The Correlation of Infectious and Inherent Agents with Acute Myocardial Infarction in Patients of Teaching Hospitals in Qazvin in 2013

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Abstract

Background: Acute myocardial infarction (AMI) is one of the most common reasons of hospitalization in western countries. The rate of early mortality (the first 30 days) caused by AMI is about 30%. Many studies have introduced the infection with *Helicobacter pylori* and mycoplasma pneumonia as causes of AMI. However, some other studies on the effect of mycoplasma pneumonia, *Helicobacter pylori*, and blood group on the incidence of heart attack showed contradictions that might be due to the ethnical and racial heterogeneities. Therefore, this study was conducted to determine the correlation of the infection with *Helicobacter pylori* and mycoplasma pneumonia and blood group with AMI in Qazvin Province, Iran. Objectives: In this respect, the infection with *Helicobacter pylori* and mycoplasma pneumonia can be taken as a risk factor for AMI thereafter if there is a strong correlation between infection with *Helicobacter pylori* and mycoplasma pneumonia and AMI, and also the high-risk blood groups can be identified, and consequently, risk factors for AMI be reduced through early treatment. Materials and Method: This case-control study was performed in teaching hospitals in Qazvin. After completing the sample size in both groups (blood serum of 90 patients with a history of infarction as the case group and blood serum of 90 other people that matched for age and sex with the first group and had no history of infarction as the control group), the studies were performed to determine the correlation of AMI with mycoplasma pneumonia through the level of IgG antibody, with *Helicobacter pylori* through the level of relevant antibodies (IgA and IgG), and with blood groups through back-type method. Results: Men and women of the case group comprised 63.3% and 36.7%, respectively, and men and women of the control group comprised 67.8% and 32.2%, respectively. The level of *Helicobacter pylori* IgG was considered negative in 1.1%, borderline in 5.6%, and positive in 93.3% in the case group and neg-

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ative in 5.6%, borderline in 10%, and positive in 84.4% in the control group. According to the Chi-square test, the difference between the two groups was significant (P < 0.05). However, the results showed that the level of *Helicobacter pylori* IgA was negative in 20%, borderline in 26.7%, and positive in 53.3% in the case group and negative in 12.2%, borderline in 20%, and positive in 67.8% in the control group. Based on the Chi-square test, the difference between the two groups in this regard was not significant (P > 0.05). The level of mycoplasma pneumonia IgG in the samples was negative in 17.8%, borderline in 5.6%, and positive in 76.7% in the case group and negative in 27.8%, borderline in 2.2%, and positive in 70% in the control group. Based on the Chi-square test, there was no significant difference between the two groups in this regard (P > 0.05). The results on testing the ABO blood groups showed that 23.3%, 21.1%, 27.8%, and 27.8% of the patients with AMI in the case group had the blood group O, AB, A, and B, respectively, and 30.7%, 13.6%, 34.1%, and 21.6% of the people in the control group had the blood group O, AB, A, and B, respectively. The analysis of results did not show a significant difference between case and control group in terms of ABO blood groups (P > 0.05). Conclusion and Recommendation: This study did not show a significant difference between the two groups in terms of the level of IgG except infection with *Helicobacter pylori*. However, more studies should be performed at local and national levels in order to find the role of risk factors of AMI in each region.

Keywords

1. Background

Acute myocardial infarction (AMI) is one of the most common reasons for hospitalization in western countries. The rate of early mortality (the first 30 days) caused by AMI is about 30%, as half of these deaths occur before patients arrive at the hospital. Moreover, about one out of 25 persons who survive in the initial hospitalization would die in the first year after AMI [1]. The survival rate particularly decreases in old patients (over 75 years old). Although the patients' survival has increased following the hospitalization over the last two decades, 5% - 10% of survivors die in the first year after AMI, and they still suffer the risk of death and relapse of AMI.

