



Homocysteine and High sensitivity C- Reactive Protein is associated with atherosclerosis in type 2 diabetes patients

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Abstract:

Introduction: Diabetes Mellitus is a metabolic disorder and is one of the major global problems, affecting 6-7% of the world population. There are several complications of diabetes, atherosclerosis is one of them. Biochemical parameters such as homocysteine and hsCRP are associated with atherosclerosis in diabetic patients.

Objectives: This study was intended to evaluate the role of homocysteine and hsCRP in type 2 Diabetic Patients with atherosclerosis.

Methodology: This case-control study was conducted on a total of 200 subjects which were divided into two groups. One Group consisted of 100 diabetic patients & second Group consisted of 100 healthy controls. Estimation of homocysteine and hsCRP were performed. Statistical evaluation was done for analysis of the results.

Result: The study documented stronger correlation between increased homocysteine level(r value= 10.26, P value = <0.001) and hsCRP levels(r value= 11.78, P value = <0.001) in diabetic patients by applying spearman's correlation.

Conclusion: The diabetic patients have significantly raised levels of homocysteine and hsCRP when compared to healthy individuals. In diabetic patient, homocysteinaemia is accompanied by increased hsCRP, suggesting activation of inflammatory pathways in progression of atherosclerosis. Increased homocysteine and hsCRP levels are associated with atherosclerosis in type 2 diabetes patients.

Keywords: Homocysteinaemia, DM, atherothrombotic diseases and cardiovascular disorders.

Introduction:

Diabetes is one of the most common non-communicable diseases and its prevalence increases continually around the world. Diabetes was the ninth leading cause of death with an estimated 1.5 million deaths as per WHO, 2019. It is affecting millions of peoples, about 6-7% of the world population (1).

Diabetes mellitus is a metabolic disease which is characterized by long term hyperglycemia with

misbalancing of carbohydrate, fat and protein metabolism resulting from defect in insulin secretion or insulin action. The most prevalent diabetes form in human is type 1 and type 2 diabetes mellitus(2).

Type 2 DM is characterized by two defects impaired insulin secretion or decrease in its peripheral action, which is known as Non Insulin Diabetes Mellitus. Diabetes leads to various microvascular and Macrovascular complications. Macrovascular disease is a major cause of death in diabetic patients.

Atherosclerosis is progressive disease of arterial wall involving the components of inflammation vascular lipid deposition and re-modeling fibrosis and thrombosis.

Diabetes is a risk factor for atherosclerosis, and atherosclerotic vascular disease, which is a major cause of morbidity and mortality among patients with diabetes mellitus. Multiple factors including hyperglycemia, hypertension, smoking, hyperlipidemia, endothelial dysfunction, and coagulation abnormalities involves in the process of accelerated atherosclerosis in diabetes (3–5).

Inflammation has been established to play an important role in the pathogenesis of atherosclerosis (6,7). There are many systemic markers of inflammation, but most common is high-sensitivity C-reactive protein (hs-CRP), which has been found to independently predict future coronary heart disease (CHD) in several prospective studies that included non-diabetic subjects (8,9,10).

C-reactive protein, an acute-phase reactant synthesized by liver, which is very sensitive marker of systemic inflammation. It might potentially be a cause underlying the etiology and manifestation of type 2 diabetes mellitus (11)hsCRP is a marker of inflammation and atherosclerosis.

In patients with type 2 diabetes mellitus, having 2 to 4 fold increased risk for coronary heart disease (CHD), plasma homocysteine level seems to predict cardiovascular events (12,13,14,15,16).

Homocysteine is a dietary amino acid produced by the breakdown of methionine (17) whose metabolic pathway involves several enzymes. Hyperglycemia elevated oxidative stress in addition to asymmetric dimethylarginine (ADMA) in the vascular endothelium. Meanwhile, elevated serum tHcy induces endothelial stress and ADMA. Oxidative metabolism of homocysteine to homocysteine and homocysteine thiolactone leads oxidative damage of vascular endothelial cells and increased proliferation of vascular smooth muscle cells.

Increased Homocysteine and hsCRP levels are seen in type 2 diabetic patients with atherosclerosis.

Material And Methods:

One case control study was conducted in the Department of Biochemistry in collaboration with Department of Medicine at Mahatma Gandhi Medical College and hospital, Jaipur. 100 diagnosed patients of Type 2 Diabetes Mellitus and 100 healthy controls were enrolled for the study.

Blood samples were collected and analyzed for the parameters by these methods:

- ❖ Homocysteine : CLIA (*Chemiluminescent Immunoassay*)
- ❖ High Sensitivity CRP (*Immunoturbidimetric Method*)

Inclusion criteria:

- Diagnosed cases of Type 2 Diabetes Mellitus.
- Age between 40 to 75 years, either gender.
- Patients who are willing to participate in the study.

Exclusion criteria:

- Age less than 40 years or more than 75 years
- Patients suffering from any other chronic diseases.

