

Yellow Fever Vaccine Safety Perception of Pregnant Women in Emergency Response Mass Vaccination in Uganda

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Abstract. Yellow fever vaccine, a live attenuated vaccine, is primarily administered to pregnant women during outbreaks. A qualitative study was conducted in pregnant women on the perception of yellow fever mass vaccination. In total, interviews with 20 women—13 semi-structured interviews and one focus group discussion with seven participants—were analyzed. This study showed that conflicting information about vaccine safety led to concern about miscarriage. Furthermore, it was believed that vaccination during gestation would concurrently immunize the fetus by transplacental antibody transfer. Consultation of health workers at the vaccination site led to diverse recommendations. When vaccinating pregnant women, clear health communication is crucial. Vaccine recommendations should be obeyed, and health workers should be trained to address emerging vaccine concerns. Pregnant women should be informed that a booster dose is recommended to achieve lifelong immunity. After pregnancy, a booster should be offered to women in endemic areas.

Yellow fever (YF) is a mosquito-borne viral hemorrhagic fever endemic in tropical regions in sub-Saharan Africa and South America.¹ More than 90% of 200,000 annually estimated cases occur in Africa.² An infection with YF virus causes significant morbidity and mortality.¹ In contrast to other arbovirus infections, there are no data if YF is more severe during pregnancy than in general adult population.³ Reports of vertical YF transmission are scarce.⁴ Yellow fever is preventable by a live attenuated vaccine, which is classically contraindicated during pregnancy because of concerns of harming the fetus.⁵ However, studies have shown that the outcomes of pregnancy and childbirth are similar to those in general population when vaccinated during gestation.^{6,7} Therefore, according to the WHO guidelines, pregnant women can be vaccinated when the risk for YF virus exposure outweighs the vaccination risk (i.e., during epidemics or when travels to endemic areas are unavoidable).⁸ In Uganda, YF is endemic with numerous reported outbreaks. In contrast to other African countries, YF vaccination is not part of routine immunization in Uganda. The vaccine is costly, and for numerous Ugandans, it is only accessible and free of charge during mass vaccination,⁹ for instance, during the reactive emergency mass vaccination in northern Uganda in 2010¹⁰ and in central and southwestern Uganda in 2016.⁹ To assist future vaccination campaigns, we investigated the perception of pregnant women toward YF emergency response mass vaccination.

This study was part of a larger qualitative research on local perception and socio-environmental factors of YF in Uganda. The field study was carried out from August to December 2017. We conducted semi-structured interviews, key informant interviews, and focus group discussions (FGDs). In total, 76 vaccine recipients, public health officers, and health workers of six districts that were affected during two recent YF outbreaks (2010 and 2016) participated. However, in this study, we focused on the perception of 20 pregnant women during the 2016 outbreak and analyzed 13 semi-structured

interviews and one focus group discussion with seven women. Interview participants (Table 1) were purposively selected from communities which experienced YF mass vaccination in 2016. Participants needed to be older than 18 years and pregnant when vaccinated. Locally trained field assistants and village health teams helped with recruitment. To verify the gestational age at the time of YF vaccination, we double-checked the date on the vaccination card with the stated gestational age and the child's current age. Semi-structured interviews and FGDs were conducted in local Bantu languages Luganda and Rukiga. Data were collected until saturation. Six key informants (district health officers, surveillance focal persons, environmental health officer, and health worker) provided in-depth knowledge of the outbreak on the district level. Interviews were audio-taped, translated, and transcribed. Data were coded and analyzed with ATLAS.ti software. Ethical approval was obtained from the Medical University of Vienna (EK 1284/2017), Mildmay Uganda Research Ethics Committee (#REC REF 0504-2017), and the National Council for Science and Technology (SS4362) in Uganda. All participants granted informed consent.

The Ministry of Health informed affected districts on the YF epidemic and called for mass vaccination. The district health officers executed the campaign on the district level. Districts used various means of health communication such as posters, radio, television, itinerant megaphones, as well as through local chairmen, health workers, and religious leaders. Thereby, different information could reach communities. The public were educated about symptoms of YF, were advised to sleep under mosquito nets, and were informed of an imminent governmental mass vaccination. Immunization was not mandatory; 70% (14 of 20) of interviewed women decided to get vaccinated while pregnant because they perceived YF as a deadly disease that killed rapidly. In addition, 55% (11 of 20) of women believed in vertical transmission of wildtype YF infection. Among those women, 35% stated transplacental transmission and 20% believed in airborne transmission postpartum through close contact. In the FGD, 42% stated that if vaccinated during gestation, then the fetus would be immunized concurrently. Women stated that according to information received by health workers vaccination near term

