Chlamydia trachomatis infection in chronically hemodialyzed patients

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Abstract

Purpose: In the general population there is association between *Chlamydia trachomatis (Ch. trachomatis)* infection and reactive arthritis (RA). RA is a systemic illness characterized by inflammatory synovitis. Arthritis tends to be oligoarticular and involves mainly the lower limbs. The aim of this study is to assess the age and sex specific prevalence of *Ch. trachomatis* infection in dialysis population and to find possible relationship between manifestation of infection and renal osteodystrophy.

Material and methods: The study was conducted in 53 patients: 22 women (W) and 31 men (M), with a mean age of 58.1 ± 15 years, treated with HD for 28.5 ± 28.2 months. The *Ch. trachomatis* infection was assessed by the detection IgG antibodies for *Ch. trachomatis*. Also some other biochemical parameters of osteodystrophy, inflammation and malnutrition were measured.

Results: The presence of a high titre of anti-*Ch. trachomatis* antibodies was found in 22 patients – 41% [G IgG (+)]. Mean level of anti-*Ch. trachomatis* antibodies was significantly higher in G IgG (+) than in seronegative patients [G IgG (-)]: 19.0 ± 8.6 vs 4.0 ± 2.1 U/ml, $p < 0.001$. There was no difference in mean age of seropositive and seronegative patients for *Ch. trachomatis* (62.4 ± 13.1 vs 56.2 ± 15.9 years). We did not observe in both groups of patients any differences in mean level of C-reactive protein (CRP): 12106.2 ± 10791.0 vs 14015.3 ± 11194.3 ng/ml. The mean ferritin level was significantly higher in G IgG (+): 624.3 ± 375.7 vs 418.3 ± 341.4 ng/ml, $p < 0.05$. Significant negative correlations were found in G IgG (+) between IgG antibodies and transferrin saturation ($r = -0.645719$, $p < 0.001$) and between CRP and calcium ($r = -0.4526$, $p < 0.05$). IgG antibodies were detected frequently in W (60%) than in M (29%). Mean level of IgG was significantly higher in seropositive W than in seropositive M (23.3 ± 7.8 vs 12.1 ± 4.2 U/ml, $p < 0.0001$). The seropositive W were older (67.9 ± 11.8 vs. 53.8 ± 11.0 years, $p < 0.02$) and seropositive W were shorter treated with HD (18.1 ± 16.6 vs 43.7 ± 30.6 months, $p < 0.02$). The mean serum calcium conc. and phosphorus were significantly lower in seropositive W (2.1 ± 0.1 vs 2.3 ± 0.2 mmol/l, $p < 0.05$ and respectively 1.3 ± 0.3 vs 1.8 ± 0.2 mmol/l, $p < 0.005$). Likewise the mean transferrin saturation (TS) was significantly lower in that group (25.7 ± 7.3 vs $38.0 \pm 11.3\%$, $p < 0.01$). There were no differences between seropositive men and women in mean serum concentrations of CRP, iPTH, albumin and hemoglobin. We found in seropositive W significant negative correlation between IgG antibodies and age ($r = -0.633$, $p < 0.02$).

Conclusions: The patients treated with HD were quite frequently shown significantly elevated level of IgG antibodies for *Ch. trachomatis*. It could have be connected with past infection. The antibodies were more commonly detected in women, particularly in younger patients. No relationship between osteodystrophy and *Ch. trachomatis* infection was found.

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Introduction

Chlamydia trachomatis (Ch. trachomatis) infection is sexually transmitted disease with chronic and often asymptomatic course [1,2]. The infection causes major complications, especially in the eye and urinogenital tract [3,4]. In the general population there

is a relationship between *Ch. trachomatis* infection and reactive arthritis (RA) [5]. RA is a systemic illness characterized by inflammatory synovitis. Arthritis tends to be oligoarticular and involve mainly the lower limbs [5,6]. It is known, that patients treated hemodialysis (HD) are more susceptible to all kinds of infections [7]. The bone disorders in dialysis population are first of all caused by renal osteodystrophy, spectrum of skeletal disorders that range from high turnover to low turnover lesions [8]. One must take into consideration that musculosceletal system complaints in patients treated HD may be caused by *Ch. trachomatis* infection as well. In the accessible literature we didn't find data about prevalence the *Ch. trachomatis* infection in patients treated HD and association between *Ch. trachomatis* infection and process of renal osteodystrophy. The aim of this study was to assess the age and sex specific prevalence of *Ch. trachomatis* infection in dialysis population. Likewise we sought possible relationship between *Ch. trachomatis* infection and renal osteodystrophy.

