John E. Deaver* and Wayne R. Cohen

Ebola virus screening during pregnancy in West Africa: unintended consequences

DOI 10.1515/jpm-2015-0118
Received April 6, 2015. Accepted May 4, 2015. Previously published online June 20, 2015.

Abstract

Objective: We hypothesized that predictive value of traditional Ebola virus disease (EVD) screening in West African pregnant women is low because febrile and hemorrhagic complications of pregnancy that can mimic EVD are common.

Methods: Proportions of various categories of pregnancy loss from a hypothetical cohort of West African gravidas were used to construct a Kaplan-Meier curve. The incidence rate of each category was determined by multiplying its proportion by the overall incidence rate, calculated from the inverse of the area under the curve. Incidence rates of Ebola-like illnesses during pregnancy were obtained by multiplying their percentages by the incidence rates of categories of loss with which they coincide.

Results: During pregnancy about 1.5% of suspected EVD cases would prove to have EVD. Most of the remaining 98.5% would have hemorrhagic and febrile complications of pregnancy.

Conclusion: Current guidelines consider obstetrical interventions inappropriate in suspected EVD during pregnancy. However, because the overwhelming majority of cases suspected by screening do not have EVD and might benefit from obstetrical intervention, policy makers must consider whether the small risk to properly protected health care workers from the 1.5% with true EVD justifies withholding potentially life-saving care from the 98.5% who ultimately test negative for EVD.

***Corresponding author: John E. Deaver,** MD, MS, Asociación Siempre Salud, Chincha, Peru and Department of Obstetrics and Gynecology, Bayhealth Milford Memorial Hospital, Milford, DE, USA Tel.: +1-281-764-1962, E-mail: john.deaver@siempresalud.org. http://orcid.org/0000-0002-5067-9176; and Asociación Siempre Salud, Chincha Alta, Peru

Wayne R. Cohen: Department of Obstetrics and Gynecology, University of Arizona College of Medicine, Tucson, AZ, USA

Keywords: Africa; Ebola; false-positive reactions; hemorrhagic fever; mass screening; predictive value of tests; pregnancy.

Introduction

An epidemic of the Zaire strain of Ebola virus began in West Africa in December 2013 and is presently concentrated in Guinea and the neighboring countries of Liberia and Sierra Leone. This epidemic of Ebola virus disease (EVD) is greater in scale and scope than past outbreaks. Fatality in cases with known outcomes is 70.8% [1], similar to that of past epidemics [2].

Ebola virus transmission occurs by contact with body fluids of symptomatic persons with EVD or with dead EVD victims. Fever and non-specific symptoms characterize the first few days, after which there is progression to abdominal pain, diarrhea, and vomiting. Gastrointestinal fluid losses are typically large [3, 4]. Clinically significant bleeding occurs as a late complication in a minority of patients. Shock develops because of gastrointestinal fluid losses and increased vascular permeability. Inadequate perfusion ultimately results in multiple organ failure, and death in the 2nd week of illness [3, 5]. Early supportive care with intravascular volume repletion and electrolyte monitoring and replacement is thought to improve outcomes of EVD [3–5]. In addition to maternal mortality, EVD in pregnancy is associated with miscarriage, fetal death, and excessive uterine bleeding [6–8]. Treatment of EVD in pregnancy is generally considered futile [6], although this view is based on limited reported experience.

Patients are screened for EVD by checking their body temperature and taking a brief history. Criteria to identify a suspected case are any of the following: (i) fever and contact with dead or living suspected or confirmed cases; (ii) fever and at least three other symptoms including malaise, fatigue, anorexia, headache, abdominal pain, muscle and joint pain, respiratory difficulty, diarrhea, and vomiting; (iii) unexplained bleeding; or (iv) sudden unexplained death [9]. In practice, many patients will not admit to contact with an EVD case because of fear of stigmatization. Therefore, irrespective of a history of contact, patients with fever and/or uterine bleeding due to pregnancy complications

(chorioamnionitis, pyelonephritis, incomplete and septic abortion, ectopic pregnancy, placenta previa, and abruptio placenta), sometimes presenting as hypovolemic or septic shock, are suspect for Ebola virus infection. Thrombocytopenia, proteinuria, and elevated hepatic transaminases occur in EVD [5], as do headaches and seizures [3, 7], all signs and symptoms associated with pre-eclampsia and the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP).

