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Sex. Transm. Inf. 2005;81:294-302
doi:10.1136/sti.2002.004077

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TROPICAL MEDICINE

Sexually transmitted infections in pregnancy: prevalence, impact on pregnancy outcomes, and approach to treatment in developing countries

S Mullick, D Watson-Jones, M Beksinska, D Mabey

Sex Transm Infect 2005;**81**:294–302. doi: 10.1136/sti.2002.004077

Sexually transmitted infections (STIs) are common in the developing world. Management of STIs in pregnancy in many developing countries has, however, been complicated by the lack of simple and affordable diagnostic tests. This review examines the prevalence and impact on pregnancy outcome of STIs in developing countries and recommends approaches to management of STIs in pregnancy for resource poor settings.

experts and reviewers suggested additional literature including project reports and published material for review.

CLINICAL PRESENTATION AND CONSEQUENCES IN PREGNANCY

Examining the impact of STI on pregnancy outcome is difficult. For ethical reasons it is not usually possible to prospectively study the effects of an untreated STI once the diagnosis has been made. Many studies have therefore been retrospective in design, where data have been collected on STIs and birth outcomes at or after delivery, and where it may have been difficult to control for other confounding factors earlier in the pregnancy that affect pregnancy outcome.

ANTIBIOTIC TREATMENT AND PREGNANCY OUTCOME

Perhaps the best evidence of the impact of maternal infection on pregnancy outcome is from studies of presumptive antibiotic treatment in pregnancy. A randomised controlled trial in the United States showed that treatment with erythromycin between 26 and 30 weeks gestation reduced the incidence of premature rupture of membranes from 16–6% ($p < 0.001$).⁷ Two studies in Africa have also shown a benefit of antibiotic therapy in pregnancy. A single dose of ceftriaxone 250 mg intramuscularly given to pregnant women in Nairobi between 28 and 32 weeks gestation participating in a randomised, double blind placebo controlled clinical trial led to a significant increase in mean birth weight (3.21 kg *v* 3.06 kg, $p = 0.01$), and non-significant reductions in the incidence of low birth weight (LBW) (4.0% *v* 9.2%, $p = 0.08$) and of postpartum endometritis (3.8% *v* 10.4%, $p = 0.05$).⁸ In a randomised clinical trial in the Rakai District of Uganda, a single oral dose of azithromycin 1 g, cefixime 400 mg, and metronidazole 2 g, which led to a reduced prevalence of STIs, was associated with significant reductions in the incidence of neonatal death (rate ratio (RR) 0.83, 95% CI 0.71 to 0.97) and low birth weight (RR 0.68, 0.53 to 0.86) and a

Sexually transmitted infections (STI) have been associated with a number of adverse pregnancy outcomes including spontaneous abortion, stillbirth, prematurity, low birth weight (LBW), postpartum endometritis, and various sequelae in surviving neonates.

Preterm birth and low birth weight are major determinants of infant morbidity and mortality, especially in developing countries where neonatal intensive care facilities are not often available. In one cross sectional study in Nairobi, Kenya, the incidence of LBW (<2500 g) was 7.5%, and the perinatal mortality in LBW children was 222 per 1000 live births.¹

STIs, including HIV, are believed to be of particular importance in determining pregnancy outcome in the developing world because the prevalence of infection is so high.² Cross sectional, randomised trials and retrospective cohort studies of antenatal clinic attenders in Africa have found that up to 40% of pregnant women have trichomoniasis and bacterial vaginosis, 2.5–17% have serological evidence of syphilis,^{3–6} while the prevalence of gonorrhoea and chlamydia ranges from 2–7% and 3–29%, respectively (table 1).

Most published studies on the relation between STIs and pregnancy outcome have come from developed countries. This paper reviews the evidence from both developed and developing countries, but focuses particularly on the few developing country studies. Literature was identified using several methods: the Pubmed database was searched using keywords “sexually transmitted infections,” “pregnancy,” and “antenatal.” Abstracts were first reviewed to select publications that reported on pregnancy outcomes. Papers reporting studies in developing countries and those most recently published were selected for review. WHO and CDC websites were also searched for relevant guidelines. Key

See end of article for authors' affiliations

Correspondence to: Saiqa Mullick, The Population Council, Frontiers in Reproductive Health, Hyde Park Lane Manor, EG001 Edinburgh Gate, Box 411744, Craighall 2024, Johannesburg, South Africa; smullick@pcjoburg.org.za

Accepted for publication 12 November 2004

Table 1 Prevalence of selected sexually transmitted infections (STI) in pregnant women in developing countries

