STIs, Bacterial vaginosis & HIV in Pregnancy

Dr. Francis J. Ndowa
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Overview of talk

- Population-based prevalence of RTIs
- Sequelae of STIs
- TV & Bacterial vaginosis in pregnancy
- Syphilis in pregnancy
- HIV in pregnancy
- Options for prevention and care
## Reminder

<table>
<thead>
<tr>
<th>RTIs</th>
<th>source</th>
<th>cause</th>
<th>examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>STI</td>
<td>Sexual partner with STI</td>
<td>Sexual contact</td>
<td>gonorrhoea, chlamydia, syphilis, HIV, herpes simplex virus infection</td>
</tr>
<tr>
<td>Endogenous</td>
<td>Normally found in vagina</td>
<td>Hormonal, medication, etc</td>
<td>candidiasis, bacteria vaginosis</td>
</tr>
<tr>
<td>Iatrogenic</td>
<td>Inside or outside the vagina</td>
<td>Self or medical instrumentation</td>
<td>Staphylococcal septicaemia, etc.</td>
</tr>
</tbody>
</table>
Purpose of surveillance

- To assess magnitude of STI burden at global, regional & country levels
- To identify vulnerable population groups
- To provide data to advocate for resources for intervention activities
- To monitor impact of intervention activities
Objectives and core components of STI surveillance

Core components

- Case reporting
- Prevalence assessments
- Etiologies of STI syndromes
- Antimicrobial Resistance monitoring

Objectives

- Magnitude of STI problem in target populations
- Inform treatment recommendations
- Improve programme management
- Improve patient care
STI Surveillance: current status

### Case reporting
- Overall weakness in IDS
- Under-reporting
  - Poor Coverage
  - Poor Representation
  - Poor Motivation
- Health seeking behaviour
  - Private
    - (GP/Pharmacy/Traditional)
  - Self-medication
- Asymptomatic/Inapparent

### Prevalence assessments
- Opportunistic data collection
- Ad hoc/Sporadic Implementation
- No Institutionalised System/Policy
- No Standard Study Design
- No Standard Laboratory Methods
- Sustainable (Lack of resources)
STI surveillance – basic

- Case reporting – syndromic (male urethral discharge, male/female genital ulcer disease)
- STI prevalence assessment and monitoring – high risk populations
- Antimicrobial resistance monitoring
- Assess and monitor etiology of syndromes
- Special studies
STI surveillance – advanced

- Case reporting – etiologic (syphilis, gonorrhoea, chlamydia, congenital syphilis)
- STI prevalence assessment and monitoring – high risk populations and general population
- Antimicrobial resistance monitoring
- Assess and monitor etiology of syndromes
- Special studies
Problems with STI surveillance

Technical problems
- capturing asymptomatic infection (esp. in women)
- health-care seeking mainly outside surveillance sites (in private sector)
- differences in risk and epidemiology for specific STIs

Health-care system problems
- logistical requirements
- financial requirements

Consequences
- very few STI surveillance programmes in resource-limited countries
Diagnoses of uncomplicated genital chlamydial infection in GUM clinics by sex and age group, UK: 1995-2002*

*Data are currently unavailable from Scotland for 2001 and 2002.

Source: HPA, UK
Resurgence Syphilis 1997-2003 by sex
UK, NL, Germany
Population-based prevalence of RTIs in resource-constrained countries

• Results from a systematic review of published and unpublished community-based studies of RTIs (1966-2000)
  – 28 studies identified
  – 10 countries represented
  – 17 studies women only
  – 3 studies men only
  – 8 studies men and women (not reported here)

(Elias, Low and Hawkes, 2003)
Population-based prevalence of RTIs, Asian Region 1989-2000

% positive on lab diagnosis

GC, CT, Syphilis, HPV, HSV2, BV, TV, Candida

What are the complications and sequelae of RTIs?

