Peripartum Infections and Associated Maternal Mortality in Rural Malawi

Thomas van den Akker, MD, MSc, MPhil, Stefan de Vroome, MSc, Beatrice Mwagomba, MBBS, Nathan Ford, PhD, and Jos van Roosmalen, MD, PhD

OBJECTIVE: To assess associations between maternal mortality and severe morbidity and human immunodeficiency virus (HIV) infection, uptake of antiretroviral therapy, obstetric infections, and nonobstetric infections in a rural Malawian district, where the estimated HIV prevalence is 21%.

METHODS: We studied the incidence and outcomes of maternal peripartum infections between September 2007 and September 2009 at the district hospital. We used a facility-based prospective cohort study design, including all cases of severe maternal peripartum infection up to 42 days postpartum, and recorded maternal and pregnancy-related characteristics. We assessed the association between mortality and covariates (including nonobstetric infection, HIV prevalence, and uptake of antiretroviral therapy) using univariable and multivariable logistic regression models.

RESULTS: In total, 140 infections occurred: 79 (56%) obstetric and 53 (38%) nonobstetric (eight unknown). Half of the women were HIV-positive. Multivariable analysis showed that nonobstetric infection was the most important explanatory variable for mortality (adjusted odds ratio [OR] 4.23, 95% confidence interval [CI] 1.53–11.73). HIV-positive women not on antiretroviral therapy were at higher risk of mortality (adjusted OR 3.02, 95% CI 1.06–8.60) but there was no significant mortality increase among those on treatment (adjusted OR 0.51, 95% CI 0.10–2.71). The most common infections were puerperal sepsis (obstetric, case fatality rate 7%) and pneumonia (nonobstetric, case fatality rate 41%).

CONCLUSION: Untreated HIV infection and nonobstetric infections are independently associated with maternal mortality. Prompt treatment of HIV and nonobstetric infections in pregnant women must be prioritized to reduce maternal mortality.

(Obstet Gynecol 2011;118:266–72)
DOI: 10.1097/AOG.0b013e3182254d03

LEVEL OF EVIDENCE: II

Although maternal mortality declined globally during the 1990s, this decline was not seen in sub-Saharan Africa, where the human immunodeficiency virus (HIV) epidemic contributed to substantial increases in maternal mortality. In these regions, declines were noted from early 2000 onward, which coincided with the scale-up of antiretroviral therapy and services to prevent mother-to-child transmission of HIV.[1]

Declines in maternal mortality have been slowest in southern sub-Saharan Africa, the region with the highest burden of HIV and acquired immunodeficiency syndrome (AIDS). In Malawi, a highly underresourced country in southern Africa with an estimated adult HIV prevalence of 12%, the rollout of antiretroviral therapy led to reductions in HIV-related mortality, including measurable declines in mortality at the population level.[2–4] However, maternal mortality in 2008 was still considerably higher than in 1990 (1,140 compared with 743 per 100,000 live births).[1]

Studies have shown that HIV is associated with an increased risk of infectious morbidity from direct obstetric causes such as postpartum endometritis and postcesarean complications.[5–7] In addition, HIV infection increases susceptibility for infectious complications not directly related to but aggravated by pregnancy. These complications are commonly referred to as nonobstetric infectious morbidity and may contribute indirectly to increased maternal mortality.[7,8] Examples of nonobstetric infectious morbidity are common infections such as pneumonia and tuberculosis as well as HIV-related opportunistic infections (eg, *Pneumocystis jiroveci* pneu-

From the Thyolo District Health Office, Ministry of Health, Thyolo, Malawi; Medecins Sans Frontières Operational Center Brussels, Brussels, Belgium; the Department of Medical Humanities, EMGO Institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands; the Department of Obstetrics, Leiden University Medical Center, Leiden, The Netherlands; and the Center for Infectious Disease Epidemiology and Research, University of Cape Town, Cape Town, South Africa.

Corresponding author: Thomas van den Akker, MD, MSc, MPhil, VU University Medical Center, EMGO Institute for Health and Care Research, Department of Medical Humanities, Van der Boechorststraat 7, 1081BT Amsterdam; e-mail: thomas_vd_akker@hotmail.com.

Financial Disclosure
The authors did not report any potential conflicts of interest.

