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Correlation of C-Reactive Protein Level with Glycemic Control in Diabetic Foot Patients and Its Sequelae: A Prospective Cross-Sectional Observational Study.

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Abstract

Background:
Diabetic foot ulcer is a serious lower-extremity complication of type 2 diabetes mellitus and is strongly influenced by infection, vascular compromise, neuropathy, and adequacy of glycemic control. C-reactive protein is an accessible inflammatory marker that can support risk assessment in patients with infected or progressive diabetic foot lesions.

Objectives:
To assess the relationship between C-reactive protein levels and glycemic control among patients with diabetic foot and to evaluate its association with healing and amputation outcomes.

Methods:
This prospective observational study included 100 patients with type 2 diabetes mellitus and diabetic foot admitted to the Department of General Surgery, King George Hospital, Visakhapatnam, from January 2024 to December 2024. Fasting blood sugar, postprandial blood sugar, and C-reactive protein were measured. Ulcer severity was graded using Wagner's classification. Patients received institutional medical and surgical care, and outcomes were classified as healed or amputated. Descriptive statistics, Fisher's exact test, and correlation analysis were used.

Results:
Fasting blood sugar ranged from 126 to 225 mg/dL, and postprandial blood sugar ranged from 200 to 398 mg/dL. Wagner grade 1 was the most common presentation. Overall, 89 patients healed, and 11 underwent amputation. C-reactive protein was above 40 mg/L in 34 patients. All amputations occurred in this elevated C-reactive protein group, while no amputation was recorded among patients with C-reactive protein below 40 mg/L. C-reactive protein showed statistically significant positive correlations with postprandial blood sugar and fasting blood sugar.

Conclusion:
Elevated C-reactive protein was associated with poor glycemic control, greater ulcer severity, delayed wound recovery, and amputation risk in diabetic foot patients.

Recommendations:
Routine combined assessment of glycemic indices, ulcer grade, and C-reactive protein should be used for early risk stratification and timely multidisciplinary care.

Keywords: *Diabetic foot; C-reactive protein; Glycemic control; Fasting blood sugar; Postprandial blood sugar; Wagner classification; Amputation; Wound healing.*
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Introduction

Diabetic foot ulcer represents one of the most disabling and resource-intensive complications of diabetes mellitus. It develops through the combined effects of peripheral neuropathy, altered plantar pressure, peripheral arterial disease, infection, impaired immunity, and delayed tissue repair. Contemporary reviews describe diabetic foot ulcer as a recurrent condition rather than a single wound episode, with considerable risk of hospitalization, amputation, and mortality after ulcer onset [1,6]. International guidelines, therefore, emphasize early recognition, structured classification, offloading, infection control, vascular assessment, and multidisciplinary management to reduce avoidable limb loss [2-5].

The pathophysiology of diabetic foot is closely related to chronic hyperglycemia. Poor glycemic control interferes with neutrophil function, collagen deposition, angiogenesis, endothelial function, and epithelial migration. These abnormalities delay granulation, increase bacterial persistence, and reduce the effectiveness of routine wound care. Hyperglycemia also contributes to neuropathy and vascular disease, which together increase the likelihood of ulcer formation, ulcer progression, and recurrent tissue breakdown [1,4]. In clinical practice, fasting blood sugar and postprandial blood sugar remain useful bedside indicators for short-term glycemic status during admission, especially when patients require frequent wound assessment, debridement, antibiotics, or surgical decision-making.

C-reactive protein (CRP) is an acute-phase reactant synthesized mainly by hepatocytes under the influence of inflammatory cytokines. In diabetic foot disease, CRP is not a disease-specific marker; however, it reflects the inflammatory burden associated with soft-tissue infection, abscess formation, osteomyelitis, and tissue necrosis. Earlier diagnostic studies showed that CRP can help differentiate infected from non-infected ulcers, particularly when clinical signs are muted in patients with diabetes [8]. A meta-analysis also supported a significant association between CRP and diabetic foot ulcer infection [14]. In adults with diabetes, elevated CRP has been linked with poorer glycemic control, suggesting that metabolic dysregulation and systemic inflammation interact in a clinically relevant manner [9].