Material and methods

The study was conducted in 53 patients: 22 women (W) and 31 men (M), with a mean age of 58.1 ± 15 years, treated with HD for 28.5 ± 28.2 months. The cause of end stage renal failure was: glomerulonephritis in 16 cases, diabetic nephropathy in 12 cases, interstitial nephritis in 9 cases, hypertensive nephropathy in 5 cases, connective tissue diseases in 4 cases, polycystic renal diseases in 4 cases and 3 underterminated cases. All patients were dialyzed with bicarbonate based dialysate, average time's session was 4 ± 0.3 minutes, low-flux polisulfone and hemophan membranes were reused. The *Ch. trachomatis* infection was assessed by the detection IgG antibodies against *Ch. tachomatis*. Some other biochemical parameters of osteodystrophy, inflammation and malnutrition were also measured: intact parathormon (iPTH), calcium (Ca), phosphorus (P), hemoglobin (Hb), albumin, normalized protein catabolic rate (nPCR), ferritin, C-reactive protein (CRP) and transferrin saturation (TS). Likewise Kt/V and mean arterial pressure (MAP) were determined. The specific IgG antibodies to *Ch. trachomatis* were detected by ELISA method with Genzyme Virotech kit. The specific IgG antibodies above 9 U/ml were considered to be positive for *Ch. trachomatis*. CRP were measured by high-sensitive ELISA method with Eucardio kit. iPTH was measured by immunochemiluminescence method with Nichols Inst kits. The normal value of iPTH in patients treated with HD was assumed to be 3-4 fold higher than normal for the healthy controls (10-65 pg/ml). nPCR and Kt/V were calculated by the Daugirdas formula according to DOQI GUIDELINES [9]. Other parameters were measured by standard automated techniques.

Statistical analysis

The results were expressed as the arithmetic mean ± standard deviation (SD). The data were analyzed statistically. To compare groups U-test of Mann-Whitney was used because of diagonal distribution of the parameters tested. Nonparametric r-Spear-

Table 1. Biochemical parameters in serum of seronegative and seropositive haemodialysis patients for *Chlamydia trachomatis*

Parameter	G-IgG(+) n=22	G-IgG(-) n=31	Statistical significance
IgG (U/ml)	19.0 ± 8.6	$4.0 \pm 2.1*$	p<0.001
hemoglobin (mmol/l)	6.6 ± 0.8	6.8 ± 0.9	N S
albumin (g/l)	34.0 ± 3.0	34.0 ± 4.0	N S
CRP (ng/ml)	12106.2 ± 10791.0	14015.3 ± 11194.3	N S
TS (%)	$25.7 \pm 7.3*$	32.1 ± 18.7	p<0.05
ferritin (µg/l)	624.3 ± 375.7	$418.3 \pm 341.4*$	p<0.05
Ca (mmol/l)	2.2 ± 0.2	2.2 ± 0.2	N S
P (mmol/l)	1.5 ± 0.4	1.6 ± 0.6	N S
iPTH (µg/l)	463.4 ± 424.3	378.6 ± 231.2	N S
nPCR (g/kg/day)	1.1 ± 0.2	1.0 ± 0.3	N S

G IgG (+) seropositive patients for *Ch. trachomatis*;
G IgG (-) seronegative patients for *Ch. trachomatis*;
Ca – calcium; nPCR – normalized protein catabolic rate;
P – phosphorus; CRP – C-reactive protein;
TS – transferrin saturation; *– statistical significance

man test was used to define correlations. The test χ-square was used to examine correlation between non measured features. Values of p<0.05 were considered to be statistically significant.

Results

The mean concentrations (conc) of measured parameters in patients were shown in *Tab. 1*. We observed that 22 patient (41%) were seropositive for *Ch. trachomatis* infection [G-IgG (+)]. The mean level of IgG antibodies for *Ch. trachomatis* was significantly higher in G-IgG (+): 19.0 ± 8.6 vs 4.0 ± 2.1 U/ml, p<0.001. There was no difference in mean age in seropositive patients and seronegative patients [G-IgG(-)]: 62.4 ± 13.1 vs. 56.2 ± 15.9 years. Likewise we did not find any differences in mean time of HD treatment and Kt/V in both groups of patients (27.8 ± 25.6 vs 29.8 ± 27.1 months and 1.3 ± 0.2 vs 1.2 ± 0.2 respectively). The serum CRP above correct level (4000 ng/ml) was in 41 patients (77%). There was no any significant differences in mean serum level of CRP in seropositive and seronegative patients (12106.2 ± 10791.0 vs 14015.3 ± 11194.3). The mean serum ferritin level was significantly higher in G-IgG (+): 624.3 ± 375.7 vs 418.3 ± 341.4 ng/ml, p<0.05. We did not find any significant differences in both groups of patients in mean arterial pressure (MAP): 91.2 ± 15.8 vs 97.2 ± 10.4 mmHg and mean serum levels of other measured parameters. We found in G IgG (+) significant negative correlations between level of IgG antibodies and TS (r=-0.6457, p<0,001) and between CRP and Ca (r=-0.4526, p<0.05).