Coronary artery atherosclerosis is the most important predisposing factor for acute myocardial infarction, and various risk factors have been introduced for it, including lipid metabolism disorders, changes in the concentration of lipoproteins, cholesterol, and leptin, genetic factors, diabetes, age, sex, and smoking habits. In recent years, numerous studies have examined the involvement of chronic infections in atherosclerosis, and most of these studies have also examined chronic inflammation caused by persistent infections with some microorganisms. Inflammation of vessel wall is an important factor in development of atherosclerosis, instability of arterial clots (atheroma), and rupture of plaques after local thrombosis that are clinically manifested by acute coronary syndrome. Vascular endothelial cell injury is the major factor in development of atherosclerotic plaques and often results in fibro-proliferative inflammatory response [2].

Helicobacter pylori is a helical-shaped, gram-negative, facultative, flagellated, and motile bacterium that causes different gastrointestinal conditions.

Helicobacter pylori causes immune cells to increase serum antibodies, including IgA, IgM, and IgG. Many studies have examined the role of *Helicobacter pylori* as a risk factor for coronary artery disease, and some reported its significant role. It is believed that HP causes coronary artery disease through increasing the activity and accumulation of platelets [3]-[8].

Mycoplasmas are the smallest free organisms without hard cell wall. These bacteria have a three-layered membrane containing sterol. Mycoplasma pneumonia causes atypical pneumonia in humans. Mycoplasma firstly penetrates into the epithelial cells of the airways. It destroys the cells and triggers an inflammatory reaction throughout the area and, in some cases, penetrates into the blood flow. Mycoplasmas need cholesterol to grow and can cause endothelial dysfunction [9] [10]. Leukocyte migration along with increased monocyte binding,

failure to produce nitric oxide, dilation of vessels, and gradual progress of the inflammation occur following the endothelial dysfunction [10].

The activation of endothelial cells by pro-inflammatory cytokines with infectious agents reduces the anti-thrombosis function of heart tissue [11] [12]. In other words, the endothelial dysfunction arising from the inflammation disturbs the balance of normal cellular activity in the endothelium, affects the anticoagulant property of the tissue negatively, and develops pre-coagulation conditions [12] [13]. Chlamydia pneumoniae and mycoplasma pneumonia have been presented as bacterial risk factors for AMI, in several studies that show their role in development of atherosclerosis and the subsequent AMI [10] [14]-[19].

Some studies introduced the ABO blood groups as the genetic factors involved in the incidence of AMI. The ABO blood groups were the first blood groups introduced by Landsteiner. Later, studies showed that blood group was a risk factor for some diseases, such as peptic ulcer and diabetes [20]. Many studies have been performed on the blood group as a risk factor of cardiovascular diseases, and some of these studies have controversial results.

2. Objectives

There are a lot of contradictions on the effect of mycoplasma pneumonia, *Helicobacter pylori*, and blood group on the incidence of myocardial infarction in many studies, which can be attributed to ethnical and racial issues. Therefore, this study was performed to determine the correlation of AMI with mycoplasma pneumonia (through specifying the level of IgG), *Helicobacter pylori* (through specifying the level of IgA and IgG), and blood groups (through back-type method) in Qazvin. If there is a strong correlation found between AMI and *Helicobacter pylori*, mycoplasma pneumonia and blood groups, these infections will be treated considering that they are risk factors for AMI, high risk blood groups will be identified, and infections will be treated timely in order to reduce the incidence of AMI.

3. Materials and Methods

This case-control study was performed in teaching hospitals in Qazvin in 2013. Firstly, the blood sera of patients with infarction (based on the inclusion criteria of the study, the AMI was diagnosed if there were at least two of the following conditions: 1) a significant increase in cardiac enzymes, 2) clinical symptoms, such as chest pain and perspiration, and 3) changes in electrocardiogram; people with a history of using antibiotics were excluded) were collected and frozen as the samples of the case group. The blood sera of some other patients in other wards of the hospital with the same age and sex as the first group and without a history of AMI were collected as the samples of the control group.(from ethical point of view we only used diagnostic patient samples sent for other purposes.