Outcome prediction in diabetic foot requires more than wound inspection alone. Ulcer depth, infection, ischemia, Wagner grade, glycemic indices, and inflammatory markers together guide the intensity of treatment and timing of surgical intervention [3,5,7]. Previous cohort studies reported that infection, peripheral arterial disease, and systemic inflammatory response influence healing, hospital stay, and amputation risk [10-12]. Nevertheless, local hospital-based data remain valuable because bacterial burden, access to care, referral timing, and treatment pathways differ across clinical settings.

The present study was undertaken with the objective of correlating CRP levels with glycemic control in patients with type 2 diabetes mellitus presenting with diabetic foot. The study also aimed to determine the association of CRP levels with conservative healing and amputation outcomes, and to describe the distribution of fasting blood sugar, postprandial blood sugar, Wagner grade, CRP category, and final clinical outcome among admitted diabetic foot patients.

Materials and Methods

Study design and setting

This hospital-based prospective cross-sectional observational study was conducted in the Department of General Surgery, King George Hospital, Visakhapatnam, Andhra Pradesh, India, a tertiary care teaching hospital affiliated with Andhra Medical College. The hospital serves as a major referral center for coastal Andhra Pradesh and neighboring regions, providing specialized medical and surgical services to both urban and rural populations. The study was conducted over a period of one year, from January 2024 to December 2024, to evaluate the relationship between inflammatory status, glycemic control, diabetic foot severity, and short-term clinical outcomes among admitted diabetic foot patients.

Study Population and Sample Size

The study population comprised patients with type 2 diabetes mellitus presenting with diabetic foot lesions and requiring admission under the Department of General Surgery. A total of 100 patients were included in the study.

The sample size was calculated using the single population proportion formula:

$$n = Z^2P(1-P)/d^2$$

Assuming a prevalence of elevated CRP among diabetic foot patients of 50%, with a 95% confidence level (Z=1.96) and absolute precision of 10%, the minimum required sample size was estimated to be 96 participants. Considering possible exclusions and incomplete data, a total sample size of 100 patients was included. Consecutive sampling was employed, and all eligible patients admitted during the study period

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were recruited until the required sample size was achieved.

Eligibility criteria

Patients were eligible when they had type 2 diabetes mellitus under treatment, presented with diabetic foot, and provided written informed consent. Patients were excluded when they had clinical or biochemical evidence of sepsis from a source other than diabetic foot, active autoimmune disease such as rheumatoid arthritis, systemic lupus erythematosus, or systemic sclerosis, or when written consent was not provided.

Clinical assessment and investigations

All patients underwent history taking, clinical examination, and foot assessment. Admission fasting blood sugar, postprandial blood sugar, and CRP values were recorded. Blood sugar and CRP estimation were performed using standard institutional laboratory methods. Diabetic foot severity was graded according to Wagner's classification, a widely used clinical grading system for stratifying ulcer depth, abscess, osteomyelitis, localized gangrene, and extensive gangrene [5,7]. Wound swab or pus culture and sensitivity, routine blood tests, and radiological evaluation were performed as clinically indicated. The use of inflammatory markers in diabetic foot assessment is supported by previous studies evaluating CRP in ulcer infection [8,14].

Treatment protocol and outcome assessment

Patients were managed according to the institutional protocol with medical optimization, glycemic control, antibiotics guided by culture and sensitivity when available, wound dressing, debridement, and surgical intervention whenever indicated. Serial blood sugar values were documented during admission. CRP levels were followed during treatment until discharge. The outcome was categorized as healed or amputated. Healing indicated adequate clinical improvement with wound recovery under conservative or surgical wound care, whereas amputation indicated removal of the affected part because of advanced infection, gangrene, tissue loss, or non-salvageable disease.

