STIs, Bacterial vaginosis & HIV in Pregnancy

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Saiqa Mullick (Pop Council)
Overview of talk

- Global epidemiology of STIs/RTIs
- Population-based prevalence of RTIs
- Sequelae of STIs
- TV & Bacterial vaginosis in pregnancy
- Syphilis in pregnancy
- HIV in pregnancy
- Options for prevention and care
Estimated Cases of Curable Bacterial STIs among Adults, 1999

Incidence bacterial STIs: ~340 million
Reminder

RTIs = Reproductive Tract Infections

- Endogenous infections
- Iatrogenic infections
- Sexually transmitted infections (STIs)
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
Models of STI surveillance

• Routine systematic recording and reporting
  – of STI patients at health-care facilities
  – of specific diseases
  – of syndromes and associated sequelae

• Special studies
  – proportions of persons infected with STIs in different population groups
  – most common microbial causes of STI syndromes
  – monitoring prevalence of antimicrobial resistance
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

Consequence
- very few STI surveillance programmes in resource-poor 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
Diagnoses of uncomplicated gonorrhoea in GUM clinics by sex and age group, UK: 1995-2002*

*Data are currently unavailable from Scotland for 2000, 2001. Source: HPA, UK
Rates of diagnoses of infectious syphilis (primary & secondary) by sex and age group, GUM clinics, United Kingdom*, 1995 - 2002

* Data are currently unavailable from Scotland for 2001 and 2002

Data source: KC60 statutory returns and ISD(D)5 data. HPA, UK.
STIs in young people in the UK – increasing trends

Fig 3. Recent trends in major acute STIs in young people, 16-19 years. E, W &NI.

Source: HIV/STI Division, CDSC
Resurgence Syphilis 1997-2003 by sex
UK, NL, Germany

incidences per 100,000 population

Measuring STIs in Resource Poor Settings

• Problem: lack of surveillance systems, or [gender-specific] problems with existing surveillance

• Solution: use results from “special studies” at national or international level

• Action: results are used to calculate burden of disease (important for planning and resource allocation)
Population-based prevalence of RTIs in resource poor 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)

- Uganda 1973
- Uganda men 1973
- Egypt 1993
- Nigeria 1995
- Tanzania 1997
- Tanzania men 1997
- Somalia 1990 men
- Somalia 1990

Countries and years:
- Uganda 1973
- Uganda men 1973
- Egypt 1993
- Nigeria 1995
- Tanzania 1997
- Tanzania men 1997
- Somalia 1990 men
- Somalia 1990

RTIs:
- 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

Developed
- Other tubal damage: 11%
- Bilat. tubal occlusion: 25%

Africa
- Other tubal damage: 36%
- Bilat. tubal occlusion: 49%

Asia
- Other tubal damage: 25%
- Bilat. tubal occlusion: 14%

Latin America
- Other tubal damage: 29%
- Bilat. tubal occlusion: 15%

East Med
- Other tubal damage: 22%
- Bilat. tubal occlusion: 20%
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
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)
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
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,
Bacterial vaginosis and pregnancy

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,
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
Pregnant woman

Symptomatic
- High risk of adverse outcome
  - Screen for vaginosis
    - Positive: Treat for BV
    - Negative: No treatment necessary

Asymptomatic
- Low risk of adverse outcome
  - No screening (controversial)

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

BUT

– 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.
- Soft, papular lesions, known as condylomata lata, develop in moist areas such as the genitals and axillae.
Secondary syphilis cont

- Mucous patches, also called snail-track ulcers, are painless erosions and occur in the mouth and genitals.
- Condylomata lata and snail-track ulcers contain *T. pallidum* and are highly infectious.
- Systemic involvement can result in headache, laryngitis, bone pains and inflammation in the liver and kidneys leading to syphilitic hepatitis and the nephrotic syndrome.
- The symptoms and signs all resolve after a few weeks to 12 months.
Results of implementing 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

Burden of HIV in pregnancy

HIV prevalence among pregnant women in South Africa, 1990 to 1999

Source: Department of Health, South Africa

<table>
<thead>
<tr>
<th>Year</th>
<th>HIV prevalence (%)</th>
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<tr>
<td>90</td>
<td>0.7</td>
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<tr>
<td>91</td>
<td>1.7</td>
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<tr>
<td>92</td>
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</tr>
<tr>
<td>99</td>
<td>22.4</td>
</tr>
</tbody>
</table>
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

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

Source: Blattner, Durban 2000, LbOr4
Antenatal Antiretroviral Treatment and Perinatal Transmission in WITS, 1990-1999

Blattner W. XIII AIDS Conf, July 2000, Durban S Africa (LBOr4)

<table>
<thead>
<tr>
<th>Type ARV vs None</th>
<th>None (N=391)</th>
<th>ZDV Mono (&lt;4/94) (N=206)</th>
<th>ZDV Mono (&gt;4/94) (N=529)</th>
<th>Multi- ART (N=179)</th>
<th>HAART (N=187)</th>
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<tbody>
<tr>
<td>p value:</td>
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</tr>
<tr>
<td>None</td>
<td>21%</td>
<td>19%</td>
<td>8%</td>
<td>4%</td>
<td>1%</td>
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<tr>
<td>Type ARV vs None</td>
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<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Type ARV vs None

p value:
Method of Infant Feeding and HIV Transmission in Breastfeeding Children

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

- 1 Day: 8% Never Breastfed, 7% Exclusive Breastfed, 7% Mixed Feeding
- 6 Mos: 19% Never Breastfed, 19% Exclusive Breastfed, 26% Mixed Feeding
- 15 Mos: 19% Never Breastfed, 25% Exclusive Breastfed, 36% Mixed Feeding

Transmission rates:
- 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>
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<tbody>
<tr>
<td></td>
<td>Spontaneous Abortion</td>
</tr>
<tr>
<td>Bacterial vaginosis</td>
<td></td>
</tr>
<tr>
<td>Syphilis</td>
<td>X</td>
</tr>
<tr>
<td>Gonorrhoea / Chlamydia</td>
<td></td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td></td>
</tr>
<tr>
<td>Herpes Simplex Virus</td>
<td></td>
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<tr>
<td>HIV/AIDS</td>
<td>X</td>
</tr>
</tbody>
</table>
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