SHORT RESEARCH ARTICLE

Mycoplasma Genitalium and Chlamydia Trachomatis Prevalence, Co-Infection and Relevant Factors in An Epidemiology Study (2016 - 2019) In Ho Chi Minh, Vietnam

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ABSTRACT

Chlamydia trachomatis and *Mycoplasma genitalium* are two common types of sexually transmitted infections. However, currently in Vietnam, there is no report on the rate of patients infected by the two types of bacteria. In this study, there were 6194 patients visiting the STI clinic of the HCMC Hospital of Dermato-Venereology, Vietnam, from 2016 to 2019. The results show that the proportion of patients positive with CT and MG is independent on time. The infection rate is mainly at the age of 21 - 30 (53.4%). The CT infection rate in female and male is equal (17.3% vs 17.4%) while the rate of MG in female is lower (5.1% vs 7, 8%). The rate of patients co-infected with either CT or MG is 4.5%, 17% and 5.7% respectively, time independence. This study may give better understandings of the epidemiological characteristics of MG and CT in Vietnam.

Key words: *Chlamydia trachomatis, Mycoplasma genitalium,* sexually transmitted infections, co-infections

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INTRODUCTION

Sexually transmitted infections (STIs) are also known as sexually transmitted diseases that are transmitted from person to person through sexual acts in the genitals, mouths or anus. According to World Health Organization (WHO), more than 1 million people have a STI every day worldwide [https://www.who.int/news-room/fact-sheets/detail/sexually-transmitted-infections-(stis)]. Although some sexually transmitted infections (Chlamydia, Mycoplasma, syphilis, etc.) are treatable, they can cause acute inflammation such as cervicitis, urethritis, and ulcers. genitalia, even lead to serious complications and long-term sequelae such as epididymitis, pelvic inflammatory disease, ectopic pregnancy, premature birth, even infertility.[1-4]

Chlamydia trachomatis (CT) is a gram-negative, obligate intracellular parasite.[5] This is a common sexually transmitted infection, a common cause of urethritis in male and cervicitis in female.[6] In addition, *Mycoplasma genitalium* (MG) is getting more and more attention due to their resistance to antibiotics, which is a common cause of non-gonorrhea urethritis in male.[7] They are so difficult to cultivate that there are only a few large centers in the world where MG can be successfully cultured.[8]

Additionally, one study found that STIs affect the quality of sex and fertility of the patient severely.[9] As a result, the issues related to STIs should be placed at a critical position in the formulation of national and international public health strategies. In 2015, WHO conducted a meta-analysis and found that the global prevalence of CT in women and men was 4.2% and 2.7% respectively.[10] In South-East Asia, the rate with a random effect model was 0.8%.[11] Statistics on Embase, Medline, IndMED, African Index Medicus and LILACS from 1 January 1991 to 12 July 2016 revealed the percentage of patients infected with MG which was 1.3%, including pregnant women 0.9%, men with men (MSM) in the community 3.2%, commercial sex workers (CSWs) in the community 15.9%.[12] In 2016, the WHO set its vision, goals, targets and strategies to prevent, control and manage the sexually transmitted infections by developing the Global Health Sector Strategy on STI.[13] The strategy aims at rapidly scaling up evidence-based interventions and providing services to end the public health concerns in STI by 2030. In accordance with the primitive aim, it is essential to provide "information for focused action", more data on STI burden, including STI prevalence estimates to both general and high-rich populations in rural and urban areas.[13]

Based on studies, we have found that the infection rate in CT and MG-infected patients, aged mainly from 21 to 30 independent on time. The CT infection rate in man and woman is equal, meanwhile the rate in woman infected with MG is lower than that in man and the co-infection rate in CT and MG is lower compared to the one found in an American study. This study is to evaluate the prevalence, co-infection as well as related epidemiological factors of CT and MG through retrospective analysis of patients who come to the STIs clinic at HCMC Hospital of Dermato-Venereology, Vietnam.

