

# Anemia among patients admitted to the Emergency department in a tertiary care hospital with high C-reactive protein

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## ABSTRACT

**Introduction:** Patients presenting to the Emergency department represent a heterogeneous group with diverse acute and chronic morbid or multimorbid conditions indicating underlying inflammation. Inflammation is reflected by elevated levels of C-reactive protein (CRP) in the blood. As inflammatory conditions are frequently associated with anemia, characterized by a reduction in hemoglobin (Hb) concentration or red blood cell (RBC) count, this study aimed to assess the prevalence of anemia among patients admitted to emergency department at Tribhuvan University Teaching Hospital with inflammation, as indicated by high CRP, and to evaluate the correlation between CRP levels and anemia markers. **Methods:** A laboratory-based cross-sectional study was conducted using data from patients who underwent simultaneous testing for CRP, Hb, and RBC count between January 2023 and July 2023. CRP was measured by immunoturbidimetric method, Hb by sodium lauryl sulfate-hemoglobin (SLS-Hb) method and RBC was counted based on the principle of electrical impedance. Data were entered into Microsoft Excel® 2013 and analyzed using SPSS version 22 for both descriptive and inferential statistics. **Results:** A total of 609 patients had concurrent CRP, Hb, and RBC measurements. Elevated CRP levels (>1mg/L) were detected in 604(99.2%) patients. Among CRP positive individuals, 359(59.43%) were anaemic. Spearman rho correlation analysis showed a statistically significant but weak negative correlation of blood CRP concentration with hemoglobin ( $r=-0.094$ ,  $p=0.02$ ) and RBC count ( $r=-0.136$ ,  $p=0.001$ ). **Conclusions:** Anemia was found to be a common comorbid condition in more than half of the patients with inflammation as indicated by high CRP. However, CRP levels demonstrated only a weak inverse association with hemoglobin and RBC count, suggesting that while inflammation and anemia frequently coexist, the relationship between them is modest.

**Keywords:** Anemia, C-reactive protein, inflammation.

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## INTRODUCTION

Admissions to the Emergency department (ED) encompass a highly heterogeneous population with diverse demographics and a wide range of acute and chronic comorbid conditions that demand immediate medical attention.<sup>1</sup> Inflammation underlies nearly all morbidities, acting as a key pathophysiological mechanism in disease progression and severity.<sup>2</sup> While many studies focus on isolated disease entities, patients presenting to the ED often exhibit multiple overlapping pathologies that are poorly characterized but inflammation will be a core condition.<sup>3</sup> Laboratory investigations, particularly blood-based analyses, are pivotal in diagnosing such patients, influencing approximately 70% of medical decisions in clinical practice.<sup>4</sup>

C-reactive protein (CRP), a hepatic acute-phase reactant, serves as a sensitive biomarker of systemic inflammation and is widely utilized in emergency settings offering superior sensitivity and faster kinetics in detecting acute inflammatory responses.<sup>5</sup> Sustained elevation of

CRP has been implicated in numerous chronic pathologies, including cardiovascular disease, atherosclerosis, chronic kidney disease (CKD), and neurodegenerative disorders such as Alzheimer's and Parkinson's disease.<sup>6</sup> Conversely, acute CRP surges often indicate infections, trauma, or burns.<sup>7</sup> CRP with lower limit of detection, evaluating inflammation in otherwise healthy individuals, typically in the range of less than 1mg/L to 10mg/L is also called hs-CRP as per FDA- 2005.

Anemia is a major global public health concern, affecting billions worldwide and profoundly impacting quality of life and disease prognosis.<sup>8</sup> It is defined by a reduction in hemoglobin concentration (<12 g/dL in females, <13 g/dL in males) or red blood cell count.<sup>9</sup> The aetiology of anemia is multifactorial, encompassing nutritional deficiencies, blood loss, genetic hemoglobinopathies, and inflammatory states.<sup>9</sup> Inflammatory conditions are frequently associated with anemia, characterized by a reduction in hemoglobin (Hb) concentration or red blood cell (RBC) count. In emergency medicine, timely recognition and evaluation of both anemia and status of systemic inflammation are vital for optimizing patient management and improving clinical outcomes.<sup>3</sup>

Therefore, this study aimed to assess the status of anemia among patients presenting with systemic inflammation as indicated by elevated CRP levels in the emergency department of Tribhuvan University Teaching Hospital (TUTH) and to evaluate the correlation between CRP concentration and hemoglobin levels.