Upon completion of the sample size of both groups, Abcam's anti-Mycoplasma pneumonia IgG and *H. pylori* IgG and IgA Human *in vitro* ELISA (Enzyme-Linked Immunosorbent Assay) kits were designed for the accurate qualitative measurement of antibodies against Mycoplasma pneumonia and *H. pylori*. A 96-well plate has been precoated with Mycoplasma pneumonia and *H. pylori* antigens to bind cognate antibodies. Controls or test samples were added to the wells and incubated. Following washing, a horseradish peroxidase (HRP) labelled anti-Human IgG or IgA conjugates were added to the wells, which binds to the immobilized specific antibodies. TMB was then catalyzed by the HRP to produce a blue color product that changes to yellow after adding an acidic stop solution. The density of yellow coloration is directly proportional to the amount of IgA and IgG of samples captured in plate.

Blood groups were determined through back-type method. In this method the liquid part of blood without cells (serum) is mixed with blood cells that is known to be type A and type B. Persons with type A blood have anti-B antibodies, and those with type B blood have anti-A antibodies. Type O blood contains both types of antibodies. These two steps can accurately determine blood type.

The results of each patient's blood group; the level of specific antibodies; and demographic and clinical information including the age, sex, and level of CPK and CPK-MB enzymes were written in their questionnaires (presented at the end of manuscript), and analyzed using SPSS software.

4. Results

The results showed that men and women of the case group comprised 63.3% and 36.7%, respectively; and men

and women of the control group comprised 67.8% and 32.2%, respectively. Based on Chi-square test, there was no significant difference between the case and control group (P > 0.05) (**Table 1**). Mean age of the patients in the case and control group was 58.6 years and 58 years, respectively, and the Chi-square test did not show a significant difference in this regard (P > 0.05). The significant increase in cardiac enzymes, which was one of diagnostic parameters for AMI in patients (including CPK and CPK-MB), was examined in the case and control groups; mean level of CPK in the case and control group was 1368 and 80, respectively, and mean level of CPK-MB in the case and control group was 132 and 5, respectively. The difference between the two groups was quite significantin terms of both enzymes (P < 0.05) (**Table 1**).

Helicobacter pylori infection, as determined by the level of IgG, was negative in 1.1%, borderline in 5.6%, and positive in 93.3% in the case group and negative in 5.6%, borderline in 10%, and positive in 84.4% in the control group. According to the Chi-square test, the difference between the two groups was significant (P < 0.05) (**Table 2** and **Figure 1**).

The results showed that the level of *Helicobacter pylori* IgA was negative in 20%, borderline in 26.7%, and positive in 53.3% in the case group and negative in 12.2%, borderline in 20%, and positive in 67.8% in the control group. Based on the Chi-square test, the difference between the two groups in this regard was not significant (P > 0.05) (**Table 2** and **Figure 2**).

Table 1. Age distribution in the case and control group.

Group	Number	Mean	Standard deviation
Case	90	58.57	15.779
Control	90	57.98	14.973
Total	180	58.12	15.344

Table 2. Overall results.

