Correlation Between Inflammatory Markers and CBC indices (WBCs and platelets) in Severely Malnourished Children

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Abstract:

Background: Malnutrition is a prevalent worldwide health problem caused by a lack of or excess of essential nutrients. This condition can be identified through a clinical examination or by measuring biochemical or anthropometric factors.

Aim and **Objectives:** To assess the efficacy of quantitative C-reactive protein as a prognostic indicator for severe infections in kids with acute severe malnutrition and to establish a correlation among inflammatory markers and complete blood count indices, particularly platelets and WBCs, in these kids.

Patients **and Methods:** This prospective analytic research was performed on sixty cases separated into two groups: The 1st group with systemic onset of infection (30 patients) and the 2nd group without systemic onset of infection (30 patients) at Assiut University Children's Hospital in a period of one year from January 1st, 2022, up to December 31st, 2022.

Results: There was highly statistically significant variance (p= <0.001) among both groups regarding WBC. Both groups had statistically insignificant variation according to platelet count (PLT) and aggregation index. CRP demonstrated a significant positive association with WBCs and PLT, while CRP demonstrated a significant negative association with HCT. ESR showed a significant positive association with WBCs and PLT, while ESR showed a significant negative correlation with HCT.

Conclusion: There is a positive correlation between inflammatory markers, including ESR, CRP, and serum ferritin, and CBC indices, including WBC and platelets, while for HCT, there is a negative correlation between it and the inflammatory markers in severely malnourished children.

Keywords: Malnutrition, CBC indices, inflammatory markers.

Introduction:

Malnutrition is a prevalent global health issue resulting from and/ or excess deficiency of essential nutrients, which can be clinically detected or manifested through anthropometric or biochemical measurements **[1].**

SAM is characterized by a weight for height that is significantly under the median WHO growth standards (under -3z scores), visible severe wasting, the presence of nutritional edema in both feet, a middle upper arm circumference less than 11.5 centimeters, and a loss of over forty percent of the expected weight. It reduces the immune system's efficacy and prevents the host's ability to respond adequately to infectious pathogens. Conversely, infections alter nutritional status and can lead to a deficiency. Therefore, the combination of malnutrition and infection frequently works together to significantly raise the rates of illness and death, especially in infants and children **[2].**

Malnutrition diminishes immune function and prevents the host from

mounting a sufficient protective response to infections. Symptoms of infection are usually nonspecific or absent in kids with severe acute malnutrition (SAM). Therefore, empirical therapy applies **[3].**

Very few investigations have examined C-reactive protein as a diagnostic tool for identifying infection in malnourished kids. This is made worse because severe acute malnutrition, specifically edematous malnutrition, can be related to decreased concentrations of acute-phase proteins **[4].**

Malnutrition leads to alterations in the body, involving modifications in the hematologic profile. The white cell alterations observed in protein energy deficiency are diverse and can be related to various causes **[5].**

The synergistic association between PEM and infections and the development of thymic atrophy in kids with PEM is a significant cause. The platelet count and function are similarly affected in severe acute malnutrition. Many researchers have shown a correlation between infections and blood platelet activation and have concluded that platelet destruction occurs during infection and in a hyper-coagulable condition **[6].** Furthermore, platelets in the blood have immunological capabilities and play a role in interacting with pathogens and human defense mechanisms **[7].** In cases of protein energy deficiency, additional research has demonstrated a reduction in certain platelet activities, particularly ADP and collagen-induced platelet aggregations **[8].**

This research aimed to assess the efficacy of quantitative C-reactive protein as a prognostic indicator for severe infections in kids with acute severe malnutrition and to establish a correlation among complete blood count indices and inflammatory markers, particularly platelets and WBCs, in these kids.

Patients and Methods

This prospective analytic research was performed on sixty cases, separated into two groups: 1st group with systemic onset of infection (30 patients) and 2nd group without systemic onset of infection (30 patients) at Assiut University Children's Hospital, over one year from January 1, 2022, up to December 31, 2022. The study was approved and monitored by the Medical Ethics Committee, Assiut Faculty of Medicine, IRB no: 17101548.

