Cost-effectiveness of screening for Chlamydia trachomatis in adolescent females in Slovenia

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SUMMARY

The aim of the study was to evaluate the cost-effectiveness of screening at an estimated asymptomatic *Chlamydia trachomatis* prevalence of 6% in a cohort of 67,870 adolescent females by using the cost-effectiveness analysis (CEA). There were two screening strategies evaluated; screening by means of a direct immunofluorescence (DIF) assay and screening by means of a polymerase chain reaction (PCR). Both screening strategies have proved cost-effective when considering the current prices of DIF and PCR assays in Slovenia (population 2 million). Screening by means of DIF would generate a saving of 3.7 million US dollars, whereas with the PCR such saving would amount to 660,000 US dollars.

KEY WORDS

***Chlamydia trachomatis*, screening, cost-effectiveness, adolescent females**

Introduction

Chlamydia trachomatis exists as an intracellular parasite of cuboidal epithelium cells in human body only. It is known to cause trachoma, inclusion conjunctivitis, urinary and genital inflammatory diseases, lymphogranuloma venereum, neonatal pneumonia, arthritis, there is also a possible association with the development of cervical cancer (1,2).

In mastering and controlling sexually transmitted *C. trachomatis* infections, asymptomatic infections represent the greatest problem. In women, up to 70% of cervical infections and about 30% of pelvic inflammatory diseases develop asymptomatically (3). The most severe complications of chlamydial tubal inflammation are those of ectopic pregnancy and infertility (4).

As several sexually transmitted *C. trachomatis* infections develop with no evident signs of infection, it is essential that such infections are detected and treated in time, if we are to master them, and above all, their consequences. And this is precisely what screening for *C. trachomatis* infection is aimed at: to reduce the occurrence of the infection, as well as treat the infected persons and their sexual partners in time and thus prevent the sequelae of such infection (5).

Screening of both adult and adolescent females can be considered cost-effective not only at high but also at low prevalence of 3% to 6% (5, 6, 7, 8). The economic analyses of screening programmes are based on the evaluation of costs and results of procedures imple-

mented to achieve the set health objectives. As the case with all preventive programmes, the invested funds should be justified on the grounds of improved health status in the target population (9).

Materials and methods

In the cost-effectiveness analysis (CEA), direct costs were taken into consideration, which include the cost of laboratory testing, the cost of other diagnostic procedures as well as the cost of medical treatment, as recognized by the Institute of Health Insurance of Slovenia in accounting the costs of health services. In Slovenia, the Institute of Health Insurance is the only payer of health services. Furthermore, indirect costs were also considered, incurred by the absence from work due to illness (sick leave). The strategy of screening adolescent females anticipated two methods of detecting the persons infected: the direct immunofluorescence (DIF) assay and the polymerase chain reaction (PCR) method.

According to the estimate of the Institute of Health Insurance of Slovenia, the financial burden brought upon the state due to lost working days in Slovenia in 2001 was 264 million US dollars. The average gross income was 840 US dollars. There was an average of 25 US dollars paid per employed insured person per day of sick leave (10).

In treatment of infected persons and their partners only the cost of such medication was considered, which is available on prescription only and in Slovenia paid for to the pharmacies by the Institute of Health Insurance of Slovenia and thus considered no direct cost for the patient (11,12). Such costs were compared to the costs of female adolescent screening. The costs of consumer material, specimen transportation as well as traveling expenses due to treatment outside the place of permanent residence were not evaluated.

The average direct costs in adolescent females, incurred as a result of *C. trachomatis* infection, originate from the treatment of cervicitis, acute pelvic inflammatory diseases, ectopic pregnancy, infertility and chronic pain in women (3,5). The costs of treating neonates, born to mothers with chlamydial cervicitis, were not considered, as the costs associated with such infections had been evaluated in adolescent females aged from 15 to 19 years (13). In Slovenia, only 0.7% of those give birth to a child (14).

With regard to chlamydial cervicitis, from 30% to 50% of infected adolescent females were anticipated to visit a gynecologist and undergo treatment on an outpatient basis (3).

