Published in final edited form as:

Am J Reprod Immunol. 2017 July ; 78(1): . doi:10.1111/aji.12699.

Challenges in Conducting Research on Sexual Violence and HIV and Approaches to Overcome Them

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Abstract

Studies have implicated sexual violence as a strong correlate of HIV acquisition in women. Characterizing how such violence affects the female immune system may provide insight into the biological mechanisms of HIV transmission and ultimately improve global HIV prevention strategies. Little research has been done in this domain, and the obstacles to investigation can be daunting. Here we describe methodological challenges encountered and solutions explored while implementing a study of dysregulation of immune biomarkers potentially indicative of increased HIV susceptibility in women following sexual assault. Challenges included accessing sexual assault survivors and defining sexual assault, promoting study participant well-being during research engagement, reducing selection and information bias, collecting and processing biological samples, and adjusting for confounders such as reproductive tract infections and emotional and physical abuse. We found that many survivors of sexual assault welcomed the attention from study staff and felt empowered by the opportunity to help other women at risk for violence. Well-trained research staff and well-articulated community and medical partnerships were key methods to overcoming challenges while promoting the safety and welfare of vulnerable study participants.

Keywords

Biomarkers; Gender-based violence; HIV; Immune System; Sexual assault

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INTRODUCTION

Multiple studies have implicated sexual violence as a strong correlate of HIV acquisition in women ^{1–6}. Given the 35% global prevalence of violence against women ⁷, characterizing the mechanisms whereby such violence affects the acquisition of HIV is important to the development of global HIV prevention strategies. Possible explanations for the association include both behavioral and biological correlates of abuse ^{8,9}. Perpetrators may be at higher risk for HIV due to factors such as alcohol abuse and social norms about masculinity that may contribute to sexual violence and other sexual behaviors associated with HIV ⁴. Survivors may also engage in sexual behaviors that put them at risk due to structural factors such as economic stressors or as a consequence of violence, often mediated by psychological and substance abuse conditions ^{10–13}. Furthermore, women in violent relationships may be less able to negotiate condom use or access other preventive measures, such as pre-exposure prophylaxis (PrEP), thus also increasing their risk of HIV ^{14,15}.

Biological explanations for the association between sexual violence and HIV acquisition have generally focused on injury to the cervicovaginal tract ^{6,16}, which creates portals of entry. This may be especially evident when other sexually transmitted infections are present ¹⁷. These infections cause an inflammatory, immune-activated microenvironment that promotes congregation of immune cells which are targets for HIV infection ¹⁸. Recent research is examining the role of inflammation and immune activation in the acquisition of HIV, under the hypothesis that a dysregulated immune microenvironment resulting from the stress that accompanies penetrative sexual assault may independently increase the risk of HIV acquisition ^{19–22}.

Sexual violence occurs in women of all age groups; however, incidents in older women are particularly under-reported ²³. Postmenopausal women are especially vulnerable to injury, immune compromise and HIV susceptibility following sexual assault. Immunologically, the loss of estrogen with aging leads to decreased levels of protective antimicrobials, commensal lactobacilli and cervical mucus production ^{20,24}. Considerable thinning of the vaginal epithelium coupled with vaginal dryness leads to greater trauma ¹⁶, and the aging process severely impairs wound-healing abilities ^{25,26}.

Understanding the nature of the immune response following sexual violence could lead to better post-assault care and to the development of new HIV prevention tools and interventions. Additionally, it may even result in discovery of novel immune biomarkers associated with sexual assault, which could be useful in identifying women who might otherwise go untreated. Research in this field is hampered, however, by the many challenges inherent in studying women following sexual assault, both in general and in the context of HIV infection. Due to the stigma and trauma associated with sexual violence, women who have experienced abuse are often both hidden and vulnerable, making them difficult to reach and presenting ethical and logistic challenges in studying them. In this paper, we describe challenges we encountered while investigating biomarkers relevant to HIV susceptibility in women who have recently experienced sexual violence and suggest approaches to overcome these in future research.

