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Research article

FREQUENCY OF CO-INFECTION WITH UROGENITAL CHLAMYDIAL INFECTION AND OTHER SEXUALLY TRANSMITTED INFECTIONS AND ASSESSMENT OF ASSOCIATED RISK FACTORS

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Chlamydia trachomatis is one of the most common sexually transmitted infection (STI) pathogens worldwide. Co-infection with multiple STI pathogens increases the risk of complications and the spread of infections necessitating research of risk factors for effective prevention and control.

We analyzed 1,201 medical histories of patients who sought treatment at a specialized dermatovenereological center between 2005 and 2022. Logistic regression was used to assess the independent influence of each analyzed factor.

Co-infection with multiple pathogens was detected in 7.8 % of patients, more frequently among women (68.1 %) and individuals aged 18–29 years (71.3 %). The main co-infections in patients with urogenital chlamydial infection were anogenital (venereal) warts (80.9 %), anogenital herpes infection (20.2 %), and gonococcal infection (14.8 %). Logistic analysis revealed that the likelihood of co-infection was higher among women (OR = 4.84), minors (OR = 3.26), individuals aged 18–29 years (OR = 1.97), those with regular sexual activity (OR = 1.56), and those not in a marital relationship (OR = 2.72).

This study identified factors associated with co-infection with multiple STI pathogens in patients with chlamydial infection, including female sex, age 18–29 years, being unmarried, and having regular sexual activity. The results emphasize the need for early screening for chlamydial infection and other STIs, as well as preventive measures for high-risk groups.

Keywords: *Chlamydia trachomatis, sexually transmitted infections (STIs), co-infection, risk factors, epidemiology, urogenital chlamydial infection, incidence, risk assessment.*

Genitourinary chlamydial infection (caused by *Chlamydia trachomatis* (*C. trachomatis*)) is the most common sexually transmitted infection (STI) worldwide. In 2020, WHO estimated nearly 129 million new cases of C. trachomatis infection emphasizing the issue being truly global [1]. In the Russian Federation, official incidence of the infection amounted to 17.1 cases per 100,000 people in 2023 [2]. However, its actual prevalence can

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be considerably higher due to predominantly asymptomatic disease course, drawbacks of early diagnostics and screening as well as differences in systems for epidemiological surveillance. As reported in epidemiological studies, which have been conducted on samples made of people from various population groups, prevalence of the disease is estimated to vary between 3.8 and 7.1 % in the country, which is comparable with findings reported in European and North American studies [3–7].

Despite the overall decline in the incidence of chlamydial infection in Russia from 2005 to 2022, a reverse trend has been identified in Moscow: the incidence grew from 10 to 14 per 100,000 people between 2018 and 2022[1]. This growth is rather alerting since the infection can induce severe reproductive complications including pelvic inflammatory diseases and infertility as well as promote susceptibility to HIV infection and other STI [8–10].

The high percentage of asymptomatic disease cases creates a significant difficulty in controlling genitourinary chlamydial infection; this makes it harder to perform timely diagnostics and treatment [11, 12]. Genitourinary chlamydial infection (GCI) is predominantly detected in young people, which makes this age group a primary target of relevant prevention and treatment [13–15].

Infection with *Chlamydia trachomatis* simultaneously with other sexually transmitted pathogens considerably increases risks of complications such as pelvic inflammatory diseases, infertility, and ectopic pregnancy [16]. Moreover, co-infection increases risks of getting infected with other STI due to a greater viral load and mucosa lesions, which create favorable conditions for pathogen penetration [17, 18]. For example, co-infection with *Neisseria gonorrhoeae* or simple herpes virus can aggravate the clinical course of genitourinary chlamydial infection and lead to more severe clinical manifestations [19]. These data emphasize the necessity to examine risk factors and peculiarities of co-infection with several pathogens in order to develop more effective prevention and treatment strategies.

In this study, we aimed to identify frequency and risk factors of *C. trachomatis* co-infection with other STI pathogens in patients who applied for treatment to specialized dermatological-venerologic clinics.