In the remaining females not undergoing treatment, 20% of infected females develop an acute pelvic inflammatory disease (5,15). For a half of those, outpatient treatment was anticipated, whereas for the rest treatment on an inpatient basis. In that case, no costs due to absence from work were taken into consideration, as the acute inflammatory disease was assumed to develop in adolescent females not yet employed.

The consequences of pelvic inflammatory disease as a result of *C. trachomatis* infection can at a later stage show as infertility, ectopic pregnancy; women are suffering from chronic pelvic pain. There were 20% of women estimated to experience chronic pain, ectopic pregnancy was estimated to occur, on average, in 15% of women, whereas 20% of women were estimated to suffer from infertility (5).

The costs of diagnostic procedure and treatment of an adolescent female for chlamydial cervicitis as well as treatment of her partner with azithromycin were estimated at 50 US dollars. In 10% of adolescent females, such costs would increase by 14 US dollars due to developing moniliasis as a result of azithromycin therapy.

The cost of treating acute pelvic inflammatory disease on an outpatient basis was estimated at 44 US dollars, whereas the cost of hospitalization at 970 US dollars. In Slovenia, in accounting the costs of services the Institute of Health Insurance of Slovenia pays the "cases" to service providers for all hospitalized patients. A "case" includes all activities provided for the insured person in the period of his/her stationary inpatient treatment (16).

With all later complications (chronic pain, infertility, ectopic pregnancy), we, in addition to direct costs, also considered the absence from work due to health problems as recognized by the Institute of Health Insurance of Slovenia in the sick-leave accounting.

In women with chronic pain, the costs including at least 14 days of sick leave were estimated at 310 US dollars.

With regard to ectopic pregnancy and diagnosing of infertility, where in both cases at least 1 month of sick leave was anticipated, the estimated costs amounted to 1,520 US dollars. With reference to infertility treatment, there were 4 attempts of in vitro fertilization anticipated at the costs of the Institute of Health Insurance of Slovenia, these connected with a month's absence from work (17). In Slovenia, there are three centers to provide such services of infertility management. The average cost at the time of the concluded laboratory portion of the attempt amounts to 1,400 US dollars (Elena Nikolavčič, personal information). In Slovenia, women are within the scope of compulsory health insurance entitled to four attempts of in vitro fertilization per pregnancy in their fertile period (18).

With the screening costs, we took into account the cost of laboratory testing with the PCR and the DIF methods as well as the cost of treating the infected persons and their partners with 1 g of azithromycin.

The cost of PCR method to test urine specimens for *C. trachomatis* in Slovenia is 80 US dollars. The average cost of DIF assay to identify *C. trachomatis* in cervical smear is 32 US dollars. The cost of treating an infected adolescent female and her partner with azithromycin is 28 US dollars.

The calculations to evaluate the cost-effectiveness of screening by comparing the screening costs to the costs associated with the infection sequelae were made by using computer programme Office Pro 97 Microsoft Excel (Win 32, Authorization No. 97922239AAB0001, License No. 97923634, SL3).

Results

On the basis of the 2.6% prevalence found by using the PCR method on urine specimens of 1272 adolescent males (confidence interval from 1.7 to 3.5, $p<0.05$) and the results of the cross-sectional epidemiological study in adolescent females (19, 20), it was estimated that in Slovenian adolescent females aged from 15 to 19 years there were at least 6% infected with *C. trachomatis*. Such estimation also originates from the information that in the age group from 15 to 19 years the number of females infected with *C. trachomatis* was 3- to 9-fold when compared to males from the same age group (21). With regard to the estimated prevalence, the cohort of 67,870 adolescent females in Slovenia includes at least 4,072 with *C. trachomatis* infection.

Of the infected population, only 35% (1,425) are being treated for cervicitis. The acute pelvic inflammatory disease was anticipated in 530 adolescent females, 529 women will have chronic pain at a later stage, 397 women will experience an episode of ectopic pregnancy, whereas due to chronic pelvic inflammatory disease 529 women will suffer from infertility and will undergo 4 attempts of in vitro fertilization at the cost of the Institute of Health Insurance of Slovenia (Table 1).

