

INFECÇÃO POR *CHLAMYDIA TRACHOMATIS* E *NEISSERIA GONORRHOEAE* EM UTENTES DE UMA CONSULTA DE DOENÇAS DE TRANSMISSÃO SEXUAL - ANÁLISE DE DEZ ANOS

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RESUMO – Introdução: Estudos recentes têm apontado para um aumento da incidência de infecções por *Chlamydia trachomatis* (CT) e *Neisseria gonorrhoeae* (NG). **Objetivos:** Determinar a prevalência de infecção por CT e NG em utentes de uma consulta de Doenças de Transmissão Sexual (DST) num Hospital Universitário. **Métodos:** Foi realizado um estudo transversal nos utentes de uma clínica de DTS ao longo de um período de 10 anos. Os diagnósticos foram efectuados recorrendo a análise de amplificação de ácidos nucleicos (PCR). **Resultados:** Na população estudada houve um predomínio do sexo masculino (83,3%). A prevalência global da infecção por CT e NG foi de 1,6% e 0,8%, respectivamente, e após implementação do rastreio a todos os utentes observados, a prevalência de infecção por CT subiu para 3%. Adicionalmente, 53% dos utentes assintomáticos foram diagnosticados como portadores da infecção, 78% com infecção por CT e 22% com infecção por NG ($p < 0,05$). O rastreio sistemático resultou no diagnóstico e no tratamento de uma média de 13,7 indivíduos assintomáticos. **Conclusão:** Contrariamente ao observado na infecção por NG, os autores encontraram um aumento da prevalência da infecção por CT, após implementação do rastreio sistemático de todos os utentes da consulta. A triagem para a infecção por CT possibilitou a identificação e tratamento das infecções assintomáticas por este microorganismo. Os autores sugerem o rastreio sistemático de todos os utentes das consultas de STD para a infecção por CT.

PALAVRAS-CHAVE – *Chlamydia Trachomatis*; *Neisseria gonorrhoeae*; Infecções por Clamídia; Gonorreia.

CHLAMYDIA TRACHOMATIS AND NEISSERIA GONORRHOEAE INFECTIONS IN ATTENDEES OF A SEXUALLY TRANSMITTED DISEASES CLINIC - A TEN YEAR TREND ANALYSIS

ABSTRACT – Background: Reports indicating incidence of *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) infections have been increasing. **Objectives:** To determine the prevalence of CT and NG infected individuals attending a Sexually Transmitted Disease (STD) clinic in a University Hospital. **Methods:** A cross-sectional study was conducted on attendees of the STD clinic throughout a 10 year period. Diagnoses of CT and NG infections were enabled upon nucleic acid amplification analysis (PCR). **Results:** In our study population there was a male predominance (83.3%). Overall prevalence of CT and NG infection was 1.6% and 0.8%, respectively. A prevalence of 3% of chlamydia infection was recorded when routine screening was implemented. More so, 53% of individuals displayed asymptomatic infection, 78% of which had chlamydia infection and 22% had gonococcal infection ($p < 0.05$). Routine screening of STD attendees has resulted in the diagnosis and treatment of an average of 13.7 asymptomatic individuals.

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Conclusion: Unlike gonococcal infection we found an increase of chlamydia infection prevalence when routine screening was implemented. Screening of STD attendees for CT provided the opportunity to identify and treat asymptomatic *Chlamydia* infections. Systematic screening of STD attendees of both genders for CT should be offered.

KEY-WORDS – *Chlamydia* Infections; *Chlamydia trachomatis*; Gonorrhea; *Neisseria gonorrhoeae*; Ambulatory Care Facilities.

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INTRODUCTION

Chlamydia trachomatis (CT) and *Neisseria gonorrhoeae* (NG) infections are the most frequent bacterial sexually transmitted diseases¹ with increasing incidence as recently reported. In the United States, experts estimate an annual incidence of 2.8 million new chlamydia infections and 720 000 new gonococcal infections, the majority of which are asymptomatic². Thus, given the highly asymptomatic nature of the pathogen, the reported prevalence of genital chlamydia infections in the population is likely underestimated.

Chlamydia infection, and to a lower degree, gonococcal infection, are associated with some urogenital complications. In women, complications include pelvic inflammatory disease and ectopic pregnancy, whereas in men epididymitis, orchitis, prostatitis and proctitis have been described. Infertility and sexually acquired reactive arthritis (SARA) are known to occur in both gender as a consequence of these infections. Moreover, chlamydia and gonococcal infections increase 3- to 6-fold the transmission or acquisition risk of human immunodeficiency virus (HIV)³.

