

## The Comparison of Acute Myocardial Infarction Serum Anticardiolipin Antibody with Healthy Subjects, in Gorgan (Northern Iran)

<sup>1</sup>Ali Reza Ahmadi, <sup>1</sup>Hamid Reza Joshaghani, <sup>2</sup>Azad Reza Mansourian, <sup>3</sup>Aref Salehi, <sup>4</sup>Nasser Behnampour

<sup>1</sup>Laboratory Sciences Research Center, Golestan University of Medical Sciences, Gorgan, Iran <sup>2</sup>Metabolic Disorder Research Center, Golestan University of Medical Sciences, Gorgan, Iran <sup>3</sup>Cardiovascular Research Center, Gargan Medical School

Golestan University of Medical Sciences, Gorgan, Iran

<sup>4</sup>Hematology and Oncology Research Center, Golestan University of Medical Sciences, Gorgan, Iran

**Abstract:** Artherosclerosis considered one of the most important causes of morbidity and mortality in industrial and developing countries. The rate of myocardial infarction in some countries is about 2 million annually with 1/4 of them is leading to death. This study was a case-control research, which was carried out as cross-sectional project in two groups, healthy and case subjects. The mean age and standard deviation of patients and control groups were nearly equal (55±10). The ELISA technique was applied to measure the serum antibody level. The sample populations in each group were exactly the same (120 person in each group). The gender distribution in case and control group was 44 female, 76 male and 45 female and 75 male, respectively. The Mean±SD of IgM in case group and control groups were 3.10± 2.54 and 1.54±1.00, respectively. The Mean±SD for IgG in case and control groups were 5.90±3.84 and 3.08±1.95, respectively. The differences, between the mean of IgM and IgG in two groups of cases and control statistically were significant (p = 0.0001 ). In case group the Mean±SD for IgM for men and woman were 2.98±1.97 and 3.17±2.83, respectively, which this differences statistically, were not significant. In case group the Mean±SD for IgG were 5.14±3.45 and 6.35. The above findings indicated that the average of both IgG and IgM are higher among men compared to women. Due to high prevalence of acute coronary syndrome in Iran, the determination of anticardiolipin antibody (IgG) are applied for suspected acute coronary syndrome patients and further prevention measure should be taken for patient with higher serum anticardiolipin antibody.

**Key words:** Artherosclerosis, myocardial infarction, anticardiolipin antibody, northern Iran

### INTRODUCTION

Artherosclerosis considered being one of the most important causes of morbidity and mortality in industrial and developing countries. The rate of myocardial infarction in U.S. is about 2 million annually with 1/4 of them is leading to death (Cannon, 2003, El-Sayed *et al.*, 2007). The prevalence of coronary vascular disease in central Iran is about 9.3%. It is reported that 38% of all death in Iran are due to heart diseases. The reasons behind artherosclerosis are genetically related, acquired risk factors, such as high blood cholesterol. Due to nutritional habitual; high blood pressure, obesity, diabetes, cigarettes smoking, low physical activity, some inflammatory mechanisms can disrupt the regulation of fat within the vein and initiate the artherosclerosis lesion (Sherer and Shoenfeld, 2002). The recent studies indicate the role plagued by immunological responses in induction of artherosclerosis. These latest response include the chemical component of CRP, other infectious agents, such

as *Chlamydia pneumonia* and autoantibodies. The various auto-antibodies genes, which can cause and mediate the cardiovascular disease, are including cardiolipin, OXLDL,  $\beta$ 2GPI and HSP (Jara *et al.*, 2006; Su *et al.*, 2006). Antiphospholipids immunoglobulin is examples of such autoantibodies. These autoantibodies can be found in healthy subjects as well but their concentration are low and are found partially is short period of time with the individual blood circulation. The phospholipid autoantibodies of non-autoimmune origin are seen in such disorder as HIV and in some cancers (George *et al.*, 1997; Salehi and Mirzaei, 2007; Jara *et al.*, 2006).