STD	Prevalence (%)	Reference	Country	Sample size	Asymptomatic (%)
Syphilis	2.4	Sullivan, 2003 ³	Vanuatu	547	4.0
	7	Fonck, 2000 ⁴	Kenya	621	
	3.3	Gray, 2001 ⁵	Uganda	4033	
	6.5	Rastogi, 2003 ¹⁰⁹		350	
	3.8	Latif, 1999 ¹¹⁰	Zimbabwe	1656	
	5*	Msuya, 2002 ¹¹¹	Tanzania	382	
	2.5–17	Watson-Jones, 2002 ⁶	Tanzania	380	
<i>Chlamydia trachomatis</i>	21.5	Sullivan, 2003 ³	Vanuatu	347	4.3
	9	Fonck, 2000 ⁴	Kenya	621	
	6.2	Blankhart, 1999 ¹¹²	Central Africa Republic	481	
	2.7	Gray, 2001 ⁵	Uganda	4033	
	20.8	Plummer, 1987 ²⁰	Kenya	1013	
	18.8	Rastogi, 2003 ¹⁰⁹		350	
	5.3	Latif, 1999 ¹¹⁰	Zimbabwe	1656	
	10.1	Farley, 2003 ²⁴	United States	1631	
	7–31	Marai, 2001 ¹¹³		77	
Gonorrhoea	5.9	Sullivan, 2003 ³	Vanuatu	347	1.7
	1.7	Gray, 2001 ⁵	Uganda	4033	
	6.7	Plummer, 1987 ²⁰	Kenya	1013	
	3.9	Latif, 1999 ¹¹⁰	Zimbabwe	1656	
	2.3	Farley, 2003 ²⁴	United States	1631	
	3.1	Blankhart, 1999 ¹¹²	Central Africa Republic	481	
	7	Fonck, 2000 ⁴	Kenya	621	
	10–20	Shulz, 1987 ¹¹		621	
Bacterial vaginosis	48.5	Gray, 2001 ⁵	Uganda	4033	4.5
	1.7	Rastogi, 2003 ¹⁰⁹		350	
	4.3	Latif, 1999 ¹¹⁰	Zimbabwe	1656	
	21.1	Blankhart, 1999 ¹¹²	Central Africa Republic	481	
	9	Fonck, 2000 ⁴	Kenya	621	
	24	Mayaud, 1998 ²⁵	Mwanza, Tanzania	660	
Trichomoniasis	27.5	Sullivan, 2003 ³	Vanuatu	347	10.7
	15.9	Gray, 2001 ⁵	Uganda	4033	
	1.7	Rastogi, 2003 ¹⁰⁹		350	
	13.0	Latif, 1999 ¹¹⁰	Zimbabwe	1656	
	9.9	Blankhart, 1999 ¹¹²		481	
	23	Fonck, 2000 ⁴	Kenya	621	
Herpes simplex virus	43.5	Rodrigues, 2002 ⁵⁵		763	0.5
	0.9	Latif, 1999 ¹¹⁰	Zimbabwe	1656	
	6.7–53.4	Mindel 2000 ⁶⁰		2616	
HIV	42.5	Latif, 1999 ¹¹⁰	Zimbabwe	1656	38.3
	15–30	Fawzi, 2002 ⁵³	African counties		
	22	Fonck, 2000 ⁴	Kenya	621	
	12.2	Blankhart, 1999 ¹¹²	Central African Republic	481	
	24.3	Ayisi, 2003 ¹¹⁴	Kenya	2466	

*5% of the syphilis prevalence also includes women who attended maternal and child health clinics and those attending family planning clinics (n = 382).

non-significant reduction in preterm delivery (RR 0.77, 0.56 to 1.05).⁵

Syphilis

Syphilis has long been known to be an important risk factor for adverse pregnancy outcome.^{9–11} The natural history of syphilis acquired in pregnancy is believed to follow the sequential stages of primary, secondary, and latent syphilis that have been observed in untreated, non-pregnant adult cases.

