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BRIEF REPORT

Risk of Sexually Transmitted Zika Virus in a Cohort of Economically Disadvantaged Urban Residents

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To understand the disease burden of sexually transmitted Zika virus (ZIKV), we prospectively followed a cohort of 359 adult and adolescent residents of an urban community in Salvador, Brazil, through the 2015 ZIKV epidemic. Later, in 2017, we used a retrospective survey to associate sexual behavior during the epidemic with ZIKV infection as defined by immunoglobulin G3 NS1 enzyme-linked immunosorbent assay. We found that males who engaged in casual sexual encounters during the epidemic were more likely (adjusted odds ratio, 6.2 [95% confidence interval, 1.2–64.1]) to be ZIKV positive, suggesting that specific groups may be at increased risk of sexually transmitted infections.

Keywords. Zika; sexual transmission; sexual behavior.

Zika virus (ZIKV) is an arbovirus associated with congenital abnormalities [1]. Substantial evidence indicates that ZIKV can be transmitted sexually [2]. Current models support this finding and suggest that sexual transmission increases the disease burden; however, critical parameters of ZIKV infection in these models, such as sexual transmission rate, are not available [3–5].

To improve control of ZIKV and to better inform these models, it is therefore essential to understand how risky sexual behaviors, such as lack of condom use or having multiple sexual partners, are associated with the spread of sexually transmitted ZIKV infections. In this study, we characterize sexual behaviors associated with increased risk of ZIKV infection in a cohort of economically disadvantaged urban residents in Salvador, Brazil. We also compare infection rates between ZIKV and dengue virus (DENV) among participants to understand the ways in which differences in transmission methods may differentiate the spread of these 2 diseases.

METHODS

In a 2015 study, we characterized the attack rate (>70%) and transmission dynamics of ZIKV in a community in Salvador, Brazil, by performing multiple prospective serosurveys with 1453 individuals [6]. For the current study, we invited 443 (30.5%) randomly selected participants from this previous project. Among them, 84 (19.0%) were unable to participate, leaving 359 (81.0%) individuals who met our inclusion criteria of having participated in at least 2 serosurveys between March 2015 and October 2015 (73% of residents were infected by ZIKV during this period [6]), having available ZIKV seroconversion results, being >13 years old, and responding to our questionnaire on sexual behavior.

To quantify DENV exposure among our participants during the ZIKV epidemic, we had to account for their high likelihood of prior DENV exposure. Previous work by our team described the prevalence of 4 DENV serotypes within the nearby Pau da Lima community, with an annual incidence of 70.2 cases per 10 000 inhabitants [7]. Because this high rate of DENV infection was likely also present within our study community, the seroprevalence of total anti-DENV immunoglobulin G (IgG) antibodies would presumably be very high. Thus, to differentiate recent DENV infections from prior exposures, we used a previously described NS1 IgG3 assay [8]. Likewise, we developed our ZIKV IgG3 assay using this methodology as well [6, 8].

Participants provided their sociodemographic characteristics including sex, age, marital status, schooling, ethnicity, and clinical symptoms during 2015 serosurveys. Follow-up household visits and interviews were performed between February and April 2017 to collect data on sexual behavior during (August 2015–January 2016) and after (March–July 2016) the ZIKV epidemic. We used questions from the National Survey of Knowledge, Attitudes, and Practices of HIV and other Sexually Transmitted Infections (Pesquisa de Conhecimentos, Atitudes e Práticas na População Brasileira 2013) to evaluate the number of sexual partners, type of partner (fixed or casual), and condom usage (condom use in each sexual intercourse or condomless) [9]. Interviews were performed by trained health professionals who conducted them in a safe and comfortable

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place within the participants' own homes, to ensure the privacy and confidentiality of their answers and who used memory triggers to enhance recall.

