Burden of Antibiotic Resistance on Women’s Health

Scope of the Problem

Infections in the female genital tract – RTI (reproductive tract infections) – include endogenous infections as well as iatrogenic and sexually transmitted infections (STI).

Infections during pregnancy may also lead to pre-term delivery, stillbirth and death of the infant in sepsis. As long as the prevalence of antibiotic resistance is almost unknown, and the urgent need of new effective antibiotics is not being provided for, adequate treatment of the mother and her child cannot be guaranteed.

Improvement of maternal health as stated in Millennium Development Goal (MDG) 5 will be difficult to achieve for such reasons.

Antibiotic resistance may also be a serious problem when women contract sexually transmitted infections (STI), especially gonorrhoea. Untreated or unmanageable infections may lead to pelvic inflammatory disease, causing chronic pain and discomfort, infertility, and ectopic pregnancies. Newborn babies may become blind.

An estimated 3 million treatment failures due to resistant gonorrhoea occur each year in the world and will incur an additional cost of US$ 500 million. When treatment guidelines recently had to be changed in the US due to increasing resistance to ciprofloxacin, the cost of treatment increased fivefold. The risk of HIV-transmission increases considerably if STI are impossible to treat adequately.
main causes of maternal deaths worldwide.  

Infections include metritis, pelvic cellulitis and abscess, peritonitis following uterine perforation, and septicaemia. 

STI and other infections of the genital tract

Untreated infections increase the probability of acquisition and transmission of HIV. 

An estimated 340 million cases of curable STI occur annually in adults. Most are in south and south-east Asia and sub-Saharan Africa. Infections may lead to acute and chronic symptoms and long term consequences. 

As many as 70% of infections in women may be asymptomatic. Infections during pregnancy can have adverse effects and may cause infections in the newborn baby. 

Syphilis during pregnancy may result in stillbirth, neonatal death or congenital syphilis. 

STI caused by *Clamydia trachomatis* and *N. gonorrhoeae*:

If not treated adequately, complications may lead to pelvic inflammatory disease (PID), infertility, chronic pain and ectopic pregnancies. 40-50% of ectopic pregnancies can be attributed to earlier PID. Transmission of infection to the infant during birth may lead to blindness and in the case of *C. trachomatis* also to pneumonia. 

**Epidemiology**

Sepsis following abortion

An estimated 19-20 million unsafe terminations take place each year in the world, and around 68,000 women die as a consequence, which accounts for about 13% of all pregnancy related deaths in the world. Deaths due to abortion are most common in the Caribbean and Latin America. The specific cause of death is often unknown but is considered to be haemorrhage or sepsis in most cases. In a study in Malawi, 77.1% of the deaths after abortions were due to sepsis. 

There is so far no knowledge about the impact of antibiotic resistance when fatal infections occur. 

Puerperal sepsis and infections during pregnancy

More than 500,000 women die each year due to complications during pregnancy and childbirth. Sepsis is estimated to be the cause of maternal deaths in 0.5-15% of cases. It is significantly more common in Africa, Asia, Latin America and the Caribbean than in developed countries. 

Infection occurs even more often after Caesarean section. On rare occasions amniocentesis may also lead to serious infections. 

**STI**

An estimated 62 million cases of gonorrhoea occur each year in the world. 

In the US, reported rates of gonorrhoea and *C. trachomatis* infections among women were respectively 124.3 and 515.8 per 100,000 in 2006. Infection may be 10-100 times more common in low-income communities according to the WHO. 

Syphilis

More than 1 million infants are born with congenital syphilis each year in the world. 

In the US, syphilis in women is much more uncommon than in men and increased by 11.1% in 2006 to one case per 100,000. Three hundred and forty nine cases of congenital syphilis were reported there in 2006. 

**Common Pathogens**

Infections are often caused by several species of bacteria. *E. coli*, beta haemolytic streptococci, *S. aureus* and anaerobes are all common pathogens. Other agents include Klebsiella spp., enterococci, and *N. gonorrhoeae*. *C. trachomatis* and Mycoplasma species may also be responsible, as may (rarely) Clostridia. 

