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SERUM HIGH SENSITIVE C-REACTIVE PROTEIN (hs-CRP) IN MALE PATIENTS WITH CORONARY HEART DISEASE

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ABSTRACT

Pathogenesis of atherosclerosis involves mainly the inflammatory processes. In this regard, the degree of inflammation especially in coronary heart disease (CHD) and other ischemic disorders is widely considered to be associated with the variations in C-reactive protein (CRP). However, precise correlation of age-related high sensitivity CRP (hs-CRP) levels with the severity of injury is not clearly known. Hence, we carried out present study in age-matched male adult patients with CHD and compared this data with the normal male healthy adult control subjects (C). The results showed that aging increases the hs-CRP levels with significant positive linear correlation in patients with CHD as well as healthy control subjects. However, highly significant age-based increase of hs-CRP (mg/L) in CHD patients as compared to C subjects revealed the role of inflammation via change in hs-CRP. Conclusively, we investigated the involvement of hs-CRP in male adult patients with CHD, and suggest that the inflammation seems a major factor causing atherosclerotic conditions in CHD.

Keywords: hs-CRP, age, inflammation, coronary heart disease, age related hs-CRP variations

INTRODUCTION

Pathogenesis of atherosclerosis involves mainly the inflammatory processes (Libby, 2012; Willeit *et al*., 2016), and modifiable risk factors associate independently and strongly with C-reactive protein (CRP) levels in CHD patients (Blaum *et al*., 2021; Serafi *et al*., 2021). Whereas the CRP is widely considered as associated with the degree of inflammation especially in coronary heart disease (CHD) and other ischemic disorders, and is considered as a marker of acute and chronic inflammation (Danesh *et al*., 2004). It has been revealed that high inflammatory burden represented as CRP ≥2 mg/L independently associates with risks of cardiovascular complications (Emerging Risk Factors Collaboration *et al*., 2010) and coronary heart disease (Sabatine *et al*., 2007), and reducing inflammation e.g. via decreasing hs-CRP without influencing lipid levels may decrease the risk of cardiovascular disease, though the inflammatory hypothesis of atherothrombosis is still unproved (Ridker *et al*., 2017). However, precise correlation of high sensitivity CRP (hs-CRP) levels with the severity of injury is not clearly known. It was revealed that atherosclerosis is not developed only by dyslipidaemia (Paramsothy *et al*., 2010) but it is also associated much in response to inflammation via plague complexity and instability (Lombardo *et al*., 2004). Hence, CRP the indicator of systemic inflammation is quite helpful in predicting atherosclerosis (Khera *et al*., 2006).

It has been suggested that even a small increase in of hs-CRP in view of its high sensitivity serves as an indicator for predicting complications and diseased conditions especially coronary heart disease (Hussain, 1991; Mahmood *et al*., 1998; Hussain, 2010; Kincl *et al*., 2010; Koc *et al*., 2010; Harutyunyan *et al*., 2011; Sohail and Hussain, 2013; Sohail *et al*., 2019). On the other side, controversial results for the role of hs-CRP in cardiac ischemic disorders have also been documented (Harutyunyan *et al*., 2011; Rashidinejad *et al*., 2013). Higher hs-CRP levels were obtained as prediction for progressive motor deficit deterioration (PMD) along with penetrating artery infarction (PAI) (Gong *et al*., 2019). Both male and female CHD patients showed various inflammatory and behavioral mechanisms with even small associations of hs-CRP and other markers (Mommersteeg *et al*., 2019). Furthermore, the patients with SIHD (stable form of ischemic heart disease) under DAPT (dual-antiplatelet-therapy) manifested increased hs-CRP (Golukhova *et al*., 2018). The hs-CRP estimated in men showed increase in the development of venous thromboembolism (VTE) with a linear association (Kunutsor *et al*., 2017). Moreover,

increased hs-CRP were obtained though not related to CHD severity in patients of mean age 60.3 years (Bouzidi *et al*., 2020).

It is important to realize that most of the studies related to CRP in ischemic disorders were carried out in Europe and America but the CRP levels were higher in Asians compared to European people (Chambers *et al*., 2001). In view of this reason, we attempted to assess the levels of hs-CRP in normal male subjects and the male subjects with CHD. We were also interested to know whether patients with CHD without obesity or over-weight status may have high serum hs-CRP. This information was required to verify that ischemic disorders and atherosclerosis occur in certain people mainly due to dysfunction in inflammatory disorders manifesting change in the levels of inflammatory markers including hs-CRP beside dyslipidaemia.

