ORIGINAL ARTICLE

ASSESSMENT OF C-REACTIVE PROTEINS IN RECENTLY DIAGNOSED TYPE-1 DIABETIC CHILDREN AS A RISK MARKER OF EARLY ATHEROSCLEROSIS

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Background: Cardiovascular disease (CVD) is a leading cause of mortality and morbidity in diabetes mellitus (DM). Studies indicate that atherosclerosis has slowly altered from a model of chronic degenerative disease affecting patients with advanced ages to a model of subclinical chronic inflammatory disease present in childhood. DM is a risk factor for atherosclerosis and asymptomatic low grade inflammation occurs prior to unconcealed vascular lesions in these patients. A low grade inflammation can be determined by serum C-reactive protein (CRP). The aim of this study was to evaluate serum CRP levels in recently diagnosed type-1 diabetic children to predict early cardiovascular complications. **Methods:** In this cross-sectional study, serum CRP levels were determined in 39 diabetic children and 40 healthy children as control. CRP concentrations were determined by ELISA by an automated ELISA analyzer. The values were expressed as mean±standard deviation and data from patients and controls was compared by *t*-test. **Results:** Serum CRP levels were significantly elevated in diabetic children as compared to controls ($p<0.001$). **Conclusion**: Serum CRP can be used as a potent biochemical markers in addition to other traditional risk factors like dyslipidemia, hypertension, obesity and smoking to detect high risk patients**.**

Keywords: CRP, type-1 diabetes, cardiovascular disease, inflammatory markers.

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INTRODUCTION

Diabetes mellitus is a risk factor for atherosclerosis and asymptomatic low grade inflammation occurs prior to unconcealed vascular lesions in these patients.[1] Subclinical inflammation involves the commencement and progression of atherosclerosis. The acute phase proteins play an important role in host protection such as direct neutralization of inflammatory agents, diminution of the degree of local tissue damage and contribution in tissue repair and regeneration. In addition, establishment of complement proteins results in migration of neutrophils, macrophages and plasma proteins.[2] Immunohistochemical studies have confirmed the involvement of CRP in inflamed tissues, atherosclerotic vessels and in the infarcted myocardium.[3] In 2007, Picardi *et al* demonstrated that despite good metabolic control, 1 year of overt type-1 diabetes is sufficient to increase CRP levels especially in males.[4] CRP levels are elevated in young patients with type-1 diabetes possibly analogous with early-stage advanced carotid atherosclerosis.[5,6]

In addition to ultrasonographic assessment of atherosclerosis, CRP has been revealed to be a risk factor for CVD.[7,8] Elevated CRP is related with atherosclerosis events such as higher intima media thickness (IMT)[9,10] and multifarious plaque.[11,12] Serum CRP has established to be a self-determining marker of the degree of atherosclerosis in patients with coronary, cerebrovascular and peripheral arterial disease. The American Heart Association (AHA) proclamation contains recommendations for the use of CRP in the diagnosis and management of cardiovascular disease.[13] To classify risk, cut points for CRP according to estimated values in the adult people have been recommended: low risk (<1.0 mg/l), average risk (1.0–3.0 mg/l) and high risk (>3.0mg/l). A CRP level >10 mg/l usually indicates the presence of a noteworthy acute phase response and further evaluation is required to conclude the cause.[14]

The aim of this study was to evaluate serum CRP levels in recently diagnosed (duration of diabetes <two years) type 1 diabetic children to foresee early cardiovascular complications.

MATERIAL AND METHODS

This cross-sectional study was carried out on 79 subjects in the department of Physiology University of Health Sciences Lahore (UHS). The study was approved by the Ethical Committee and the Research Board of UHS Lahore. Seventy-nine consecutive children were selected and divided into 2 groups. Group-1 included thirty nine children with type-1 diabetes mellitus (19 males and 20 females) with age 9–16 years having diabetes for more than one year.

