

## Original Research Article

# Evaluating the Diagnostic and Prognostic Role of C-Reactive Protein and Fibrinogen Degradation Product Sickle Cell Disease Management

## Abstract

### Introduction

Abnormal hemoglobin is a hallmark of sickle cell disease (SCD), a genetic blood abnormality that can cause a number of clinical consequences, such as vaso-occlusive crises and an elevated risk of infection. One potential biomarker for evaluating disease activity and consequences in SCD patients is C-reactive protein (CRP), an acute-phase reactant that is frequently increased in inflammatory conditions.

### Aim/Objectives

The purpose of this study is to assess the diagnostic and prognostic value of FDP and CRP levels in sickle cell disease patients at the University College Hospital in Ibadan, Nigeria. Among the specific goals are measuring the levels of fibrinogen degradation products (FDP) and CRP in patients with sickle cell disease (SCD), figuring out how demographic characteristics like age and sex affect these measurements, and investigating the relationship between these parameters and clinical symptoms.

### Method

There were 131 participants in the descriptive cross-sectional study, including 40 healthy controls and 91 persons with SCD diagnoses. Purposive random sampling was used to gather the data, and independent t-tests, correlation analysis, and descriptive statistics were used to analyze the results at a significance level of 5%.

### Results

The data suggested that 2.2% of SCD patients exhibited abnormal CRP levels. However, no significant difference was identified in mean CRP levels between SCD patients and healthy controls ( $p=0.400$ ). However, there was a significant difference ( $p=0.001$ ) in the mean FDP levels between the two groups. Furthermore, among SCD patients, no discernible relationships between CRP levels and sex or age were discovered.

### Conclusion

Fibrinogen degradation products levels are suggestive of thrombotic events in this population, whereas CRP levels may not differ substantially between SCD patients and healthy people. The findings imply that when it comes to addressing SCD complications, FDP monitoring may be more clinically useful than CRP. This emphasizes the necessity of more study to develop successful intervention plans based on these biomarkers in order to enhance patient outcomes.

**Keywords:**Sickle Cell Disease, C-Reactive Protein, Fibrinogen Degradation Products, Biomarkers, Prognosis, Hematology.

## **Introduction**

A complex genetic disorder that primarily affects people of African descent, sickle cell disease (SCD) is characterized by hemoglobin S production, which results in sickle-shaped red blood cells and a number of complications, such as chronic pain and vaso-occlusive crises [1][2]. Two to three percent of Nigerians suffer from sickle cell anemia, and in some areas, carrier rates can reach 20 to 30 percent [3]. Because SCD pain is complex, it necessitates a biopsychosocial approach that takes into account social, psychological, and medical aspects that affect how pain is perceived[4]. Although hydroxyurea and opioids are already used as treatments, other approaches like amino acid therapy have the potential to reduce pain [1]. Despite the lack of proven biomarkers, research into biomarkers for acute pain episode prediction is still ongoing [5]. The special difficulties that SCD patients experience must be addressed through a multidisciplinary approach, especially in underprivileged populations [2][4]. In diseases like sickle cell disease (SCD), C-reactive protein (CRP) is an essential biomarker for inflammation. Its levels can reveal the severity of the illness and possible side effects like vaso-occlusive crises[6][7].

Acute inflammatory reactions are reflected in elevated CRP levels, which are mostly produced in the liver [8][9].

According to research showing its predictive usefulness, monitoring CRP in SCD patients may help determine their risk of cardiac events [10]. Furthermore, D-dimer and other fibrin degradation products (FDPs) are important for assessing thrombotic events, which are frequent in SCD because of elevated coagulation activity[11]. A crucial knowledge gap regarding how these biomarkers can improve clinical management strategies is highlighted by the understudied interaction between CRP and FDPs in SCD [10].

This research aims to assess the diagnostic and predictive functions of FDP and CRP levels in sickle cell disease management at the University College Hospital in Ibadan, Nigeria. Through investigating the correlation between these biomarkers and clinical outcomes, this study aims to improve our comprehension of their usefulness in tracking the course of disease and guiding treatment choices.

## **2.0 MATERIALS AND METHODS**

### **2.1 Study Design and Area**

The Hematology Day Care Unit of the University College Hospital in Ibadan, Nigeria, was the site of this study, which used a descriptive cross-sectional design. The area was chosen because of the high incidence of sickle cell disease and the accessibility of pertinent clinical resources.

### **2.2 Study Design**

A cross-sectional study of sickle cell disease patients was conducted in order to assess C-reactive protein (CRP) and fibrinogen degradation products (FDPs) as possible disease management biomarkers.

