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RISK FACTORS AND AETIOLOGICAL AGENTS OF URETHRITIS IN MEN WITH URETHRITIS IN BRAŞOV COUNTY

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Abstract:

Introduction*: Despite advances in the diagnosis and treatment of urethritis, they remain a global public health problem worldwide. Patients with urethritis have a higher risk sexual behavior than the general population.*

Aim*: The aim of the study was to evaluate the risk factors and the etiological pathogens of urethritis in men among Brașov county.*

Patients and methods*: A retrospective study was conducted in Medlife-PDR Clinic from Brașov, România, from Jan 2016 to Nov, 2020. 111 male patients aged from 17 to 78 years (mean age 34.5±10.26) presenting with dysuria, micturition discomfort and/or urethral discharge were included in the study.*

Results*: The highest incidence of urethritis was among men aged 21-40 years. The acquisition of urethral infection was related to their young age, low educational level, multiple sexual partners and lack of condom use, most having extramarital relations including commercial sex. N. gonorrhoeae was identified as a causative agent in 18 (16.22%) patients with urethritis, C. trachomatis in 39 (35.14%) patients, Mycoplasma spp. in 5 (4.5%) patients, Ureaplasma spp. in 30 (27.03%) patients, Trichomonas vaginalis in 6 (5.4%) patients. A concurrent infection with N. gonorrhoeae and C. trachomatis was identified in one patient (0.01%). In 12 patients (9.9%) other infectious agents were identified and in one case the aetiological agent could not be identified (0.01%).*

Conclusion*: By identifying risky sexual behaviors, clinicians may be able to provide educational counseling as well as assistance in the diagnosis and treatment of urethritis.*

Key words: *sexually transmitted diseases, urethritis.*

1. Introduction

Urethritis is a common male presentation to clinics which specialize in sexually transmitted diseases (STDs). Urethritis in men is a well-recognized

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clinical syndrome usually presenting with urethral itching, dysuria and, with variable frequency, urethral discharge, but may be asymptomatic. Although there are other situations in which urethral irritation occurs, the term urethritis is reserved for urethral inflammation caused by STDs. Traditionally, based on its aetiology, urethritis is subdivided into gonococcal (GU) and non-gonococcal urethritis (NGU) due to infections with *Chlamydia trachomatis, Trichomonas vaginalis, Mycoplasma genitalium, Mycoplasma hominis* or *Ureaplasma urealyticum* [8]. Other rare infections that cause urethritis include herpes simplex virus types 1 and 2, adenovirus, lymphogranuloma venereum, syphilis, mycobacterial infection, and bacterial infections (usually gram-negative rods) [8].

Despite all the advances in medicine, STDs are a serious public health problem especially among younger population in all societies of the world. The aim of the study was to evaluate the risk factors and the etiological pathogens of urethritis in men among Brașov county.

2. Patients and methods

This retrospective study was conducted in Medlife-PDR Clinic from Brașov, România, from Jan 2016 to Nov, 2020. 111 male patients aged from 17 to 78 years (mean age 34.5±10.26) presenting with dysuria, micturition discomfort and/or urethral discharge were included in the study. Patients were divided into 4 groups according to age. Asymptomatic contacts and those with non-urethral symptoms were excluded.

Data obtained from all participants included sexual orientation, number of sexual partners in the past 6 months, past history of STDs, past history of urethritis, marriage, incubation period of urethritis, urethritis symptoms, history and duration of symptoms, any abnormalities on genital examination and microbiological diagnoses were recorded. The study was conducted with the agreement of the institutional ethics commission.

A sample of urethral discharge was taken from each patient. When discharge was not seen spontaneously, urethra was milked to confirm its presence.

A specimen of urethral discharge was collected for Gram and Giemsa-stained microscopic examinations. A diagnosis of GU was confirmed by the presence of Gram-negative intracellular diplococci, whereas NGU was diagnosed by their absence but presence of 5 or more polymorphonuclear leukocytes per microscopic field. The positive result of *T. vaginalis* infection was defined as the presence of one or more trichomonads with characteristic morphology and jerky motility. Other specimens of urethral discharge were also collected for nucleic acid amplification tests for *N. gonorrhoeae*, *C. trachomatis*, *Mycoplasma spp.* and *Ureaplasma spp.* detection. Urinalysis and urine culture were also performed. Blood sample to detect simultaneous infection with syphilis, HIV and B hepatitis was collected from all patients.

The characteristics of the study subjects were presented as mean ± standard deviation for continuous variables and as frequency for categorical variables.

3. Results

The sexual behavior characteristics as derived from anamnesis are shown in Table 1.