The majority of phospholipid antibodies are seen in a one autoimmune antibody named, Antibody Phospholipid Syndrome (APS). The other characteristic of APS are thromboembolic and pregnancy abortions. The APS considered as mediator of autoimmunity and artherosclerosis (George and Shoenfeld, 1997). The antiphospholipids are integrated with various forms of

cardiovascular diseases, such as myocardial infarctions. (Sherer and Shoenfeld, 2003; Vaarala *et al.*, 1995). Anti Cardiolipin Antibody (ACA) is an antibody raised against cardiolipin and in disease such as APS, autonomous abortion, thrombosis and lupus. Anticardiolipin antibody can be divided into two categories; 1) class-I: of Immunoglobulin M (IgM). Immunoglobulin G (IgG), Immunoglobulin A (IgA). 2) Dependent or non-dependent to  $\beta$ -2-glycoprotein. This test is requested when the signs of a traumatic accident, such as pain, inflammation in lower organs, respiratory disorder, accompanied with pain are indicated. It is also advised on repeated pregnancy abortion and lupus. Considering the high scale of acute coronary heart diseases and in particular acute myocardial infarction and possible role played by anticardiolipin in acute coronary syndromes (Erkkila *et al.*, 2005, Levine and Jacobs, 2001; Sherer and Shoenfeld, 2003, Wu *et al.*, 1997; Sherer *et al.*, 2001) and particularly due to the absence of a documented para clinical tests and reference into the relation between cardiovascular disorders and the blood antibody level, this present research project was designed to address such queries in this region of northern Iran.

## MATERIALS AND METHODS

**Type of research:** This study was a case control study which was cross-sectionally carried out in two groups. Due to technical difficulties and the absence of other types of heart diseases, the sample population in the case groups predominantly were from those patients with acute myocardial infarctions.

**Method of sampling:** On the base of statistical parameter the exact number of patient was calculated to be 116 but for sake of security and avoiding any mistake 120 patients were selected. Ethical procedure was applied in this study and all patients were informed on the study procedure and the patients entered in this on their own choice. All the patients were matched on such variables as, age and gender.

**Data collection:** A questioner was used for every patient, clinical examination and serological measurement was done by cardiologist and clinical laboratory. The information within the questionnaires, the medical examination files, laboratory tests, were arranged and

entered into SPSS statistical software and presented as a tables and figures. The statistical Kolmogorov-Smirnov test was used to compare the mean of two antibodies of IgM and IgG.

**Statistical analysis:** Initially the serum of two antibodies of IgG, IgM should have been compared; therefore the normal range and positive results in this study should have been determined before the actual measurement Kolmogorov-Smirnov test was applied for the determination of normal range in this study. Using this statistical equation the following results was designed.

### Positive results:

- $>5 \text{ GPL mL}^{-1}$
- $>15 \text{ MPL mL}^{-1}$

### Normal range:

- $\leq 15 \text{ MPL mL}^{-1}$
- $\leq 15 \text{ GPL mL}^{-1}$

## RESULTS

The mean age and standard deviation of patients and control groups were nearly equal ( $55 \pm 10$ ). The sample population in each group was exactly the same (120 person in each group). The gender distribution in case and control groups were 44 female, 76 male and 45 female and 75 male, respectively. In this study the matching among case and control was performed properly according to Table 1 and even the gender matching was also were established to obtain the proper results. The Mean $\pm$ SD of Immunoglobulin M (IgM) in case group and control groups were  $3.10 \pm 2.54$  and  $1.54 \pm 1.00$ , respectively. The Mean $\pm$ SD for Immunoglobulin G (IgG) in case and control groups were  $5.90 \pm 3.84$  and  $3.08 \pm 1.95$ , respectively. The differences, between the mean of IgM and IgG in two groups of cases and control statistically were significant ( $p < 0.0001$ ). In case group the Mean $\pm$ SD for IgM for men and woman were  $2.98 \pm 1.97$  and  $3.17 \pm 2.83$  respectively which this differences statistically were not significant ( $p < 0.697$ ). In case group the Mean $\pm$ SD for IgG were  $5.14 \pm 3.45$  and  $6.35 \pm 4.01$ , respectively. The above findings indicated that the average of both IgG and IgM are higher among men compared to women but this