Variables

The primary outcome variables were wound healing and amputation. The primary predictor variable was serum C-reactive protein level. Other study variables included fasting blood sugar, postprandial blood sugar, Wagner ulcer grade, age, sex, and final clinical outcome. CRP was categorized as <40 mg/L and >40 mg/L for outcome analysis.

Bias

Selection bias was minimized by consecutively recruiting all eligible patients admitted during the study period. Measurement bias was reduced by using standardized laboratory methods for the estimation of blood glucose and C-reactive protein levels. Uniform clinical criteria, including Wagner's classification, were used for ulcer assessment. Data collection was performed using a structured proforma to ensure consistency and completeness.

Ethical Considerations

Ethical approval for the study was obtained from the Institutional Ethics Committee of Andhra Medical College and King George Hospital, Visakhapatnam, Andhra Pradesh, before commencement of the study.

Informed Consent

Written informed consent was obtained from all study participants before enrollment. Participants were informed regarding the objectives of the study, confidentiality of collected information, voluntary participation, and their right to withdraw from the study at any time without affecting their treatment.

Statistical analysis

Data were entered and analyzed using Microsoft Excel and SPSS version 26.0. Qualitative variables were expressed as frequencies and percentages. The association between CRP category and outcome was tested using Fisher's exact test. Correlation analysis was performed to assess the relationship of CRP with fasting blood sugar and postprandial blood sugar. A p-value of 0.05 or less was considered statistically significant.

Results

During the study period, 112 patients with diabetic foot were assessed for eligibility. Eight patients did not fulfill the inclusion criteria, and four patients declined participation. Consequently, 100 eligible patients were enrolled and included in the final analysis.

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A total of 100 diabetic foot patients were included in the final analysis. All patients underwent glycemic assessment, CRP measurement, ulcer grading, and outcome evaluation during admission. The fasting blood sugar values ranged from 126 to 225 mg/dL. The largest proportion of patients belonged to the 167-186 mg/dL group, followed by the 147-166 mg/dL group. The distribution of fasting blood sugar is presented in Table 1.

Table 1. Distribution of study subjects according to fasting blood sugar

Fasting blood sugar (mg/dL)	Number of patients	Percentage
126-146	19	19.0
147-166	25	25.0
167-186	26	26.0
187-206	16	16.0
>206	14	14.0
Total	100	100.0

Values are expressed as numbers and percentages.

Postprandial blood sugar values ranged from 200 to 398 mg/dL. The 241-280 mg/dL category was the most frequent group, followed by 281-320 mg/dL. A notable proportion of patients had values above 320 mg/dL, indicating poor post-meal glycemic control in several admitted patients. The distribution is shown in Table 2.

Table 2. Distribution of study subjects according to postprandial blood sugar

Postprandial blood sugar (mg/dL)	Number of patients	Percentage
200-240	16	16.0
241-280	28	28.0
281-320	26	26.0
321-360	16	16.0
>360	14	14.0
Total	100	100.0

Values are expressed as numbers and percentages.

Wagner grade 1 was the most common clinical presentation, accounting for 44 patients. Grade 2 lesions were seen in 27 patients, while grade 3 lesions were present in 18 patients. Advanced limb-threatening disease, represented by grades 4 and 5, was less frequent but clinically important because these grades indicate gangrene and extensive tissue involvement. The Wagner grading profile is summarized in Table 3.

Table 3. Distribution of study subjects according to Wagner's grading

Wagner grade	Number of patients	Percentage
Grade 1	44	44.0
Grade 2	27	27.0
Grade 3	18	18.0
Grade 4	4	4.0
Grade 5	7	7.0
Total	100	100.0

Values are expressed as numbers and percentages.