### **2.3 Sample Size Determination**

In order to guarantee enough power for identifying group differences, a sample size of 131 participants was established using the proper statistical procedures. 40 healthy people served as controls, and 91 persons with sickle cell disease were included.

### **2.4 Study Subjects**

Purposive random sampling was used to select participants from the outpatient clinic.

#### **2.4.1 Inclusion Criteria**

Adults with a verified diagnosis of sickle cell disease who were at least 18 years old met the inclusion criteria, while controls were healthy people with normal hemoglobin levels.

#### **2.4.2 Exclusion Criteria**

Individuals with acute infections, recent operations, or other hematological diseases were removed to minimize confounding variables.

### **2.5 Materials and Equipment**

Blood collection tubes, centrifuges, and assay kits for FDP and CRP analysis were among the supplies utilized in the study. For hemoglobin electrophoresis, standard lab equipment such electrophoresis apparatus was used.

## **2.6 Ethical Consideration**

Igbinedion University, Okada's Institutional Review Board granted ethical approval. All subjects gave their informed consent before being enrolled in the study.

## **2.6 Clinical Laboratory Investigation**

Several analytical methods were used in the clinical laboratory investigations:

### **2.6.1 Sample Collection and Analysis**

Venipuncture was used to obtain blood samples, which were processed in two hours to guarantee accurate results.

### **2.6.2 Analysis of C-Reactive Protein**

Enzyme-linked immunosorbent assay (ELISA) technology was used to measure CRP levels accurately, adhering to product directions.

### **2.6.3 Hemoglobin Electrophoresis**

The subjects' hemoglobin genotype was verified by hemoglobin electrophoresis, which guaranteed an accurate sickle cell disease status classification.

### **2.6.4 Fibrin Degradation Product Assay (ELISA)**

ELISA was used to measure the FDP levels in the participant blood samples, enabling accurate assessment of these indicators.

## **2.7. Statistical Analysis**

Descriptive statistics, such as means and standard deviations, and inferential statistics, such as independent t-tests and correlation analyses, were used to examine the data at a significance level of 5%. Strong interpretations of the connections between CRP, FDP levels, and clinical outcomes in the treatment of sickle cell disease were made possible by this all-encompassing approach.

### 3. Results

**Table 1: Descriptive statistics of CRP and FDP of subjects and control**

Statistics	Subjects		Control	
	CRP	FDP	CRP	FDP
Mean	2.31	0.66	2.10	1.28
Median	2.10	0.40	1.85	1.32
Mode	2.10	0.01	3.10	0.35
Std. Deviation	1.30	0.62	1.24	0.75
Minimum	0.01	0.01	.01	0.12
Maximum	5.10	3.2	4.30	2.89

The table showed the descriptive statistics of CRP and FDP of subjects and control in which mean  $\pm$  standard deviation of CRP of subject vs control ( $2.31 \pm 1.30$  vs  $2.10 \pm 1.24$ ). Also mean  $\pm$  standard deviation of FDP of subject vs control ( $0.66 \pm 0.62$  vs  $1.28 \pm 0.75$ ). The mode and median of subjects CRP was same at value 2.10 while the mode and median of control CRP was at value 3.10 and 1.85 respectively. The mode and median of subjects FDP was at value 0.1 while the mode and median of control FDP was at value 1.32 and .35 respectively. The range of CRP of subjects was 0.01 to 5.10 while control was 0.01 to 4.30. Also the range of FDP of subjects was 0.01 to 3.23 while control was 0.12 to 2.89.

**Table.2: Comparing difference in mean CRP and FDP between the group.**

Variables	Group	N	Mean	Std. Deviation	95%CI	Range	p-value
C-reactive protein levels	Subject	91	2.31	1.30	2.03-2.6	.01-5.10	0.400
	Control	40	2.10	1.24	1.71-2.50	.01-4.30	
FDP	Subject	91	.66	.72	.51-.81	.01-3.23	0.001
	Control	40	1.28	.75	1.04-1.53	.12-2.89	

There is no significant difference in mean C-reactive protein levels between sickle cell patients and individual without sickle cell diseases (2.31 vs 2.10,  $p=0.400>5\%$ ). There is a significant difference in mean fibrinogen degradation product (FDP) between sickle cell patients and individual without sickle cell diseases (0.66 vs 1.28,  $p=0.001<5\%$ ).

