

The level of *C.pneumoniae*, Cytomegalovirus, and *H.pylori* antibody in a patient with coronary heart disease

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Abstrak

Aterosklerosis sampai saat ini merupakan penyebab utama morbiditas dan mortalitas di negara maju. Meskipun modifikasi faktor risiko di negara maju telah dapat menurunkan kekerapan aterosklerosis namun penurunan ini mulai menunjukkan grafik yang mendatar. Keadaan ini merangsang para peneliti untuk mencari faktor pajanan lingkungan termasuk faktor infeksi yang dapat mempengaruhi proses aterosklerosis. Telah dilakukan penelitian potong lintang dari bulan Maret 1998 sampai Agustus 1998 terhadap 122 orang pasien yang secara klinis menunjukkan penyakit jantung koroner yang menjalani kateterisasi jantung, terdiri dari 92 orang laki-laki dan 30 orang perempuan dengan rerata umur 55 tahun. Pasien diperiksa secara klinis dan laboratorium (gula darah, kolesterol, trigliserida dan antibodi terhadap *C.pneumoniae*, Cytomegalovirus dan *H.pylori*). Pada penelitian ini didapatkan perbedaan kadar kolesterol, trigliserida dan HDL antara kelompok stenosis koroner dan non stenosis. Sedangkan kadar antibodi *C.pneumoniae*, Cytomegalovirus, *H.pylori* tidak berbeda bermakna. Penelitian ini belum dapat menyimpulkan pengaruh antibodi terhadap aterosklerosis karena pada kelompok non stenosis tidak dapat disingkirkan kemungkinan terjadinya aterosklerosis mengingat rerata umur subyek penelitian 55 tahun. Penelitian mengenai interaksi infeksi dengan risiko tradisional serta gender dan nutrisi diperlukan untuk mendapat jawaban yang lebih jelas tentang pengaruh infeksi terhadap aterosklerosis. (*Med J Indones* 2002; 11: 211-4)

Abstract

Atherosclerosis is still the chief cause of morbidity and mortality in developed nations. Even though in developed nations the modification of risk factors is able to reduce the prevalence rate of atherosclerosis, such reduction is starting to slow down. Such condition has stimulated researchers to identify environmental exposure, including infection, that can influence the process of atherosclerosis. This cross sectional study was conducted from March to August 1998, on 122 patients that clinically demonstrate coronary heart disease and have underwent cardiac catheterization, 92 males and 30 females with an average age of 55 years. Patients undergo clinical and laboratory evaluation (blood glucose, cholesterol, triglyceride, and antibody for *C.pneumoniae*, Cytomegalovirus, and *H.pylori*). We found a significant difference in cholesterol, triglyceride, and HDL levels in those with coronary stenosis and those without. However, we did not find a significant difference in the levels of *C.pneumoniae*, Cytomegalovirus, and *H.pylori* antibodies. This study is unable to conclude the influence of these antibodies on atherosclerosis, since in the non-stenosis group, we cannot eliminate the possibility of atherosclerosis, since the average age of study subject is 55 years. Studies on the interaction between infection and traditional risk factors as well as gender and nutrition is needed to find a clear answer of the influence of infection in atherosclerosis. (*Med J Indones* 2002; 11: 211-4)

Keywords: Level of *C.pneumoniae*, Cytomegalovirus, *H.pylori* antibody, coronary heart disease.

Atherosclerosis is still the chief cause of morbidity and mortality in developed nations. In Indonesia, even though infectious disease is still the chief health problem, degenerative disease, including atherosclerosis, has become an important health problem. The most recent development and management of coronary heart disease, both in reducing risk factors, establishing a diagnosis, and intervention is still unsatisfactory. Surgical intervention requires complete facilities at high costs. Even though in developed

nations the modification of risk factors is already able to reduce the prevalence rate of atherosclerosis, such reduction is starting to slow down.¹⁻³ Such condition has stimulated researchers to identify environmental exposures including infection, that can influence the process of atherosclerosis.⁴⁻⁶ Sero-epidemiological and pathological studies as well as laboratory animal studies and clinical data demonstrate that chronic infection by *C.pneumoniae*, Cytomegalovirus, and *H.pylori* may play a role in the pathogenesis of atherosclerosis. Even though there has been many studies associated with the process of atherosclerosis, the exact relationship between atherosclerosis and infection is still unclear.