METHODOLOGY

Patients: The retrospective study was conducted on patients who visited STIs clinics at HCMC Hospital of Dermato-Venereology, Vietnam from January 2016 to December 2019. These patients included both male and female with symptoms: vaginitis, cervicitis, dysuria and pelvic inflammatory disease in female and urethral discharge, itching, burning urination, difficulty urinating in male and asymptomatic (including patients who came to the examination for other conditions such as syphilis, genital warts, genital fungal infections, ... or having a sex partner who has a sexually transmitted disease or visits for screening). Patients who were tested for the second time or more during treatment were counted only once. The statistics is made as follows: negative if all tests are negative, positive if there is at least one positive test.

Ethics statement: The study was approved by the Human Research Ethics Committee of HCMC Hospital of Dermato-Venereology, Vietnam. The study was conducted according to the bio-medical ethics of Vietnamese laws (item 3, article 3, circular 45/2017/TT-BYT). Clinical information and data from patients who visited STIs clinics at HCMC Hospital of Dermato-Venereology from 2016 to 2019 were analyzed and assessed for scientific purposes.

Specimen collection and detection of CT and MG: The samples were taken from urethral swabs, vaginal swabs, and cervical swabs with a cotton swab. Transfer the swab into an Eppendorf tube containing 0.5 ml of sterile 0.9% NaCl solution or 0.3 mL of Transport medium sample storage solution. Add 200µL of the patient sample to 10µL Internal control, then add the mixture to the sample tube, transfer the sample to the SaMag-12 (Sacace Biotechnologies) tray to obtain the total DNA. Then identify CT and MG by real-time PCR method (machine Mx3005P-Agilent Technologies), sample is mixed with Multiplex kit (Sacace). Read the results by linear scale analysis.

Statistical analysis: All statistical analyses were performed using the R software. The rates were calculated by dividing the number of positive patients by the number of patients tested; however, the CT and MG co-infection rates were calculated by three different ways according to the total number of people infected with one of the two diseases, out of the total number of people with only MG and out of the total number of people with only CT disease. The age-adjusted rate for male or female is calculated according to data of patients who came to STIS at

HCMC Hospital of Dermato-Venereology from 2016 - 2019. Age stratified into groups: ≤20, 21-30, 31-40, >40. Confidence interval (CI) is calculated at 95%. On the one hand, groups are compared by the χ2-test, on the other hand when comparing the proportions we use the Z-test, *P*-values less than 0.05 are considered statistically significant

RESULTS

A total of 6194 patients visited and tested real-time PCR CT and MG at STIs clinics of HCMC Hospital of Dermato-Venereology, including 4420 female patients and 1774 male patients. The rates of CT and MG infections in both sexes were 17.3% (1074/6194) (95% CI 16.4% - 18.3%) and 5.9% (364/6194) (95% CI 5.3% - 6.5%). The rates of CT and MG infection were 17.4% (309/1774) (95% CI 17% - 19%) and 7.8% (138/1774) (95% CI 6.6% - 9.1%) in male; 17.3% (763/4420) (95% CI 16% - 18%) and 5.1% (226/4420) (95% CI 4.5% - 5.8%) in female.

Prevalence from 2016 to 2019: From 2016-2019, see **Fig 1a.**, the percentage of patients positive for CT and MG generally did not depend on time over the years. This means that the respective rates are computed each year for four years with an equal distribution. To confirm this, we use χ2-test, with *P*-value >0.05, we accept the above statement. In other words, the proportion of patients infected with MG and the rate of patients infected with CT were unchanged over the years. Also, from **Fig 1a**., it shows that, if counted each year, the proportion of patients infected with CT is higher than the rate of people infected with MG. If calculating these two rates for all the 4 years, the rate of people infected with CT is 17.3%, much higher than the rate of people infected with MG of 5.9%.

