Clinical guidance for use of virus-like particle chikungunya vaccine in pregnant and breastfeeding women

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Clinical guidance for use of virus-like particle chikungunya vaccine (CHIK-VLP) in pregnant women

Presentation of chikungunya among pregnant women

- Clinical disease similar to non-pregnant individuals

Outcomes of chikungunya virus infection during pregnancy

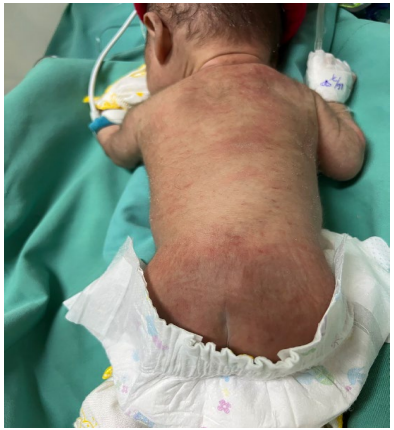
- Adverse outcomes such as fetal loss, stillbirth, or preterm birth documented but rare
  - Mouse studies and examination of placentas from infected women suggest placenta is refractory to chikungunya virus infection[1,2]

- Infection commonly results in adverse neonatal outcomes if pregnant woman infected around time of delivery
  - Intrapartum transmission occurs in ~30%–50% cases[3–6]
  - Mechanism hypothesized to be maternal blood entering fetal circulation by placental barrier breaches from uterine contractions during labor

1. Fritel X et al, Emerg Infect Dis 2010; 2. Couderc T et al, PLoS Pathog 2008; 3. Gerardin P et al, PLoS Medicine 2008; 4. Ramful D et al, Ped Infect Dis J 2007; 5. Torres JR et al, Int J Infect Dis 2016; 6. Senanayake MP et al, Ceylon Med J 2009.

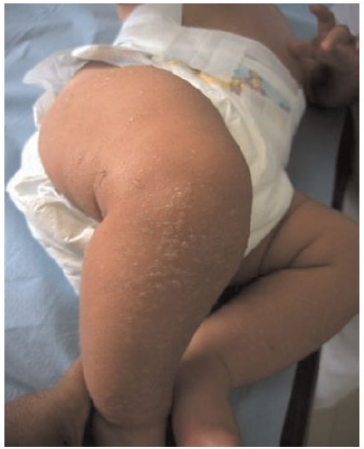
Disease in neonates infected via intrapartum transmission

- Severe and sometime fatal illness
  - In one prospective study 53% (10 of 19 neonates) had severe disease[1]
- Presentations include encephalopathy, sepsis-like illness, cardiac, dermatologic, and hemorrhagic manifestations
- Neurocognitive outcomes often poor, particularly if initial clinical presentation with encephalopathy



Bin S et al, Clin Case Rep 2023

Jebain J et al, ID Cases 2020

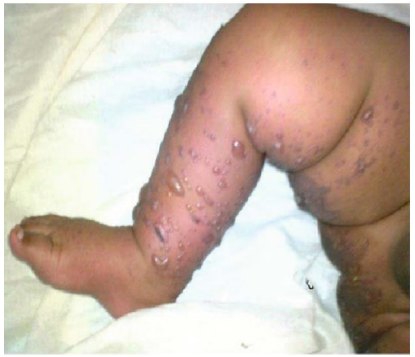


Villamil-Gomez W et al, J Trop Ped 2015

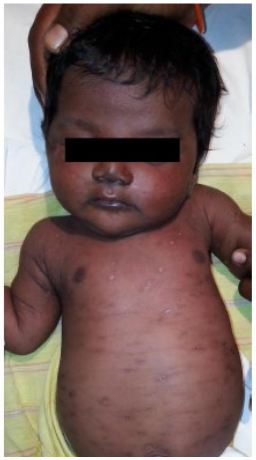
1. Gerardin P et al, PLoS Medicine 2008

Chikungunya and young infants

- Young infants infected via mosquito-borne transmission also at risk for severe disease, particularly during first few months of life
- Clinical presentations similar to infected neonates



Valamparampil JJ et al, Ind J Ped 2009



Gupta D et al, Ind J Ped 2015

CHIK-VLP vaccination during pregnancy: Immunogenicity

- No data available on immunologic response to CHIK-VLP administered to pregnant women

- General principles of maternal vaccination and experience with other vaccines
  - Transplacental transfer of antibodies confers protection with most vaccines
  - Examples of benefits: Decreased hospitalization rates in infants (e.g., influenza, COVID-19, RSV vaccines) and decreased preterm birth risk (e.g., COVID-19 vaccine)

CHIK-VLP vaccination during pregnancy: Safety

- Data insufficient to determine whether any safety risks from vaccination during pregnancy as pregnancy an exclusion criteria in clinical trials
- Only one pregnant woman inadvertently vaccinated, was in 1st trimester
  - Phase ll study with formulation of vaccine* different to licensed product
  - History of 2 ectopic pregnancies
  - Last menstrual period 11 days prior to vaccination
  - Ectopic pregnancy detected 24 days after vaccination and assessed as unrelated to vaccination