Meta analysis demonstrated a relationship between an increase in *C.pneumoniae* antibody and the prevalence of coronary heart disease.⁷ Saiko first reported a case control study in post-acute myocardial infarction and chronic coronary heart disease that demonstrated an increase in pneumoniae antibody compared to control subjects.⁸ Shor first reported *C.pneumoniae* in atherosclerosis lesion under the electron microscope.⁹ Ramirez found that *C.pneumoniae* can be cultured from atherosclerotic plaques.¹⁰

Cytomegalovirus is associated with primary atherosclerosis, post angioplasty re-stenosis and post-transplantation atherosclerosis. On the other hand, the association of *H.pylori* and atherogenesis is not as strong as the relationship between *C.pneumoniae* or CMV.^{7,11}

In Indonesia, examinations for *C.pneumoniae*, CMV and *H.pylori* antibody associated with coronary heart disease has not been frequently reported.

METHODS

This study is a cross sectional study on patients that clinically demonstrate coronary heart disease and undergo cardiac catheterization. This study was conducted from March to August 1998. All study subjects that met the criteria were incorporated in the study (consecutive sampling) after stating informed consent. Patients that underwent cardiac catheterization undergo clinical and laboratory evaluation (blood glucose, cholesterol, triglyceride, and antibody for *C.pneumoniae*, Cytomegalovirus, and *H.pylori*). Evaluation for *C.pneumoniae*, cytomegalovirus, and *H.pylori* antibody were performed using the Elisa method. The statistical analysis used was the t-test and logistic regression.

RESULTS

There were 122 an study subjects that participated in this study. Most of the study subjects were male with an average age of 55 years. There were more non-

smokers than smokers. The initial data of the patients in this study can be found in Table 1.

Table 1. Baseline characteristics of study subjects (n=122)

Age (years)	55.03 ± 10.65
Sex	
Male	92 (75.4%)
Female	30 (24.6%)
Smoking	
Yes	51 (41.8%)
No	71 (58.2%)
History of hypertension	
Yes	62 (50.8%)
No	60 (49.2%)
Total cholesterol level	201.68 ± 42.25
HDL cholesterol	41.10 ± 10.93
Triglyceride	191.27 ± 91.55
Blood sugar	137.89 ± 56.35
Fibrinogen	340.36 ± 105.97
<i>C.pneumoniae</i>	1.63 ± 0.69
Cytomegalovirus	2.88 ± 2.26
<i>H.pylori</i>	32.35 ± 10.07

The group with coronary stenosis compared to those without coronary stenosis did not demonstrate a significant difference in cholesterol and triglyceride level, as seen in Table 2.

Table 2. The difference between groups with coronary stenosis and those without

Criteria	Coronary stenosis (n=83)	No coronary stenosis (n=39)	P
Age (years)	56.18 ± 9.60	52.58 ± 13.19	0.09
Blood sugar	135.90 ± 56.35	142.12 ± 56.37	0.572
Total cholesterol	206.15 ± 43.29	192.17 ± 77	0.088
Triglyceride	204.08 ± 95.55	164.02 ± 76.57	0.024
HDL	39.65 ± 10.74	44.02 ± 10.83	0.031
LDL	126.59 ± 40.34	115.15 ± 35.42	0.132
Fibrinogen	351.86 ± 117.94	315.87 ± 69.54	0.080

There was no significant difference in the antibody levels in groups with stenosis and without, as seen in Table 3.

Table 3. The difference in the antibody levels in the group of patients with and without stenosis

Criteria	Coronary stenosis (n=83)	No coronary stenosis (n=39)	P
<i>C.pneumoniae</i>	1.6233 ± 0.7200	1.6533 ± 0.6292	0.812
CMV	2.8217 ± 2.2835	3.0179 ± 1.9896	0.656
<i>H.pylori</i>	38.3133 ± 118.6253	19.6487 ± 35.7222	0.339

DISCUSSION

This study is a cross-sectional study. Evaluation of the levels of *C.pneumoniae*, CMV, and *H.pylori* antibodies was conducted prior to heart catheterization examination. *C.pneumoniae*, CMV, and *H.pylori* antibodies was evaluated by the evaluation of IgG antibodies evaluation, signifying past infection. In this study, we were not able to demonstrate a significant difference in the anti- *C.pneumoniae*, CMV, and *H.pylori* IgG levels in groups with and without stenosis. Even though this group was classified into those with coronary stenosis and those without, it does not mean that those in the group without stenosis did not suffer from atherosclerosis. Coronary stenosis is an advanced stage of the atherosclerotic process.