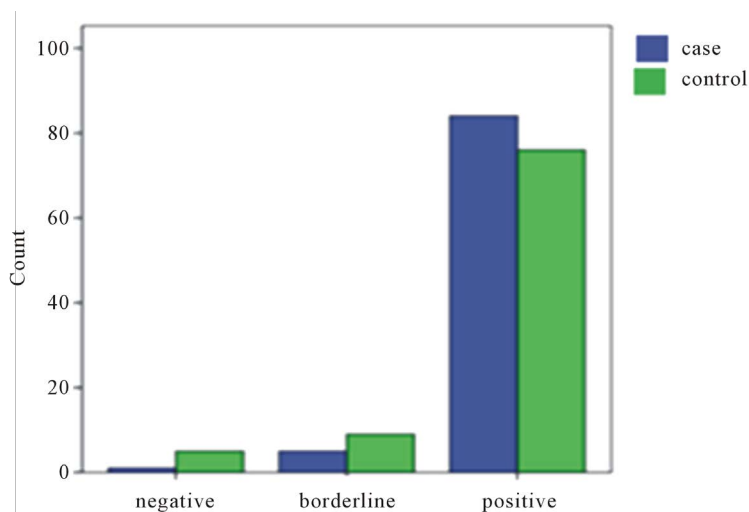|	Group					
	Case		Control		Total	
	Number	Percentage	Number	Percentage	Number	Percentage
Men	57	63.3	61	67.8	118	65.6
Women	33	36.7	29	32.2	62	34.4
Negative IgG.HP	1	1.1	5	5.6	6	3.3
Borderline IgG.HP	5	5.6	9	10	14	7.8
Positive IgG.HP	84	93.3	76	84.4	160	88.9
Negative IgA.HP	18	20	11	12.2	29	16.1
Borderline IgA.HP	24	26.7	18	20	42	23.3
Positive IgA.HP	48	53.3	61	67.8	109	60.6
Negative IgG.MP	16	17.8	25	27.8	41	22.8
Borderline IgG.MP	5	5.6	2	2.2	7	3.9
Positive IgG.MP	69	76.7	63	70	132	73.3
O blood group	27	30.7	21	23.3	48	27
AB blood group	12	13.6	19	21.1	31	17.4
A blood group	30	34.1	25	27.8	55	30.9
B blood group	19	21.6	25	27.8	44	24.7

Figure 1. Comparison of the case and control groups in terms of the level of IgG.HP.
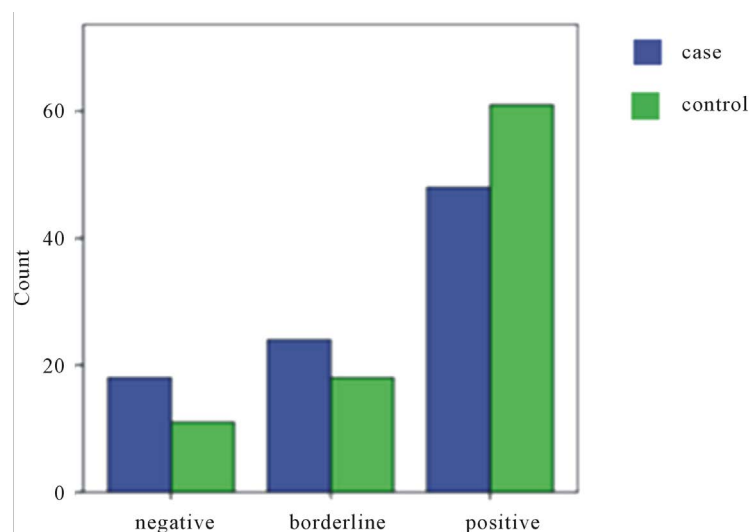

Figure 2. Comparison of the case and control groups in terms of the level of IgA.HP.

The level of mycoplasma pneumonia IgG, which showed the infection in patients, was negative in 17.8%, borderline in 5.6%, and positive in 76.7% in the case group and negative in 27.8%, borderline in 2.2%, and positive in 70% in the control group. Based on the Chi-square test, there was no significant difference between the two groups in this regard (P > 0.05) (**Table 2** and **Figure 3**).

The results on testing the ABO blood groups showed that 23.3%, 21.1%, 27.8%, and 27.8% of the patients with AMI in the case group had the blood group O, AB, A, and B, respectively, and 30.7%, 13.6%, 34.1%, and 21.6% of the people in the control group had the blood group O, AB, A, and B, respectively. So the analysis of results did not show a significant difference between case and control group in terms of ABO blood groups (P > 0.05) (**Table 2** and **Figure 4**).

