Association of Mycoplasma pneumoniae Infection with Myocardial Infarction

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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 atheroderosis 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[3]. 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]; additionally 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].
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 capta kit for Mycoplasma was used for detection of IgG antibodies to *M. pneumoniae* and a value of more than 10 U mL\(^{-1}\) 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 |
|----------------------------------------------------------|
| 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[31]. 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 pneumoniae, M. pneumoniae* 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* seropositivity 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 infection.[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.

**REFERENCES**

1. Selwyn, A.P. and E. Braunwald, 2005. Ischemic Heart Disease. In: Harrison's Principle of Internal Medicine, Fauci, A.S., E. Braunwald and J.D. Wilson et al. (Eds.). 16th Edn., Mc Grow Hill Company, Philadelphia, USA., ISBN: 0-07-139141-X, pp: 1434-1444.
2. Antman, E.M. and E. Braunwald, 2005. ST-Segment Elevation Myocardial Infarction. In: Harrison's Principle of Internal Medicine, Fauci A.S., E. Braunwald and J.D. Wilson et al. (Eds.). 16th Edn., Mc Grow Hill Company. Philadelphia, USA., ISBN: 0-07-139141-X, pp: 1448-1459.
3. Goyal, P., S.C. Kale, R. Chudhry, S. Chauhan and N. Shah, 2007. Association of common chronic infections with coronary artery disease in patients without any conventional risk factors. Indian J. Med. Res., 125: 129-136. http://www.ncbi.nlm.nih.gov/pubmed/17431281
4. Danesh, J., 1999. Coronary heart disease, Helicobacter pylori, dental disease, *Chlamydia pneumoniae* and cytomegalovirus: Meta analyses of prospective studies. AM. Heart J., 138: S434-S437. http://www.ncbi.nlm.nih.gov/pubmed/10539843
5. Fong, I.W., 2000. Emerging relation between infectious diseases and coronary artery disease and atherosclerosis. CMAJ., 163: 49-56. http://www.ncbi.nlm.nih.gov/pubmed/10920732

6. Momiyama, Y., R. Ohmori, H. Taniguchi, H. Nakamura and F. Ohsuzu, 2004. Association of Mycoplasma pneumoniae infection with coronary artery disease and its interaction with chlamydial infection. Atherosclerosis, 176: 139-144. http://www.ncbi.nlm.nih.gov/pubmed/15306186

7. Atkinson, T.P., M.F. Balish and K.B. Waites, 2008. Epidemiology, clinical manifestations, pathogenesis and laboratory detection of Mycoplasma pneumoniae infections. FEMS. Microbiol. Rev., 32: 956-973. http://www.ncbi.nlm.nih.gov/pubmed/18754792.

8. Waites, K.B., 2008. Ureaplasma infection. http://www.medscape.com/article/231470-overview

9 Clyde, W.A., 1993. Clinical overview of typical Mycoplasma pneumoniae infections. Clin. Infect. Dis., 17: S32-S36. http://www.ncbi.nlm.nih.gov/pubmed/8399935

10. Dominguez, A., S. Minguell, J. Torres, A. Serrano, J. Vidal and L. Salleras, 1996. Community outbreak of acute respiratory infection by Mycoplasma pneumoniae. Eur. J. Epidemiol., 12: 131-134. http://www.ncbi.nlm.nih.gov/pubmed/8817190

11. Baum, S.G., 2005. Mycoplasma Pneumoniae and Atypical Pneumonia. In: Principle and Practice of Infectious Diseases, Mandel, G.L., J.E. Bennett and R. Dolin (Eds.), 6th Edn., Churchill Livingstone, New York, ISBN: 0-443-06643-4, pp: 2271-2280.

12. Goulet, M., R. Dular, J.G. Tully, G. Billowes and S. Kasatiya, 1995. Isolation of Mycoplasma pneumoniae from the human urogenital tract. J. Clin. Microbiol., 33: 2823-2825. http://www.ncbi.nlm.nih.gov/pubmed/8576326

13. Ghadimi, H., F. Bishehsari, F. Allameh, A.H. Bozorgi and N. Sodagari et al., 2006. Clinical characteristics, hospital morbidity and mortality and up to 1 year follow-up events of acute myocardial infarction patients: The first report from Iran. Coron Artery Dis., 17: 585-591. http://www.ncbi.nlm.nih.gov/pubmed/17047441

14. Esteghamati, A., M. Abbasi, M. Nakhjavan, A. Yousefizadeh, A.P. Basa and H. Afshar, 2006. Prevalence of diabetes and other cardiovascular risk factors in an Iranian population with acute coronary syndrome. Cardiovasc. Diabetol., 17: 5-15. http://www.ncbi.nlm.nih.gov/pubmed/16842631