Materials and methods. An unselected study sample was made of 1201 medical histories of patients who voluntarily underwent clinical tests to identify STI with subsequent treatment of genitourinary chlamydial infection (GCI) (ICD-10 code A56.0-8) of various localizations at the State Scientific Center of Dermatovenerology and Cosmetology of the RF Ministry of Health between 2005 and 2022.

A case-control study was selected as a method for investigating what factors could influence risks of getting infected with chlamydia and other STI pathogens. Independent effects produced by each analyzed factor were investigated by using logistic regression; to get more precise results, weighted logistic regression (where weight given to variables when examining factors influencing co-infection was equal to 11.78). Co-infection with other sexually transmitted infections (STI) was selected as a dependent variable.

Selection criteria were met for 1201 patients who applied to the clinical and diagnostic center of the State Scientific Center of Dermatovenerology and Cosmetology. The patients were divided into two groups. The control included 1107 patients (92.17 %; 95 % CI: 90.55–93.59 %) with diagnosed genitouri-

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nary chlamydial infection (A56.0-8); the main group was made of 94 patients (7.83 %; 95 % CI: 6.4–9.45 %) with diagnosed chlamydial infection together with other STI (A60; A63; A59; A54; A51).

We analyzed the following variables: sex, age, STI in medical history, chlamydial infection in medical history, complications (for diagnosed A56.1 per ICD-10), marital status, age of the first sexual contact, regularity of sexual contacts, the number of sexual partners, surgery on the genitourinary system in medical history, chicken pox in medical history.

Statistical analysis, creation of graphs, tables and diagrams as well as analysis of the study results were accomplished with Microsoft Excel 2010 and IBM SPSS Statistics 22 software packages. Significance in the case-control study and logistic regression was estimated using the Chi-square test (χ^2) and Fischer's exact test for small samples. The Wald test was employed to calculate confidence intervals.

Results and discussion. One thousand two hundred and one patients with genitourinary chlamydial infection (GCI) were almost evenly distributed per sex: 634 (52.75 %) men and 568 (47.25 %) women. Young patients (aged 18–29 years) prevailed in the groups; minors accounted for 7.2 %. Sexually transmitted infections (STI) appeared in patients' medical history in 23.1 % of the cases and re-infection with chlamydia was detected in 8.9 % of the patients.

Genitourinary chlamydial infection (GCI) combined with other STI was established in 94 patients (7.82 %; 95 % CI: 6.3–9.3). GCI was the most frequent together with anogenital (venereal) warts, 80.9 % (74 patients); genital herpes, 20.2 % (19 patients); gonococcal infection, 14.8 % (14 Patients). GCI combined with two other STI was established in 18.1 % (17 patients); three other STI, 1.06 % (1 patient). Co-infections were more frequent among women (11.3 % (of all women); 95 % CI: 8.9–14.1, against 4.7 % (of all men); 95 % CI: 3.3–6.6 among men). The average age of patients with co-infection was 24.5 (16 to 55, the median age was 24 years). The lowest medium age was established among patients with anogenital warts, 21.75 years (16 to 34, the median age was 19 years) (Table 1).

Factors that increased risk of co-infection with chlamydial infection and other STI pathogens included female sex (*OR* = 2.6; 95 % CI: 1.6–4.0), age between 18 and 29 years (*OR* = 1.8; 95 % CI: 1.1–3.1), being single (*OR* = 2.9; 95 % CI: 1.5–6.2), chicken pox in medical history (*OR* = 2.04; 95 % CI: 1.5–3.9). Other analyzed indicators did not have any statistical significance (Table 2).

Independent influence exerted by each analyzed factor was examined by using logistic regression. It should be noted that only those patients, for whom all factors included in the analysis are known, can be considered in a logistic regression model. To get more authentic results, we selected only those factors for our analysis, which allowed minimal reduction in the number of patients in both groups (Figure 1).

The results obtained by logistic regression analysis showed that female sex and being single were two independent factors, which increased the risk of co-infection with several STI by 4.88 (95 % CI: 1.9–12.4) times and 3.12 (95 % CI: 1.1–9.3) times accordingly.