We evaluated the association between risk factors (sexual behaviors) and ZIKV exposure (anti-ZIKV IgG3). We also evaluated DENV exposure as an alternative outcome for non–sexually transmitted flavivirus infection, to control for mosquito exposure as a confounding factor. Both the ZIKV and DENV IgG3 assays were previously validated in this cohort [6]. Relationships between outcomes and exposure factors were assessed using Pearson χ^2 test or Fisher exact test. To measure associations, we used odds ratios (ORs) and 95% confidence intervals (CIs). In cases where the evaluated frequency was equal to 0, we used ORs calculated with the Haldane–Anscombe correction. Multivariate analyses were performed to evaluate the relationship between ZIKV infection and the examined risk factors, and associations were calculated as adjusted ORs (aORs). Variables (including sociodemographic and sexual behavior factors) with $P < .10$ in bivariate analysis were included in the multivariate analysis. This was created using a forward-selection method using likelihood ratio as the criterion for adding significant variables to the model. We also compared intrahousehold relationships to test whether sexual relationships (eg, husband-wife) were more likely to exhibit concordance in ZIKV infection statuses than nonsexual relationships (eg, mother-daughter). To compare seroconcordance between sexual and nonsexual relationships, we used a generalized linear mixed model (GLMM) using a binomial distribution with the logit link function that included the household cluster effect as a random group intercept.

This study was reviewed and approved by the institutional review boards of Yale University (1006006956) and the Oswaldo Cruz Foundation and Brazilian Ministry of Health (45217415.4.0000.0040 and 55904616.4.0000.0040).

RESULTS

Among our 359 participants, 138 (38.4%) were male, 170 (47.4%) self-identified as black, mean age was 30 years (standard deviation, 16 years), and 274 (76.3%) reported having had sex at least once in their lifetime. Furthermore, 207 (57.7%) were ZIKV IgG3 positive. DENV IgG3 results were available for 302 individuals (84.1%), of whom 67 (22.2%) were positive (Supplementary Table 1).

Participants who reported having sex with >1 partner were more likely to be ZIKV positive (ZIKV positive, 8/113 [7.1%] vs ZIKV negative, 0/89 [0%]; $P = .02$) (Table 1). A marginal statistical difference was also identified between the proportion of participants who reported having had casual sex (ZIKV positive, 15/113 [13.3%] vs ZIKV negative, 5/88 [5.7%]; $P = .07$) (Table 1). Sex-stratified analysis found that males who reported interacting with >1 sexual partner were more likely to be ZIKV positive than males with a single sexual partner ($P = .04$). This analysis also found that males engaging in casual sexual relations during the epidemic were more likely to be ZIKV positive (OR, 5.8 [95% CI, 1.2–28.4]) and that of 12 males who reported engaging in casual sexual relations, 5 (41.7%) did not use condoms regularly (Table 1). After adjusting for schooling, the multivariate analysis confirmed this association between males engaging in casual sexual relations and ZIKV infections (aOR, 6.2 [95% CI, 1.2–64.1]). In the female group, we did not identify sexual behaviors associated with ZIKV, although having <6 years of formal schooling doubled the probability of a positive ZIKV result with marginal significance (aOR, 2.1 [95% CI, 1.0–4.6]; $P = .05$) (Table 2).

We analyzed sexual behavior during and after the epidemic and found no difference in sexual behaviors between these periods (Supplementary Table 2). Finally, in the household analysis, we were able to identify 165 pairwise relationships containing at least 1 individual infected with ZIKV with 78 (47.2%) seroconcordant and 87 (52.7%) serodiscordant pairwise relationships. We did not identify a statistically significant difference between sexual and nonsexual intrahousehold relationships in the GLMM analysis for the ZIKV seroconcordance (Supplementary Table 3).

DISCUSSION

In areas where mosquito-borne transmission is the main route of ZIKV transmission, determining the relative contribution of sexual transmission is challenging. Our findings, in a community of economically disadvantaged urban residents, suggest that sexual behaviors may be associated with ZIKV infection. This association was driven specifically by males engaging in risky sexual behavior, defined as lack of condom use, engagement with multiple sexual partners, and participation in casual sexual encounters. Among our study participants, males reported higher rates of risky sexual behaviors. Furthermore, among all members of our sample, engaging in casual sexual encounters increased the likelihood of testing positive for ZIKV 6-fold (Table 2). Although we only found a significant relationship between ZIKV infection and casual sex, we also found high rates of other risky behaviors in ZIKV-positive residents. Given the reports of sexual transmission of ZIKV, it is unsurprising that ZIKV infection is associated with these casual encounters, and our results are consistent with previous findings for other sexually transmitted infections and with current ZIKV models [3–5, 10]. While previous studies highlighted the role of infected males in sexual transmission because of higher viral persistence in genital secretions of males than in those of females [2], our findings also suggest an additional contribution of males to ZIKV transmission through risky sexual behaviors. These findings support the inclusion of gender and behavioral differences in mathematical models of ZIKV transmission [5, 11]. Recent household analyses in northeast Brazil [12] found that

