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Original Research Article

Correlation of CRP level with glycemic control in diabetic foot patients and its sequelae

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ABSTRACT

Background: Diabetes mellitus is a major public health problem globally and in Indian population and diabetic foot is reported as the most common cause of non-traumatic amputation of the lower limbs in India. There is renewed interest in various inflammatory markers and their association with various chronic complications of diabetes mellitus. There is a scarcity of data on the subject in Indian population.
Methods: The current study was a cross sectional study of 100 patients admitted to a Diabetic foot in Department of General Surgery, Stanley medical college and Hospital between January 2012-November 2012. The CRP level and fasting and plasma glucose levels were considered as the relevant variables for statistical analysis.
Results: A total of 100 patients were included in the final analysis. The proportion of subjects with Wagners, grade 1, grade 2, 3, 4 and 5 ulcers were 48%, 27%, 16%, 3% and 6% respectively. Among the study population, 73% of patients had CRP value greater than 40 and 27% patients had CRP value less than 40. The proportion of subjects with Higher CRP level (>40) showed increasing trend with increasing level of fasting blood sugar and post prandial blood sugar in the study population. The proportion of people who underwent amputation was 27.5% in people with CRP value >40 and it was only 6.85% of people with CRP value <40, the association between CRP values and amputation was statistically significant. (P value 0.046).
Conclusions: The study has established a strong positive association between poor blood sugar control and elevated CRP levels in the study population. The study has also documented a positive association between higher CRP levels and amputation.

Keywords: Amputation, C-Reactive protein, Diabetic foot, Diabetes mellitus

INTRODUCTION

Inflammation has been found to be an essential factor in the atherosclerotic disease pathogenesis.[1,2] High-sensitivity C-reactive protein (CRP) is an acute-phase response protein that is considered both a marker of inflammation and an independent predictor of cardiovascular disease (CVD), including myocardial infarction, stroke, peripheral arterial disease, and sudden cardiac death in apparently healthy people.[3-5] CRP may also act directly on atherosclerosis, inhibiting prostacyclin synthesis in endothelial cells and promoting adhesion molecule expression, resulting in endothelial dysfunction.[6-9] Growing evidence indicates that diabetic individuals have higher concentrations of CRP than nondiabetic individuals, suggesting an increased role of inflammation in the accelerated atherosclerosis seen in these patients.[10-14] Diabetes is a serious public health problem that has been increasing exponentially across the globe. The risk of CVD is two- to four times higher in type 2 diabetics and >50% of all diabetic patients die of CVD.[15] One of the common complications of long term

diabetes is diabetic foot and bacterial infections are the commonest foot infections of patients with diabetes in clinical practice.[16] These infections and their squeal cause considerable disability and often the reason for lower-limb amputation.[17]

Even with appropriate treatment, some patients must undergo major amputation or a limb salvage operation.[18] These operations are not only a huge emotional and social burden to the patients due to physical impairment, but also a financial burden.[19] We hypothesized that prolonged hyperglycemia can initiate active micro inflammation systemically as indicated by a rising in CRP levels and such inflammation might be associated with the various complications of the diabetic foot.

The objectives of the present study were to assess the association between glycemic control and serum CRP levels in patients with type 2 Diabetes mellitus presenting with diabetic foot and to correlate the level of CRP with sequelae of diabetic foot in the study population.

METHODS

The current study was a cross sectional study of 100 patients admitted with a Diabetic foot in Department of General Surgery, Stanley medical college and Hospital between January 2012 to November 2012. Subjects who were critically ill were excluded from the study. The study was approved by Institutional Human Ethics committee and informed written consent was obtained from all the eligible participants.

After obtaining the informed consent, each participant underwent thorough clinical examination. 5 ml of venous blood was drawn under asceptic conditions and was transported to the laboratory for routine blood investigations. Blood sugar values both fasting and post prandial and c reactive protein levels were checked in all patients. Patients underwent appropriate evaluation as per the hospital protocol and were appropriately managed. The CRP level and fasting and plasma glucose levels were considered as the relevant variables for statistical analysis.

Descriptive analysis was done by mean and standard deviation for quantitative variables and frequency and proportions for categorical variables. The values were grouped into categories using standard cut-off values. The association between blood sugar levels and CRP levels was done by cross tabulation and comparison of percentages using Chi square test. The data was analyzed using IBM SPSS statistical software version 21.

RESULTS

A total of 100 patients were included in the final analysis. The fasting blood sugar value ranges from 127 to 225. minimum value is presentation 127 and the maximum value 225.patients are categorized into five groups to find the distribution and they are shown in the table below. The proportion of subjects with fasting blood sugar between 126 to 146, 147 to 166, 167 to 186 was 21%, 27% and 22% respectively. Among 17% of the study population, the fasting blood sugar levels were 187 to 206 and 13% of the subjects had fasting glucose >206 gm/dl. Similarly, patients are classified into five groups based on the post prandial blood sugar values.