The effectiveness of community based screening in reducing the incidence and consequences of CT infection is well documented⁴. Nowadays, nearly every major U.S. public health organization recommends routine screening of sexually active young women for chlamydia infection⁵⁻⁷. There are no widely accepted guidelines for gonococcal infection screening⁸.

DIAGNOSTIC TECHNIQUES

Nucleic acid amplification techniques (NAATs) such as polymerase chain reaction (PCR) are now widely available and are currently being used for diagnosis of genital chlamydia and gonococcal infections. Tests can be performed in urine, urethral, vaginal, rectal, conjunctival or pharyngeal specimens and their superiority over other techniques has been demonstrated⁹. Recently however, new strains of CT have emerged (the Swedish variant), leading to false negative results since most commercially available NAATs fail to detect them. To overcome this, new real-time PCR assays for detection of CT have been developed¹⁰.

In some European countries, there are no clear guidelines for screening these bacterial infections, and as such, screening programs differ among medical centres. Herein, we aimed to determine the prevalences and predictors of CT and NG infections among the attendees of the STD clinic in Hospital de S. Joao, Porto, throughout a 10 year period. More so, we set out to evaluate whether routine screening in both genders should be extended to other health institutions.

MATERIAL AND METHODS

We carried out a retrospective review of all medical records of STD clinic attendees diagnosed with microbiological infections by NAATs, namely CT and NG. Several

variables were analysed, including age, gender, sexual behaviour, clinic manifestations, treatment and follow-up.

COBAS® AmpliCor (Roche, Basel, Switzerland) had been used for the diagnosis of CT and NG infections from 2001 through 2006 in every patient, and respective partner, suspected of having one of the infections. Ever since, artus 3000 TM® (Qiagen, Hamburg, Germany), a real-time PCR for CT detection and an 'in house' method for NG detection have been systematically performed to all STD attendees regardless of complaints. Since 2004, CT serovars are also being determined. The specimens collected include first-void urine, vaginal, urethral or rectal swabs.

Statistical analysis was performed using SPSS software version 17.0 using the χ^2 test. P values of <0.05 were considered statistically significant.

RESULTS

Of the 2711 attendees throughout the 10 year study period, 60 had positive laboratory PCR results to either CT or NG infection; 39 were diagnosed with chlamydia infection (10 between 2001 and 2006 and 29 after 2007), 21 with gonococcal infection (13 between 2001 and 2006 and 8 after 2007). Additionally, co-infection by both microbial agents was observed in 4 patients.

The overall prevalence of CT and NG infections was 1.6% and 0.8% respectively. From 2007 onwards, routine screening of both infections in first-void urine was implemented and a prevalence of 3% and 0.8% were recorded for chlamydia infection and gonococcal infection, respectively.

Table 1 depicts the comparison of socio-demographic, behavioural characteristics and clinical data between the two groups of bacterial genital infection. We found a clear male predominance (83.3% of individuals) in our study population; five of them (8.3%) were emigrants, mainly from African countries, 3 of which were non-Caucasian.

As far as age is concerned, CT infections were more frequent around the 30ies, whereas two peaks were found for NG infection, one in the 20ies and another in the 50ies. However, no differences in median age were found.

Thirty-four patients (56.6%; 34/60) had completed primary school, while 26 (43%; 26/60) had high school or university graduation, however no differences were observed for either chlamydia or gonorrhoea group of patients.

Regular sex partner was predominantly reported, namely boy/girlfriend (38%; 23/60) or spouse (16%; 10/60). However, in the gonorrhoea infected partici-

pants there was a predominance in the married group over the occasional partners group, ($p < 0.05$). The majority of participants (87%; 52/60) reported being heterosexual in both groups of bacterial infections.

The most frequently reported symptoms were discharge, dysuria and pruritus. Patients with gonorrhoea displayed symptoms more frequently than the chlamydia participants (67% vs 36%; $p < 0.05$). Dysuria, discharge and purulent discharge were more often reported by the attendees with gonorrhoea infection ($p < 0.05$). Pruritus, which was the least reported complaint, was equally distributed among the groups.

Individuals diagnosed with chlamydia infection were frequently more infected with other sexually transmitted infections (STI) than individuals with gonococcal infection ($p < 0.05$). Diagnosed co-infections were also distinct between groups. In chlamydia infection participants, genital warts were the most common co-infection (33%; 13/39) followed by syphilis (15%; 6/39). In contrast, the gonorrhoea group of participants displayed a predominance of chlamydia co-infection (4/21), followed by genital warts (2/21). Only 7% (4/60) of the attendees were co-infected with both chlamydia and gonorrhoea. Concurrent HIV infection was only found in attendees from the chlamydia infection group (8%; 3/39).