STUDY DESIGN

Funding and ethical statement—This paper was informed by the implementation of two separately funded but interrelated studies [DC-CFAR: AI117970 (Greenberg/Ghosh); NIH: R56AI111933-01 Ghosh)]. The studies were conducted according to the principles expressed in the Declaration of Helsinki and approved by the Institutional Review Boards of The George Washington University (081328, 071408) and MedStar Health Research Institute (2014–216). All participants provided written informed consent. In the description below, we have collapsed the two studies into a single multi-armed study for ease of understanding.

Study aims and activities—The purpose of the study was to compare immune biomarkers indicative of HIV susceptibility between women who had experienced forced vaginal penetration during the preceding 12 weeks (cases) and women who had never experienced forced or coerced vaginal penetration (controls). We investigated inflammatory biomarkers that are known to enhance HIV, endogenous antimicrobials that are known to inhibit HIV, and biomarkers involved in tissue repair and wound healing pathways. Clinical specimens were also collected to confirm HIV negative status using the HIV 1/O/2 (HIV-1/O/2) Antigen/Antibody (Fourth Generation) Preliminary Test With Cascade Reflex© (LabCorp, Burlington, NC) and to test for *Bacterial vaginosis*, *Candida albicans* and *glabrata*, *Trichomonas vaginalis*, *Chlamydia trachomatis*, and *Neisseria gonorrhoeae* using the NuSwab Vaginitis Plus (VG+)© (LabCorp, Burlington, NC). The specimens were sent to LabCorp for analysis, and clinical staff followed up with participants, providing clinical recommendations as needed.

Arm 1 was cross-sectional in design. Following provision of informed consent, community-recruited participants ages 18 to 45 completed a brief computer self-administered interview (CASI) to provide epidemiologic data and determine eligibility/case/control status. Eligible cases and controls then provided blood, cervicovaginal lavage and cervical swab samples for biomarker analysis. Arm 2 was longitudinal, with two additional aims: to observe fluctuations in immune biomarkers over the course of the menstrual cycle in pre-menopausal women and to compare these biomarkers between pre- and postmenopausal women. Pre-menopausal participants in this arm completed a total of five visits each at two-week intervals, calculated to coincide with the follicular and luteal stages of the cycle. Postmenopausal women were also sampled every two weeks to match the sampling intervals of the pre-menopausal group. Arm 3 included women who reported a recent sexual assault and presented to the Emergency Department (ED) of MedStar Washington Hospital Center (MWHC) in Washington DC for medical forensic examinations and evidence collection. Participants consented to provide blood and cervical swab samples for research purposes during the course of their exam in the ED. Participants from all arms of the study received gift checks at each visit: \$20 for completing the CASI, \$80 for providing samples, or \$100 for both.

Inclusion and exclusion criteria—Participants had to be HIV-negative, with uterus and at least one ovary intact, not pregnant, not breastfeeding, and either pre-menopausal (18 to

45 years old with regular menstrual periods) or postmenopausal (50 to 90 years old with no periods for at least one year). Initially, our intention was to exclude women who tested positive for any reproductive tract infection (RTI) or presented with genital tract lesions or mucopurulent discharge suggestive of an infection; however, during implementation of the study we relaxed this requirement as discussed below.

Ascertainment of case/control status—For community-recruited participants, case/control status was determined by two questions in the CASI: 1) “Have you ever been forced without your consent to have vaginal sex (with or without a condom)?” and 2) “When was the last time this happened to you?” Participants were considered cases if they indicated they had experienced forced vaginal penetration during the past four weeks (later changed to 12 weeks as discussed below) and controls if they reported never having experienced forced vaginal penetration. To maximize the contrast, women who had experienced forced vaginal penetration in the more distant past were excluded from the study. For women presenting to the hospital emergency department, a forensic nurse determined case status based on patient report and any other available information.

