

# Association between Recent Group A Beta-Hemolytic

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## Abstract

**Background:** Acute and chronic infections have been linked to development of atherosclerosis and precipitation acute coronary syndromes. Our aim was to investigate if there is an association between group A beta-hemolytic Streptococcus infection and acute myocardial infarction (AMI).

**Methods:** 110 consecutive patients diagnosed as either first time ST elevation or non-ST elevation AMI were included as the study group. 100 consecutive patients diagnosed as hypertension were included as the control group. Presence of acute or subacute Group A beta-hemolytic streptococcus infection was searched by throat culture and immunoturbidimetric antistreptolysin O (ASO) titers.

**Results:** Frequency of positive throat culture and ASO assay positivity was not different between groups [2 (1.8%) vs. 1 (1%),  $p=1$  and 9 (8%) vs. 5 (5%),  $p=0.416$ , respectively]. Absolute ASO titer levels were significantly higher in the AMI group (132±99 vs. 87±88 Todd units/ml,  $p=0.01$ ).

**Conclusion:** Recent group A beta-hemolytic streptococcus infection is not associated with AMI.

## INTRODUCTION

There is growing evidence suggesting that inflammation, in addition to playing a major role in pathogenesis of atherosclerosis, can trigger acute coronary events. Several earlier small studies have suggested that there may be a transient increase in the risk of a AMI after infection.<sup>1,2,3,4,5,6</sup> Many recent investigations have focused on chronic and acute infections and vaccinations as promoters of inflammatory process and their role in cardiovascular events. Common general infections such as urinary tract and respiratory tract infections have shown to be associated with a transient increase in acute coronary events.<sup>7,8,9</sup> Data on common specific infections, however, is scarce. The aim of the present study was to determine if a recent Group A beta-hemolytic streptococcus infection is associated with an increased risk of acute myocardial infarction.

## MATERIAL AND METHODS

110 consecutive patients admitted to coronary care unit of Sisli Etfal Hospital with the diagnosis of first time ST elevation or non-ST elevation AMI in march and may of 2005 were included in the study. 100 consecutive patients

over 40 years of age with a new diagnosed or known hypertension examined at the polyclinic of Turkish Heart Foundation at the same time interval were included as the control group. Informed consent was obtained from all patients and the study protocol was approved by both institutes' committee on human research. Patients were diagnosed as ST elevation AMI if both a ST elevation (greater than or equal to 2 mV in leads V1 to V4 and greater than or equal to 1mV in other leads) in two or more contiguous leads and an elevated troponin T level were present. Non-ST elevation AMI diagnosis was made if ST segment depression or T wave abnormalities along with elevated troponin T level were present.<sup>10</sup> Patients were excluded from the study group if they had a known prior AMI on history or ECG and if cardiogenic shock, severe heart failure or life threatening arrhythmia was present. Patients were excluded from control group if they had any known coronary artery disease. The general exclusion criteria was presence of liver or renal disease, any autoimmune disease, using any immune modulating drugs and statins. During history taking patients were asked if they had a sore throat in the past 5 days. If they had, a pharyngeal examination was done and a swab for culture was taken from

patients with pharyngeal hyperemia. Within the first 24 hours, a blood sample was obtained for ASO titers and routine laboratory analysis. Antistreptolysin O titers were measured by immunoturbidimetric assay method using a Cobas-Integra 400 Plus, Roche Diagnostics. Titers over 250 Todd units were considered positive.<sup>11</sup>

## STATISTICAL ANALYSIS

Statistical analysis was performed by Statistical Program for Social Sciences (SPSS version 10.0) software. Qualitative data were expressed as percentage and analyzed by chi square test. Quantitative data were analyzed with students t test and expressed as mean standard deviation. A P value < 0.05 was considered statistically significant. The correlation between AMI and ASO titer levels, throat culture and ASO positivity were calculated using multivariate stepwise logistic regression analysis.

## RESULTS

Groups were well matched according to baseline characteristics except for number of hypertensives, which was significantly higher in control group. This was a natural result of the chosen method; including only hypertensive patients in the control group. Baseline characteristics are listed in table I. There wasn't any statistical difference in number of patients with positive throat culture and number of patients with positive ASO titer between two groups [2 (1.8%) vs. 1 (1%), p=1 and 9 (8%) vs. 5 (5%), p=0.416, respectively]. The absolute ASO titer level was significantly higher in AMI group compared to control group (132 99 vs. 87 88 Todd units/ml, p=0.01). Results are shown in table II. After logistic regression analysis; among the variables, throat culture positivity, ASO positivity and ASO titer levels, only ASO titer level was significantly related to AMI (p=0.001). Results are shown in table III.