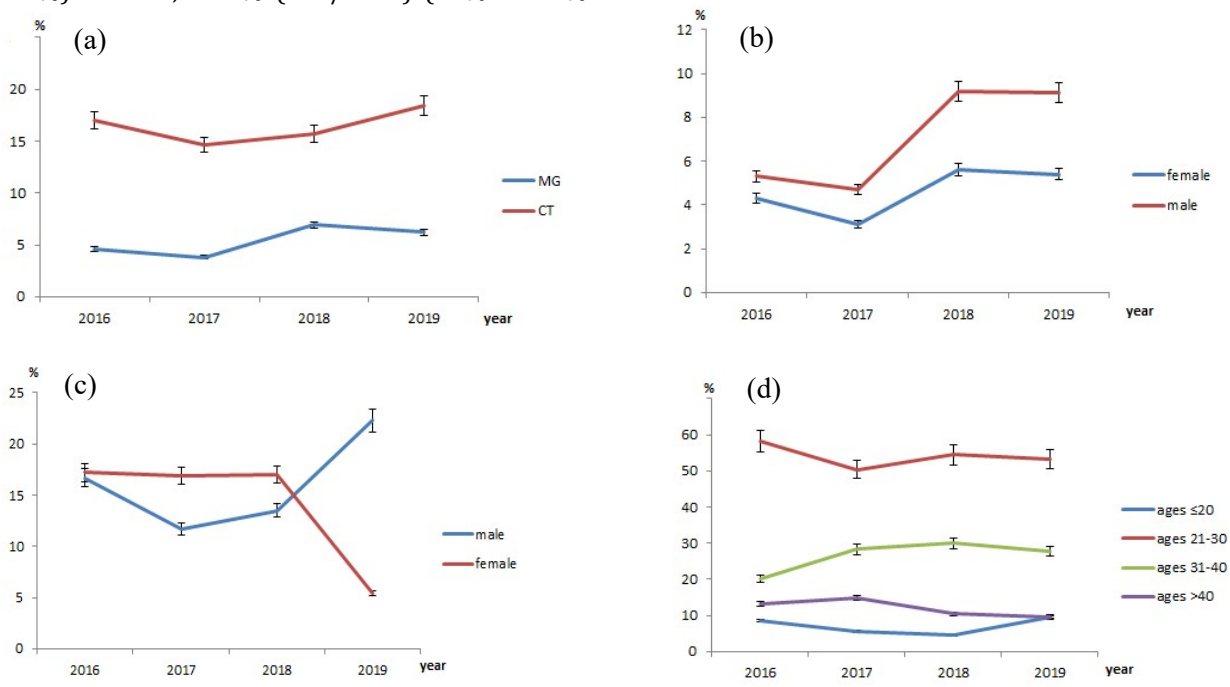

Figure 1: The adjusted prevalence of MG and CT from 2016 to 2019

(a) Infection from 2016 to 2019; (b) MG in male and female; (c) CT in male and female, (d) MG and CT by age groups.

Gender differences in prevalence: First of all, from the data in **Fig 1.**, we use χ2-test with the calculated *P*-values are all larger 0.05, we accept the rates of female infected with MG, female infected with CT, male infected with MG, male CT infections are equally distributed over the years. In other words, these rates have not changed over the years.

For MG disease, patients came to the examination for 4 years, the proportion of female infected with MG was less than that of male (5.1% female, 7.8% male). If calculating these rates by year, the results in **Fig 1b.,** show that from 2016 to 2019, the proportion of patients infected with MG among female was lower than that among male. To confirm this, with the note that since the rates are considered time-independent, instead of comparing the two ratios of each pair of years, we only need to compare these two ratios calculated for all the four years. Specifically, the above statement is accepted when we use Z-test with *P*-value close to 0.

