

Effect of Chlamydia Pneumonia Infection on Myocardial Infarction

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Abstract: Artherosclerosis is the major cause of cerebrovascular accidents and major problems of industrial countries. In USA %75 of peoples suffered from it and it causes %42 of all deaths in developing countries such as India. As such as developed countries growth in life standards and socioeconomic levels is yield that cardiovascular disease be as a threaten fact to life. Despite a lot of many efforts on decreasing metabolic risk factors of cardio vascular deaths, Decrease in mortality from cardiovascular disease has reached to plateau level. In USA not only mortality from chronic disease such as artherosclerosis but also mortality from infectious disease has a reverse relationship with economic and educational level of people. For this reason relation of MI with other risk factors such as infections were been interested. This was a case- control study. Sixty patients with MI and 60 matched cases were selected from other words of Boali hospital. All of the patients whom bean admitted with myocardial infarction diagnosis in the time of study selected and information's about them recorded in a researcher made questionnaire. Serum sample from patients and control case were sent to determinations of IgG Anti Chlamydia antibodies with enzyme immune assay. Control case were selected from other words of hospital with matching in go and sex and same test in serum sample was done. Sixty patients and 60 controls were evaluated. In any groups 48 persons (80%) were men and 12 persons (20%) were women. Mean ago of cases were so 58.83+/-12.6 (SD) and mean ago of con tools were 59.08+-11.59. All of the patients in any groups had anti Chlamydia antibodies (IgG) (titer great her than 5U mL⁻¹). Difference of means IgG level in two groups in t test was not significant t (p value %85). In this study all of the cases and controls had anti Chlamydia antibodies. (IgG) that maybe related to cold temperature and high level of population co existence in cold seasons.

Key words: Myocardial infarction, chlamydia pneumonia, Ig G, antibodies, immune assay

INTRODUCTION

Cardiovascular diseases are causes of 29% of all mortality occurred in all over the world, and are the second cause of death after infectious and parasite causes (WHO, 1997). Atherosclerosis is the main cause of vascular accidents and is from major problems of industrial countries. In the US among 4 persons 1 of them suffer from atherosclerosis and this phenomenon is cause of 42% of all death (AHA, 2001). In the developing countries like India life standards and socioeconomic condition improvement increases risk factors of cardiovascular diseases (Reddy and Yusuf, 1998).

Atherosclerosis is a inflammatory disease of vessels and role of numerous risk factors like diabetes, hypertension, hyperlipidemia and cigarette has been proved (Umesh *et al.*, 2003). However among some

individuals with atherosclerosis known risk factors like cigarette, high risk dietary, having no exercise, hypercholesterolemia, hypertension diabetes and genetic factors aren't seen. On the other hand despite of numerous attempts in control of metabolic risk factors, mortality rate curve resulted from cardiovascular diseases, have changed to plateau state in the western countries(5).

Furthermore in the America, both mortality induced by chronic disease like atherosclerosis and mortality induced by infectious diseases have inverse relation with outcome and literacy level of persons, and this subject has elicited this hypothesis that there is correlation between environmental factors like infectious diseases and process of atherosclerosis (CDCP, 1998) and has culminated in collection of epidemiologic and laboratory evidences and discovering of relation between another non-contagious disease and infection

(Siabhan *et al.*, 2001) and some microorganisms like Chlamydia pneumonia, Cytomegalovirus, bacterial agents of mouth infection like Streptococcus Sangius, and Porphyromonas gingivalis, Helicobacter pylori and Herpes simplex type I and II are suspected. Response of this question that whether present of microorganisms components in the atherosclerosis plaques is an accidental phenomenon or has an active role in formation of these plaques hasn't been known yet (CDCP, 1998). From the view point of pathology, microbes may invade vessels wall directly or indirectly and with Endotoxins or lipopolysacharyd releasing into circulation make Endothelium damage. Systemic responses to infection may result in changes in fats profiles through cytokines release and predispose vascular environment to coagulation and contribute aggravation of thrombus formation or atherosclerosis process (Ignatius, 2002). According to above issues present study has performed to evaluate correlation between Chlamydia pneumonia infection and Myocardial infarction. This is case-control studies which in 60 patients and 60 controls were evaluated. All patients hospitalized with acute myocardial infarction diagnosis in the C.C.U ward of Boali hospital within study period, and their diagnosis have been proved through clinical manifestations, E.C.G and heart enzymes increase, were selected and their data were recorded in the researcher edited questionnaire (Fig. 1).

