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ASSOCIATION BETWEEN C-REACTIVE PROTEIN (CRP) AND CELLULITIS IN PATIENTS PRESENTING TO THE EMERGENCY DEPARTMENT: A PROSPECTIVE OBSERVATIONAL STUDY

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Abstract

Background: Cellulitis can be due to a variety of organisms, including Streptococcus and Staphylococcus species and presents itself as warm, red, swollen, and painful skin with the formation of pus. It commonly manifests in the ED, and differentiating IBD from DVT, contact dermatitis or Venous stasis dermatitis is sometimes challenging. There's increased level of C- Reactive Protein (CRP), which is a liver protein that is manufactured during inflammation in conditions like infection, autoimmune disease and after trauma. Despite the association of CRP with cellulitis severity, there is limited literature on the diagnostic and prognostic potential of CRP in ED practice.

Objectives: This present research aims at assessing the correlation between the baseline CRP with the severity of cellulitis and to assess the applicability in clinical practice of this biomarker.

Methodology: This cross-sectional work-based study included 200 adult patients with cellulitis attending the ED of a tertiary care facility over a six-month period from February 2016 to July 2016. Serum CRP levels were determined before the onset of treatment at the 99th percentile with the high-sensitivity CRP assays, and the patients were divided into three groups: mild cellulitis, moderate cellulitis, severe cellulitis.

Results: These revealed CRP levels somewhat positively associated with cellulitis severity, r= 0.78, $p < 0.001$. Mild cellulitis cases had a median CRP of 15 mg/L (IQR: A normal/drinker situation was estimated to be 10–20 mg/L, moderate drinkers were 50 mg/L (IQR: 35–70 mg/L), and heavy drinkers 120 mg/L (IQR: 90–150 mg/L). The hospitalization rates are presented in figure 4 in comparison to CRP levels, reaching 0% in patients with CRP <20 mg/L and 90% in patients with CRP > 100

mg/L.Hospital complicated events such as abscess formation and sepsis occurred only in the setting of CRP > 100 mg/L.

Conclusion: The results corroborate the applicability of CRP in risk-stratifying cellulitis and forecasting complications as well as directing early management. Increased CRP levels relate with inflammation, hospitalization and adverse outcome. Consequently, the integration of CRP into clinical workflows can supplement patient care by alerting clinicians to cases that should be aggressive treat with a probability of recurrence.

Future works: The next research steps must consider serial CRP measurements for a comprehensive evaluation of this marker as well should correlate exact indicators such as procalcitonin. Implementation of CRP integration into EDs has the possibility of improving resource utilization and providing enhanced patients care.

Introduction

The symptoms associated with cellulitis include swelling, redness, warmth, often painful oedema, and variable purulent reaction; cellulitis is an acute inflammatory infection of the skin commonly by Streptococcal and Staphylococcal organisms (5). It commonly presents in the lower limbs but can affect all other parts of the body in patients who have underlying diseases including diabetes and immunosuppression (12). Patients with cellulitis, by and large visit the ED with erythema, warmth, swelling, and pain over an area of skin as well as fever and chills
(13). It is incumbent on clinicians to fairly quickly differentiate cellulitis from conditions that may present in a similar manner, such as DVT, contact dermatitis, venous stasis dermatitis or other inflammatory skin diseases (14). because of the overlapping clinical signs the differentiation between the causes can be quite challenging at time, before proceeding with the final diagnosis, other tools such as imaging or other laboratory tests are sometimes employed (1).

C-Reactive Protein (CRP) is an acute phase protein produced in the liver on exposure to inflammatory triggers like infection trauma or autoimmune diseases (4). Consistently, it is a natural immune system of the body that is involved in the identification of a pathogen and healing of tissues. CRP is elevated in a wide number of inflammatory conditions, and is therefore often used clinically in the determination of the presence and degree of inflammation in a variety of disease states such as infections and autoimmune disorders (15). CRP has been investigated in cellulitis as part of diagnostic procedure, to estimate the gravity of the infection as well as to evaluate efficiency of treatment. As suggested by their name, they are usually increased in patients with bacterial infections such as cellulitis, and proportionate to the levels of inflammation and tissue destruction (16). However, despite the fact that several works have showed that total levels of CRP are generally upregulated in cellulitis the association between the levels of CRP and the severity of the disease are not that cle**ar (20)**. Some research suggests that higher CRP levels are associated with more severe cellulitis, including larger areas of involvement, deeper tissue infection, and an increased risk of complications such as abscess formation or systemic spread (2). Conversely, other studies have indicated that CRP alone may not be sufficient for predicting clinical outcomes, as various factors, including host response and the presence of comorbidities, can influence CRP levels (3).