15. Salari, M.H. and R. Samimi, 2001. Comparison of mycoplasma hominis and ureaplasma urealyticum in infertile women and control group. Hakim Res. J., 4: 322-326. http://www.sid.ir/En/ViewPaper.aspx?ID=61173&v arStr=3;SALARI%20M.H.,SAMIMI%20R.;HAKI M,WINTER%202001;4;322;326

16. Waiters, K.B. and D.F. Talkington, 2004. Mycoplasma pneumoniae and its role as a human pathogen. Clin. Microbiol. Rev., 17: 697-728. http://www.ncbi.nlm.nih.gov/pubmed/15489344

17. Layani-Milon, M.P., I. Gras, M. Valette, J. Luciani, J. Stagnara and M. Aymard, 1999. Incidence of upper respiratory tract Mycoplasma pneumoniae infections among outpatients in Rhone-Alpes, France, during five successive winter periods. J. Clin. Microbiol., 37: 1721-1726. http://www.ncbi.nlm.nih.gov/pubmed/10325314

18. Immuno-Biological Laboratories, Inc. (IBL-America). http://www.manta.com/coms2/dnbcompany_hxd416

19. Basinkevich, A.B., R.M. Shakhnovich, V.R. Martynova and N.I. Kolkova et al., 2003. Role of Chlamydia, mycoplasma and cytomegalovirus infection in the development of coronary artery disease. Kardiologiia, 43: 4-9. http://www.ncbi.nlm.nih.gov/pubmed/14671556

20. Parker, P., J. Puck and F. Fernandez, 1981. Cerebral infarction associated with Mycoplasma pneumoniae infection. Pediatrics, 67: 373-375. http://www.ncbi.nlm.nih.gov/pubmed/7243475

21. Nakahata, C., E. Kitaka, H. Fujii, T. Sakano and T. Usui, 1983. A case of cerebral infarction associated with Mycoplasma pneumoniae infection. Hiroshima J. Med. Sci., 32: 277-279. http://www.ncbi.nlm.nih.gov/pubmed/6643107

22. Dowd, A.B., R. Grace and W.D. Rees, 1987. Cerebral infarction associated with Mycoplasma pneumoniae infection. Lancet, 2: 567. http://www.ncbi.nlm.nih.gov/pubmed/2887855

23. Ode, B. and S. Cronberg, 1976. Infection and intracranial arterial thrombosis. Lancet, 2: 863-864. http://www.ncbi.nlm.nih.gov/pubmed/61548

24. Grau, A.J., F. Buggle, S. Heindl, C. Steichen-Wiehn and T. Banerjee et al., 1995. Recent infection as a risk factor for cerebrovascular ischemia. Stroke, 26: 373-379. http://www.ncbi.nlm.nih.gov/pubmed/7887855

25. Ramires, J.A. and L. Higuchi Mde, 2002. Mycoplasma pneumoniae and Chlamydia pneumoniae are associated to inflammation and rupture of the atherosclerotic coronary plaques. Rev. Esp. Cardiol., 55: 2-9. http://www.ncbi.nlm.nih.gov/pubmed/15626350
26. Pourahmad, M., 2005. A study on the relationship between acute myocardial infarction and *Chlamydia pneumoniae*. Sci. Med. J. Ahwaz Jondi Shapur Uni. Med. Sci., 4: 147-151. http://dbase.irandoc.ac.ir/00789/00789957.htm

27. Jaremo, P., 2001. Evidence that *Chlamydia pneumoniae* affects platelet activity in patients with acute myocardial infarction and ST segment elevations. Scand J. Infect. Dis., 33: 747-48. http://www.ncbi.nlm.nih.gov/pubmed/11728040

28. Ashkenazi, H., B. Rudendky, E. Paz, D. Raveh, J.A. Balkin, D. Tzivoni and A.M. Yinnon, 2001. Incidence of immunoglobulin G antibodies to *Chlamydia pneumoniae* in acute myocardial infarction patients. Isr. Med. Assoc. J., 3: 818-821. http://www.ncbi.nlm.nih.gov/pubmed/11729576

29. Ciervo, A., P. Visca, A. Petrucca, L.M. Biasucci, A. Maseri and A. Cassone, 2002. Antibodies to 60 kilodalton heat shock protein and outer membrane protein 2 of *Chlamydia pneumoniae* in patients with coronary heart disease. Clin. Diagn. Lab. Immunol., 9: 66-74. http://www.ncbi.nlm.nih.gov/pubmed/11777831