Surveillance and outbreak reports

INCREASE IN REPORTED GONORRHOEA CASES IN SWEDEN, 2001 - 2008

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Gonorrhoea is on the rise in Sweden and in many other European countries. The present report describes and evaluates the gonorrhoea trends in Sweden from 2001 to 2008 when an increase of 32% was reported. Up to 86% of the cases were reported in men, with the highest proportion among heterosexually infected men (41-59% during these years). Heterosexually infected men more often acquired gonorrhoea abroad, especially in Thailand, whereas women and men who have sex with men were more likely to acquire the infection within Sweden. The recent increase in gonorrhoea cases in Sweden is most likely due to adoption of more risky sexual behaviour (e.g. an increase in the number of sexual partners and the number of new/casual sexual partners and/or low use of condoms) in the Swedish population. Further research regarding more effective identification and description of sexual transmission chains and sexual networks is needed in order to follow the spread of infection and to recognise more effective interventions to prevent the spread of gonorrhoea and also other sexually transmitted infections.

Introduction

Gonorrhoea is a bacterial sexually transmitted infection (STI) that showed a steady decline in incidence during the 1970s, 1980s and early 1990s in Sweden. This epidemiological trend was also seen in many other, especially high- and middle-income, countries worldwide [1]. However, after an all-time low incidence in 1996 (2.4 per 100,000 population) with most of the cases acquired abroad, the gonorrhoea incidence in Sweden started to increase again (Figure 1) [2].

A similar increase has also been described from many other high- or middle-income, industrialised countries since the mid- or late 1990s. In north-western Europe, this re-emergence of gonorrhoea was primarily due to outbreaks among men who have sex with men (MSM), but also due to increased transmission among young heterosexuals of both sexes [2-4]. In 2005, it was estimated that 95 million gonorrhoea cases among adults occurred worldwide, with the majority of cases in Sub-Saharan Africa, South and South-East Asia, Latin America and the Caribbean [5].

Resistance of the aetiological agent of gonorrhoea, the bacterium *Neisseria gonorrhoeae*, to antimicrobials used in the traditional treatment (penicillin, tetracycline, and fluoroquinolones) of the infection is now prevalent worldwide. Most worrying, the level of resistance and/or reduced susceptibility of *N. gonorrhoeae* also to newer treatment alternatives, such as azithromycin and extended-

spectrum cephalosporins (cefixime and ceftriaxone), has increased worldwide [6-8].

This report summarises the gonorrhoea surveillance data in Sweden for the last eight years (2001-2008).

Methods

Gonorrhoea is a notifiable infection in Sweden, in accordance with the Swedish Communicable Diseases Act, and the present surveillance system has been described elsewhere [2,9]. The gonorrhoea case definition used in Sweden since 1997 includes any person meeting the laboratory criteria. The laboratory criteria are as follows: a) *N. gonorrhoeae* has been isolated from a clinical specimen using culture, b) *N. gonorrhoeae*-specific antigen or nucleic acid has been demonstrated in a clinical specimen, and/or c) *N. gonorrhoeae* Gram-negative intracellular diplococci have been identified in a urethral smear from a symptomatic male. The Swedish laboratory confirmation also requires use of appropriate diagnostics. Quality-assured culture remains the recommended diagnostic method and accounts for most of the reported cases during each year. Positive nucleic acid amplification tests (NAATs) are recommended to be confirmed (using other method or a NAAT targeting another suitable gene). The Swedish gonorrhoea case

FIGURE 1
Incidence of reported gonorrhoea cases in Sweden, 1990-2008

definition is identical to the case definition of the European Union (EU) [10,11].

Data from the national computer-based surveillance system SmiNet was used to describe epidemiological trends for the period from 2001 to 2008. In this system, gonorrhoea cases are described by age, sex, reporting county, self-reported route of transmission (divided into heterosexual transmission, homosexual transmission and vertical transmission (mother to child), and country of acquisition (consistent with incubation period and anamnesis). Unfortunately, the electronic database can contain only one laboratory notification, and notifications from other sites for the same case are disregarded, which makes it impossible to draw any conclusions from the site of infection (therefore these data are not presented).