Lowest value 203 and highest sugar level 394. The distributions are shown in the table above. The proportion of subjects, with blood sugar level between 200 to 400 was 18%. About 31% and 23% of the subjects had post prandial blood sugar between 241 to 280 and between 2821 to 320 gm/dl. The proportion with post prandial sugar level between 321 to 360 and above 360 were 15% and 23% respectively (Table 1).

Table 1: Descriptive analysis of fasting blood sugar in study population (N=100).

Parameter	Number	Percentage
Fasting blood sugar		
126-146	21	21%
147-166	27	27%
167-186	22	22%
187-206	17	17%
>206	13	13%
Post-prandial blood sugar		
200-240	18	18%
241-280	31	31%
281-320	23	23%
321-360	15	15%
>360	13	23%

The proportion of subjects with Wagners, grade 1, grade 2, 3, 4 and 5 ulcers were 48%, 27%, 16%, 3% and 6% respectively. Among the study population, 73% of patients had CRP value greater than 40 and 27% patients had CRP value less than 40. Out of 100 patients 13% got amputated and 87% patients wound healed without complications (Table 2).

Table 2: Descriptive analysis of Wagner's grading in study population (N=100).

Wagner's grading	No of patients	Percentage
Grade 1	48	48%
Grade 2	27	27%
Grade 3	16	16%
Grade 4	3	3%
Grade 5	6	6%
CRP value		
< 40	73	73%
>40	27	27%
Outcome		
Amputated	9	9%
Healed	91	91%

The proportion of subjects with Higher CRP level (>40) showed increasing trend with increasing level of fasting blood sugar in study population. It was only 14.29% in people with fasting sugar level, between 126 to 146 gm/dl and increased constantly and was 61.54% in people with fasting blood sugar level >206mg/dl. The association between fasting blood sugar level and CRP values was statistically significant (P value 0.020).

The proportion of subjects with Higher CRP level (>40) showed increasing trend with increasing level of post prandial blood sugar in study population from 11.11% in people with PPBS 200 to 240 to 61.54% in people with PPBS more than 360.

The association between PPBS and CRP values was statistically significant (P value 0.012) (Table 3).

Table 3: Association between sugar levels and CRP values in the study population (N=100).

Parameter	CRP > 40 (%)	CRP < 40 (%)	Chi-square value	P value
FBS (Fasting blood sugar)				
126-146 (N=21)	3 (14.29)	18 (85.71)		
147-166 (N=27)	5 (18.52)	22 (81.48)		
167-186 (N=22)	5 (21.74)	18 (78.26)	11.561	0.020
187-206 (N=17)	6 (35.29)	11 (64.71)		
>206 (N=13)	8 (61.54)	5 (38.46)		
PPBS (Post prandial blood sugar)				
200-240	2 (11.11)	16 (88.89)		
241-280	6 (19.35)	25 (80.65)		
281-320	5 (21.74)	18 (78.26)	12.702	0.012
321-360	6 (40)	9 (60)		
>360	8 (61.54)	5 (38.46)		

The proportion of people who underwent amputation was 27.5% in people with CRP value >40 and it was only 6.85% in people with CRP value <40, the association between CRP values and amputation was statistically significant (p value 0.046) (Table 4).

Table 4: Association between CRP value and amputation in study population (N=100).

CRP value	Amputation (%)	No amputation (%)	Chi square value	P value
>40 (N=27)	8 (27.5)	21 (72.5)	8.02	0.046
< 40 (N=73)	5 (6.85)	68 (93.15)		

DISCUSSION

Diabetes and its complications is one of the most common cause of death. Prevalence of Diabetes worldwide is around 252 million. prevalence of diabetes in India is 42 million and age of distribution is middle and elderly people. There is 20% risk of developing diabetic ulcer in diabetic patients over a period of time One of the earliest discovered biomarkers used to diagnose infection is CRP.[20] Diabetic foot is a common but serious complication in lower extremity with 15-25% are estimated to experience such ulcers during their lifetime.[21] Autonomic neuropathy, poor glycemic control, high pressure in soles are the factors which contributes to development of ulcer and one of the cause of non-traumatic amputation of lower limb. The finding indicate a significant level of correlation between glycemic control CRP level and outcome in terms of wound healing and amputation.

Of the 100 patients with diabetic foot (DF), 27 had CRP levels higher than 40, of which nine had their foot amputated, while among others the wounds healed after surgical treatment. Lin C W et al. after analyzing 90 diabetic foot patients and concluded that reduced c reactive protein level (<50mg/l) indicates good prognosis in diabetic foot patients. Baris A kinci, of Dokuz Eylul university hospital (2003-2008) observed 165 ulcer patients and concluded that post treatment CRP values were strongly related to amputations.