5. Discussion

This study examined the correlation of AMI with *Helicobacter pylori* and mycoplasma pneumonia and blood group. Using the case-control method, a number of patients with a history of AMI and a number of patients without a history of AMI were respectively selected as the case and control group. The case-control method was
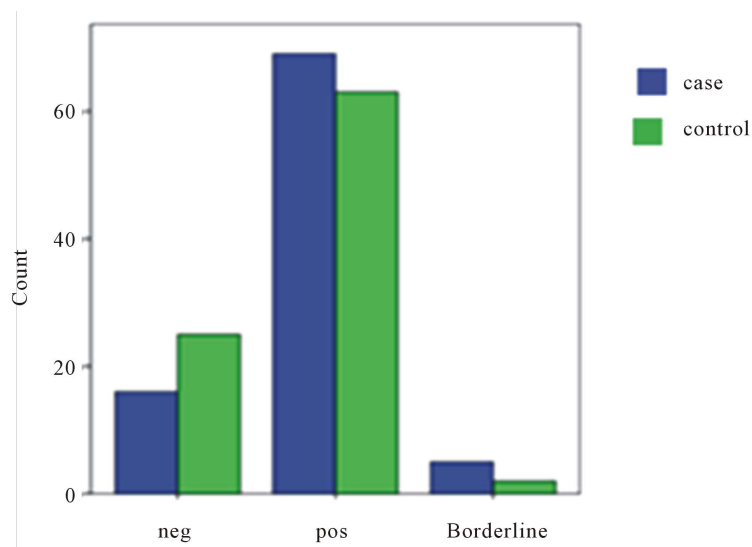
Figure 3. Comparison of the case and control groups in terms of the level of IgG.MP (mycoplasmapneumonia).
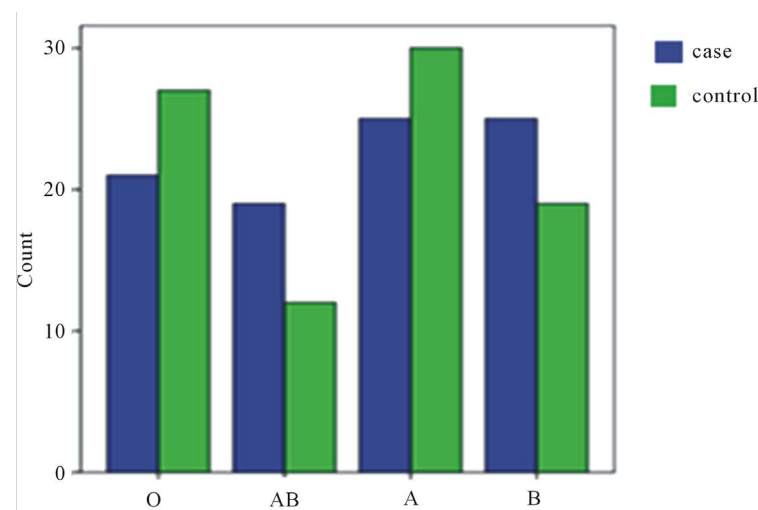

Figure 4. Comparison of the case and control groups in terms of the blood group.

used in order to express the variation in independent variables and find the risk factor of the disease.

Some of the methods that determine infection with *Helicobacter pylori* directly or non-serologically include biopsy, culture, PCR for *Helicobacter pylori*, one-minute urease test of the biopsy sample, and urease breath test, which are followed by technical, administrative, and financial problems for a case-control study.

Sayah *et al.*'s study was the most recent case-control study performed in Qazvin on 80 patients going to Qazvin's Bu Ali Hospital using the urease breath test. Results of current study showed the probable effect of *Helicobacter pylori* on the course of atherosclerosis and introduced the *Helicobacter pylori* as a transmittable risk factor for the coronary heart disease [21].

A part of the present study examined the serological reaction of body against the infectious agent, particularly the two classes A and G *Helicobacter pylori* antibodies separately and in combination.

However, despite the importance of the serological diagnosis of infectious agents, the body immune response against the agent might affect the serological diagnosis and consequently the specificity of the test. This might be the main reason for the differences and contradictions in studies [22]-[24].

Results of the present study showed a significant difference between the case and control group in terms of

the level of *Helicobacter pylori* IgG. The result conformed to that of some studies [5] [25]-[30] and disagreed with some other studies [24] [31] [32]. It seems that these studies differ from one another in terms of the sample size and also the sampling method for the case and control group.

