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Evaluation of Effect of Influenza-Like Virus in Adults: A Case Control Study on Adults with Myocardial Infarction Problems

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Key words
Influenza-like virus, Risk factors, Adults, Myocardial infarction

ABSTRACT

Influenza is a virus that attacks the nasal passages, including the throat and lungs. Influenza-like virus in adults is partly due to changes in the body's defense system. The present study was performed to evaluate influenza-like virus effects in adults. This case-control study was performed on 50 patients admitted to the Third Affiliated Hospital of Henan University of Traditional Chinese Medicine during the autumn and winter seasons with myocardial infarction and 50 patients as controls. History, tests, and clinical examinations in both groups did not show diabetes, hypertension, dyslipidemia, or smoking. For both groups, Influenza-like experiments were performed in the form of fever with cough or sore throat. The mean age was 53.7 ± 8.99 years in the case group and 54.1 ± 8.89 years in the control group. 25 patients (50%) in the case group and 6 patients (12%) in the control group had influenza-like infection and the comparison between the two groups showed a statistically significant difference (CI=1.165-8.551, OR=4.5, P=0.005). The frequency of influenza-like infections in both sexes was higher in the case group than the control group (men CI = 1.032-6.742, OR = 3.8, P = 0.002 and women CI = 1.102-11.155, OR = 5.7, P = 0.003). The influenza-like test was more than twice as positive in the case group as in the control group. Therefore, influenza-like infection is a risk factor for heart attack and getting an influenza vaccine is recommended for people who are prone to heart disease.

INTRODUCTION

Influenza infects the respiratory tract by RNA virus of the Orthomyxoviridae family so that it is highly contagious (WHO, 2015). The virus mostly affects the nose, throat, bronchi and especially the lungs and the disease occurs immediately with high fever, muscle cramps, headache, restlessness, cough without sputum, sore throat and rhinitis (Hay *et al*., 2001). Influenza virus belongs to the group of RNA viruses, which include 3 genera out of 5 of the Orthomyxoviridae family, the most important influenza A. The wild and aquatic bird species are natural hosts for these viruses, which are transmitted between species thus creating a pandemic and eventually infectin human communities (Russell *et al*., 2004).

Today, acute myocardial infarction (MI) is considered as one of the causes of high mortality and important clinical problems in the world (Jinnouchi *et al*., 2013; Jamil *et al*., 2013; Lopez *et al*., 2006). Despite the therapeutic advances, prevention is still the best way to manage and treat MI and therefore it is important to identify its risk factors (Shojaie *et al*., 2009). The hypothesis that influenza causes acute MI and death developed in the early 1930s, and the relationship between seasonal influenza activity and cardiovascular mortality was first mentioned (Collins, 1932; Housworth and Langmuir, 1974; Stem and Gaskill, 1978; Alling *et al*., 1981; Majdid *et al*., 2007; Warren-Gash *et al*., 2001; Foster *et al*., 2013). A systematic review of the observed studies shows that cardiovascular complications occurred in about 18% of hospitalized patients due to pneumonia (Corrales-Medina *et al*., 2011).

Studies done at London Medical School have reported several different organisms that cause respiratory infections, including influenza virus and *S. pneumoniae* which are also responsible for causing inflammation in the heart. This condition can lead to blood clots in the heart

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muscle, increasing the risk of heart attack and stroke. The new findings show that influenza or pneumonia increases the risk of heart attack up to a week after infection and the risk of stroke for up to a month (Warren-Gash *et al*., 2009; Madjid *et al*., 2007; Foster *et al*., 2013). MI is permanent and irreversible cell destruction and death in a part of the heart muscle (myocardium), which occurs due to loss of blood flow and the occurrence of severe ischemia in that part of the heart (Foster *et al*., 2013; Warren-Gash *et al*., 2013). Blood circulation may appear suddenly and without any previous symptoms, or after a few angina (chest pain). The main cause of stroke is the closure of the arteries that feed the heart. Other than medication, balloons and open-heart surgery (replacement of blocked arteries) are used to remove the obstruction. MI is a pervasive complication that causes thousands of deaths each year (Warren-Gash *et al*., 2009, 2012).