Antibodies for *Ch. trachomatis* were detected generally in group of W. The mean serum levels of measured parameters in seropositive W and seropositive M for *Ch. trachomatis* were shown in *Tab. 2*. We found that 60% of W and 29% of M were seropositive for *Ch. trachomatis*. Mean level of IgG antibodies was significantly higher in seropositive W: 23.3 ± 7.8 vs 12.4 ± 4.2 U/ml, p<0.0001. The seropositive W were older then

Table 2. **Biochemical parameters in serum seropositive women and seropositive men for *Chlamydia trachomatis***

Parameter	G IgG (+) women n=13	G IgG (+) men n=9	Statistical significance
IgG antibody for *Ch.trachomatis* (U/ml)	23.3±7.8	12.1±4.2*	p<0.0001
hemoglobin (mmol/l)	6.5±0.6	6.9±0.9	N S
albumin (g/l)	30.3±.3.0	35.0±0.3	N S
CRP(ng/ml)	12490.3±12024.4	11482.0±9171.0	N S
TS (%)	25.7±7.3*	38.0±11.3	p<0.01
ferritin (μg/l)	604.6±312.7	660.8±499.0	N S
calcium (mmol/l)	2.1±0.1	2.3±0.2*	p<0.05
phosphorus (mmo/l)	1.3±0.3 *	1.8±0.2	p<0.005
iPTH (μg/l)	426.2±412.1	367.0±349.3	N S
nPCR (g/kg/day)	1.0±0.2	1.1±0.2	N S

G IgG (+) – seropositive patients for *Ch. trachomatis*;
G IgG (-) – seronegative patients for *Ch. trachomatis*;
nPCR – normalized protein catabolic rate;
CRP – C-reactive protein; iPTH – intact parathormone;
TS – transferrin saturation; * – statistical significance

seropositive M (67.9±11.8 vs 53.8±11.0 years, p<0.02) and they were shorter treated with HD (18.1±16.6 vs 43.7±30.6 months, p<0.02). The mean serum levels of Ca and P were significantly lower in seropositive W (2.1±0.1 vs 2.3±0.2 mmol/l, p<0.05 and respectively 1.3±0.3 vs 1.8±0.2 mmol/l, p<0.05). Likewise the mean TS was significantly lower in seropositive W (25.7±7.3 vs 38.0±11.3%, p<0.01). There were no differences in mean MAP in seropositive men and seropositive women (92.1±15.1 vs 89.6±17.8 mmHg). We did not observe in both groups of patients any significant differences in mean serum levels of other measured parameters (*Tab. 2*). We found in seropositive W significant negative correlation between IgG antibodies for *Ch. trachomatis* and age (r=-0.633, p<0.02).

Discussion

Ch. trachomatis is a powerful immunogen, which stimulates the host's immunological processes [10]. The primary infection leads to a local inflammatory reaction due to penetration and reproduction of the bacteria in the epithelial cells. The IgA and IgG antibodies neutralize the primary infection. The serological tests are useful to identify the specific IgG antibodies in diagnosis of *Ch. trachomatis* infection [11,12]. The antibodies can not be used as a sign of current infection, they often persist for years after the infection has resolved. But in most cases the host's reaction to the primary infection is transient and does not causes tissue damage [10]. Locally produced antibodies limit the spread of *Chlamydia* infection, but do not eliminate the bacteria completely. The chronic infection leads to progressive damage of epithelial cells and can lead to serious and costly sequels.

There is a high prevalence of inflammation in the hemodialysis population [7]. The source of inflammation in dialysis patients is multifactorial. The immunodeficiency state recognized in hemodialysis patients can promote the development of *Ch. trachomatis* infection. We observed that in our hemodialysis

patients 41% were infected with *Ch. trachomatis*. Prevalence of *Ch. trachomatis* infection among young adults in Poland is high, the Ig G antibodies against this pathogen were detected in 26% young adults (13). In general population there is high prevalence of *Ch. trachomatis* in younger women [1,2,13,14]. Likewise we observed that *Ch. trachomatis* antibodies were detected in women, but the seropositive women were older and shorter treated with HD then the seropositive men. We observed that the immunological reaction presence of this pathogen was significantly more expressed in younger subjects. We have found in seropositive women lower serum concentrations of calcium and phosphorus and transferrin saturation than in seropositive men. There was no link between time of HD treatment and titre of anti-*Ch. trachomatis* antibodies.