Laboratory confirmation of EVD is done by reverse transcriptase polymerase chain reaction (RT-PCR) testing. To achieve adequate sensitivity, patients with symptoms for fewer than 3 days and negative RT-PCR tests for Ebola virus require retesting in 48 h [10].

Current guidelines [6], based on small published series from past outbreaks [7, 8] and field experience during the current epidemic, recommend that interventions such as labor induction, amniotomy, surgery, operative vaginal delivery, and fetal monitoring should not be performed in a pregnancy with suspected or confirmed EVD. The rationale is that any risk of EVD in health care workers is unacceptable because treatment will not prevent the uniformly poor outcomes of EVD in pregnancy [6].

What are the consequences for women whose screening assigns them to the suspected case category, but who are later shown by specific testing not to have the virus? Unfortunately, many of the pregnancy complications that present as Ebola-like illness, such as septic abortion, ectopic pregnancy, placental bleeding, or chorioamnionitis, often evolve acutely, and require prompt treatment. The interval during which obstetrical intervention is likely to be most beneficial has often elapsed before true-positive cases can be reliably distinguished from false-positive ones.

The consequences of this fact may be substantial. Based on observations at Princess Christian Maternity Hospital in Freetown, Sierra Leone in 2014, most situations in which potentially beneficial obstetrical interventions were withheld occurred in cases of suspected EVD later determined to have had false-positive results of screening by temperature and history. In this study we quantify the predictive value of EVD screening during pregnancy by calculating incidence rates of EVD and Ebola-like illness in pregnant women in Sierra Leone. In doing so, we provide insight into the potential hazards of a high-sensitivity, low-specificity screening approach for pregnant women.

Materials and methods

This study did not directly involve human or animal subjects or medical records. All data were available from previously published sources. Thus, informed consent was unnecessary, and the study was exempt from Institutional Review Board or Ethics Committee review.

Calculating the incidence rate (cases/10,000 pregnant women/week) of a pregnancy-specific illness is challenging because of the variable duration of pregnancy. We estimated by literature review the proportion of pregnancies lost from a hypothetical cohort of West African pregnant women from spontaneous and induced abortion, ectopic pregnancy, and preterm and term live born and stillborn deliveries. We constructed a Kaplan-Meier curve of cumulative probability of survival (continuation of pregnancy) in weekly intervals from the beginning of the 4th week (100% of cohort still pregnant) until the end of the 43rd gestational week when all deliveries were considered to have occurred. We defined early fetal loss to be between 5 and 13 weeks' gestation, preterm delivery between 24 and 36 weeks, and term delivery between 37 and 43 weeks. To simplify the construction of the curve we assumed a uniform distribution of losses within each category.

In this format, the area under the curve is person-weeks. The inverse of person-weeks is the overall incidence rate of loss from the cohort (losses/10,000 person-weeks). Specific incidence rates of loss categories (abortion, ectopic pregnancy, and preterm and term delivery) were obtained by multiplying their individual proportions by the overall incidence rate. Proportions of pregnancy-specific illnesses [placenta previa, abruptio placentae, septic abortion, HELLP syndrome, and chorioamnionitis] that can masquerade as EVD and result in positive initial screening were obtained by literature review and multiplied by the incidence rates of the categories of losses with which they coincide to determine the incidence rates of pregnancy-specific illnesses. Only the proportion of HELLP syndrome that occurs in normotensive women was considered to be Ebola-like in presentation. Treated pyelonephritis is not normally associated with pregnancy loss and can occur throughout pregnancy. Therefore, to determine the incidence rate of pyelonephritis the reported proportion of pregnancies with pyelonephritis was divided by cumulative person-weeks from 4 to 43 weeks as determined from the area under the Kaplan-Meier curve.

Results

The calculated expected weekly incidence rates (cases/10,000 person-weeks) for EVD and Ebola-like illnesses in Sierra Leonean pregnant women are shown in Table 1, where the predictive value of screening is 0.8/52.1 (1.5%). The incidence rate of EVD reflects the reported peak incidence in Sierra Leone from November 10 to 30, 2014, during which period there was an average of 485 new cases weekly [11]. We considered the entire Sierra Leone population of 6,092,000 [12] to have been at risk.

