ORIGINAL ARTICLE

Cystatin C: An Early Marker of Cardiac Complications in Diabetics

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ABSTRACT

Introduction: Cardiovascular disease is one of the common complications of Diabetes mellitus. Serum Cystatin C level has been suggested as a marker for cardiac complications in diabetes. **Material and Methods:** We studied serum Cystatin C level in Diabetics to find if correlation exists between cardiac complications and elevated Cystatin C levels. **Results:** A total of 50 diabetics were studied out of whom 25 had cardiac complications and the rest did not have cardiac complications. No significant difference was observed between Serum Cystatin C levels of diabetics with cardiac complications (mean 1·5±0·45) and diabetics without cardiac complications (1·4±0·46) although Cystatin C levels were found to be elevated in diabetic cases. **Conclusion**: Keeping in view the significant difference (p=0·000) in Cystatin C levels of healthy and diabetic patients, it is reasonable to accept the importance of Cystatin C as an indicator of diabetes and its associated complications.

Keywords: Cystatin C, Cardiac complications, Diabetes mellitus, Ischemic heart disease

INTRODUCTION

Diabetes mellitus has been designated as a major risk factor for cardiovascular disease by American Heart Association. Synergism between hyperglycemia and other known risk factors namely obesity, hypertension and hypertriglyceridemia increases the cardio vascular morbidity and mortality in diabetics.[1]

Cystatin C belongs to Cystatin family of cystein protease inhibitors which is a 13kDa proteinof 120 amino acid and is produced at a constant rate by all nucleated cells,[2-4] Cystatin C has a role in tissue remodelling.[5,6] There is increased production of inflammatory cytokines following a vascular injury and there is increased production of elastolytic cysteine proteases. This is counter balanced by increased production of Cystatin C.[7,8] An imbalance between protease and inhibitors may affect the cardiovascular system.[6,7,9]

Most of the markers studied previously for establishing the presence of cardiovascular diseases were not fool proof. In metabolic syndrome and type 2 diabetes mellitus which are a syndrome complex of hyperglycemia caused by insulin resistance, cardiovascular complications are important because of the cost involved in diagnosis and treatment. The economic loss associated has lead to search of specific markers which would depict probability of cardiovascular complications in diabetics and patients with metabolic syndrome. Most markers are invasive in nature although a few non invasive markers have been studied as well.

Cystatin C has been extensively studied in metabolic syndrome and insulin resistance and studies have shown that Cystatin C has similar value as marker in diabetes as in metabolic syndrome in cardiovascular morbidity[10-15] Cystatin C levels in serum may denote myocardial tissue damage following ischemic events and can be a marker for cardiovascular morbidity and mortality.[16-18] A significant difference was found between Cystatin C levels of Diabetic controls and diabetic subjects with cardiac complications by Rafat et al.[19] There are certain conditions where Cystatin C is increased like in smokers, patients with nephropathy, retinopathy and those on glucocorticoids.[20-22]

It has been suggested that Cystatin C is a useful marker for identifying individuals at a higher risk for cardio vascular events even in patients who do not have other risk factors, as elastolytic proteases and inhibitors play an important role in vascular remodelling and atherosclerosis.[6]

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The present study was done to establish whether serum Cystatin C could be used as a non invasive markers for cardiovascular complications in Diabetics.

MATERIAL AND METHODS

Blood sample of 100 subjects 50 healthy persons and 50 diabetic patients were analysed. The sample of 50 healthy persons was drawn from among the persons working in various units of HIMS. The diabetic subjects were grouped into two those with cardiac complications (n=25) and those without cardiac complications (n=25). Diabetics with cancers, pregnancy, neurological disorder, diabetics with nephropathy (as indicated by increased serum creatinine levels) and those who were smokers and on glucocorticoid therapy were excluded. Cardiac complications were identified by ECG and echocardiography.

Study Tools

Cystatin C was estimated in serum of patients and control subjects by in vitro latex enhanced turbidimetry method by Diazyme'sCystatin C assay – other parameters like estimation of blood glucose, BUN, serum creatinine, urinary creatinine, urinary albumin and serum total cholesterol, HDL cholesterol, triglycerides were done on automated chemistry analyser. HbA_{IC} was done by HPLC and hsCRP by ELISA. Clinical and experimental data was collected as per a specified format. Baseline characteristics are mentioned in the table.

In 50 healthy and 50 diabetic subjects Cystatin C was estimated (Table 1). In healthy subjects the range was 0·37-1·8 mg/lit. In diabetics the serum Cystatin C range was 0·77-2·6 mg/L. Statistically significant (t= 9·5; p<0·001) difference was seen in Cystatin C levels between healthy and diabetic subjects.

Although the Cystatin C level in diabetics with cardiac complications is marginally higher but the difference between two groups is statistically insignificant (p=0·836) (Table 2).

Table 1: Results comparison of mean cystatin C levels between healthy and diabetic subjects

	Mean±S.D (n=50)		CI	
	Healthy	Diabetes subjects	Lower	Upper
CystatinC	0·77±0·45	1·48±0·26	0·566	0·863

t=9.5; P<0·001

DISCUSSION

The Cystatin C levels in diabetic subjects compared with healthy subjects was significantly raised in our study (p=<0·001). Studies by Servias et al (p<0·003), Tanindi et al (p<0·001) also found a significant difference in Cystatin C in patients with or without metabolic syndrome.[23]

In our study we could not find a significant difference in Cystatin C levels between diabetics with cardiac complications and those without cardiac complications (p=0·836). Kim et al also have reported lack of association between serum Cystatin C levels and coronary artery disease in diabetics.[24] However this is in contrast to observations of Tanindi et al.[23] They studied patients of metabolic syndrome and compared serum Cystatin C (p=0·005) between metabolic group with cardiac ischemia and without cardiac ischemia wherein they found a relationship. Rafat el all also found a significant difference (p<0·001) in Cystatin C levels among diabetic controls and diabetics with complications (nephropathy and cardiac complications).[19]

CONCLUSION

The serum Cystatin C levels of diabetic subjects (1·4±0·45) in our study was higher than healthy subjects (0·77±0·26). Keeping in view the significant difference (p=0·001) in Cystatin C levels of healthy and diabetic patients, it is reasonable to accept the importance of Cystatin C as an indicator of diabetes and its associated complications.

But from the present study no significant difference was observed between serum Cystatin C levels of diabetes with cardiac complications (mean 1·5±0·45) and without cardiac complications (1·4±0·00) (p=0·836), so Cystatin C cannotoutrightly be used as a predictor of cardiac complications among diabetic patients. Some more investigations may be warranted to arrive at precise inferences. It may be required to enlarge the sample size as also to draw it from a wider association of the society.

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Table 2: Comparison of Cystatin C between diabetics with and without cardiac complications

	Diabetics with cardiac complications		Diabetics without cardiac complications		95% CI	
	Range	Mean±S.D	Range	Mean±SD	Lower	Upper
Cystatin C	0·77-2·6 mg/L	1·5±0·45	0·89-2·4 mg/L	1·47±0·46	0·235	0·290

t=0·208; P=0·836

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