Relation between Chlamydia pneumoniae infection and mild to moderate hypertension

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Abstract

introduction: *Chlamydia pneumoniae* was first described in 1986. Serological studies indicate that it is one of the most prevalent infectious agents worldwide, with a wide range of clinical manifestations, including exacerbations of chronic obstructive pulmonary disease and chronic asthma. Several groups have demonstrated serological associations with coronary artery disease, 7±10 strokes and transient cerebral ischemia, and asymptomatic carotid atherosclerosis. Our study was designed to test the association of this organism with HT in sylhet MAG Osmani Medical College hospital, Sylhet. **Materials and Methods:** This was a cross sectional descriptive and comparative study conducted in the Department of Microbiology, Sylhet MAG Osmani Medical College, Sylhet, Bangladesh during the period from January 2013 to December 2013. For this purpose 49 patients with history of hypertension and 51 age-sex matched subjects without history of hypertension were selected according to inclusion and exclusion criteria and categorized as case group (group-A) and control group (group-B) respectively. **Result :** Distribution of patients by seroprevalence of IgG anti-Chalmydia antibody. In hypertension group 27 (56.0%) patients were positive for IgG anti-Chalmydia antibody; while in non hypertensive group29 (57.0%) patients were positive for IgG anti-Chalmydia antibody. There was no significant association of seropositivity of IgG anti-Chalmydiaantibody between two groups (p=0.859). **Conclusion:** These data does not support the associations of mild to moderate hypertension with previous *Chlamydia pneumoniae* infection.

Key Ward: *Chlamydia pneumoniae*, hypertension, anti-Chalmydia antibody

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Introduction

Chlamydia pneumoniae is an obligate intracellular Gram-negative bacterium that infects humans as a respiratory pathogen. It has a biphasic life-cycle, existing as either an EB ('elementary body') or a RB ('reticulate body'). The EB is the extracellular infectious non-replicating form which, when internalized by a susceptible cell, differentiates into the metabolically active RB. The RB replicates, by binary fission, forming an intracellular microcolony (inclusion) and then re-differentiates, after 48–72 h, back into EB forms, which are released from the infected cell to begin another infection cycle. Under certain conditions, RBs do not re-differentiate directly into EBs, but form interim non-replicating 'persistent bodies', allowing the bacterium to maintain a chronic latent infection[1]. Exposure to *Chlamydia pneumoniae* is common, with 50% of individuals seropositive by 20 years of age and approximately 80% by 80 years of age[2].

Chlamydia pneumoniae generally causes mild upper respiratory tract infections, which range in severity from asymptomatic disease to, occasionally, severe pneumonia. *Chlamydia pneumoniae* has been estimated to account for 10% of community-acquired pneumonia and 5% of pharyngitis, bronchitis and sinusitis[3], and because it can maintain a chronic or latent infection, recurrence of the disease is frequent, despite treatment with antibiotics. A link between vascular disease and infection with other chlamydial species was suggested in the 1940s and 1960s and, with the isolation of *Chlamydia pneumoniae* from the respiratory tract in 1983, it was speculated that this bacterium may also play a role in cardiovascular disease[4].

Hypertension exemplifies probably better than any other disorder the complexity of polygenic disease. In 95% of cases, no single cause can be identified; although factors such as consumption of alcohol and caffeine, salt intake, smoking, obesity, and physical inactivity may clearly contribute to increasing blood pressure. The notion that infections may predispose to hypertension is not new. For example, such a role has been proposed for Helicobacter pylori: of 33 patients in one urban general practice with unequivocal H. pylori gastritis, 42% had sustained hypertension compared with 12% of dyspeptic patients

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without H. pylori[5]. Schreiber et. al. reported that intravenous injections of either live or heat-killed group B -hemolytic streptococci in newborn lambs caused significant dose-dependent increases in systemic vascular resistance and mean systemic arterial pressure and that these effects were partly blocked by leukotriene D4 receptor antagonists, suggesting that leukotrienes might mediate hypertension in this infection[6]. This is one of several immunologic changes that might be relevant to the infectious origin of essential hypertension. Furthermore, chronic chlamydial infections have a marked propensity to cause fibrosis (as seen, for example, in the cicatricial scarring of the cornea that characterizes trachoma and in fibrosis of the Fallopian tubes in pelvic inflammatory disease due to C. trachomatis). It is therefore reasonable to speculate that C. pneumoniae within vascular endothelial cells might, by a similar process, lead to an increase in vascular resistance. There are wide variations in the prevalence and incidence of hypertension in different parts of the world. Both in the United Kingdom and United States, it is more common among black people than in the white population. C. pneumoniae antibodies have been associated with Afro-Caribbean origin, raising the possibility that a genetic predisposition to this infection may contribute to the development of hypertension[7].