For CT disease, see **Fig 1c.**, among 1072 CT-positive patients, there was no difference in the prevalence rate in female and male (17.3% female vs 17.4% male). This statement is accepted when we use Z-test to compare CT infection rates of male and female over 4 years with the calculated value of *P*-value =

0.91. With the same attention that the prevalence of this disease for male and female has remained constant over the years, we can conclude that the rate of CT infection of two male and female is equal over time with statistical significance.

Age differences in prevalence: In this study we divided patients into 4 age groups: ≤20, 21-30, 31-40 and >40. From the results of **Fig 1d**., it is shown that the proportion of patients infected with CT and MG depends on age. If we calculate the infection rate for all the 4 years, the highest infection rate is at the age of 21-30 (56.3%, 774/1374), followed by the age of 31-40 (25.6%, 352/1374), the age over 40 (9.2%, 127/1374) and the lowest is at the age of 20 (8.8%, 121/1374). The proportion of patients infected with CT and MG gradually decreased with age. If we calculate the rate for all the 4 years, the highest rate is of patients aged 21-30 (56.3%, 774/1374), next 31-40 (25.6%-352/1374), age >40 (9.2%, 127/1374) and the lowest ≤20 (8.8%, 121/1374). The rate of patients infected with CT and MG decreased with age (in groups of 20 and more). The rate of 21-30 was twice as much as that of 31-40 and 6 times as much as that of over 40. Over the years, the proportion of patients infected with CT and MG in the 21-30 age group is higher than other age groups (58.3% in 2016, 50.3% in 2017, 54.6% in 2018 and 57.3% in 2019). There is a statistical note that, if using $\chi 2$-test, we accept the infection rate by age from 21 to 30 with an equal distribution over 4 years with calculated *P*-value of 0.8741. In other words, the rate of infection by each age group is constant year by year. Moreover, we have similar conclusions for ages ≤20, 31-40 and over 40 with the corresponding *P*-value calculated as 0.4094, 0.5611, and 0.4559.

In terms of gender by age, female patients aged 21-30 years were infected with CT and MG accounted for 60% (563/938), while that for male accounted for 48.4% (211/436). Using Z-test with *P*-value <0.05, we can conclude that the rate of infection at this age of female is greater than that of male. In addition, the prevalence of MG infection by age group was 9% (33 patients), 54.6% (199 patients), 26% (95 patients), and 10% (37 patients) respectively. The corresponding CT was 9.2% (99 patients), 56.7% (609 patients), 25% (269 patients) and 8.8% (95 patients). In terms of statistics, using Pearson $\chi 2$-test, the obtained P-value is 0.21, we can accept that the age distribution of MG and CT is the same.

Prevalence of co-infections: In all 4 years, among 1376 infected ones, there were 364 infected with MG, 1074 with CT, and 62 patients infected with both diseases. Thus, the ratios of co-infected patients to the total number of infected patients with either of the 2 diseases, with MG, and with CT are 4.5% (62/1376), 17% (62/364) and 5.7% (62/1074) respectively. In terms of each year, the ratio of co-infected people to the total number of people infected with either of the diseases from 2016-2019 is 3.1% (4/127), 2.1% (3/141), 5% (12/236) and 4.9% (43/872) respectively. Meanwhile, when calculating the rate of co-infection on the total number of people infected with MG over the years, the result is respectively 14.3% (4/28), 10% (3/30), 15.8% (12/76), 18.7% (43/230) and if calculating the ratio of co-infection to the number of people infected with CT, the corresponding results are 3.9% (4/103), 2.6% (3/114), 9.6% (12/172) and 6.3% (43/685). Using $\chi 2$-test, with *P*-values of 0.66, 0.44, and 0.17, respectively, we have no basis to deny that the ratio of co-infection to the total number of people infected with either of the diseases, the total number of MG infected patients or the total number of the CT infected has an equal distribution over time. This means we accept that the rate of co-infection according to the three above calculation methods is the same through the 4 years; in other words, that the rate is unchanged for the 4 years.