The proportion of subjects with Higher CRP level (>40) showed increasing trend with increasing level of fasting blood sugar in the study population. The association between fasting blood sugar level and CRP values was statistically significant. (p value 0.020).

The proportion of subjects with Higher CRP level (>40) showed increasing trend with increasing level of post prandial blood sugar in study population from 11.11% in people with PPBS 200 to 240 to 61.54% in people with PPBS more than 360. The association between PPBS and CRP values was statistically significant. (p value 0.012).

Early diagnosis and adequate treatment are therefore essential to prevent amputation.

CONCLUSION

The study has established a strong positive association between poor blood sugar control and elevated CRP levels in study population and the study has also documented positive association between higher CRP levels and amputation.

Limitations

The major limitation of the study was the role of various potential confounders like demographic factors, co-morbidities etc. could not be evaluated by appropriate statistical methods, due to relatively smaller sample size. The role of potential bias due to convenient sampling also could not be quantified.

Recommendations

There is a need for further large scale prospective studies on the subject to understand the exact role of CRP and its association with complications of diabetes, independent of the potential confounding variables.

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REFERENCES

1. Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. New England J Med. 2005;352(16):1685-95.
2. Atherosclerosis RR. An inflammatory disease. New Engl J Med. 1999;340:115-26.
3. Pai JK, Pischon T, Ma J, Manson JE, Hankinson SE, Joshipura K, et al. Inflammatory markers and the risk of coronary heart disease in men and women. New England J Med. 2004;351(25):2599-610.
4. Ridker PM WP, Grundy SM. Should C-reactive protein be added to metabolic syndrome and to assessment of global cardiovascular risk?. Circulation. 2004;109:2818-25.
5. Schulze MB, Rimm EB, Li T, Rifai N, Stampfer MJ, Hu FB. C-reactive protein and incident cardiovascular events among men with diabetes. Diabetes Care. 2004;27(4):889-94.
6. Jialal I DS, Venugopal SK. C-reactive protein: risk marker or mediator in atherothrombosis?. Hypertension. 2004;44(1):6-11.
7. Venugopal SK DS, Jialal I. C-reactive protein decreases prostacyclin release from human aortic endothelial cells. Circulation. 2003;108:1676-8.
8. Pasceri V WJ, Yeh ET. Direct proinflammatory effect of C-reactive protein on human endothelial cells. Circulation. 2000;102:2165-8.
9. Verma S, Wang CH, Li SH, Dumont AS, Fedak PW, Badiwala MV, et al. A self-fulfilling prophecy. Circulation. 2002;106(8):913-9.
10. Aronson D, Bartha P, Zinder O, Kerner A, Shitman E, Markiewicz W, et al. Association between fasting glucose and C-reactive protein in middle-aged subjects. Diabetic Medicine. 2004;21(1):39-44.
11. De Rekeneire N, Peila R, Ding J, Colbert LH, Visser M, Shorr RI, et al. Diabetes, hyperglycemia, and inflammation in older individuals. Diabetes Care. 2006;29(8):1902-8.
12. King DE MAr, Buchanan TA, Pearson WS. C-reactive protein and glycemic control in adults with diabetes. Diabetes Care. 2003;26:1535-9.
13. Bruno G, Fornengo P, Novelli G, Panero F, Perotto M, Segre O, et al. C-reactive protein and 5-year survival in type 2 diabetes: the Casale Monferrato Study. Diabetes. 2009;58(4):926-33.
14. Ford ES. Body mass index, diabetes, and C-reactive protein among US adults. Diabetes care. 1999;22(12):1971-7.
15. Haffner S LS, Ro¨nnemaa T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med. 1998;339:229-34.
16. Mendes JJ, Marques-Costa A, Vilela C, Neves J, Candeias N, Cavaco-Silva P, et al. Clinical and bacteriological survey of diabetic foot infections in Lisbon. Diabetes Research Clinical Practice. 2012;95(1):153-61.
17. Bengalorkar GM NK. Diabetic foot infections-A review. Int J Biol Med Res. 2011;2(1):453- 60.
18. Singh N AD, Lipsky BA. Preventing foot ulcers in patients with diabetes. JAMA. 2005;293:217-28.
19. Driver VR, Madsen J, Goodman RA. Reducing amputation rates in patients with diabetes at a military medical center. Diabetes Care. 2005;28(2):248-53.
20. Standage SW WH. Biomarkers for pediatric sepsis and septic shock. Expert Rev Anti Infect. 2011;9(1):71-9.
21. Cavanagh PR LB, Bradbury AW, Botek G. Treatment for diabetic foot ulcers. Lancet. 2005;366:1725-35.

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