Left untreated, syphilis has a dramatic impact on pregnancy outcome. The consequences of untreated maternal infection include stillbirth, LBW, preterm birth and also congenital infection in a proportion of surviving infants. Historically, one third of pregnancies are believed to result in second trimester spontaneous abortion or perinatal death, one third in a congenitally infected infant, and one third in an uninfected infant.¹⁰ Data from developing countries confirm that maternal syphilis still remains an extremely important cause of perinatal morbidity and mortality.^{6 12–14} The most significant consequence of untreated syphilis in

resource poor settings is stillbirth but the infection has also been associated with LBW, preterm birth, and intrauterine growth retardation (IUGR) in Africa.^{6 15} As in developed countries, mothers with high non-treponemal test titres, as seen in earlier stages of infection, are most at risk of having an adverse pregnancy outcome.^{6 16}

The impact of untreated syphilis in pregnancy at the population level may be considerable. In a prospective population based study in Malawi and a retrospective cohort study in Tanzania, 21% of perinatal deaths, 26–51% of stillbirths, 24% of preterm live births, 17% of all adverse pregnancy outcomes, and 11% of neonatal deaths have been attributed to untreated high titre (a rapid plasma reagin (RPR) test titre of $\geq 1:8$ and a positive treponemal assay) maternal syphilis.^{6 15}

Chlamydia trachomatis

Chlamydia trachomatis infection in pregnancy leads to cervicitis and cervical discharge but a high proportion of women are asymptomatic. Information on the impact of untreated chlamydial infection on pregnancy outcome has mainly come

from non-developing countries. The infection has been associated with stillbirth, premature delivery, premature rupture of the membranes, and LBW. Three large prospective studies of the impact of *C trachomatis* on pregnancy outcome have been reported from the United States. A study of 801 women enrolled between 22 weeks and 30 weeks gestation found that *C trachomatis* infection was associated with both intrauterine growth retardation (adjusted odds ratio (aOR) 2.4, 95% CI 1.3 to 4.2) and preterm delivery (aOR 1.6, 95% CI 1.0 to 2.5).¹⁷ A study of 534 women found that *C trachomatis* infection was associated with low birth weight (aOR 2.7, 95% CI 1.3 to 5.7), premature rupture of membranes (aOR 2.4, 95% CI 1.1 to 5.4) and preterm labour (<34 weeks) (aOR 4.0, 95% CI 1.7 to 9.2).¹⁸ However, a third study involving 1365 women found no association between cervical *C trachomatis* infection and adverse pregnancy outcome.¹⁹ In Nairobi, *C trachomatis* infection was found to be associated with postpartum endometritis.²⁰

Maternal *C trachomatis* infection can also affect the neonate, leading to infant pneumonia and ophthalmia neonatorum (ON)²¹; 30–50% of infants born to infected women will develop chlamydial ON, which is usually less severe than gonococcal ON. Cross sectional and prospective studies in Nairobi and the Gambia found the incidence of chlamydial ON to be 8.1 and 2.7 per 100 live births, respectively.^{22–23}

Neisseria gonorrhoeae

The clinical pattern of gonorrhoea in pregnant women is similar to non-pregnant women, with up to 45% of cases being asymptomatic.²⁴ In an antenatal clinic in Tanzania, symptoms of vaginal discharge, itching, and lower abdominal pain were no more common in women with than in women without cervical infection with *Neisseria gonorrhoeae* or *C trachomatis*.²⁵ Documented sequelae of untreated *N gonorrhoeae* infection in pregnancy noted in case reports include preterm delivery, premature rupture of the membranes, LBW, postpartum endometritis, and gonococcal ON.²⁶

A case-control study of women delivering in hospital in Nairobi, Kenya, enrolled 166 women who delivered infants weighing <2500 g, and 175 control women. *N gonorrhoeae* was isolated from 11% of cases and 4% of controls (OR 2.9, 95% CI 1.2 to 7.2).²⁷ The authors concluded that gonorrhoea was responsible for 14% of cases of LBW in this population. A prospective study in South Africa looked at the relation between gonorrhoea diagnosed at the first antenatal clinic attendance and pregnancy outcome in 167 women. Five of nine women with gonorrhoea delivered a preterm infant compared with 24 of 158 uninfected women (RR 6.0, 95% CI 1.5 to 34.0). Women with gonorrhoea delivered significantly smaller babies (mean weight 2252 g v 2,970 g, $p < 0.005$).¹³ Gonorrhoea has also been associated with upper genital tract infection in postpartum women in a prospective study in Kenya.²⁰

Gonococcal ON occurs in 30–50% of infants born to infected mothers. The incidence of gonococcal ON was 3.6 per 100 live births in Nairobi and 2.1% in the Gambia.^{22–23} Gonococcal ON is a severe disease that may lead to corneal ulceration or perforation, and hence to blindness. A large controlled clinical trial in Nairobi found that ON could be prevented by instilling either 1% silver nitrate solution, or 1% tetracycline ointment into the eyes of infants at the time of delivery.²⁸ However, since that study was conducted, the prevalence of tetracycline resistant strain of *N gonorrhoeae* has increased dramatically in many parts of the developing world and 2.5% povidone-iodine solution appears to be an effective alternative.²⁹