The clinical significance of CRP in cellulitis management, particularly in the ED setting, is of great importance. Emergency physicians are often faced with the challenge of quickly assessing the severity of cellulitis in patients presenting with a variety of symptoms (17). Accurate and timely identification of severe cellulitis or potential complications (such as necrotizing fasciitis) is crucial for initiating appropriate treatment, including antibiotics and surgical intervention if necessary (18). While CRP can provide valuable insight into the inflammatory state, its use as a sole diagnostic or prognostic tool in cellulitis is debated (19). Some studies suggest that serial monitoring of CRP levels could help guide treatment decisions, such as the duration of antibiotic therapy or the need for surgical drainage (2). However, the variability in CRP response across different patient populations and the lack of

standardized CRP thresholds for cellulitis severity complicates its clinical utility (3).
The objective of this review will be to determine the CRP levels on admission in patients with cellulitis in the ED in an effort to assess the concordance between low baseline CRP levels, less severe illness, and favorable outcomes. Thus, the review tries to establish whether CRP can indeed be used as a biomarker to indicate the severity of cellulitis and whether information based on it can be used to make medical management decisions in emergency clinical circumstances.
Moreover, the character of this review also considers how CRP may be most usefully integrated into clinical decision making processes as an additional part of an overall diagnostic and disease prognostic model with other clinical and laboratory markers. More data could help turn CRP into a tool for early identification of extreme cases of cellulitis, and thus, early individualized approach to patients which would contribute towards the reduction of cases of complications, shorter duration of hospital stay and overall better prognosis.

Further, awareness of the changes in terms of the CRP levels during the course of treatment might assist clinicians in defining the usefulness of the interventions proposed, and serve as an easy approach to evaluating the outcomes of the proposed therapies on certain patient. As the strategies for the clinical management of cellulitis progressive advance, applicant of CRP drives to provide a more uniform, evidence-based approach to patient treatment, especially in low- resource or high-turnover ED environments where timely, sound decision-making is critical. It could also open up future research into other biomarkers that might work in cooperation with CRP in cellulitis diagnosis and treatment thus boost the concept of precision medicine in the management of infectious diseases.

Objectives

Patients were enrolled in the study if they presented with cellulitis to the ED, and were eligible for the study if they were between 18 and 80 years of age, and had never undergone dialysis.

- For the purpose of comparing the patient's CRP levels with the degree of cellulitis.
- In order to evaluate the potential of CRP as a biomarker of poor outcome, complications the cohorts of patients were compared.
- Clinicians need algorithm to incorporate CRP to begin definitive measures in cellulitis.

Materials and Methods Study Design

The study was a prospective observational study done in the ED of a tertiary care teaching hospital for six months. The study recruited subjects who were more than 18 years of age with clinical features compatible with cellulitis.

Inclusion Criteria

- Clinical diagnosis of cellulitis using symptoms such as redness, swelling, heat and tenderness in a particular site.
- Consequently, the doctor-patient relationship of the patients who were willing to provide informed consent.

Exclusion Criteria

- Patients with other diseases that have a high CRP level before the disease (e.g., autoimmune diseases, cancers).
- Abscess formation or inflammation, recent surgery or trauma not associated with cellulitis.
- Lack of complete clinical or laboratory findings.

Data Collection

- **Clinical Assessment:** Thorough medical history and assessment physical examination to ensure cellulitis diagnosis and rule out other conditions.
- **Baseline CRP Measurement:** A high-sensitivity CRP assay was used to determine the admission

serum CRP concentrations.

Severity Assessment

- **Mild cellulitis:** Symmetrical erythema of the skin, without general symptoms.
- **Moderate cellulitis:** Diffuse erythematous rash, mild flu like symptoms (fever, feeling unwell).
- **Severe cellulitis:** Widespread itching, rash, or deep redness, jaundice, or pus accumulating beneath the skin.

