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ASSOCIATION OF *MYCOPLASMA PNEUMONIAE* INFECTION WITH ISCHEMIC HEART DISEASES

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ABSTRACT

Association of atherosclerosis and coronary artery disease well known main pathophysiologic basis for Ischemic Heart Diseases and Myocardial Infarction and due to major risk factors such as high plasma level of low density lipoprotein, low plasma level of high density lipoprotein, cigarette smoking, hypertension and diabetes mellitus, infection with few infectious agents such as *Mycoplasma pneumoniae* that might associated with atherosclerosis consider as another risk factor for ischemic heart diseases. Aim of this study is to investigate the role of this organism and its association to the risk of exposure to *Mycoplasma pneumonia* infection for ischemic heart diseases in Saudi population. This was a case-control study in which 96 patients studied and they were in two groups: first group (or case group), include 48 units patients who had been admitted in hospital by diagnosis of Ischemic Heart Diseases including Unstable angina and Myocardial Infarction (STEMI, NSTEMI) and second group (or control group), include 48 healthy units patients who had no modifiable risk factors history of Ischemic Heart Disease and they matched by first group, for age index. IgG antibodies to *Mycoplasma pneumoniae* was assessed by ELISA technique in both groups. In the case group, 15 cases out of 48 and in control group 3 out 48 were positive for antimycoplasma antibody and in both groups. There was significant statistic difference in antimycoplasma antibody level. In the groups ($p = 0.004$) and the relative risk of mycoplasma infection for Ischemic heart diseases estimated to be 5. It seems that *Mycoplasm pneumoniae* infection is a risk factor for Ischemic Heart Disease, in Saudi population. This is the first report study of such a disease in Saudi Arabia.Further studies will needed to evalute the risk of coinfection by *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* and also better to evalute the effects of the risk of these infection and conventional risk factors for Ischemic Heart Disease in this country.

Keywords: *Mycoplasma pneumoniae,* Ischemic Heart Disease, Risk Factor

1. INTRODUCTION

Ischemic Heart Diseases (IHD) is a coronary artery disease which is a well-established major cause of death and disability in both developed and developing countries (Backer, 2009). In United States, Twelve million individuals in the United States and 143 million worldwide have Coronary Artery Disease (CAD) (Selwyn and Braunwald, 2005). Regardless of declines in developed countries, both CAD mortality

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and the prevalence of CAD risk factors continue to rise rapidly in developing countries (Spence *et al*., 1999).

In this country, Cardiovascular Disease (CVD) and Coronary Heart Disease (CHD) are major health problems. The most recent WHO statistics for Saudi Arabia have reported a total death rate of 156.87 per 100,000 persons (36%) death from CVD, with diabetes being responsible for a further 5% of deaths (Rawas *et al*., 2012).

As it was clearly known the main pathophysiologic bases for IHD and Mycocardial Infarction (MI) is (CAD) that causes reduction in oxygen supply to cardiac tissue which leads to clinical manifestations of myocardial ischemia (Selwyn and Braunwald, 2005). Furthermore, the most common causes of the CAD is atherosclerosis with major risk factors including high plasma level of Low Density Lipoprotein (LDL), low plasma level of High Density Lipoprotein (HDL), cigarette smoking, hypertension and diabetes mellitus (Selwyn and Braunwald, 2005).

Beside the well-established conventional risk factors for atherosclerosis, studies have suggested that infection with *Chlamydophila pneumoniae*, *Helicobacter pylori* and *Cytomegalovirus* can initiate or maintain the atherosclerotic process (Danesh, 1999; Fong, 2000; Awadalla *et al*., 2011).

In recent studies, there is data in literature concerning the association between IHD and Mycocardial infarction with *Mycoplasma pneumonia*, another atypical bacterium which might associate with atherosclerosis either alone or coexistence with other conventional risk factors (Momiyama *et al*., 2004; Goyal *et al*., 2007; Pourahmad *et al*., 2009). *Mycoplasma pneumoniae* which is the smallest and simplest self-replicating microorganism, can exist as a persistent asymptomatic infection, resulting in chronic inflammation as well as *Chlamydia pneumonia* (Waiters and Talkington, 2004; Waites *et al*., 2008). This pathogen is out of 17 known human mycoplasmas species, is a significant respiratory pathogen in persons of all ages, causing respiratory diseases and it may induce clinically significant manifestations in extra-pulmonary sites by direct invasion and/or immunologic effects.Macrophage activation,cytokine induction and super-antigen properties are some factors related to the pathogenicity of mycoplasmas (Razin *et al*., 1998; Waiters and Talkington, 2004; Waites *et al*., 2008).

In Saudi Arabia, To our knowledge there has been no previous and information studies about of the association of exposure to *M. pneumoniae* with IHD and its complications and there is lack of national data available from community based on the prevalence of CAD in this country (Al-Nozha *et al*., 2004) and in a study it found the overall prevalence of CAD was 5.5% from a patients with statistically significant modifiable risk factors (Al-Nozha *et al*., 2004).