All patients presented a negative urine cure test following one month treatment and in none of them it was isolated Lymphogranuloma venereum serovar (L1-L3).

All patients diagnosed with chlamydia infection were prescribed azithromycin (1 g orally in a single dose) and all gonococcal infections were treated with ceftriaxone (250 mg intramuscular in a single dose).

ASYMPTOMATIC CHLAMYDIA AND GONORRHOEA INFECTIONS

Asymptomatic chlamydia and gonorrhoea infections were found in 53% (32/60) of individuals, 78% (25/39) of whom had CT infection and only 22% (7/21) NG infection ($p < 0.05$). In five attendees, the diagnosis of asymptomatic genital infection was accomplished through partner notification.

Table 2 displays the differences between symptomatic and asymptomatic individuals with genital chlamydia or gonococcal infection.

We found that asymptomatic STD attendees with chlamydia or gonococcal infections were either married or live-in partners more frequently, and presented more concurrent STIs than symptomatic attendees (Table 2). There were no statistically significant differences between

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Table 1 - Comparison of socio-demographic and behavioural characteristics and clinical data between *C. trachomatis* and *N. gonorrhoeae* infected patients

		<i>Chlamydia trachomatis</i>		<i>Neisseria gonorrhoeae</i>		P Value*
		n	%	n	%	
Male		31	79	18	86	NS
Age	Median (years)	35		39		
Marital status						NS
	Married / Live-in partner	11	28	7	33	
	Not married / No live-in partner	28	72	14	67	
Education level						NS
	Primary school	23	59	11	52	
	Highschool/ University	16	41	10	48	
Sexual orientation						NS
	Heterosexual	34	87	18	86	
	MSM	5	13	3	14	
Number of partners in the previous 6 months						
	0	2	5	1	5	
	1	2	5	8	38	
	2 – 4	20	51	12	57	
	>4	15	39			
Partner						0,03
	Steady	24	62	8	38	
	Ocasional	15	38	13	62	
Other STI		26	67	7	33	0,08
Symptoms	Present	14	36	14	67	0,02
	Discharge	14	36	14	67	0,02
	Dysuria	7	18	8	38	0,04
	Pruritus	6	15	1	5	NS

*= χ^2 test; STI= Sexually Transmitted Infection; MSM= Men who have sex with Men; NS = Not significant

the two groups of asymptomatic bacterial genital infection regarding socio-demographic and behavioural characteristics.

DISCUSSION

Prevalence and incidence of CT and NG infections can be variable, depending on the different settings

in which the studies are performed. In a population based survey, Fenton *et al*¹¹ reported an incidence of CT infection in female and male patients aged 18-44 years of 2.2% and 1.5%, respectively. These values appear higher when the study is restricted to the female gender, younger age and to particular medical environments, namely gynaecology or dermatology consultations. The scenario for gonorrhoea infection however is similar, with reported values from 0.2 to 1.5%¹²⁻¹³.

Table 2 - Comparison of socio-demographic characteristics and clinical data between symptomatic and asymptomatic STD attendees with genital chlamydia and/or gonococcal infections

		Symptomatic infection (n=28)		Asymptomatic infection (n=32)		P Value*
		n	%	n	%	
Male		23	82	27	84	NS
Age	Median (years)	32		37		NS
Marital status						0,05
	Married / Live-in partner	5	18	13	40	
	Not married / No live-in partner	23	82	19	59	
Education level						NS
	Primary school	14	50	18	56	
	Highschool/ University	14	50	14	44	
Sexual orientation						NS
	Heterosexual	25	89	26	81	
	MSM	3	11	6	19	
Number of partners in the previous 6 months						NS
	1	15	54	16	50	
	More than 1	13	46	16	50	
Partner						NS
	Steady	16	57	17	53	
	Occasional	12	43	15	47	
Other STI		14	50	20	63	0,02

*= χ^2 test; STI - Sexual Transmitted Infection; MSM - Men who have Sex with Men; NS= Not significant

In our study population, there was a male predominance and a prevalence of 1.6% and 0.8% for chlamydia and gonococcal infections, respectively. However, there was an increase of chlamydia infection diagnoses towards the end of the decade, which actually corresponded to the time point when systematic chlamydia and gonococcal infections screening was implemented to all STD attendees. If the analysis is restricted to the last 4 years of the study (matching the period of systematic screening), there is a prevalence of 3% and 0.8% for chlamydia and gonococcal infections, respectively. Thus, systematic screening to all STD attendees has resulted in the diagnosis and treatment of an average of 13.7 individuals that would otherwise have remained infected. Interestingly, the prevalence of gonococcal infection remained stable, confirming the symptomatic nature of this infection, previously reported by Orellana and colleagues¹⁴.

