to lack of an anamnestic response to GC[7].

The high frequency of antibiotic use in the study population likely confounded the incidence of N. gonorrhoeae. In addition, the small sample of coinfections provides little power to elaborate on the temporality of N. gonorrhoeae and C. trachomatis infections. However, our study suggests an interaction between N. gonorrhoeae and C. trachomatis infections. Future studies should explore the mucosal and systemic immunologic correlates and temporal relationship between these infections in other at-risk populations.

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