RESULTS

Sample size and current status of recruitment—We initially aimed to recruit a total of 34 cases and 30 controls (Table 1). Recruitment began in July 2014. At the time of preparation of this manuscript we had finished recruitment for all controls and enrolled 21 pre-menopausal cases (eight from the hospital and 13 from the community) and three postmenopausal cases (one from the hospital and two from the community). Throughout the implementation of this study, we identified several salient challenges and adopted methods to overcome them (Table 2). The remainder of the paper will discuss these with the intention of informing future research.

Challenges to Community-Based Recruitment

Considering our very specific target population, we initially used three approaches to focus our efforts: recruiting at universities, peer referral, and partnering with community domestic violence and sexual assault service organizations. Later we experimented with online advertising.

Recruiting university students—The Association of American Universities recently found that 11% of undergraduate women surveyed had experienced unwanted sexual penetration by force or incapacitation since entering school, and other researchers have reported similar findings^{27,28}. In an effort to reach this group, fliers were posted around the undergraduate campus local to the study. These fliers were initially vague about the purpose of the study in order to protect the privacy of the study participants and avoid the stigma associated with sexual assault.

As expected, we easily accrued controls, but after several months we had enrolled no cases using our four-week window, and increasing this to 12 weeks did not improve recruitment. Adjusting the fliers to be more specific about sexual assault produced only a marginal

improvement; two cases were recruited at the local campus and two more cases when the study was expanded to three additional college campuses. Among the women screened out of the study, seven had experienced forced vaginal penetration three to six months prior to the study, and at least 10 in the more distant past, suggesting that women were increasingly interested in participating as time elapsed from their reported sexual assault. Importantly, because we identified fewer cases than anticipated from our university-based recruitment, we accrued a control population that was disproportionately young, healthy, and self-identified as White compared to our case population.

Incentivized peer referral—An incentivized referral structure that had worked successfully in previous studies conducted by members of the study team (not involving sexual violence) was not effective for recruitment. Study participants were given up to five coupons to distribute to family members, friends, or social networks. Those referring ultimately eligible participants received \$10 per recruitment in addition to the incentive for their own study participation. However, from the 75 participants we enrolled, we received only eight referrals, none of whom were eligible cases.

Partnering with community organizations—Working with local domestic violence agencies, housing shelters, and organizations for homeless women, we received numerous referrals for study. Our most successful collaboration involved direct referrals from District of Columbia Forensic Nurse Examiners, a local nonprofit organization that performs medical forensic examinations on victims of sexual assault. This resulted in nurse referrals of 18 women over a period of six months, of whom four enrolled and three completed the study. Unfortunately, many of the women who learned about the study through this and other community organizations had multiple barriers to study enrollment and participation. These included the necessity to relocate for safety reasons, difficulties reaching the clinic despite transportation reimbursement, substance abuse, and no phone or other means of communication following the initial expression of interest.

Recruiting postmenopausal women—Recruiting postmenopausal women for our study proved especially challenging. After several months we had enrolled only one control based on our fliers and none from partnering with community organizations. To address the problem we revised both the language and the style of the fliers, enlarging the print and highlighting the benefits of the study to older women. We distributed the revised fliers throughout the city and along metro corridors, posting them in places where older women were known to congregate: gyms and weight loss centers, public libraries, community centers, and retirement communities. This resulted in the enrollment of the four controls needed to complete this group, but no cases. However, we were eventually successful in recruiting cases by placing an online classified advertisement on Craigslist.

Online advertising—During the final three months of active community-based recruitment, we placed an advertisement for volunteers on Craigslist. This resulted in the most rapid accrual of cases of any method used: two postmenopausal and five premenopausal women over the next several weeks. Online advertising may be useful in reaching both older and younger women who are looking for ways to contribute to the

community or to supplement their incomes. One concern with this approach was that women recruited in this way might be unduly motivated by financial considerations and might be induced to misrepresent their sexual experiences; however, to minimize this possibility, all participants were blinded to the specific eligibility criteria.

