ETHICAL ISSUES INFLUENCING WILLINGNESS TO PARTICIPATE IN HIV VACCINE TRIAL RESEARCH AMONG SELECTED RISK POPULATIONS IN OYO STATE, NIGERIA

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ABSTRACT

The development of a safe, effective, and accessible HIV vaccine has become one of the most urgent global health need. This is in view of the almost five million new HIV infections and three million deaths from AIDS occurring every year worldwide. This study was based on the need to understand the ethical issues influencing HIV vaccine acceptance and willingness to participate in HIV vaccine trial as this will foster trust which is imperative for successful ethical trial of HIV vaccine among populations that will be primary targets of the vaccine trial .This study was carried out to assess the ethical concerns, knowledge gaps, attitude towards HIV vaccines and willingness to participate in future HIV vaccine trials among selected risk populations in Oyo state, Nigeria.

Descriptive study that employed both quantitative and qualitative approaches was carried out. Multiple sampling methods were adopted to select the study population as appropriate, since they belong to different groups. Seven Focus Group Discussions comprising of eight discussants each were held among students (male & female), commercial sex workers, long distance workers, people living with HIV (male & female) and market women. Three key informant interviews were also conducted among health professionals. Information gathered were transcribed and content analysis of the focus group discussions were done by the researcher. The information obtained guided the design of a semi- structured questionnaire which was used to gather information from 230 respondents comprising students, commercial sex workers, long distance workers, people living with HIV and market women; respondents were randomly selected . Descriptive statistics was used to summarise the data and Chi square was used to test for associations between categorical variables at 0.05 level of significance.

Majority of the respondents (83.0 %) have not heard about vaccine trial but most (93.0%) were able to define HIV and 68.0 % stated that they will be willing to participate in HIV vaccine trial .Willingness to participate was strongly associated with knowledge of vaccines against childhood killer diseases (X^2 =9.21,P =0.003) and not that of HIV vaccine trial. Willingness to participate in vaccine trial was reported more among male sex (5.06, P =0.025, OR = 2.06) and students (X^2 =3.04, P =0.018). There were also associations between willingness and the perception of vaccine being safe (X^2 =27.88,P = 0.000), ensuring protection from harm during trial (X^2 =35.89,P = 0.000) , and ability to withdraw from trial (X^2 =18.55,P = 0.000). Availability of social and family support if infected (X^2 =13.94, P =0.000), assurance that vaccine will strengthen their immune system against AIDS (X^2 =22.92, P =0.000) , provision of free treatment if infected (X^2 =12.64,P =0.001) , client's testing HIV positive (X^2 =6.12,P =0.014) and respondent's believe that their participation in the trial will make HIV become preventable (X^2 =12.47, P =0.001) were associated with willingness. No association was found between willingness to participate and getting money during trial (P= 0.685), stigma (P=0.379) and knowledge of HIV status (P=0.302) and HIV vaccine trial (P= 0.703).

Deficiencies in knowledge identified and the high level of willingness to participate in vaccine trial by the study population point raised some ethical concerns and point to the potential value of preparatory work before introduction of HIV vaccine. Appropriate health educational campaign of vaccine trial concepts to create awareness before HIV vaccine begins in Nigeria is recommended.

Keywords: HIV vaccine trials, HIV/AIDS knowledge, Willingness to participate.

Introduction

The HIV and AIDS pandemic is a major public health problem worldwide, more so in sub-Saharan Africa where more than 70 percent of all people living with HIV and AIDS reside (USAIDS, 2010). More than thirty years after the start of the epidemic, HIV/AIDS still remains one of the most important threats to health around the globe. Despite moderate successes in decreasing individual-level risk (Stoneburner & Low-Beer , 2004), and international efforts to address structural factors (Cohen & Scribner 2000 ; Gupta,1995) the epidemic continues unabated. Burden of HIV and AIDS in Nigeria is still too high; it may be estimated that over 300,000 infections and 200,000 deaths occurred in 2005 (USAIDS, 2010). The high burden of HIV and AIDS calls for dedicated and sustained acceleration of prevention strategies against the transmission of the virus.

In this light, an affordable and effective HIV vaccine remains vitally important to curtailing the population-level spread of infection. Despite acknowledging the need for an HIV vaccine and in spite of 25 years of research the development of an HIV vaccine is still in its infancy.The progress of the vaccine trial has been slow in many resource-poor countries. (USAIDS, 2010; Tucker & Mazithulela, 2004) and the acceptance of such vaccine by the populace remains unknown.

Statement of Problem

Following the promulgation of the Nuremberg code in 1947, the ethics of research on human subjects has been a challenging and often contentious topic of debate. (Benatar and Singer, 2010).The high burden of HIV infection globally has guided the impetus of many biomedical researchers to conduct researches on a safe, effective and accessible HIV vaccine. The trial of the HIV vaccine is going on in many countries. Since Africans will benefit from the vaccine, it is necessary and fair that they will be part of the trial.

Successful trial is dependent on valuable human relationship, participation and cooperation. This participation should be based on valuable interaction between the medical researchers and the participants and Trust is a key component in such relationship. Trust improves public compliance and is central to professional integrity on the part of the researcher. However, the value of trust is gradually been threatened by unethical research conduct. Since public trust is essential in promoting research there is the need to explore the avenues by which the research enterprise can build trust, hence the need for this study on ethical issues influencing willingness of selected risk population to participate in HIV vaccine trial and to create awareness before the actual commencement of the trials.

Objective of the study

General

To assess the ethical concerns, attitude towards HIV vaccines and willingness to participate in future HIV vaccine trials among selected risk populations in Oyo State.