**Table 3: Comparing difference in mean CRP and FDP between the male and female.**

Variables	Group	N	Mean	Std. Deviation	95%CI	t-test	p-value
C-reactive protein levels	Male	62	2.40	1.30	2.01-2.4	0.932	.354
	Female	29	2.12	1.32	1.61-2.30		
FDP	Male	62	.71	.78	.41-.71	.873	0.385
	Female	29	.57	.59	1.02-1.43		

There is no significant difference in mean C-reactive protein levels (CRP) between male sickle cell patients and female sickle cell patients (2.40 vs 2.12,  $p=0.454 >5\%$ ). There is no significant difference in mean fibrinogen degradation product (FDP) between male sickle cell patients and individual female sickle cell patients (0.71 vs .57,  $p=0.873 >5\%$ ). The implication of the results was that outcome of C-reactive protein levels or fibrinogen degradation products (FDP) were subjected to gender difference.

**Table 4:Relationship between some haematological parameters**

Parameters	CRP	FDP r(p-value)	Age r(p-value)
CRP	1	.085(.425)	-.060(.574)
FDP		1	.142(.181)
Age			1

There is no significant correlation between C-reactive protein levels and fibrinogen degradation product (FDP) ( $r=.085$   $p=.425>0.05$ ) among sickle cell patients in University College Hospital, Ibadan, Oyo state. There is no significant correlation between C-reactive protein levels and age ( $r=.060$   $p=.574>0.05$ ) among sickle cell patients in University College Hospital, Ibadan, Oyo state. There is no significant correlation between C-reactive protein levels and age ( $r=.142$ ,  $p=.181>0.05$ ) among sickle cell patients in University College Hospital, Ibadan, Oyo state. The implication of the results was that C-reactive protein levels or fibrinogen degradation product (FDP) respectively have independent outcome and also age had no influence on the changes of C-reactive protein levels and fibrinogen degradation product (FDP).

## Discussion

At the University College Hospital in Ibadan, Nigeria, the study assessed the diagnostic and prognostic functions of fibrinogen degradation products (FDPs) and C-reactive protein (CRP) in the treatment of sickle cell disease (SCD). The importance of FDP, a measure of thrombotic activity, and CRP, an acute-phase reactant, in comprehending and treating SCD problems was examined. According to the findings, there was no significant difference in the mean CRP levels between SCD patients and healthy controls ( $p=0.400$ ). The results pertaining to fibrin degradation products (FDP) and C-reactive protein (CRP) in sickle cell disease (SCD) patients underscore the intricacy of inflammatory indicators in this illness.

Since CRP has a known role in inflammation, it is useful during vaso-occlusive crises even though its levels did not differ significantly between SCD patients and healthy controls, suggesting that it is not a reliable diagnostic marker on its own in steady-state conditions[12][13]. However, the significantly decreased FDP levels ( $p=0.001$ ) in SCD patients raise concerns regarding the disease's predicted thrombotic activity, pointing to possible special pathophysiological adaptations or limitations in the study design [14][15]. Further research into these biomarkers is necessary to better understand their significance for disease management and therapeutic options, as evidenced by the raised CRP during crises and the chronic inflammatory state in SCD[16][12].

Additionally, the study found no significant difference in CRP and FDP levels between male and female SCD patients ( $p=0.354$  and  $p=0.873$ , respectively), and no correlation between the biomarkers' levels and age among the SCD patients. These results suggest that the biomarkers' variations are independent of age and sex, supporting their potential use as universal markers in the SCD population. The lack of correlation between FDP and CRP levels further highlights their independent pathways of action, with FDP being a marker of fibrinolysis and thrombotic activity, while CRP reflects inflammation. These differences highlight the complexity of SCD pathophysiology, where multiple systems are involved.

## **Conclusion**

Although they have different functions as diagnostic and prognostic markers, CRP and FDP provide information about the inflammatory and thrombotic processes in SCD. Although steady-state SCD patients' CRP levels did not differ much, their prospective use in emergency situations is still encouraging. Despite being surprisingly lower in SCD patients, FDP levels highlight the need for additional study to determine their clinical significance. These results highlight the value of managing sickle cell disease (SCD) with a multimodal strategy that incorporates biomarkers and clinical evaluations.

## **Recommendation**

To fully assess the dynamics of C-reactive protein (CRP) and fibrinogen degradation products (FDP), future studies should involve sickle cell disease (SCD) patients in both steady-state and crisis settings. To aid in the early detection of problems, routine monitoring of these biomarkers ought to be incorporated into standard care procedures. To determine their predictive usefulness, research should also look into the relationship between CRP and FDP levels and clinical outcomes such the incidence of vaso-occlusive crises, organ damage, and mortality. Research findings will be more broadly applicable if sample size and geographic variety are increased. This will also address possible geographical differences in SCD presentation. Last but not least, creating standardized procedures for analyzing FDP and CRP levels will improve their clinical usefulness and improve patient care.