Chlamydia pneumoniae was first described in 1986. Serological studies indicate that it is one of the most prevalent infectious agents worldwide, with a wide range of clinical manifestations, including exacerbations of chronic obstructive pulmonary disease and chronic asthma.6 Several groups have demonstrated serological associations with coronary artery disease, strokes and transient cerebral ischemia, and asymptomatic carotid atherosclerosis[8]. Our study was designed to test the association of this organism with HT in sylhet MAG Osmani Medical College Hospital, Sylhet. We subjected the patients with mild to moderate hypertension according to their history of hypertension as well as their history of taking hypertensive drug.

Materials and Methods

This was a cross sectional descriptive and comparative study conducted in the Department of Microbiology, Sylhet MAG Osmani Medical College, Sylhet, Bangladesh during the period from January 2013 to December 2013. For this purpose 49 patients with history of hypertension and 51 age-sex matched subjects without history of hypertensionwere selected according to inclusion and exclusion criteria and categorized as case group (group-A) and control group (group-B) respectively. Inclusion criteria includes patients withhistory of hypertension for at least 1 year or more, Any age irrespective of sex and age and sex matched subjects having normal blood pressure. Immunoglobulin G (IgG) antibodies against *Chlamydia pneumoniae* was tested using the DIA pro *Chlamydia pneumoniae* enzyme-linked immunosorbent assay (Milan, Italy) according to manufacturer's instructions.

Study procedure

After explaining the purpose of the study written informed consent was taken. All patients with mild to moderate hypertension were evaluated. The clinical histories of the patients were noted. Each patient was examined thoroughly. General demographic details, smoking habits and past medical history such as diabetes mellitus and hypertension; past and family history of ischemic heart disease or any other disease was recorded.

Hypertension was Documented by, History of hypertension diagnosed and treated with medication, diet or exercise and Blood pressure >140 mmHg systolic and or >90 mmHg diastolic on at least 2 occasions by palpatory method (inflate the cuff rapidly to 70 mm of Hg. And increase by 10 mmHg, increments while palpating the radial pulse. Level of pressure noted at which the pulse disappears and subsequently reappears during deflation is systolic blood pressure). Also those patient who was on anti-hypertensive pharmacological therapy was included in our study.

Estimation of serum *Chlamydia pneumoniae*IgG antibody

Immunoglobulin G (IgG) antibodies against *Chlamydia pneumoniae* was tested using the DIA pro *Chlamydia pneumoniae* enzyme-linked immunosorbent assay (Milan, Italy) according to manufacturer's instructions.Serum samples were be diluted and then incubated with the highly purified *C. pneumoniae* outer membrane protein antigens coated in the microwells with negative and positive controls. After washing, the bounded IgGs were further complexed with antihuman IgG antibodies labeled with HRP. A substrate solution was used reacting with HRP to produce color correlating with the presence of anti-*Chlamydia pneumoniae* IgG in the sample. The results were determined by calculating an index value from optical density values relative to control materials. An index of ≥ 0.9 was considered reactive, and <0.9 was considered negative. Seropositivity was defined as the presence of either IgG antibodies.

Results

This was a cross sectional descriptive and comparative study conducted in the Department of Microbiology, Sylhet MAG Osmani Medical College, Sylhet, Bangladesh during the period from January 2013 to December 2013 with a view to evaluate association between IgG anti C pneumoniae antibody and mild to moderate hypertension . For this purpose 49 patients with mild to moderate hypertension were selected according to inclusion and exclusion criteria and categorized as case group (group-A). Age and sex matched 51 subjects without hypertension were also selected and categorized as control group (group-B). The outcome of the study was as follows:

Table 1 Showed the age of the patients ranged from 32 to 70 years with the mean age of 49.35 (SD ± 8.53) years in hypertension group (group A); whereas the age ranged from 31 to 70 years with the mean age of 47.28 (SD ± 9.49) years in without hypertension group. The mean age of the patients in both groups was almost similar

(p=0.686)

In table-2 shows the frequency distribution of patients according to sex. There were 41(84.0%) male and 8 (16.0%) female in hypertensiongroup; whereas 38 (74.0%) male and 13 (26.0%) female in patients without hypertension group. The sex of the patients of hypertension group and without hypertension group did not show any statistically significant difference (p=0.261).

In group-A, 23 (48.0%) patients were smoker and 26 (52.0%) patients were non-smoker; whereas in group-B, 22(42.0%) patients were smoker and 29 (58.0%) patients was non-smoker. There was no significant difference of smoking status between the groups (p=0.702). Distribution of patients by smoking status is shown in table-3.

