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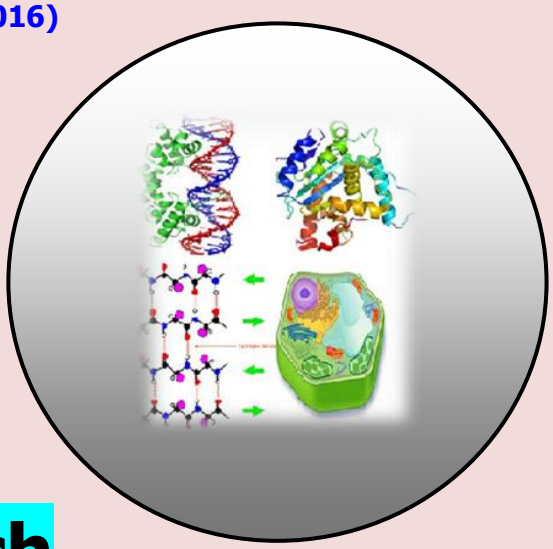

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A Cross Sectional Study Showing Association of C - reactive protein (C-RP) with Prediabetes and Diabetes in Indian Population

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ABSTRACT

C-reactive protein, a systemic inflammatory marker is synthesized by liver and play important role in pathogenesis of diabetes. Very few studies were conducted in India to show the association of CRP with prediabetes. The present study was coined to show the association of CRP with prediabetics and diabetics in Indian population. A cross sectional study, comprising of total 79 subjects was carried out in department of Physiology, KGMU, Lucknow. Among total 79 subjects, 63 were diabetics and 16 were prediabetics as per ADA guidelines (2010). Subjects with conditions or factors affecting metabolic parameters and CRP concentration were excluded from study. After the 8 hours of fasting, venous blood was withdrawn to measure fasting blood sugar. The postprandial blood sugar was estimated 2 hours after post OGTT with 75 gram glucose. Serum CRP concentration was measured by nephelometry method. For quantitative parametric datas student "t" test and for non parametric datas Mann- whitney U test was used. The Chi square test was used for categorical datas. The CRP concentration was comparatively higher (10.51±8.98 mg/l) in diabetics than 6.76±5.95 mg/l in prediabetics. (p=0.117). The CRP concentration increased in both prediabetic and diabetic group. It indicates that CRP is positively correlated with serum blood sugar level.

Keywords: Diabetes, Prediabetes and C-reactive protein.

INTRODUCTION

Diabetes, a metabolic syndrome is a huge problem worldwide. According to International Diabetes Federation (2013), India ranked on 2nd position (65.1 million) after the China (98.4 million).[1]

A study done by ICMR (2011) reported the national burden of diabetics and prediabetics. The datas showed that in India, 62.4 million were diabetics and 77.2 millions were prediabetics.[2]

Low grade inflammation play important role in the development of type II diabetes.[3] Many prospective studies have showed that increased CRP level was associated with increased risk of developing type II diabetes.[4-7] A study concluded that CRP concentration increased parallel as fasting or post load glucose levels increased in Japanese population.[8]

C-reactive protein (CRP) is synthesized by liver and play significant role in inflammation. Numerous studies have reported that the level of plasma CRP predicts the risk of development of type II diabetes in middle aged and elderly subjects.[4, 9-12] The level of various inflammatory parameters including CRP increased parallel to the various stages of glucose intolerance.[13-15] This study was designed to show an association of serum C – reactive protein with prediabetic and diabetic stage of glucose intolerence in Indian population.

MATERIAL AND METHODS

This is a cross sectional study, carried out in the department of Physiology in collaboration with department of Pathology and Medicine at King George's Medical University, Lucknow. On the basis of well defined inclusion and exclusion criteria, among total 79 consistents, 16 were pre-diabetics and 63 were diabetics.

Inclusion criteria

All diabetic and prediabetic subjects as per ADA guidelines (2010)

Exclusion criteria

Patients having systemic inflammation/ inflammatory diseases, patients with hypothyroidism or vit.B12 deficiency, chronic alcoholic, liver disease, chronic kidney disease etc were excluded.

Definition

Subjects were classified on the basis of the American Diabetic Association (ADA) Guidelines (2010) into pre-diabetic and diabetic groups.

Pre-diabetics were defined as those having fasting blood glucose level 100-125mg/dl or 2 hours oral glucose tolerance test with 75 gm of glucose, 140-199 mg/dl.

Diabetic patients were defined as those having fasting blood glucose ≥126 mg/dl or 2 hours oral glucose tolerance test with 75 gm of glucose, ≥ 200 mg/dl.