ISSN: 0029-7844/11

monia) and neoplasms such as Kaposi sarcoma and HIV-associated lymphoma.[9–12] For most of these complications, the natural course in the HIV-infected pregnant woman is not well understood.[13]

To better understand the contribution of obstetric and nonobstetric infections attributing to maternal mortality and severe morbidity, and the relative contribution of HIV and AIDS to this disease burden, we conducted an operational research assessment of all cases of severe maternal peripartum infection that occurred at Thyolo District Hospital, Malawi, over a period of 2 years.

MATERIALS AND METHODS

Thyolo District Hospital is located in southern Malawi, a low-income country in sub-Saharan Africa, and serves an area of 600,000 inhabitants. The adult HIV prevalence stood at 21% in 2004.[14] In the district hospital 4,363 deliveries occurred in 2009 supported by nurse–midwives, clinical officers, and one volunteer expatriate physician with experience in obstetrics.[15] Services at this public hospital are provided free of charge. In 2003, Médecins Sans Frontières and the Ministry of Health embarked on a joint mission to scale up access to antiretroviral therapy, reaching district-wide coverage in August 2007, defined as the fulfillment of 80% of urgent treatment needs.[2] Antenatal care, services for prevention of mother-to-child transmission, and antiretroviral treatment are provided at hospital, health center, and health post levels.

Sisterhood surveys conducted in the district reflect an increase in maternal mortality in sub-Saharan Africa that is associated with a rise in HIV prevalence.[1,16,17] The locally reported maternal mortality ratios were 561 per 100,000 live births in 2006 compared with 409 per 100,000 in 1989.[16,17] A review of facility-based maternal mortality and severe acute maternal morbidity in Thyolo found that peripartum infections had replaced obstetric hemorrhage as the primary cause of maternal mortality considering that this was likely a result of the increased HIV prevalence. Of 46 mortality cases, 23 were the result of infectious causes and 10 were the result of hemorrhage. The remainder were the result of eclampsia, uterine rupture, and other less common causes.[18] However, neither national nor local studies specified which types of infection contributed to increased maternal mortality and morbidity nor the contribution made by HIV to the different types of infection.

Protocols for HIV testing and treatment used in Thyolo follow the national guidelines of the Ministry of Health. Opt-out HIV testing and counseling is offered to all women attending the antenatal clinic and ideally performed on the first antenatal contact unless the woman already tested positive previously or received testing and counseling in the previous 3 months. On testing positive, eligibility for antiretroviral therapy is established based on World Health Organization clinical criteria (women in World Health Organization stages III–IV)[19] and immunologic criteria (all women are offered treatment if the CD4 level is below 250 cells/mm^3; this threshold was raised by the Malawi Ministry of Health to 350 cells/mm^3 after the study period). CD4 count is only performed at the district hospital, so samples from peripheral sites have to be transported for analysis. Women attending antenatal care at these sites return to the primary care clinics 3 weeks after having their samples taken to receive CD4 results and have their treatment eligibility assessed.

This study of peripartum infections forms part of an enquiry into severe acute maternal morbidity and mortality.[15,18] in Thyolo District Hospital. The 4M-study addresses maternal mortality and severe acute maternal morbidity according to disease-specific criteria (uterine rupture, [severe pre-]eclampsia, major obstetric hemorrhage, and maternal peripartum infection) up to 42 days postpartum.[18]

For this present part of the 4M-study, we included all cases of severe maternal peripartum infection that occurred at this hospital between September 1, 2007, and September 1, 2009. We defined severe maternal peripartum infection as any infection in a pregnant or recently delivered woman up to 42 days postpartum for which intravenous antibiotics or intravenous malaria treatment were prescribed or surgical treatment was performed irrespective of duration of pregnancy or other maternal factors. In addition, we included Kaposi sarcoma and HIV-associated lymphoma into the study as complications of HIV. Minor wound infections that did not require surgical débridement or medical treatment were excluded.

We included cases on occurrence of an infection. For included cases, we extracted relevant data during admission from all available medical records, including antenatal register, labor graph, and admission file. We verified the completeness of these data on discharge of the woman or at the time of her death. To minimize bias toward obstetric cases, we also screened the medical department on a daily basis for pregnant or recently aborted women admitted with infections.

We recorded maternal characteristics (age, parity, HIV status, whether or not on antiretroviral therapy), and characteristics of pregnancy and delivery (maternal mortality, unwanted pregnancy, antenatal visits, and involvement of traditional birth attendant or health

center). All diagnoses were evaluated by applying the locally developed criteria shown in Box 1, which are applicable to the local setting and were used to verify the diagnosis made by the attending clinician.