The costs of screening and infection treatment in a cohort of adolescent females, when using the DIF assay on cervical smear specimens, would at the current price of DIF assay in such population amount to 2.3 million US dollars. Thus, such screening would already at present generate a saving of 3.7 million US dollars. A presently implemented DIF screening strategy in adolescent females would prove cost-effective at the prevalence as low as 2.4% (Figure 1).

With screening in a cohort of adolescent females by implementing the PCR method on urine specimens, the required funds would amount to 5.3 million US dollars. When compared to costs associated with complications (6 million US dollars), there would be a saving of 660,000 US dollars. At a prevalence of 5.3%, the screening costs would equal the saving generated, if any (Figure 2).

Discussion

In economic evaluation of adolescent female population based screening we have, on the assumption of a 6% prevalence of asymptomatic infection in such population, evaluated the cost-effectiveness of screening by means of DIF assay on cervical smear specimens and PCR assay on urine specimens. We anticipated to have tested all adolescent females in the cohort, which is, however, difficult to achieve in practice.

According to the first screening strategy, the detection of persons infected with *C. trachomatis* was based on DIF assay on cervical smear specimens, which is at our estimated prevalence rate considered a suitable method with regard to sensitivity and specificity (22). There are ten laboratories in Slovenia to implement such tests within the scope of public health service network.

The costs without screening in a cohort of 67,870 adolescent females at a 6% prevalence of *C. trachomatis* were estimated at 6 million US dollars, whereas the estimated costs of DIF assay screening including treatment of an infected adolescent female and her partner with azithromycin were 2.3 million US dollars. The DIF screening strategy proved highly cost-effective, as it would generate a saving of 3.7 million US dollars. The problem with this strategy, however, lies in the aforementioned inability of encompassing the population as a whole, whereas the advantage is that of a developed laboratory network.

The major problem with screening strategies planned is in the response rate of the population to be screened. The majority of opportunistic screening programmes have to encounter too low number of participants in such programmes, as the recruitment solely depends on coincidental visits of individuals. According to J. Paavonen, gynecological checks would cover less than a half of females aged from 15 to 25 years (5).

In Finland, the evaluation of universal screening strategy, which anticipated 75% of women participating on the assumption of a 5% prevalence of *C. trachomatis*, led to the conclusion that the PCR screening strategy on urine specimens might prove cost-effective already at the prevalence as low as 3.9% (5). Furthermore, one attempt of in vitro fertilization was anticipated for every woman suffering from infertility, and not four attempts as the case in our country. The cost of such attempt was estimated at 2,444 US dollars.

In extensive cross-sectional epidemiological study, J.M. Marazzo with associates observed a 6.6% prevalence of women infected with *C. trachomatis*. The infection was diagnosed by using the DIF assay. In their estimation, the universal screening of women has proven most cost-effective, regardless of the age of the participants (8).

According to Dutch studies, preventing one of the anticipated late complications as a result of *C. trachomatis* infection would require examination of 479

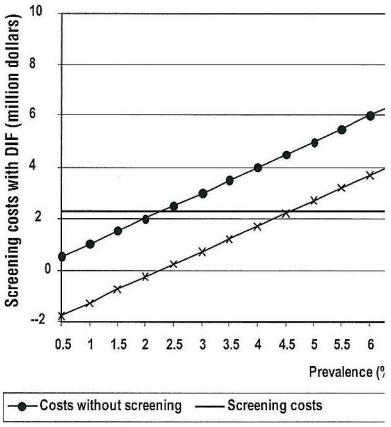

Figure 1. Prevalence effect on total costs of screening by means of DIF assay to detect *C. trachomatis* in a cohort of 67,870 adolescent females and on costs without screening.

DIF=direct immunofluorescence

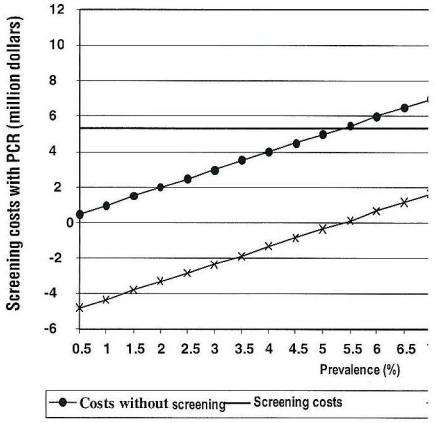

Figure 2. Effect of *C. trachomatis* prevalence on cost-effectiveness of the PCR screening strategy in a cohort of 67,870 adolescent females in Slovenia. PCR=polymerase chain reaction

women aged from 15 to 40 years. The costs associated with such examination were estimated at 15,800 US dollars. An average of 2 attempts of in vitro fertilization was foreseen, with 70% of infertile women to decide on undergoing such treatment (we anticipated all infertile women would decide on undergoing such treatment as infertility was to have been identified in women, younger than 30 years).