Biochemical analysis

After ethical approval from the institute and taking informed consent from the patients, total 5 ml. venous blood sample was drawn from each patient. 2 ml. blood was collected in fluoride vial for measuring blood sugar level and 3 ml. blood was taken in plain vial for measuring CRP level. Serum and plasma was separated and stored at -80 degree Celsius. Fasting blood sugar (FBS) and postprandial blood sugar (PPBS) estimation was done by glucose oxidaseperoxidase method (Merck Kit). Estimation of C-reactive protein was done by the commercially available Kit (Agappe Diagnostics Ltd. India) with the help of MISPA instrument base on nephelometry method.

Statistical Analysis

Continuous data were summarized as Mean± SD (standard deviation). Groups were compared by independent Student's't' test and the results were also validated with non parametric Mann-Whitney U test. Discrete (categorical) observations were summarized in % and compared by chi-square ($\chi 2$) test. Pearson correlation analysis was used to assess association between the variables. Diagnostic evaluation of C-RP levels was done by ROC (receiver operating characteristic) curve analysis. A two-sided ($\alpha=2$) $p<0.05$ was considered statistically significant. SPSS (version 18.0) and STATISTICA (version 6.0) statistical software were used for the analyses.

RESULT

The demographic variables such as age, sex and blood sugar level both fasting and postprandial were briefly represented in **table 1**. The mean age ± SD of pre-diabetic and diabetic groups were 49.50 ± 11.57 yrs of age and 55.14 ± 10.79 yrs of age, respectively. The mean age of diabetic group was comparatively higher than Pre diabetic group but statistically the difference was not significant. ($p=0.069$) The percent of male population was higher than female population in both the groups.

The mean level of both FBS and PPBS were statistically higher in Diabetic group than Pre diabetic group. ($p<0.05$) On comparing, the mean age and % age of males and females were found similar between the two groups. **Table 2 s**howed the distribution of C-reactive protein (C-RP) in both the groups. The mean CRP was comparatively higher in Diabetic group than Pre diabetic group but statistically levels did not differ between the groups ($p=0.117$). The diagnostic accuracy (cut off value) of C-RP levels for pre diabetics and diabetics were summarized in **table 3** and shown graphically in **Fig. 2** respectively. The cut off value (criterion) of C-RP level was >6.1 Mg/l and at this value it is discriminating diabetics with 66.67% sensitivity (95% CI=53.7-78.0) and 81.25% specificity (95% CI=54.3-95.7).

Table 1. Distribution of age, gender, FBS and PPBS in pre-diabetic and diabetic patients

Characteristics	Pre diabetics (n=16)	Diabetics (n=63)	χ2/t value	P_ value
Age (yrs)	49.50 ± 11.57	55.14 • ± 10.79	1.84	0.069
Gender:				
Male	11 (68.8%)	49 (77.8%)	0.57	0.451
Female	5 (31.3%)	14 (22.2%)	0.57	0.451
FBS (mg/dl)	111.50 ± 10.56	142.66 ± 44.39	2.77	0.007*
PPBS (mg/dl)	168.75 ± 17.34	216.04 ± 52.89	3.51	0.001*

*Significant ($p<0.05$), Values are in % (Categorical data) and Mean ± SD (Continuous data), FBS (Fasting Blood Sugar), PPBS (Postprandial Blood Sugar)

Figure 1. Diagnostic accuracy of CRP levels for prediabetics and diabetics.

