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Pediatric HIV Type 1 Vaccine Trial Acceptability among Mothers in Kenya

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Abstract

Vaccination of infants against human immunodeficiency virus type 1 (HIV-1) may prevent mother-to-child HIV-1 transmission. Successful trials and immunization efforts will depend on the willingness of individuals to participate in pediatric vaccine research and acceptance of infant HIV-1 vaccines. In a cross-sectional study, pregnant women presenting to a Nairobi antenatal clinic for routine care were interviewed regarding their attitudes toward participation in research studies and HIV-1 vaccine acceptability for their infants. Among 805 women, 782 (97%) reported they would vaccinate their infant against HIV-1 and 729 (91%) reported willingness to enroll their infant in a research study. However, only 644 (80%) would enroll their infants if HIV-1 testing was required every 3 months and 513 (64%) would agree to HIV-1 vaccine trial participation. Reasons for not wanting to enroll in a pediatric HIV-1 vaccine trial included concerns about side effects (75%), partner objection (34%), and fear of discrimination (10%), HIV-1 acquisition (8%), or false-positive HIV-1 results (5%). The strongest correlate of pediatric vaccine trial participation was maternal willingness to be a vaccine trial participant herself; in univariate and multivariate models this was associated with a 17-fold increased likelihood of participation (HR 17.1; 95% CI 11.7–25; $p < 0.001$). We conclude from these results that immunizing infants against HIV-1 and participation in pediatric vaccine trials are generally acceptable to women at high risk for HIV-1 infection. It will be important to address barriers identified in this study and to include male partners when mobilizing communities for pediatric HIV-1 vaccine trials and immunization programs.

INTRODUCTION

Children In Sub-Saharan Africa and other regions with generalized human immunodeficiency virus type 1 (HIV-1) epidemics are at risk for acquiring HIV-1 through mother-to-child transmission.[1] Vaccination of infants against HIV-1 may be one way to reduce HIV-1 acquisition or attenuate disease progression among children during the first years of life.[2–5] The success of pediatric vaccine research and future HIV-1 immunization programs that target infants will depend in part on the willingness of parents to have their child participate in a clinical study and on parental acceptance of infant HIV-1 vaccines.

To our knowledge, no studies have examined attitudes toward infant vaccination against HIV-1. However, parental perceptions have been shown to be important predictors of uptake

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of infant immunizations against other common childhood illnesses. [6–9] Parents' beliefs in the protective value and safety of vaccination significantly influence having an up-to-date immunization record for their child,[6,8] while insufficient information has been cited as an important reason for not accepting newer vaccines.[6] HIV-1 vaccine acceptability studies among adults also contribute to our understanding of what may influence parents' decisions to accept HIV-1 immunization for their child once a vaccine is developed.[10–16] Several studies have found that health beliefs, such as low perceived susceptibility to HIV-1 and concerns about safety and efficacy, impact adult HIV-1 vaccine acceptance.

Additional data come from studies evaluating how willing parents would be to vaccinate adolescents and preadolescents against HIV-1 and other sexually transmitted infections (STI). Such studies have focused on sexual rather than vertical HIV-1 transmission risk and were carried out in the United States where the HIV-1 epidemic has been concentrated in high-risk groups, unlike in sub-Saharan Africa.[17–23] Not surprisingly, acceptance of HIV or STI vaccines was not universal with negative responses being associated with parents' perceiving their child to be at low risk for HIV or STI, and positive responses being associated with vaccine efficacy, severity of the disease, and the absence of behavioral interventions to prevent specific infections.[18,20]

The goals of the current study were to define parental attitudes towards HIV-1 vaccines for infants and to determine willingness of parents to participate in pediatric HIV-1 research and vaccine trials. This is the first study to address HIV/AIDS vaccine acceptability among pregnant women and to work towards pediatric HIV-1 vaccine preparedness in an African setting within a population with high rates of vertical HIV-1 transmission. Such preparedness is essential if pediatric vaccines are to be developed, studied, promoted, and utilized in sub-Saharan Africa and other parts of the world where pediatric HIV-1 infection contributes disproportionately to childhood morbidity and mortality.