Proof that associated *C.pneumoniae* infection and atherosclerosis was conducted sero-epidemiologically, through direct detection of bacterial components in the atherosclerotic lesion and isolation of the bacteria from carotid and coronary atherome tissue. Many sero-epidemiological studies have associated increased *C.pneumoniae* serology with myocardial infarction, coronary heart disease, and stroke. Prospective studies that have been performed do not provide strong evidence that support a relationship between *C.pneumoniae*, cytomegalovirus, and *H.pylori* infection with coronary heart disease. In *C.pneumoniae* infection, the risk-ratio towards coronary heart disease is 1.22 (95% CI 0.96-1.54), the risk ratio for cytomegalovirus is 0.91 (95%, CI 0.69-1.19), and the risk ratio for *H.pylori* is 1.13 (95%, 0.93-1.38).¹² Even though we must understand the diagnostic criteria, the limit of the titer used may be different. We also have to take into consideration the possibility of confounding factors such as smoking, and also the number of samples being studied.¹⁴ In addition, when performing the evaluation, we also need to consider the fact that over 50% adults have antibodies against *C.pneumoniae*. The evaluation of antibody levels should be conducted serially, since there is a tendency for re-

infection, thus causing fluctuation of the antibody serum.^{12,13} Melnich reported that patients that undergo coronary bypass surgery have an increased CMV antibody of 70%, compared to 43% in control subjects.¹⁴ Pathological studies using PCR for CMV found 57% in atherosclerotic plaques and 36% in control subjects. Zhou reported that CMV infection is a strong independent risk factor for the development of post-atherectomy re-stenosis.¹⁵ In patients positive for CMV, atherosclerosis of the graft occurs in 68.8% cases, while occurring in only 36.8% in patients with negative CMV.¹⁶ Mendal reported that patients with positive *H.pylori* serology, there is a twofold risk of coronary heart disease.¹⁷ Patel reported a correlation between *H.pylori*, *C.pneumoniae*, and coronary heart disease.¹⁸ Rathbone et al, reported no correlation between *H.pylori* and coronary heart disease.¹⁹

Pasari reported infection of a bacteria more virulent that Cag-A positive strain of *H.pylori* demonstrating a significant correlation with coronary heart disease.²⁰ From the pathological evaluation of 50 patients with abdominal aortal aneurysm, the DNA of *H.pylori* was not found in the atherosclerosis plaque.⁷ The presence of microbes or their components in atherosclerotic lesions is estimated to be the initiating factor for the exacerbation of disease, but can not directly be concluded as the causative agent.

Influencing factors in the risk of coronary heart disease in this study was total cholesterol, HDL cholesterol, and triglyceride. This was in accordance with various studies that have taken place. It seems that infectious agents are not sufficient to cause atherosclerosis by themselves, but instead do so in conjunction with other risk factors for the development of atherosclerosis, such as smoking, hyperlipidemia, hypertension, etc.

Studies on human subjects, such as this one, are usually focused on advanced stages of atherosclerosis. Animal studies, on the other hand, are able to study earlier stages of the disease. Such condition needs to be understood, since the exposure to infection during childhood is common. In addition, available studies do not sufficiently consider past infection, whether it is active, persistent, recurrent, or latent. To be able to produce more reliable results, we need to conduct studies with serial antibody level evaluation of a larger number of samples, on homogenous population, with early onset of the disease. The Center for Disease Control and Prevention and Laboratory Center for Disease Control, which conducted a workshop in

Canada, recommended to increase the reproducibility and comparability of *C.pneumoniae* studies.²¹⁻²²

Studies conducted now a days are those that study the interaction between infection, traditional risk factors, and other determinants of host susceptibility, such as gender and nutrition.

CONCLUSION

In this study conducted on 122 people undergoing heart catheterization, we found a significant difference in cholesterol, triglyceride, and HDL levels between those with coronary stenosis and those without.

However, we did not find a significant difference in the levels of *C.pneumoniae*, CMV, and *H.pylori* antibodies. This study is unable to conclude the influence of these antibodies on atherosclerosis, since in the non-stenosis group, we cannot eliminate the possibility of atherosclerosis, since the average age of study subjects is 55 years. Studies on the interaction between infection and traditional risk factors as well as gender and nutrition is needed to find a clear answer of the influence of infection in atherosclerosis.

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