On the assumption of urine specimens tested by using the lygase chain reaction (LCR) method in a cohort of 161,065 women, they concluded that at the estimated 2.2% prevalence of *C. trachomatis* the universal screening programme for detection of *C. trachomatis* in the cohort would not be cost-effective (23).

In our evaluation, it was anticipated that all women would decide on undergoing in vitro fertilization, and that at least four times, which they are entitled to in accordance with the Slovenian legislation and the rights arising from the compulsory health insurance (18). Costs were also estimated for the case of the second attempt of in vitro fertilization having proved successful and the woman giving birth to a child. In such case, however, the costs do not differ considerably from the costs associated with four attempts of in vitro fertilization. After successfully performed in vitro fertilization, the majority of pregnant women in Slovenia are namely on sick leave from 28 to 42 days respectively prior to the date of delivery, and receive a sick pay.

The consequences in babies, live born to an infected adolescent female with cervicitis, were not considered in our calculations. According to statistical data, 507 adolescent females aged from 15 to 19 years gave birth

Table 1. Estimated costs of infection sequelae at the estimated 6% prevalence of *C. trachomatis* in a cohort of 67,870 adolescent females in Slovenia.

Infection sequelae	No. of persons	Costs per person	Costs total*
Cervicitis	1425	50	71,250
Moniliasis treatment	143	14	2,002
Acute pelvic inflammatory disease outpatient treatment	265	44	11,660
Acute pelvic inflammatory disease hospitalization	265	970	257,050
Chronic pelvic pain	529	310	164,000
Ectopic pregnancy	397	1520	603,440
Infertility - identification	529	1520	804,080
Infertility – 4 attempts	529	1400	740,600
Costs total (in million)*			6.000.000

*US dollars

to a live born baby in Slovenia in 2000, which in this cohort represents 0.7% of adolescent females (14).

In Slovenia, the calculated average incidence rate of ectopic pregnancies in the 1990s was 10.5/10,000 women in their fertile period, which represents an average of 458 women with ectopic pregnancy per year. The cost associated with one ectopic pregnancy was estimated at 1,520 US dollars, such pregnancy being a possible sequelae of *C. trachomatis* infection in 180 women.

The implementation of urine-based PCR screening strategy in adolescent females would improve the sensitivity as well as increase costs, which were with such strategy estimated at 5.3 million US dollars. In Slovenia, only the Medical Faculty in Ljubljana presently implements the PCR assay in diagnosing chlamydial infections. Besides the problem of capturing the population as a whole in this strategy, there is also the disadvantage of an underdeveloped laboratory network for such diagnostics and, of course, the high cost of PCR assay. Nevertheless, a saving of 660,000 US dollars would still be generated.

The urine-based PCR screening strategy in adolescent females would also prove cost-effective at the prevalence of asymptomatic infections slightly lower than estimated (5.3%). Although no saving would be generated in such case, both screening and timely treatment would nevertheless prevent several health problems.

Conclusions

Screening programmes are an opportunity for health care education, a benefit which can hardly be measured in money and on a short term-basis. Economic evaluations of screening strategies and analyses are based on estimation, a more or less successful approximation of the actual situation. Due to great importance of sexually transmitted *C. trachomatis* infections in public health care system in Slovenia, the economic burden of such infections needs to be evaluated. Our evaluation of screening strategies may prove helpful in elaborating a national doctrine of mastering sexually transmitted *C. trachomatis* infections. Here again, the old and already familiar problem of financing arises. And this is, also in Slovenia, one of the key reasons why the screening programmes are not implemented in practice although they have proven cost-effective.

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