Challenges to Hospital-Based Recruitment

After assessment of sensitivity and acceptability, we partnered with staff at MedStar Health Research Institute, District of Columbia Forensic Nurse Examiners, and MedStar Washington Hospital Center Emergency Department to conduct a pilot feasibility study involving women presenting for medical forensic examinations within four days following sexual assault. Women who met the inclusion criteria and who were deemed by the research coordinator to be capable of providing informed consent were offered participation in the study. Participation consisted of providing blood from a vein in the arm and cervical swab samples, which were collected by the forensic nurse at the end of the exam to avoid compromising forensic evidence. Since the women were already having blood and cervical specimens obtained for the medical forensic exam²⁹, the collection of additional specimens for research was not thought to impose a substantial burden. Furthermore, to minimize psychological distress, participants were not asked to provide CASI data. Although we felt this omission was necessary, it limited our ability to measure potential confounders such as depression, medication and drug use, and sexual and abuse histories.

Some women who presented to the emergency department were unable to consent due to intoxication or a traumatized emotional state. Among those capable of consent, many chose not to have a medical forensic exam and were excluded from the study to avoid compromising evidence, in case they changed their minds within the prescribed 96-hour window for evidence collection. Thus, a minority of patients was offered the study; however, most of the women who were approached consented to participate.

One challenge we encountered in this group was an incomplete recall of events that had occurred during the assault. Memory of any traumatic event is often found to be scattered or incomplete, and sexual assault is no exception³⁰. The involvement of alcohol or other drugs in at least four of the nine incidents (44%) may have also contributed to this incomplete memory. Sometimes the women were not sure whether vaginal penetration had occurred, nor could this be definitively ascertained by examination. Studies indicate that it can be difficult to discern between injuries sustained from recent consensual sex and non-consensual assault^{16,31–33}. Forensic evidence kits were only processed if the victim decided to press charges, and for legal reasons we did not have access to the results that might have confirmed the presence of semen or foreign DNA. Furthermore, the absence of semen does not prove that vaginal penetration did not occur, since the perpetrator may have used a condom or not ejaculated. Given these uncertainties, we depended on the statements of the survivors and the expertise of the forensic nurses to determine eligibility. This is a gap in the field that we seek to address by identification of biomarkers associated with sexual trauma.

A second challenge was the potential contamination of specimens with semen and other substances (discussed under *Clinical and Laboratory Challenges*, below). In spite of these drawbacks, this strong partnership resulted in a relatively rapid accrual of cases.

Vulnerability of Cases

Vulnerability of cases was of particular concern in the design and implementation of the study. Not only were the women potentially traumatized by recent violent events, but many had additional vulnerabilities including lack of income, lack of safe housing, and ongoing involvement in abusive relationships, which is often attributable to financial dependence. Stigma regarding rape and intimate partner violence persists and frequently serves as a barrier to seeking care and treatment. Survivors of sexual violence have higher rates of substance abuse, depression and other mental health issues than the general population^{34–36}, posing additional challenges to recruitment and retention in research.

Ensuring a high level of training for research staff and being prepared to provide care and counseling referrals were essential. Excellent resources³⁷ were identified for training. Close partnerships with local domestic violence and sexual assault service organizations were key. Several queries came from women who had experienced assault and expressed some interest in the study, but mostly wanted to find out about HIV testing and referral into care. These women were connected with appropriate services regardless of whether they participated in the study. It is noteworthy that not all staff persons were comfortable with the idea of asking women who had recently experienced assault to participate in research of this nature, feeling it was simply too sensitive a time to approach them even with comprehensive ethical oversight. This is an important training point, highlighting the critical element of research team member comfort with the study goals and methods.