Therefore it is important to investigate the possible risk and relation of exposure to*M. pneumonia* infection for CAD and MI so we conducted this study to recognize the role of this organism and its association to the risk exposure to (IHD) in Abha (a city in southwest region of Saudi Arabia) among Saudi population.

2. MATERIALS AND METHODS

This is a case-control study, in which 96 patients studied. The study conducted during one year (March, 2011-FEB, 2012) in Cardiologic ward at Asser Central Hospital in Abha (a cityin southwest region of Saudi arabia). The units selected by simple nonrandomized sampling technique. They were in two groups: first group (or case group), include 48 units who had been admitted in hospital by diagnosis of acute Coronary Syndrome (IHD) such as unstable ungina, Myocardial Infarction (STEMI, NSTEMI) and second group (or control group) include 48 healthy units who had not any positive history of IHD and they matched by first group, for age index. Inclusion Criteria in first group were: Typical Chest pain for IHD, positive Electrocardiogram (ECG) and serum biomarkers for myocardial infarctiIon.Upon ECG signs; the case group was divided into two groups: ST elevated and NonST elevated myocardial infarction (STEM and NSTEMI respectively) (Antman and Braunwald, 2005).

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 (3 mL) collected for analysis for serologic markers of *M. pneumoniae*.

IgG antibodies to *M. pneumoniae* were assessed by ELISA technique; Vircell Microbiologists kit for Mycoplasma was used for detection of IgG antibodies to *M. pneumoniae* and a sample with antibody index value of more than 11 was considered seropositive as having

IgG specific antibodies against *M pneumonia* on manufacturer's guidelines vircel microbiologists.

All our information was Statistically analyzed by using the Statistical Package for the Social Sciences version 13.0 (SPSS software, Inc., Chicago, IL, USA). SPSS software and for statistic analysis, t-test and chi square test was used. Results with P value less than 0.05 was considered as statistically significant.

3. RESULTS

Ninety six 96 patients were studied. Mean age of the patients in case group was 62.54±11.19 and in control group was 64.68±13.65.There was not significant statistic difference for age between two groups (p = 0.26) **Fig. 1**.

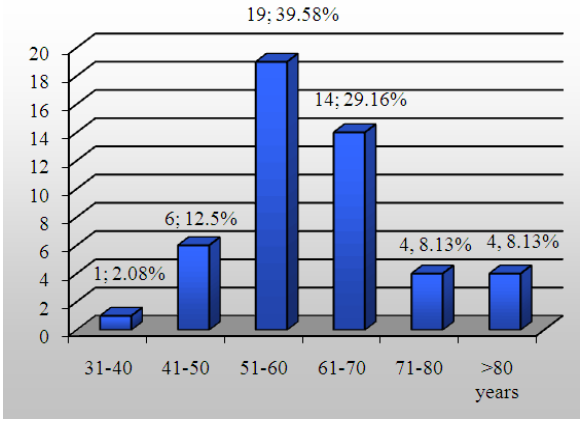

Fig. 1. Age wise distribution of Patients in case group (n = 48)

Table 1: Antimycoplasma antibody in case and control groups (n = 48; n = 48)

	Antimycoplasma ab		
Group	Positive	Negative	Total
Case	15	33	48
Control	3	45	48

P = 0.004

Table 2: Antimycoplasma antibody in STEMI, NSTEMI and Unstable angina

	Antimycoplasma ab		
MI type	Positive (%)	Negative (%)	Total
STEMI	10 (40)	15 (60)	25
NSTEMI	1(8.3)	11(91.6)	12
Unstable angina	4(36.3)	7 (63.6)	11
Total	15	33	48

P = 0.138

In case group (patients with diagnosis of acute Coronary Syndrome (IHD) such as unstable ungina, Myocardial Infarction -STEMI, NSTEMI) 15 cases out of 48 and in second group (control group) 3 units out of 48 were positive for antimycoplasma antibody and this difference was statistically significant (p = 0.004) (**Table 1**). The relative risk of antimycoplasma antibody for myocardial infarction in our patients. OR = 5(95% C.I = 1.54-16.16).

Fasting blood glucose and serum total cholesterol levels in both case and contro lgroups were within normal limits.

In this study from 48 patients with Myocardial Infarction, 25(52%) patients had STEMI and 12(25%) patients had NSTEMI, 11(23%) patients had Unstable angina; 10, 1,4 patients had positive antimycoplasma antibody in STEMI, NSTEMI and Unstable angina groups respectively, but the difference was not statistically significant (p = 0.138) (**Table 2**).

4. DISCUSSION

Many studies are conducted to evaluate the risk-factor for IHD and MI in populations, some of these studies designed to evaluate the other than risk factors for IM, among these factor is infection as risk factor that need further investigation and for this purpose we conducted this study to recognize the role of infectious agent and its association to the risk exposure to (IHD).

On the other hand, other studies have reported the relation between infections such as *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* a with IHD and MI and they evaluate the effect of these infectious agents in CAD, however, few studies will contribute to evaluate the relative risk of these agents with IHD and MI.

