Retrospective Cohort Study of Lassa Fever in Pregnancy, Southern Nigeria

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Release date: July 16, 2019; Expiration date: July 16, 2020

Learning Objectives

Upon completion of this activity, participants will be able to:

- Compare maternal and fetal outcomes for 2 broad patterns of clinical presentation in 30 pregnant patients with LF: patients with complications vs patients with milder, nonspecific symptoms, according to a retrospective study of cases seen at ISTH n Nigeria between January 2009 and March 2018
- Describe predictors of maternal and fetal outcomes in 30 pregnant patients with LF treated with early ribavirin and a conservative obstetric approach at ISTH in Edo State, Nigeria, between January 2009 and March 2018, according to a retrospective study
- Identify clinical implications of maternal and fetal outcomes in 30 pregnant patients with LF treated with early ribavirin and a conservative obstetric approach at ISTH in Edo State, Nigeria, between January 2009 and March 2018, according to a retrospective study.

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Lassa fever in pregnancy causes high rates of maternal and fetal death, but limited data are available to guide clinicians. We retrospectively studied 30 pregnant Lassa fever patients treated with early ribavirin therapy and a conservative obstetric approach at a teaching hospital in southern Nigeria during January 2009–March 2018. Eleven (36.7%) of 30 women died, and 20/31 (64.5%) pregnancies ended in fetal or perinatal loss. On initial evaluation, 17/30 (56.6%) women had a dead fetus; 10/17 (58.8%) of these patients died, compared with 1/13 (7.7%) of women with a live fetus. Extravaginal bleeding, convulsions, and oliguria each were independently associated with maternal and fetal or perinatal death, whereas seeking care in the third trimester was not. For women with a live fetus at initial evaluation, the positive outcomes observed contrast with previous reports, and they support a conservative approach to obstetric management of Lassa fever in pregnancy in Nigeria.

Lassa fever (LF), a viral hemorrhagic fever endemic to West Africa (*1*–*3*), was first reported in 1969 from northern Nigeria (*4*,*5*). Since that time, LF has been documented in several countries in West Africa, including Sierra Leone, Liberia, Guinea, Mali, and, more recently, Benin and Togo (*6*–*9*). Historical reports of LF in pregnancy have described poor maternal and fetal outcomes; an early direct comparison in Sierra Leone reported a 50% mortality rate in pregnant women (n = 30), compared with 16% among nonpregnant women (n = 234) (*10*). A subsequent study conducted in Sierra Leone in 1988 observed a smaller disparity of a 21% mortality rate in pregnant women (n = 68) versus 13% among nonpregnant women (n = 79) but found a worse mortality rate (30%, n = 40) for mothers in the third trimester and an overall fetal and neonatal mortality rate of 87% (*11*). Although the Sierra Leone study demonstrated the considerable contribution of LF to overall maternal mortality rates at a single hospital, since then, large studies of pregnant patients with LF have been lacking, leading to difficulty in estimating the actual regional burden on maternal health. This problem is exacerbated by the large variability in Lassa virus across regions (*12*) and the often nonspecific early signs and symptoms of the disease, including overlap with other common infectious diseases in the region, such as malaria, influenza, and bacterial sepsis (*2*,*13*).

Pathophysiologically, the poor outcome of LF in pregnancy has been attributed to the higher viral loads often observed in pregnant compared with nonpregnant patients, possibly because of the poorly understood immunologic changes in pregnancy or the affinity of the virus for the highly vascularized placenta (*14*,*15*). Also, the overlap of symptoms such as nausea, headache, and abdominal pain with complicated or even uncomplicated pregnancy might further delay identification or diagnosis and result in worse outcomes when the infection is severe (*16*).

The management of LF in pregnancy requires making difficult decisions with sparse data for guidance. The antiviral drug ribavirin represents the only established pharmacologic therapy for LF and is believed to substantially reduce overall mortality rates (*17*,*18*), although the mechanism of action is not clear and data on safety of the drug in pregnancy are limited (*19*). The 1988 Sierra Leone study, which has been the largest LF case series in the literature to date, found that delivery, spontaneous abortion (miscarriage), and evacuation of the uterus all improve maternal outcome (*11*); the study recommended active obstetric management, particularly because the authors observed high fetal mortality rate irrespective of the modality of management (*2*). However, patients in the study did not receive ribavirin before delivery because of published evidence of teratogenicity in animal studies (*19*). To improve maternal and fetal outcomes and explore their relationship to clinical signs and symptoms, we retrospectively analyzed >9 years of records at a hospital in Nigeria that treated a substantial number of LF cases and applied both a more conservative approach to obstetric management and more liberal antepartum use of ribavirin.

Methods

Irrua Specialist Teaching Hospital (ISTH) is a tertiary-care federal hospital that served as the LF national referral center for the duration of our study. Providers at ISTH and outside facilities in >30 states refer specimens for Lassa virus (LASV) testing by reverse-transcription PCR (RT-PCR) for patients who fit our previously described case definition (*20*); outside patients who test positive by RT-PCR are often referred to ISTH for management. Two authors (S.O.

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DOI: https://doi.org/10.3201/eid2508.181299