**Antibiotic resistance**

Effective and early treatment of STI is essential to decrease the transmission of the actual disease, and of HIV. The choice of antibiotic for treatment depends on knowledge of local resistance patterns. As an example, since 2007 ciprofloxacin is no longer recommended by the CDC as the first-line treatment for gonorrhoea in the US due to high level of resistance. The same decision had to be made in India. 

Penicillins have remained effective for the treatment of early syphilis. 

Resistance among aerobic Gram-negative bacteria like *E. coli* is common and several strains are also resistant to third-generation cephalosporins (see factsheet on MRGN). *E. coli* carried as part of the normal flora can be resistant, and maternal colonisation with resistant bacteria may lead to neonatal sepsis. 

Prophylactic treatment given against Group B streptococci may lead to neonatal infections with resistant bacteria, e.g. *E. coli*. 

The number of community- and hospital-associated methicillin resistant *S. aureus* (MRSA) infections is increasing in the post-partum period. 

Two out of 305 women screened had vaginal colonisation with MRSA. 

Penicillinase-producing *N. gonorrhoeae* (PPNG) emerged in 1976. Surveillance programmes in several countries, and the global gonococcal antimicrobial surveillance programme (GASP) of the WHO monitor development of resistance among *N. gonorrhoeae*. In the US, 19.6% of *N. gonorrhoeae* were resistant to penicillin, tetracycline or both in 2005, an increase from 15.9% in 2004. In the
UK, 17.9% of isolates were penicillin-resistant in 2005 but the figure fell to 9.5% in 2006. Tetracycline resistance was present in 36.9% of isolates, again a decrease from 48%.2 In India, penicillin resistance increased significantly to 68.4% in 2003 but decreased to 18.2% in 2006. In other parts of Asia, 9-90% of isolates are penicillin-resistant, as are over 35% in sub-Saharan Africa.2

Resistance to fluoroquinolones is increasingly prevalent globally. The prevalence in Hongkong and other parts of China is 99%. In India resistance to ciprofloxacin increased to 97.2% in 2006.34

Overall quinolone resistance among N. gonorrhoeae has increased steadily to around 13% in the US in 2006 and to 21.7% in the UK in 2005.27

Confirmed resistance to ceftriaxone has still not been recorded worldwide but isolates with intermediate susceptibility have been identified.28 In India, 5.5% of isolates were less susceptible in 2006.34 Resistance to cefixime has not yet been identified.

Isolates with higher azithromycin MIC were also found to have increased over the years, and 5% of the isolates were resistant to azithromycin in Europe in 2004.29 In the Caribbean and South America, these figures vary from 16% to 70%.2

Resistance to spectinomycin varies from 0% to about 5%.2

Antibiotic resistance among C. trachomatis is still low, but in vitro resistance to macrolide antibiotics has been detected.30 Since 2002 treatment failures have occurred in the US when early syphilis has been treated with azithromycin. A high prevalence of the resistant bacteria has also been found in Ireland.31

**QUANTITATIVE CONSEQUENCES OF RESISTANCE**

Quantification of morbidity, mortality or costs due to antimicrobial resistance associated with infections during pregnancy or delivery is impossible for the time being because of lack of reliable data. Difficulties include inadequate diagnostics, uncertain aetiology of infections, other coexisting conditions (haemorrhage, eclampsia etc) and sometimes lack of proper records.

Based on figures from the USA, an assumption of 3 million treatment failures globally each year due to antibiotic resistance in gonorrhoea has been made. This would incur an extra cost of US$ 500 millions each year.35 The cost of treatment of resistant gonorrhoea is five times higher when ciprofloxacin has had to be replaced by ceftriaxone. The cost of treatment of MRSA infections is probably three times higher than that incurred by susceptible strains.

**Urgent needs**

- Train caregivers in appropriate infection control and rational drug use.
- Improve diagnostic capacity and documentation of infection, aetiological agents and their antimicrobial susceptibilities.
- Develop hospital-based and community-based surveillance systems to monitor antibiotic resistance trends, antibiotic use and treatment failure rates.
- Perform clinical trials to identify the most effective drugs/combinations for specific indications.
- Develop locally relevant guidelines, taking into account local susceptibility patterns, availability and cost of drugs, diagnostic facilities etc.
- Develop new medicines which can cure STI and other infections suffered by women.

The risk of HIV-transmission increases considerably if STI are impossible to treat adequately.
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