MATERIALS AND METHODS

Enrollment and follow-up visits

This study was nested in a cohort study evaluating the suitability of pregnant and postpartum women for participation in HIV-1 prevention trials. Pregnant women attending a public antenatal clinic in Nairobi, Kenya provided written informed consent for study participation and were interviewed with a questionnaire by a study nurse or physician in Swahili or English, depending on the participant's language preference. Those women agreeing to HIV-1 voluntary counseling and testing (VCT) were tested using parallel rapid HIV-1 enzyme-linked immunosorbent assays (ELISA) and asked to return 2 weeks after enrollment for additional HIV-1 prevention counseling. Questions regarding attitudes and acceptability of pediatric research participation and immunization against HIV-1 were asked only at the enrollment visit prior to HIV-1 testing.

Statistical analysis

Independent t tests and Chi-squared tests were used to define associations between maternal factors and expressed willingness to participate in pediatric research or vaccinate their child against HIV-1 with a vaccine when available. Those factors that were statistically significant in univariate analyses ($p \leq 0.05$) were included in a multivariate logistic regression model. If two or more factors were highly collinear, only one was incorporated into the final model.

RESULTS

Cohort characteristics

From December 2003 to April 2004, 805 pregnant women presenting to the antenatal clinic were enrolled into the study after providing written informed consent (Table 1). Among these, the median age was 23 years [interquartile range (IQR) 20–27] and 716 (79%) women were married, with 30 months (IQR 14–60) as the median duration of their current relationship. On average, the women had a history of two lifetime sexual partners (IQR 1–3) and two pregnancies (IQR 1–3) when including the current pregnancy (Table 1). Only 139 (17%) perceived themselves to be at risk for HIV-1 acquisition during the last 1 year. Five hundred eighty-five (72%) women accepted HIV-1 testing and 97 (17%) of these were HIV-1 seropositive.

Attitudes toward pediatric research and childhood immunization against HIV-1

Among the 805 women enrolled in the study, 782 (97%) responded that they would be willing to have their child vaccinated against HIV-1 if a safe, effective vaccine were available and 729 (91%) were willing to have their child participate in a research study. Of the 794 women with a regular sexual partner, 601 (76%) responded that study participation would require approval from their spouse or partner (Table 2). Overall, 488 (62%) believed their partner would support participation in pediatric research and 251 (32%) did not know how their partner would respond.

A lower proportion of these women was willing to have their child participate in a study requiring frequent HIV-1 testing or in a trial involving immunization of their child with an investigational HIV-1 vaccine (Table 2). Overall, 644 (80%) responded positively to research participation when study participation included HIV-1 testing every 3 months and 513 (64%) responded they would be willing to enroll their child in an HIV-1 vaccine trial. The majority of women did not provide an explanation for their unwillingness to participate in a research study that included HIV-1 testing every 3 months (Table 3). For the subset who did respond, reasons identified included time constraints [8 (8%)] and concerns about partner objections to study participation [7 (7%)]. Among the 240 women who did not want their child in an HIV-1 vaccine trial, 175 (79%) were concerned about side effects, 82 (34%) indicated that their partner would object to participation, 24 (10%) were concerned about discrimination, and 18 (8%) feared HIV-1 acquisition as a result of immunization (Table 3).

Correlates of willingness to participate in HIV-1 vaccine trials

Women stating that they were willing to be participants in HIV-1 research were more likely to respond that they would allow their child to be enrolled in a pediatric study or HIV-1 vaccine trial (Table 4). For HIV-1 vaccine trials, women who would participate were 17-fold more likely to report willingness to have their child participate in an HIV-1 vaccine trial [odds ratio (OR) 17.2, 95% confidence interval (CI) 11.9–24.7, $p < 0.001$]. Additional correlates of participation in vaccine trials included younger age ($p = 0.002$), fewer years of formal education ($p = 0.004$), and earlier sexual debut ($p = 0.003$) (Table 4). Women who tested HIV-1 seropositive after the interview and those perceiving themselves at higher risk for HIV-1 acquisition were not more likely to agree to participation than women who were HIV-1 seronegative ($p = 0.4$ for both).

Using a multivariate model to assess those correlates that were significantly associated in univariate analysis, we found a persistent association between the woman's willingness to be a participant in an HIV-1 vaccine study and her interest in having her child participate ($p < 0.001$) (footnote to Table 4). Younger age was also found to be associated with willingness to enroll in a pediatric vaccine study ($p = 0.01$) (footnote to Table 4).