We used univariable logistic regression to model the individual associations of baseline variables with maternal mortality; variables were stratified into discrete categories as follows: age younger than 20 and older than 20 years; presence or absence of nonobstetric infections; nulliparity; HIV and treatment status (HIV-negative, HIV-positive on antiretroviral therapy, HIV-positive not on antiretroviral therapy), health center involvement, antenatal care visits (yes or no) and involvement of traditional birth attendants (yes or no). Using these results, we constructed a multivariable logistic regression model using stepwise forward selection. Given the relatively small sample size, we compared these findings against an exact logistic regression model.[20] Data were entered in Microsoft Excel and analyzed using STATA 11. All reported *P* values are exact and two-tailed, and for each analysis, $P<.05$ was considered significant.

The study was performed in accordance with the guidelines for operational research of the National Research Council and the Health Sciences Research Committee of the Ministry of Health of Malawi and with the Helsinki Declaration of 1975, as revised in 2000.[21,22] We obtained approval from the National Health Sciences Research Committee from the Ministry of Health, Malawi, which ruled that formal ethics approval was not necessary for this type of study.

Box 1. Inclusion Criteria for Different Types of Infection

A. Puerperal sepsis treated intravenously with antibiotics and at least two of the following symptoms: fever (body temperature above 38.3°C or twice above 38°C), uterine tenderness, purulent vaginal discharge
B. Pneumonia treated with intravenous antibiotics and at least four of the following symptoms: cough, fever, tachypnea, dyspnea, crackles at auscultation
C. Bacterial meningitis confirmed by lumbar puncture or, when lumbar puncture was not done, in the presence of all of the following: fever, headache, nuchal rigidity
D. Tuberculosis (TB) confirmed by a sputum smear positive for acid-fast bacilli or with at least four of the following: X-ray suggestive of TB, weight loss, night sweats, chronic cough, no response to first-line antibiotics
E. Wound infection: visibly infected wound with fever and treated with intravenous antibiotics or surgical débridement
F. Severe malaria with or without confirmation by positive blood film or rapid test but with at least three of the following: fever, anemia, headache, vomiting, diarrhea
G. Septic abortion complete or incomplete expulsion of the embryo (up to 28 weeks), fever, and treated with intravenous antibiotics
H. Tetanus confirmed by medical doctor, with three of the following: trismus, opisthotonus, risus sardonicus, nuchal rigidity
I. Kaposi sarcoma (KS): clinical diagnosis; pink to black papules, macules, plaques, or nodules typical of KS
J. Gastroenteritis: fever and diarrhea treated with antibiotics
K. Fever of unknown origin after excluding all of the above

RESULTS

A total of 140 cases met the criteria for severe maternal peripartum infection, representing 36% of all 386 cases of severe maternal morbidity and maternal mortality that occurred at the district hospital over the 2-year observation period.

Median age was 25 years (range, 13–48 years) and more than one in five women was a teenager. Median parity was two (range, 0–9). Fifteen women (11%) had not attended any antenatal care and only 22 (16%) had met the recommended number of four antenatal visits. Fifty-one infections (36%) occurred in women with unwanted pregnancies (Table 1).

More than half (56% [79 of 140]) of peripartum infections were obstetric infections; more than one third (38% [53 of 140]) were nonobstetric infections. In eight cases, insufficient information was available to differentiate between obstetric and nonobstetric infection. HIV status was known for 128 women (91%), among whom 68 (53%) were HIV-positive. HIV prevalence in women with nonobstetric infections (58.5%) was considerably higher compared with women with obstetric infections (39.2%) (Table 2).

Fifteen of 23 infection-related maternal deaths (65%) were the result of nonobstetric infections and classified as "indirect." Seven deaths were classified as "direct"; one case could not be classified as a result of incomplete information. Among the 23 women who died, 15 (65%) were HIV-positive, five (22%) HIV-negative, and three (13%) had unknown HIV status. HIV-positive women were more than three times as likely to die compared with HIV-negative women (odds ratio [OR] 3.1, confidence interval [CI] 1.1–9.2; $P=.03$) (Table 2).