*20µg dose of unadjuvanted vaccine

Vaccination during pregnancy: Developmental and reproductive toxicology (DART) studies

- DART study in rabbits
  - Administered equivalent of human dose of vaccine on 5 occasions (i.e., twice prior to mating, twice during gestation, and once during lactation)
  - Postnatal survival rate within 28 days was lower for kits born to vaccinated mothers (**42%**; 95% CI: 32%–53%) compared with kits in control group (**69%**; 95% CI 58%–80%)
  - No adverse effects on other postnatal development parameters
- DART study in rats
  - Reduced pup survival rates not observed

Groups for whom clinical guidance will be relevant

- Travelers and laboratory workers
- Persons in U.S. territories and states with risk of chikungunya virus transmission

Objectives of vaccinating pregnant women against chikungunya

- Protect pregnant woman from disease
- Avoid maternal infection around time of delivery to prevent intrapartum virus transmission and severe disease in newborn
- Transplacental transfer of antibodies might also protect young infant from mosquito-borne transmission and severe disease

Proposed clinical guidance for use of CHIK-VLP in pregnant women

Pregnant women should avoid the risk for chikungunya virus infection, if possible (e.g., by avoiding travel to an area with virus transmission particularly during an outbreak).

Proposed clinical guidance for use of CHIK-VLP in pregnant women (2)

Pregnancy is a **precaution** for vaccination with CHIK-VLP based on the lack of safety and immunogenicity data in pregnant women and potential safety concerns from the toxicology study in rabbits.

In general, vaccination should be deferred until after delivery. However, in specific circumstances it might be warranted. If the risk of infection is high and exposure cannot be avoided, a health care provider should discuss with a pregnant woman the potential risks of chikungunya virus infection and the potential benefits and risks of vaccination so that vaccination can be considered.

CHIK-VLP should ideally be administered a minimum of 2 weeks prior to the expected date of delivery, and preferably earlier, to allow protection around the time of delivery.

Proposed clinical guidance for use of CHIK-VLP in pregnant women (3)

If pregnant women choose to be vaccinated, **deferring vaccination until after the 1st trimester** (after 14 weeks gestation) might be preferred until there are further data to clarify any potential concerns from the animal toxicology data. In addition, it is estimated that 20%–25% of all pregnancies lead to pregnancy loss, and the highest rates occur in the 1st trimester, so avoiding vaccination in the 1st trimester would avoid any association with an unrelated pregnancy loss.

Proposed clinical guidance for use of CHIK-VLP in pregnant women (4)

If both CHIK-VLP and CHIK-LA are available, **vaccination with CHIK-VLP would be preferred**. Although there are no data, this is based on general principles that vaccination with non-live vaccines is preferred over vaccination with live vaccines for pregnant women.

Guidance maximizing benefits while minimizing potential risks of vaccination during pregnancy

1. Avoid risk of chikungunya virus exposure, if possible
2. In general, defer vaccination until after delivery
3. If exposure risk high, consider vaccination given risk for severe adverse outcomes of infection particularly if intrapartum transmission occurs
4. If consider vaccination, where possible avoid 1st trimester and ideally administer >2 weeks before delivery
5. If both CHIK-VLP and CHIK-LA available, vaccination with non-live CHIK-VLP preferred

Clinical guidance for use of CHIK-VLP in breastfeeding women

Chikungunya and breastfeeding

- Chikungunya viral ribonucleic acid (RNA) detected in breast milk on very rare occasions[1,2]
  - No studies have reported detection of replicating virus
- Case report describes mother with chikungunya and chikungunya virus RNA detected in her breast milk who was breastfeeding her 3-month-old infant[1]
  - No symptoms or laboratory evidence of infection in infant

1. Campos GS et al, Pediatr Infect Dis J 2017; 2. De Paula Souza et al, Transl Res 2023.

CHIK-VLP and breastfeeding

- No data on any benefits or risks of breastfeeding after vaccination with CHIK-VLP, including whether chikungunya antibodies present in breast milk post-vaccination
- In toxicology studies in rabbits and rats, no impact of vaccination on lactation was observed

Objectives of vaccinating breastfeeding women

- To protect the woman from chikungunya
- Possible added benefit to reduce risk of infection for young infant by transfer of protective antibodies through breast milk

Proposed clinical guidance for use of CHIK-VLP in breastfeeding women*

Breastfeeding women and their infants should avoid the risk for chikungunya virus infection, if possible (e.g., by avoiding travel to an area with transmission particularly during an outbreak).

Best practice guidelines[1] for immunization note that non-live vaccines pose no risk for mothers who are breastfeeding or their infants.

*Breastfeeding not a contraindication or precaution for vaccination with CHIK-VLP

1. https://www.cdc.gov/breastfeeding/breastfeeding-special-circumstances/vaccinations-medications-drugs/vaccinations.html

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