Prevalence of asymptomatic infection during the study period was 1.2%. It was mainly diagnosed in young males presenting other STDs. Fernandes and colleagues reported an incidence of 13.5% and 3% of asymptomatic chlamydia and gonococcal infections, respectively¹⁵. However, the study was performed in females randomly assigned with more than 4 sexual partners. In addition, Huneus *et al* reported a 7% prevalence of chlamydia infection in young asymptomatic females¹⁶. CT prevalence in asymptomatic young men has been reported around 3% to 5%¹⁷⁻¹⁸. The majority of our study population, however, was male, highlighting that CT prevalence in this gender should not be underestimated, despite reported lower than in females.

Screening young women for chlamydia infection has been shown to be cost-effective, by preventing pelvic inflammatory disease, which is a major cause of

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infertility and chronic pelvic pain¹⁹. Although screening has increased significantly, there remains a proportion of women at risk who still lack access to it^{20, 21}. More so, screening of young men may be crucial as a strategy to prevent chlamydia infection in young women. However, evidence to support recommendations of screening in men is still scarce.

The economic burden of pelvic inflammatory disease and infertility has recently drawn a lot of debate. In the UK, the cost of treating complications from this infection was estimated to be around 50 to 100 million pounds per year throughout the last decade of the twentieth century²². The average cost of this screening in our STD clinic is 108 euros per person. Since opportunistic screening has been shown to be cost effective at infection prevalence between 2% and 6% (10), we suggest it is worthy to screen all STD attendees. We obtained a 3% prevalence of chlamydia infection in the systematic screening throughout the last 4 years of the study, and furthermore, the most frequent patient profile was: male gender, in the 30ies, single, heterosexual, with basic scholarship qualification and with concurrent STI(s). Whether chlamydia and gonococcal screening should be targeted to this particular patient profile or, instead, offered to all sexually active citizens in primary care centres can only be assessed in a few years from this time. We believe extensive data obtained in this era, when PCR testing is no longer an extravagance, will be crucial to provide insight into this issue.

Although European STD Guidelines do not recommend a routine cure test upon successful chlamydia and gonococcal infections treatment²³, we performed a cure test upon 4-6 weeks of treatment in all individuals both for reassurance and follow up of partner's notification. We did not obtain any positive result following treatment.

We acknowledge some limitations in our study. Namely, female screenings with cervical swabs as well as self-collected vaginal swab are regarded as the two most reliable methods for diagnosis of CT infection in women. Nonetheless, we believe that urine samples are easier and more comfortable for this gender²⁴. Moreover, Haugland *et al*²⁵ recently reported that screening accuracy is higher when first void urine is used, even though the specificity is lower than that obtained with cervix samples.

We also postulate that the observed increase in chlamydia infection reflects the systematic screening to all STD attendees initiated in 2007. Maintenance of this screening strategy will provide more accurate results regarding real progress status of infection in society.

CONCLUSIONS

Sexually transmitted infections represent a major public health concern in modern societies. Awareness of HIV infection contributes to a slight brake in the acquisition of STIs such as syphilis and HPV, however new sexual habits are contributing to the emergency of other diseases. CT and NG infections are distributed worldwide, and are associated to the new challenges societies are facing. Moreover, both these infections can be silent and asymptomatic eventually leading to serious consequences in patients. There remains a lot of debate concerning the need for universal screening in an era invaded by major economic turmoil. However, we are confident that screening of both females and males is crucial given that these asymptomatic individuals represent a vehicle of infection.

Unlike gonococcal infection we found an increase of chlamydia infection prevalence when routine screening was implemented using urine-based nucleic acid amplification tests. Screening of STD attendees for CT provided the opportunity to identify and treat asymptomatic Chlamydia infections.

Nowadays, screening of asymptomatic sexually active women for CT infection in some European countries is available in public health institutions. There is no standing recommendation for routine screening of males, but STD clinics are important venues in which to perform screening for CT in asymptomatic males provides the opportunity to identify and treat substantial numbers of CT infections.

We expect this study provides new understanding concerning status of these emergent bacterial infections and insights into prevention strategies.

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