Statistical Evaluation:

Results obtained by statistically and expressed as mean \pm SD (standard deviation). The probability value ≤ 0.05 was considered as statistically significant. The correlation was analyzed by the “Spearman’s Correlation”.

Results:

In group A (healthy controls) 48% was male and 52% was female. In group B (diabetic patients) 51 % was male and 49% was female.

On comparing serum hsCRP levels and homocysteine of type 2 diabetic patients with control group, hsCRP was significantly higher in diabetic patient ($r=11.78$, $P<0.001$) as compared to control group and Serum Homocysteine was also significantly higher among diabetic patient ($r=10.26$, $P<0.001$).

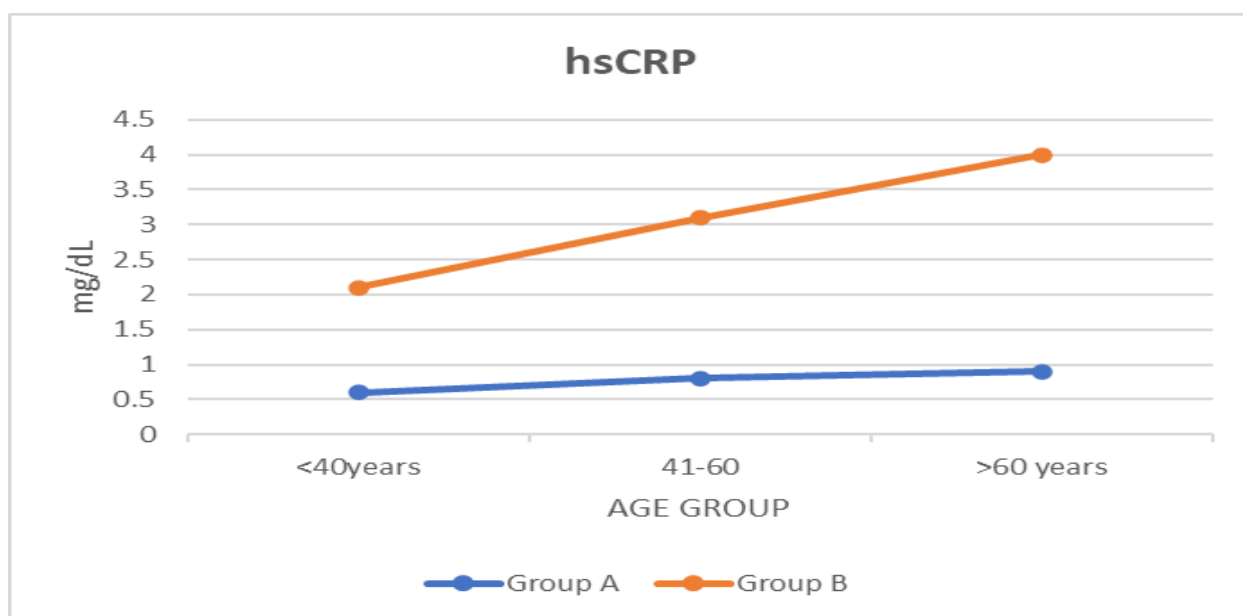
Observations:

Table 1 : Sex Distribution

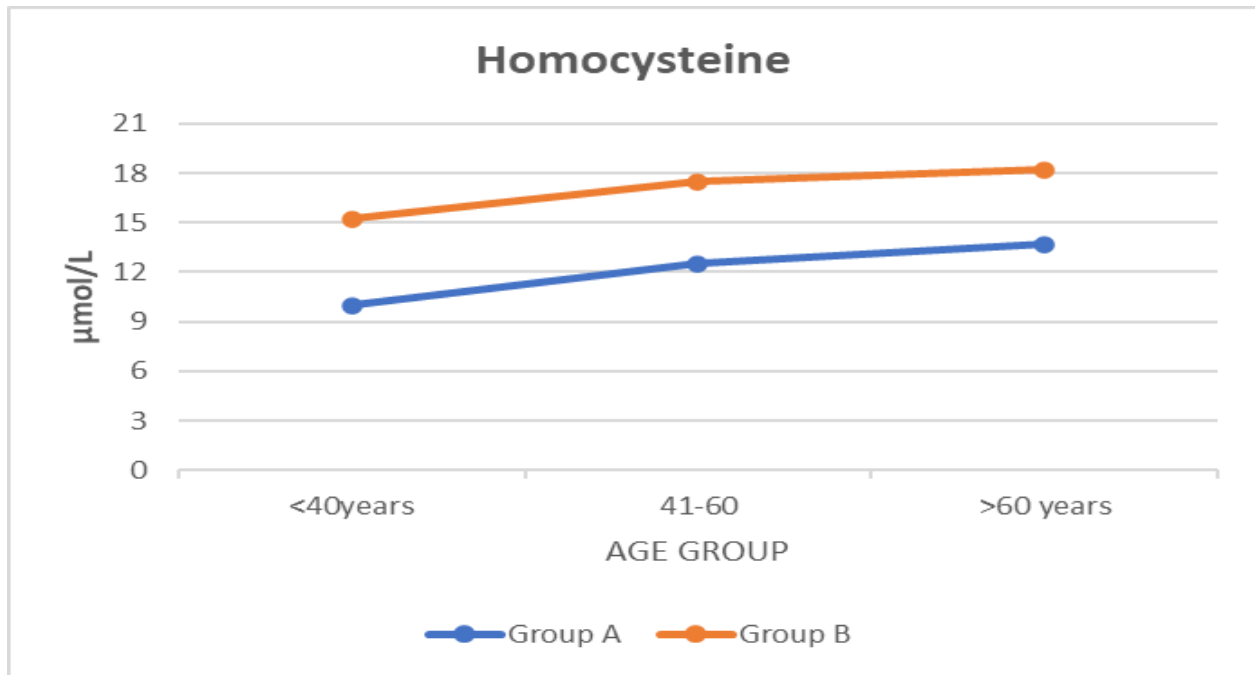
Sex	Group A (n=100)		Group B (n=100)	
	Number	%	Number	%
Male	48	48	51	51
Female	52	52	49	49
Total	100	100	100	100