Bacterial vaginosis

Bacterial vaginosis (BV) is the most prevalent cause of vaginal discharge in developing countries. Up to 50% of pregnant women have been found to have BV in sub-Saharan Africa.^{5–25–30} In developed countries it has been implicated as a cause of preterm birth, LBW, premature rupture of the membranes (PROM), postpartum sepsis, and spontaneous miscarriage. Treatment with oral metronidazole or clindamycin has been shown to reduce the incidence of preterm delivery in women with BV in case-control, prospective, and controlled clinical trials.^{31–37} In the clinical trial in Rakai, treatment with single dose metronidazole, combined with azithromycin 1 g and cefixime 400 mg, reduced the incidence of LBW and neonatal death.⁵ In a multicentre randomised placebo controlled trial in Indonesia, 2% clindamycin vaginal cream administered to women with BV at 14–26 weeks gestation, the results showed that this was effective for treating BV but did not reduce the incidence of preterm delivery or LBW as it did not eradicate upper genital tract infection.³⁸

There have been few studies of the impact of BV on pregnancy outcomes in developing countries. BV was associated with premature delivery in a prospective study in Indonesia, especially when diagnosed early in the second trimester between 16–20 weeks gestation.³⁹ No effect of BV was seen later in pregnancy, in contrast with studies in the United States. BV may have most impact on pregnancy when combined with another potential risk factor such as previous preterm or LBW delivery or when there is co-infection with *Trichomonas vaginalis*.^{34–40}

Trichomoniasis

Trichomonas vaginalis infection is highly prevalent in antenatal clinic (ANC) attenders in many developing countries (table 1). The WHO estimates that *T vaginalis* accounts for approximately half of all curable sexually transmitted diseases worldwide.² The primary symptom of trichomoniasis in women is vaginal discharge^{41–42} but approximately half of all women will be asymptomatic.^{25–42–43}

T vaginalis has been associated with preterm delivery and LBW in prospective cross sectional and cohort studies.^{41–44–46} Similar findings from a case-control study have been observed in Africa where *T vaginalis* in pregnant Congolese women was associated with delivery of a LBW infant.⁴⁷ It has been estimated that *T vaginalis* may be responsible for 20–25% of cases of premature delivery in Africa.⁴⁸ However, treatment of asymptomatic *T vaginalis* infection with metronidazole in a randomised controlled trial failed to reduce the incidence of preterm delivery in mothers in the United States.⁴⁹

Herpes simplex virus

Herpes simplex virus (HSV) type 2 has an extremely high prevalence in resource constrained settings, especially in sub-Saharan Africa where up to 75% of women aged over 25 years may be infected.^{50–51} The proportion of genital ulcers caused by HSV-2 is believed to be increasing in Africa^{52–53} and this may be due to its synergistic relation with HIV infection. HSV has been shown to be associated with HIV acquisition in a cross sectional population based sample, an unmatched case-control study nested within a randomised trial cohort and a meta-analysis of 31 studies^{54–56} and clinical recurrences are more frequent in HIV infected individuals. The virus is usually vertically transmitted to the neonate from an infected mother during delivery. As such, the optimal strategy for reducing the morbidity of neonatal herpes is to prevent the neonate from acquiring HSV infection at delivery. A meta-analysis of prospectively designed, randomised, clinical trials detailing the use of aciclovir in pregnancy for women with HSV found that antiviral prophylactic treatment with aciclovir beginning at 36 weeks gestation was effective in

Table 2 Estimated risk and timing of mother to child transmission of HIV

Timing	Transmission rate (%)		
	No breastfeeding	Breastfeeding through 6 months	Breastfeeding through 18–24 months
During pregnancy	5–10	5–10	5–10
During labour	10–20	10–20	10–20
Through breastfeeding			
Early (first 2 months)		5–10	5–10
Late (after 2 months)		1–5	5–10
Overall	15–30	25–35	30–45

Source: De Cock *et al.*⁷¹

reducing clinical HSV recurrences at the time of delivery, caesarean delivery, recurrent genital herpes, and the risk of viral shedding at delivery.⁵⁷

Neonatal herpes is a severe illness presenting with pulmonary disease, seizures, fever, intracranial findings, and a high case fatality rate following contact with infected genital secretions during delivery.⁵⁸ One prospective cohort study in the United States found that 5% of women from whom HSV was isolated at the time of labour had neonates with HSV infection.⁵⁹ Risks of viral shedding and transmission to the infant are greatest when the mother has primary genital lesions during delivery, especially if she acquires infection towards the end of her pregnancy,⁶⁰ in which case 5–50% of infants will be infected,^{61 62} and lower for recurrent herpes. There are few data on the proportion of pregnant women in developing countries who acquire HSV during pregnancy or on the incidence or prevalence of neonatal HSV.