DISCUSSION

Overall, we found that the majority of pregnant women in this Nairobi-based study were willing to participate in research (>90%) and were receptive to having their child immunized with a safe and effective HIV-1 vaccine (>95%). A lower proportion of women was willing to have their child participate in studies requiring frequent blood draws for HIV-1 testing or in an HIV-1 vaccine trial (80% and 64%, respectively). The most frequently cited reason for not wanting to participate in a vaccine trial was fear of side effects, mentioned by approximately 80% of women. Other barriers included concerns about their male partner's response, stigmatization, and fear of HIV-1 acquisition. Prior to initiating recruitment for pediatric vaccine studies, it will be important to address these specific concerns within the community through education and outreach efforts.

Our findings also suggest that special recruitment strategies may be required for pediatric HIV-1 vaccine studies. Thirty-four percent of women refusing to participate in a pediatric vaccine trial believed that their male partner would object and reported this as a primary reason. In addition, 76% of 750 women responding that they would participate in a research study believed they would need the prior approval of their spouse or partner. Approximately two-thirds of these women believed that their spouse would be in favor and the remaining one-third was uncertain of his response. As male partners were not interviewed in this study we were unable to assess their perspective. Additional studies exploring male attitudes toward participation in vaccine trials will be important to help clarify this. It will also be necessary to target men when launching community out-reach and educational programs directed at potential pediatric research participants. Using couple counseling to identify parents who are willing to participate in vaccine trials is another strategy that may work well. Couple counseling in the antenatal setting has been associated with increased uptake of interventions to prevent vertical as well as heterosexual transmission and may enhance recruitment and retention in clinical trials for HIV-1 vaccines.[24]

The most significant correlate for participation in pediatric studies was the woman's willingness to be enrolled in research herself. This suggests that discussing pediatric study participation from the perspective of the parents may contribute to successful mobilization. In addition, identifying those parents willing to participate in research may be a useful strategy for recruitment into pediatric vaccine studies. Other correlates of participation in HIV-1 and vaccine studies were younger age and fewer years of education. One explanation for this is that younger, less educated individuals believe themselves to be at higher risk for HIV-1 acquisition and therefore their perception of the risk–benefit ratio is more favorable.

This cross-sectional study of pediatric vaccine acceptability and willingness to participate in vaccine research has its limitations. As noted earlier, men were not interviewed as part of this study and attitudes of male partners are likely to be important determinants of a woman's willingness and ability to enroll her child in a vaccine study. In addition, participants were interviewed before learning their HIV-1 status, making it difficult to know whether women who knew they were HIV-1 seropositive and at risk for vertical HIV-1 transmission would have responded differently. It is possible they would have been more receptive toward participation in HIV-1 vaccine trials and infant vaccination against HIV-1. Finally, our study could not address whether behavior will change for women participating in pediatric HIV-1 vaccine trials. Specifically, will women choose to breastfeed over formula feed if their child participates in an HIV-1 vaccine trial, thus increasing risky behavior because they perceive a protective benefit from having their child vaccinated with a candidate vaccine? This concern has come up in HIV-1 vaccine studies among adults and will need to be further examined in mother–infant prevention studies.

In conclusion, as vaccine research continues, feasibility studies such as this one will help prepare for future pediatric vaccine studies in sub-Saharan Africa. Pediatric HIV-1 vaccine trials pose unique scientific, ethical, and logistical challenges,[2] making it important to educate communities most affected by HIV-1 and to address specific concerns well before introducing an HIV-1 vaccine. Evaluating parental attitudes toward participation in research and particularly in vaccine trials may help to shape these educational efforts and may guide trial design and community preparation. Furthermore, while immunization campaigns against childhood illnesses have been successful in Kenya and other developing countries, there is no guarantee that availability of an HIV-1 vaccine will lead to widespread public acceptance. Many factors are likely to contribute and effectiveness of HIV vaccine programs will ultimately depend on the availability and willingness of individuals to accept vaccination.