## METHODS

### Ethical approval

Ethical approval for this study was obtained from the Institutional Research Committee of the Institute of Medicine (IOM), Tribhuvan University, Kathmandu, Nepal (Ref. No. 93(6-11) E2,080/81). All procedures were conducted in accordance with institutional ethical guidelines and the principles outlined in the Declaration of Helsinki.<sup>10</sup>

### Study design and data collection:

This was a laboratory database-based cross-sectional study conducted in the Emergency Unit Laboratory of the Department of Biochemistry at Tribhuvan University Teaching Hospital. The emergency laboratory performs biochemical testing for patients presenting to the hospital's emergency department.

Data were retrieved from the laboratory records of patients

who underwent simultaneous testing for CRP, Hb, and RBC count between January to July, 2023. Only patients who had all three parameters tested concurrently were included in the analysis. Cases with incomplete testing (i.e., only CRP, Hb, or RBC count) or samples originating from hospital wards were excluded. Convenient sampling was applied.

To preserve patient confidentiality, only age, sex, and laboratory values were recorded for analysis. All identifiable patient information was excluded before data handling.

### Laboratory analysis of CRP, Hb, and RBC Count:

For CRP estimation, serum samples were analyzed using an immunoturbidimetric assay on an automated clinical chemistry analyzer (Beckman Coulter AU480, USA).<sup>11</sup> Hb and RBC count were measured from EDTA-anticoagulated whole blood using a fully automated hematology analyzer (HORIBA ABX Pentra XL 80, Japan).<sup>12</sup> Hb estimation employed the sodium lauryl sulfate-hemoglobin (SLS-Hb) method, which is internationally standardized and cyanide-free.<sup>13</sup>

Grading of anemia was performed according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) classification:<sup>14</sup>

- Mild: Hb 10.0 g/dL to the lower limit of normal
- Moderate: Hb 8.0–10.0 g/dL
- Severe: Hb 6.5–7.9 g/dL
- Life-threatening: Hb <6.5 g/dL

Inflammation severity was categorized based on CRP levels as per previously established clinical cut-offs:<sup>7,15</sup>

- Normal: <0.3mg/L
- Normal/minor elevation: 0.3-1 mg/L
- Moderate elevation: 1.1-10mg/L
- Marked elevation: >10mg/L
- Severe elevation: >50mg/L

### Data analysis

All collected data were entered into Microsoft Excel® 2013 and subsequently analyzed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were applied to summarize demographic and laboratory variables. The relationship between CRP and hematological parameters (Hb and RBC count) was evaluated using Spearman's rank correlation coefficient. A p-value <0.05 was considered statistically significant.

## RESULTS

### Demographic profile

Out of 609 patients, 283(46.47%) were males and 326(53.53%) were females, with a median age of 50 years (range: 9–81 years).

### Inflammation profile

Among the patients enrolled, the minimum level of CRP was 1mg/L and maximum level of CRP recorded was 424.14mg/L. There were only 5(0.82%), who had CRP level at 1mg/L indicating normal/ minor elevation. Similarly, frequency of patients with increased CRP level indicating moderate, marked and severe inflammation are tabulated in Table 1, where 365(59.93%) demonstrated severe acute inflammation with CRP levels exceeding 50 mg/L. Inflammation without anemia was noted in 245(40.22%) cases.

### Anemia status

Anemia was observed in 361(59.27%) patients, irrespective of CRP levels (males=169, females=192). Two male patients presented with anemia at CRP level of 1.0 mg/L. The distribution of anemia grades across varying CRP categories is detailed in Table 1. Among the 361 anemic patients, 220(60.94%) patients had mild anemia, 102(28.25%) had moderate anemia, 29(8.03%) had severe anemia, and 10(2.77%) exhibited life-threatening anemia, as outlined in Table 1. Figure 1 illustrates that mild anemia predominated across both sexes and all age categories, independent of inflammation severity. However, 90% of life-threatening level of anemic patients were found in category of severe inflammation.