In this paper, we present data on the self-reported sexual route of transmission (not on sexual identity) when we are referring to homosexually infected men (MSM) and heterosexually infected men. Furthermore, the number of people tested and the number of people positive for *N. gonorrhoeae* are reported on a voluntary basis to the Swedish Institute for Infectious Disease Control, by the 29

laboratories in Sweden performing diagnostics for *N. gonorrhoeae*. These data are presented as number of people tested (by sex) and as positivity rate (proportion of people positive for *N. gonorrhoeae*). The annual incidence was calculated using all reported gonorrhoea cases per 100,000 population/men/women (population data from Statistics Sweden, www.scb.se).

The presented antimicrobial resistance data are from the Swedish Reference Laboratory for Pathogenic Neisseria, Örebro University Hospital, Örebro, which annually reports trends and characteristics including antimicrobial resistance data of all examined Swedish *N. gonorrhoeae* isolates [12,13]. It is recommended by the Swedish Reference Laboratory that all gonococcal isolates should be examined for antimicrobial resistance. Although most isolates are actually tested, the results from a few laboratories are not available for this report.

Results

In the period from 2001 to 2008, a total of 4,936 gonorrhoea cases were reported to the national electronic surveillance system SmiNet. The gonorrhoea incidence during this period increased by 32% from 5.9 to 7.8 cases per 100,000 population (notably, this corresponds to a 225% increase since 1997) with several smaller incidence peaks in 2000 (6.6/100,000), in 2003 (6.6/100,000), in 2005 (7.6/100,000) and in 2008 (7.8/100,000). Overall during the study period, a steady upward trend in the incidence was observed (Figure 1).

Age

During 2001-2008, the median age for infected women was 27 years (range: 14-61 years), for heterosexually infected men 34 years (range: 15-80 years), and for MSM 32 years (range: 15-77 years). The highest incidences as well as the largest increase in incidence in both sexes were observed in the age groups of 15-24 year-olds and 25-34 year-olds, and were consistently higher among men (Figure 2).

Sex and self-reported route of transmission

Between 2001 and 2008, the male-to-female ratio varied from 4.1 to 6.2. The mean proportion of men in general and MSM was 83% (range: 80-86%) and 44% (range: 38%-56%), respectively (Figure 3). The proportion of female cases increased from 16% in 2001 to 20% in 2008.

Geographic spread

The majority of the gonorrhoea cases between 2001 and 2008 were reported from the counties with the highest number of population. Accordingly, Stockholm county (21% of Sweden's population) reported a mean of 68% of all gonorrhoea cases per year (range during 2001-2008: 61-73%), Skåne county (13% of Sweden's population) reported 10% (range: 6-16%), and Västra Götaland county (17% of Sweden's population) reported 10% (range: 5-16%).

Country of acquisition of the infection

In the period from 2001 to 2008, a mean of 60% of the cases had acquired the infection in Sweden, 34% abroad, and for 6% this information was not available. Women and MSM more often acquired gonorrhoea in Sweden (71% of the female cases and 79% of MSM). In contrast, heterosexually infected men more often acquired infection abroad (56%). No major longitudinal trends were identified regarding the country of acquisition of

FIGURE 2

Gonorrhoea incidence in women (n=877) and men (n=4,020) by age group in Sweden, 2001-2008*

* Cases under 15 years and over 64 years (n=39) are not included in the figure.

