Original Article

Ebola virus disease and pregnancy outcome: A review of the literature

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ABSTRACT

Introduction: Ebola virus disease (EVD) is a disease of humans and other primates caused by Ebola viruses. The most widespread epidemic of EVD in history occurred recently in several West African countries. The burden and outcome of EVD in pregnant women remains uncertain. There are few reports to date on maternal and fetal outcomes among pregnant women with EVD, hence the justification for this comprehensive review of these published studies.

Materials and Methods: Published literature in Englishthat reported on maternal and or fetal outcome among pregnant women with EVD up to May 2016 were searched in electronic databases (Google Scholar, Medline, Embase, PubMed, AJOL, and Scopus). Studies that did not meet the inclusion criteria were excluded. We extracted the following variables from each study: Geographical location, year of the study, settings of the study, participants, maternal and fetal outcome.

Results: A total of 12 studies reported on 108 pregnant women and 110 fetal outcomes. Six of the studies were case reports, three retrospective studies, two cross-sectional studies, and one was a technical report. There were 91 (84.3%) deaths out of the 108 pregnant women, while only one (0.9%) fetal survival was reported out of 110. The survival rate among the 15 patients that had spontaneous abortion/stillbirth or induced delivery was 100%.

Conclusion: There was a poor maternal and fetal outcome among pregnant women with EVD, and fetal evacuation significantly improves maternal survival.

Key words: Africa; Ebola; fetal; maternal; outcome.

Introduction

Ebola virus disease (EVD) is a disease of public health importance that affect humans and other primates which is caused byEbola viruses. The causative agent of Ebola is an RNA virus of the family Filoviridae and genus Ebola virus. Ebola virus has five different strains: Zaire Ebolavirus (EBOV), Tai Forest Ebola virus (TAFV), Sudan Ebola virus (SUDV), Reston Ebola virus (RESTV), and Bundibugyo Ebola virus (BDBV) and all are pathogenic to humans, except for RESTV.[1] However, the vast majority of past Ebola outbreaks in humans are with EBOV, BDBV, and SUDV.[2]

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The disease was first identified in 1976 during two simultaneous outbreaks in sub-Saharan Africa, one in Nzara and the other in Yambuku, a village near the Ebola River, from which the disease takes its name.[3] Between 1976 and 2013, there were 24 outbreaks. The 2014 Ebola virus disease (EVD) epidemic was the 24th outbreak, described as the largest, longest, and most complex, killing more people than all previous Ebola outbreaks combined.[4] Several West

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African countries were affected, primarily Guinea, Liberia, Sierra Leone with secondary cases in Mali, Nigeria, Senegal, Spain, and the United States.[5] Fatality in cases with known outcomes is 70.8%,[6] similar to that of past epidemics.[7]

Ebola virus is transmitted among humans through close and direct physical contact with body fluids from a symptomatic individual. In Africa, the caregiver role of women both in domestic and hospital settings put them at a higher risk of acquiring the infection. Poor infection prevention practices at antenatal clinics was said to be the reason for the disproportionate increase in infection among pregnant women in the 1976 Zaire Ebola outbreak rather than a biological consequence of pregnancy.[8] This is supported by epidemiological data from a recent epidemic, which demonstrated the equal distribution of EVD between the sexes.[9] A high Ebola virus load was shown in the amniotic fluid of two pregnant women, and in one of these cases, it was after viral clearance from blood in the convalescent phase.[10] Therefore, it is likely that fetal infection occurs through the placenta. It is not known if a mother can infect her baby with ebola virus through breast milk. However, EBV was found in breast milk as long as 40 days after the patient became asymptomatic and the virus was no longer present in blood,[11] suggesting that babies born to EVD survivors may also be at significant risk.

The burden of EVD in pregnant women is unknown due to the low numbers of pregnant women affected and limitations in data collection during the previous outbreaks. There are very few studies to date reporting on maternal and fetal outcomes among pregnant women with EVD, hence the justification for this comprehensive review of these published studies.

Materials and Methods

We considered all published papers in English that reported maternal and or fetal outcome among pregnant women diagnosed with Ebola virus disease up to January 2016. Electronic databases (Google Scholar, Medline, Embase, PubMed, AJOL, and Scopus) were searched. Reference lists of selected studies were also checked for other potentially relevant studies. Keywords used in the search included: Ebola virus disease, Ebola hemorrhagic fever, pregnancy, fetal death, fetal outcome, maternal mortality, maternal outcome.

Two authors independently reviewed the studies and extracted the information. Areas of disagreements were resolved by discussion and consensus.

From our search, 56 studies were found, 47 of which were excluded because they did not meet the inclusion criteria. Extracted data were imputed into SPSS version 16 and analyzed.

We extracted the following variables from each study: geographical location, year of the study, settings of the study, participants, maternal and fetal outcome.