## Figure 1

Table 1: Baseline characteristics of groups

Variable	AMI group (n=110)	Control group (n=100)	P value
Age, years	63±11	61±10	0.091
Men/women	75/35	58/42	0.126
Smokers, n (%)	54(49)	47 (47)	0.762
FPG (mg/dl)	113±31	106±31	0.071
Hypertensives, n (%)	57(52)	100 (100)	0.0001
LDL (mg/dl)	165±34	159±30	0.187
HDL (mg/dl)	42±8	44±9	0.243
Triglyceride (mg/dl)	146±39	134±61	0.099

AMI=Acute myocardial infarction, FPG=Fasting plasma glucose, LDL=Low density lipoprotein, HDL=High density lipoprotein

## Figure 2

Table 2: Throat Culture and ASO titer results

Variable	AMI group (n=110)	Control group (n=100)	P value
Positive throat culture, n(%)	2 (1.8%)	1 (1%)	1
Positive ASO titer, n(%)	9 (8%)	5 (5%)	0.416
Absolute ASO titer level, Todd units/ml	132±99	87±88	0.001

AMI=Acute myocardial infarction, ASO= Antistreptolysin o

## Figure 3

Table 3: Logistic regression results

Variable	Odds ratio	95 % CI	P value
Throat culture positivity	0.49	0.43-0.72	0.620
ASO positivity	0.9	0.07-1.48	0.358
ASO titer level	3.5	0.48-12.2	0.001

ASO= Antistreptolysin o

## DISCUSSION

Studies investigating chronic infections have shown that microorganisms including Herpes Simplex Virus, Cytomegalovirus, Chlamidia Pneumoniae, Porphyromonas gingivalis, Helicobacter Pylori, Mycoplasma Pneumoniae and Epstein Barr Virus are linked to acute coronary syndromes.<sup>12,13,14,15,16,17,18,19</sup> Studies on acute infections, however, have conflicting results. Meier et al. have suggested that upper respiratory tract infections increase

AMI risk but urinary tract infections don't. They also reported that the risk was increased for a period of 10 days after the infection.<sup>7</sup> In a recent study, subclinical urinary tract infection was found to be 3 times more frequent in acute coronary syndrome patients compared to controls.<sup>8</sup> In another large study, urinary tract and upper respiratory tract infections were found to be a risk factor for AMI but no increase in the event rate was detected after influenza, tetanus, and pneumococcal vaccinations. For the upper respiratory tract infection, the risk was highest during the first three days of infarction but stayed elevated for 3 months.<sup>9</sup> The general opinion after these studies was that the effect of infections on cardiovascular event risk may be generic and is not linked to specific types of infection. However; in our opinion, it's early to reach such a conclusion because there are many different pathogens causing acute urinary and respiratory tract infections and studies focusing on specific pathogens and comparing them are lacking.

The hypotheses postulated to account for the association between inflammation and coronary events include endothelial dysfunction, cytokine interactions with coagulation factors and activation of proteases that may promote plaque destabilization. In an experimental model, the vaccination of healthy volunteers induced a short-lived inflammation that was associated with profound suppression of endothelium-dependent relaxation.<sup>20</sup>

It is known that inflammation is not a constant process but fluctuates in response to infections or to other proinflammatory stimuli. Most probably, the potency of an infection to cause plaque destabilization depends on the magnitude, type and duration of inflammation it produces. For example, the mild transient inflammation and associated suppression of endothelium dependent relaxation induced by vaccination does not appear to translate into a detectable increase in the risk of cardiovascular events. Different microorganisms cause different immune responses. Therefore, studies on specific infections are needed, at least for the common pathogens.

Our study was the first in the medical literature to investigate the possible role of Group A beta-hemolytic streptococcus infection on pathogenesis AMI. We undertook the study during the spring months when upper respiratory infections are diagnosed most frequently. We based our study on throat cultures and ASO titers. As known, ASO is an antigen produced as an immune response to the enzyme streptolysin o, produced by Group A beta-hemolytic streptococcus.

Titers rise after 1 week of infection peak at 2-3 weeks and fall to preinfection levels within 6-12 months. Therefore, elevated ASO titers signify a Group A beta hemolytic streptococcus infection 1 week to 1 year before the time of the test.

Our study results suggest that a recent Group A beta-hemolytic streptococcus infection is not associated with an increase in the risk of first time acute myocardial infarction. The possible explanation is that Group A beta-hemolytic streptococcus infection either does not produce a strong enough, long enough or the "right" type of inflammation to cause plaque rupture.

Another interesting finding of our study was that although ASO positivity was similar in both groups, ASO titer levels were significantly higher in AMI group. Meaning, AMI patients had higher circulating antistreptolysin o antibodies. This may be interpreted as a higher state of systemic inflammation and is in accordance with the evidence that inflammation is linked to acute coronary events.

Study limitations: Our patient group was small in number.

## CONCLUSIONS

Acute or subacute Group A beta-hemolytic streptococcus infection is not associated with an increase in the risk of acute myocardial infarction. Larger studies to confirm ours and investigate other pathogens are needed.

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