DISCUSSION

STIs remain a serious worldwide public health problem.[14] In Vietnam, in recent years, along with the social development, people have become more open-minded on sexual relations; however, this also contributes to an increase in the incidence of sexually transmitted infections. Among them, CSWs and their clients, MSM, drug users, migrant workers and young people are considered to be at a high risk of STIs.[15] Therefore, a critical solution is needed to prevent the spread of STIs from these high-risk populations to common populations in Vietnam and throughout the world. However, the epidemiology of sexually transmitted diseases in Vietnam is very statistically limited with little information. This study investigates retrospectively the epidemiological factor of CT and MG of patients who examined at the STIs, which can provide more basic scientific information on STIs to help the government with some solutions to control the spread of sexually transmitted diseases.

CT is the most common cause of non-gonorrhea urethritis. MG is one of the main causes of non-gonorrhea urethritis in the world but an uncommon STI in general. The risk of sexual transmission is lower for CT.[16,17] This study also shows similar results, patients infected with MG were not as common as those infected with CT (364 vs 1074 respective 5.9% vs 17.3%). The proportion of patients infected with MG for the 4 years in female is lower than that in male. This rate is consistent with many previous studies in the US[18,19] and Australia[20].

This study showed that the incidence of CT infection was 17.3%, which is lower than the US study (21.6%)[19] but higher than the study in China[21]. We do not know what factors made the difference and require further studies to evaluate.

In this study, the proportion of patients infected with CT and MG did not depend on time factor. Therefore, this is an important data and a premise for future research on STIs (CT and MG) in Vietnam. In addition,

this result shows that communication in STIs prevention has not been highly effective, which requires more authorities' attention.

Age is one of the factors affecting the rate of sexually transmitted infection. Many previous studies have shown that young people have the highest risk of infection.[22,23] Our research results show that at the age of 21-30, the rate of CT and MG infection is the highest (53.4%), consistent with previous studies in the world.[21,24] Besides, in this age group, the rates of CT and MG infection did not differ in sex and had the highest rate of co-infection. In the youngest age group (≤20 years old), the incidence of CT and MG infection is the lowest. In addition, in other age groups, the incidence of CT and MG infection in both sexes decreases with the increasing of life expectancy. This study result is consistent with a study in the US[19], China[21] and New Zealand[24]. The correlation between sexually active age and STIs can be attributed to both physiological and behavioural factors. First, the young have a higher sex life demand than older do. Second, young people often tend to have unsafe sex such as having sex with many sex partners, not using condoms during sex. Therefore, we strongly recommend the need for sex education and screening programs for sexually transmitted infections for young people aged 21-30 to prevent the spread in the community, reducing the burden of treatment costs for patients as well as for society.

The rate of co-infection to the total number of people with one of the two diseases, with MG and with CT disease is 4.5%, 17% and 5.7% respectively. The rate of co-infection in this study is many times as high as that in the Siberian[25] and Dutch[26] studies. The data from this study can help clinicians in diagnosing and treating more effectively.

Our research is limited because it is a retrospective study; therefore, there are no interviews or questionnaires for patients about marital status, educational level, and risk factors and we could not make further research to evaluate the factors that can affect the prevalence of infection and co-infection. In addition, because the study subjects only included patients who came to the STI clinic of a hospital, these statistics cannot be considered as the most general, even though they were from one of the major hospitals where most of Vietnam's STIs are examined and treated.

Conclusion

In summary, the incidence of CT and MG infection does not depend on time but ages: high in the age group from 21 to 40 and the highest in group from 21-30. The rate of MG infection in female over the years is lower than that in male whereas the rate of CT infection in female and male is the same. The rate of co-infection to the total number of people with one of the two diseases, with MG and with CT disease is 4.5%, 17% and 5.7%, respectively. This study can help epidemiologists, clinicians to have a better understanding of the current epidemiological features of CT and MG in Vietnam and thereby provides further information for more effective prevention, diagnosis and treatment.

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