Specific Objectives

1. To identify ethical issues influencing willingness to participate in HIVVTs among selected risk populations in Oyo State.
2. To determine the willingness of populations at risk of HIV infection to participate in future HIVVTs among selected risk populations in Oyo State.
3. To identify predictors influencing willingness to participate in HIVVTs among selected risk populations in Oyo State.
4. To identify ethical issues that can deter participation in HIVVTs among selected risk populations in Oyo State.

Significance of study

The broad impact of HIV and the difficulty in controlling or eliminating it as a health threat stimulated an ongoing series of HIV prevention and treatment clinical trials. Some of these trials test new pharmaceuticals designed to slow the progression of the disease in those who are infected and also to prevent the infection in non-infected individuals. This research will assess the concerns, knowledge gaps, attitude towards HIV vaccines and willingness to participate in future HIVVTs among populations at risk of HIV infection in Oyo state, Nigeria. The findings stand to provide information to guide the development of programmes to create awareness and policy formulation on HIV/AIDS vaccine trial.

Literature Review

Ethical conduct of research is based on a variety of codes and reports, these includes the Nuremberg code, the Declaration of Helsinki, the Belmont Report, the Council of International Organizations on Medical Sciences' Guidelines for Biomedical Research Involving Human Subjects' (hereafter referred to as 'CIOMS'), and the National Bioethics Advisory Commission's report titled 'Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries' (hereafter referred to as 'NBAC').

The Nuremberg code emphasizes that the voluntary consent of the human subject is absolutely essential in medical research. This means that the person involved should have legal capacity to give consent, should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior forms of constraint or coercion; should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him or her to make an enlightened decision. The World Medical Association Declaration of Helsinki developed as a statement of ethical principles provided guidance to physicians and other participants in medical research involving human subjects. The guide explained that medical research involving human subjects includes research on identifiable human material or identifiable data and stated that it is the duty of the physician to promote and safeguard the health of the people. The physician's knowledge and conscience should be dedicated to the fulfillment of this duty. In medical research on human participants, considerations related to the well-being of the human participant should take precedence over the interests of science and society.

The Belmont Report identified three principles or general prescriptive judgments that are relevant to research involving human subjects, these are principles of respect for persons, beneficence and justice. Respect for persons incorporates at least two ethical convictions; first, that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection. Beneficence requires that persons be treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making

efforts to secure their wellbeing. Two general rules have been formulated as complementary expressions of beneficent actions are do no harm and maximize possible benefits and minimize possible harms.
Justice describes who ought to receive the benefits of research and bear its burdens. This is a question of justice, in the sense of "fairness in distribution" or "what is deserved."

The Council for International Organizations of Medical Sciences (CIOMS) guideline was set out in cooperation with WHO, to prepare guidelines ‘‘to indicate how the ethical principles that should guide the conduct of biomedical research involving human participants, as set forth in the Declaration of Helsinki, particularly in developing countries, given their socioeconomic circumstances, laws and regulations, and executive and administrative arrangements’’. The National Bioethics Advisory Commission (NBAC) developed a schema to describe the character of the personal information associated with particular samples of human biological materials as they exist in clinical facilities or other repositories and in research. The NBAC offered recommendations to improve the interpretation and implementation of the existing federal regulations as they apply to research using human biological materials.

Despite all these guidelines, there are several cases of unethical conduct of researches/trials around the world, in both developed and developing countries. Some examples of unethical trials include the Letrozole trials in India, Hepatitis E vaccine trial in Nepal, Nevirapine PMTCT trials in Uganda, Tenofovir trials in Cameroon, Thailand, and Nigeria, Ragaglitazar trials in thirty two countries including India and the Trovafloxacin trials in Nigeria.

Empirical Studies

Smit, Middelkoop, Myer, Seedat, Bekker and Stein (2006) carried out a study on willingness to participate in HIV vaccine trials in a peri-urban South African community and found out that Willingness was associated with increasing age, male gender, and increasing knowledge about vaccines generally and HIV vaccines specifically. Heather, Jaspan, Jessica , Berwick , Myer , Mathews, Flisher, Wood & Bekker (2006) carried out a study to determine human immunodeficiency virus (HIV) prevalence, sexual risk behaviors, and attitudes toward HIV vaccine trials among 11–19 year-olds in a peri-urban community near Cape Town, South Africa. Of the 356 adolescents that participated, the majority of adolescents (79%) were willing to participate in an HIV vaccine trial. Increasing age and length of residence in the community were significantly associated with willingness to participate.

Another study on incentives and disincentives to participate in prophylactic HIV vaccine research by Jenkins , Temoshok, & Virochsiri (2005) revealed that willingness to participate was related to self-perceived benefits from joining a preventive vaccine trial, as well as to concerns about product safety and social discrimination that might result from participation. Men were more willing to participate than women, and there was a trend toward greater willingness to participate in those who were less educated.

Findings from a study conducted to determine the anticipated participation in a prophylactic AIDS vaccine trial and to identify perceived benefits and barriers to enrollment of HIV-seronegative volunteers at risk of HIV infection in northern Thailand by Celentano, Beyrer, Natpratan, Eiumtrakul, Sussman, Renzullo, Khamboonruang & Nelson in 1995 yielded the following result: Awareness of vaccines (88-97%) and AIDS vaccine development efforts (62-77%) were common and viewed to be

a complement to behavior change (74-94%). Approximately 25% of subjects would definitely join a trial if asked, and an additional 38% would accept an AIDS vaccine if they were convinced it would be safe and effective. Important barriers to participation included concerns with discrimination (16-45%), short- (37-60%) and long-term (30-55%) vaccine side-effects, fear of disability and death (36-58%), and beliefs that partners would refuse to have sex (24-49%) after immunization. The principal inducement to join a trial was health insurance (62%).