Table 1

Demographic and sexual behavioral characteristics

	Risk factors	n=111 (%)
Age (years)	< 20	3 (2.7)
	21-30	45 (40.54)
	31-40	42 (37.84)
	> 40	21 (18.92)
Marital status	Married	41 (36.94)
	Concubinage	19 (17.12)
	Unmarried	51 (45.94)
Sexual orientation	Heterosexual	109 (98.2)
	Homosexual	2 (1.8)
	Bisexual	0 (0)
Education	Primary	9 (8.1)
	Secondary	72 (64.86)
	Higher	30 (27.03)
No. of sexual partners in the last 6 months	1	6 (5.4)
	2	67 (60.36)
	>2	38 (34.23)
Use of condoms	Yes	2 (1.8)
	No	109 (98.2)
Past history of urethritis	Yes	7 (6.3)
	No	104 (93.7)
Past history of STDs	Yes	17 (15.32)
	No	94 (84.68)

The majority of patients (78.38%) were in 21-30 and 31-40 year age groups. 36.94% of patient were married, 17.12% lived in cohabitation and 45.94% were unmarried. Most men with urethritis had secondary education (64.86%), while 27.03% had higher education and only 8.1% had primary education. Regarding their sexual orientation 109 (98.2%) subjects were heterosexual and only 2 patients (1.8%) reported homosexual relations. 105 (94.6%) men had more than one sexual partner in the last 6 months, most having casual intercourse or commercial sex. Only 7 (6.3%) of them had a history of urethritis and 17 (15.32%) had a history of other STDs. 109 (98.2%) of them did not use condom protection during infectious sexual contact. The other 2 men (1.8%) who used a condom for genital intercourse were exposed without a condom to orogenital intercourse.

The etiological agents of urethritis identified following laboratory investigations are presented in Table 2.

N. gonorrhoeae was identified as a causative agent in 18 (16.22%) patients with urethritis, *C. trachomatis* in 39 (35.14%) patients, *N. gonorrhoeae* and *C. trachomatis* in 1 (0.01%) patient, *Mycoplasma spp.* in 5 (4.5%) patients, *Ureaplasma spp.* in 30 (27.03%) patients, *Trichomonas vaginalis* in 6 (5.4%) patients.

Table 2

Aetiological pathogens of urethritis

Aetiological agent	n=111 (%)
N. gonorrhoeae	18 (16.22)
C. trachomatis	39 (35.14)
N. gonorrhoeae + C. trachomatis	1 (0.01)
Mycoplasma spp.	5 (4.5)
Ureaplasma spp.	30 (27.03)
Trichomonas vaginalis	6 (5.4)
Others	11 (9.9)
Unknown	1 (0.01)

A concurrent infection with *N. gonorrhoeae* and *C. trachomatis* was identified in one patient (0.01%). In 12 patients (9.9%) other infectious agents were identified: *Klebsiella spp.* (2.7%), *Staphylococcus aureus* (2.7%), *Escherichia coli* (1.8%), *Haemophilus parainfluenzae* (0.01%), *Candida spp.* (1.8%). In one case the aetiological agent of urethritis could not be identified (0.01%).

The clinical form of presentation was acute urethritis in 30 patients (27.03%), subacute urethritis in 34 patients (30.63%) and chronic urethritis in 47 patients (42.34%). Clinical characteristics depending on aetiological pathogens are presented in Table 3. *N. gonorrhoeae*

infection has mainly caused acute urethritis (88.89%). *C. trachomatis* infection presenting as acute urethritis in 4 patients (10.26%), as subacute urethritis in 15 patients (38.46%) and chronic urethritis in 20 patients (51.28%). Infections with *Mycoplasma spp.* and *Ureaplasma spp.* more often caused chronic urethritis (100% and 66.67% respectively). In 3 patients (50%) with *T. vaginalis* infection diagnoses was acute urethritis. The onset of symptoms was on average 14.9±11.33 days after infectious intercourse. Depending on aetiological pathogens, the onset of symptoms was on average 3.6±2.71 days after intercourse in *N. gonorrhoeae* infection, 13.96±6.7 days for *C. trachomatis* infection, 20.67±2.12 days for *Mycoplasma spp.* infection, 5.6±9.64 days for *Trichomonas vaginalis* infection, 26.53±9.78 days for *Ureaplasma spp*. The presentation of patients at the medical consultation was on average after 11.02±6.7 days from the onset of symptoms, being shorter in cases where the symptoms were more intense (Table 3). Three (2.7%) of the men in our study had acute complications: 2 patients with acute orchiepididymitis (1 with *N. gonorrhoeae*). and 1 with *C. trachomatis*) and 1 (0.01%) with prostatitis (*N. gonorrhoeae* infection).

Clinical characteristics depending on aetiological pathogens Table 3

	N. gonorrhoeae n=18 (%)	*C. trachomatis n=39 (%)*	*Mycoplasma spp. n=5 (%)*	*Ureaplasma spp. n=30 (%)*	*T. vaginalis n=6 (%)*	*Unknown n=12 (%)*
Clinical form of urethritis:						
- Acute	16 (88.89)	4 (10.26)	0 (0)	0 (0)	3 (50)	6 (50)
- Subacute	2 (11.11)	15 (38.46)	0 (0)	10 (33.33)	2 (33.33)	5 (41.67)
- Chronic	0 (0)	20 (51.28)	5 (100)	20 (66.67)	1 (16.67)	1 (8.33)
Incubation period (days±SD)	3.6±2.71	13.96±6.7	20.67± 2.12	26.53±9.78	5.6±9.64	8.33±7.43
Duration of symptoms (days±SD)	3.42±1.89	10.1±5.96	13.8± 6.21	20.1±10.8	4.33±1.03	10.5±9.27