Plasmodium falciparum malaria is holoendemic in West Africa, and can cause perinatal mortality and morbidity [13]. Because most pregnant women have previously acquired functional immunity, they experience little febrile morbidity [13]. Therefore, malaria during pregnancy will infrequently present as Ebola-like illness and is excluded from Table 1. We assumed that the attack rates

Table 1: Incidence rates of EVD and Ebola-like illnesses.

Illness	Incidence rate[b]
EVD (peak incidence)[a]	0.80
Lassa fever	1.43
Typhoid	0.07
Abruptio placentae	2.78
Bleeding from placenta previa	1.83
Ectopic pregnancy	7.50
HELLP in normotensive	0.29
Septic abortion	11.31
Chorioamnionitis	9.30
Pyelonephritis	16.79
Total EVD and Ebola-like illness	52.10

[a]November 10–30, 2014 [11]; [b]Cases per 10,000 pregnant women per week.
EVD=Ebola virus disease.

for Lassa virus and *Salmonella typhi* in pregnancy are the same as in the general population. In Sierra Leone there are 6099–148,589 (midpoint 77,344) symptomatic Lassa virus seroconversions yearly [14]. The incidence rate of symptomatic Lassa fever is about 7.14 cases/10,000 person-weeks; 20% have a severe illness [14] for which, for purposes of Table 1, we assumed medical attention would be sought. The incidence of typhoid fever in West Africa is 38 cases/100,000 person-years [15].

Table 2 shows the proportions of losses from a hypothetical cohort of pregnant women [16, 17]. The ratio of rows A/B (0.14) is equivalent to the ratio of 14 induced abortions for every 100 live births in West African countries that, like Sierra Leone, have restrictive abortion laws [18]. Cousens et al. reported that about 2.8% of deliveries in West Africa are complicated by stillbirth [19], equivalent to the ratio of rows C/D (0.028). The preterm delivery ratio (preterm live births/all live births) averaged 17% in four low-income countries [20], equivalent to the ratio of rows E/B (0.17).

Table 3 summarizes cumulative continuation of pregnancy from 4 to 43 weeks. The area under the resulting survival curve (Figure 1) is cumulatively 26.8 person-weeks. The expected overall incidence rate of loss from the hypothetical cohort of pregnant women is 1/26.8 person-weeks, or 373 losses from the cohort per 10,000 person-weeks. Multiplication of these 373 losses by the distributions in Table 2 results in the specific incidence rates of early fetal losses and deliveries in Figure 2.

We calculated the birth rate in Sierra Leone as 149 births/1000 women of reproductive age (WRA) [21, 22]. From data in Figure 2 and a formula from the US Centers for Disease Control [23] we calculated that at any given time 189,243 persons, or 3.1% of the Sierra Leone population, are pregnant women. This estimate is comparable to that of other investigators [6]. That total multiplied by our estimated live birth incidence rate and by 52 weeks estimates 265,698 live births annually, a crude birth rate of 44/100,000 population/year, somewhat higher than that of 37.1/100,000 reported by the WHO [24].

Table 2: Proportions of losses from hypothetical cohort of pregnant women.

Row	Event category	Proportion of cohort	Subtotals
	Early fetal loss		
	Spontaneous abortion[a]	0.135	
A	Induced abortion	0.101	
	Ectopic pregnancy [16]	0.02	
	Total early losses		0.256
	Preterm delivery	0.127	
	Delivery at term and beyond	0.616	
	Total deliveries		0.743
	Total losses from cohort	1	1
	Deliveries by live born vs. stillborn		
B	Liveborn	0.722	
C	Stillborn	0.021	
D	Total deliveries		0.743
	Deliveries by preterm vs. term stratified by live born vs. stillborn		
E	Preterm live born	0.124	
	Preterm stillborn	0.003	
	Term live born	0.598	
	Term stillborn	0.018	
	Total deliveries		0.743

[a]12–15% (midpoint 13.5%) of pregnancies end in clinically recognized spontaneous abortion [17].

Table 3: Summary of cumulative probability of survival (continuation of pregnancy) by gestational age for a hypothetical cohort of West African pregnant women.

Gestational week completed	Cumulative probability of survival (continuation of pregnancy)
4	1.000
5	0.972
13	0.744[a]
14	0.744
23	0.744[b]
24	0.734
36	0.616[c]
37	0.528
43	0.000[d]

[a]Proportion of total cohort lost 0.0285 per week×9 weeks (gestational weeks 5–13)=0.256; [b]no losses gestational weeks 14–23; [c]proportion of total cohort lost 0.0098 per week×13 weeks (gestational weeks 24–36)=0.127; [d]proportion of total cohort lost 0.088 per week×7 weeks (gestational weeks 37–43)=0.616.