Table 1. Sexual Behavior During the Zika Virus Epidemic, Stratified by Sex, in Pau da Lima Community, Salvador, Brazil

Sexual Behavior During the ZIKV Epidemic	ZIKV Positive	ZIKV Negative	*P* Value	OR (95% CI)
General population				
≤6 y of schooling	114/207 (55.1)	69/152 (45.4)	.07	1.5 (1–2.2)
Had sex (August 2015–January 2016)	113/207 (54.6)	89/152 (58.6)	.45	0.9 (.5–1.3)
>1 sexual partner	8/113 (7.1)	0/89 (0)	.02[a]	10.3 (1.1–606.2)[b]
Sex with fixed partners	100/112 (89.3)	83/89 (93.3)	.33	0.6 (.2–1.7)
Condomless sex with fixed partners	87/100 (87)	70/82 (85.4)	.75	1.5 (.5–2.7)
Sex with casual partners	15/113 (13.3)	5/88 (5.7)	.07	2.5 (.9–7.3)
Condomless sex with casual partners	8/15 (53.3)	1/5 (20)	.32[a]	4.6 (.4–51.1)
Self-report of Zika-like symptoms in sexual partner	17/112 (15.2)	10/88 (11.4)	.53	1.4 (.6–3.2)
Male group				
≤6 y of schooling	44/79 (55.7)	30/59 (50.8)	.57	1.2 (.6–2.4)
Had sex (August 2015–January 2016)	39/79 (49.4)	28/59 (47.5)	.82	1.1 (.5–2.1)
>1 sexual partner	6/39 (15.4)	0/28 (0)	.04[a]	7.7 (.7–483.1)[b]
Sex with fixed partners	29/38 (76.3)	25/28 (89.3)	.18	0.4 (.1–1.6)
Condomless sex with fixed partners	24/29 (82.8)	22/25 (88)	.71[a]	0.7 (.1–3.1)
Sex with casual partners	12/39 (30.8)	2/28 (7.1)	.02	5.8 (1.2–28.4)
Condomless sex with casual partners	5/12 (41.7)	0/2 (0)	.51[a]	2.2 (.1–201.4)[b]
Self-report of Zika-like symptoms in sexual partner	4/38 (10.5)	3/27 (11.1)	.99[a]	0.9 (.2–4.6)
Female group				
≤6 y of schooling	70/128 (54.7)	39/93 (41.9)	.61	1.6 (1–2.9)
Had sex (August 2015–January 2016)	74/128 (57.8)	61/93 (65.6)	.24	0.7 (.4–1.3)
>1 sexual partner	2/128 (1.6)	0/61 (0)	.50[a]	1.9 (.1–115.8)[b]
Sex with fixed partners	71/74 (95.9)	58/61 (95.1)	.99	1.2 (.2–6.3)
Condomless sex with fixed partners	63/71 (88.7)	48/57 (84.2)	.45	1.5 (.5–4.1)
Sex with casual partners	3/74 (4.1)	3/60 (5)	.99[a]	0.8 (.2–4.1)
Condomless sex with casual partners	3/3 (100)	1/3 (33.3)	.40[a]	12 (.3–556.7)[b]
Self-report of Zika-like symptoms in sexual partner	13/74 (17.6)	7/61 (11.5)	.32	1.6 (.6–4.4)

Data are presented as No. of positive answers/total No. of answers (%), unless otherwise indicated.

Abbreviations: CI, confidence interval; NA, not applicable; OR, odds ratio; ZIKV, Zika virus.

[a]Fisher exact test *P* value.