MATERIALS AND METHODS

The male patients with coronary heart disease (CHD, n: 26, age: 60.65±3.50 years), along with normal male control subjects (C, n: 25, age: 60.52± 3.45 years) were included in the present study. The patients with CHD were diagnosed properly with the help of their clinical manifestations, and differential diagnosis. Proper diagnosis needed family and medical history of the patients and thorough examination including physical check-up and performing diagnostic/biochemical tests. For that purpose, expert clinicians/ physicians helped for properly diagnosing the patients.

The data of male adult subjects in the present study were those without over-weight/ under-weight status / and without obesity that was confirmed by estimating their BMI. The patients and control subjects were well informed prior to the study about the purpose and benefits of the present study program. Blood sample drawn was centrifuged and serum separated for the estimation of high-sensitive C-reactive protein (hs-CRP) serum levels (mg/L) employing standard laboratory methods. Serum levels of hs-CRP were determined using immunoturbidimetric assay (Behring-Nephelometer: BNA-2, Siemens USA).

The levels of hs-CRP serum were estimated as mean ± SD. The t and p values (using unpaired t test) were analysed. Following the general statistical procedures (Zahir *et al*., 2014), the subjects were tested for hs-CRP levels by t test for predicting the dispersion pattern of values with the determination of two tailed p values. Slope values, intercept, R^2 and P for the regression lines were recorded. Spreadsheets (that were written for Excel & were workable with Calc program) were used for analysing the data. The Y intercept, regression coefficient, Y estimator and X estimator were obtained. Serum levels of hs-CRP were determined in age-matched normal healthy male adult control subjects for comparing the serum hs-CRP levels obtained in CHD adult male patients.

RESULTS

The mean ± SD values for adult male subjects with CHD (age: 60.65 ± 3.50) and adult male control groups (age: 60.52 ± 3.45) did not differ significantly since they were age-matched. However, the serum levels (mean ± SD) of hs-CRP (mg/L) for male patients with CHD (5.24 ± 2.75) differed significantly (t: 7.69, two-tailed p <0.0001) from those in healthy control male subjects (0.97 ± 0.62).

Association for the age vs. serum hs-CRP for healthy control subjects (C) and CHD patients was assessed (Fig 1 & 2). Plot between the age and serum hs-CRP levels in C group showed a positive linear relationship with the slope value of 0.096 and R^2 as 0.2797, R as 0.5289 ($p < 0.007$; Fig.1). It revealed positive correlation of serum hs-CRP levels with the increasing age in normal male control subjects.

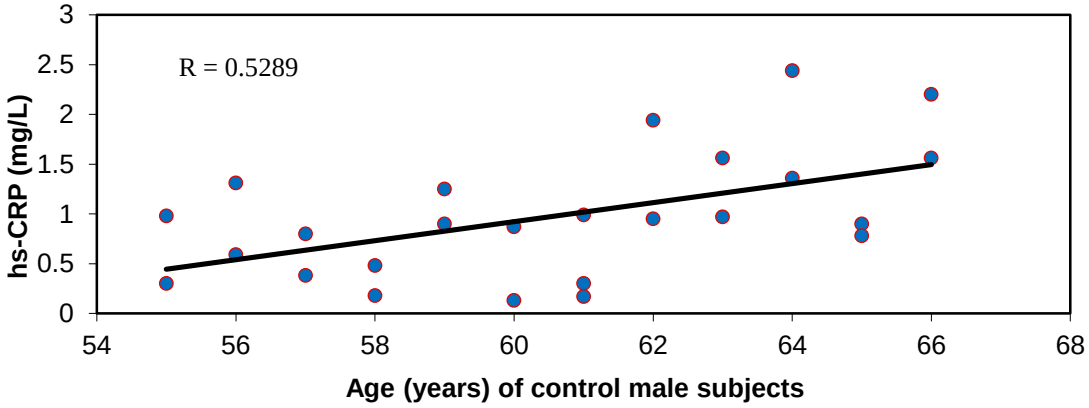

Fig.1. Association of the age and serum hs-CRP in adult male control subjects. (Regression equation: y =0.0955x – 4.8109; R^2= 0.2797).

Regression for the age against serum hs-CRP in the adult male patients with CHD showed a positive linear correlation (slope value of 0.541 and R^2 as 0.4733, R as 0.6880 ($p > 0.0001$; Fig. 2). The CHD patients revealed highly significant positive linear correlation for age vs. serum hs-CRP as compared to that in C group subjects.