Compounding the difficulties of engaging and supporting the target population was the sensitive nature of the study activities themselves, which included recalling and reporting on recent traumatic events, sharing other sensitive personal information, and undergoing a pelvic exam with cervicovaginal lavage and swab collection. Some women who inquired about the study opted not to participate after learning what was involved; however, most were not deterred. Once enrolled in the study, participants indicated that the procedures were acceptable, although some of the postmenopausal women reported discomfort associated with a non-lubricated speculum examination. The use of a non-lubricated speculum is standard for studies investigating genital tract biomarkers as the presence of lubricant in samples can compromise specimen integrity. We were able to reduce the discomfort by using the smallest available size of speculum, which was soaked in lukewarm water prior to use. Female study staff explained the procedures in advance and provided support during and after the visit. Many of the women who participated in the study expressed appreciation for the opportunity to do something positive following a negative experience. We observed that participation seemed to have a recuperative effect, allowing the women to acknowledge their experiences and interact constructively with other people while being treated with respect and normalcy. Retention of cases (7/8=88%) as well as controls (10/10=100%) was excellent in the longitudinal arm of the study, corroborating this perception.

Operationalization

Other forms of abuse—Defining sexual violence is not straightforward due to variations in the form and degree of violence and in how the behavior is perceived by the survivor, among other factors. Our narrow case definition requiring forced vaginal penetration was

based on the hypothesis that immune biomarkers in the reproductive tract would be affected by localized physical factors. However, it is possible that stress resulting from other forms of violence may affect systemic or even local biomarkers given that emotional, physical, and sexual abuse have been shown to impact the immune system³⁸. Thus emotional and physical abuse could confound the relationship between vaginal assault and dysregulation of the immune system. We therefore included questions about these types of abuse in the CASI, with the following results: 87% (13/15) of community-recruited cases reported experiencing emotional abuse and 33% (5/15) reported experiencing physical abuse within the previous two months. By comparison, 3.3% (1/30) of controls reported emotional abuse and 0.0% (0/30) reported physical abuse during the same time interval. Because of the apparent association between emotional, physical, and sexual abuse, it will be challenging to disentangle the effects of each. We will perform sensitivity analysis if possible but will be limited by our small sample size and lack of CASI data from hospital-recruited participants.

Time elapsed between assault and sample collection—Because this is a new area of research, the duration of the effects of sexual violence on immune biomarkers is not known. Thus, we aimed to collect samples as soon after the event as possible, hoping that by comparing samples obtained at different intervals in the longitudinal arm and at different time points, we might detect patterns based on time elapsed. All samples from the hospital arm of the study were obtained within 96 hours of assault, consistent with the requirements of forensic evidence collection guidelines. For community-recruited participants, we sometimes learned the exact date of assault but more often had a range of possible dates based on information obtained from community partners or the CASI. We determined that at least four of the 15 first-visit samples were obtained within four weeks and at least 12 within eight weeks of the event. For the longitudinal arm, the fifth sample was obtained 10 to 20 weeks after the event or sometimes even later due to scheduling difficulties, as described below.

Clinical and laboratory challenges

Scheduling and quality of specimens—The scheduling of visits depended upon the availability of the participant, the study coordinator, the clinician collecting the samples, and the lab scientist processing them. For the longitudinal arm of the study, scheduling was further complicated by the necessity of timing based on the participant's menstrual cycle. We wanted to observe the changes in biomarkers over the course of the cycle and therefore aimed to collect two samples during the follicular stage and two during the luteal stage for each pre-menopausal woman. To match this timing, we collected samples at two-week intervals from postmenopausal women³⁹. For all community participants, we tried to ensure that the samples were free of blood, semen and vaginal lubricant, as these can obscure the biomarkers being studied. In addition to all of the above, we had to reschedule if a participant was on antibiotics as the presence of certain medications can impact the genital immune microenvironment⁴⁰.

Assuring the concordance of all these factors while sampling as soon as possible after sexual assault proved to be a formidable challenge, but the use of a shared online calendar as well as regular communication between members of the study team facilitated the process.