Given that classical risk factors have not been able to fully explain the epidemiological diversity of the disease, other risk factors such as inflammation and systemic infections are under investigation and the cause-and-effect relationship between these infections and acute coronary syndrome has not so far been established (Kerr, 1998; Kerr *et al*., 2000). Various inflammatory factors such as CRP, ICAm-1 and cytokines such as IL-1, IL-2 and LL-6 and fibrinogen are associated with an increased risk of cardiovascular disease and accelerated atherosclerosis (Hara *et al*., 2001). The source of stimulation for the production of these inflammatory factors can not only be in the arteries, but also in extravascular sites such as chronic infections of the bronchi and urinary tract. Infectious agents can play an important role in the pathogenesis of atherosclerosis, which can be the result of a chronic infection or a low-grade chronic inflammatory process that causes endothelial dysfunction (Pieniazek *et al*., 1999). Sometimes even overlap has been reported between the pathological changes observed in obstructive vascular disease and the changes observed in infections (Eskandarian *et al*., 2007). Systemic inflammation results from chronic infections including *Chlamydia pneumoniae* and *Helicobacter pylori* (Wood, 2001; Lawson, 2016; Cammarota *et al*., 2000; Sharma and Aggarwal, 2015), cytomegalovirus (Wood, 2001; Lawson, 2016; Cammarota *et al*., 2000; Sharma and Aggarwal, 2015; Aceti *et al*., 1996), chronic gingival infections (Cook and Lip, 1996), bronchial tract infections, urinary tract infections (Aceti *et al*., 1996), hepatitis A virus (Pieniazek *et al*., 1999) and herpes simplex virus (Pieniazek *et al*., 1999; Wood, 2001). This reinforces the hypothesis that infection is involved in coronary heart disease (Gasbarrini *et al*., 1998). The development of atherosclerosis itself is expressed as a response to injury and is in fact a mild chronic inflammatory process. There is disagreement as to whether infectious agents are involved in atherogenesis and disease or play a role in the transformation of stable angina into unstable and myocardial infarction (Sims *et al*., 2005). Inflammatory processes can exacerbate the process of atherosclerosis and systemic infection, and these mild infections that have no obvious clinical symptoms can cause acute coronary syndrome. Inflammatory processes can exacerbate the process of atherosclerosis and systemic infection, and these mild infections that have no obvious clinical symptoms can cause acute coronary syndrome. Another reason for the involvement of infection in atherosclerosis is the studies done or underway that indicates a significant reduction in cardiovascular events following antibiotic treatment in patients with MI (Amman *et al*., 2000; Stone *et al*., 2002).

While several studies have shown that patients with acute MI are more likely to have the influenza or influenza-like (Cardoso *et al*., 2020; Vejpongsa *et al*., 2019; Kwong *et al*., 2018; Warren-Gash *et al*., 2012, 2013, 2018; Pearce *et al*., 2017; Nguyen *et al*., 2016; Macinture *et al*., 2013; Madjid *et al*., 2014), some other studies have reported that more evidence is needed about the effectiveness of influenza vaccines in reducing the risk of heart disease in people without vascular disease (Warren-Gash *et al*., 2009). To determine this relationship and because of the great importance of this issue, many studies have focused today on identifying such high-risk individuals. The present study was therefore, performed to evaluate influenza-like virus effects in adults with MI problems.

MATERIALS AND METHODS

This case-control study was performed during 2020 and 2021 at the Third Affiliated Hospital of Henan University of Traditional Chinese Medicine on patients with acute MI (case group) and patients with osteoarthritis who referred to the clinic of this hospital for treatment and were assessed as cardiovascularly healthy using clinical and paraclinical criteria. For the case group, the clinical inclusion criteria were pressing pain in the front of the chest lasting more than 30 min. They also had to have paraclinical criteria for ECG changes and elevated serum troponin (Arcavi *et al*., 2004) and were admitted to the hospital's CCU with a definitive diagnosis. In both groups, laboratory tests were performed after reviewing the records and in the absence of diabetes, hypertension, hyperlipidemia and smoking and after obtaining personal consent. They were selected if they met the inclusion criteria (cholesterol below 200 mg / dL, HDL above 40 mg / dL, LDL below 130 mg / dL, blood pressure below 140.90 mm / Hg, triglycerides below 150 mg / dL and fasting blood sugar below 100 mg / dL).

In both groups, the criterion for influenza-like diagnosis was based on the clinical guidelines for influenza provided by the International Classification of Health Problems in Primary Care (ICHPPC2), which measures: Fever above 38 degrees, weakness, lethargy, body aches and tiredness, dry cough, chills, headache, sore throat, chills, hoarseness, nasal congestion, chest discomfort and feeling short of breath (Van Elden *et al*., 2001). Data obtained from influenza-like diagnosis were analyzed using X^2, OR, CI, Fisher exact, Mantel Haenezel statistical methods and SPSS13 software.

