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Association of *Mycoplasma pneumoniae* Infection with Myocardial Infarction

[1]Morteza Pourahmad, [2]Abdolreza Sotoodeh Jahromy and [1]Mohammad Shojaei
[1]Department of Internal Medicine, Jahrom University of Medical Science, Iran
[2]Department of Immunology, Jahrom University of Medical Science, Iran

Abstract: Problem statement: In addition to the major risk factors for atherosclerosis such as high plasma level of low density lipoprotein, low plasma level of high density lipoprotein, cigarette smoking, hypertension and diabetes mellitus, some studies introduce other agents such as *Mycoplasma pneumoniae* as risk factors for atherodclerosis and coronary artery diseases. Aim of this study was to clarify the risk of *Mycoplasma pneumoniae* for myocardial infarction in Iranian population. **Approach:** This was a case-control study, in which 90 patients studied. (March 2005-2007). First group (or case group) include 45 units who had been admitted in hospital with diagnosis of myocardial infarction and second group include 45 units, who were healthy individuals without any positive history of ischemic heart disease. IgG antibodies was assessed by ELISA technique in both groups. **Results:** There was significant statistic difference in antimycoplasma antibody level. In the groups ($p = 0.028$) and the relative risk of mycoplasma infection for myocardial infarction estimated to be 2.7. **Conclusion:** *Mycoplasma pneumoniae* infection seems to be a risk factor for myocardial infarctin, in Iranian population. It is better to design other studies to evaluate the risk of coinfection of *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* and also the risk of these infection plus conventional risk factors for myocardial infarction in this country.

Key words: *Mycoplasma pneumoniae*, myocardial infarction, risk

INTRODUCTION

Ischemic Heart Disease (IHD) is one of the most common, serious, chronic, life-threatening illness in the world. In united states, more than 12 million persons have IHD, more than 6 million have angina pectoris and more than 7 million have sustained a Myocardial Infarction (MI)[1].

In this country, approximately 650,000 patients experience a new Acute Myocardial Infarction (AMI) and 450,000 experience a recurrent AMI each year[2].

As we know the main pathophysiologic basis for IHD and MI is Coronary Artery Disease (CAD) that causes reduction in oxygen supply to the cardiac tissue[1]. On the other hand the main cause of the CAD is atherosclerosis and we know; high plasma level of Low Density Lipoprotein (LDL), low plasma level of High Density Lipoprotein (HDL), cigarette smoking, hypertension and diabetes mellitus are the major risk factors for atherosclerosis[1].

However, a large number of CAD patients don't have any of these known risk factors, therefore, the cause of atherosclerotic CAD in these patients is difficult to explain[3]. So this question arise that is there any other risk factor for IHD?

One of the suspicious causes in these patients is infection with some the organisms.

Association of atherosclerosis and CAD has been reported with a few infectious agents such as: gram negative bacteria[4], *Chlamydia pneumoniae*, Helicobacter pylori and herpes viruses[4,5].

Mycoplasma pneumoniae is also one of the accused agents that is said may be associate with atherosclerosis[3,6] lonely or in coexistence with other conventional risk factors. It should imply that from 17 mycoplasma species which are isolated from human, the only virtual known pathogen for human is *M. pneumonia*[7,8].

M. pneumoniae is known as an important infectious cause for respiratory system[9,10] and most cases of mycoplasma respiratory infection occur singly or as family outbreaks[11]; additionaly it is also isolated from urogenital tract in human[12].

In Iran (our country), information about the epidemiology of acute MI and it's complications are very little[13] and in a study it showed that in 3% of the patients with MI none of the conventional CAD risk factors is found[14].

On the other hand the prevalence of *M. pneumoniae* infection in Iran is about 22.7%[15] which is similar to the proportion in some other countries[16,17].

Corresponding Author: Morteza Pourahmad, Jahrom University of Medical Science, Jahrom, Iran Tel: 09177916203

Therefore it seems that the evaluation of the risk of *M. pneumoniae* infection for CAD and MI is necessary, so we conducted this study to find the role of this organism in MI in Jahrom (a city in south of the Iran) as an Iranian population sample.

MATERIALS AND METHODS

This is a case-control study, in which 90 patients are studied. This study conducted during two years (March 2005-2007) in cardiologic ward in peymanieh hospital in Jahrom (a city in south of Iran). The units selected by simple nonrandomized sampling technique. They were in two groups: first group (or case group), include 45 units who had been admitted in hospital by diagnosis of myocardial infarction and second group include 45 healthy units who had not any positive history of IHD and they matched by first group, for sex, age, weight and body mass index. Inclusion criteria for first group were: Typical chest pain for IHD, positive Electrocardiogram (ECG) and serum biomarkers for myocardial infarction.

Upon ECG signs; the case group was divided into two groups: ST elevated and NonST elevated myocardial infarction (STEMI and NSTEMI respectively)[2].

Exclusion criteria for two groups were: Two blood pressure recordings of 140/90 mm Hg or higher, fasting blood glucose level more than 110 mg dL^{-1}, serum total cholesterol level more than 200 mg dL^{-1}, history of smoking and family history of coronary artery disease.

In all units (cases and controls) a fasting blood sample (5 mL) collected for analysis of blood glucose and serum total cholesterol levels as well as for serologic markers of *M. pneumoniae*.

IgG antibodies to *M. pneumoniae* were assessed by ELISA technique; Trinity biotech captia kit for Mycoplasma was used for detection of IgG antibodies to *M. pneumoniae* and a value of more than 10 U mL^{-1}[18] was considered seropositive on manufacturer's guidelines.

At last all information analyzed by SPSS software. For statistic analysis, we used t-test and chi square test.