Human immunodeficiency virus

In many African settings, HIV is now the most prevalent STI in pregnant women. Overall, 15–30% of women attending prenatal care clinics are infected with HIV.⁶³ UNAIDS reports prevalences between 18–39% in southern Africa. In east Africa prevalence seems to be declining from 30% in Uganda in 1990 to 9% in 2002. In much of west and central Africa, HIV prevalence remains lower than other parts of the continent.⁶⁴

As well as sequelae in the mother, maternal HIV infection, examined in prospective cohort and cross sectional studies, has an independent effect on birth outcome, especially where there is also chorioamnionitis.^{65 66} HIV has been associated in case-control and prospective studies with both LBW and stillbirth⁶⁷ and with spontaneous abortion.¹³ An increased risk of preterm delivery in HIV positive mothers compared to HIV negative mothers has also been observed.^{68 69} The impact of HIV on pregnancy outcome is therefore likely to be significant in high prevalence settings. With an HIV seroprevalence of 16%, 19% of adverse pregnancy outcomes in a large prospective study in Nairobi were attributable to HIV.⁷⁰

The most significant sequela of maternal HIV infection in pregnancy is mother to child transmission (MTCT) of HIV (table 2). Without intervention, rates of MTCT range from 15–30% without breastfeeding and rise to 30–45% with prolonged breastfeeding.⁷¹ MTCT is responsible for 90% of HIV infection in children worldwide.⁷² It is estimated that 5–10% of MTCT of HIV results from intrauterine transmission, 10–20% takes place during delivery, while post-delivery transmission accounts for 5–20%.⁷³ In Africa, duration of breastfeeding,⁷⁴ elevated breast milk sodium levels,⁷⁵ mastitis, maternal viral load,⁷⁶ and non-exclusive breastfeeding⁷⁷ are all risk factors for HIV transmission via breast milk. The risk of MTCT of HIV in the breastfed population is estimated to range from 25% to 48%.⁷⁸

RECOMMENDATIONS FOR MANAGEMENT IN PREGNANCY IN RESOURCE POOR SETTINGS

Table 3 summarises the recommended management of STIs in pregnancy in resource poor settings.

Screening for STI in pregnancy—syphilis and HIV

There are two main situations where screening for the management of STI in pregnancy is an option for resource poor countries. This is because there are cheap screening tests available for the diagnosis of both maternal syphilis and HIV infection.

Given the impact maternal syphilis has on pregnancy outcome, screening and treatment of syphilis in pregnant women at least once during pregnancy should be performed. In most resource poor developing countries, the RPR test is the most common screening assay. This test is cheap and simple although, like other non-treponemal tests, it is susceptible to false positive reactions from other maternal infections or autoimmune disease. These include common conditions like pregnancy, infection, measles, and malaria. Biological false positive (BFP) reactions are common in malaria endemic areas and may account for up to 30% of reactive RPR tests.⁶ Although the CDC recommends screening at the first ANC visit and again in the third trimester in high prevalence areas,⁷⁹ many developing countries are only able to screen once during pregnancy owing to late attendance of women for antenatal care, the long turn around times from taking blood to getting results, and the cost of screening more than once. The WHO and CDC recommended treatment regimen is a single intramuscular dose of 2.4 MU benzathine penicillin for primary, secondary, and early latent syphilis infection, with three doses for late latent syphilis or syphilis of unknown duration.^{79 80} This is often not implemented since many women fail to re-attend for treatment or attend too late in pregnancy to complete the course of treatment.^{81 82}

A South African study where women were asked to come back 14 days after testing for results found that the mean number of days to return was 20 and almost a fifth of women were not notified.⁸³ Onsite screening, where RPR testing is done on site at the ANC and treatment is given at the same visit, does at least assure that women get at least one dose of benzathine penicillin in pregnancy at the time of testing and avoids delays in initiating treatment because of long turn around times for results and women not returning for results.^{2 84} Another South African study suggests that pregnancy outcome is better in women who receive three rather than one dose of benzathine penicillin, although this may have been because women receiving fewer than three doses were mostly treated late in the third trimester.^{16 84} Pregnancy outcomes were similar for women treated for syphilis with single dose benzathine penicillin compared to women without serological syphilis in a recent prospective cohort study in Tanzania.⁸⁵ This intervention was found to be extremely cost effective,⁸⁶ but did not address late congenital