The results obtained by weighted logistic regression established an association between co-infection with several STI and regular sexual contacts (*OR* = 1.56 (95 % CI: 1.14–2.14)), being a minor (*OR* = 3.26 (95 % CI: 2.0–5.29)), age between 18 and 29 years (*OR* = 1.97 (95 % CI: 1.39–2.79)), female sex (*OR* = 4.84 (95 % CI: 3.47–6.74)) and being single (*OR* = 2.72 (95 % CI: 1.83–4.06)) (Figure 2).

The analysis established that the risk of ci-infection simultaneously with *Chlamydia trachomatis* and other STI pathogens was higher for women, patients aged between 18 and 29 years and single (not married) patients. Higher odds ratio for women can be caused by their greater readiness to undergo a preventive medical check-up even if they do not have any complaints concerning the genitourinary system functioning or when planning

Table 1

Profile of patients with genitourinary chlamydial infection

	Cases (percentage [95 % CI])		
	Co-infection with other STI	Without co-infection	Total
Total	94 (7.8 % [6.3–9.3])	1107 (92.2 % [90.7–93.7])	1201 (100 % [100–100])
Sex			
Male	30 (31.9 % [22.5–41.3])	604 (54.6 % [51.6–57.5])	634 (52.8 % [50–55.6])
Female	64 (68.1 % [58.7–77.5])	503 (45.4 % [42.5–48.4])	567 (47.2 % [44.4–50])
Age			
Minors	6 (6.4 % [1.4–11.3])	81 (7.3 % [5.8–8.9])	87 (7.2 % [5.8–8.7])
between 18 and 29	67 (71.3 % [62.1–80.4])	652 (58.9 % [56–61.8])	719 (59.9 % [57.1–62.6])
Older than 30	21 (22.3 % [13.9–30.8])	374 (33.8 % [31–36.6])	395 (32.9 % [30.2–35.5])
Chicken pox in medical history			
Yes	27 (28.7 % [19.6–37.9])	159 (14.4 % [12.3–16.4])	186 (15.5 % [13.4–17.5])
No	67 (71.3 % [62.1–80.4])	948 (85.6 % [83.6–87.7])	1015 (84.5 % [82.5–86.6])
STI in medical history			
Yes	24 (25.5 % [16.7–34.3])	254 (22.9 % [20.5–25.4])	278 (23.1 % [20.8–25.5])
No	70 (74.5 % [65.7–83.3])	853 (77.1 % [74.6–79.5])	923 (76.9 % [74.5–79.2])
Chlamydial infection in medical history			
Yes	5 (5.3 % [0.8–9.9])	102 (9.2 % [7.5–10.9])	107 (8.9 % [7.3–10.5])
No	89 (94.7 % [90.1–99.2])	1005 (90.8 % [89.1–92.5])	1094 (91.1 % [89.5–92.7])
Complications			
Yes	3 (3.2 % [-0.4–6.7])	30 (2.7 % [1.8–3.7])	33 (2.7 % [1.8–3.7])
No	91 (96.8 % [93.3–100.4])	1077 (97.3 % [96.3–98.2])	1168 (97.3 % [96.3–98.2])
Marital status			
Data not available	20 (21.3 % [13–29.6])	354 (32 % [29.2–34.7])	374 (31.1 % [28.5–33.8])
Married	56 (59.6 % [49.7–69.5])	369 (33.3 % [30.6–36.1])	425 (35.4 % [32.7–38.1])
Single	18 (19.1 % [11.2–27.1])	384 (34.7 % [31.9–37.5])	402 (33.5 % [30.8–36.1])
Age of the first sexual contact			
Data not available	49 (52.1 % [42–62.2])	833 (75.2 % [72.7–77.8])	882 (73.4 % [70.9–75.9])
Younger than 18 years	34 (36.2 % [26.5–45.9])	203 (18.3 % [16.1–20.6])	237 (19.7 % [17.5–22])
Older than 18 years	11 (11.7 % [5.2–18.2])	71 (6.4 % [5–7.9])	82 (6.8 % [5.4–8.3])
Regular sexual contacts			
Data not available	55 (58.5 % [48.6–68.5])	563 (50.9 % [47.9–53.8])	618 (51.5 % [48.6–54.3])
Yes	27 (28.7 % [19.6–37.9])	352 (31.8 % [29.1–34.5])	379 (31.6 % [28.9–34.2])
No	12 (12.8 % [6–19.5])	192 (17.3 % [15.1–19.6])	204 (17 % [14.9–19.1])
The number of sexual partners over the whole life time			
Data not available	76 (80.9 % [72.9–88.8])	1015 (91.7 % [90.1–93.3])	1091 (90.8 % [89.2–92.5])
More than 2	13 (13.8 % [6.9–20.8])	56 (5.1 % [3.8–6.3])	69 (5.7 % [4.4–7.1])
2 or less	5 (5.3 % [0.8–9.9])	36 (3.3 % [2.2–4.3])	41 (3.4 % [2.4–4.4])
Surgery on the genitourinary system			
Data not available	41 (43.6 % [33.6–53.6])	442 (39.9 % [37–42.8])	483 (40.2 % [37.4–43])
Yes	3 (3.2 % [-0.4–6.7])	42 (3.8 % [2.7–4.9])	45 (3.7 % [2.7–4.8])
No	50 (53.2 % [43.1–63.3])	623 (56.3 % [53.4–59.2])	673 (56 % [53.2–58.8])