Ch. trachomatis infection is frequently asymptomatic, the sequels are common and could be a serious health problem: urinogenital tract complains, acute or chronic renal interstitial inflammation, infertility, increased risk of ectopic pregnancy and ocular damage [15,16]. The *Chlamydia* infection may be a problem in patients after renal transplantation, so one must examine the presence of *Ch. trachomatis* infection in patients prepared to transplantation.

The local inflammatory reaction is most intense on days 2-4 after *Ch. trachomatis* infection onset [10]. The infected epithelial cells secrete numerous proinflammatory chemokines and cytokines including TNF-alfa, interleukin IL-1, IL-6, which in turn activate the liver to secrete CRP and other acute-phase protein like ferritin. It is now known that CRP may act as a clearance factor for endotoxin and opsonized bacterial products. Serum CRP levels in dialysis population are 5 to 10 times higher than in healthy controls [17]. But elevated CRP values are frequently found in the absence of apparent infection or inflammation. Bacterial contamination during the extracorporal circulation and bioincompatiblity explain only a very small part of high prevalence of inflammation as defined by raised CRP in those patients.

We observed that CRP concentration in our studied patients was markedly increased and exceeded the upper limit of the normal range. But we didn't observe any differences in mean level of CRP in all seropositive and seronegative patients for *Ch. trachomatis*. We didn't find association between CRP and antibodies for *Ch. trachomatis*.

The inflammation is strongly linked to atherosclerosis in dialysis population [18]. The cardiovascular risk in the dialysis population is extremely high. Cardiovascular diseases and infections remain the main mortality causes in hemodialysis patients. There are relationships between some infection factors and presence of coronary heart disease [18,19]. Increased levels of CRP and evidence of chronic *Chlamydia pneumoniae (Ch. pneumoniae)* infection have been identified as risk factors for cardiovascular diseases in the general population and in dialysis population [20,21]. The patients *Ch. pneumoniae* antibodies are associated with the severity of atherosclerosis, but this relationship was not observed for *Ch. trachomatis*. The levels of IgG, IgM, IgA antibodies for *Ch. pneumoniae*, *Ch. trachomatis* and *Ch. psittaci* were measured in blood serum patients with myocardial infarction compared with control. Patients with coronary heart disease had higher frequency of seropositivity

to *Ch. pneumoniae* and similar levels of seropositivity to *Ch. trachomatis* and *Ch. psittaci* [22]. We didn't observe any differences in MAP in seronegative and seropositive patients for *Ch. trachomatis*. The malnutrition and inadequate dialysis dose contribute to reduced immune responsiveness in HD patients [7]. We didn't find any association between Kt/V and any well recognized nutritional parameters (albumin, nPCR) or levels of IgG antibodies. We didn't observe in our groups of patients any influence of *Ch. trachomatis* on nutritional status. We have found in seropositive patients a negative link between anti-*Ch. trachomatis* antibodies and ferritin. The *Ch. trachomatis* infection causes major complications, especially in the eye and urinogenital tract [3,4]. We didn't observe any ocular damage in seropositive patients.

In the general population there is a relationship between *Ch. trachomatis* infection and musculoskeletal system disorders, especially with reactive arthritis. In reactive and postinfectious arthritis the joints are generally sterile, although the presence of bacterial antigens has been reported. In vessel walls of synovial membranes IgG and IgA deposits are found [23]. Taking this fact into consideration we tested hypothesis that seropositivity for *Ch. trachomatis* is associated with the osteodystrophy process. We haven't find any typical clinical symptoms of rheumatological disorders in our population studied. In that group of patients we recognized process of osteodystrophy with high bone turnover. Seropositivity to *Ch. trachomatis* did not significantly increase the risk associated with hyperparathyroidism. In seropositive women we found lower mean serum concentrations of calcium and phosphorus and transferrin saturation than in seropositive men.

Conclusions

The patients treated with HD have high frequency of significantly elevated level of IgG antibodies for *Ch. trachomatis*. It could have be connected with infection in the past. The antibodies were more commonly detected in women, particularly younger one. No relationship between osteodystrophy and *Ch. trachomatis* infection was found.

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