### Correlation of anemia and inflammation

Concurrent anemia and inflammation were documented in 359(58.94%) of all cases. Among these, 192(53.48%) were females and 167(46.51%) were males. Among five patients in normal/minimal inflammation category, two patients (all males) had anemia while three patients (two males and one female) did not exhibit anemia.

The frequency of anemia increased progressively with the severity of inflammation. Specifically, anemia was detected in 40% among those with normal/minor inflammation (n = 2/5), 48.05% in moderate inflammation (n = 37/77), 61.11% of patients with marked inflammation (n = 99/162) and 61.09% of those with severe inflammation (n=223/365). (Table 1) However, this trend did not reach statistical significance (chi-square = 5.51, p = 0.14).

The coexistence of anemia and inflammation appeared to increase with advancing age. A detailed age-specific distribution is presented in Table 2.

**Table 1:** Frequency of different degrees of inflammation and anemia in emergency patients (N=609)

Anemia		No inflam- mation/ minor elevation (CRP:0.3- 1mg/L)	Moderate inflam- mation (CRP:1.1- 10mg/L)	Marked inflam- mation (CRP:10.0- 50.0 mg/L)	Severe inflam- mation (CRP >50mg/L)	
NA	Total	3 (0.49%)	40 (6.56%)	63 (10.34%)	142 (23.31%)	248 (40.72%)
	Male	2 (0.32%)	15 (2.46%)	28 (4.59%)	69 (11.33%)	114 (18.71%)
	Female	1 (0.16%)	25 (4.10%)	35 (5.74%)	73 (11.98%)	134 (22%)
Mild	Total	0	27 (4.43%)	61 (10.01%)	132 (21.67%)	220 (36.12%)
	Male	0	10 (1.64%)	28 (4.59%)	69 (11.33%)	107 (17.56%)
	Female	0	17 (2.79%)	33 (5.41%)	63 (10.34%)	113 (18.55%)
Moderate	Total	2(0.32%)	8 (1.31%)	31(5.09%)	61 (10.01%)	102 (16.74%)
	Male	2(0.32%)	4 (0.65%)	11 (1.80%)	24 (3.94%)	41 (6.73%)
	Female	0	4 (0.65%)	20 (3.28%)	37 (6.07%)	61 (10.01%)
Severe	Total	0	2(0.32%)	6 (0.98%)	21 (3.44%)	29 (4.76%)
	Male	0	1 (0.16%)	4 (0.65%)	11 (1.80%)	16 (2.62%)
	Female	0	1 (0.16%)	2 (0.32%)	10 (1.64%)	13 (2.13%)
LT	Total	0	0	1(0.16%)	9(1.47%)	10 (1.64%)
	Male	0	0	0 (0.82%)	5 (0.82%)	5 (0.82%)
	Female	0	0	1(0.16%)	4 (0.65%)	5 (0.82%)
Total		5(0.82%)	77 (12.64%)	162 (26.60%)	365 (59.93%)	609 (100%)
Male		4 (0.65%)	30 (4.92%)	71 (11.65%)	178 (29.22%)	283 (46.46%)
Female		1 (0.16%)	47 (7.71%)	91 (14.94%)	187 (30.70%)	326 (53.53%)

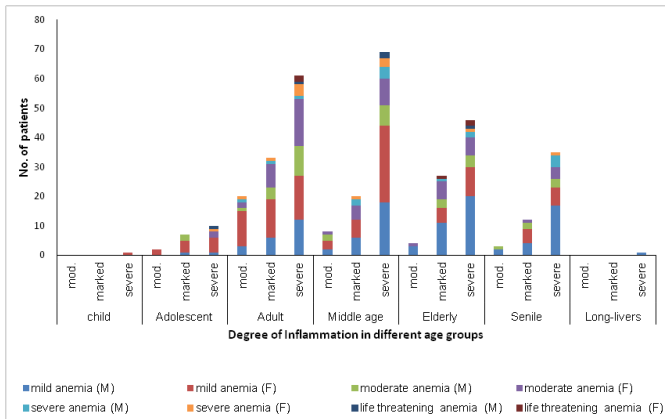
Abbreviations: NA: no anemia; LT: life threatening  
Note: Data are presented as n(%) where the percentage is calculated out of the total population (n=609).