Otuonye, Onwuatuelo, Okwuzu, Onwuamah, Adeneye, Oparaugo, Akintude, Uwandu & Fowora (2011) evaluated Adolescents' willingness to participate in HIV vaccine clinical trial preparedness in Nigeria. Of the 291 respondents interviewed, 73.5% have knowledge of HIV vaccine, and 66.2% have no perceived risk of HIV vaccine infection. Newman, Duan,Roberts, Seiden, Rudy, Swendeman, & Popova in 2006 explored perceived barriers and motivators regarding HIV vaccine trial participation among low-socioeconomic ethnic minority respondents at risk for HIV in Los Angeles. The perceived barriers to HIV vaccine trial participation, in rank order, were vaccine-induced HIV infection, physical side effects, uncertainty about vaccine efficacy, and uncertainty about other vaccine characteristics, mistrust, low perceived HIV risk, study demands, stigma, and vaccine-induced HIV seropositivity. Motivators were protection against HIV infection, free insurance and/or medical care, altruism, and monetary incentives.

METHODOLOGY

This is a cross – sectional descriptive study that employed both quantitative and qualitative approaches to data collection.

Study Setting

Ibadan is located in south-western Nigeria. It is the capital of Oyo State, and is reputed to be the largest indigenous city in Africa, south of the Sahara. Ibadan is an important commercial centre. Virtually every street and corner in the traditional core and the inner suburbs of the city is a market square or stall. Within the city there are two eight-day periodic markets - Ibuko (Bode) and Oje markets as well as many daily markets. One of the two markets, Oje was chosen for this study. Due to lots of commercial activities in Ibadan, there is availability of the at risk population for HIV in the city because people come from far and near to buy and sell in Ibadan. One of the major parks for long distance journey is the Ojoo motor park, where data was collected for this study.The premier citadel of learning, the University of Ibadan and the Ibadan Polythenic serve the populace by providing the training needs for the young and old. People come in to access qualitative education in Ibadan. The University of Ibadan was randomly selected for this study. There are two major government hospitals in Ibadan, the University College Hospital which is a teaching hospital with the core mandate for Research, Training and Service and Adeoyo State Hospital, a state owned hospital with the core mandate of clinical service provision for the populace. Both hospitals enjoy funding from President's Emergency Plan for AIDS Relief (PEPFAR) / AIDS Prevention Initiative in Nigeria (APIN) project for screening, diagnosing, counselling and treatment of people living with HIV/AIDS. Adeoyo PEPFAR / Sexually Transmitted Disease clinic was one of the study sites used for this study.

Study Population

The study population was made up of people at risk of HIV and people living with HIV. The participants were men and women representing the following subgroups:

- Male long distance drivers

- Commercial sex workers
- Market women from a major market in lbadan
- HIV positive individuals attending PEPFAR Clinic in Adeoyo government hospital, Ibadan
- Clients attending STD clinic in Adeoyo government hospital, Ibadan and
- Adolescents from a selected higher institution in lbadan.

3.3 Sample Size determination

From the sample size calculation, the sum is 206 and plus the 10% non response of 20 respondents, it is 226. Approximately 230. A total of 230 respondents were used for the study.

Sampling

The study sites were selected by ballot. Since the study population fell into distinctly different group, simple randomized sampling method was used to select forty respondents from each stratum to ensure fair representation. Subjects were then selected using systematic random sampling method except for the commercial sex workers, where convenience sampling method was adopted due to small available willing population. The sampling interval was predetermined to be every fifth person for each group, the first person was randomly selected. For the male long distance drivers, every fifth driver given a tally to load passengers at the Ojoo Long Distance Journey Park was enrolled in the study. At oje market, every fifth shop/stall was approached and market women were given a questionnaire to fill. At Adeoyo Government Hospital on the clinic day, every fifth HIV positive individuals attending PEPFAR clinic/ clients attending STD clinic that received treatment were recruited into the study and for the undergraduates students ,two halls of residence (one male and one female hostel) in University of Ibadan were utilized. Here every fifth student that entered the hall of residence was given a questionnaire to fill after having been provided information about the study.

Instrument development and data collection

The instrument used for data collection in the study was a structured questionnaire. The questionnaire was developed in English and then translated into Yoruba language. Back translation was done to ensure that the original meanings of the questions were retained. The questionnaire was made up of sections A – C. Section A contained questions on demography, section B was on knowledge of HIV/AIDS vaccine trial while section C was on willingness to participate in HIV vaccine trial. A pre-test was conducted at the sexually transmitted disease clinic in UCH, Ibadan with 10 clients to ensure reliability of the instrument. The questionnaires were administered by three trained research assistants.

Validity and Reliability of Instrument

The questionnaire was presented to experts in the field of study for review to ensure that it contained all the items relevant to the study and to review the content for face validity. Test retest method was used to measure the reliability of the instrument. Scores were analyzed using reliability coefficient.

Ethical Consideration

The proposal was reviewed by the University of lbadan /University College Hospital Ethical Review Committee after which an approval was given for the conduct of the study. Permission was also obtained from the gatekeepers of the different groups. All intending participants in the

study were given an opportunity to make an informed decision. Participation was voluntary and a written informed consent was taken from all participants after a detailed explanation of the research. Confidentiality of all data was maintained throughout the period of the research as all information was coded.

Data Analysis

Descriptive and inferential statistics were used to analyze the data using Stata statistical software. Test of hypotheses was done. Chi square was used for categorical variables and logistic regression was used to identifying variables related to willingness at p value of 0.05 level of significance. Data was presented in form of tables

RESULTS

Socio - Demographic Characteristics

Table 1 depicts that 79 (34.4%) of the respondents were male while 151 (65.6%) were female. The respondents age revealed that 73 (34.7%) of the respondents were between ages 26-35 years, 81(35.2%) were between 16-25 years, while 46(20.0%) were between 36-45 years and 30 (13.1%) were between 46-55 years. The educational level revealed that 93(40.4%) of the respondents had secondary education, 71 (30.9 %) had tertiary education, 47 (20.4%) had primary education, only 19 (8.3%) had no formal education. One hundred and thirty eight 138(60.0 %) of the respondents were married, while those that were never married accounted for 81(35.2%), 6(2. 6%) were separated, 5 (2.2%) the respondents were widowed. Majority 136(60.7%) reported to be Christians, while 88(39.3%) were Muslims. The information on occupation revealed that 87 (37.8%) were self employed/traders, 46(20.0%) were students, 14(6.1%) were civil servants, 43(18.7%) were drivers while 40(17.4%) were commercial sex workers.

