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Is *Chlamydia pneumoniae* seropositivity associated with atherothrombotic cerebrovascular infarction?

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KEYWORDS
Atherotherombotic infarction;
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Summary
Background and objective: Several studies suggested that *Chlamydia pneumoniae* (CP) infection may be a risk factor for cerebrovascular disease. Since these studies have reported controversial results, we performed this study to identify whether Cp-immunoglobulin was associated with atherothrombotic cerebrovascular infarction (ACI) in Iranian patients.
Materials and methods: Forty-five patients admitted with ACI, and 45 control without ACI were enrolled in this case—control study. Using an enzyme-linked immunosorbed assay kit (ELISA), the presence of CP-immunoglobulin (CP-IgG) in studied patient's sera was determined.
Results: The seroprevalence of CP-IgG was 35(77.7%) in the ACI group (mean age = 73.3 years) and 29(64.4%) in the control group (mean age = 70.1 years) ($P > 0.05$). There was no difference in sex, age, hypertension, smoking, hyperlipidemia, diabetes and obesity between cases and control groups ($P > 0.05$). No association was observed between CP seropositivity and ACI [OR: 1.95 (95% CI, 0.081—2.03), $P = 0.16$].
Conclusion: Our finding suggests that there is no association between ACI and positive CP-IgG in Iranian patients.

Introduction

Cerebrovascular accident (CVA) is the third cause of death worldwide. Risk factors of CVA are: blood hypertension (BH), diabetes mellitus (DM), atherosclerosis, hyperlipidemia, cigarette smoking, alcohol and recent or chronic infections [1,2]. Previous studies have described acute and chronic respiratory infection as potential risk factors for atherosclerotic vascular or cerebrovascular disease [3—5]. Several infectious agents have been found to be involved in atherogenesis over the past decades. *Chlamydia pneumoniae* (CP) is an important cause of upper respiratory tract infection and pneumonia in children and young adults and is a cause

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Table 1 Demographic characteristics and risk factors of cerebrovascular disease in studied subjects.

Risk factors	ACI group ($n=45$) *N* (%)	Control group ($n=45$) *N* (%)	*P* value
Sex, female	30(66.6)	30(66.6)	0.58
Age (years)	73.3 ± 15	70.1 ± 13.5	0.289
Hypertension	23(51.1)	19(42.2)	0.26
Hyperlipidemia	27(60)	30(66.6)	0.33
Cigarette smoker	18(40)	20(44.4)	0.41
Diabetes mellitus	20(44.4)	19(42.2)	0.50
Over weight	16(35.5)	18(40)	0.41

ACI; atherothrombotic cerebrovascular infarction, hypertension; systolic above 140 mmhg and diastolic above 90 mmhg, hyperlipidemia; serum triglyceride above 180 mg/dl and or cholesterol above 200 mg/dl, cigarette smoker; more than 10 cigarrettes per day for more than 5 years, diabetes mellitus; fasting blood sugar above 140 mg/dl, Over weight; body mass index (kg) divided by the square of the height (m^2) more than 27, *P* value lower than 0.05 is significant.

of recurrent respiratory infection in older adults [4]. Diagnosis of CP infection is currently difficult because cell culture techniques are not available for clinical use [4] and nonculture tests using antigen detection methods or DNA polymerase chain reaction (PCR) are expensive and are not available every where. Varying level of anti CP-IgG antibody titer have frequently been used as presumptive markers of persistent, or chronic infection status [5]. Recently introduced enzyme-linked immunosorbent assay (ELISA) kits are available and are more objective [3,6]. Numerous studies have linked CP infection to atherosclerosis [6]. Infection of the vascular wall with CP has been liked to stroke in epidemiological studies [7—11]. Kawashima and Kawada demonstrated a significant elevation of CP-immunoglobulin (CP-IgG) in an ischemic stroke patient [12]. Since the association between antibodies against CP and CVA is yet controversial [13—16] and because, there are no studies examining the relation ship between the presence of CP antibodies level and CVA in Iran, we conducted this case—control study. The aim of the present study was to ascertain whether CP-IgG positivity was associated with ACI in hospitalized subjects.

Materials and methods

Ninety hospitalized patients participated in this case—control study. The study population was recruited from the internal medicine department in Naft Great Hospital in Ahvaz a city southern Iran. From December 2004 to May 2005, forty-five patients with CVA and 45 control subjects without a history of CVA were investigated. Whereas cases were admitted patients with CVA, control subjects were selected from consecutive admitted patients without CVA. CVA was diagnosed by an expert neurologist clinically with or without brain CT scan. Including criteria were: age of 40 years or more and admission to the hospital under care of specialist physician. Exclusion criteria were: non-thrombotic brain infarction (e.g. septic or fat emboli) and cardiac disorders with embolism. Individuals with immunodeficiency, collagen vascular disease and other autoimmune disorders, because of the interference with IgG production were excluded. Controls who had a history of stroke or infectious disease on admission were also excluded. CVA was defined according to the American Neurology Association (ANA) as a clinical syndrome characterized by clinical signs and symptoms of focal or global loss of brain function with no apparent cause other than of vascular origin. This definition was made with either a normal brain CT scan, or evidence of an infarct in the clinically relevant area of the brain on a CT Scan. Five milliliter of clotted blood samples obtained from each case and control subjects and were preserved at $-20^{\circ}C$ until the time of serological assays. Immunoglobulin G (IgG) antibodies against CP were tested by using the DIA Pro CP enzyme-linked immunosorbent assay (Milan, Italy) according to manufacturer's instructions. Out of total samples, 10 samples were randomly selected and retested to detect CP-IgG. No difference was observed between results of duplicate tests. Sensitivity and specificity of the test was more than 98%. According to manufacturer's instructions, cut off for the CP-IgG was 10 IU. Those with titers of 10 IU or above were determined as seropositive and those with titers below the 10 IU were considered seronegative. Data about other risk factors was collected by a questionnaires including gender, age, blood pressure, body weight, smoking, triglyceride/cholesterol serum levels and blood sugar (DM = diabetes mellitus). Data was statistically analyzed by using SPSS 11.5, and compared by chi square test. A value of *P* below 0.05 was considered significant.