Group-2 included forty healthy children of the same age and sex as of group-1, without type-1 diabetes mellitus. Children with type-1 diabetes mellitus were taken from the Diabetic Clinic of

Children's Hospital and Institute of Child Health, Lahore. Subjects with history of type-II diabetes mellitus or taking medications known to affect body growth or lipid metabolism, endocrinopathies, infections, autoimmune disorders, thyroid abnormalities, connective tissue disease, liver dysfunction, or angiopathy or any major illness since birth were excluded from the study.

Written informed consent was obtained from each subject and his or her parents. The study subjects underwent a detailed clinical examination. All participants and their parents were asked to answer a questionnaire on their family history of diabetes and any other major disease (cardiovascular disease, autoimmune disease, endocrinopathy etc.) as well as on their life style characteristics e.g. physical activity, dietary habits, smoking, and economic status.

Body weight and height were recorded in all subjects. Body mass index (BMI) was calculated. Arterial blood pressure (BP), glucose levels, and HbA_{1c} were measured.

Serum CRP concentrations were determined by ELISA using commercial kits. Data was analysed using SPSS 15.0. T-test was used to determine statistically significant differences of quantitative variables between the two groups with $p \leq 0.05$.

RESULTS

Table-1 summarizes the anthropometric characteristics of type-1 diabetic subjects and nondiabetic controls. No significant differences were observed in the values of BMI, systolic blood pressure, and diastolic blood pressure between type-1 diabetics and non-diabetic controls. Mean blood glucose concentrations were significantly higher in type-1 diabetic children than in controls. HbA_{1c} levels were also significantly higher in both male and female diabetic children as compared to control groups. Serum CRP levels were significantly higher in both male and female diabetic children as compared to the control group.

Table-1: Anthropometric characteristics of type-1 diabetics and non-diabetic controls

Variable	Controls	Diabetic type-1 patients	*p*-value
Number of subjects(n)	40	39	
Age(years)	09±16	09±16	
Male	20	19	
Female	20	20	
Duration of diabetes	Nil	≥1 year	
BMI(Kg/m^2)	16.4±2.03	17.9±3.37	>0.09
Systolic blood pressure(mm Hg)	100.75±13	99.74±10	>0.05
Diastolic blood pressure(mm Hg)	63.13±8	62.82±8	>0.05

Data is expressed as mean±standard deviation

Table-2: Cardiovascular risk markers (Serum CRP mg/l) in type-1 diabetic and non-diabetic controls

Gender	Type-1 diabetics	Non diabetic controls	*p*-value
Males	0.6±0.14	0.23±0.09	0.03*
Females	1.19±0.34	0.15±0.04	0.004*

Data expressed as Mean±standard error of mean (SEM)
*statistically significant

DISCUSSION

There are many studies about cardiovascular mortality and morbidity in diabetic adults and old age population with respect to different risk factors like dyslipidemia, hypertension, metabolic disease, obesity, and hyperglycemia but the risk factors about the cardiovascular disease in type-1 diabetic children have not been studied extensively.

The present study revealed that there was significant elevation of CRP levels in type-1 diabetic children at an early age despite that short duration of disease and higher levels of elevated CRP were observed in female diabetics compared to diabetic boys which showed that they were at a greater risk of developing atherosclerosis in future. C-reactive protein is known as a novel marker of low grade inflammation, which characterizes an atherosclerotic process in its early stages. Contrary to an extensive data on inflammatory markers in diabetes type-2 and metabolic syndrome in adults, little is known so far about the inflammatory process in diabetes type-1, especially in children.[15] Elevated levels of CRP has been observed in patients with type-2 diabetes mellitus[16] this is because of the induction of acute phase response by underlying intra-arterial inflammation. Another study has shown that CRP has a direct pro inflammatory effect on human endothelial cells and affects endothelial function.[17] Elevated CRP level has also been observed in obese children and adults.[18] An interesting but untested use for CRP is to motivate persons with moderate to high risk levels to improve their life styles or to comply with drug therapies.

CONCLUSION

Elevated CRP and altered lipid profile in type-1 diabetic children may predispose them to the development of early atherosclerosis. Their measurement will improve the prediction and early interventions in high risk diabetic children.

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