Table 1: Distribution of respondents' by Socio- demographic Characteristics

Variables	Frequency N=230	Percentage 100 %
Sex		
Male	79	34.4
Female	151	65.6
Age		
16-25 years	73	31.7
26-35 years	81	35.2
36-45 years	46	20.0
46-55 years	30	13.1
Educational		
No formal education	19	8.3
Primary	47	20.4
Secondary	93	40.4
Tertiary	71	30.9
Marital status		
Married	138	60.0
Never married	81	35.2
Widowed	5	2.2
Separated /divorced	6	2.6
Religion		
Christian	136	60.7

Islam	88	39.3
Occupation		
Civil servant	14	6.1
Self Employed/ Artisan	87	37.8
Student	46	20.0
Drivers	43	18.7
Commercial sex workers	40	17.4

Table 2: Knowledge of HIV/AIDS vaccine trial concepts

Result of the analysis shown in Table 2 revealed that 127 (55.2%) respondents strongly agree that vaccines are used to describe products that are designed to prevent disease, 72 (31.3%) agree, 27 (11.7%) undecided, 2 (0.9%) disagree and strongly disagree respectively. The data also depicts that 86 (37.4%) respondents strongly agree that preventive vaccines are given to non infected individuals, 62 (27.0%) agree, 56 (24.4%) undecided, 21 (9.1%) disagree while 5 (2.2%) strongly disagree. However, 62 (27.1%) respondents strongly agree that therapeutic vaccines are given to infected individuals, 72(31.4%) agree, 88(38.4%) undecided, 5(2.2%) disagree, 2(0.9%) strongly disagree.

The findings further revealed that 9(3.9%) respondents strongly agree that vaccine trials occur in three phases, 19(8.3%) agree, 197(85.7%) were undecided. Also, 6(2.6%) of the respondents strongly agree that phase 1 trial tests how much of a new vaccine can be given with reasonable safety, 26(11.4%) agree, 191(83.4%) undecided while 6(2.6%) disagree.

The table revealed further that 17(7.5%) respondents strongly agree that phase II trial tests the effectiveness of the vaccine against the infection/disease, 23(10.1%) agree, 184(80.7%) undecided while 4(1.8%) disagree to this statement. The findings further depicts that 12(5.2%) respondents strongly agree that phase III trial tests the new vaccine against the standard therapy, 25(10.9%) agree, 187(81.7%) were undecided while the remaining 5(2.2%) respondents disagree to this statement.

Few respondents 14(6.1%) strongly agree that in vaccine trials some participants get real vaccine, while some get an inactive substance (Placebo) 23(10.1%) agree, 180 (78.6%) were undecided, 9(3.9%) disagree and 3(1.3%) respondents strongly disagreed with this statement. Result further depicts that 75(32.6%) respondents strongly agree that an HIV vaccine will protect against HIV infection, 74(32.2%) agree, 61(26.5%) were undecided, 15(6.5%) disagree while 5(2.1%) respondents strongly disagree. A total 46(20.1%) respondents strongly agree that HIV vaccine could be used to cure HIV infected people, 31(13.5%) agree, 86(37.6%) were undecided, 44(19.2%) disagree, only 22(9.6%) respondents strongly disagreed with this statement. 19(8.3%) respondents strongly agree that HIV vaccine will alter the participant HIV test result, 36(15.8%) agree, 120(52.6%) were undecided, 30(13.2%) disagree, 23(10.1%) respondents strongly disagreed with the statement. The table further revealed that 11(4.8%) respondents strongly agree that a vaccine could weaken the body's ability to fight HIV infection, 23(10.0%) agree, 113(49.4%) undecided, 41(17.9%) disagree while the remaining 41(17.9%) strongly disagree that a vaccine could weaken the body's ability to fight HIV infection.

Table 2 Knowledge of HIV/AIDS vaccine trial concepts

Item	Strongly Agree Count (%)	Agree Count (%)	Undecided Count (%)	Disagree Count (%)	Strongly Disagree Count (%)	Total Count (%)

Vaccines are used to describe products that are designed to prevent disease.	*127(55.2)*	*72(31.3)*	*27(11.7)*	*2(0.9)*	*2(0.9)*	***230(100)***
Preventive vaccines are given to non infected individuals	*80(37.4)*	*62(27)*	*56(24.4)*	*21(9.1)*	*5(2.2)*	***230(100)***
Therapeutic vaccines are given to infected individuals.	*62(27.1)*	*72(31.4)*	*88(38.4)*	*5(2.2)*	*2(0.9)*	***229(100)***
Vaccine trials occurs in three phases	*9(3.9)*	*19(8.3)*	*197(85.7)*	*3(1.3)*	*2(0.9)*	***230(100)***
Phase 1 trial tests how much of a new vaccine can be given with reasonable safety.	*6(2.6)*	*25(11.4)*	*183(83.2)*	*6(2.7)*		***220(100)***
Phase II trial tests the effectiveness of the vaccine against the infection / disease.	*17(7.5)*	*23(10.1)*	*184(80.7)*	*4(1.8)*		***228(100)***
Phase III trial tests the new vaccine against the standard therapy.	*12(5.2)*	*25(10.9)*	*187(81.7)*	*5(2.2)*	-	***229(100)***
In vaccine trials, some participants will get real vaccine, and some will get an inactive substance (Placebo).	*14(6.1)*	*23(10.04)*	*180(78.6)*	*9(3.9)*	*3(1.3)*	***229(100)***
An HIV vaccine will protect against HIV infection.	*75(32.6)*	*74(32.2)*	*61(26.5)*	*15(6.5)*	*5(2.1)*	***230(100)***
HIV vaccine could be used to cure HIV infected people.	*46(20.1)*	*31(13.5)*	*86(37.6)*	*44(19.2)*	*22(9.6)*	***229(100)***
The HIV vaccine will alter the participant HIV test result.	*19(8.3)*	*36(15.8)*	*120(52.6)*	*30(13.2)*	*23(10.4)*	***228(100)***
A vaccine could weaken the body's ability to fight HIV infection.	*11(4.8)*	*23(10.0)*	*113(49.4)*	*41(17.9)*	*41(17.9)*	***229(100)***