Table 3 WHO recommended drug treatment for STIs in pregnancy

STI	Treatment in pregnancy
Syphilis	Benzathine penicillin 2.4 million units by intramuscular injection. Three weekly doses recommended in latent syphilis of unknown duration.
Chlamydia	Erythromycin 500 mg orally four times a day for 7 days, or azithromycin 1 g orally single dose, or amoxicillin 500 mg orally three times a day for 7 days.
Gonorrhoea	Cefixime 400 mg orally as single dose, or ceftriaxone 125 mg by intramuscular injection.
Bacterial vaginosis and trichomoniasis	<i>Preferable after the first trimester</i> Metronidazole 200 mg or 250 mg orally three times a day for 7 days, or metronidazole gel 0.75%, one full applicator (5 g) intravaginally twice a day, or clindamycin 300 mg orally twice a day for 7 days. For trichomoniasis 2 g metronidazole stat recommended as first line treatment.
HSV-2	<i>Primary infection only</i> Aciclovir 200 mg orally five times a day for 7 days, or aciclovir 400 mg orally three times a day for 7 days. <i>Recurrent infection</i> Famciclovir 125 mg orally three times a day for 5 days, or valaciclovir 500 mg twice a day for 5 days.
Cautions:	
<ul style="list-style-type: none"> ● Doxycycline, tetracycline, ciprofloxacin, norfloxacin, and ofloxacin should be avoided in pregnancy and when breast feeding. ● Erythromycin estolate is contraindicated in pregnancy because of drug related hepatotoxicity; only erythromycin base or erythromycin ethylsuccinate should be used. ● Metronidazole should be avoided in the first trimester of pregnancy 	

Source: World Health Organization.¹¹⁵

syphilis or serological cure in the mothers. Further research on what constitutes an adequate treatment regimen in pregnancy is needed.

There is evidence of the safety and efficacy of short course antiretroviral prophylaxis regimens for prevention of MTCT of HIV from a number of developing countries.^{87–90} Women who are identified as being infected during pregnancy and who have clinical indications for their own therapy should be given the appropriate regimen based on the current WHO recommendations for resource poor settings shown in table 4.^{90–92} There is evidence that viral suppression is less likely in postpartum women given nevirapine containing antiretroviral regimens in those women who received nevirapine during pregnancy.⁹³ Pregnant women should therefore now be encouraged to attend for voluntary counselling and testing (VCT) for HIV infection. Initial studies in Africa have shown that uptake of this service may be high. Zambian health employees trained in VCT counselled 17 263 pregnant women, of whom 72% were tested and 24% of those tested were HIV seropositive.⁹⁴ A large study in four African countries showed that of 22 000 antenatal clients, slightly over 13 000 (61%) received pretest counselling and 7280 (33%) were tested, although this was highly variable by centre (25–90%).⁹⁵ In Kenya and Zambia between 20–50% of women who were tested did not get their results.⁹⁵ This attrition can significantly dilute the impact of interventions for PMTCT.

Post-test counselling of an HIV positive pregnant woman will include advice on breastfeeding. The WHO policy on breastfeeding is summarised as follows.^{96–97}

- Exclusive breastfeeding should be promoted and supported for 6 months. This applies to women known not to be HIV infected and those of unknown status.
- When replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding

by HIV infected mothers is recommended; otherwise exclusive breastfeeding is recommended during the first months of life.

- To minimise the risk of HIV transmission, breastfeeding should be discontinued as soon as it is feasible, taking the woman's situation into account (including risk of replacement feeding).

Syndromic management of STIs

In the resource constrained settings of many developing countries, laboratory diagnosis to confirm the aetiology of an STI related symptom is not a practical option. Simple and cheap criteria such as Gram stained vaginal smears or clinical criteria can be used to screen for *T vaginalis* using a wet preparation or BV^{98–99}; in reality even this is beyond the reach of most ANC services in resource poor settings. With the exception of syphilis, HIV, *T vaginalis*, and BV, there are currently no cheap and reliable screening tests for other STIs. Screening using culture, ELISA, and polymerase chain reaction testing are not feasible and are too costly.

