International Journal of Sciences: Basic and Applied Research (IJSBAR)

ISSN 2307-4531
(Print & Online)

http://gssrr.org/index.php?journal=JournalOfBasicAndApplied

Views and Experiences of Mucosal Sampling in HIV Clinical Research among Kenyan Volunteers

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Abstract

HIV transmission predominantly occurs across mucosal surfaces. Efforts to find an effective and efficacious HIV vaccine, requires understanding the various mechanisms of sexual HIV transmission including immune responses to various HIV vaccine candidates along the mucosal pathways. In this paper, we describe the experiences of health volunteers in three Phase 1 HIV vaccines trials and an observation study that comprised of high- risk and low risk healthy participants with regard to the collection of rectal, cervical and seminal mucosal samples. The paper emanates from a study that examined the views and experiences of volunteers in participating in HIV clinical research, at the KAVI-Institute of Clinical Research, Nairobi, Kenya. The study followed a mixed methods phenomenological research approach with a dominant qualitative strand. In the first phase, quantitative data was collected via a survey questionnaire involving 116 volunteers that helped identify 28 volunteers for the qualitative phase. Quantitative data were analyzed using SPPS while qualitative data was transcribed verbatim, thematic themes identified for coding and entered into Atlas *ti* for analysis. Participants had a mean age of 28.5 ± 5.7 years (range 20–51 years). There were more males (n =85) than females (n= 31). In general, volunteers expressed mixed reactions towards the collection and use of mucosal samples. Both none-consenting and consenting volunteers cited invasiveness of their privacy.

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Also reported were experiences of physical and psychological discomforts, with men terming the collection of semen via masturbation as unnatural and contravening individuals' religious and cultural beliefs. The findings reveal a knowledge gap among community members with use of mucosal samples and modes of collection.

Keywords: Clinical research; HIV trials; mucosal sampling; experiences.

1. Introduction

HIV infection remains a major global health concern. In 2017, an estimated 36.9 million were living with HIV worldwide with nearly 70% reportedly being residents in sub-Saharan Africa [1]. The total number of new infections recorded in the same year was 1.8 million having declined from 3.4 million in 1996. Additionally, 18.2 million people aged 15 years and above were living with HIV; accounting for close to half of the new infections that had occurred in 2017. Recent data further show a staggering slow decline of new infections in relation to expected global targets [2]. In the sub –Saharan region, Kenya included, sexual transmission remains the key driver to the HIV epidemic. Kenya has both a generalized and a concentrated epidemic that is deeply-rooted among key populations. Key populations account for a significant HIV prevalence and 30% of new infections in comparison to the general population [3]. Further, the Kenya AIDS Response Progress report [4] documents the following prevalence: Injection Drug Users (IDUs) at 18.3% men who have sex with men (MSMs) at 18.2% while for Sex Workers at 29.3%. Whilst, the last two decades have witnessed sustained global efforts in scale-up of various HIV prevention, treatment, care and support programs [5, 6, 7], the war against HIV remains [1]. Finding an effective and safe HIV vaccine remains the ultimate key to bringing HIV to a halt. Since the late 1980s, that saw the first attempt to develop a vaccine against HIV with ability of eliciting antibody response in host recipients, over 200 candidate vaccines have been developed and tried in many parts of the globe. While some of these have moved to Phase 2, only a few have made it to the Phase 3 efficacy trials and just one the RV144 producing an efficacious outcome [8,9]. Several factors that include the inability of the human body to recognize the virus to initiate immune response and the variability of the HIV virus are some of the reasons for this delay [10] in having a vaccine in place. With the knowledge that HIV transmission predominantly occurs across mucosal surfaces, the induction of effective and long-standing antibody and cellular immune responses in the genito-rectal mucosa may be the critical factor to an efficacious HIV vaccine. In Kenya, the Kenya AIDS Vaccine Initiative- Institute of Clinical Research (KAVI-ICR) at the University of Nairobi since its establishment in 1999, with the support of IAVI, conducted a number of phase 1 HIV vaccine trials, observational studies and one PrEP study. With the dynamism of HIV epidemic and transmission patterns changing globally, KAVI-ICR is continuously engaged in trying new and novel approaches in understanding the HIV virus and its behavior such as studying the human mucosa surfaces that include collecting mucosal samples from various parts of the body such as rectal-anal; cervical, nasal and sperms. Although available data from the clinics [11] report acceptance and tolerance for invasive mucosal sampling, there is scanty literature on how volunteers perceive and experience this phenomenon. This paper attempts to provide an understanding on how volunteers perceive and experience mucosal sampling especially those thought to emanate of invasive body parts. The table 1 below details the various samples that volunteers were requested to provide, pre/post collection conditions and methods of collection.