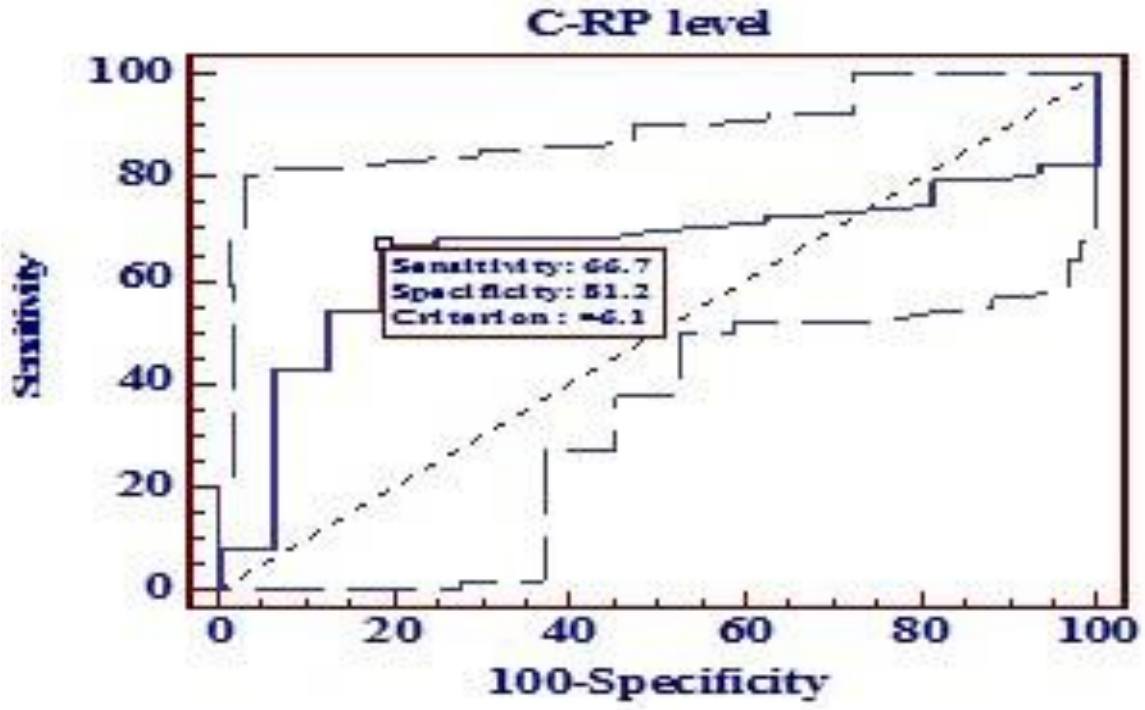

Table 2. Distribution of CRP levels in pre-diabetic and diabetic patients.

Characteristics	Pre diabetics (n=16)	Diabetics (n=63)	t value	p value
CRP (mg/l)	6.76 ± 5.95	10.51 ± 8.98	1.58	0.117

*Values are in Mean ± SD, C-RP (C - reactive protein)

Table 3. Diagnostic accuracy of CRP levels for diabetics and pre diabetics.

Variables	Criterion (cut off value)	Sensitivity (95% CI)	Specificity (95% CI)	AUC	"P" value	+LR	-LR	+PV	–PV
C-RP	>6.1 (Mg/l)	66.67 (53.7-78.0)	81.25 (54.3-95.7)	0.656	0.029	3.56	0.41	93.3	38.2

*p value <0.05(Significant), +LR: Positive likelihood ratio, -LR- Negative likelihood ratio, +PV: Positive predictive value, -PV: Negative predictive value

DISCUSSION

In this prospective cross sectional study the CRP level did not differ significantly between the diabetic and pre-diabetic group but it was comparatively higher in diabetic group than pre diabetic group *i.e.* there is increasing trend of c-reactive protein in pre-diabetic stage to diabetic stage of glucose intolerance. These findings of our study is supported by previous study which showed that CRP levels were significantly higher in both diabetic men and women as compared to their nondiabetic counterparts.[16] Similarly a nested case control also reported the positive correlation of CRP with development of type II diabetes.[4] Increased CRP level was also associated with increased risk of development of type I diabetes.[17] Diabetes is more common in obese individuals however we did not include the obesity as a variable in our study. A study suggested the positive correlation of obesity, CRP level and development of diabetes.[18] However; some studies demonstrated an independent role for CRP in the development of diabetes.[19, 20] In our study, CRP level was higher in pre-diabetic patients than in normal individuals. This observation is supported by previous cross sectional study which demonstrated that elevated hsCRP levels are independently associated with risk of IFG and IGT in Indians.[21] Significant atherogenic changes (which is represented by hsCRP level occurred in patients with IFG & IGT than in patients with NGT.[22] The cut off value (criterion) of CRP level in our study was >6.1 mg/l and at-this value it is discriminating diabetics with 66.67% sensitivity and 81.25% specificity. There are some limitations in our study such as the sample size was small and some other important risk factors like obesity and metabolic syndrome were not included in the study. Although it was multifactorial but as per our study findings, it may be concluded that high CRP levels may play a significant role in progression of diabetes. The findings may be used as a predictor of diabetes at its earlier stage, but further studies with large sample size are required to establish the CRP levels as a predictor for diagnostic purpose.

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REFERENCES

IDF Diabetes Atlas. 6th edition. 2013

Anjana, R.M., Pradeepa, R., Deepa, M., Datta, M., Sudha, V. and Unnikrishnan, R. (2011). Prevalence of diabetes and prediabetes (impaired fasting glucose and/or impaired glucose tolerance) in urban and rural India: phase I results ICMR-INDIAB study. Diabetologia; 54:3022-7.

John, C.P. and Pickup Dphil Frcpath (2004). Inflammation and activated innate immunity in the pathogenesis of type II diabetes. Diabetes Care 2004; 27: 813–23.

Pradhan, A.D., Manson, J.E., Rifai, N., Buring, J.E. and Ridker, P.M. (2001). C-reactive protein, interleukin 6 & risk of developing type II diabetes mellitus, J. Am. Med. Assoc, 286; 327–34.