Table 3: Participation in clinical trial research

Table 3 shows the distribution of respondents, 211 (93.4%) respondents have not participated in clinical trial before while 15 (6.6%) have participated. From the responses only four people actually participated in the UCH SAP project which was a clinical trial, Others participated in drug promotions. The table further revealed that 157(68.6%) of the respondents will be willing to participate in HIV vaccine trial research while 72 (31.4 %) of the respondents will not be willing to participate in HIV vaccine trial research

Table 3: Participation in clinical trial research

Previous participation in clinical trial	**Frequency**	**Percentage**
Yes	15	6.6

No	211	93.4
Total	**226**	**100**
Willingness to participate in HIV trial vaccine		
Yes	157	68.6
No	72	31.4
Total	**229**	**100**

Table 4: Ethical issues influencing decision to participate in HIV vaccine trial

Table 4 depicts the importance of some variables in the respondents' decision to participate in HIV vaccine trial research. The respondents perceived as important that the lesser the chance that the vaccine will cause problem 122(53.0%) while 108(47.0%) responded as not important. 152(66.1%) respondents believe that it is important that HIV vaccine research be safe while 78(33.9%) said it is not important. 164(71.3%) respondents believe that it is important that HIV vaccine should be protective while 66(28.7%) felt that it was not important.

The table further revealed that 137(60.1%) respondents believed as important that HIV vaccine strengthens the immune system while 91(39.9 %) stated that it is not important. 149(64.8%) respondents believed that it was important that they are guaranteed that they will be protected from harm during the trial while only 81(35.2%) respondents said it was not important.

The findings also depicts that 124(54.1%) respondents said it was important that they have the ability to withdraw from the trial if they become dissatisfied with the research process while 105(45.9%) believed that it was not important. 98(43.0%) respondents believed as important that earlier vaccine were not 100% effective , 130(57.0%) respondents said it was not important in their decision to participate in vaccine trial. 126(55.5%) respondents believed that it was important that HIV will become preventable through their participation, while 101(44.5%) said it was not important. 166(73.1%) respondents said getting free counseling and HIV tests during the trial was important while 61(26.9%) respondents said it was not important. 70(30.6%) respondents believed as important getting money during the trial while 159(69.4%) respondents said it was not important.171(75.0%) said getting current information about HIV research was important while only 57(25.0%) respondents said it was not important. 177(77.9%) respondents said that getting free medical treatment during the trial will aid their decision, 53(23.0%)said it was not important in their decision to participate in HIV trial vaccine.101(44.5%) respondents believed that it was important to consider the stigma attached to HIV infected individuals before participate in HIV trial vaccine while 126(55.5%) respondents did not support this statement. 123(53.7%) respondents believed as important social and family support if they eventually become infected, 106(46.3%) respondents said it was not important. 179(77.8%) respondents believed that free medical treatment/care if they get infected might aid their decision, while 52(22.2%) said it was not important. 66(28.7%) respondents claimed that they will consider the ability of the vaccine to make them test HIV positive, even if they were not infected while 164(71.3%) respondents believed it was not important.

Table 4: Ethical issues influencing decision to participate in HIV vaccine trial.

Items	Not important (%)	Important Count (%)	Total Count (%)
There is less chance that the vaccine could cause problem.	*108(47.0)*	*122(53.0)*	***230 (100)***

HIV vaccine research is safe.	*78(33.9)*	*152(66.1)*	***230 (100)***
HIV vaccine could be protective.	*66(28.7)*	*164(71.3)*	***230 (100)***
HIV vaccine strengthens the immune system.	*91(39.9)*	*137(60.1)*	***228 (100)***
Guarantee that I will be protected from harm during the trial.	*81(35.2)*	*149(64.8)*	***230 (100)***
Ability to withdraw from the trial, if I become dissatisfied with the research process.	*105(45.9)*	*124(54.1)*	***229 (100)***
Earlier vaccines were not 100% effective.	*130(57.0)*	*98(43.0)*	***228 (100)***
HIV will become preventable through my participation	*101(44.5)*	*126(55.5)*	***227 (100)***
Getting free counseling and HIV tests during the trial.	*61(26.9)*	*166(55.5)*	***227 (100)***
Getting money during the trial.	*159(69.4)*	*70(30.6)*	***229 (100)***
Getting current information about HIV research.	*57(25.0)*	*171(75.0)*	***228 (100)***
Free medical treatment during the trial.	*53(23.6)*	*177(77.0)*	***230 (100)***
The stigma attached to HIV infected individuals.	*126(55.5)*	*101(44.5)*	***227(100)***
Social and family support if I eventually become infected.	*106(46.3)*	*123(53.7)*	***229(100)***
Free medical treatment/ care if I get infected.	*52(22.2)*	*179(77.8)*	***230(100)***
The vaccine could make me test HIV positive, even if I was not infected**.**	*164(71.3)*	*66(28.7)*	***230(100)***

Test of Association

Cross tabulation of some variables with willingness were tested for their association.