Table 1: Types of mucosal samples collected, sites of collection and methods

Type of sample/ site	Pre/ post Collection Conditions	Method of collection
Cervical-vaginal secretions	• Avoid sex day before collection	• Soft-cup (in place 1 hour) • Sponge placed in cervix area for a few minutes for non IUD users • Aspirator for non IUD users
Colo-rectal biopsis(M/F)	• Anema to clean the rectum • For biopsy return to clinic 1-2 days after for healing evaluation • Abstain from anal sex till healed • Use lubricants and condoms in case of anal sex after biopsy	• Sponge placed in rectum a few minutes • Biopsy upto10 samples size of uncooked rice grains collected from rectum wall.
Semen	• Avoid sex day before collection	• Through Masturbation

2. Materials and Methods

2.1 Study Setting and Population

This study took place at the KAVI- Institute of Clinical Research sites at KAVI-KNH University of Nairobi School of Medicine and at the KAVI- Kangemi at the Kangemi County Health facility, Nairobi, Kenya. Study participants were male and female adult volunteers, screened and found eligible to participate in four studies that included three Phase 1 vaccines trials – B002, B003, Sendai/S001 and one observation–Protocol J. Majority of the participants were low risk HIV uninfected except for the Protocol J that enrolled low risk, high risk uninfected and HIV seropositive individuals. The inclusion criteria for study participants entailed all that were screened and eligible for enrolment. They included those that had declined enrolment or dropped after enrolment.

2.2 Study design

This study applied a descriptive phenomenological research design following the mixed methods phenomenological research approach (MMPR). Data was sequentially (quantitative-Phenomenology) collected to allow for the sampling and data collection of the qualitative (phenomenological) data as proposed [12]Mayoh

and his colleagues 2015). In the first phase, quantitative data was collected from 116-screened eligible volunteers recruited from the four KAVI studies via a survey questionnaire tool. The data collected The data was used to refine the in-depth interview tool and further guide in the identification of 28 participants for the phenomenological phase to provide a rich account of their experiences. All interviews took place at the trial sites, in quiet and secured rooms. All qualitative interviews were audio recorded and accompanying notes taken. Appropriate data management and analysis procedures were undertaken. For completeness, the quantitative data was cleaned before entering into the SPSS Version 17.0. The audio-recorded interviews, were on the other hand, transcribed verbatim and cleaned for analysis. Using a descriptive phenomenological analysis approach, each transcript read entirely to make a sense of the whole. This followed the delineation of data and transforming it to meaning units into sensitive statements reflecting individuals' lived experiences. This process enabled the development of coding sheet for coding and subsequent entry into Atlas *Ti* for management and analysis. This followed was by a synthesis of the general structure of the experience based on the constituents of the experiences identified.

2.3 Ethical considerations

Ethical review and approval for this study was from the Kenyatta National Hospital Ethics Research Committee (KNH-ERC- ref P298/05/2013). To uphold ethical research standards, the research team that included the researcher and the research assistants went through the code of ethical conduct that included undertaking the online research ethics course. All study participants were adequately consented prior to data collection.

3. Results

3.1 Participants' characteristics

The participants' ages ranged from 20-51 years with significant proportions of males (73%) to females (27%). Their mean and median ages were 28.5 and 28 respectively. Majority (96%) were heterosexual as those reporting single marital status (54%) being were slightly more than the married (41%). Their levels of education attainment ranged from incomplete primary to college/ University. Majority had complete secondary education (n=49), closely followed by those with college education (n=38). The forms occupation included casual work (n=30), small businesses (n=27), formal employment (n=34) with a significant number (n=25) were at the time unemployed and/or studying. Close to 47% (n=54) of the participants had monthly incomes Ksh. 10,000 and below; 32% (n=37) had incomes of Kshs. 10,000 and above while about 22% (n=25) had no incomes at the time.

3.2 Reported acceptance for collection of mucosal samples

Although overall there was a high enrolment of males to females across the four studies, women were more receptive to collection of samples from the genitals sites. In the Protocol J study for instance all the seven (n=7) women agreed to cervical samples collection, while for the semen it was by less than half (n=5) of the men. Across the four studies, the Protocol J recorded the highest number of volunteers agreeing to provide rectal (n=12), cervical (n=7) and semen (n=5) samples as displayed in Table 2 below.