Among community-recruited participants, the samples were occasionally contaminated or a visit had to be rescheduled due to unexpected menstrual bleeding or recent sexual activity. We attempted to minimize this problem by reminding participants 48 hours prior to each appointment to abstain from having sex, lubricating, and douching. Trusting relationships were developed between the participants and research staff, who acknowledged the unpredictable nature of menstrual cycles and sexual encounters and emphasized the importance of communicating when complications arose. As a result, we were able to reduce, though not eliminate, these challenges to the laboratory validity of samples.

In the case of women sampled at the hospital, our protocol presented a paradox because blood and semen resulting from sexual assault and lubricant from the medical forensic exam made it difficult to observe the effects we were studying. Unfortunately, the nature of the research prevented us from excluding these factors as would typically be done in studies investigating mucosal immune biomarkers. Because these factors are intrinsic to this research, every effort should be made to develop and improve upon assays that can validate biomarkers in this type of sample. To this end, we hope to obtain valuable information by comparing the samples from the hospital with the relatively “clean” (free of blood, semen, and lubricant) samples from community.

Similarly, although the screening process excluded participants who reported RTIs, 44% of participants tested positive for infections with the NuSwab, including 22% (1 case and 9 controls) who tested positive for *Candida spp.* only and were asymptomatic. Among the 15 community-recruited cases, 53% tested positive for any other RTI (*Bacterial vaginosis*: 53%; *Chlamydia trachomatis*: 6.7%; *Neisseria gonorrhoeae*: 0.0%; *Trichomonas vaginalis*: 13%) as did 10% of the 30 controls (*Bacterial vaginosis*: 10%; *Chlamydia trachomatis*: 0.0%; *Neisseria gonorrhoeae*: 0.0%; *Trichomonas vaginalis*: 3.3%). As a result, first visit samples were sometimes contaminated. For the longitudinal arm of the study, we then faced a choice: collect the remaining samples on the original schedule or wait two weeks for a course of antibiotic treatment, which we prescribed or referred. Although we knew the RTIs were likely to act as confounders, we adhered to the original schedule for pre-menopausal women to meet time points through the menstrual cycle and thus preserve comparability between participants. For postmenopausal women, we waited for treatment.

Collection methods—Several different methods may be used for obtaining genital fluids including CVL, cervical or vaginal swabs obtained by a clinician, and vaginal self-swabs⁴¹. All have been used successfully to detect secreted genital immune mediators⁴². As swabs were already collected routinely for the medical forensic exams at MWHC, we considered the collection of additional swabs to be the least invasive approach for these vulnerable women in the immediate aftermath of assault. For community-recruited participants our clinicians collected CVL using 0.9% normal saline (BD Biosciences, Franklin Lakes, NJ) followed by two cervical swabs, allowing us to compare the two collection methods. CVL sampling was found to be acceptable and well tolerated, and we were able to detect multiple biomarkers in both types of samples.

Once collected, the samples had to be transferred as soon as possible to the laboratory for processing. The community samples were collected at a clinic near the laboratory and could

be walked over immediately, but the MWHC samples had to be picked up, often at night or on weekends, by our staff trained in handling and shipping bio-specimens. In case of possible pick-up delays, we provided the research nurses with a small refrigeration unit for storage of the cervical swabs and a rocker for blood samples. However, we were able to pick up all samples within two hours of collection. Once the samples arrived at the laboratory, processing typically took four to six hours depending upon the experiments being conducted, necessitating late nights for the laboratory staff.

DISCUSSION

Several studies have successfully recruited survivors of sexual assault using community-based methods, especially after preliminary strategic assessment and with support from local leaders^{43,44}. Our results suggest that recruitment among the general population becomes less feasible the narrower the window of time elapsed from the event and thus underscore the importance of working with organizations that provide access to recently assaulted individuals. Furthermore, recruitment of controls from low-prevalence populations should be avoided as it may lead to selection bias. Peer referral, although not effective for us, has proved useful in other studies^{45, 46–48}.