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Clinical outcome assessment showed that most patients recovered with healing, while 11 patients required amputation. CRP analysis showed that 34 patients had CRP values above 40 mg/L, whereas 66 patients had CRP values below 40 mg/L. Table 4 provides the distribution of the outcome and CRP category.

Table 4. Distribution of study subjects according to outcome and CRP category

Variable	Category	Number of patients	Percentage
Outcome	Healed	89	89.0
Outcome	Amputated	11	11.0
CRP value	<40 mg/L	66	66.0
CRP value	>40 mg/L	34	34.0

CRP: C-reactive protein; values are expressed as numbers and percentages.

A clear association was observed between elevated CRP and adverse outcomes. All 11 amputations occurred among patients with CRP values above 40 mg/L. Among patients with CRP below 40 mg/L, every patient healed, and no amputation was recorded. The association between CRP and outcome was statistically significant, as shown in Table 5.

Table 5. Association between CRP category and clinical outcome

CRP category	Amputated	Healed	Total	p value
>40 mg/L	11 (32.4%)	23 (67.6%)	34 (100.0%)	<0.001
<40 mg/L	0 (0.0%)	66 (100.0%)	66 (100.0%)	
Total	11 (11.0%)	89 (89.0%)	100 (100.0%)	

The p-value was calculated using Fisher's exact test.

Correlation analysis demonstrated statistically significant positive relationships between CRP and both glycemic indices. CRP showed a modest positive correlation with postprandial blood sugar and fasting blood sugar. Although the strength of correlation was low, both associations reached statistical significance, supporting a measurable link between hyperglycemia and systemic inflammation in this study population. The correlation findings are shown in Table 6.

Table 6. Correlation of CRP with glycemic parameters

Variable correlated with CRP	r value	p value	N
Postprandial blood sugar	0.221	0.027	100
Fasting blood sugar	0.232	0.020	100

Correlation analysis was used to assess the relationship between CRP and glycemic indices.

Overall, the results indicate that higher CRP was associated with poorer clinical outcomes, particularly amputation, and that higher fasting and postprandial glucose values were linked with elevated inflammatory status. Patients with lower CRP values responded favorably to treatment and had better wound recovery during admission.

Discussion

This observational study evaluated the relationship of CRP with fasting and postprandial glycemic status and short-term clinical outcome among 100 admitted diabetic foot patients. The findings demonstrate that CRP was clinically meaningful in outcome stratification. Of the 34 patients with CRP above 40 mg/L, 11 underwent amputation, while no amputation occurred in the 66 patients with CRP below 40 mg/L. This statistically significant association indicates that a higher inflammatory burden accompanied the more severe and non-salvageable diabetic foot presentations in this cohort.

The present findings are biologically plausible. Hyperglycemia impairs innate immune function, reduces leukocyte chemotaxis and phagocytosis, worsens endothelial dysfunction, and delays collagen remodeling. In diabetic foot disease, these changes prolong infection,

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support tissue necrosis, and delay the formation of healthy granulation tissue. International guidance stresses that diabetic foot infection should be diagnosed clinically but supported by structured assessment, ulcer classification, and selected laboratory markers when the picture is unclear [2,3,5]. In the current study, CRP demonstrated a modest but statistically significant positive correlation with both fasting blood sugar and postprandial blood sugar, reinforcing the link between metabolic instability and inflammation.

The role of CRP in diabetic foot has been supported by earlier diagnostic and prognostic literature. Jeandrot et al. reported that CRP helped distinguish infected from non-infected diabetic foot ulcers, with higher diagnostic performance than routine leukocyte parameters in selected groups [8]. Zhang et al. also concluded from meta-analysis that CRP was significantly associated with diabetic foot ulcer infection [14]. In parallel, King et al. observed that elevated CRP concentrations increased with poorer glycemic control among adults with diabetes, suggesting an interface between systemic inflammation and hyperglycemia [9]. The current study extends this concept to hospitalized diabetic foot patients by showing that higher CRP was related not only to glycemic indices but also to limb outcome.