Then their blood samples were taken and were analyzed for Anti Chlamydia pneumonia IgG Ab through immunoassay way and its results were recorded. Samples were taken at morning and immediately send lab of hospital. After separating serum, IgG Ab titer measured in the immunoassay method with Kit of Dia.Pro S.r.l Company that its specificity and particularity were 98% and its coefficient of variation is 4 to 12%. On the basis of Kit producer advice titers ≥ 5 Unit/liter are known as positive. Control group has been selected from patients hospitalized in other wards of that hospital that have been matched (Age and Sex) with case group who have no

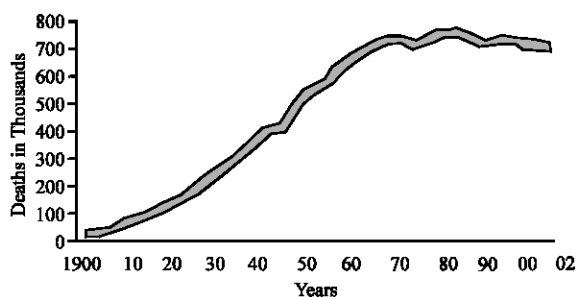


Fig. 1: Deaths from diseases of heart united states: 1990-2002

known cardiovascular disease and no Electrocardiographic signs supporting heart disease and Pneumonia and their blood sample were analyzed for Anti Chlamydia IgG.

RESULTS

Sixty patients and 60 controls were evaluated which 48 was male (80%) and 12 was female (20%) from every group. Age range of case and control group was 35-80. Age average of case group was 58.83 year (standard deviation = 12.06) and control group age average was 50.08 year (standard deviation =11.59). All patients of case and control group had positive Anti Chlamydia IgG antibody. IgG average among case group was 40/20 (Standard deviation =28/15) and IgG average of control group was 39/25(Standard deviation =29/99) (Table 1).

IgG average among tw0 groups was compared by "t student" test that no meaningful difference was seen between two groups (p=0.85).Also age average was compared between two group using "t test" that no meaningful difference was seen between two groups. OR rate for titers more than 10, 20, 50 U mL⁻¹ was as following, respectively:

$$\begin{aligned} \text{OR} &= 1.16 \text{ CI: } (0.394-3.444) \\ \text{OR} &= 1.35 \text{ CI: } (0.631-2.894) \\ \text{OR} &= 1.08 \text{ CI: } (0.493-2.383) \end{aligned}$$

In all of above rates confidence interval contain number 1 and then there was no meaningful difference between two groups for exposure to Chlamydia pneumonia infection. As it is known Chlamydia pneumonia is from important pathogens producing respiratory infections, and now it has been isolated from Atheromatous plaques in coronary and carotid arteries (Jackson *et al.*, 1997). In numerous studies performed on samples extracted from autopsy, atherectomy, Endartrectomy and surgery, there were pathobiologic evidences of bacteria in plaque by positive immunocytochemical staining (staining with specific monoclonal antibody) or positive PCR (Lee *et al.*, 1998). Also several studies have been performed for positive rate (for Anti Chlamydia pneumonia Antibody) of serum samples in patients afflicted by acute myocardial infarction and paradoxical results have been obtained. In

Table 1: Comparision beteen two groups (Age, IgG)

	Cases	Controls	P value
Age Average	12.06	11.59	p>0.05
Standard deviation	58.83	59.08	
IgG Average	28.15	29.99	p>0.05
Standard deviation	40.02	39.25	

the prospective study of Danesh *et al* published with a meta-analysis among 502 patients afflicted by coronary disease with 1005 control IgA titer was positive for 44% of cases and 33% of controls. Odds ratio was obtained for this risk as 1.84 that accompany 1.4-2.4 confidence interval however in spite of its implication for infection and coronary disease relation hasn't been so powerful predictor (Danesh *et al.*, 2002). In the primary studies reports which imply that increase of Anti Chlamydia antibody coincide with severity or more incidences of cardiovascular diseases overcame studies that imply no coincident, but recent reports imply two-edged doubtful responses. The important point is this without a standard microimmunofluorescence test beside cut-off titers variation to regard tests positive, have made incongruence between reports of different researchers (Sandeep, 2002) and this study doesn't exempt this principle. Problems in serology tests results interpretation for Chlamydia pneumonia and different ways for Antibody's existence determining have caused results contain different cut-off points. For example Schumacher et al in their study on 197 patients afflicted by heart coronary diseases with mean age of 55, have found that difference in prevalence of antibodies against Chlamydia antigen was meaningful between afflicted patients and normal controls but this difference wasn't meaningful for antibodies against external membrane proteins (Schumacher *et al.*, 2001). Epidemiologic studies foreshadow the public spread of Chlamydia throughout the world as most of people are afflicted before 20 year and Reinfection by Chlamydia occurs repeatedly. Incidence rate of new Chlamydia infection in the study by Grayston at Seattle has been evaluated and on this basis in every year 9% of 5-9 year old children and 6% of 10-14 year old are afflicted by this disease. Findings of prevalence rate study show that, all persons are afflicted by this infection within their life and reinfection is indeed probable too. High rate of positive antibody titer among males older than 20 may be related with more incidence rate of atherosclerotic disease, and this relation is more probable in males in comparison with females (Thomas, 2000). The first hypothesis for relation between atherosclerosis and Chlamydia infection has been propounded by Saikku *et al.* (1998) that has shown patients afflicted by coronary disease have more probable positive Anti Chlamydia antibody in comparison with others (Saikku *et al.*, 1988).