Where services are offered for the treatment of STIs in pregnancy in developing countries, this should rely on syndromic management, based on the provision of treatment for the main organisms that cause specific signs and symptoms (syndromes) associated with certain STIs. Vaginal discharge and genital ulceration are the most frequent syndromes encountered in pregnancy in developing countries. Management of STIs using this approach alleviates the need for expensive laboratory testing and helps health-care workers to standardise the treatment for each syndrome.¹⁰⁰ Syndromic management algorithms have several limitations including the fact that they will miss asymptomatic infections.¹⁰¹ There are also particular limitations with the use of syndromic management algorithms for the treatment of vaginal discharge as these are particularly poor

Table 4 Recommendations for use of antiretroviral (ARV) drugs in pregnant women in different clinical scenarios in resource constrained settings

Clinical situation	Recommendation
Newly diagnosed HIV infected pregnant women without indication for ARV treatment	<p>Mother</p> <ul style="list-style-type: none"> ● ZDV ± 3TC+NVP from 32 weeks gestation, through delivery (1), (2), (3); stop NVP and continue ZDV + 3TC for 3 days after delivery ● alternatively: ZDV + 3TC from 34–36 weeks boosted with single dose NVP at onset of labour ● alternatively: ZDV from 34–36 weeks boosted with single dose NVP at onset of labour ● Single dose NVP in settings where none of the more potent ARV combinations are feasible or available <p>Infant</p> <ul style="list-style-type: none"> ● Single dose NVP within 72 hours of delivery and one week daily ZDV (extend ZDV for a second week with a second dose of NVP 5–7 days after the first one if ZDV + 3TC + NVP was the maternal regimen and breastfeeding has been initiated) ● If delivery occurred within 2 hours of maternal single dose of NVP, infant should receive an additional dose of NVP immediately after birth as well as the routine dose within 72 hours
Newly diagnosed HIV infected women, with indications for ARV treatment, who may become pregnant	Exclude pregnancy before starting treatment. Avoid EFZ Prefer ZDV + 3TC ± NVP regimen.
Newly diagnosed HIV infected pregnant women with indications for ARV treatment	Delay start of treatment until after the first trimester of pregnancy Proceed as for non-pregnant adults (1), (2), (3) except EFV
Newly diagnosed HIV infected pregnant women, with indications for ARV treatment, who did not initiate therapy during pregnancy	In both cases proceed as for non-pregnant adults (WHO guidelines) with first line regimen recommended
<ul style="list-style-type: none"> ● received short course MTCT prophylaxis ● did not receive any MTCT prophylaxis 	Initiate ARV treatment as soon as possible, including in postpartum period
HIV infected pregnant women newly diagnosed at the time of delivery	If there is time, offer rapid test; if no time, rapid test as soon as possible (and acceptable) after delivery. If test positive, initiate post-exposure prophylaxis in infant: single dose NVP within 72 hours of delivery plus 1 week ZDV.
HIV infected women on ARV treatment for their own disease	Exclude pregnancy before starting treatment. EFV should be avoided in women who can potentially become pregnant Discontinue drugs with teratogenic potential (EFV) or with known adverse potential for the pregnant mother (d4Tiddl) Consider switching to regimens which include ZDV, 3TC or NVP

EFV, efavirenz; NVP, nevirapine; 3TC, lamivudine; ZDV, zidovudine.

(1) Start NVP with half dose for the first 2 weeks as recommended for adults in WHO guidelines.

(2) Monitor closely clinical and biochemical tolerance in the first month of ARV use

(3) Stop NVP in case of NVP associated toxicity, continue ZDV only until labour

Source: World Health Organization.⁹¹

at identifying women with cervicitis. In order to reduce the number of women with cervicitis a “risk assessment” approach has been used, and in some settings has been able to reduce the proportion of women overtreated.¹⁰¹ However, this approach still lacks sensitivity and specificity and should not be used as a diagnostic or screening tool.¹⁰⁰ The effectiveness of syndromic management also depends on the healthcare seeking behaviour of the local population, the integration of STI treatment services within ANC services, and on the efficacy of the drugs chosen. Choosing appropriate drugs for STI treatment should depend on local antibiotic sensitivities but these are not known in many resource poor settings. Syndromic management guidelines are currently under review for the management of genital HSV infection,¹⁰¹ but are unlikely to affect the current management of HSV in pregnancy unless there is evidence of genital ulceration during the pregnancy. In this situation, women would be treated for syphilis, chancroid, and HSV syndromically. There are no guidelines for prevention of neonatal HSV in most resource poor settings and there are few data on the efficacy of syndromic management regimes for preventing adverse birth outcomes.