Table 1. Characteristics of Women Included in the Study (n=140)

Characteristic	No. (%)*	HIV Status			Thyolo Maternal Population [% (95% CI)]
		Positive	Negative	Unknown	
Age (y)					31.3 (combined)†
Younger than 20	30 (21)	2	21	7	
20 to younger than 25	38 (27)	21	14	3	
25 to younger than 30	32 (23)	23	8	1	30.7†
30 or older	40 (29)	22	17	1	27†
Parity					
0	30 (21)	8	20	2	NA
1–4	67 (48)	40	22	5	
More than 4	38 (27)	19	18	1	
Unknown	5 (4)	1	0	4	
Antenatal clinic attendance					
0	15 (11)	5	4	6	7‡
1 or more	104 (74)	52	51	1	93‡
No. of visits					
4 or more	22 (16)	14	8	0	57‡
Unknown	21 (15)	11	5	5	NA
Attitude toward pregnancy					
Wanted and planned	46 (33)	22	23	1	
Wanted but unplanned	14 (10)	5	9	0	
Unwanted	51 (36)	29	19	3	
Unknown	29 (21)	12	9	8	
Traditional birth attendant involved					
Yes	16 (11)	6	7	3	21.3 (16.8–26.4)†
No	114 (81)	57	51	6	78.7†
Unknown	10 (7)	5	2	3	NA
Health center involved					
Yes	67 (48)	30	35	2	32 (26.8–37.6)†
No	66 (47)	34	25	7	68†
Unknown	7 (5)	4	0	3	NA

HIV, human immunodeficiency virus; CI, confidence interval; NA, not available.
* Values may not add up to 100% because of rounding.
† Data taken from baseline report for the Community-Based Maternal and Newborn Care Learning Program, March 2008.
‡ Data taken from World Health Organization Malawi country profile on maternal and newborn health.

In four cases no diagnosis was recorded in the medical files and we resorted to retrospectively applying the criteria shown in Panel 1 (one puerperal sepsis, one septic abortion, two fever of unknown origin). In all other cases, the clinical diagnosis corresponded with these criteria. Puerperal sepsis and pneumonia were the first and second most frequent types of infection. Among the 56 women who sustained puerperal sepsis, 52 (93%) survived (case fatality rate 7%). By contrast, only 10 (59%) of 17 women with pneumonia survived (case fatality rate 41%). All of eight tuberculosis cases occurred in HIV-positive women. Women with nonobstetric infections were four times more likely to die than women with obstetric infections (OR 4.1, CI 1.5–10.8, P=.004) (Table 2).

Our multivariable logistic regression model confirmed nonobstetric infection as the most important explanatory variable for mortality (adjusted OR 4.2, 95% CI 1.5–11.7). (This result did not differ significantly if an exact logistic regression model was fitted: adjusted OR 4.1, 95% CI 1.4–13.4). Being HIV-positive and on antiretroviral therapy was not independently associated with mortality (adjusted OR 0.5, 95% CI 0.1–2.7) but there was an independent association between mortality and being HIV-positive but not on antiretroviral therapy (adjusted OR 3.0, 95% CI 1.1–8.6) (Table 3).

Of 12 women with unknown HIV status, nine (75%) had not attended any antenatal clinic and attendance was unknown for two; one had attended but had not been tested (reason unknown). Of the 68 women who tested HIV-positive, eight (12%) were only tested after the complication already had occurred. Of the other 60, the exact timing of the test was unknown in five cases (8%); 20 women (33%) had tested positive before pregnancy, three (5%) had tested positive during the first trimester, and 32 (53%) had tested positive later during pregnancy. These latter 32 women had not attended antenatal clinics

Table 2. Causes of Severe Maternal Infection and Human Immunodeficiency Virus Prevalence (n=140)