Results

Twelve studies were found that reported on maternal and or fetal outcome among pregnant women with EVD. Among these 12 studies, there were five case reports, three retrospective studies, two cross-sectional studies, and one technical report [Table 1]. Countries covered by the studies include DRC, Liberia, Sierra Leone, Guinea, and Uganda.

Out of the 108 pregnant women reported in the studies reviewed, there were 91 (84.3%) deaths.The survival rate among the 15 patients that had spontaneous abortion/ stillbirth or induced delivery was 100%. In one study, no pregnant woman was reported, but one of the patients was reported to have a miscarriage before admission. While in another study, a case of Ebola RNA negative mother with a history of contact who was delivered of EVD positive baby was reported. Therefore, a total of 110 fetal outcomes were reported out of which 52 (47.3%) from the 1976 Zaire outbreak died undelivered. Of the remaining 58 reported fetal outcomes, 31 (53.4%) were spontaneous abortions, 12 (20.7%) were stillbirths, one (1.7%) was a perinatal death, while 13 (22.4%) were neonatal deaths.There was only one reported fetal survival 1 (1.7%). The overall survival rate among the 110 reported fetal outcomes is therefore 0.9%. One study reported a mortality rate of 70% among non-pregnant women.

Discussion

There are few studies that report the outcome of EBV infection in pregnant women. Here, we report a comprehensive review of the published literature on maternal and fetal outcome among ebola virus disease patients. We found a maternal mortality rate of 84.3%, while of the 58 reported fetal outcomes there was only 0.9% survival rate. Most of the studies were case reports.

Several infectious diseases, such as hepatitis, tuberculosis, and malariahave been reported to be severe in pregnant than non-pregnant women.[23,24] Pregnant women infected with Ebola more often have serious complications, such as hemorrhagic and neurologic sequelae, than do non-pregnant patients.[25] Similar trends have been documented among pregnant women with Lassa fever. In fact, the first reported case of Lassa fever was described in a pregnant patient,

Table 1: A summary of studies reporting pregnancy outcome in EVD

Study	Site/Country/Year	Sample size	Type of study	Maternal outcome	Pregnancy outcome
Mupapa *et al*.[12]	Kikwit/DR Congo/1995	105 All women 15 (14%) pregnant	Retrospective	14/15 mortality within 10 days All the 15 developed vaginal and uterine bleeding	-10/15 spontaneous abortion at 1st or 2nd trimester. -4/15 fetal loss at third trimester -1/15 neonatal mortality on the third day with a fever
Akerlund *et al*.[13]	Liberia/2015	One case reported	Case report	Died	Still birth
Oduyebo *et al*.[14]	Sierra Leone/2015	One case reported	Case report	Survived	Still birth
Baggi *et al*.[10]	Guinea/2014	Two cases reported	Case report	Both survived	Two still births
Paul Roddy *et al*.[15]	Bundibugyo/ Uganda/2007-2008	26 laboratory confirmed cases	Cross-sectional	None of the recruited patients was pregnant at the time of admission	One case of miscarriage reported before the patient was admitted
Bulletin of the WHO[16]	Yambuku/Zaire/1976	177 cases; 82 (46%) pregnant	Technical report	73/82 (89%) mortality	-19/82 abortions -11/11 died within 19 days of delivery -7/11 of the neonates had a fever- (suspected to be Ebola)
Baize *et al*.[17]	Guinea, 2014	15 patients; 1 pregnant		Survived	1/1 spontaneous abortion
Bower *et al*.[18]	Sierra Leone, 2015	One case report With hx of contact with EVD, no symptoms, delivered EVD positive baby	Case report	Mother Negative for RNA, but history of contact	1/1 stillbirth
Séverine Caluwaerts *et al*.[19]	Sierra Leone, 2015	Two cases reported	Case report	Both survived	2/2 stillbirths
Francesconi *et al*.[20]	Uganda, 2003	One case	Retrospective case identification	1/1	1/1 neonatal death
Wamala *et al*.[21]	Uganda, 2010	One case	Active surveillance, medical chart review (Retrospective)	1/1	1/1 perinatal death
Muehlenbachs *et al*.[22]	Uganda, 2000 DRC, 2012	1 1	Case report	0/1 1/1	1/1 still birth 0/1

and case fatality rate was higher particularly in the third trimester than for non-pregnant women. However, this is in contrast to EVD where mortality is reported to be high in all trimesters of pregnancies.[12,25,26] Also, mothers with Lassa fever improved rapidly after induced/spontaneous abortion or normal delivery.[26] Similarly, in this review there were 15 reported maternal survivals following a fetal loss.

Similar to what we found, a high frequency of abortion has been observed during infection with other hemorrhagic fevers, such as Lassa fever.[26] We also noted all the reported live deliveries died during the neonatal period; however, it is not clear whether these deaths were EVD related or resulted from the many other causes of high infant mortality recognized in resource-poor countries. In EVD, several factors such as pyrexia, intravascular coagulopathy, and EBV infection in fetuses may explain this high incidence of abortions.