**In adults**
- Pelvic inflammatory disease (PID)
- Ectopic pregnancy
- Spontaneous abortions
- Post-partum infections
- Infertility (male & female)
- Cancers (cervical, anal, penile, liver)
- Increased HIV transmission

**In children**
- Stillbirths
- Prematurity, low birth weight
- Congenital syphilis
- Conjunctivitis and blindness
- Pneumonia
Fallopian tube damage as a cause of female infertility in the world

Cates W et al, Lancet, 1985
Trichomoniasis

- Caused by *Trichomonas vaginalis*
- Is usually sexually transmitted
- Incubation period 3-28 days
- Affects women more than men
- Presents with a vaginal discharge
  - Scanty to profuse, usually yellow-green tinted
  - can be atypical depending on host factors
Trichomoniasis

- Can present with vulval erythema, oedema and excoriations
- Cervix may be involved – "strawberry cervix"
- Asymptomatic in 50% of cases
- Accounts for 15-20% of cases of vaginitis
- Associated with a 2-6 fold increase in risk of HIV transmission*

*Van Der Pol et al. JID 2008, 197:548–54
Trichomonas vaginalis and Pregnancy

- Associated with low birth weight
- Preterm delivery
- Preterm delivery of low birth weight baby
- Perinatal transmission – only with female offspring in about 5% of cases
  - May present with Vg discharge in infant
  - Usually self-limiting in the infant (3-4 weeks)
Trichomonas vulvitis

- acute inflammation of the vulva, perineum and perianal area (intertrigo secondary to associated vaginal discharge)

- common manifestation - vulvitis, oedema, excoriations and severe pruritus
Trichomoniasis

A profuse greyish-white discharge, with a green tint, resulting from infection with *T. vaginalis*
Trichomonas vaginalis

Wet mount
- T. vaginalis - a polymorphic organism - changing shape as it moves in amoeboid fashion
- usually recognized from the movement of the flagellae
Candida vulvitis
• Characteristic, floccular, white vaginal discharge
• Labia are swollen and erythematous
• commonly associated with acute pruritus and vaginal discharge
• Discharge - minimal to copious,
• often severe erythema of the vulva.
• Cervix is not affected

NB. Three satellite lesions on top of the right thigh
Candida vulvitis with crural intertrigo

- Labia are swollen and erythemaous
- Erythema spreading to the inguinal and perianal regions
- No visible vaginal discharge

NB Papular erythematous rash on the upper thighs
Bacterial vaginosis

- A clinical polymicrobial syndrome characterized by:
  - an increase in gram-negative anaerobic bacteria (Gardnerella vaginalis, Mobiluncus spp, Prevotella spp, Bacteroides, Peptostreptococcus, Fusobacterium, Porphyromonas, Mycoplasma hominis, etc.)
  - a reduction in the concentration of Lactobacilli

- It is the most common cause of abnormal vaginal discharge in women of reproductive age
  - asymptomatic in about 50% of women
Bacterial vaginosis

Cervix covered with a discharge associated with BV
- white to grey, homogeneous (nonflocular),
- thin and adherent
Normal flora: Gram-stained smear showing a pure flora of Gram-positive rods of lactobacilli

Gram-stained smear showing mixed intermediate flora - Gram-positive and Gram-negative organisms

Bacterial vaginosis (Probably Nugent score = 8)
Bacterial vaginosis

Gram-stained smear showing mixed bacterial flora associated with severe BV. (Probably Nugent score = 10)

- a "salt and pepper" appearance from the mixture of Gram-negative and Gram-positive bacteria.
- No lactobacilli seen.
Diagnosis of Bacterial Vaginosis

Clinical criteria
Amsel's criteria (3 of 4)

- Homogeneous thin vaginal discharge
- Vaginal pH > 4.5
- “Fishy” odour upon contact of the sample with KOH 10% (positive whiff test)
- Epithelial cells covered with bacteria (Clue cells)

Amsel R, 1983 Am J of Medicine, 74:14
Diagnosis of Bacterial Vaginosis

Clinical criteria

Nugent's criteria - assigns a score of 0-10 based on different bacterial morphotypes seen in the stained smear. A score of:

0-3 Normal
4-6 intermediate
7-10 is consistent with bacterial vaginosis

• Good intra-observer agreement
• High reproducibility
• Sensitivity of 85-90%
• Specificity of more than 90%
Bacterial vaginosis and pregnancy

