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Assessment of C - Reactive Protein and Albumin in Diabetic Subjects

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ABSTRACT

Hyperglycemia which usually characterizes Diabetes Mellitus (DM) stimulates the release of the inflammatory cytokines which result in the induction and secretion of acute phase proteins. Therefore, this study aimed at assessing the levels of C- reactive protein (CRP) and Albumin in Type -2 DM subjects. A total of 68 individuals were recruited; 26 were newly diagnosed type- 2 DM, 22 with type- 2 DM on treatment (Metformin) and 20 non diabetic subjects served as control. Fasting blood samples were collected from each participant for the determination of FBS by Glucose- peroxidase method, CRP by Enzyme linked immunosorbent assay (ELISA) method and Albumin by Bromocresol-Green method. The height and weight of each subject were measured using height gauge and bathroom scale to calculate body mass index. The result revealed that CRP was significantly higher in newly diagnosed type -2 DM subjects ($P< 0.001$) and type- 2 DM subjects on treatment when both groups were compared with controls while the reverse was the case for serum albumin. There was positive significant correlation ($P< 0.05$) and negative significant correlation ($P<0.01$) between CRP of the subjects with FBS and Albumin respectively. Elevated CRP and decreased albumin level were seen in Type -2 DM subjects. It was observed that CRP level was significantly reduced in DM subjects on treatment showing that the use of antidiabetic agent has a lowering effect on CRP. Therefore, the study concluded that CRP may serve as a useful marker of inflammation during diagnosis and management of type- 2 DM.

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic diseases in which there is high level of blood sugar (hyperglycemia) over a prolonged period resulting from defects in insulin secretion, insulin action or both[1,2]. DM is a chronic debilitating disease that affects large number of people of all socio-economic class throughout the world. In Africa, the total number of individuals with diabetes is 19.8 million; this number is expected to double by 2035 and in the recent time, diabetes is considered to be accountable for 8.6% of all deaths in the African region among people between age 20-79 years[3]. Nigeria has a prevalence of 5% as at 2013 and this has been estimated to increase to 5.5% by the year 2035[4]. However, from 2012 to 2014, diabetes prevalence was reported to be 5.27% in Nigeria while the rate in Ekiti state is at 2.24% to 3.19%.[5]

The pathophysiological hallmarkers of type 2 DM are insulin resistance and beta cell dysfunction[6]. It has been reported that the mechanisms of islet β cell failure are different in the progression of both type 1 and type 2 DM[7]. Diabetes is associated with a pro-inflammatory state and endothelial dysfunction. Hyperglycemia stimulates the release of the inflammatory cytokines which result in the induction and secretion of acute phase reactants by adipocytes. Type 2 DM alters the function of immune cell and produce inflammation which is chronic, low grade and associated with insulin resistance which develops during stress[8,9,10,11]. The insulin resistance overtime leads to complications that are caused by poorly controlled DM, persistence hyperglycemia which triggers the production of acute phase reactants[12]. The elevated synthesis of pro-inflammatory cytokine and acute phase proteins characterize the early stage of Type 2 DM and exhibit a graded increase with the disease progression[13].

Acute phase proteins (APPs) play important roles in various stages of the inflammatory reaction. In general, the main function of APPs is to defend the host against pathological damage, assist in the restoration of homeostasis and in the regulation of different stages of inflammation[14]. According to a report, the acute-phase proteins (C-reactive protein and albumin) are sensitive marker of inflammation and tissue damage[15]. Moreover, small elevations in C-reactive protein (CRP) concentrations have been shown to indicate increased risk for cardiovascular disease and possibly colon cancer[16]. CRP is also considered to be a major inflammatory cytokine that functions as a non specific defense mechanism in response to tissue injury or infection[17]. A major mechanism by which CRP plays a critical role in type

2 DM is primarily by the action on pancreatic β-cell[18,19]. CRP significantly inhibits cell proliferation and increases the rates of apoptotic cell death[20]. During the acute phase response, the demand for amino acids for synthesis of the positive APPs is markedly increased, which necessitates reprioritization of hepatic protein synthesis. Thus, albumin synthesis is down-regulated and amino acids are shunted into synthesis of positive APPs[21]. It has been reported that during the acute phase response 30–40% of hepatic protein anabolic capacity is used for the production of positive APPs[22]. Therefore, the assessment of serum CRP and Albumin will be of immense value in the diagnosis and management of type 2 DM.