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TABLE 1
Demographics of pregnant women

Pregnant women (n = 20)	
Age	Median age, 28 (range = 21–37) years
Parity	Median parity, 3.2 (range = 1–6) children
Occupation	35% small business, 30% farmer, 25% housewife, and 10% teacher
Education level	65% > primary level of schooling (range = primary school–higher education)
Time of yellow fever vaccination	First trimester (30%), second trimester (35%), or third trimester (35%)
District and subcounty	Masaka (Kyanamukaaka, Kyesiga, Masaka municipality, and Buwunga) Kalangala (Bujjumba and Mugoye) Rukungiri (Kebisoni, Bwambara, and Buyanja)

would protect newborns. Therefore, women stated to have gotten vaccinated as a preventive measure for themselves and the fetus. Free access to an expensive vaccine and obtaining a YF certificate for traveling had a positive impact on vaccination-seeking behavior. It was believed that without vaccination YF could be easily contracted, which would require expensive hospital treatment. One woman thought that without a certificate people would not be treated in hospital, whereas another woman indicated that children would not be able to attend school. All women stated to have no precise knowledge of the vaccine, and protective duration varied. Nevertheless, immunization was considered as beneficial. Women indicated that children older than 6 months and adults should be vaccinated.

Vaccination criteria for pregnant women were contradictory within districts. According to some health officials, all pregnant women were excluded from mass vaccination, whereas others claimed that everyone got vaccinated. Particularly, information regarding vaccination at the first trimester or third trimester was controversial; 35% (7 of 20) of women consulted health workers at the vaccination site. The women stated that health workers did not mention abortion as a risk of YF vaccination. Interviewed women indicated that health workers did not discourage them, but they observed how health workers advised other pregnant women against immunization (Table 2). Conflicting recommendations on vaccine safety in pregnancy augmented allegations that the vaccine was contraindicated and could cause abortion. Women stated four contributing factors concerning miscarriage after immunization (Figure 1). 1) The vaccine itself could be harmful: It was believed that the fetus receives the vaccine concurrently through a shared umbilical cord. However, the vaccine dose was perceived as too strong and harmful for the fetus. As prevention, one woman demanded a weaker vaccine during gestation. In addition, the vaccine was believed to cause abortion by preventing labor. 2) To have been vaccinated by mistake: Women stated that they felt guilty for unintentionally putting their offspring at risk after hearing conflicting information about the vaccine safety during gestation. 3) To fall ill after immunization: Experiencing symptoms of fever, weakness, and pain augmented concerns. 4) To know someone who miscarried: Solely, one woman's friend miscarried after immunization in her second trimester.

Overall, 65% (13 of 20) of women were concerned about miscarriage. However, five of them indicated they would bear possible consequences of abortion as long as they are protected of YF. Worries diminished when time passed without miscarrying. Nevertheless, concerns about the fetus proceeded. In the end, 80% (16 of 20) of women delivered healthy

children. Four newborns showed either signs of icterus, fever, umbilical hernia, or skin rash. Affected women attributed icterus and fever in newborns to the vaccine without consulting health workers. However, 20% (4 of 20) of women indicated to have never taken rumors about abortion seriously because they heard them from community members and not health workers.

Our study showed that unclear information led to incorrect perception of YF vaccination. Health officials were unaware of the WHO recommendation that pregnant women can be vaccinated against YF during outbreaks.⁸ Inconsistent vaccination criteria and information within the district amplified rumors of miscarriage. Women received diverse advice from health workers at vaccination posts. As a result, women were anxious and confused after immunization. Previous studies showed that health workers are the greatest influential source of information.¹¹ Health workers should be trained according to guidelines and be able to address vaccine concerns accurately. Ethical guidance on immunization and implementation of vaccines in pregnant women should be considered.^{12,13} Women assumed to be protected from YF after vaccination. However, previous studies showed a varying proportion of developed antibodies during pregnancy with a lower seroconversion rate later in gestation.^{14,15} The WHO recommends a booster dose for all women who were vaccinated during pregnancy.¹⁶ Affected women and district health officers were unaware of this recommendation, and there was no strategy in place to offer boosters after pregnancy. This lack of information could prevent women from receiving another vaccine dose in future campaigns. According to the WHO, in concurrent outbreaks in Angola and the DRC, fractional vaccine doses were administered to counteract insufficient stockpiles, whereas pregnant women received whole doses, but no boosters.¹⁷ Our study showed that pregnant women believed their fetus was immunized by transplacental antibody transfer. Health workers augmented this belief. Studies showed that maternal immunization, an antibody transfer via placenta and breast milk, protects newborns for a short period.¹⁸ However, there are no data on the efficiency of transplacental antibody transfer after YF immunization and its duration in infants.¹⁹ The perception of long-lasting immunity in offspring may lead women to not vaccinate their child in a future YF campaign. The risk of encephalitis in newborns by the transmission of a live attenuated vaccine strain via breast milk, which has been reported in case studies,²⁰ should be considered when offering boosters. Demographics had no impact on the perception of mass vaccination. A strength of this study is that we conducted interviews at three different outbreak sites with diverse mass vaccination campaigns. However, qualitative