Table 5 :Association between socio demographic characteristics of respondents and willingness to participate in HIV trial vaccine.

The association was tested using logistic regression analysis to measure the association between socio- demographic variables and willingness to participate in HIV trial vaccine as shown in Table 5 Sex and occupation were significantly associated with willingness, with male sex (OR 2.06, P = 0.025) more willing than females and students (OR 1.26, P = 0.018) more likely to be willing than other occupational groups.

Table 5: Analysis of each of the socio-demographic characteristics on willingness to participate in HIV vaccine

Variable	**Reference**	**Odds Ratio (OR)**	**95% Confidence Interval (CI)**	**X^2 value**	**P value**
Sex	Male	2.06	1.09 – 3.86	5.06	.0254*
Age					
26– 35years		1.30	0.52 - 3.28		
36– 45years	16– 25years	1.92	0.81 - 4.60	1.13	.3383
46 + years		2.02	0.84 - 4..91		
Education					
Primary	No formal education	2.37	0.79 - 7.08		
Secondary		2.58	0.94 - 7.10	1.35	.2595

Tertiary		2.83	0.99 - 8.09		
Marital status					
Married	Not married	0.98	0.56 – 1.72	0.00	.9529
Religion					
Muslim	Christian	0.99	0.56 – 1.75	0.00	.9745
Occupation					
CSW	Civil Servants	0.34	0.14 - 0.83		
Driving		0.61	0.21 – 1.76	3.04	.0183*
Trading		0.23	0.09 - 0.63		
Student		1.26	0.23 – 6.97		

*** Significant at p<0.05**

Table 6: Association between knowledge of vaccine/vaccine trial and willingness to participate in HIV vaccine trial.

Table 4.3.4 depicts the association between knowledge of vaccine/vaccine trial and willingness to participate in HIV vaccine trial. The table reveals (X^2 = 9.21, P = 0.0030) for knowledge of vaccine and willingness which is significant and (X^2 = 0.15, P = 0.7029) for knowledge of vaccine trial and willingness, this signifies that, a significant association between knowledge of vaccines and willingness to participate in HIV vaccine trial.

Table 6: Cross tabulation knowledge of vaccine/vaccine trial and willingness to participate in HIV vaccine trial

Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	X^2 value	P value
Vaccine	2.10	1.40 – 4.4	9.21	.0030*
Vaccine Trial	0.80	0.30-2.10	0.15	.7029

Table 7:Association between some ethical issues and willingness to participate in HIV trial vaccine

The cross tabulations of some ethical issues and willingness were presented in Table 4.3.5. Significant associations exist between willingness to participate in HIV vaccine trial and most of the variables. There was a significant association between respondents perception of vaccines being safe and willingness to participate in HIV trial vaccine (X^2 = 27.88, P =0.0000). Respondents will be five times more willing to participate in HIV vaccine, when they are sure of the safety of this vaccine trial (OR 5.36).The cross tabulation of ability of vaccine to strengthen the immune system with willingness revealed an association, the association was tested with chi-square test at 5% level of significance, It revealed that the association is significant (X^2 = 22.92, P = 0.0000). This indicates that there is a significant association between ability of the vaccine to strengthen the immune system and willingness to participate in HIV trial vaccine. Respondents

will be four times more willing to participate if they know the ability of the vaccine (OR 4.16). The relationship between protection from harm during the trial and willingness to participate in HIV trial vaccine also revealed an association, (X^2 = 35.89, P = 0.0000, OR 6.54) this depicts that there is a significant relationship between protection from harm during the trial and willingness to participate in HIV trial vaccine. This implies that respondents will be six times more willing to participate in vaccine trial if protection from harm can be guaranteed. Family/social support if infected during the HIV trial vaccine and willingness to participate in HIV trial vaccine was also significant(X^2 = 13.94, P = 0.0002, OR 2.97). Hence, there is significant relationship between family/social support if infected during the trial and willingness to participate in HIV trial vaccine. People will be twice more willing in the presence of family/social support if infected as the family system is highly valued in African culture and safely guided.

The association between provision of incentive and willingness was not significant (X^2 = 0.16, P = 0.6854). This indicates that there is no significant association between provision of monetary incentive and willingness to participate in HIV trial vaccine. However, significant associations exist between other trial benefits and willingness to participate in HIV trial vaccine. Free counseling and HIV test (X^2 = 9.21, P = 0.0027, OR 2.59), current information on HIV during trial (X^2 = 4.78, P = 0.0299, OR 2.00),free medical treatment during trial(X^2 = 11.00, P = 0.0011, OR 2.96) , free medical treatment and care if infected during trial (X^2 = 12.64, P = 0.0005, OR 3.25), These depicts that there are significant associations between trial benefits and willingness to participate in HIV trial vaccine.

Table 7: Cross tabulation of willingness to participate in HIV trial vaccine with some ethical issues

Ethical issues influencing willingness	Reference	Odds Ratio (OR)	95% Confidence Interval (CI)	X^2 value	P value
Safety of vaccine	Important	4.99	2.74 – 9.10	27.88	.0000*
Ability of vaccine to strengthen immune system	Important	6.53	2.31 – 7.49	22.92	.0000*
Guaranteed protection from vaccine	Important	6.54	3.53 – 12.19	35.9	.0000*
Ability to withdraw from trial	Important	3.65	2.02 – 6.59	18.55	.0000*
Efficiency of earlier vaccines	Important	3.39	1.80 – 6.38	14.40	.0002*
HIV becoming preventable	Important	2.83	1.58 – 5.06	12.47	.0005*
Free counseling and testing during trial	Important	2.59	1.40 – 4.81	9.21	.0027*
Getting money as incentive	Important	1.13	0.62 – 2.09	0.16	.6854