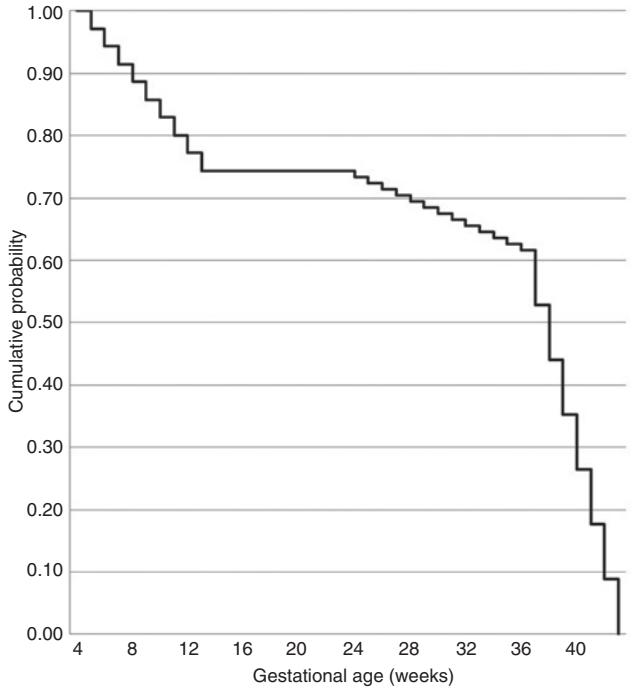

Figure 1: Kaplan-Meier curve of cumulative probability of survival (continuation of pregnancy) for a hypothetical cohort of West African pregnant women.

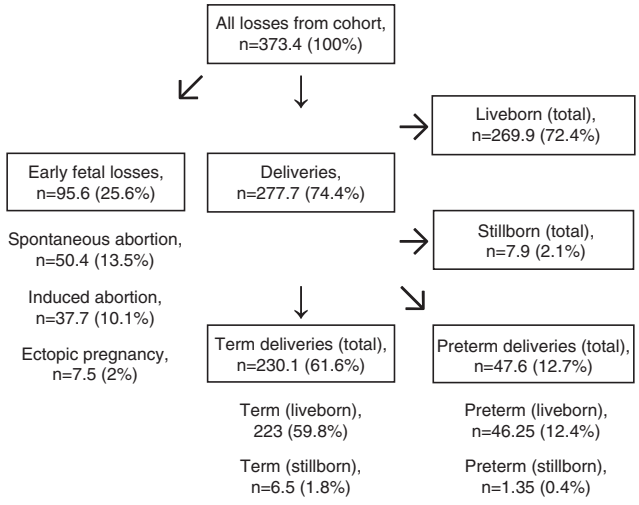

Figure 2: Incidence rates of losses from cohort of pregnant women as cases/10,000 person-weeks (n), percentage of all losses in parentheses.

The incidence rate of ectopic pregnancy in Table 1 was taken from Figure 2. The incidence rates of other pregnancy-specific Ebola-like illnesses in Table 1 were obtained by multiplying percentages of illness by the specific incidence rates of the categories of losses (Figure 2) with which they coincide. Percentages of illness from our literature review are shown in Table 4. Placenta previa, abruptio placenta, and HELLP syndrome generally occur in late pregnancy (≥24 weeks).

In West Africa, where prenatal screening for bacteriuria is not routinely performed, an estimated 10–20% of pregnancies are affected [31]. About 30% of untreated cases develop pyelonephritis [32], a risk factor for preterm delivery. With early treatment, however, these pregnancies can be expected to continue. The proportion of the cohort with pyelonephritis (0.045 using midpoints of ranges), was divided by person-time of pregnancy at risk (26.8 person-weeks) to determine the incidence rate in Table 1.