FIGURE 3

Reported gonorrhoea cases by sex and self-reported route of transmission in Sweden, 2001-2008 (n=4,936)

gonorrhoea and way of transmission (Figure 4). For men who had acquired gonorrhoea abroad by heterosexual transmission, the most common countries of infection were Thailand (22-32% of these cases over the years) and the Philippines (3-5% of these cases). The other heterosexually infected male cases acquired gonorrhoea in countries worldwide that were implicated less frequently, e.g. 1-2% in northern European countries (Denmark, Finland, Iceland, Norway and Sweden), 1-4% in western European countries (United Kingdom, Spain, France, Germany, Portugal, Italy), and 0-1% in eastern European countries (Baltic States, Poland, Bulgaria) (range for 2001-2008). MSM who acquired gonorrhoea abroad most frequently acquired it in Denmark (1-8% of the cases), Spain (1-4% of the cases) and Germany (0.5-3% of the cases). Among men with unknown route of transmission, the majority had acquired gonorrhoea in Sweden (range for 2001-2008: 5-67%) and in Thailand (range: 0-33%).

Laboratory-based reporting of test volumes (voluntary)

According to the voluntary reporting from the laboratories, the number of persons tested for *N. gonorrhoeae* in Sweden increased by 15% from 48,925 in 2001 to 56,084 in 2008. The peak in the number of people tested in 2007 was likely due to the reports in late 2006 of the new variant of *Chlamydia trachomatis* (nvCT), which resulted in high numbers of false-negative results. In 2007, when new genetic assays detecting the nvCT had been

introduced, many people were re-tested (testing volumes for *C. trachomatis* significantly increased in 2007), and were most probably also tested for gonorrhoea at the same time. All 29 laboratories performing testing for *N. gonorrhoeae* reported most of the requested data and, accordingly, the coverage was as high as 97-100% in the period from 2001 to 2008, although reporting was voluntary. Of those tested, 60-64% were women. Despite the fact that more women were tested for *N. gonorrhoeae*, only 0.3-0.4% were found to be positive. In contrast, 2.2-2.9% of the tested men were positive (Figure 5), which may also reflect that gonorrhoea is more commonly symptomatic in men than in women. In general, no major trends were seen in the positivity rates for women or men from 2001 to 2008. Furthermore, during the study period, there has not been any major change in the laboratory methods used for diagnosis.

Antimicrobial resistance of Swedish *Neisseria gonorrhoeae* isolates

Between 2001 and 2008, all Swedish isolates reported by the Swedish Reference Laboratory (n=2,242) were susceptible to spectinomycin (100%), 99.96% to ceftriaxone (i.e. only one isolate in 2008 displayed an intermediate susceptibility/resistance in vitro), 98.7% to cefixime, and 94.8% to azithromycin. However, the level of intermediate susceptibility to cefixime increased from 0% to 4% and the resistance to azithromycin increased from 0% to 3% (0-10% intermediate susceptibility), over the years. The level of beta-lactamase production, intermediate susceptibility and resistance to ampicillin, and intermediate susceptibility and resistance to ciprofloxacin varied from 22% to 39%, 66% to 82%, and 50% to 71%, respectively, over the study period [12,13].

Discussion

The incidence of reported gonorrhoea cases in Sweden has increased by 32% over the last eight years (2001-2008), from 5.9 to 7.8 cases per 100,000 population, an increase of 225% compared to the all-time low incidence in 1996 (2.4 per 100,000 population) [2]. Similar increasing patterns have also been observed in other Nordic countries such as Denmark and Norway [4,14] as well as in other EU countries [3,15,16]. The main contributors to the recent increasing trend in Sweden, in particular in the period from 2005 to 2008, were heterosexually infected men but also women: the proportion of heterosexually infected men increased from 41% to 59% and the proportion of female cases increased from 16% to 20% during these years. MSM also contributed to the increase in gonorrhoea cases. However, the proportion of these cases decreased from 56% to 42% in the past four years (2005-2008).