a pregnancy. Age between 18 and 29 years and extra-marital sexual contacts are likely to be associated with frequent change of sexual partners, neglected barrier contraception, low vigilance and low readiness to have any check-up for having a STI and consequently, a higher risk of co-infection with several such diseases simultaneously.

Chicken pox in medical history was associated with an elevated risk of co-infection with chlamydial infection together with other STI. However, a significant association between chicken pox in medical history and risks of co-infection was established only in the case-control study. It did not persist when logistic regression was used. This may indicate

Table 2

Factors associated with risks of co-infection with chlamydial infection and other STI pathogens, the case-control study

Indicator	Odds Ratio [95 % CI]	*p* value
Female sex	2.55 [1.635–4.042]	0.00001303
Age younger than 18 years	1.319 [0.516–3.372]	0.3572
Age between 18 and 29 years	1.829 [1.114–3.094]	0.008917
Being single	2.887 [1.469–6.232]	0.001137
Chicken pox in medical history	2.04 [1.471–3.846]	0.0001101
Complications	1.184 [0.354–3.953]	0.4851
STI in medical history	1.151 [0.6982–1.853]	0.284
Chlamydial infection in medical history	0.5538 [0.1946–1.305]	0.1017
The first sexual contact prior to 18 years of age	1.081 [0.5278–2.334]	0.4173
More than 2 sexual partners over the whole life time	1.664 [0.5566–5.595]	0.1812
Regular sexual contacts	1.227 [0.6142–2.561]	0.2836
Surgery on the genitourinary system in medical history	0.8901 [0.2119–2.691]	0.4539

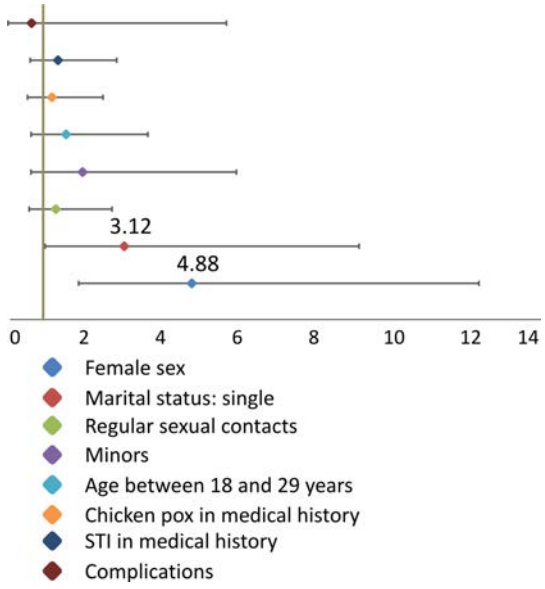

Figure 1. Logistic regression showing risk factors that influence risk of co-infection simultaneously with GCI and other STI (R^2 = 0.1 (Hosmer & Lemeshow); 0.48 (Cox & Snell); 0.121 (Nagelkerke); Chi-square – 26.792; $p < 0.001$)