Formal partnerships with domestic violence and sexual assault service organizations might be more effective than the informal approach we used. In particular, the creation of satellite offices, where screening and study activities could take place on site, would reduce or eliminate many of the barriers to participation we encountered. Ideally, controls would be recruited from the same populations, thus reducing selection bias. Since many domestic violence service organizations serve non-English speaking communities, the availability of translated materials and bilingual, culturally sensitive study staff would have the dual advantages of reaching more potential participants and providing more generalizable results. Care would have to be taken in such collaborations to avoid any sense of coercion or undermining of trust between the organizations and the women they serve.

Problems associated with hospital-based recruitment included the inability to collect CASI data and difficulty in ascertaining whether vaginal penetration had occurred. CASI data is important for determination of possible confounders and effect modifiers but was not collected in order to avoid potentially imposing additional distress during a moment of crisis. It might be possible to collect this data later, perhaps by including information about further participation in the informed consent form or inviting women to participate during follow-up care. Making the survey available to this group online would likely increase participation. Ascertainment of penetration might be enhanced by testing a swab for semen immediately or by establishing a partnership with the forensic crime laboratory to obtain results confirming the presence of semen or foreign DNA. However, failure to recover semen does not necessarily exclude the possibility that vaginal penetration had occurred²⁹. In addition, we hypothesize that even in the absence of semen, genital injury or other stress-related inflammation may cause changes in the immune microenvironment. If we identify such changes in immune biomarkers, these might be helpful in redefining forensic guidelines for determination of vaginal penetration.

The relationships between sexual assault, immune system response, and HIV susceptibility may be obscured by participant characteristics such as age, hormonal status, hormonal contraception, RTIs and other comorbidities, substance abuse, stress, social support, and socio-demographic factors. Our experience indicates that it may not be feasible to exclude women with RTIs or samples containing semen from research. It may even be undesirable, given the prevalence of these factors in the target population, since it would greatly limit generalizability. Improved laboratory techniques to measure immune biomarkers in the presence of these substances should be sought. The strong correlation we found between different emotional, physical, and sexual violence may be partly explained by selection bias. However, to the extent such a correlation exists in the general population, a large sample size would be helpful in disentangling the separate and interactive effects. It would further provide statistical power to detect small effects while adjusting for the presence of RTIs and other covariates. Given the limitations to recruitment potential in any single location, the development of multi-site consortia may be critical to the advancement of research in this area.

CONCLUSIONS

Our study confirms that research into the relationships between sexual assault, immune biomarkers and HIV acquisition is possible though not without challenges. Moreover, we found that many survivors of sexual assault felt empowered by participating and welcomed the chance to help other women experiencing violence. When biological samples or other data must be collected within a short time after assault, well-articulated collaborations with organizations that serve sexual assault survivors are essential. Safeguards for the trust, privacy, and well-being of potential study participants must be incorporated into study design. To sustain active involvement by partners, good communication channels should be maintained, adequate resources provided, and activity records kept.

Screening activities should be brought to potential study participants rather than requiring them to incur costs in time and money before eligibility is ascertained. In addition to removing unnecessary burdens for women who do not meet inclusion criteria, this would increase study participation, reduce selection bias, and potentially reduce exposure misclassification.

Future research should be directed at developing larger studies and sample repositories which would provide power to differentiate between the effects of various causal factors.

Acknowledgments

This study was funded by NIH (R56AI111933-01; PI: Ghosh) and by an award from the District of Columbia Center for AIDS Research, an NIH funded program (AI117970). We acknowledge Alexandra Clement and Monika Juzumaite for help with recruitment and consenting of participants and Mariel Jais and Jason Daniels for processing samples and performing laboratory assays. This study could not have been conducted without the enormous support of personnel from MedStar Washington Hospital Center and District of Columbia Forensic Nurse Examiners. We would like to thank the participants without whom this study would not have been possible.