RESULTS

In total, influenza-like tests were performed on 100 patients; among them, 50 had acute myocardial infarction (case group, 38 male and 12 female) and 50 had degenerative joint disease (control group, 37 male and 13 female). There was no difference in the mean age of patients in both groups (case and control). The age range of patients was from 40 to 75 years; with a majority in the age group of 49-40 years in the male group (38 in the control group and 37 in the case group) and a majority in the age group of 69-60 years in the female group (12 in the control group and 13 in the case group) (Table I). During the influenza-like tests, 3 patients in the case group and 1 patient in the control group had diabetes and were excluded from the study. In the case group, 22 patients (47%) out of the remaining 47 patients were infected with influenza-like and in the control group, 7 patients (17%) out of 49 patients were infected with influenza-like, which this difference was statistically significant (Table II).

Table I. Demographic status of participants by group, age and gender.

Group	Gender	N	Min age	Max age	Mean ±S.D
Control	Male	38	40	49	44.5 ± 8.23
	Female	12	60	69	64.5 ± 6.54
Case	Male	37	41	49	45 ± 9.11
	Female	13	62	68	65 ± 7.42

Table II. Frequency distribution of influenza-like disease for participants in two groups.

influenza like results	Control	Case	Total	
Negative	42 (86%)	25 (53%)	67 (70%)	P = 0.008
Positive	7 (14%)	22 (47%)	29 (30%)	OR = 3.538
Total	49	47	96	CI = 1.333-8.653

The results also showed that in both groups of men and women with myocardial infarction, the incidence of influenza-like disease in the case group was higher than the control group (Table III).

Table III. Frequency distribution of influenza-like disease in study groups by sex.

Gender	influenza like test	Control group	Case group	
Male	Negative	31 (84%)	19 (54%)	P = 0.074
	Positive	6 (16%)	16 (46%)	OR = 3.6 CI = 1.0232 – 7.116
Female	Negative	10 (83%)	5 (42%)	P = 0.04
	Positive	2 (17%)	7 (58%)	OR = 10 CI = 1.138 – 117.253
	Mantel Haenezel			P = 0.007, CI = 1.332-2.998

DISCUSSION

The present study showed that 22 patients (47%) in the case group had influenza-like disease, while the number of patients with influenza-like disease in the control group was 7 (14%) (P=0.008, OR=3.538, CI=1.333-8.653). It can be found that influenza-like as an independent risk factor increases the risk of heart attack in both groups. The Warren-Gash *et al*. (2009) study provided evidence that influenza (including influenza-like illness and acute respiratory infection) causes acute myocardial infarction or cardiovascular death. Madjid *et al*. (2004) showed that influenza-like may play a causal role in the development of atherosclerosis and its complications. In the study of Kwong *et al*. (2018) as in the present study, there is a significant association between respiratory infections, especially influenza and acute MI (AMI). A study by Pearce *et al*. (2017) showed that severe respiratory infections may cause cardiovascular events and identified the influenza virus as an important contributing factor. Based on the results of another study by Warren-Gash *et al*. (2012), influenza and other acute respiratory infections can act as stimulants of AMI; this effect may be stronger for influenza than for other infections; the people coded as influenza were associated with higher rates of AMI.

Another result of the present study was that the prevalence of influenza-like illness among patients was reported to be 30%. In the study of Cardoso *et al*. (2020), the prevalence of influenza was reported to be 0.3%. According to the study results, patients with Acute AMI and influenza simultaneously had an unfavorable prognosis in the hospital compared to patients without influenza. Vejpongsa *et al*. (2019) also reported that the prevalence of

influenza was 0.5%. However, the difference in prevalence was due to the type of disease studied because the type of disease in the present study was influenza-like but in the studies of Cardoso *et al*. (2020) and Vejpongsa *et al*. (2019) was influenza.

Another finding of the present study is that the prevalence of AMI was higher in men than women. There are conflicting results on the incidence of MI in both men and women. Chaikhouni *et al*. (1993) and Al-khadra (2003) in their study stated that in most cases, the prevalence of heart disease occurred in men (96.2%), which in the study of Sezavar *et al*. (2004) found the same finding, while other studies such as Doughty *et al*. (2002) and Kantiz *et al*. (1996) reported a higher percentage of women. In the above studies, the reason for the difference in the prevalence of MI in men and women is probably related to the reasons for the distribution of risk factors in women or men in these communities.

CONCLUSION

In patients with myocardial infarction (case group), the incidence of influenza-like was almost three times higher than in the control group; therefore, influenza-like is an independent risk factor for heart disease. As a result, getting the influenza vaccine in people who are prone to heart disease seems necessary to diagnose and treat influenza-like.

Statement of conflict of interest

The authors have declared no conflict of interest.

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