Evidence of an association between BV
• first trimester miscarriage
• mid-trimester (16-20 wk) abortion
• preterm birth - specifically preterm delivery < 30 wk that results in births of newborns < 1000 g
• Preterm rupture of membranes
• chorioamnionitis
• Postpartum endometritis
• Post-abortion infections
• Post-procedural infections

Kurki T 1992 Obstet Gynecol 80: 173,
It has been speculated that BV
- facilitates access of bacteria into the amniotic cavity
- remains in the uterine cavity as a chronic infection

Kurki T 1992 Obstet Gynecol 80: 173,
Managing asymptomatic BV infection in pregnant women

We should NOT screen for bacterial vaginosis in asymptomatic women since there is no difference in the rate of pre-term birth?
Managing asymptomatic BV infection in pregnant women

Some studies show that treatment of pregnant women with BV, who have a history of preterm delivery (high risk), might reduce the risk for prematurity.

- Screening and treating in pregnancy
  - might be beneficial for asymptomatic, high risk women
  - should be conducted at the earliest part of the 2nd trimester to be of benefit
Simplify decision and management with a locally agreed flowchart for health workers.
Is BV still important for pregnant women?
BV and HIV

Evidence that BV and HIV are related

• Theoretical basis
• Epidemiological observations
• Therapeutic intervention studies
Theoretical basis

BV characterised by:
- absence of Lactobacilli
- low $\text{H}_2\text{O}_2$
- high pH

Conditions believed to be conducive to increased susceptibility to HIV infection
Epidemiological Observations

Epidemiological association found in cross-sectional and prospective studies

- Relationship is dose-dependent
  - severe BV is associated with increasing risk of HIV infection
  - relative risk of HIV acquisition = 2 to 4

**Therapeutic intervention studies**

- One study (Uganda):  
  - No difference in HIV acquisition in either treatment or control groups  
  - BV therapy is not highly effective (cure rates at one month or more post-therapy)

Wawer et al. Lancet 1999
Association between BV and HIV acquisition?

Community study in Rakai, Uganda
• 4718 women 15-59 years
• Nugent criteria for diagnosis of BV

HIV: 14.2 % in women with normal flora
26.7 % in women with severe BV (Nugent 9-10)
\( p < 0.001 \)

Sewankambo, N Lancet 1997 350: 546a
Bacterial Vaginosis: Need to switch the direction of our research?

- There is an association between BV and preterm birth, but it is not cause-effect.

- The association between BV and a higher acquisition rate for HIV suggests that the loss of lactobacilli or the presence of BV could increase susceptibility.

- There is a difference in local immunity response in women with BV: Alteration in the balance between sialidase and IL-8?

(Cauci, Culhane)
Vaginal and iatrogenic infections

Vaginal infections
- are most common cause of RTIs in women
- are associated with adverse outcomes of pregnancy
- are associated with increased susceptibility to HIV infection
- are associated with high health-care costs to individual women and to health-care system
- due to iatrogenic infections, contribute heavily to burden of maternal morbidity and mortality (*true magnitude unknown*)
Syphilis in pregnancy
Transmission

- Syphilis is considered most infectious for sexual transmission in the primary, secondary and early latent stages.
- Estimates of the proportion of sexual contacts who become infected range from 6 to 62% for contacts of early syphilis cases.
- Little data on transmission probabilities for men-to-women and vice versa or on how infectious the late stages of syphilis are.
Secondary syphilis

- The second stage of infection, during which the infection is widely disseminated, develops after approximately 6 weeks to 6 months.
- Classically there is a widespread macular rash over the trunk and limbs and sometimes over the palms and soles, mucous membranes.
- Soft, papular lesions, known as condylomata lata, develop in moist areas such as the genitals and axillae.
Implementation of antenatal syphilis screening

• Survey of 22 MoH in sub-Saharan Africa:
  – vast majority have ANC syphilis screening policies
  – most pregnant women do not get screened
  – estimated 2,000,000 or more women with active syphilis are pregnant each year - 1,640,000 have their infection undetected during pregnancy.
  – syphilis is the leading cause of perinatal mortality, causing 21% of perinatal mortality.

