Antibodies to *Chlamydia pneumoniae* are Associated with Increased Intima Media Thickness in Asymptomatic Indian Individuals

V. C. S. Srinivasarao Bandaru, MSc, PhD,* Subhash Kaul, MD, DM, FRCP, FAAN,* Vemu Laxmi, MD,† M. Neeraja, MSc,† M. Uma Mahesh, MD, DNB,‡ Suvarna Alladi, DM,* and Demudu Babu Boddu, MD, DM*

Chlamydia pneumoniae has been found to be associated with cerebrovascular and cardiovascular diseases in seroepidemiologic studies. The aim of this study was to investigate whether this organism is associated with increased intima media thickness (IMT) of carotid arteries in asymptomatic individuals. Serum titer of antibodies to *C pneumoniae* antibodies IgA and IgG in 100 asymptomatic individuals older than 40 years was measured by microimmunofluorescence. These subjects also had their IMT measured by B-mode ultrasound in the common carotid artery on both sides. Comparison of baseline characteristics between the group with abnormal IMT (>0.08 cm) and group having normal IMT (≤0.08 cm) showed significant association of *C pneumoniae* antibodies and hypertension with the former (i.e., abnormal IMT group). Multiple logistic regression (stepwise method) established *C pneumoniae* as an independent risk factor for increased IMT. To conclude, this study demonstrated that *C pneumoniae* infection is associated with an increase of IMT in the common carotid artery. **Key Words:** *Chlamydia pneumoniae*—asymptomatic individuals—intima media thickness—erythrocyte sedimentation rate—C-reactive protein—microimmunoflourescence.

Many studies published in the last decade have incriminated chronic infection as a causative factor for myocardial infarction and stroke.[1,2] The support for the role of *Chlamydia pneumoniae* in causing the vascular events comes from the fact that many elementary bodies related to *C pneumoniae* have been detected in atherosclerotic plaques and fatty streaks in the aorta, coronary arteries of autopsy cases, coronary arterectomy specimens, and carotid endarterectomy specimens.[3,4] The exact mechanism is not clear but there is evidence that infections may contribute to atherosclerotic process and may facilitate plaque rupture and thrombosis.[5] A recent meta-analysis indicated that *C pneumoniae* may be causative for arterial disease, although further research is needed.[5]

An increased intima media thickness (IMT) is believed to be an early stage in the pathophysiology of atherosclerosis, and ultrasound measurement of IMT is increasingly being used in clinical research as a surrogate marker of early atherosclerosis.[6]

The aim of this study was to investigate whether elevated titers of antibodies to *C pneumoniae* are associated with increased IMT in asymptomatic individuals older than 40 years in a sample of the Indian population.

Methods

Selection of Subjects

The study was conducted in our neurology department, a referral university teaching hospital in south India. In all, 100 consecutive, asymptomatic individuals, older than 40

From the *Departments of Neurology, †Microbiology; and ‡Radiology, Nizam's Institute of Medical Sciences Panjagutta, Hyderabad India.

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Address correspondence to Subhash Kaul, MD, DM, FRCP, FAAN, Nizam's Institute of Medical Sciences, Panjagutta, Hyderabad, India 500082. E-mail: subashkaul@hotmail.com.

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Table 1. *Comparison of baseline characteristics of asymptomatic individuals having abnormal and normal intima media thickness*

Parameters	Abnormal IMT, n = 50 (%)	Normal IMT, n = 50 (%)	OR	95% CI	*P value
Men	36 (72)	39 (78)			
Women	14 (28)	11 (22)			
Mean age, y (SD)	60.4 (10.1)	54.7 (8.1)			.004
Age range, y	44-82	41-75			
Chlamydia pneumoniae	18(36)	5(10)	5	1.7-15	.004
Hypertension	25(50)	10(20)	4	1.6-9.7	.003
Diabetes	12 (24)	7 (14)	1.93	0.6-5.4	.3
Smoking	12 (24)	14 (28)	0.8	0.3-1.9	.8
Alcoholic	11 (22)	13 (26)	0.8	0.3-2	.8
Hypercholesterolemia	23 (46)	15 (30)	1.9	0.8-4.5	.1
Hyperhomocysteinemia	14 (28)	11 (22)	1.4	0.8-3.5	.6

Abbreviations: CI, confidence interval; IMT, intima media thickness; OR, odds ratio.
*Chi-square test.

years, were enrolled into this study, provided they had no or history of stroke or transient ischemic attack in ocular or hemispheric distribution. This study was approved by the institutional ethical committee and study period was from January 2005 to January 2006.

Data were collected through interviews of subjects by a trained research fellow, clinical assessment by the stroke neurologist, and a detailed medical record review. Standardized questions were adapted from the behavioral risk factor surveillance system[7] by the Centers for Disease Control and Prevention regarding the following conditions: hypertension, diabetes, hypercholesterolemia, peripheral vascular disease, cigarette smoking, and cardiac conditions such as myocardial infarction and coronary artery disease. Standard techniques were used to measure blood pressure, height, weight, fasting blood specimen lipids (including total cholesterol, low-density lipoprotein, high-density lipoprotein, very low-density lipoprotein, and triglycerides), and glucose.[8] Serum homocysteine estimation and electrocardiography was performed in all subjects.

Hypertension was defined as per the guidelines of Joint National Committee VI to VII.[9] Diabetes was diagnosed according to World Health Organization criteria.[10] Hypercholesterolemia was defined as per the 2001 guidelines of the National Institutes of Health.[11] Hyperhomocysteinemia was defined as greater than 15 mg/100 mL of serum in those younger than 60 years, and greater than 20 mg/100 mL of serum in those older than 60 years.[12,13] Smokers were defined as those reporting daily smoking.[14] Alcoholics were defined as those in whom alcohol consumption was more than 50 g/day.[15] When possible, data were obtained directly from subjects, by use of the standardized data collection instruments. When the subjects were unable to provide answers, proxy or close blood relation knowledgeable about the subject's history was interviewed.

Table 2. *Multiple logistic regression analysis (stepwise method), establishing* Chlamydia pneumoniae *as an independent risk factor for increased intima media thickness*

Variables	OR	95% CI
Dependent variable IMT		
Independent variables:		
age, sex, hypertension, diabetics, smoking, alcoholic, hyperhomocysteinemia, hypercholesterolemia,		
Final variable indicated in the model		
Chlamydia pneumoniae IgG	4.0	1.3-12.5

Abbreviations: CI, confidence interval; IMT, intima media thickness; OR, odds ratio.

Color Doppler

The ultrasonographic examination was performed by a qualified radiologist, experienced in neurosonology, and the findings were confirmed by the stroke neurologist, certified in neurosonology by the American Society of Neuroimaging. The sonographic evaluation was done

Table 3. *Correlations of C-reactive protein and* Chlamydia pneumoniae *positivity with intima media thickness*

	Abnormal IMT, n = 50 (%)	Normal IMT, n = 50 (%)	*P value
Chlamydia pneumoniae-positive CRP positive	18 (36)	5 (10)	.004
Chlamydia pneumoniae-negative CRP positive	10 (20)	3 (6)	.07

Abbreviations: CRP, C-reactive protein; IMT, intima media thickness.
*Chi-square test.