Table 1: The matching among case and control in general in one hand and between two genders of male and females

	Sex	Count	Mean $\pm$ SD	p-value	p-value (caset+control)
Case	Female	44	55.29 $\pm$ 9.800	0.813	0.99
	Male	76	54.84 $\pm$ 10.27		
Total			55.01 $\pm$ 10.06		
Control	Female	45	55.24 $\pm$ 9.700	0.833	
	Male	75	54.84 $\pm$ 10.37		
Total			54.99 $\pm$ 10.09		

Table 2: Status of antiphospholipids antibodies of immunoglobulin G (IgG) and immunoglobulin M (IgM) among male and female in case and Control groups

Sex	Case		Control	
	IgM	IgG	IgM	IgG
<b>Female</b>				
Mean	2.98	5.14	1.67	3.06
N	44.00	44.00	45.00	45.00
Std.deviation	1.97	3.45	1.23	1.97
<b>Male</b>				
Mean	3.17	6.35	1.46	3.09
N	76.00	76.00	75.00	75.00
Std.deviation	2.83	4.01	0.84	1.95
<b>Total</b>				
Mean	3.10	5.90	1.54	3.08
N	120.00	120.00	120.00	120.00
Std.deviation	2.54	3.85	1.00	1.95

Table 3: Serum immunoglobulin G (IgG) and immunoglobulin M (IgM) concentration level among patient and healthy subjects

Parameters	IgG		IgM	
	High	Normal	High	Normal
Case count	12 (10)	108 (90)	13 (10.8)	107 (89.2)
Control count	1(0.8)	119 (99.2)	1(0.8)	119 (99.2)
p-value	<0.002		<0.001	
Odds ratio for group (case/control)	13.222		14.458	
95% confidence Interval	1.691-103.385		1.860-112.380	

Values in brackets are percentage

difference statistically was not meaningful (p 0.095) (Table 2). In this research project the serum IgG and IgM concentration was determined among case and control groups and the results were tabulated in Table 3 which is shown that there is a statistically significant correlation between patients and healthy subject's antibodies level.

In control group (Table 2) the Mean±SD of IgM for women and men were 1.67±1.23 and 1.46±0.84, respectively which statistically were not significant (p 0.266). The Mean±SD for were 3.04±1.95 and 3.06±1.97, which again it was not statistically significant (P+0.917). The comparison of mean of IgM and IgG in both group of case and control among women and men were as follow.

**Women:** The Mean±SD for IgM is both case and control groups were 2.98±1.97 and 1.67±1.23; these findings statistically were significant (p 0.0003). The Mean±SD for IgM in both case and control groups were 5.14±3.45 and 3.06±1.97, respectively; this latter difference statistically were significant (p 0.0007).

**Men:** The Mean±SD of IgM in both case and control group were 3.17±2.83 and 1.46±0.83 which statistically were significant (p 0.00001). The Mean±SD for IgM in both groups of case and control were 6.35±3.09 and 3.09±1.95, respectively.

## DISCUSSION

Acute myocardial infarction and Unstable Angina (UA) are among wide range of recognized diseases, collectively known as acute coronary syndrome. The

pathophysiology of this diseases are due to displace, or disruption of atheroma from coronary internal vascular system. Acute coronary syndromes are among the most common form of sudden death and it is well established that about 50% of AMI patients die before reaching to the hospitals. Earlier studies on the serum Anticardiolipin antibody, level in AMI and its normal range and the relationship of this antibody with AMI and related morbidity and mortality are found to have contradictory, results (Brey *et al.*, 2001; George and Shoenfeld, 1997). Our study indicated that there are a significant different between the serum cardioliipin antibody of AMI patient compared with the control group. In our study we found that there is a significant correlation between the A $\square$ 11 and IgG, IgM serum concentration levels. Also in this study we found that Patient/Healthy ratio was found to be 13.22 and 14.458, for IgG and IgM, respectively compared to the subjects which they have normal IgG and IgM serum concentration levels. Anticardiolipin antibody is considered as a major characteristic of antiphospholipids syndrome and in the other hand there is a tendency toward thrombosis onset. It is probable, that anticardiolipin antibody play an important role in occurrence and intensity of AMI due to vascular abnormality.