Discussion

Current screening protocols for EVD in West Africa, a low medical resource setting, are designed to be simply applied, and to relinquish specificity at the expense of high sensitivity. There are obvious virtues to this approach, in as much as screening to identify fever and pertinent medical history should identify the great majority of potential cases of EVD, allowing them to be managed in a setting in which supportive care can be effectively administered and transmission to others minimized. In setting public health policy, however, the potential hazards of this approach must be considered, particularly in the case of pregnant women. The fate of women who are identified as suspected EVD patients but who later are found to have some other disease is unknown. Our calculations suggest this is not a trivial problem.

Of all suspected EVD cases referred into Ebola treatment centers (ETCs) 37–54% will have negative RT-PCR results [4, 33, 34]. Many have an endemic febrile illness [13–15]. According to our estimates, EVD in Sierra Leone may account for only 1.5% of suspected cases of EVD during pregnancy. Thus, 98.5% of pregnant women identified as possibly having EVD by standard primary screening will have other diseases, many of which are treatable and require prompt attention to avoid serious morbidity and mortality. The largest proportion of Ebola-like illnesses (71.8%) are pregnancy-specific infections (septic abortion, chorioamnionitis, and pyelonephritis). Another 2.9% are endemic infections with Lassa virus and *S. typhi*, which are treatable with antimicrobials; 14.4% are ectopic pregnancies; and 9.4% are late-pregnancy complications of placenta previa, abruptio placentae, and HELLP syndrome.

It is interesting that despite the scale of the current epidemic there have been only five pregnant women

Table 4: Proportions of pregnancy-specific Ebola-like illnesses.

Illness	Proportions of illness (midpoint)	Formula for incidence rate of illness
Placenta previa	0.14–0.30% (0.22%) [25] of pregnancies have placenta previa that persists until delivery; bleeding is episodic (we assume three episodes).	0.0022*total deliveries*3
Abruptio placentae	1% [26] of total deliveries.	0.01*total deliveries
HELLP in normotensive	HELLP 0.5–0.9% (0.7%) of total deliveries, 10–20% (15%) of these in normotensive women [27].	0.007*0.15*total deliveries
Septic abortion	60% of induced abortions are performed by non-physicians (a proxy for unsafe abortion) [18], 50% of unsafe abortions are complicated [18], 100% of complications are septic (described as sepsis, pelvic collection, uterine gangrene, tuboovarian abscess and/or retained products of conception) [28].	0.60*induced abortions*0.50*1
Chorioamnionitis	One-third of preterm deliveries are due to preterm premature rupture of membranes (PROM) [29], 15% of preterm PROM develop clinical chorioamnionitis [30]; 2–4% (3%) of term deliveries are complicated by chorioamnionitis in labor [30].	(0.333*preterm deliveries*0.15)+(0.03*term deliveries)

"Total deliveries", "induced abortions", "preterm deliveries", and "term deliveries" refer to their respective incidence rates in Figure 2.

identified in three published series of more than 843 ETC patients [3, 4, 33], whereas 25–42 would have been expected, given that 3–5% of the population are pregnant [6]. Those few pregnant women have appeared in ETCs may reflect, in part, the prevailing notion that it is futile to care for them.

Even if further study confirms the validity of considering intervention during pregnancy with known EVD to be futile, this study demonstrates that intervention is both appropriate and likely to be beneficial in 98.5% of suspected cases of EVD identified by traditional screening. Moreover, the optimal opportunity to intervene for the benefit of the mother or fetus is likely to occur before a confirmatory negative test of Ebola virus will have been obtained. It is still uncertain how intervention in these suspected cases would alter the risk calculus for patients and health care workers.

The risk of EVD in health care workers is low when they follow recommended infection control practices and wear appropriate personal protective equipment (PPE) during care of non-pregnant individuals suspected to have EVD [35], even though half or more of such patients will be identified as true EVD cases [4, 33, 34]. This begs the question of whether obstetrical interventions represent an unacceptable risk to health workers using the same infection prevention practices when only 1.5% of patients actually have EVD.

It is reasonable to assume, although it has not been demonstrated, that obstetrical interventions in patients with EVD confer additive risk of transmission to health care workers because Ebola virus is present in blood and amniotic fluid and procedures potentially increase the risk that PPE will be breached.

The precise toll extracted by current policies is impossible to calculate, but it is probably substantial. For example, Sierra Leone has one of the world's highest maternal mortality ratios (1100 maternal deaths/100,000 live births in 2013) [36]. The most common causes were hemorrhage, sepsis, unsafe abortion, and eclampsia [37], the very conditions that are likely to be confused with EVD and to have treatment withheld or delayed. In pregnant women with suspected EVD, the risk of infecting health workers by the few patients with EVD needs to be balanced against the risks of non-intervention in the vast majority without EVD.