Getting current information on HIV	Important	2.00	1.07– 3.74	4.78	.0299*
Free medical treatment during trial	Important	2.96	1.55 – 5.63	11.00	.0011*
Stigma associated with HIV	Not Important	1.29	0.73 – 2.26	0.78	.3785
Social & family support if infected	Important	2.97	1.67 – 5.28	13.94	.0002*
Free medical care if infected	Important	3.25	1.69 –6.25	12.69	.0005*
Testing false positive due to participation	Not Important	2.35	1.19 – 4.65	6.12	.0141*

*** Significant at p<0.05**

DISCUSSIONS

Socio - demographic characteristics of the respondents

The sociodemographic characteristics of the respondents in this study points to the fact that majority of the respondents are females both at FGD and survey. The highest numbers of respondents were between ages 26- 35years at survey but at FGD majority were between 36 – 45 years. The mean age was 33 years. Majority of the respondents had some level of formal education, at survey secondary level and at FGD secondary level of education. This may not be unusual for communities in southwest, Nigeria or Oyo state where free education has been in existence since 1955. The information on marital status revealed that majority of the respondents was married both at survey and FGD. The rate of divorce was not high among the studied population. Majority of the respondents were self employed/ artisans but it is worthy to note that unemployment rate was high.

Knowledge of HIV/Vaccine trial concepts

Knowledge of HIV/AIDS was high among study population. This was also evident during the focus group discussions as most of the respondents' defined HIV infection, while the major source of information was electronic/print media. Majority of the respondents perceived themselves at risk of HIV infection and were aware of their HIV status and had their blood tested for HIV. However, a percentage still claimed not to be at risk of HIV and have not blood test for HIV. These corroborated Otuonye et al (2011) findings on the preparedness of adolescents' to participate in HIV vaccine clinical trial in Nigeria. Of the 291 respondents 73.5% had knowledge of HIV vaccine, and have no perceived risk of HIV vaccine infection (66.2%). Few respondents (31.3%) know their HIV status.

An important key finding in this study is the level of knowledge of vaccine trial concepts. Most respondents have heard about vaccines but not vaccine trials. Most respondents do not know the benefits and risks associated with vaccine trial. Also, only a few are aware of HIV vaccine trial, this may be due to the fact that none is presently going on in Nigeria. The respondents were not familiar with the types of vaccines and phases of vaccine trial, though a few claimed to have participated in clinical trial. Even the few that claimed to have participated in clinical trial were not well informed about clinical trial concepts. This is supported by findings from the FGDs and surprisingly by the key informant interviews conducted among health professionals.

The cross tabulation of knowledge of vaccine/HIV vaccine trial revealed an association between knowledge of vaccine and willingness but not HIV vaccine trial. This study identified a wide knowledge gap among the study population; this contradicts the findings from a South African study by Smit et al (2011) that identified increasing knowledge about vaccines generally and HIV vaccines specifically. This contradiction may be due to the fact that different clinical trials are going on in South Africa. There is the need for aggressive educational campaign on vaccine trials concepts so that participants will be able to make informed decisions before participation in future clinical trial.

Ethical issues influencing willingness to participate in HIV vaccine trial

Some variables were strongly associated with willingness to participate in HIV vaccine trial. These include safety of vaccine, protection from harm during trial, ability to withdraw from trial, social and family support if infected, assurance that vaccine will strengthen their immune system against AIDS, efficiency of earlier vaccines, free counseling and testing, provision of free treatment if infected, self perception of risk for HIV, clients' being HIV positive and respondents' believing that their participation in the trial will make HIV become preventable. Of importance is the respondents' ability to withdraw from the trial if they become dissatisfied with the research process, and the availability of some incentives. It is worthy to also note that there was a significant association between knowledge of vaccines (not vaccine trial concepts) and willingness to participate in HIV vaccine trial. Willingness was observed among the male sex than females and also among civil servants than other occupational groups.

An analysis of these factors influencing willingness to participate raises some important ethical concerns as bioethicist. What are the ethical issues concerning the HIV vaccine trial and how can we deal with these issues raised by the research respondents? Answering these questions necessitate the application of the ethical principles. The Belmont Report identified three principles that are relevant to research involving human subjects. These three basic principles, among those generally and are particularly relevant to the ethics of research involving human participants are the principles of respect for persons, beneficence and justice.

Respect for persons incorporates at least two ethical convictions; first, that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection. The principle of respect for autonomy promotes the idea that every person is free, independent and has the right to make their own decisions. The principle of respect for autonomy requires researchers to recognize the freedom of individuals to decide if they want to take part in a research study. It also stipulates protections for individuals with reduced autonomy. The deficient in the knowledge level of vaccine trials concepts and increased willingness by the respondents raises the issue of more vulnerability to exploitation, and the need to protect their right to adequate information before participation in the trial. Also, majority of the respondents want their right to be able to withdraw from the trial, if they become dissatisfied during the trial protected. This is also line with this principle of respecting participants' autonomy.