## Disclaimer (Artificial intelligence)

Option 2:

Author(s) hereby declare that generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

Author (s) hereby declare that generative AI technologies such as large language models, etc. have been used during the writing or editing of manuscript. This explanation will include the name, version, model and source of the generative AI technology and as well as all input prompt provided to the generative AI technology

1. Open AI's ChatGPT-4.1 and Perplexity
2. Laptop and Phone
3. Summarise, Paraphrase and correct grammatical errors

## Disclaimer (Artificial intelligence)

Option 1:

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

Option 2:

Author(s) hereby declare that generative AI technologies such as Large Language Models, etc. have been used during the writing or editing of manuscripts. This explanation will include the name, version, model, and source of the generative AI technology and as well as all input prompts provided to the generative AI technology

Details of the AI usage are given below:

- 1.
- 2.
- 3.

## References

1. Zhang B, Bubb C, Yao S-H, Dong V, Patel P, Shahani AK, et al. Evaluating the therapeutic effects of amino acid treatment on vaso-occlusive pain in sickle cell disease: a systematic review and meta-analysis protocol. *Protocols.io*. 2024; doi: 10.17504/protocols.io.kxygxyo5ol8j/v1.
2. Belfer I, Chen W, Chen W, Chen W, Edwards E. Unmet need: mechanistic and translational studies of sickle cell disease pain as a whole person health challenge. *J Pain*. 2024; doi: 10.1016/j.jpain.2024.104603.
3. Jain D, Gupta M, Madkaikar M, Jena RK, Khargekar N, Saraf SL, et al. Sickle cell disease in India: current status and progress. *Lancet Haematol*. 2024; doi: 10.1016/s2352-3026(24)00109-1.
4. Mulchan SS, Coco M, Boruchov D. Pain in sickle cell disease. *Oxford Medicine*. 2024; doi: 10.1093/med/9780197649176.003.0024.
5. Bhat V, Sheehan VA. Can we use biomarkers to identify those at risk of acute pain from sickle cell disease? *Expert Rev Hematol*. 2024; doi: 10.1080/17474086.2024.2372322.
6. Zhou H, Tang Y, Xu T, Cheng B. C-reactive protein: structure, function, regulation, and role in clinical diseases. *Front Immunol*. 2024; doi: 10.3389/fimmu.2024.1425168.
7. Levinson T, Wasserman A. C-reactive protein velocity (CRPv) as a new biomarker for the early detection of acute infection/inflammation. *Int J Mol Sci*. 2022; doi: 10.3390/ijms23158100.
8. Bhattacharya S, Munshi C. Biological significance of C-reactive protein, the ancient acute phase functionary. *Front Immunol*. 2023; doi: 10.3389/fimmu.2023.1238411.
9. Xi X, Tan T. C-reactive protein: issues of laboratory diagnostics. *Terapevt*. 2023; doi: 10.33920/med-12-2305-01.

10. C-reactive protein levels in adults with sickle cell disease visiting the University College Hospital, Ibadan, Nigeria. *Biomed Sci Clin Res.* 2023; doi: 10.33140/bscr.02.03.13.
11. Rizo-Téllez SA, Sekheri M, Filep JG. C-reactive protein: a target for therapy to reduce inflammation. *Front Immunol.* 2023; doi: 10.3389/fimmu.2023.1237729.
12. Gaber J, Al-Basheer O, Abdelgadir OE, Musa M, Abdel Rahim MM, Abdelgadir RE, et al. C-reactive protein level and WBC count as biomarkers for vaso-occlusive crisis among patients with sickle cell disease. *Am J Med Med Sci.* 2015;4.
13. Okocha CE, Manafa PO, Ozomba J, Ulasi TO, Chukwuma GO, Aneke JC. C-reactive protein and disease outcome in Nigerian sickle cell disease patients. *Ann Med Health Sci Res.* 2014; doi: 10.4103/2141-9248.141523.
14. Hlouedjè WH, Lokonon JE, Senou M, Abissi G, Medoatinsa E, Tchogou PA, et al. Some markers of inflammation in patients with sickle cell disease at Zou-Collines departmental hospital in Benin. *Int J Res Med Sci.* 2022; doi: 10.18203/2320-6012.ijrms20221475.
15. Conran N, Belcher JD. Inflammation in sickle cell disease. *Clin HemorheolMicrocirc.* 2018; doi: 10.3233/CH-189012.
16. Aboderin FI, Oduola T, Davison GM, Oguntibeju OO. A review of the relationship between the immune response, inflammation, oxidative stress, and the pathogenesis of sickle cell anaemia. *Preprints.* 2023; doi: 10.20944/preprints202307.1039.v1.