In the present study *Mycoplasma pneumonia* the Odd's ratio for *Mycoplasma pneumonia* infection in our patients with MI was revealed that the infection with this agent might be a risk factor for IHD and MI (OR = 5.00).

A similar study was conducted in Iran, in which seropositivity to *Mycoplasma pneumonia* was significantly higher (p<0.05) in CAD patients with MI than in those without MI and the risks (Odd's ratio0 of this infection has been accounted to be 2.7 (Pourahmad *et al*., 2009), although patients studied were of both sex, there was no significant statistic difference in sex proportion in the studied groups (p = 0.26). In another previous study, conducted in patients of same

contrary; the relative risk of *Chlamydia pneumonia* infection for MI (OR = 2.3) (Pourahmad, 2005) was lower than that for *Mycoplasma pneumonia*.

In another study conducted in Japan, *Mycoplasma pneumonia* seropositivity was more prevalent in patients with CAD than without CAD (14% versus 6%, $p<0.01$). The highest prevalence was found in patients with MI. In contrast, the prevalence of *Chlamydia pneumonia* seropositivity was similar in patients with and without CAD (62% versus 59%) (Momiyama *et al*., 2004).

On the other hand, coinfection of *Mycoplasma pneumonia* and *Chlamydia pneumonia* might occur in patients and may be an important cofactor for CAD, In the study conducted by Momiyama *et al*. (2004) it was found that among patients with *Chlamydia pneumonia* seropositivity, *Mycoplasma pneumonia* seropositivity was more prevalent in patients with CAD than without CAD (17% versus 5%, $p<0.01$), whereas among patients without *Chlamydia pneumonia*, *Mycoplasma pneumonia* seropositivity did not differ between patients with and without CAD (9% versus 6%). The study found that *Mycoplasma pneumonia* seropositivity was associated with CAD only in patients with *Chlamydia pneumonia* seropositivity (odds ratio = 5.1, 95% CI = 1.8-14.9). Thus, the study was suggested that coinfection by *Mycoplasma pneumonia* and *Chlamydia pneumonia* may be an important cofactor for CAD.Therefore, the risk of coinfection for IHD and MI, need to be determine.

It should be take in consideration that several case reports described an association between cerebral ischemia and *Mycoplasma pneumonia* infections (Nakahata *et al*., 1983; Dowd *et al*., 1987; Tanir *et al*., 2006). But Grau and his colleagues, on the other hand, had not detect any association between *Mycoplasma pneumonia* infection and cerebrovascular ischemia (Grau *et al*., 1995). Higuchi and his colleagues suggests that the association of *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* may increase the virulence of these microorganisms, favoring proliferation, plaque inflammation and possibly plaque rupture. Mycoplasmas were present mainly in the lipid core of the ruptured thrombosed plaque. Vulnerable atheromas are rich in cholesterol and may favor the growth of mycoplasmas, since the organisms require cholesterol or related sterols for growth (Higuchi *et al*., 2000; Brown *et al*., 2010). However, recent study in India found that there was no direct evidence of the involvement of *Mycoplasma pneumonia*, *Chlamydia pneumonia* and other infective agents and viruses in CAD. The study suggests It is possible that such infections produce an indirect adverse effect on the lipid profile (Padmavati *et al*., 2012).

In this study, we assessed the IgG antibodies to *Mycoplasma pneumonia* infection by ELISA technique; as detection of specific antibody by this assay is a reliable and useful method for diagnosis of *Mycoplasma pneumonia* respiratory disease in human (Cassell *et al*., 1996), it was found the method offers several major advantages over other antibody detection methods: objectivity, immunoglobulin class and subclass specificity and increased sensitivity (Cassell *et al*., 1996) Specific antibodies of IgG have been detected by ELISA in patients older than 40 years and often have 56% of cases response only, whereas children and teenagers respond predominantly with IgM antibodies (Cassell *et al*., 1996), In our study the mean age of the patients in case and control groups was 62.54±11.19 and 64.68±13.65 respectively, with no significant statistic difference for age between the groups ($p = 0.26$) and this will reveal the detection of IgG antibodies to the patients at older age and confirm the risk of association of the *Mycoplasma pneumonia* infection in patients for MI. The present study was matched with the result reported by other studies that the association between IHD and *Mycoplasma pneumonia* independent of the role of several conventional risk factors; wither the *Mycoplasma pneumonia* infection may have alone and/or cofactor effects with conventional risk factors, in patients with IHD and MI who has these conventional risk factors will need further studies to be undertaken.

5. CONCLUSION

Our results showed that *Mycoplasm pneumoniae* infection is a risk factor for IHD. This what is apparently the first study performed for *Mycoplasma pneumoniae* in association with IHD in Saudi Arabia. Further work study is needed to evalute the risk of coinfection by *Mycoplasma pneumoniae* and *Chlamydia pneumonia*. Furthermore, evalution the effects of the risk of these infection and conventional risk factors for IHD in this country should be determined.

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