Other strategies to control STI in pregnancy

Other strategies to reduce the impact of STI in pregnancy have included vaginal washing with chlorhexidine to reduce MTCT of HIV in Nairobi.¹⁰² This showed no overall reduction in intrapartum MTCT of HIV. There have been several studies of presumptive antibiotic treatment in pregnancy. A Kenyan trial of a single presumptive dose of cefetamet-pivoxil versus placebo in women with a previous history of LBW or stillbirth found lower rates of LBW, gonorrhoea at delivery, and postpartum endometritis in women who received the antibiotic.¹⁰³ A larger randomised mass treatment trial of a single cycle of presumptive treatment (azithromycin 1 g, cefixime 400 mg, and metronidazole 2 g) in Rakai, Uganda, resulted in significant reductions in maternal cervical and vaginal infections and infant ON.¹⁰⁴ The rates of early neonatal mortality and LBW were also significantly reduced.⁵

In neonates, the WHO recommends that all cases of conjunctivitis in the newborn should be treated for both *N gonorrhoeae* and *C trachomatis*. The recommended treatment regimen for gonococcal conjunctivitis is ceftriaxone 50 mg/kg by intramuscular injection as a single dose to a maximum of 125 mg or alternatively kanamycin 25 mg/kg as a single dose

by intramuscular injection to a maximum of 75 mg. Neonatal chlamydial conjunctivitis should be treated with erythromycin syrup, 50 mg/kg per day orally, in four divided doses for 14 days or alternatively trimethoprim 40 mg with sulfamethoxazole 200 mg orally twice a day for 14 days.¹¹⁵ Prophylactic silver nitrate, tetracycline or erythromycin eye drops are recommended for infants in populations with high prevalence of *C trachomatis* and gonorrhoea,^{104 105} although this simple intervention is rarely implemented.

Contact tracing, or partner notification, is recommended as an integral part of STI control, including the management of STI in pregnancy. There have been few evaluations of this strategy in the developing world. Studies in sub-Saharan Africa have generally shown low attendance of contacts for syphilis treatment.⁸⁶ A concerted health education campaign in Zambia managed to increase the proportion of contacts attending.¹⁰⁶ Whether this was sustained long term and what proportion were infected are not known. The social consequences of passing a contact notification slip to a sexual partner have not been measured in developing countries where gender inequality may mean that these can seriously compromise the relationship. This has been highlighted in Kenya where 10% of women who informed their partners of their HIV status experienced relationship disruption or violence.¹⁰⁷ Information on the acceptability, effectiveness, and consequences of contact tracing for syphilis and other STI in developing countries is clearly needed.

CONCLUSION

In summary, there is a high prevalence of STIs in many developing countries. These continue to have an impact on pregnancy outcome. The approach to diagnosis and management is likely to differ from country to country depending on available resources. Most developing countries rely on the syndromic approach to manage STIs in pregnancy. This approach, however, is notoriously poor in identifying infections particularly with *N gonorrhoeae* and *C trachomatis* and will miss a high proportion of infection because a significant proportion of infections are asymptomatic. Risk assessment approaches have been used to reduce the proportion of women with cervicitis who are overtreated using the syndromic management approach but this approach still lacks sensitivity and specificity. Further, the syndromic approach currently does not address HSV, which is becoming increasingly common. Recent evidence from a prospective study of women with symptomatic STIs in Ethiopia showed that genital ulcer disease was significantly associated with treatment failure using syndromic management.¹⁰⁸

There is an urgent need for affordable, rapid, point of care screening tests for STI screening in resource constrained antenatal care settings. Studies have confirmed the effectiveness of antenatal screening and treatment for syphilis and HIV on pregnancy outcome. Integration of antenatal screening services for these infections and the provision of syndromic management for other STIs in antenatal clinics should be prioritised.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the contributions of Ms Michele Seibou, Population Fellow, Michigan University and Ms Sibekezelu Msomi of the Reproductive Health and HIV Research Unit.

Authors' affiliations

S Mullick, The Population Council, Frontiers in Reproductive Health, Hyde Park Lane Manor, Edinburgh Gate, Craighall, Johannesburg, South Africa

D Watson-Jones, London School of Hygiene and Tropical Medicine, London, UK and African Medical and Research Foundation, Mwanza, Tanzania

M Beksinska, Reproductive Health Research Unit, Durban, Suite 1301, Maritime House, Salmon Grove Durban, South Africa

D Mabey, London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT, UK

Series editor: David Lewis

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