[b]OR calculated with the Haldane–Anscombe correction and Fisher exact test.

household members living with a seropositive patient had an increased risk of Zika and chikungunya infection and that this risk increases when the relationship between the individuals is sexual [12]. In contrast, our household analysis did not find a significant effect of the type of relationship. We think that this may be due to the fact that there are other environmental and social factors for individuals living in these economically disadvantaged communities, which may confound the effect of intrahousehold relationship type. This is also consistent with the high recorded incidence of ZIKV among participants in our study (57.7%).

Although the findings of our study are important, it is also essential to note its limitations. One limitation is the potential for recall bias, which can occur during retrospective reporting of individual behaviors. That said, we took careful steps to reduce recall bias, and interviews used specific memory triggers

Table 2. Risk Factors Associated With a Zika Virus Positive Result in Multivariate Analysis

Characteristics	ZIKV Positive	ZIKV Negative	*P* Value	OR (95% CI)	*P* Value	aOR (95% CI)
Female group[a]						
≤6 y of schooling	38/74 (51.4)	20/60 (30.3)	.03	2.1 (1.0–4.3)	.05	2.1 (1.0–4.6)
Sex with casual partners	3/74 (4.1)	3/60 (5)	.99[c]	0.8 (.2–4.1)	.99	0.8 (.1–6.5)
Male group[b]						
≤6 y of schooling	21/39 (53.8)	13/28 (53.8)	.73	1.3 (.5–3.5)	.46	1.7 (.5–5.5)
Sex with casual partners	12/39 (30.8)	2/28 (7.1)	.03[c]	5.8 (1.2–28.4)	.02	6.2 (1.2–64.1)

Data are presented as No. of positive answers/total No. of answers (%), unless otherwise indicated.

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio; ZIKV, Zika virus.

[a]One hundred thirty-four females who had sex during August 2015–January 2016.

[b]Sixty-seven males who had sex during August 2015–January 2016.

[c]Fisher exact test.

to enhance recall. In addition to recall bias, small sample size and large CIs were a further limiting factor in our study, which affects the generalizability of our findings. Notably, we did not find any association between sexual behavior and ZIKV infection in the female population. This may be due to limited sample size or to women underreporting this type of relationship [10]. Sample size also limited our ability to evaluate the relative contribution of sexual behavior in the context of other potential risk factors (eg, number of mosquito bites, resident movement). Finally, we note that our methodology identified correlational associations between variables; however, these relationships are not necessarily causative. As a result, it is possible that outside factors such as degree of risk aversion drive both an individual's likelihood of engaging in risky sexual behavior and their likelihood of taking precautions against mosquito-borne infections.

There were also many variables on which we were unable to collect data. For example, we were not able to consider the spatial distribution of ZIKV infection within our study. We also did not collect data on sexual preferences and orientation, although prior studies suggest the possibility of long-term disease persistence within communities of men who have sex with men, [2, 4], as well as other potential confounders such as sexual frequency or transactional sex. Notwithstanding, when we analyzed the same associations for DENV infection, they were not significant. Previously, a case report described an incidence of sexual transmission of dengue; however, this finding has not been replicated in epidemiological studies [13]. Thus, although ZIKV and DENV are ecologically similar arboviruses that share the same primary transmission vector, sexual transmission forms a relevant secondary transmission method in ZIKV infection that we do not find in DENV.

The World Health Organization advocates that persons of reproductive age receive information about the sexual transmission of ZIKV to improve parental planning. Our data suggest that the behaviors of individuals did not experience significant changes in the context of the epidemic. More studies to prospectively follow the change in the behavior before, during, and after epidemics are necessary to develop government policies and improve access to information about the disease in economically disadvantaged urban communities. One previous study that evaluated contraceptive sales in Brazil found an increase in demand for contraception that might be associated with the ZIKV epidemic [14], In contrast, however, a 2016 study of women of reproductive age in northeast Brazil found that despite high levels of knowledge about ZIKV and the congenital alterations, few women changed their attitudes about pregnancy and contraceptive use [15]. Similarly, we also did not find any difference in frequency of risky behaviors between the epidemic and postepidemic periods. Overall, long-term studies are necessary to evaluate changes in sexual behaviors despite ZIKV reduction rates.

This study provides the first glimpse of the population-level relationship between males reporting multiple partners or casual sex and ZIKV transmission, which should be further investigated to inform mathematical models and governmental recommendations pertaining to the risk of sexual ZIKV infection in vulnerable populations.

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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