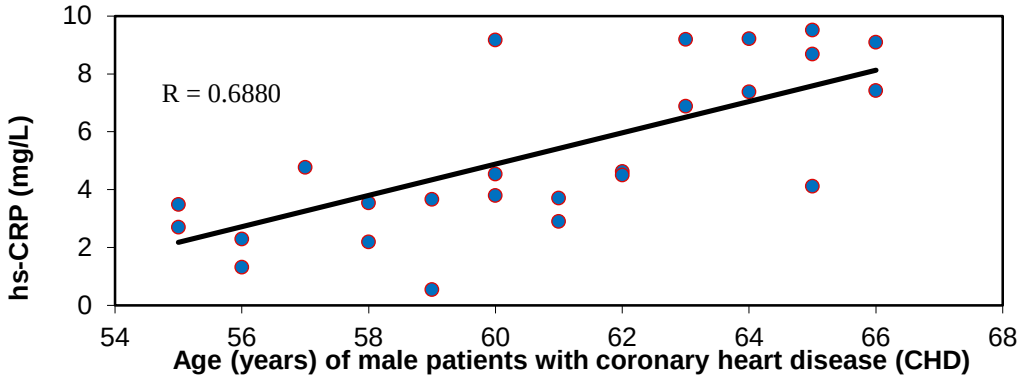

Fig.2. Association of the age and serum hs-CRP in adult male patients with coronary heart disease. (Regression equation: y =0.5415x – 27.607; R^2= 0.4733).

DISCUSSION

Extent of inflammation investigated in the present study in coronary heart disease has also been suggested by other investigators (Lombardo *et al*., 2004; Blaum *et al*., 2021) since dyslipidaemia is not the sole cause of atherosclerosis (Paramsothy *et al*., 2010). Hence, we were interested to investigate the role of hs-CRP serving as an indicator of systemic inflammation in atherosclerosis (Khera *et al*., 2006). In view of this, we were also interested to estimate the correlation and the extent of correlation of age with serum levels of hs-CRP in adult male patients with coronary heart disease.

It is quite informative that the male patients in the present study were not obese or over-weight/ under-weight but they still showed significant increase in serum hs-CRP levels with the increase in age. Estimation of hs-CRP in normal healthy male patients was included for comparing the levels of hs-CRP and hence the inflammatory status. Furthermore, it was revealed in the present study that the estimation of hs-CRP levels in normal subjects may also serve as predictor in healthy people for a possibility of their cardiac/ ischemic complications in future. Our these findings have resemblance with the investigations that high level of inflammation represented as CRP independently associates with the risks of cardiovascular complications (Emerging Risk Factors Collaboration *et al*., 2010) and coronary heart disease (Sabatine *et al*., 2007), and inflammation is reduced by decreasing hs-CRP (Ridker *et al*., 2017).

Involvement of hs-CRP in male patients with coronary heart disease in the present report is in accordance with the existing information about the important role of hs-CRP in inflammation and degree of inflammation (Danesh *et al*., 2004; Hussain *et al*., 2007; Sohail *et al*., 2013; Matsuo *et al*., 2016; Oemrawsingh *et al*., 2016; Attia *et al*., 2020; Blaum *et al*., 2021; Serafi *et al*., 2021). Controversial results for the role of hs-CRP in cardiac/ ischemic disorders were obtained (Kincl *et al*., 2010; Rashidinejad *et al*., 2013). However, our results are similar to some of the reported investigations (Kincl *et al*., 2010; Koc *et al*., 2010; Harutyunyan *et al*., 2011; Blaum *et al*., 2021).

Our data though with limited age range shows similar status for inflammation as described earlier by Gao *et al*. (2014) and other investigators (Wada *et al*., 2008; Lavallée *et al*., 2013). Elevated hs-CRP investigated in patients with coronary heart disease (Kunutsor *et al*., 2017; Golukhova *et al*., 2018; Mommersteeg *et al*., 2019; Attia *et al*., 2020; Bouzidi *et al*., 2020; Blaum *et al*., 2021) are quite similar to the present results in male patients with coronary heart disease. These reports and our present study explain the involvement of hs-CRP in atherosclerotic process in coronary artery disease and related complications.

Conclusively, we suggest the role of hs-CRP with the influence of age in adult male patients with coronary heart disease. Hence, inflammation manifested in the form of increased hs-CRP and such other factors seems a major factor causing atherosclerotic conditions in coronary heart disease.

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