**Table 2:** Anemia of inflammation in different age groups (N=609)

Age group (years)	Child (0-12)	Adolescent (13-24)	Adult (25-44)	Middle Age (45-60)	Elderly (61-75)	Senile (76-90)	Long livers (> 90)
Total patients [n=609]	3	40	210	160	121	74	1
Anemia and inflam- mation [n=359]	1 (33.33%)	19 (47.50%)	113 (53.80%)	98 (61.25%)	77 (63.63%)	50 (67.56%)	1 (100%)
Inflam- mation without anemia [n=245]	2 (66.66%)	21 (52.50%)	94 (44.76%)	60 (37.50%)	44 (36.36%)	24 (32.43%)	0
Anemia without inflam- mation [n=2]	0	0	1 (0.47%)	1 (0.62%)	0	0	0
No anemia, no inflam- mation [n=3]	0	0	2 (0.95%)	1 (0.62%)	0	0	0

Note: Data are presented as n (%) where the percentage is calculated out of the total patients within the age group [child (n=3), adolescent (n=40),

adult (n=210), middle age (n=160), elderly (n=121), senile (n=74), long  
livers (n=1)].



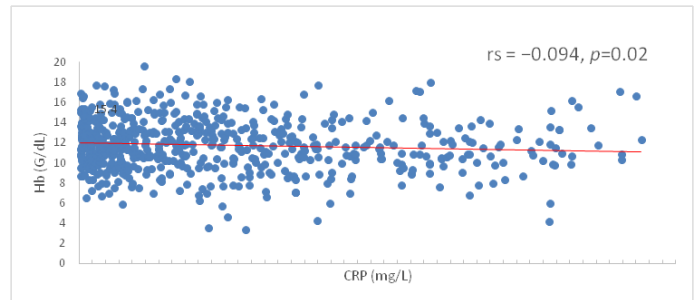
**Figure 1:** Severity of anemia of inflammation in different age groups of males and female emergency patients. Abbreviations: mod: moderate, M: males, F: female

**Correlation of CRP with Hb and RBC Count**

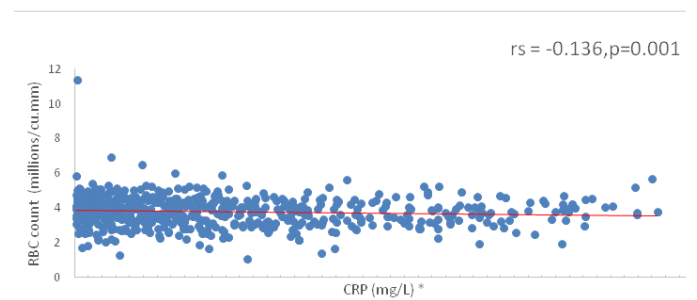
The median CRP was 74.95 mg/L (Q1: 24.58 mg/L, Q3: 160.33 mg/L), median Hb was 11.70 g/dL (Q1: 10.15 g/dL, Q3: 13.35 g/dL), and the median RBC count was 3.86 million/cu.mm (Q1: 3.27, Q3: 4.34). Spearman’s rho correlation analysis revealed a statistically significant but very weak negative correlation between CRP and Hb ( $r = -0.136, p = 0.001$ ; Figure 3).

There were only five patients categorized as no inflammation, all having CRP level at 1mg/L within which anemia was seen in two people with average Hb of 9.1g/dl and average RBC count as 3.54 million/cu.mm. In the male group with inflammation without anemia, the median CRP level was 69.97mg/L (Q1:30.84mg/L, Q3: 131.37mg/L), median Hb level was 14.8g/dl (Q1: 13.95 g/dL, Q3: 15.87 g/dL), the median RBC count was 4.55 million/cu.mm (Q1: 4.17, Q3: 4.91). In the female group with inflammation without anemia, the median CRP level was 65.07mg/L (Q1:17.41mg/L, Q3: 134.67mg/L), median Hb level was 13.0g/dl (Q1: 12.4 g/dL, Q3: 13.87 g/dL), the median RBC count was 4.20 million/cu.mm (Q1: 3.91, Q3: 4.49).