4. Discussions

Despite advances in the diagnosis and treatment of urethritis, they remain a global public health problem worldwide. Each year, about 62 million of new cases of GU and 89 million new cases of NGU are reported worldwide, but probably both types of infections are underreported [9]. Promiscuity, early onset of sex life, multiple sexual partners, homosexuality and a history of STDs are the most important factors that contributed to their spread [5]. Patients with urethritis have a higher risk sexual behavior than the general population. In the study group, the acquisition of urethral infection was related to their relatively young age, low educational level, the number of sexual partners and lack of condom use. Urethritis may occur in any sexually active person, but the highest incidence was among men aged 21-40 years. 94.6% of subjects had multiple sexual partners in the last 6 months, most having extramarital relations including commercial

sex. The number of sexual partners is a major high-risk factor and is probably the most studied marker in measuring the risk of acquiring urethritis. The high rate of those who did not use a condom in our group is certainly a cause for concern and most likely reflects educational issues. Patients with a prior history of STDs are at an increased risk of contracting another or concurrent STDs, so a high level of suspicion for another STDs should be maintained and tests for syphilis, HIV infection and hepatitis B should be performed.[9] Only a relatively small proportion of our patients had a history of STDs. One patient was diagnosed with secondary syphilis and one with HIV infection. Homosexual men are more likely to have contracted an STDs, including urethritis [9]. In our research, two subjects were declared to be homosexual, both being diagnosed with acute GU.

Although there was a steady decrease in the incidence of GU from 2000 to 2009, it subsequently had intermittent increases. Of all the etiological agents of urethritis, *N. gonorrhoeae* has the greatest versatility to acquire resistance to antimicrobial substances and a high antigenic variability by which it bypasses the host's defense mechanisms. [5] Currently, the prevalence of *N. gonorrhoeae* strains that are resistant to available antibiotics, until recently considered effective (cephalosporins, cyclines, macrolides, fluoroquinolones), is estimated to be very high which causes a great concern.[5] The frequency of NGU in our study was the highest (83,78%) while the rate of *N. gonorrhoeae* infection was 16.22%. The etiological agents of NGU in the group investigated by us were: *C. trachomatis – 35.14%, Ureaplasma spp. - 27.03%, Mycoplasma spp. – 4.5%* and *Trichomonas vaginalis – 5.4%.* In 9.9% of men with urethritis in which none of the classic etiological agents of urethritis were identified, other infectious agents (Gram-negative bacilli, *Staphylococcus aureus, Candida spp.*) were isolated from urine culture.

C. trachomatis has long been considered the main aetiological agent of NGU with 20 to 50% of patients being positive for this infectious agent.[6] Testing for pathogens other than *N. gonorrhoeae* and *C. trachomatis* is controversial and is generally reserved for patients with resistant or recurrent unexplained symptoms.[2] *T. vaginalis* can also cause urethritis in men, but is more difficult to detect. Recently, *M. genitalium* has gained recognition as an infectious pathogen that can be isolated from 10 to 30% of patients with NGU [6]. Several studies have concluded that *M. genitalium* is a common cause of NGU and that its eradication is associated with improved symptoms.[7] *Ureaplasma spp.* are commonly identified in men with urethral symptoms, but their exact role as a pathogen has not been fully defined [1]. The definition of *Ureaplasma spp.* as a pathogen in the context of NGU or a cause of infertility in men remains controversial, largely due to the high historically rates of isolation of these bacteria from the urethra of healthy men [1]. Although the current opinion is not to recommend routine testing for *Ureaplasma spp.* in men with urethritis, this should be recommended in cases where no other pathogens have been identified [1].

Symptoms of urethritis usually occur from 2 days to 2 weeks after contact with an infected partner, but the patient may also be asymptomatic. In GUs the symptoms are usually acute, with abrupt onset of dysuria and purulent discharge, with onset on average after 3 days after infectious contact. The intensity of the symptoms determines them to seek an

early curative treatment. Incubation period of NGUs is more variable and is often longer (between 2 and 35 days), symptoms are milder (subacute or most often chronic), and a longer duration of symptoms until treatment is initiated. Many men with NGU develop urethral symptoms within 4 days, so the incubation period is not a reliable factor in the etiological diagnosis.[4] Usually, urethritis does not associate systemic symptoms (fever, chills, sweating, nausea). If they exist, these symptoms suggest disseminated gonococcal infection, pyelonephritis, orchiepididymitis or other systemic infection.

Most of the time, urethritis recovers without complications, even without treatment. Complications have been reported in 1-2% of men suffering from urethritis. The most common complication reported is urethral stricture due to the formation of post-inflammatory scars. Other potential complications are prostatitis, acute orchiepididymitis, proctitis, infertility, sperm abnormalities, disseminated gonococcal infection and Reiter's syndrome [2, 3].

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