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Table 1

Recruitment goals and number of participants enrolled, Washington DC, 2014–2016

Arm 1				
Cross-sectional (1 visit). Community-recruited, pre-menopausal women.				
	Cases		Controls	
Goal:	20		20	
Enrolled:	13 ^a		20	
Arm 2				
Longitudinal (5 visits). Community-recruited women.				
	Pre-menopausal		Postmenopausal	
	Cases	Controls	Cases	Controls
Goal:	2 ^b	5	2 ^c	5
Enrolled:	6 ^a	5	2	5
Arm 3				
Cross-sectional (1 visit). Hospital-recruited women (cases).				
	Pre-menopausal		Postmenopausal	
Goal:	5 ^d		5	
Enrolled:	8		1	

^aThe pre-menopausal cases from Arm 2 were also included in Arm 1, (first visit only).^bLater revised to 5.^cLater revised to 3.^dLater revised to 20.

Table 2**Challenges to Conducting Sexual Violence Research, Washington DC, 2014–2016**

Challenge	Solution
<i>Community-based recruitment</i>	
Difficult to access recent survivors of sexual assault (within past 12 weeks)	Partner with organizations that serve survivors of domestic violence and sexual assault, including setting up satellite offices. Develop multi-site consortia to increase sample size.
Stigma associated with sexual violence	Public education to raise awareness of prevalence and reduce stereotypes about survivors. Recruitment materials can normalize with statements about prevalence; e.g. 'one in five women'.
Maintaining privacy of study participants	In-person communication (no phone messages) or through email when authorized by participant. Study activities conducted in private locations, soundproof rooms.
Potential for misrepresentation of exposure by non-cases	Keep financial incentives modest in keeping with time and effort required by participants. Simultaneous recruitment of cases and controls. Blinding participants to specific inclusion criteria.
Transportation issues, homelessness, no means of contact	Partner with organizations that serve survivors of domestic violence and sexual assault sexual, including setting up satellite offices. Provide reimbursement for transportation.
Selection bias	Recruit cases and controls from same base populations. Do not recruit controls from low-prevalence populations.
Postmenopausal women less likely to participate in research	Target older women specifically in recruitment materials. Use large print. Advertise strategically in places frequented by older women, including electronic mailing lists and online classified ads.
<i>Hospital-based recruitment</i>	
Limited data collected due to vulnerability of participants	Include access to medical records in consent form. Consider adding information about follow-up activities in consent form or inviting women to participate when receiving follow-up care. Provide online access to computer self-administered interview (CASI).
Ascertaining case status	Self-report using CASI. Partner with organizations that have experience in assessing sexual violence. Research to find biomarkers of sexual assault.
<i>Vulnerability of cases</i>	
Vulnerability of cases	Work with community organizations. Train research staff. Be prepared to provide care and counseling referrals.
Sensitive questions	Train research staff. Advise study participants in advance about nature of questions. Remind them they do not have to answer any question they do not want to. Be prepared to provide referrals.
Uncomfortable pelvic exam	Use experienced, female clinicians and staff. Use smallest available speculum and lubricate with warm water to minimize discomfort
<i>Operationalization and measurement</i>	
Confounding by other forms of abuse	Collect data on emotional, physical abuse and adjust in analysis.
<i>Clinical and laboratory challenges</i>	
Scheduling issues	Good communication. Shared calendar. Appointment cards. Reminders.
Reproductive tract infections	Need large sample size to evaluate interactive effects of sexual violence and reproductive tract infections. Given the prevalence of infections, novel techniques to discern any biological effects of sexual trauma in the presence of infection should be sought.
Quality of specimens	Participant education. 48-hour reminders. Rescheduling as necessary. Given that semen is likely to be present after sexual assault, novel techniques to discern the effects of violence in the presence of semen should be sought.
Transportation, storage of specimens	Provide courier training. Provide refrigeration and rockers for temporary storage on site.
Collection methods	Both CVL and provider-collected swabs effective.