Although pregnant women are not immunosuppressed in the real sense of the word, immunologic changes of pregnancy may induce a state of increased vulnerability to certain intracellular pathogens. This results from a shift from cell-mediated immunity toward humoral immunity. This phenomenon is often referred to as the Th1-Th2 shift of pregnancy and is likely to contribute to maternal tolerance of the fetus by suppressing the antifetal cell-mediated immune response. However, these immunological changes could may make the placenta a preferred site for viral replication, and it also helps explain so as to why illness and death increase during pregnancy and improvement is observed after pregnancy ends.

Knowledge about the novel and emerging infections in pregnancy is limited compared to common infectious diseases. Such lack of knowledge causes concern, given that an altered response to infectious diseases during pregnancy may require altered responses to emerging infectious disease threats. During outbreaks, public health policy and practice and the implications for clinical care rarely consider the unique issues of pregnancy and the newborn until very late.[27] For example, during the early stages of the H1N1 pandemic, there were no clinical guidelines or special recommendations for pregnant women until it was recognized that pregnant women had a poorer prognosis than non-pregnant adults.[28,29] This has also been observed during

the early days of HIV epidemics. In the recent West African Ebola outbreaks because of the fear of transmission and the perception that pregnant women and infant born to EVD women have a low chance of survival, most pregnant women with suspected Ebola were turned away from healthcare facilities.[30] However, there is now supporting evidence that shows the high efficacy of simple supportive management approaches such as fluid resuscitation even in the absence of specific antiviral treatment.[31–33] In some reports survival rates can be as high as 70% to 80%.[34]

Compared with what is known about common disease threats, knowledge about currently recognized emerging infectious diseases is quite limited. Because the effects of emerging infections in pregnant women might remarkably be different from that of the general population, pregnancy needs to be considered a potential risk for disease vulnerability as well as the associated morbidity and mortality. Unfortunately, pregnancy issues are often not usually taken into consideration in outbreak investigations, prospective studies, or emergency preparedness planning.

Conclusion

There are few published reports on maternal and perinatal outcomes among pregnant women. Almost all the reports showed poor maternal and perinatal outcomes. There is a need for maternal health considerations in outbreak investigations and management of emerging and re-emerging infections like EVD for a more inclusive description of the course and effect of the disease in sub-saharan Africa.

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Conflicts of interest

There are no conflicts of interest.