Table 2 : Homocysteine and hsCRP levels in diabetic and healthy group

Parameter	Group A Control (n=100)	Group B Cases (n=100)
	Mean ± SD	Mean ± SD
hsCRP(mg/L)	0.77 ± 0.43	3.21 ± 1.05
Homocysteine (µmol/L)	10.86 ± 1.72	16.25 ± 1.52



Graph 1 : hsCRP levels in diabetic and healthy group



Graph 2 : Homocysteine levels in diabetic and healthy group

Discussion:

Hyperglycemia is an important risk factor for atherosclerosis. Atherosclerosis and cardiovascular diseases are main cause of morbidity and mortality in diabetic patients. Atherosclerosis is considered to be an inflammatory process triggered by response to injury. The present study was planned to evaluate the levels of serum hsCRP and homocysteine in 100 type 2 diabetic patients and compared them with 100 control group. Patients were selected on the basis of predefined exclusion and inclusion criteria and after obtaining informed consent. The mean age in type 2 diabetic patients and the healthy individuals group was comparable

Table.1 exhibits the distribution of cases on the basis of gender. The number of females was higher (52%) in diabetic patients whereas number of males was higher (51%) in healthy controls. Table.2 & Fig.2 exhibits that, when serum homocysteine levels were compared between type 2 diabetic patients and healthy individuals, then a statistically significant increase was found in patients group. Homocysteine is formed by demethylation of methionine. It's a thiol-containing amino acid. It is metabolized by 2

major pathways: remethylation and transsulfuration. Homocysteine (Hcy) plays an important role in the development of atherosclerosis and vascular injury. It is also an important atherosclerotic factor found in diabetes patient.

A study by Akalin A et al.(18), reported that plasma Homocysteine levels were significantly elevated in diabetic patients with atherosclerotic vascular disease. They concluded in their study that Hcy may lead to atherosclerosis by operating through alternative mechanisms other than inflammation. Similar findings were reported by Hoogeveen E et al (14). They suggested that, a high serum total homocysteine level is an independent risk factor for cardiovascular disease and High serum tHcy may be a stronger (1.6-fold) risk factor for cardiovascular disease in patient with type 2 diabetes mellitus.

Another study by Soinio M et al.(19), reported the increase in Homocysteine levels in patients of Coronary Heart Disease in Type 2 Diabetes Mellitus. They concluded that in this large cohort of patients with type 2 diabetes; plasma homocysteine level was a strong and independent risk factor for CHD events.

Table:2 & Fig:3 represented that, when the levels of serum hs-CRP were compared between type 2 diabetic patients and healthy individuals, then a statistically significant increased was found in patients group. There are many inflammatory markers but high sensitivity C- reactive protein was found to be an independent predictor of coronary heart disease events in several prospective studies (20,21,22).

A study by Effoe V et al. (23), demonstrated that the levels of hs-CRP increased in patients with diabetes type-2, when compared with non-diabetic patients. They concluded that a positive association between low-grade systemic inflammation (as measured by

the level of hs-CRP) and incident type 2 diabetes. Another study by SOINIO M et al.(19), concluded that In the large cohort of type 2 diabetic patients, hs-CRP was an independent risk factor for CHD deaths.

Conclusion:

A strong correlation was found between increased homocysteine and hsCRP. In diabetic patient, homocysteinemia is accompanied by increased hsCRP, suggesting activation of inflammatory pathways in progression of atherosclerosis.

Increased homocysteine and hsCRP levels are associated with atherosclerosis in type 2 diabetes patients.

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