Although MIF method is used as the most sensitive diagnostic method for evaluation of infection precedent but evidences which can distinguish previous infection from chronic infection aren't available in this method too.

In the study of Ridker *et al.* in Boston 15,000 people were evaluated in cohort shape and titer of anti Chlamydia IgG were measured among them. In the next follow up period (for 12 year) 343 persons were afflicted by MI attack and anti Chlamydia IgG antibody prevalence (titer = $1 \cdot 16^{-1}$) was 68% among them, that is like rate seen in American middle-aged men. Risk assessment on the basis of IgG, has shown that IgG positive rate aside from its levels is the same in patients and control group and for 1/16 titer, 69.4% of cases and 67.4% of controls have positive antibody. In cited study Relative Risk (RR) for effect of Chlamydia on MI incidence in 1/16, 1/32, 1/128, 1/256 titers were 1.1, 1, 1.1, 1 and 1.8 respectively which non of them aren't statistically meaningful and study has resulted in this hypothesis that previous contact with Chlamydia haven't had important effect in the chronic inflammation shape and has refused hypothesis of Chlamydia as a risk factor for MI (Ridker *et al.*, 1999).

As from 60 evaluated cases in autopsy 37% had microorganism that from these 84% were IgG positive, 57 and 5% had positive IgA and positive IgM, respectively, and altogether 94.9% of them have one of antibodies, while all positive instances for antibody in patients without Chlamydia in vascular atheroma were 54.9%. In this study that serum samples have been got and frozen from 1- 26 years ago, with multivariate analysis and with necessary modifications for age, cigarette smoking and time interval between death and sample extraction, titers higher than $1 \cdot 128^{-1}$ and $1 \cdot 256^{-1}$ had 3.65 and 9.40 OR, respectively, that after elimination of insignificant factors, the only effective factor among risk factors was high IgG titer with value more than 1/256 (OR=8.01 and Confidence interval=2.46-25.99) highly accompanied Chlamydia Pneumonia existence I the Atheromatous plaque (Davidson *et al.*, 1998).

Hans et al measured IgG and IgA antibody against Herpes Simplex I and II, Cytomegalovirus, Epstein bar virus, Haemophilus influenza, Chlamydia Pneumonia, Mycoplasma pneumonia and Helicobacter pylori, beside C Reactive Protein (CRP) and followed patients approximately for 3.1 year, results showed that the more positive antibody against more microbes the more is mortality, thus death probability in persons with 0-3, 4-5 and 6-7 microbial contacts was 3.7, 7.2 and 12.6% respectively. In patients with more than 5 microbial contact and positive serology in comparison with persons with lower than 4 microbial contact death probability due to heart disease was 5.1 times more (CI: 1.4-18.3 and $p = 0.002$). Positive CRP has no predictor role and results were greatly influenced by anti Herpes antibodies (Hans *et al.*, 2001).

In the study performed by Noogh et al at Rafsanjan, mean serum IgG in 3 groups (29-persons) include patients afflicted by MI, patients afflicted by Ischemia and control group were 37.7, 11.4 and 3.6, respectively ($p < 0.001$) and there was a meaningful difference between these three groups. In this study titer higher than 5 U mL^{-1} have been regarded positive and relation between Chlamydia infection precedent and heart stroke has been assessed. In aforementioned study 100% of MI group, 65.6% of Ischemia group and 31% of control group had titers more than 5 U mL^{-1} .

CONCLUSION

In present study all case and control patients, had positive anti Chlamydia IgG, therefore results of study don't support relation between this infection and myocardial infarction. Positive result in all studied individuals may result from high Chlamydia infection prevalence in our region because of cold weather and high compactness of peoples gathering in warm places due to this weather.

Assessing this study and present incongruous literature it is concluded that existence of Chlamydia pneumonia in some Atheromatous plaques is definite, but this question saying "Why in some patients, in spite of positive serology of Chlamydia pneumonia, this bacteria isn't seen in plaques" will be accountable with Immunologic rules; thus only in some individuals affliction by Chlamydia aggravate Atheromatous plaques formation.

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