• More than 500,000 fetal deaths a year, globally, from congenital syphilis

Effect of pregnancy on HIV

• HIV-positive women do not seem to have a worse prognosis from HIV on account of becoming pregnant

• Short-course treatments to prevent infection of a newborn are not the best choice for the mother’s health

• Medications taken only during labour and delivery may precipitate resistance to future treatment options for the mother

• Combination therapies are the standard treatment
Complications of pregnancy and delivery found among HIV positive (mainly symptomatic) women compared to HIV negative women: 1990-99

- More frequent and severe reproductive tract infections
- More severe and more frequent blood loss, sepsis and delayed wound healing after caesarean section, and induced abortion
- Lower fertility rate ratios
- Insufficient weight gain in pregnancy
Complications of pregnancy and delivery found among HIV positive (mainly symptomatic) women compared to HIV negative women: 1990-99

- Higher rates of ectopic pregnancy
- Greater risk of post-partum haemorrhage and post-partum sepsis
- More frequent and severe anaemia and malaria, and possibly tuberculosis.
- Complications of AIDS-related conditions, such as bacterial pneumonia
The variable risk of MTCT of HIV (with and without preventive interventions)

- no ARV, prolonged breastfeeding
- ARV, prolonged breastfeeding
- no ARV, no breastfeeding
- ARV, no breastfeeding
- ARV, no breastfeeding, C-section

[Bar chart illustrating the risk of MTCT of HIV under different conditions with and without preventive interventions.]

Infected  Uninfected  0%  25%  50%  75%  100%
ARV Use and HIV Transmission (WITS, USA)

Source: Blattner, Durban 2000, Int Conf AIDS Jul 9-14; (abstract no. LbOr4)
Antenatal Antiretroviral Treatment and Perinatal Transmission in WITS, 1990-1999

Blattner W. XIII AIDS Conf, July 2000, Durban S Africa (LBOor4)

<table>
<thead>
<tr>
<th>Type ARV vs None</th>
<th>% Transmission</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>None (N=391)</td>
<td>21%</td>
<td></td>
</tr>
<tr>
<td>ZDV Mono (&lt;4/94) (N=206)</td>
<td>19%</td>
<td>0.76</td>
</tr>
<tr>
<td>ZDV Mono (&gt;4/94) (N=529)</td>
<td>8%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Multi- ART (N=179)</td>
<td>4%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>HAART (N=187)</td>
<td>1%</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>
Method of Infant Feeding and HIV Transmission in Breastfeeding Children

Coutsoudis A. XIII AIDS Conf, July 2000, Durban S Africa (LbOr6)

At 6 months:
- Exclusive vs Mixed: 0.6 (0.3-1.0)
- Exclusive vs Never: 1.2 (0.6-2.2)
## RTIs and HIV and adverse outcome of pregnancy

<table>
<thead>
<tr>
<th>RTI</th>
<th>Possible Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous Abortion</td>
<td>Stillbirth</td>
</tr>
<tr>
<td>Pre-term rupture of membranes</td>
<td>Prematurity &amp; Low birthweight</td>
</tr>
<tr>
<td>Congenital or neonatal infection</td>
<td></td>
</tr>
<tr>
<td><strong>Bacterial vaginosis</strong></td>
<td>X</td>
</tr>
<tr>
<td><strong>Syphilis</strong></td>
<td>X</td>
</tr>
<tr>
<td><strong>Gonorrhoea / Chlamydia</strong></td>
<td>X</td>
</tr>
<tr>
<td><strong>Trichomoniasis</strong></td>
<td>X</td>
</tr>
<tr>
<td><strong>Herpes Simplex Virus</strong></td>
<td>X</td>
</tr>
<tr>
<td><strong>HIV/AIDS</strong></td>
<td>X</td>
</tr>
</tbody>
</table>

- **X** indicates presence of an outcome.
- **RTIs** include Bacterial vaginosis, Syphilis, Gonorrhoea / Chlamydia, Trichomoniasis, Herpes Simplex Virus, and HIV/AIDS.
What can be done to reduce adverse outcomes of pregnancy associated with RTIs?
A public health perspective on STI prevention and care

- Total Population
- Number infected with STI
- Aware of infection
- Seek care
- Correctly diagnosed
- Correctly managed

Primary prevention efforts
- Vaccination
- Selective mass treatment (PPT)

Screening
- Improve HCSB
- Improve diagnosis
- Improve case management
- Improve partner management