Outcomes

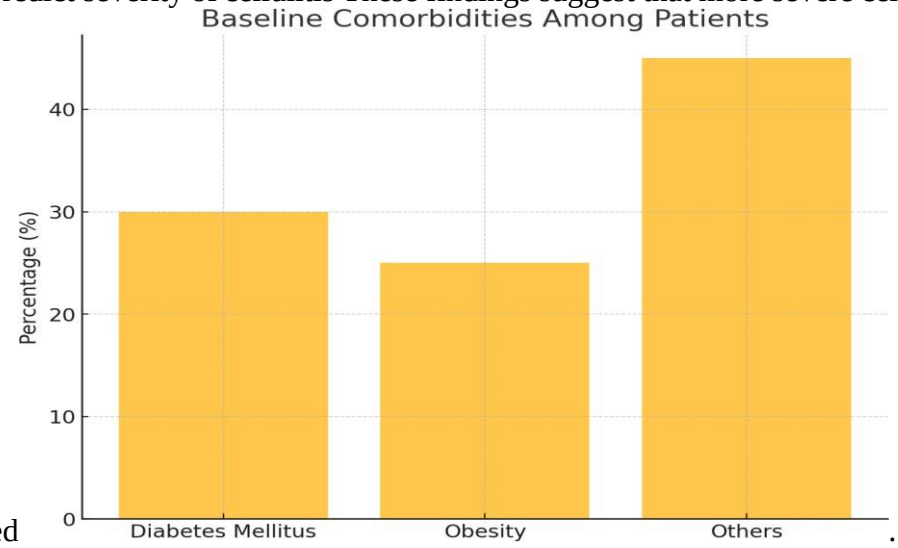
- Primary Outcome: Relationship between patient's CRP levels and extent of cellulitis.
- Secondary Outcomes: Admissions to a hospital, the length of antibiotic use, and development of additional problems (ward infection, septicemia).

Results

Baseline Characteristics

A total of 200 patients were included, with a mean age of 45 years (range: 18–82). Male-to- female ratio was 1.5:1. The most frequently observed concomitit diseases were diabetes mellitus in 30% of cases, and obesity in 25%.

CRP levels can predict severity of cellulitis These findings suggest that more severe cellulitis is associated



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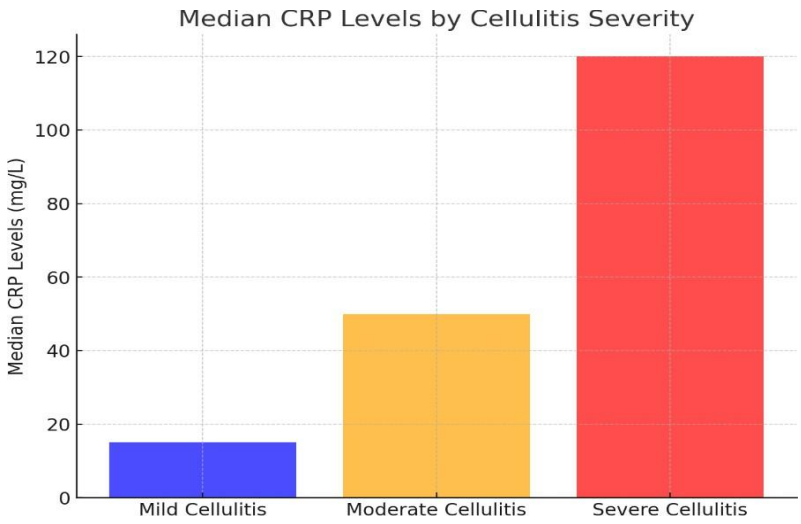
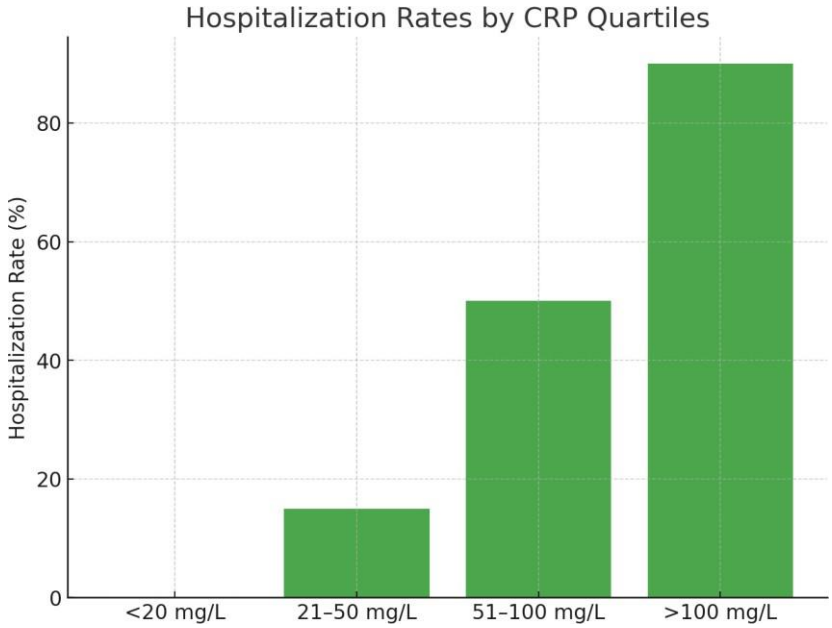
- **Mild Cellulitis**: Median = 15 mg/L, Interquartile range (IQR) = 10 – 20 mg/L