Table 2: Volunteers' reported acceptance for mucosal sampling

Study Name	Survey Tool Respondents		Reported acceptance for mucosal collection		
	Number of females n=31	Number of males n=85	Rectal (19)	Cervical (14)	Semen (8)
B002	9	27	3	1	1
B003	13	28	2	5	2
S001	2	18	2	2	0
Protocol J	7	12	12	7	5

3.3 Views and Experiences with Mucosal sampling

Upon enrolment into the four studies, the volunteers were further, invited to join the mucosal sub-studies. Like any other study, they were for a second time consented to allow for personal determination. This entailed providing adequate information that included the samples to be collected, purpose, collection procedures and tools of collection. Other information provided were on safety and risk factors, individual rights to participate or decline, right to choose the samples they could provide, right terminate their participation in the mucosal sub study and yet remain in the study initially enrolled study. Although the requested mucosal samples included those from the nasal and salivary glands, those emanating from the genital and rectal sites aroused mixed reactions, with many questioning the purpose for their collection. These views varied with the type sample, mode of collection and understanding the purpose for which they were required. Moreover, these varied with the sexes across both the consenting and non –consenting volunteers. The excerpt below points to some of the expressed views I had problems with some of the samples they were requesting. They are samples that are so difficult to provide. They were many like sperms and you ask yourself, surely, how will they collect it? Then there were rectal samples- that were shocking! I cannot remember well but there was a way they said they could insert a gadget through the anus to get the sample. I tried to figure out that process and I found it hard. (B003, Single Male, Chef) *Semen collection While from the consenting process, the volunteers had received information about the purpose for which the semen was required, for some, were fears that perhaps it was for sell. One male from the Protocol J explained, that before being fully explained to, he had questions For the semen, I had many questions. It was something unusual because you know, some things are unfamiliar and furthermore you have never seen them before…..because you know there are stories the selling of semen but they explained it deeply so I could understand and I did. They convinced us enough and I accepted (Protocol J, Married, Discordant male, 36 years old.)*

Even though providing mucosal samples was an option, for some it had served a reason for some volunteers to decline enrolment, cited discomfort with the whole idea of having to produce semen via a non-sexual environment with some terming it unclean, un-cultural and unreligious as shared by two male volunteers.

I declined to join the study because I did not understand how I was going to be able to give semen ...masturbation is against my religion (Protocol J Married Male) To be honest I just felt uncomfortable giving the semen…..I just felt uncomfortable there is that right to refuse and nothing will be done to you because you will still enjoy the privileges you had before like check-ups….I gave out saliva (B002, Married Male, 26 years old) Besides the psychological discomfort, some consenting men expressed difficulties in producing the semen in spite of having shown the willingness. *Tell us about your challenges with providing samples During the participation, they introduced an aspect of collecting saliva and sperms. That one was hectic because you see somebody who is not used to just producing sperms like that without having sex…..… it was challenging. I tried… but it reached a point that it was hard because you could stay in a room for around thirty minutes trying to ejaculate and there is nothing, the sample is like the very little so they said that I just continue producing the saliva which was easy (B003, Single Male 22 years old)*

For others, the requirement to abstain from sexual intercourse a day before the scheduled day of collection presented a social burden of having to disclose to sexual partners their participation in the study and whole aspect of postponing sexual engagement in wait for semen collection. More difficult to explain was the aspect of masturbation, as was shared by a married male from the Protocol J study below: *How do you start explaining to your partner that today no… that tomorrow I am going to give semen through masturbation? It was difficulty; I had to find other excuses for not having sex (Protocol J, Maried Male) Cervical secretions* The collection of cervical secretion was via soft cup that the women had an option for self-sampling or provider assisted. Although generally painless, women that had consented reported feelings of physical discomfort and invasion of personal privacy. One female volunteer explained that although the procedure was painless, she had felt uncomfortable with the whole process which she added had only been was made easier with having a female provider collect the samples as opposed to a male. The excerpt below explains this: *Besides blood, tell us about the other samples you provided or were to provide Saliva and if you were willing rectal samples, cervical samples and semen for the men... if one were willing. For me, I gave all… (laughs) for me because I was dealing with a female, I was just ok. There was no pain it was just normal though I was not that comfortable but since I was willing to participate and it was voluntary so I had to… but I was not that much comfortable when they were inserting those things in me but I was not forced to (B002, Single mother, 27 years old- sales lady)*

Another female respondent was of similar opinion citing the importance of the attending clinician being of the same sex as indicated below:*the soft cup, putting it in is usually … uncomfortable.....the good thing is that for me the doctor that was doing it was a woman…I used not to mind it... I did not see if there was much problem ….even now I prefer a woman (S001, Single Female, 23 years old- Teacher)*