The principle of beneficence states the necessity of maximizing the benefits and minimizing the harms of research. The research participants stated that the will be five times more willing if they are sure of the safety of the vaccine, the guarantee that the vaccine will strength the immune system and they will be protected from harm. Participation in HIV vaccine trial exposes both the participants and the host community to some level of risks. Physiological risks for individual participants include the chance of developing rapidly progressing or established infection if a vaccine is subsequently exposed to HIV, serious infection if a participant has undetected HIV infection and is vaccinated, injuries due to research-related activities, as well as repeated injections

and associated pain or malaise. Psychosocial risks for individual participants includes: attendant discrimination of individuals perceived to be at high risk of HIV infection, vaccine-induced seropositivity on conventional screening methods and associated negative consequences such as the potential for discrimination in employment, health care and also stress may result between partners in a relationship as a result of the participation of one partner in a trial. Stigma and discrimination that may result if participation becomes publicly known, and they are perceived to be HIV-infected or at high risk of HIV infection. Risks to the community from which participants are drawn include stigma that may attach to them from the manner in which they are portrayed in the press and scholarly journals, and stigma attached to participating communities that may be identified as high risk. The benefits of HIV vaccine trial as expressed by the respondents are free counseling and testing during the trial, current information on HIV, free medical treatment during the trial and medical care if infected. Researchers must act in ways that promote the welfare of research trial participants and others who may benefit in the future from the research. A balance must be struck between any potential benefits of participating in research and any potential risks. There was no association between willingness to participate and getting money during trial, stigma and knowledge of HIV status .This corroborates findings from other studies on willingness such as Heather et al (2006) in Capetown, Jenkins et al (1995) ,Celentano et al (1995) in Northern Thailand, and Newman et al (2006) in Los Angeles. Though there was no association between willingness and monetary incentive; participants should be adequately compensated for travel, time and inconvenience relating to trial participation.

Justice describes who ought to receive the benefits of research and bear its burdens. Willingness among the male sex was five times more than females and three times among civil servants than other occupational groups. In the fairness of distribution, since women and other occupational groups other than civil servants will benefit from the vaccine, they should be part of the trial.

What all these imply is that the world is patiently waiting and eager to find a lasting solution to the HIV epidemics through an ideal vaccine to prevent and treat those already infected. This places a lot of responsibility on clinical researchers to ensure safety and protection for research participants during clinical trials in order not to betray public trust. Researchers' should carry out clinical trials responsibly as dictated in our ethical guidelines for responsible conduct of research. National and local ethical review boards should put in place additional regulatory measures to protect research participants.

Willingness to participate in HIV vaccine trial

Willingness was slightly more than average among studied population at survey but not at FGD. The hypothesis tested on the relationship between socio demographic characteristics of respondents and willingness to participate in HIV trial vaccine revealed significant associations between sex, occupation and willingness. The male sex was more willing than the female, and students were more willing than other occupational groups. No significant association between age, education, marital status and willingness occurred. Though from the observed frequencies, increased willingness were revealed among the older age group (46+ years) and respondents' exposure to tertiary level of education. This is line with Smits et al (2011) findings in a peri-urban South African community that willingness was associated with increasing age and male gender. Heather et al (2006) also identified that increasing age was associated with age. The hypotheses tested on the association between risk perception, knowledge of HIV status and willingness to participate in HIV trial vaccine revealed that there is significant association between risk perception and willingness to participate in HIV trial vaccine this implies that there is a significant association

between knowledge of HIV status and willingness to participate in HIV trial vaccine. This can be explained using the health belief model which stated the link between perceived susceptibility and likelihood of adopting an action. This implies that those that perceived themselves as being at risk of HIV are likely to have blood tested for HIV and will be more willing to participate in HIV vaccine trial. This is supported by the fact that they were already diagnosed. This point to the need to create more awareness on individual susceptibility to HIV infection.

Study Limitation

As with all studies, this study has its limitations. First, the study was designed to examine willingness to participate in HIV vaccine trial in Ibadan. The study faces the limitation of generalizing the result as the views of the people in Oyo State or Nigerian populace. Secondly, most of the data were obtained through participants' self report and some might have been unintentionally biased in some of their responses especially during the FGDs. Despite these constraints in the study, the researcher believes that these results are still valuable contributions to the literature on willingness to participate in HIV vaccine trial in Nigeria.

SUMMARY AND CONCLUSIONS

This study sought to assess the ethical issues influencing willingness of selected risk populations to participate in HIV vaccine trial. It was found that knowledge of vaccine trial concepts was poor among the studied population. Willingness to participate in HIV vaccine trial was above average.

The sociodemographic variables associated with willingness were sex and occupation. The predicting variables of willingness were also identified. These included safety of vaccine, protection from harm during trial, ability to withdraw from trial, social and family support if infected, assurance that vaccine will strengthen their immune system against AIDS, efficiency of earlier vaccines, free counseling and testing, provision of free treatment if infected, self perception of risk for HIV, client's being HIV positive and respondent's believe that their participation in the trial will make HIV become preventable. There was no association between willingness to participate and getting money during trial, as well as stigma or knowledge of HIV status.

Conclusion

In conclusion, the result generated from the data in this study is expected to contribute to the growing body of literature on ethical issues influencing willingness to participate in HIV vaccine. Deficiencies in knowledge identified and the high level of willingness to participate in vaccine trial by the study population will make them more vulnerable and point to the potential value of preparatory work before introduction of HIV vaccine in Nigeria.

Recommendations

Based on the findings of this study, the following recommendations are made towards future HIV vaccine trials.

- The National and Local Ethics Review Boards should put in place additional regulatory mechanism to protect research participants especially the at risk populations.
- The educational component of providing full relevant information relating to the trial in a language understandable to the participants before consent is given should be strictly observed. Opportunity must be given to ask questions and receive answers throughout the research process.
- All participants must be linked up with an existing facility to receive treatment and support services throughout the period of the trial. For those that are infected, they should be given access to treatment during and after trial at no cost the participants.

- Sponsors and investigators must ensure that treatment and care for HIV infection is provided to participants who become HIV-infected during the course of an HIV vaccine trial. Sponsors and investigators should provide, or ensure access to, high-quality treatment and care for participants who become infected during the course of an HIV preventive vaccine trial, including ART.
- Reducing the risk of HIV infection among participants is an essential ethical component of HIV vaccine trial. This is especially critical given that phase III efficacy trials rest on some exposure to HIV infection. In order to manage the perceived conflict of interest between risk reduction and scientific goals of the research, and to promote the welfare of participating individuals, investigators are morally compelled to provide optimal risk-reduction measures to participants.

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