Thorand, B., Lowel, H., Schneider, A., Kolb, H., Meisinger, C., Frohlich, M., et al. (2003). C-reactive protein as a predictor for incident diabetes mellitus among middle-aged men: results from the MONICA Augsburg cohort study, 1984–1998, Arch. Intern. Med. 2003; 163 : 93–9.

Nakanishi, S., Yamane, K., Kamei, N., Okubo, M. and Kohno, N. (2003). Elevated C-reactive protein is a risk factor for the development of type II diabetes in Japanese Americans. Diabetes Care; 26: 2754–7.

Laaksonen, D.E., Niskanen, L., Nyyssonen, K., Punnonen, K., Tuomainen, T.P., Valkonen, V.P., et.al. (2004). C-reactive protein and the development of the metabolic syndrome and diabetes in middle-aged men. Diabetologia 2004; 47: 1403–10.

Doi, Y., Kiyohara, Y., Kubo, M., Tanizaki, Y., Okubo, K., Ninomiya, T., et. al (2005). Relationship Between C-Reactive Protein And Glucose Levels In Community- Dwelling Subjects Without Diabetes: Diabetes Care. 2005; 28 :1211-3.

Barzilay, J.I., Abraham, L., Heckbert, S.R., Cushman, M., Kuller, L.H., Resnick, H.E., et. al (2001). The relation of markers of inflammation to the development of glucose disorders in the elderly: the Cardiovascular Health Study. Diabetes 2001; 50: 2384– 9.

Freeman, D.J., Norrie, J., Caslake, M.J., Gaw, A., Ford, I., Lowe, G.D., et. al (2002). C-reactive protein is an independent predictor of risk for the development of diabetes in the West of Scotland Coronary Prevention Study. Diabetes 2002; 51:1596–1600.

Festa, A., D'Agostino, R., Tracy, R.P. and Haffner, S.M. (2002). Elevated levels of acutephase proteins and plasminogen activator inhibitor-1 predict the development of type II diabetes: the Insulin Resistance Atherosclerosis Study. Diabetes 2002; 51:1131– 7.

Thorand, B., Lowel, H., Schneider, A., Kolb, H., Meisinger, C., Frohlich, M., et. al. (2003). C-reactive protein as a predictor for incident diabetes mellitus among middle-aged men. Arch Intern Med 2003; 163 : 93–9.

McMillan, D.E. (1989). Increased levels of acute phase serum proteins in diabetes. Metabolism 1989; 38 :1042–6.

Ford, E.S. (1999). Body mass index, diabetes, and C-reactive protein among U.S. adults. Diabetes Care; 22: 1971–7.

Kurktschiev, T., Henkel, E., Koehler, C., Karrei, K. and Hanefeld, M. (2002). Subclinical inflammation in newly detected type II diabetes and impaired glucose tolerance. Diabetologia; 45 :151.

Mahajan, A., Tabassum, R., Chavali, S., Dwivedi, O.P., Bharadwaj, M., Tandon, N., et. al (2009). High sensitivity C-reactive protein levels and type II diabetes in urban North Indians. J. Clin. Endocrinol. Metab. 2009; 94 : 2123-7.

Kilpatrick, E.S., B.G. Keevil, C. Jagger, R.J. Spooner and M. Small (2000). Determinants of raised C-reactive protein concentration in type 1 diabetes. Q. J. Med. 2000; 93: 231-6.

Trayhurn, P. and Beattie, J.H. (2001). Physiological role of adipose tissue: white adipose tissue as an endocrine and secretary organ. Proc. Nutr. Soc. 2001; 60 : 329-39.

Barzilay, J.I., Abraham, L., Heckbert, S.R., Cushman, M., Kuller, L.H., Resnick, H.E. and Tracy, R.P. (2001). The relation of markers of inflammation to the development of glucose disorders in the elderly: the cardiovascular health study. Diabetes 2001; 50: 2384-9.

Hu, F.B., Meigs, J.B., T.Y. Li, Rifai, N. and Manson, J.E. (2004). Inflammatory markers and risk of developing type II diabetes in women. Diabetes 2004; 53: 693-700

Jaiswal, A., Tabassum, R., Podder, A., Ghosh, S., Tandon, N. and Bharadwaj, D. (2012). Elevated level of C-reactive protein is associated with risk of prediabetes in Indians. j.atherosclerosis; 222:495-501.

Chakarova, N., Tankova, T., Atanassova, I. and Dakovska, L. (2009). Serum lipid and hsCRP levels in prediabetes – impaired fasting glucose (IFG) and impaired glucose tolerance (IGT). j.diabres; 86:56-60.

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