In the male group with inflammation and anemia, the median CRP was 89.74 mg/L (Q1:28.89 mg/L, Q3:169.13 mg/L), median Hb level was 8.55/dl(Q1:9.3g/dl, Q3:11.7g/dl), the median RBC count was 3.1 million/cu.mm (Q1:2.96,Q3:3.9). In the female group with inflammation and anemia, the median CRP was 77.69mg/L (Q1:24.26mg/L, Q3:179.70mg/L), median Hb level was 10.4g/dl(Q1:9.1g/dl,Q3:11.5g/dl), the median RBC count was 3.43 million/cu.mm (Q1:2.96, Q3:3.81).



CRP level (\*at interval of 10mg/L)



level (\*at interval of 10mg/L)

**DISCUSSION**

This study investigated the prevalence of anemia among patients presenting with inflammation, as indicated by elevated CRP levels, in the emergency department of TUTH. Systemic inflammation is one of the common conditions seen in emergency visit.<sup>16</sup> The prevalence of anemia observed as 59.3% in this study aligns with global and regional data indicating that over one-third of the general population and up to 60% of hospitalized or chronically ill patients experience anemia.<sup>17,18,19</sup> Our findings suggest a strong coexistence of inflammation and anemia. Elevated CRP levels during inflammation inhibit intestinal iron absorption and impair its mobilization from macrophages, leading to functional iron deficiency which may lead to decrease hemoglobin.<sup>20-21</sup>

In these patients with high CRP, there was predominance of mild anemia which did not alter with increasing severity of inflammation as indicated by CRP more than 50mg/L. This result is consistent with the other reports in literatures where they have mentioned that a mild to moderate form of anemia is associated with inflammation.<sup>3,20-23</sup>

Although anemia was more common in those with higher CRP levels (Table 1), the correlation between CRP concentration and hemoglobin or red blood cell (RBC) count was weak (Figure 2 and 3) compared to similar study done in emergency patients which has shown negative

correlation of moderate strength.<sup>3</sup> Thus, while inflammation and anemia frequently coexist, the strength of relationship between is modest. Our correlation ( $r_s = -0.094$ ,  $p = 0.02$ ) result between non-disease specific inflammation status (CRP) with hemoglobin (Hb) is similar to studies reporting on disease specific inflammatory conditions, such as in hemodialysis patients,<sup>27</sup> chronic kidney disease,<sup>28</sup> and even in an apparently healthy population.<sup>29</sup>

Anemia may also have been contributed by coexisting nutritional deficiency like iron deficiency or hemolysis or gastrointestinal bleeding etc. but they were not identified in our study which is the major limitation of this study as the missed clinical details would have improved our impact of the result. However, based on other studies,<sup>24-26</sup> anemia coexisting with inflammation may be present even in the background of chronic GI bleeding, iron deficiency anemia, or hemolytic anemia. In these cases, however, the primary cause plays a vital role than mere inflammatory status. There were 8% of patients with severe anemia and 2.8 % of patients with life-threatening anemia among patients with inflammation. Here again, we lacked clinical details that would have better identified the inflammation as a primary or secondary factor.

We also observed that the frequency of anemia coexisting with inflammation increased with increasing age which may be due to phenomenon called inflammaging as ageing is exposed with increased inflammatory burden and multiple comorbidities.<sup>12,29,30</sup>

Our study also revealed a higher frequency of anemia among females compared to males, consistent with demographic patterns observed globally, where reproductive age and menstrual blood loss contribute to increased anemia risk in women.<sup>18</sup>

Thus, the results emphasize the importance of routinely evaluating hemoglobin and CRP levels in emergency patients. Early recognition of anemia in individuals with inflammation can guide appropriate management, such as iron supplementation, addressing the inflammatory source or monitoring of the inflammatory status, which can potentially improve clinical outcomes.

## CONCLUSIONS

Anemia is observed in more than half of patients exhibiting inflammatory responses, yet the severity of inflammation demonstrates only a modest association with anemia.

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## AUTHORS' CONTRIBUTION

SK did concept and design, literature search, data collection, analysis, interpretation and preparation of manuscript. ETT did concept and design, literature search, data analysis and interpretation, manuscript preparation and editing. RKD, AB, MR, AN, VKS did data analysis and interpretation, manuscript preparation and editing. All the authors have read and approved the final draft.

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