MATERIALS AND METHODS

The ethical approval for the study was obtained from the ethical committee of the College of Medicine and Health Sciences, Afe Babalola University, Ado-Ekiti (ABUAD), Nigeria. The study involved 68 participants at Ekiti State University Teaching Hospital (EKSUTH). Each participant was informed about the nature of the study and they gave their consents before blood samples were collected from them. The subjects were grouped into newly diagnosed type 2 diabetic subjects (26), type 2 diabetic subjects on treatment (22) and apparently healthy subjects without the history of diabetes (20) which served as control subjects.

Blood samples were collected for the measurement of fasting plasma glucose, CRP and albumin from all participants. The weight and height of the participants were also measured using the height gauge and bathroom scales. Body mass index (BMI) was calculated for each individual by using weight/height (kg/m^2). Plasma glucose was determined using the Glucose oxidase-peroxidase method[23]. Serum CRP was determined using Enzyme-linked Immunosorbent Assay (ELISA) method[24]. Albumin was determined using colorimetric method[25].

STATISTICAL ANALYSIS

The results obtained were subjected to statistical analysis using the statistical package for social sciences (SPSS) version 20. The data generated were expressed as mean ± standard deviation (SD) while students't-test and correlation (r) were used to compare and relate the serum levels of all variables. Statistical significance level was set at $p < 0.05$.

RESULTS

Table 1 shows the correlation of CRP with Fasting Blood Glucose and Albumin in newly diagnosed type 2 DM, type 2 DM on treatment and control subjects.

Figure I show the results of all parameters between newly diagnosed type 2 DM subjects, type 2 DM subjects on treatment and control subjects. Fasting Blood Glucose, CRP and Albumin were statistically significant (P< 0.001) compared with control while BMI was not significant.

TABLE 1: CORRELATION OF CRP WITH FBS AND ALBUMIN IN ALL GROUPS.

Group	Correlation r (P value)	
	FBS	Albumin
CRP of Newly- diagnosed DM subjects (n=26)	0.744**(0.04)	-0.805**(0.001)
CRP of DM On- Treatment subjects (n=22)	0.552 (0.079)	-0.009 (0.978)
CRP of Control subjects (n=20)	0.021 (0.929)	-0.012 (0.958)