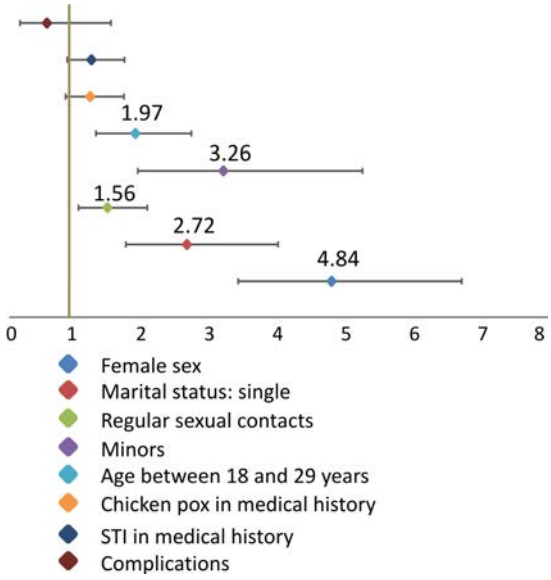

Figure 2. Logistic regression with weighted risk factors influencing the risk of co-infection simultaneously with GCI and other STI (R^2 = 0.17 (Hosmer & Lemeshow); 0.179 (Cox & Snell); 0.239 (Nagelkerke); Chi-square – 187.539; $p < 0.001$)

either certain effects produced by confounders, which were not considered, or the applied model being not being powerful enough to reveal weaker associations. Therefore, the results require further analysis involving additional variables and a larger sample.

Logistic regression analysis found an association between co-infection with several STI, female sex and being single. Although the model is significant, the codetermination coefficients (R^2) show that it explains only a small part of the analyzed variation. This indicates there might be other significant risk factors, which were not included in the analysis.

To achieve make our analysis and study more precise, weighted logistic regression was employed; this made it possible to consider impacts exerted by different factors more profoundly. This approach confirmed the results obtained by the case-control study and revealed additional significant associa-

tions: regular sexual contacts (*OR* = 1.56) and being a minor (*OR* = 3.26) turned out to be associated with elevated risks of co-infection with several STI pathogens. Minor patients face a considerably higher risk of co-infection as compared with people aged between 18 and 29 years. This difference may be due to anatomic and physiological peculiarities of the genital organs as well as low awareness, tendency to neglect barrier contraception (largely due to difficulty in buying relevant means). Another reason might be difficulties in performing STI prevention check-ups when it concerns young patients (both psychological and financial), which make young people more susceptible to sexually transmitted infections. Use of weighted logistic regression raised the explanatory capability of the model considerably, which is confirmed by the determination coefficients growing up to R^2 = 0.179 (Cox & Snell) and R^2 = 0.239 (Nagelkerke). High statistical significance of the model is confirmed by the Chie-square test results (χ^2 = 187.539; $p < 0.001$). These data give evidence that the model is reliable and capable of adequately describe relationships between key risk factors and likelihood of co-infection.

Conclusions. Co-infection with other STI pathogens was established in 7.8 % of the analyzed patients with genitourinary chlamydial infection; more frequently, it occurred together with anogenital (venereal) warts (80.9 %), anogenital herpes (20.2 %) and gonococcal infection (14.8 %).

Female sex, age between 18 and 29 years, being a minor, regular sexual contacts and being single are key independent risk factors of co-infection with simultaneously *C. trachomatis* and other STI pathogens.

Our findings give evidence of the necessity to intensify prevention aimed at reducing levels of co-infection with several STI pathogens. Given that women and young people are the most susceptible population groups, prevention programs should include some educational initiatives targeted at them. Such activities should be aimed at promoting barrier contraception and safe sex concepts (having one regular sexual partner, both partners having regular check-ups to identify STI) [20]. It is also important to develop a system for early testing and preventive check-ups and to implement programs for raising awareness and motivation of both partners to have an examination and, if necessary, treatment. This will help effectively break the chain of infection transmission.

A complex approach based on the findings reported in this study can make for reduction in incidence, prevention of complication and protection of reproductive health.

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