References

1. Ansari AA. Clinical features and pathobiology of Ebola virus infection. J Autoimmun 2014;55:1-9.
2. Briand S, Bertherat E, Cox P, Formenty P, Kieny M, Myhre J, *et al*. The International Ebola Emergency. N Engl J Med 2014;371:1180-3.
3. World Health Organization. Ebola virus disease; 2015.
4. Liu S, Deng C, Yuan Z, Rayner S, Zhang B. Identifying the pattern of molecular evolution for Zaire Ebola virus in the 2014 outbreak in West Africa. Infect Genet Evol 2015;32:51-9.
5. World Health Organization. Interim infection prevention and control guidance for the care of patients with suspected or confirmed filovirus hemorrhagic fever in health-care settings, with afocus on Ebola; 2014. p. 1-24.
6. WHO Ebola Response Team. Ebola virus disease in West Africa– The first 9 months of the epidemic and forward projections. N Engl J Med 2014;371:1481-95.
7. World Health Organization. Ebola virus disease fact sheet No. 103. Updated September 2014. Available at: http://www. who.int/mediacentre/factsheets/fs103/en. [Last Accessed on 2016 July 15].
8. World Health Organization. Ebola hemorrhagic fever in Zaire, 1976. Bull World Health Organ 1978;56:271-93.
9. World Health Organisation. Ebola Situation Report, http://apps.who.int/ebola/current-situation/Ebola situation report 8 April 2015. [Last accessed on 2016 July 15].
10. Baggi FM, Taybi A, Kurth A, Van Herp M, Di Caro A, Wölfel R, *et al*. Management of pregnant women infected with Ebola virus in a treatment center in Guinea, June 2014. Euro Surveill 2014;19:20983.
11. Bausch DG, Towner JS, Dowell SF, Kaducu F, Lukwiya M, Sanchez A, *et al*. Assessment of the risk of Ebola virus transmission from bodily fluids and fomites. J Infect Dis 2007;196:S142-7.
12. Mupapa K, Mukundu W, Bwaka MA, Kipasa M, De Roo A, Kuvula K, *et al*. Ebola hemorrhagic fever and pregnancy. J Infect Dis 1999;179:S11-2.
13. Akerlund E, Prescott J, Tampellini L. Shedding of Ebola Virus in an Asymptomatic Pregnant Woman. N Engl J Med 2015;372:2467-9.
14. Oduyebo T, Pineda D, Lamin M, Leung A, Corbett C, Jamieson D. A Pregnant Patient With Ebola Virus Disease. Obstet Gynecol 2015;126:1273-5.
15. Roddy P, Howard N, Van Kerkhove MD, Lutwama J, Wamala J, Yoti Z, *et al*. Clinical Manifestations and Case Management of Ebola Haemorrhagic Fever Caused by a Newly Identified Virus Strain, Bundibugyo, Uganda, 2007–2008. PLoS One 2012;7:e52986.
16. Bulletin of the WHO.
17. Baize S, Pannetier D, Oestereich L, Rieger T, Koivogui L, Magassouba N, *et al*. Emergence of Zaire Ebola Virus Disease in Guinea. N Engl J Med 2014;371:1418-25.
18. Bower H, Grass JE, Veltus E, Brault A, Campbell S, Basile AJ, *et al*. Delivery of an Ebola virus–positive stillborn infant in a rural community health center, Sierra Leone, January 2015. Am J Trop Med Hyg 2016;94:417-9.
19. Caluwaerts S, Fautsch T, Lagrou D, Moreau M, Modet Camara A, Günther S, *et al*. Dilemmas in Managing Pregnant Women With Ebola: 2 Case Reports. Clin Infect Dis 2016:903-5.
20. Francesconi P, Yoti Z, Declich S, Onek PA, Fabiani M, Olango J, *et al*. Ebola hemorrhagic fever transmission and risk factors of contacts, Uganda. Emerg Infect Dis 2003;9:1430-7.
21. Wamala JF, Lukwago L, Malimbo M, Nguku P, Yoti Z, Musenero M, *et al*. Ebola hemorrhagic fever associated with novel virus strain, Uganda, 2007-2008. Emerg Infect Dis 2010;16:1087-92.
22. Muehlenbachs A, Olimpia de la Rosa Vázquez, Bausch DG, Schafer IJ, Paddock CD, NyakioJP, *et al*. Ebola Virus Disease in Pregnancy: Clinical, Histopathologic, and Immunohistochemical Findings. J Infect Dis 2017;215:64-9.
23. Brabin BJ. Epidemiology of infection in pregnancy. Rev Infect Dis 1985;7:579-603.
24. Foster SO. Malaria in the pregnant African woman: Epidemiology, practice, research, and policy. Am J Trop Med Hyg 1996;55:1-3.
25. White SR, Henretig FM, Dukes RG. Medical management of vulnerable populations and co-morbid conditions of victims of bioterrorism. Emerg Med Clin North Am 2002;20:365-92.
26. Price ME, Fisher-Hoch SP, Craven RB, McCormick JB. A prospective study of maternal and fetal outcome in acute Lassa fever infection during pregnancy. BMJ 1988;297:584-7.
27. Money D. Ebola in Pregnancy: Have We Learned Any Lessons? J Obstet Gynaecol Can 2015;37:105-7.
28. Jamieson DJ, Uyeki TM, Callaghan WM, Meaney-Delman D, Rasmussen SA. What obstetrician-gynecologists should know about Ebola: A perspective from the Centers for Disease Control and Prevention. Obstet Gynecol 2014;124:1005-10.
29. Centers for Disease Control and Prevention. Interim guidance: Considerations regarding 2009 H1N1 influenza in intrapartum and

postpartum hospital settings. Atlanta (GA): CDC; 2014. Available at: http://www.cdc.gov/h1n1flu/guidance/obstetric.htm. [Last accessed on 2014 December 11].

30. Lang J. Ebola in the maternity ward. NewYorker; 2014. Available at: http://www.newyorker.com/tech/elements/ebola-maternity-ward. [Last accessed on 2016 June 6].
31. Boseley S, O'Carroll L. Number of Ebola deaths could be cut by use of basic measures, say experts. Guardian; 2014. Available at: http://www.theguardian.com/world/2014/dec/05/ebola-deaths-basic-medical-measures-lancet. [Last accessed on 2016 June 6].
32. Lamontagne F, Clément C, Fletcher T, Jacob ST, Fischer WA 2nd, Fowler RA. Doing today's work superbly well—treating Ebola with current tools. N Engl J Med 2014;1565-6.
33. Chertow DS, Kleine C, Edwards JK, Scaini R, Giuliani R, Sprecher A. Ebola virus disease in West Africa—clinical manifestations and management. N Engl J Med 2014;371:2054-7.
34. World Health Organization (WHO).Ebola response roadmap situation report. Geneva(CH): WHO; 2014. Available at: http://apps.who.int/iris/bitstream/10665/144806/1/roadmapsitrep_3Dec2014_eng.pdf?ua=1. [Last accessed on 2016 June 6].