**. Correlation is significant at the 0.01 level (2-tailed).
*. Correlation is significant at the 0.05 level (2-tailed).

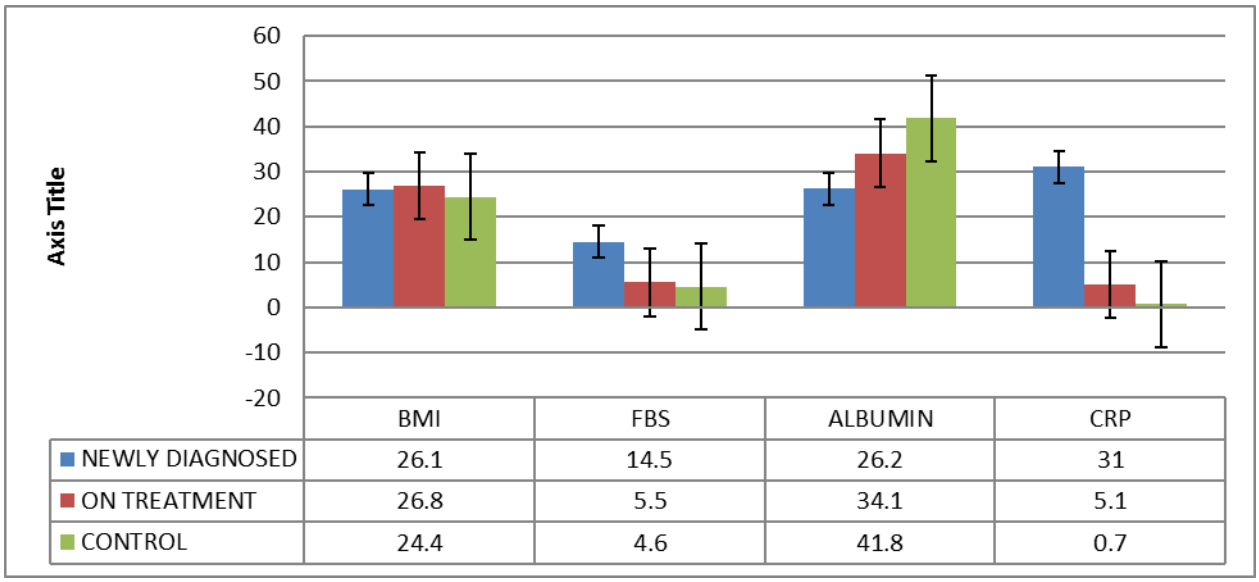

FIGURE 1: FBS, CRP, ALBUMIN AND BMI IN TYPE 2 DM AND CONTROL SUBJECTS

DISCUSSION

In this study, significant increase in CRP and FBS were observed in newly diagnosed type 2 DM subjects and type 2 DM subjects on treatment compared with control while there was significant decrease in albumin on the other hand. It has been shown that Type 2 DM alters the function of immune cell and produces inflammation which is chronic, low grade and associated with insulin resistance[11]. APPs which are inflammatory markers are thus synthesized in response to tissue damage and inflammation. This triggers cytokines and APPs such as CRP and Albumin which characterizes the early stage of type 2 DM and exhibits a graded increase in the disease progression[13]. During DM, persistent hyperglycemia causes increased production of positive acute phase reactants. This can be the reason for the increase in the CRP observed in the type 2 DM. Furthermore, it has been shown that an independent interrelationship exits between CRP levels and insulin resistance[26]. In addition, high blood glucose is known to accelerate chronic inflammation[27,28]. This study supports the works which showed the relationship between rising CRP levels and the onset of diabetes. Monitoring of conventional CRP levels during routine examination can lead to early diagnosis of diabetes. The role of antidiabetic agents on CRP can never be overemphasized because treatment has positive outcome in reducing the CRP level to lower risk value. This study agrees with another research which shows that CRP is relatively increased in poorly or non- controlled DM[29]. This implies that subjects with non-controlled diabetes are at a greater risk of disease progression and therefore more prone to its attendant complications.

It has also been shown that APPs concentration varies in response to inflammation which may have contributed to the decrease level of albumin type 2 DM. Negative APPs such as albumin shows decreased concentrations in newly diagnosed type 2 DM based upon the inflammatory response[30]. It has been shown that during the acute phase response, the demand for amino acids synthesis of positive APPs such as CRP is markedly increased, which necessitates reprioritization of hepatic protein synthesis. Thus, albumin synthesis is down-regulated and amino acids are shunted into synthesis of positive APPs[21]. If albumin level is reduced, there is the possibility that the liver has been affected and the synthetic function of the liver has been grossly affected[31]. This is because the liver has high functional reservoir for albumin which in turn makes albumin a useful parameter in assessing the synthetic function of the liver. This also shows that the antidiabetic agent (metformin) taken by the subjects

have positive effect on the liver to increase the albumin concentration in those type 2 DM on treatment.

It has been shown that BMI is the best measure of overweight and obesity, hence the reason for its measurement in this study. According to some researchers, overweight and obesity are risk factors for developing Type 2 DM[32,33,34] but there was no significant difference in BMI when control subjects were compared with both newly diagnosed type 2 DM subjects and those on treatment. The CRP has a significant positive correlation with FBS in newly diagnosed type 2 DM subjects but a significant negative correlation with albumin. However, CRP in type 2 DM subjects on treatment and control subjects did not show significant correlation with FBS and albumin. Lower CRP values among those on treatment compared to the newly diagnosed suggest that antidiabetic drugs have a lowering effect on CRP. However, CRP was not correlated with BMI in this study since it did not show significant increase or decrease in the subjects. Thus, CRP may serve as a marker of identifying individuals about to develop type 2 DM and also for monitoring treatment effectiveness.

CONCLUSION

It was established in this study that individuals with type 2 DM (either newly diagnosed or on treatment) have significantly higher CRP and lower albumin levels compared with individuals without DM. It was also established that CRP level was significantly reduced in Type 2 DM subjects on treatment showing that the use of antidiabetic agent has a lowering effect on CRP. Furthermore, CRP was positively correlated with FBS while it showed negative correlation with albumin. Therefore, the study concluded that CRP may serve as a useful marker of inflammation during diagnosis and management of type 2 DM.

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