RESULTS

Ninety patients were enrolled and completed this study, 55(61%) out of them were male and other 35(39%) were female. In case group (patients with diagnosis of myocardial infarction) 31 units (68.9%) were male while the other 14 units (31.1%) were female. In second group (control group) 24 units (53.3%) were male and 21 units (47.7%) were female.

Table 1: Antimycoplasma antibody in case and control groups

		Antimycoplasma ab		
Group		Positive	Negative	Total
Case	Male	11	20	31
	Female	10	4	14
Total		21	24	45
Control	Male	5	19	24
	Female	6	15	21
Total		11	34	45

p = 0.028

Table 2: Antimycoplasma antibody in STEMI and NSTEMI

	Antimycoplasma ab		
MI type	Positive (%)	Negative (%)	Total
STEMI	17 (45.9)	20 (54.1)	37
NSTEMI	4 (50)	4 (50)	8
Total	21	24	45

p = 0.83

There was no significant statistic difference in sex proportion in the groups. (p = 0.26).

Mean age of the patients in case group was 62.29±13.24 and in control group was 61.71±12.29. There was not significant statistic difference for age between two groups (p = 0.83).

Fasting blood glucose and serum total cholesterol levels in case and control groups were within normal limits.

In case group 21 cases out of 45 and in control group 11 units out of 45 were positive for antimycoplasma antibody and this difference was statistically significant (p = 0.028) (Table 1).

We also accounted the relative risk of antimycoplasma antibody for myocardial infarction in our patients. OR = 2.7 (95% C.I. = 1.103-6.634).

In this study from 45 patients with MI, 37 (82%) patients had STEMI and 8 (18%) patients had NSTEMI; 17 and 4 patients had positive antimycoplasma antibody in STEMI and NSTEMI groups respectively but the difference was not statistically significant (p = 0.83) (Table 2).

DISCUSSION

Many studies are conducted for evaluation of the risk factors in myocardial infarction and some of these studies try to clarify the risk factors other than the known risk factors for MI. Infections seem to be questionable risk factors that their effect is not clarify yet and more investigations are needed, this study conducted for this purpose.

Many studies are conducted for evaluating the effect of infectious agents such as *M. pneumoniae* and C. *pneumoniae* in cardiovascular diseases and MI; but

there are a few studies to evaluate the relative risk for these agents in patients with MI.

In this study we accounted the Odd's ratio for *M. pneumoniae* infection in patients with MI and it revealed that infection by this agent may be a risk factor for MI. (OR = 2.7).

A similar study was conducted in India in which; combined seropositivity to C. *pneumonia* and *M. pneumoniae* was significantly higher ($p<0.05$) in CAD patients with MI than in those without MI; but the risks (Odd's ratio) of these infections have not been accounted in this study[3]. Another study that is conducted in Moscow; Russia, concluded that there is association between infection and coronary heart disease. This study revealed that in comparison with controls; patients with coronary heart disease had higher frequency of seropositivity to *Chlamydia pneumonia*, *M. pneumonia* and cytomegalovirus ($p<0.05$). It also revealed that infectious burden (quantity of antibodies per one patient) is significantly higher in patients with M.I., unstable and stable angina than in controls[19].

In another study that is conducted in Japan; *M. pneumoniae* seropositity was more prevalent in patients with CAD than patients without CAD (14% versus 6%, $p<0.01$). In this study the highest prevalence is found in patients with MI[6].

It should imply that several case reports have described an association between cerebral ischemia and Mycoplasma infections[20-23]. But, on the other hand, Grau and his colleagues had not detected any association between infection with *M. pneumoniae* and cerebrovascular ischemia[24].

Mycoplasma is the only bacterium that needs cholesterol for proliferation. Ramires hypothesized that the association of *M. pneumoniae* and *C. pneumoniae* increases their virulence in inducing inflammation and rupture of the plaque[25].

In another study that has been conducted in our city (Jahrom); the relative risk of *C. pneumoniae* infection for MI (OR = 2.3)[26] was lower than that for *M. pneumoniae* in this study.

It should be keep in mind that this study and some other similar studies are conducted on the patients with deletion of the role of conventional risk factors; whereas *M. pneumoniae* infection may have summative and/or synergistic effects with conventional risk factors. Thus for better evaluation of these effects another study in myocardial infarction patients who has conventional risk factors should be designed.

On the other hand, sometimes coinfection of *M. pneumonia* and *C. pneumonia* may happen in a patient. In a study that is conducted by Mamiyama *et al*.[6] it is revealed that among patients with *C. pneumoniae* seropositivity, *M. pneumoniae* seropositivity is more prevalent in patients with CAD than patients without CAD, whereas among patients without *C. pneumoniae* seropositivity, *M. pneumoniae* seropositivity did not differ between patients with and without CAD. Thus this study suggests that; coinfection by *M. pneumoniae* and C. *pneumoniae* may be an important cofactor for CAD[6]. Then the risk of their coinfection for MI and infection of each of them alone as a risk for MI, seems to be necessary to reveal. It is also better to evaluate the effect of these infections in premature MI.

CONCLUSION

At last; by attention to the results of this and other studies we suggest to study more, to evaluate the effect of infections and anti-infection agents (specially anti *M. pneumoniae*) on cardiovascular system.

In some studies that *C. pneumonia* has been accounted as a risk factor for MI, antichlamydia; antibiotics, have been applied to decrease CAD risk[27-29].

Today we have vaccines for *M. pneumoniae*. These vaccines induce specific antibody responses, but protection against infection is limited to no more than 50% of vaccine recipients[11].

One suggestion is that to evaluate the effect of vaccination against *M. pneumoniae* for prevention of cardiovascular diseases and MI.

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