Type of Infection	n (%)	HIV-Positive [n (%)] (n=68)	Case Fatality			Case Fatality Rate [% (95% CI)]
			HIV-Positive	HIV-Negative	HIV Status Unknown	
Direct (obstetric) causes						8.9 (4.0–16.7)
Puerperal sepsis	56 (40.0)	24 (42.9)	3	1	0	
Wound infection	10 (7.1)	1 (10.0)	0	0	0	
Septic abortion	8 (5.7)	4 (50.0)	0	0	0	
Tetanus	2 (1.4)	0 (0)	0	1	0	
Fever of unknown origin	2 (1.4)	2 (100)	1	0	0	
Other direct causes*	1 (0.7)	0 (0)	0	0	1	
Total direct	79 (56.4)	31 (39.2)	4	2	1	
Indirect (nonobstetric) causes						28.3 (17.4–41.5)
Pneumonia	17 (12.1)	13 (76.5)	6	1	0	
Bacterial meningitis	8 (5.7)	3 (37.5)	2	1	2	
Tuberculosis	8 (5.7)	8 (100)	0	0	0	
Severe malaria	11 (7.9)	0 (0)	0	0	0	
Kaposi sarcoma	4 (2.9)	4 (100)	2	0	0	
Gastroenteritis	1 (0.7)	1 (100)	0	0	0	
Other indirect causes†	4 (2.9)	1 (25.0)	0	1	0	
Total indirect	53 (37.9)	31(58.5)	10	3	2	
Unknown	8 (5.7)	6 (75.0)	1	0	0	

HIV, human immunodeficiency virus; CI, confidence interval.
* Sepsis arising from an intrauterine death.
† One case of liver cirrhosis likely resulting from hepatitis B, one case suggestive of TB but not fulfilling criteria, one case of epilepsy, and one case of meningitis of unclear origin in an HIV-negative patient.

during the first trimester. Of the 68 HIV-positive women, 16 women (16 of 68 [24%]) had already started antiretroviral therapy before pregnancy. None of the remaining 52 women had a record of an antenatal clinical assessment for treatment eligibility; 29 (56%) had a CD4 result recorded in their personal antenatal record book. Of these 29 women, 13 (45%) had a CD4 count below 250 cells/mm^3 and were thus eligible for antiretroviral therapy. Of these 13 women, two died before or within 3 months of the start of treatment.

Table 3. Outcome of Univariable and Multivariable Analysis for the Association Between Mortality and Covariables

	Univariable Analysis	Multivariable Analysis
Age younger than 20 y	0.5 (0.1–1.8)	
Nonobstetric infection	4.1 (1.5–10.8)	4.2 (1.5–11.7)
Nulliparity	0.5 (0.2–1.7)	
HIV-negative	Reference	Reference
HIV-positive not on ART	3.3 (1.2–8.6)	3.0 (1.1–8.6)
HIV-positive on ART	0.8 (0.1–3.9)	0.5 (0.1–2.7)
Health center involved	0.9 (0.3–2.3)	
No antenatal care visits	1.2 (0.2–6.1)	
Traditional birth attendant involvement	2.6 (0.7–9.2)	

HIV, human immunodeficiency virus; ART, antiretroviral therapy. Data are adjusted odds ratio (95% confidence interval).

DISCUSSION

Our study found that obstetric infections were more common than nonobstetric infections, but nonobstetric infections were more likely to result in maternal mortality. In addition, we found that HIV increases the risk of acquiring both obstetric and nonobstetric infections. Moreover, HIV-positive women are at a higher risk of death once infection is acquired, but uptake of antiretroviral therapy reduces this risk dramatically.

Our results illustrate that achieving a reduction in HIV-related maternal mortality and morbidity remains a challenge despite scaled-up access to antiretroviral therapy. Missed opportunities occur in different steps of the HIV treatment protocol: some women do not attend antenatal services; many do not attend in the first trimester; a few women are not tested despite attending antenatal care; finally, among those who tested HIV-positive, the procedure to establish eligibility for antiretroviral therapy by CD4 in this resource-limited setting is complicated, resulting in considerable delay in establishing eligibility. The result is that only a minority of women starts treatment early in pregnancy.

Delays in starting treatment are the result of patient-related factors (eg, not attending antenatal care until later in pregnancy) as well as factors related to the health system (eg, shortages of HIV tests, CD4

reagents and other supplies, the need to transport CD4 samples to a central laboratory and report results back to the health services). Possible solutions to reduce these delays include promoting early antenatal attendance; increased access to point-of-care CD4 testing, which will reduce transport needs and losses to follow-up[23]; and measures to prevent stock ruptures.

The recently simplified World Health Organization protocol for prevention of mother-to-child transmission recommends that antiretroviral therapy be initiated in all HIV-positive pregnant women regardless of clinical or immunologic criteria and continued throughout pregnancy and breast feeding.[24] This protocol, which has not yet been implemented in Malawi and a number of other resource-limited, high HIV burden countries, would contribute substantially to reducing delays in establishing antiretroviral therapy initiation among pregnant women.