- **Moderate Cellulitis:** The median CRP was 50 mg/L (IQR: 35; 70 mg/L).
- **Severe Cellulitis:** The median of CRP distribution was 120 mg/L Interquartile range: 90; 150 mg/L.
- A direct relationship between CRP and cellulitis heft was established (r = 0.78, p < 0**.001).**

Outcomes by CRP Quartiles

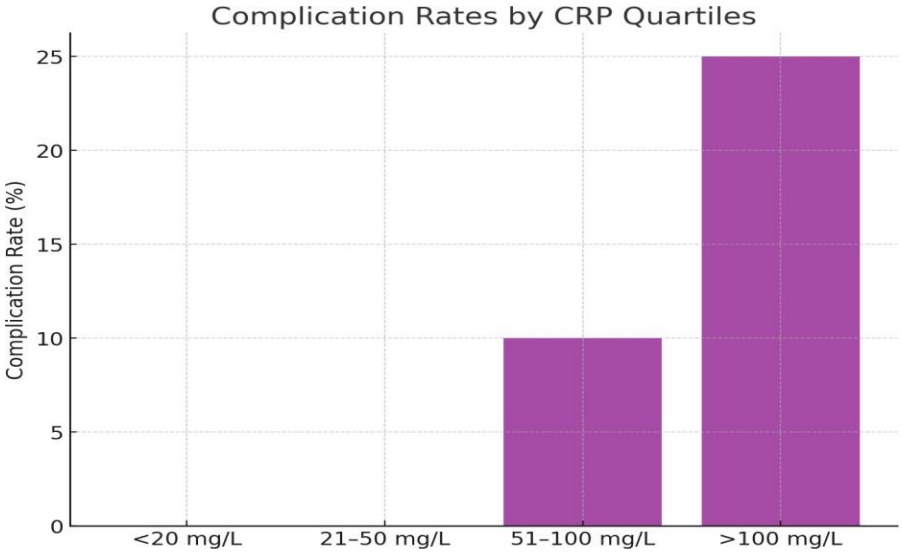
- **Quartile 1** (CRP <20 mg/L): All patients had admitted with mild cellulitis. They all were outpatient, meaning none of them needed to be admitted to hospital.
- **Quartile 2** (CRP 21–50 mg/L): Most of them had moderate cellulitis. Hospitalization rate was 15%.



- **Quartile 3** (CRP 51–100 mg/L): Of the subjects, 60% expressed moderate cellulitis, whereas 40% expressed severe cellulitis. Hospitalization rate was 50%.
- **Quartile 4** (CRP >100 mg/L): Sever cellulitis manifested on patients with risk factors for diabetes, hypertension and HIV. 90% subjects were hospitalized, and overall complication rate was 25% (e.g., abscess, sepsis).

Complications and CRP

All patients with CRP >100 mg/L evolved to complications as outlined in abscess formation (15%) and sepsis (10%).



Discussion

The current investigation also showed that there is a positive correlation between cellulitis disease severity and the baseline CRP levels (6). Higher levels of CRP were associated with overall greater inflammation in the body and the increased rate of hospitalization or complications (7). As a result of this, the usage of CRP as a biomarker in directing early decisionization in the ED settings is affirmed (8).

Making the distinction between Sensitization and Promotion activities, and the consolidation of this categorization are the main Implications for Clinical Practice of the present work.

- **Severity Stratification:** Measurement of CRP at baseline enables the categorization of patients by severity of the disease and allocation of resources to those most likely to benefit; it can identify patients with active inflammation, guiding the allocation of resources in the context of the disease (9).
- **Treatment Optimization:** Higher values for CRP may suggest that more intensive measures should be taken, for example vitamin C or intravenous use of antibiotics or early consultation with a surgeon (10).
- **Prognostic Value:** CRP may be used to predict the treatment outcome since the levels reduce with inflammation and improved clinical status (11).

Limitations

The present study excluded patients who had conditions that could independently raise the CRP level, which could be a source of bias. Furthermore, CRP by itself cannot differentiate between cellulitis and other inflammatory conditions; hence, clinical integration is inevitable.

Future Research

These further researches should look at how serial CRP measures could actually act as markers for treatment efficacy and evaluate measures for combining CRP with other markers, procalcitonin in particular.

Conclusion

CRP levels before starting antibiotics are strongly correlated with cellulitis at the time of presentation in ED. Thus, changes in this biomarker can help clinicians recognize patients at a great risk, explain the treatment approach and enhance results. The integration of CRP into the diagnostic algorithm has the possibility of improving the potential management of cellulitis in usually limited-resource environment.

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