Colon- Rectal sampling Rectal samples were collected from consenting males and females volunteers. Even though there were mentions of psychological discomfort, the actual process was said to be painless *There was no any effect. No pain and there are tools which they use to collect samples The tool is like a gun which they put behind you and they have two sponges and plastic and that sponge they pass it through that gun then they swap. Takes about five minutes (S001 Single male) there are those like rectal…..as in they are not comfortable (S001, Single Female, 23 years old -Teacher)* Describing the process of colorectal sample collection, a male volunteer from the S001 study found it to have been painless following sedation. *For biopsy, they collect samples from*

the wall of the intestine to see if the vaccine has any effect on the wall of small intestine. That takes place in the lab, where you are injected with some sleeping medicine when you are asleep the procedure takes place. You are given some pills to take which help you to clean the intestine… you are given the day before so when you come tomorrow you are clean so there is no interference with the procedure. There is no pain because when they are doing it you are not aware of it. After entering the lab you are injected with sleeping medicine, there is a tool they insert directly into your anus and it goes directly into the small intestine (S001 Single male) One of the requirements for pre and post collection of colorectal biopsy collection was sexual abstinence, more so among MSM community that practice anal sex. For those selling sex, this requirement, presented both a social economic dilemma challenging their income opportunities and seen be an inconvenience resulting into income loss. One MSM from the protocol J explained that he had bled after providing the biopsy further indicated that although he had been asked to abstain to allow healing he went on to have sex as the reimbursement received was not make up for what he could lose. *you are told to avoid sex but for me I had sex throughout because what I would get was more than I would get suppose I avoided sex (Protocol J MSM, 27 years old-Gay activist)* Besides the fears and misgivings with sampling, for some participation was of benefit as it had provided an opportunity for health assessment. A male volunteer with the Sendai study was to explain that in spite of the requirements of abstaining from food on the day before sample collection he was able to know his health condition. *I have learnt a lot and of course they had told us that if you participate you will get to know if you have any health problem…..In the process of collecting biopsy, the colon was examined, and that gave me a chance to know if I have a problem in my colon or not. (S001, Single male, age 24, stage actor)*

4. Discussion

This paper provides a view of the experiences of volunteers regarding mucosal sample collection for HIV clinical research evaluation. Knowledge as to how volunteers view their participation experiences provides outcome based insights into the effectiveness of the efforts of human protection as well as opportunities to enhance their clinical research experience [13]. Studies evaluating feasibility for collecting mucosal samples among health volunteers in health volunteers in African [14, 11] have recorded acceptability and tolerability on the uptake of various samples. However, findings from this study reveal that in spite of the reported acceptance, volunteers harbor mixed feelings more so with samples collected from the anal-rectal sites. Although semen collection is commonly used infertility treatments that mostly occur in developed countries, it is, rarely collected from health volunteers creating fears that perhaps the semen was for sale. These fears resonate with those surrounding the collection blood. Indeed, narratives of community fears and mistrust of research doctors exist in the African settings, raising ethical concerns as has been extensively discussed in literature [15, 16, 17, 18]. Tied to the collection of semen, is process of collection via masturbation that some male volunteers termed unnatural and contra version of individuals religious beliefs. Although masturbation is an old and common behavior for achieving sexual pleasure, for many communities it remains a taboo, that is seldom discussed or practiced in public [19,20] thus explaining the reactions of the participants in the present study. The fact that some males had declined enrollment is an important pointer to addressing community information needs regarding human biological samples especially those emanating from sites considered invasive. Findings from this study showed, although the collection of cervical samples was highly accepted by the female volunteers, feeling of physical discomfort were felt. Besides the physical discomfort, reported also were experiences of psychological

discomfort associated to nakedness which to a small extent resolved by being attended by a female provider. Although self- sampling was an option for the female participants, they preferred it collected by a clinician suggesting a lack of self-confidence. Adoption of self-sampling is feasible and has been shown to be successful [21], suggesting the need to increase acceptability for its use. One of the requirements for those providing semen, cervical and colon rectal samples was to abstain from sex a day before the appointed day of collection and few days after collection to allow for healing. Despite learning about the rationale for post biopsy collection sexual abstinence, for some especially those with partners it presented a social burden of having to explain why sex cannot happen. Besides the burden of having to explain to sexual partners, it also had economic implications for those MSM who sold sex and exposure to risk. This general behavior of volunteers failing to adhere to study protocol requirements are not new and suggesting further research on risk perception among clinical research volunteers

5. Conclusions

Although the findings from this study are not conclusive, they point to a number of grey areas of science that need contextualizing. In order to increase acceptability and willingness for the collection of mucosal samples among volunteers in future studies, there is need for community education regarding the collection and use of biological samples in medical and clinical research. Social science research should be inbuilt into clinical trials to provide understanding of the social behavioral issues surrounding participation and trial procedures and their impact on trial outcomes.

Acknowledgements

We acknowledge the KAVI-Institute of Clinical Research for supporting this study by providing access to the volunteers that were interviewed and the resources. Gratefully acknowledged are the volunteers that wholeheartedly shared their experiences of being clinical research volunteers.

Source of funding

This work was supported the IDRC through the KAVI-Institute of Clinical Research, University of Nairobi.

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