The majority of the heterosexually infected men acquired gonorrhoea abroad, with the majority of cases acquired in Thailand, sometimes through sexual contacts with female commercial sex workers (FCSWs; it is occasionally but not consistently possible to collect these data). This is most worrying because Thailand has a high prevalence of human immunodeficiency virus (HIV) infection and many other STIs among commercial sex workers. For instance, recent estimates among FCSW in Thailand revealed an HIV prevalence of 4.7% among venue-based FCSW and of 43% among street-based FCSW [17]. Accordingly, the heterosexual Swedish men may, in addition to gonorrhoea, also acquire HIV and other STIs that they could transmit to others after their return to Sweden. A similar pattern has also been observed in Norway [4]. This provides support for targeted prevention interventions

FIGURE 4

Gonorrhoea reported to be acquired in Sweden and abroad by sex and route of transmission, 2001-2008 (n=4,936)

FIGURE 5

Number of persons tested and positivity rate for *Neisseria gonorrhoeae* among men and women in Sweden, 2001-2008

among Swedish men going abroad, especially to Thailand and the Philippines.

The high proportion of MSM (38-56% during the study period) among the men gonorrhoea cases in Sweden is also a reason for concern. Some MSM have not consistently adopted safe sex practices and therefore maintain continuous possibilities for transmission of STIs and HIV [3]. An increasing number of casual sexual partners, anonymous sexual partners, and non-use of condoms are likely to have contributed to the recent increases in STIs among MSM [3,18]. Preventive programmes with adapted educational messages tailored specifically to MSM would be beneficial.

From 2001 to 2008, gonorrhoea cases were reported from all over Sweden with a higher number of cases reported from the counties with the largest cities, such as Stockholm county, Skåne, and Västra Götaland. This correlates well with the reported syphilis cases in Sweden [9], suggesting that cities with a large population provide an environment where free sexual behaviour is more readily accepted. In addition, sexual networks tend to be larger in the cities and the chances of contact with risk groups for STI transmission are higher.

The increase in gonorrhoea and other STIs in Sweden could be due to several reasons. One of the most important reasons might be the adoption of more risky sexual behaviour which has been observed in studies among MSM in Sweden [19]. For example, practise of unprotected anal sex during the last 12 month was reported by 59% of responding MSM with an average number of three to four partners during the last 12 month, as well as practise of unprotected anal sex with a partner with unknown HIV-status (during the last sexual contact) [19]. The present study observed more risky sexual behaviour not only among MSM but also among heterosexually infected men and women. The increase in the number of sexual partners overall and in the number of new/casual sexual partners combined with an insufficient use of protection is certainly one of the factors contributing to the spread of gonorrhoea. Regular assessments and studies of sexual knowledge, behaviour, attitudes, and the risks of HIV/AIDS and STIs that have been performed in Sweden since 1989 provide comprehensive and valuable insights into these factors [20,21]. These studies showed that in the years from 1989 to 2003, the prevalence of casual sexual contacts (unspecified type of sexual contacts) without condom use rose significantly, especially in the age groups under 35 years (both men and women) [20]. Furthermore, the proportion of 18-19 year-old men and women who had more than three sexual partners during the last 12 months increased between 1989 and 2007 from 17% to 23% in men and from 13% to 26% in women [21]. These studies, as well as surveillance data for gonorrhoea (and other STIs), support the need for targeted prevention interventions in vulnerable groups of the Swedish population.

The upward trend of gonorrhoea in Sweden during the period analysed in this study cannot be explained by changes in the national gonorrhoea case definition or the diagnostic methods. Nevertheless, another possible contributing factor is a rise in the number of people tested for *N. gonorrhoeae* (by 59% in 2001-2008), which is partly a result of an improved access to health care.

Gonorrhoea is on the rise in many European countries [3,4,14,22,23]. There are also major concerns worldwide regarding the high level of antimicrobial resistance in *N. gonorrhoeae*, and it

is crucial for effective treatment to perform antimicrobial resistance surveillance locally, nationally and internationally. Accordingly, gonorrhoea needs special attention from health care professionals, health promoters, surveillance facilities and diagnostic laboratories. Further research regarding more effective identification and description of sexual transmission chains and sexual networks is needed in order to follow the spread of infection and to recognise more effective interventions to prevent the spread of gonorrhoea as well as other STIs.

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