Present study did not show a significant difference between the case and control group in terms of the level of *Helicobacter pylori* IgA (P > 0.05). A few studies have focused on IgA [31] [32]. In this respect, it seems that although a moderate correlation can be assumed between *Helicobacter pylori* in terms of IgG seropositivity and incidence of MI, the correlation is not definite, and such a correlation should be proved through broader clinical trials and using more definitive parameters.

In another part of the present study, serological reactions were used to examine infection with mycoplasma pneumonia considering that this bacterium could increase the antibody in patients' serum, and acute attacks caused by coronary artery atherosclerosis often occurred after middle age, and there was a high risk for infecting with mycoplasma pneumonia in these ages. Moreover, it seems that the measurement of the IgG antibodies specific to mycoplasma pneumonia provides useful information about any previous infections with this microorganism, as many studies only measured the above antibody [10] [16]. However, some other studies have also determined the level of other antibodies, such as IgA and IgM [33].

The analysis of the difference between the infection with mycoplasma pneumonia and incidence of AMI showed no significant difference between the case and control group in terms of the level of IgG antibody (P > 0.05). In this regard, 76.7% of the case group and 70% of the control group were positive for IgG, and there was no difference between the case and control group in terms of the mean level of the antibody. Ponka *et al.*'s study also did not show any significant correlation between the case and control group in terms of IgG antibody titer [10].

Chlamydia pneumoniae and mycoplasma pneumonia are bacterial agents, and several studies have been conducted on their role as predisposing factors of atherosclerosis and MI [9] [10] [15]-[17] [34]. Interestingly, infection with the two agents concurrently seems to have a stronger impact than infection with one of these agents; however, the present study did not examine the effect of infection with chlamydia pneumonia. Some studies introduced the effect of mycoplasma and chlamydia as a risk factor [9] [15]-[17] and some studies did not show any significant correlation. In Poorahmad *et al.*'s study, chlamydia pneumonia increased the risk of AMI less than mycoplasma did (OR = 2.3) [10] [34]-[36].

Hosseinian *et al.*'s study showed that failure to perform a standard immunofluorescence test and also the variability of cut-off values in taking the ELISA tests positive were problems that were considered as the causes of differences in interpretation of the results of serological tests in different studies [34]. Therefore, regarding the contradictions in determining the effect of the level of mycoplasma antibodies, it seems that the main role of these agents in incidence of cardiovascular involvements is determined through indicating the pathogen or genome of the disease at the site of involvement (atheromatous plaques), which is very difficult in practice.

The possession of a specific blood group has been introduced as one of the genetic factors involved in heart diseases, and many studies have been performed to examine the correlation of blood group with cardiovascular diseases [20] [37]-[46]. Some studies found a specific blood group as a risk factor for heart diseases [37]-[42]. However, some other studies did not find any significant correlation between blood group and heart diseases [20] [45] [46]. Results of the present study showed no significant correlation between ABO blood groups and AMI (P > 0.05). The studies performed on the effect of blood group on the incidence of AMI found that blood groups A, B, and AB as the most involved blood groups in AMI [39] [42] [47]-[55]. The studies showed a correlation between the blood group and heart disease found different groups of blood as the risk factor; one reason might be the different distribution of blood groups in different parts of the world [55]-[58]. Some studies showed a correlation between blood group and thrombosis of the lower extremities [59]-[61]. An increase in factor VIII and von Willebrand factor and decrease in APTT have been observed in patients without the blood group O (with other ABO blood groups), which increased the risk of thrombosis [47] [59]-[65].

In studies performed by Allen *et al.* [50] Tarjan *et al.* [43] and Rosen berg *et al.* [52] and some other studies, blood group A increased the risk of heart diseases. Despite the lack of correlation between blood groups and AMI in the case and control group in the present study, the frequency of the blood group A in the case group was higher than other blood groups (34.1%).

6. Conclusion and Recommendation

This study did not show any significant difference between the two groups in terms of the level of IgG except

for the infection with *Helicobacter pylori*. However, more studies should be performed at local and national levels in order to find the role of risk factors of AMI in each region.

Acknowledgements

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