The policy of delaying obstetrical interventions until EVD has been definitively excluded is well-intentioned, and has been promulgated as a means to protect patients from futile interventions and health care workers from unnecessary risk. It is likely, however, that it has had the opposite effect for patients by delaying urgent appropriate management of treatable complications of pregnancy. Until a rapid single-step point-of-care test for Ebola becomes available the best option would be to develop a refined screening algorithm based on unique characteristics of pregnant women to improve specificity. This issue has a complex ethical dimension that is beyond the scope of this report, and which must be considered in policy making. It is equally important that care protocols be guided by an informed risk-benefit analysis that considers the unique needs of pregnant women.

References

[1] 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.

[2] World Health Organization. Ebola virus disease fact sheet No. 103. Updated September 2014. Available at: http://www.who.int/mediacentre/factsheets/fs103/en. Published 2014. Accessed on January 15, 2015.

[3] 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.

[4] Bah EI, Lamah MC, Fletcher T, Jacob ST, Brett-Major DM, Sall AA, et al. Clinical presentation of patients with Ebola virus disease in Conakry, Guinea. N Engl J Med. 2015;372:40–7.

[5] Fowler RA, Fletcher T, Fischer WAN, Lamontagne F, Jacob S, Brett-Major D, et al. Caring for critically ill patients with Ebola virus disease. Perspectives from West Africa. Am J Respir Crit Care Med. 2014;190:733–7.

[6] Caluwaerts S, Lagrou D, Van Herp M, Black B, Caluwaerts A, Taybi A, et al. Guidance paper Ebola Treatment Center (ETC): pregnant and lactating women. Brussels: Médecins Sans Frontières, 2014.

[7] Mupapa K, Mukundu W, Bwaka MA, Kipasa M, De Roo A, Kuvula K, et al. Ebola hemorrhagic fever and pregnancy. J Infect Diseas. 1999;179(Suppl 1):S11–2.

[8] WHO International Study Team. Ebola hemorrhagic fever in Zaire, 1976. Bull World Health Organ. 1978;56:271–93.

[9] World Health Organization. Global Alert and Response (GAR). Ebola response roadmap – situation report 19 November 2014. Available at: http://www.who.int/csr/disease/ebola/situation-reports/en/?m=20141119. Published 2014. Accessed on January 15, 2015.

[10] World Health Organization. Interim Guideline. Laboratory diagnosis of Ebola virus disease. 19 September 2014. Available at: http://apps.who.int/iris/bitstream/10665/134009/1/WHO_EVD_GUIDANCE_LAB_14.1_eng.pdf. Published 2014. Accessed on January 16, 2015.

[11] World Health Organization. Ebola Data and Statistics. Data Published 21 January 2015. Data on new cases per epi week for Sierra Leone. Available at: http://apps.who.int/gho/data/node.ebola-sitrep.ebola-country-SLE-20150121?lang=en. Published 2015. Accessed on January 13, 2015.

[12] World Bank. Sierra Leone: country at a glance. Available at: http://www.worldbank.org/en/country/sierraleone. Published 2015. Accessed on January 15, 2015.

[13] Snow RW, Omumbo JA. Chapter 14 Malaria. In: Jamison DT, Feachem RG, Makgoba MW, Bos ER, Baingana FK, Hofman KJ, et al., editors. Disease and mortality in sub-Saharan Africa. 2nd ed. Washington, DC: World Bank; 2006.

[14] Richmond JK, Baglole DJ. Lassa fever: epidemiology, clinical features, and social consequences. Brit Med J. 2003;327:1271–5.

[15] Crump JA, Luby SP, Mintz ED. The global burden of typhoid fever. Bul World Health Organ. 2004;52:346–53.

[16] Marion LL, Meeks GR. Ectopic pregnancy: history, incidence, epidemiology, and risk factors. Clin Obstet Gynecol. 2012;55:376–86.

[17] Regan L, Rai R. Epidemiology and the medical causes of miscarriage. Baillieres Best Pract Res Clin Obstet Gynaecol. 2000;14:839–54.