The question remains whether women would then need a CD4 count to assess eligibility postpregnancy. There is increasing evidence to suggest that provision of antiretroviral therapy at higher CD4 counts is justifiable for medical, public health, and human rights reasons and the potential to keep all women on treatment postdelivery is being discussed by experts in Malawi and several other countries.[25,26] In this way, the need to perform CD4 counts would be removed. The extra investment needed to implement this option may be cost-effective as a result of reduced laboratory costs, reduced costs associated with a simplified management approach that would allow antiretroviral therapy among pregnant women to be overseen by less trained health cadres, and reduced attrition and mortality among women who have to wait for or never get a CD4. The findings of this study lend support to the argument that such an approach would contribute to reducing current and future (maternal) mortality.

The high proportion of infections occurring in women with unwanted pregnancies and teenagers underlines the need to increase access to acceptable and convenient family planning methods. In this respect, many obstacles have yet to be overcome; some health workers still promote "abstinence" instead of offering family planning, others will only offer family planning to women beyond adolescence, and yet others are uncomfortable to offer family planning methods in addition to promoting condom use out of fear of spreading double messages.

Our study has several limitations. First, there may be a bias toward recording obstetric infections compared with nonobstetric infections and infections later in pregnancy compared with early infections, because infections in the obstetric departments may have been included in the study more promptly. Second, like all observational studies, our analysis is subject to potential bias resulting from unmeasured confounding and missing data. Third, our study was conducted in a setting with a high incidence of HIV infection and nonobstetric infections, and thus the generalizability of our findings may be limited beyond such contexts. Fourth, our relatively small sample size means that although the overall estimates of the adjusted association between mortality and nonobstetric infection are statistically significant, there is considerable variability around the estimates. Finally, our study relies on deaths recorded at the health facility and thus was unable to account for out-of-facility deaths such as septic abortions as a complication of unsafe abortions carried out in the community. Although we had foreseen that including clinical presentations of malaria without laboratory confirmation could lead to an overestimation of the incidence of this disease, only 11 cases of severe malaria were included in the study.

Untreated HIV infection and nonobstetric infections are independently associated with maternal mortality. Prompt treatment of HIV and nonobstetric infections in pregnant women must be prioritized to reduce maternal mortality. Recent arguments have been made to suggest that HIV and AIDS funding should be redirected toward services to improve maternal and child health.[27] Our study provides further evidence that, in settings of high HIV prevalence, these two goals are inextricably connected.

REFERENCES

1. Hogan MC, Foreman KJ, Naghavi M, Ahn SY, Wang M, Makela SM, et al. Maternal mortality for 181 countries, 1980–2008: a systematic analysis of progress towards Millennium Development Goal 5. Lancet 2010;375:1609–23.
2. Bemelmans M, van den Akker T, Ford N, Philips M, Zachariah R, Harries A, et al. Providing universal access to antiretroviral therapy in Thyolo, Malawi through task shifting and decentralization of HIV/AIDS care. Trop Med Int Health 2010;15:1413–20.
3. Mwagomba B, Zachariah R, Massaquoi M, Misindi D, Manzi M, Mandere BC, et al. Mortality reduction associated with HIV/AIDS care and antiretroviral treatment in rural Malawi: evidence from registers, coffin sales and funerals. PLoS One 2010;5:e10452.
4. Jahn A, Floyd S, Crampin AC, Mwaungulu F, Mvula H, Munthali F, et al. Population-level effect of HIV on adult mortality and early evidence of reversal after introduction of antiretroviral therapy in Malawi. Lancet 2008;371:1603–11.
5. Semprini AE, Castagna C, Ravizza M, Fiore S, Savasi V, Muggiasca ML, et al. The incidence of complications after caesarean section in 156 HIV-positive women. AIDS 1995;9:913–7.