In a study the effective role of anticardiolipin antibody and its relationship with arthrosclerosis in mice it was demonstrated that the mice which were immunized with anticardiolipin antibody and having the higher, titer of anticardiolipin antibody and arthrosclerosis intensity were observed among mice compared to control group (Sherer and Shoenfeld, 2002; George *et al.*, 1997). In agreement with our study it is demonstrated that

higher anticardiolipin antibody serum concentration is considered as risk factor, in AMI and in elderly men. (Sherer and Shoenfeld, 2002). In separate study on 63 patients afflicted with the ACS, which were admitted to the CCU during 2003-04, the average anticardiolipin antibody among patient were  $4.35 \pm 2.7$  and in the control group it was  $3.38 \pm 3.1$  which demonstrated to have significant differences ( $p = 0.038$ ). This average for men in case and control group were  $4.47 \pm 2.22$  and  $3.08 \pm 2.17$ , respectively which statistically were significant ( $p = 0.002$ ).

In latter study, there was not a meaningful difference among female in case and control group,  $4.1 \pm 3.58$  vs.  $3.69 \pm 3.89$  ( $p = 0.634$ ). The latter finding are in agreement with our general population average and also men average but our finding about women is contradicted other results, because, in our study we found an significant difference among women in case and control group ( $p = 0.0007$ ). In our study we found also a statistically significant correlation of higher level of IgG and IgM levels among AMI patients which is an interesting finding which can be used in laboratory investigation for AMI patient clinical setting. Also we should mention that in our study we found that there is not meaningful correlation between IgG and IgM levels and AMI among women but there is a meaningful correlation between IgG and IgM serum level and AMI among men, which is an interesting finding.

This disagreement can be explained as follow, in Salehi and Mirzaei (2007) study the sample population of case and control were not equal 63 vs. 103. The other explanation is that, in our study in spite of extra clinical and Para clinical examination such as ANA test, we were not able to discriminate the coexistence of other disease such as lupus but we are in opinion that the former possibility can fit these differences. One further clue to this disagreement may be relay on the differences on the women mean age in case and control group. In other study by Ghaemian *et al* it was demonstrated that there was a statistically significant differences between serum anticardiolipin antibody among patient with AMI and control group ( $p = 0.01$ ) It was found that there was, a significant increase of serum anticardiolipin antibody of AMI patient with control group ( $37.14 \pm 30.18$  vs.  $13.14 \pm 3.02$ ) and based on their findings it was concluded that anticardiolipin antibody serum level can be considered as a risk factor for ischemic heart diseases and it is suggested it can be considered as marker for the subsequent syndrome vascular thrombolytic lesion

(El-Sayed *et al.*, 2007). The latter findings are in agreements with our data from this study, which indicated that the AMI patients have high anticardiolipin antibody serum level, compared with control group but it

should mentioned that we measured IgM was measured in addition to IgG which was determined by Elsheikh *et al.* (2010).

## CONCLUSION

Based on our finding we can indicate that the mean serum level of IgM and IgG were 4.55-0.55 and 9.9- 1.15 respectively. The sensitivity and specificity for this spectrum of reference rang was calculated as 90%. It is concluded that due to high prevalence of acute coronary syndrome in Iran particularly among men the determination of anticardiolipin antibody (IgG, IgM) are to be applied for the suspected acute coronary syndrome patients and further prevention measure should be taken for the patients with higher serum anticardiolipin antibody.

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