[18] Henshaw SK, Singh S, Oye-Adeniran BA, Adewole IF, Iwere N, Cuca YP. The incidence of induced abortion in Nigeria. Int Fam Plan Perspec. 1988;24:156–64.

[19] Cousens S, Blencowe H, Stanton C, Chou D, Ahmed S, Steinhardt L, et al. National, regional, and worldwide estimates of stillbirth rates in 2009 with trends since 1995: a systematic analysis. Lancet 2011;377:1319–30.

[20] Lawn JE, Gravett MG, Nunes TM, Rubens CE, Stanton C. Global report on preterm birth and stillbirth (1 of 7): definitions, description of the burden and opportunities to improve data. BMC Pregnancy Childbirth. 2010;10(Suppl 1):S1.

[21] UNICEF. At a glance: Sierra Leone. Available at: http://www.unicef.org/infobycountry/sierraleone_statistics.html. Published 2013. Accessed on January 15, 2015.

[22] World Health Organization. African health observatory. Comprehensive analytical profile: Sierra Leone. Introduction to country context. Available at: http://www.aho.afro.who.int/profiles_information/index.php/Sierra_Leone:Introduction_to_Country_Context. Published copyright 2010–2014. Accessed on March 27, 2015.

[23] Centers for disease control and prevention. National center for chronic disease prevention and health promotion, division of reproductive health. Estimating the number of pregnant women in a geographic area. Available at: http://www.cdc.gov/reproductivehealth/emergency/PDFs/EstNoofPregWom_508.pdf. Published 2013. Accessed on January 15, 2015.

[24] World Health Organization. Global health observatory data repository. Sierra Leone statistics summary (2002 – present). Available at: http://apps.who.int/gho/data/node.country.country-SLE. Published 2014. Accessed on January 16, 2015.

[25] Chie L, Levine D. Sonography of the lower uterine segment. Ultrasound Clin. 2006;1:303–19.

[26] Ananth CV, Oyelese Y, Yeo L, Pradhan A, Vintzileos AM. Placental abruption in the United States, 1979 through 2001: temporal trends and potential determinants. Am J Obstet Gynecol. 2005;192:191–8.

[27] Haram K, Svendsen E, Abildgaard U. The HELLP syndrome: clinical issues and management. A review. BMC Pregnancy Childbirth. 2009;9:8.

[28] Fasubaa OB, Akindele ST, Ezechi OC. Illegal induced abortion in Nigeria: an examination of its consequences and policy implications for social welfare and health policy makers. J Hum Ecol. 2003;14:433–42.

[29] Mercer BM. Preterm premature rupture of the membranes: current approaches to evaluation and management. Obstet Gynecol Clin North Am. 2005;32:411–28.

[30] Newton ER. Chorioamnionitis and intraamniotic infection. Clin Obstet Gynecol. 1993;36:795–808.

[31] Gilbert NM, O'Brien VP, Hultgren S, Macones G, Lewis WG, Lewis AL. Urinary tract infection as a preventable cause of pregnancy complications: opportunities, challenges, and a global call to action. Glob Adv Health Med. 2013;2:59–69.

[32] Mittal P, Wing DA. Urinary tract infections in pregnancy. Clin Perinatol. 2005;32:749–64.

[33] Schieffelin JS, Shaffer JG, Goba A, Gbakie M, Gire SK, Colubri A, et al. Clinical illness and outcomes in patients with Ebola in Sierra Leone. N Engl J Med. 2014;371:2092–100.

[34] Medecins San Frontieres. Global bio-disaster response urgently needed in Ebola fight, 2 September 2014. Available at: http://www.msf.org/article/global-bio-disaster-response-

urgently-needed-ebola-fight. Published 2014. Accessed on November 20, 2014.
[35] Medecins Sans Frontiéres. Ebola crisis update – 13th January 2015. Available at: http://www.msf.org/article/ebola-crisis-update-13th-january-2015. Published 2015. Accessed on March 25, 2015.
[36] World Health Organization. Sierra Leone: health profile. Available at: http://www.who.int/gho/countries/sle.pdf?ua=1. Published 2015. Accessed on January 16, 2015.
[37] Reproductive and Child Health Program. Ministry of health and sanitation. Nationwide needs assessment for emergency obstetric and newborn care services in Sierra Leone. Freetown: Sierra Leone ministry of health and sanitation, August 2008.

The authors stated that there are no conflicts of interest regarding the publication of this article.