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Table 1

Sociodemographic Characteristics of Cohort

Characteristic	Median (IQR) [a] or number (%)
Age (years)	23 (20–27)
Education duration (years)	8 (7–11)
Married	716 (89%)
Employed or self-employed	281 (35%)
Rooms in house	1 (1–1)
Monthly rent (U.S. dollars)	21 (13–27)
Number of pregnancies	2 (1–3)
Age at sexual debut (years)	17 (16–19)
History of a sexually transmitted infection	65 (8%)
Number of lifetime sexually partners	2 (1–3)
Duration of relationship with current partner (months)	30 (14–60)
Perceives self to be at risk for HIV acquisition during last 1 year	139 (17%)
HIV-1 seropositive[b]	97 (17%)

[a] IQR, interquartile range.

[b] Data available for 585 (72%) of participants.

Table 2

Attitudes of 805 Pregnant Women in Nairobi Toward Participation in Pediatric Research Studies and HIV Vaccination for Their Child

	Number of women (%)		
	Yes	**No**	**Undecided**
Would allow infant to participate in a research study	729 (91%)	34 (4%)	42 (5%)
Permission from male partner would be required[a]	601 (76%)	177 (22%)	16 (2%)
Believe male partner would support study participation[a]	488 (62%)	50 (6%)	251 (32%)
Would allow infant to participate in study requiring HIV-1 testing of infant approximately every 3 months	644 (80%)	99 (12%)	58 (7%)
Would allow infant to participate in study requiring immunization of infant with HIV-1 vaccine	513 (64%)	240 (30%)	52 (6%)
Would be willing to have infant vaccinated with safe, effective HIV-1 vaccine outside the research setting	782 (97%)	8 (1%)	14 (2%)

[a]Only women with current partners were included in denominator, N = 794.

Table 3

Reasons for Not Wanting to Participate in Pediatric HIV-1 Research or an HIV-1 Vaccine Trial or Receive an Immunization Against HIV-1

Reason	Number (%)[a]
Not willing to have child participate in research with HIV-1 testing[b]	*N* = 99
Cannot spare the time	8 (8%)
Partner would object	7 (7%)
Does not want child in a study	6 (6%)
Not willing to have child participate in HIV-1 vaccine trial	*N* = 240
Concerns about side effects	179 (75%)
Partner would object	82 (34%)
Fear of discrimination	24 (10%)
Fear HIV-1 acquisition 2° vaccine	18 (8%)
Fear of false HIV-1 results	12 (5%)

[a] Sum of responses may exceed 100% because women may have provided more than one response.

[b] The majority of women were not able to provide a specific reason for why they were unwilling.

Table 4

Correlates of Willingness to Participate in a Pediatric HIV-1 Vaccine Trial[a]

	Willing to enroll child in HIV-1 vaccine trial		
	Yes	**No**	
	Median (IQR)		***p* value**
Maternal characteristics and attitudes			
Age (years)	23 (20–26)	24 (21–24)	0.002
Education completed (years)	8 (7–10)	8 (8–12)	0.004 [b]
Age at sexual debut (years)	17 (16–19)	18 (16–20)	0.003
Number of pregnancies	2 (1–3)	2 (1–3)	0.07
Lifetime sexual partners	2 (1–3)	2 (1–3)	0.15
Duration of current relationship (months)	29 (12–16)	36 (17–64)	0.30
	Number (%)		**Odds ratio (95% confidence interval); *p* value**
Perceives self at risk for HIV-1	92 (19%)	47 (16%)	1.2 [0.8–1.7]; 0.40
HIV-1-seropositive status	67 (18%)	30 (15%)	1.2 [0.8–2.0]; 0.39
Willing to be a participant in HIV-1 research	448 (88%)	210 (71%)	2.8 [2.0–4.1]; <0.001
Willing to be a participant in adult HIV-1 vaccine trial	447 (88%)	85 (29%)	17.2 [11.9–24.7]; <0.001
Willing to receive an adult HIV-1 vaccine	502 (98%)	274 (94%)	3.5 [1.6–7.6]; 0.001

[a] In a multivariate model including age (years), education completed (years), age at sexual debut (years), and maternal willingness to be a participant in an HIV-1 vaccine trial, age was inversely correlated (OR 0.95; 95% CI 0.91–0.98; $p = 0.01$) and the woman's willingness to be a participant in a vaccine trial was positively correlated (HR 17.1; 95% CI 11.7–25; $p < 0.01$).

[b] Statistical analysis used the independent *t* test to compare mean duration, which was 8.5 years for those willing versus 9 years for those not willing to participate.