TABLE 2
A selected excerpt of pregnant women's knowledge and perception on reactive emergency yellow fever immunization

Yellow fever	They told us that this disease (YF) has come to the area. It kills people and once you get it you have to die. So, I was forced to take the vaccination, because I feared to die. People went (to be vaccinated), because they heard that some of their friends had died (of it). (Vaccinated during the first trimester, Rukungiri)
Vertical transmission	Yellow fever can be transmitted, because what your body contains during gestation is always shared (by umbilical cord) with the baby. That's how YF can be transmitted from mother to child. (Vaccinated during the third trimester, Kalangala)
Fetus immunized	I thought that since I was vaccinated while pregnant my child was also vaccinated. (FGD)
Reason for immunization	I got vaccinated because I was scared of the disease and I was concerned because I was pregnant. (Vaccinated during the second trimester, Masaka) I decided to get vaccinated even if I get an abortion, at least me personally I will remain healthy, so that I don't contract YF and spread it to others. (FGD) People, who missed the vaccination during mass vaccination, will not be able to get treatment when they get YF in the future. (Vaccinated during the first trimester, Rukungiri) We were told that if you don't get vaccinated against YF and you contract it (YF) hospital bills will be expensive. Without a yellow fever certificate, you cannot travel abroad. If you don't keep your certificate safe you will not receive treatment (for YF) in case, you contract YF. (FGD)
Vaccine knowledge	All I know is that once you receive the YF vaccine you are protected from the disease, but I am not informed on how long the vaccine lasts. (Vaccinated during the second trimester, Kalangala) I think it (a booster dose) is required after a 5-year interval. (Vaccinated during the third trimester, Kalangala)
Vaccine recommendation	Since I was vaccinated once it was enough. (Vaccinated during the third trimester, Rukungiri) Initially I thought that each and everybody could be vaccinated. Soon after vaccination I realized that vaccination was targeting pregnant women greater than 4 months of gestation, babies greater than 6 months and adults. (Vaccinated during the first trimester, Kalangala) I was told (by health workers) that since I was near term, I could get vaccinated and thereby even protect the unborn child from contracting YF. (FGD) Health workers told pregnant women, who were near term, not to receive the vaccine. Whereas, my pregnancy was just an early pregnancy. (Vaccinated during the first trimester, Rukungiri)

YF = yellow fever; FGD = focus group discussion.

findings cannot be generalized. A limitation of this study is that additional in-depth ethnographic interviews were not possible. Future research should include the perception of pregnant women on vaccine safety.

In summary, health officials should adhere to the official YF vaccination criteria. Vaccine information needs to be precise, easily understood, and unambiguous to reduce misconception. Health workers should be trained to address vaccine concerns during gestation. Pregnant women should be informed that lifelong immunity cannot be guaranteed, and a booster dose should be offered in endemic areas. Women need to be sensitized that maternal immunization does not lead to long-lasting immunity in offspring.

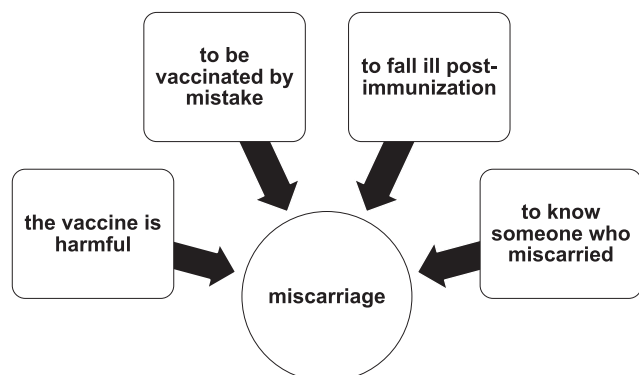


FIGURE 1. Perception of contributing factors to miscarriage after yellow fever vaccination.

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