Wagner's grading further supports the clinical interpretation of the results. Most patients presented with grade 1 or grade 2 lesions, yet all amputations were confined to patients with elevated CRP and advanced disease. Previous outcome studies have shown that infection severity, peripheral arterial disease, ulcer depth, and systemic inflammatory response are major determinants of amputation and length of stay [10-12]. The observed amputation rate of 11% emphasizes the importance of early diagnosis, repeated wound review, debridement when indicated, culture-directed antimicrobial therapy, and glycemic optimization. CRP is not a substitute for clinical judgment, vascular assessment, or imaging; rather, it functions as a practical adjunct that alerts clinicians to greater inflammatory activity and poorer prognosis.

Generalizability

Generalizability is strongest for tertiary-care surgical units managing admitted diabetic foot patients with similar case-mix, laboratory access, and treatment pathways. The findings are less directly transferable to community clinics, primary-care screening settings, or highly specialized limb-salvage centres with advanced vascular reconstruction services. Still, the consistent relationship between elevated CRP, poor glycemic control, severe ulcer grades, and amputation supports its practical relevance across comparable inpatient settings, especially where prompt laboratory reporting is available.

Conclusion

This study concludes that CRP is a useful adjunctive marker for risk stratification in diabetic foot patients. Elevated CRP above 40 mg/L was strongly associated with amputation, whereas patients with CRP below 40 mg/L healed without limb loss. Both fasting and postprandial blood sugar showed significant positive correlations with CRP, indicating an interaction between poor glycemic control and systemic inflammation. Wagner grade, glycemic profile, CRP value, and clinical wound assessment should be interpreted together to identify patients needing intensified monitoring, early debridement, culture-guided antibiotics, strict glycemic correction, and timely surgical decision-making. These findings support routine CRP monitoring in admitted diabetic foot patients, particularly when severe infection or delayed healing is suspected.

Limitations

The single-centre design restricts external inference. The sample size was modest, and follow-up ended at discharge, limiting assessment of recurrence and late healing. CRP was measured in relation to available treatment records, while HbA1c and microbiological details were not analysed as primary variables. Residual confounding from vascular status, ulcer duration, nutrition, antibiotic exposure, and timing of referral remains a relevant concern.

Recommendations

Diabetic foot patients should undergo early combined assessment of fasting blood sugar, postprandial blood sugar, CRP, ulcer grade, vascular status, and infection severity at admission. Patients with CRP above 40 mg/L require closer monitoring, aggressive glycemic correction, culture-guided antimicrobial therapy, prompt debridement, and early surgical review. Routine documentation of serial CRP trends can strengthen clinical decision-making and help identify delayed responders. Future studies should include larger multicentre cohorts, HbA1c, microbiological patterns, vascular parameters, and post-discharge follow-up to develop a validated risk prediction model for healing, recurrence, and amputation. Multidisciplinary foot-care pathways should be strengthened in tertiary hospitals.

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in the study and the laboratory, nursing, and theatre staff who assisted in patient care, investigations, wound management, surgical support, data collection, record maintenance, and documentation during admission.

Abbreviations

ABI: Ankle-brachial index
CRP: C-reactive protein
DFU: Diabetic foot ulcer
FBS: Fasting blood sugar
HbA1c: Glycated hemoglobin
IDSA: Infectious Diseases Society of America
IWGDF: International Working Group on the Diabetic Foot
PAD: Peripheral arterial disease
PPBS: Postprandial blood sugar
SPSS: Statistical Package for the Social Sciences

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The study had no funding.

Conflict of interest

The authors declare no conflict of interest.

Author contributions

AR: Conceptualization, data collection, literature review, statistical analysis, interpretation of results, manuscript drafting, and revision.
SSR: Study design, supervision, interpretation of findings, critical review, and final approval of the manuscript.
VVP: Literature review, data interpretation, manuscript preparation, critical revision, and final approval.

Data availability

Data is Available

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