Table-4 showed the distribution of patients by seroprevalence of IgG anti-Chalmydia antibody. In hypertension group 27 (56.0%) patients were positive for IgG anti-Chalmydia antibody; while 29 (57.0%) patients were positive for IgG anti-Chalmydia antibody in without hypertension group. There was no significant association of seropositivity of IgG anti-Chalmydia antibody between two groups (p=0.859).

Table 1: Distribution of the patients on the basis of age

Age in years	Study group		p-value
	Group-A (n=49)	Group-B (n=51)	
Mean (years)	47.28(SD ± 9.49)	49.35(SD ± 8.53)	*p=0.686

*X^2 test were employed to analyze the data.

Table 2: Distribution of the patients according to sex

Sex	Study group		Total	
	Group-A (n=49)Frequency (%)	Group-B(n=51) Frequency(%)		
Male	41 (84.0)	38(74%)	79*	p=0.261
Female	8 (16.0)	13(26%)	21*	
Total	49 (100.0)	51(100.0)	100*	

*χ^2 (Chi- square) test was employed to analyze the data.

Table 3: Distribution of patients by smoking status

Smoking status	Study group		*p-value
	Group-A (n=49) Frequency (%)	Group-B (n=51) Frequency (%)	
Smoker	23 (48.0)	22 (42.0)	
Non-smoker	26 (52.0)	29 (58.0)	p=0.702
Total	49 (100.0)	51 (100.0)	

*Chi-square (χ^2) Test was employed to analyse the data

Table 4: Distribution of patients by seroprevalence of IgG anti-Chalmydia antibody

IgG anti-Chalmydia antibody	Study group		Odd ratio (95% CI)	p-value
	Group-A (n=50)	Group-B (n=50)		
Positive	28 (56.0)	16 (32.0)	2.71 (1.20-6.11)	p=0.016
Negative	22 (44.0)	34 (68.0)		
Total	50 (100.0)	50 (100.0)		

*χ^2 (Chi- square) test was employed to analyze the data.

Discussion

There are wide variations in the prevalence and incidence of hypertension in different parts of the world. Both in the United Kingdom and United States, it is more common among black people than in the white population. C. pneumoniae antibodies have been associated with Afro-Caribbean origin, raising the possibility that a genetic predisposition to this infection may contribute to the development of hypertension[9]. In a large Finnish study that showed a clear association of high titers of chlamydial IgG and IgA antibodies with chronic coronary artery disease and acute myocardial infarction, there was no correlation with other risk factors for these conditions, including

hypertension[10].

The authors of the Finnish study did not specify the criteria for diagnosing hypertension in their report, but another study by Cook, et al. of chronic severe hypertensive patients have detected such an association. They found of the matched HT patients, 43 (35.0%) had serological evidence of previous infection, 9 (7.3%) acute (re)infection, and 71 (57.7%) no infection. Of the matched control subjects, 22 (17.9%) had evidence of previous infection, 11 (8.9%) acute (re)infection, and 90 (73.2%) none. Regression analysis suggested associations of HT with previous C. pneumoniae infection (OR, 2 z 5; 95% confidence interval [CI], 1.3 to 4.7) but not with acute (re)infection (OR, 1.0; 95% CI, 0.4 to 2.6)[11].

In our study we found distribution of patients by seroprevalence of IgG anti-Chalmydia antibody. In hypertension group 27 (56.0%) patients were positive for IgG anti-Chalmydia antibody; while 29 (57.0%) patients were positive for IgG anti-Chalmydia antibody in non-hypertension group. There was no significant association of seropositivity of IgG anti-Chalmydiaantibody between two groups (p=0.859).These data does not support the associations of mild to moderate hypertension with previous *Chlamydia pneumoniae* infection. Future clinical studies will be necessary to define the importance of this risk across a range of populations.

Conclusion

Among These data does not support the associations of mild to moderate hypertension with previous *Chlamydia pneumoniae* infection. For the past 20 years, numerous studies have evaluated the role and importance of *Chlamydia pneumoniae* in cardio vascular risk factors, but it is a major challenge to either prove or disprove a causal role for a common agent in a highly prevalent disease. In view of important limitations in study design and execution, these results cannot rule out an important pathogenic role. Considering the totality of present evidence, *Chlamydia pneumoniae* is neither alone sufficient nor is it necessary to cause cardio vascular events or its clinical consequences in humans. However, *Chlamydia pneumoniae* is highly likely to be a modifiable risk factor that may be amenable to future therapies focused on either eradication (antibiotic therapy or early immunization) or modifying the vascular inflammatory response to infection. Future clinical studies will be necessary to define the importance of this risk across a range of populations.

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