6. Louis J, Landon MB, Gersnoviez RJ, Leveno KJ, Spong CY, Rouse DJ, et al. Perioperative morbidity and mortality among human immunodeficiency virus infected women undergoing cesarean delivery. Obstet Gynecol 2007;110:385–90.
7. Lapaire O, Irion O, Koch-Holch A, Holzgreve W, Rudin C, Hoesli I. Increased peri- and post-elective cesarean section morbidity in women infected with human immunodeficiency virus-1: a case-controlled multicenter study. Arch Gynecol Obstet 2006;274:165–9.
8. Moodley J, Pattinson RC, Baxter C, Sibeko S, Abdool KQ. Strengthening HIV services for pregnant women: an opportunity to reduce maternal mortality rates in Southern Africa/sub-Saharan Africa. BJOG 2011;118:219–25.
9. Walson JL, Brown ER, Otieno PA, Mbori-Ngacha DA, Wariua G, Obimbo EM, et al. Morbidity among HIV-1-infected mothers in Kenya: prevalence and correlates of illness during 2-year postpartum follow-up. J Acquir Immune Defic Syndr 2007;46:208–15.
10. Ahmad H, Mehta NJ, Manikal VM, Lamoste TJ, Chapnick EK, Lutwick LI, et al. Pneumocystis carinii pneumonia in pregnancy. Chest 2001;120:666–71.
11. Bryant AE, Genc M, Hurtado RM, Chen KT. Pulmonary Kaposi's sarcoma in pregnancy. Am J Perinatol 2004;21:355–63.
12. Pollack RN, Sklarin NT, Rao S, Divon MY. Metastatic placental lymphoma associated with maternal human immunodeficiency virus infection. Obstet Gynecol 1993;81:856–7.
13. McIntyre J. Mothers infected with HIV. Br Med Bull 2003;67: 127–35.
14. National Statistical Office. Malawi Demographic and Health Survey 2004. Available at: http://www.measuredhs.com/pubs/pdf/FR175/FR-175-MW04.pdf. Retrieved March 1, 2011.
15. van den Akker T, Mwagomba B, Irlam J, van Roosmalen J. Using audits to reduce the incidence of uterine rupture in a Malawian district hospital. Int J Gynaecol Obstet 2009;107:289–94.
16. Beltman J, van den Akker T, Lam E, Moens M, Kazima J, Massaquoi M, et al. Repetition of a sisterhood survey district level in Malawi: the challenge to achieve MDG 5. BMJ Open 2011; May 5, 2011 [Epub ahead of print].
17. Chiphangwi JD, Zamaere TP, Graham WJ, Duncan B, Kenyon T, Chinyama R. Maternal mortality in the Thyolo District of southern Malawi. East Afr Med J 1992;69:675–9.
18. van den Akker T, van Rhenen J, Mwagomba B, Lommerse K, Vinkhumbo S, van Roosmalen J. Reduction of severe acute maternal morbidity and maternal mortality in Thyolo district, Malawi: the impact of obstetric audit. PLoS One 2011; June 3, 2011 [Epub ahead of print].
19. World Health Organization. WHO case definitions of HIV surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children. Geneva (Switzerland): World Health Organization; 2007.
20. Mehta CR, Patel NR. Exact logistic regression: theory and examples. Stat Med 1995;14:2143–60.
21. Republic of Malawi, Ministry of Health, National Health Sciences Research Committee. Summary guidelines for writing a research proposal. Lilongwe (Malawi): Republic of Malawi, Ministry of Health, National Health Sciences Research Committee; 2001.
22. Republic of Malawi, National Research Committee of Malawi. Procedures and guidelines for the conduct of research in Malawi. Lilongwe (Malawi): Republic of Malawi, National Research Committee of Malawi; 2002.
23. Zachariah R, Reid SD, Chaillet P, Massaquoi M, Schouten EJ, Harries AD. Viewpoint: Why do we need a point-of-care CD4 test for low-income countries? Trop Med Int Health 2011;16: 37–41.
24. World Health Organization. Antiretroviral drugs for treating pregnant women and preventing HIV-infection in infants. Recommendations for a public health approach. 2010 version. Geneva (Switzerland): World Health Organization; 2010.
25. Ford N, Calmy A, Hurst S. When to start antiretroviral therapy in resource-limited settings: a human rights analysis. BMC Int Health Hum Rights 2010;10:6.
26. Alcorn K. Malawi plans 'test and treat' approach for pregnant women to cut mother-to-child HIV transmission. XVIII International AIDS Conference Vienna; 2010. Available at: www.aidsmap.com/Malawi-plans-test-and-treat-approach-for-pregnant-women-to-cut-mother-to-child-HIV-transmission/page/1494940/. Retrieved March 19, 2011.
27. Denny CC, Emanuel EJ. US health aid beyond PEPFAR: the Mother & Child Campaign. JAMA 2008;300:2048–51.