Inclusion Criteria: all children between the ages of six months and five years who were admitted with a diagnosis of severe acute malnutrition. The diagnosis of severe acute malnutrition was determined utilizing the most recent criteria established by the World Health Organization, which include measuring the height, length, and mid-upper arm circumference and assessing the presence of bilateral pitting edema and severe wasting. Two types of severe acute malnutrition can occur in kids. The first type is called non-edematous malnutrition, or marasmus. It is described by severe wasting and is currently defined by a weight-for-length/height z score of less than three based on the WHO growth standard or a mid-upper arm circumference of less than 11.5 centimeters. The second type is called edematous malnutrition, also known as Kwashiorkor. The presence of bilateral pitting edema defines it. Marasmic Kwashiorkor is used to characterize kids who exhibit wasting and edema.

Exclusion Criteria: kids with moderate and mild malnutrition, kids under six months or above five years, kids with malnutrition secondary to serious underlying conditions involving congenital anomalies, inborn errors of metabolism, malignancies, inherited autosomal disorders like cystic fibrosis, chronic diarrheal illnesses like celiac illness, congenital cardiac disorders, and chronic kidney illness.

Methods:

Investigation: CBC, ESR, CRP, serum ferritin, and platelet function tests (adhesions, aggregation).

The initial characteristics of the studied children were that they had dietary causes of malnutrition.

Classification of children with malnutrition: The study compared two groups of children, first with systemic onset of infection and second without systemic onset of infection.

The plan to determine the spectrum of nutrient deficiency: The response is to rely on CBC parameters, mainly WBCs, platelets, serum ferritin, and CRP.

Follow-up period: it is fixed at presentation (baseline) after 6 months. Follow-up data included full clinical examination, anthropometric measures: body weight, height, head and chest circumference, and mid-upper arm circumference. Follow-up for investigation (CBC, ESR, CRP) was after 6 months from the onset of the infection.

The specifity and sensitivity of (CRP, ESR, CBC parameters, and platelet function tests): Comparison between the two groups of severely malnourished kids with and without systemic infection to determine whether kids with acute severe malnutrition can mount an acute phase reactant response, namely C-reactive protein, and to assess the usefulness of quantitative C-reactive protein as a predictor of severe infections in kids with acute severe malnutrition, as well as to understand the hematological profile of severely malnourished kids. It results in various pathophysiological alterations in the body systems, involving significant alterations in hematological parameters.

Research Outcome Measures:

Primary (main): The primary goals of this investigation were to establish a correlation among markers of inflammation and complete blood count measurements in malnourished kids. Additionally, the research aimed to determine if children with severe acute malnutrition can produce an acute-phase reactant response, specifically C-reactive protein. Furthermore, the research aimed to assess the effectiveness of quantifying CRP levels to predict severe infections in children with severe acute malnutrition. To establish a correlation among inflammatory markers and complete blood count indices, including white blood cell count (WBC) and platelet count, in kids.

The objective is to assess if children with severe acute malnutrition can produce an acute-phase reactant response, namely CRP. Additionally, we aim to determine the value of measuring C-reactive protein levels as a predictor for severe infections in kids with severe acute malnutrition and to gain knowledge into the hematological profile of severely malnourished kids.

It leads to different pathological changes in the body systems, involving considerable alterations in hematological markers.

Secondary (subsidiary): The objective is to reduce the incidence of illness and death in severely malnourished kids.

Ethical Considerations: Confidentiality (dealing with data and data dissemination should be confidential). Participants will get a statement describing the research methodology. Each patient provided informed consent. The research should only be carried out by scientifically certified and trained individuals. The research depends on relevant pre-clinical studies conducted on animals. The full consent form should be included in the proposal at this place.

Data Management and Analysis: The mean ± standard deviation (range) was used to present continuous data, while categorical data were expressed as frequency. x^2 was employed to evaluate the frequencies of various categories. ANOVA and the Student T-test were implemented to evaluate variations among means. SPSS version 20 was employed to conduct all statistical analyses. Statistical significance was determined for all tests implemented when the P value was less than 0.05.

Results

Both groups had a statistically insignificant distinction regarding sex, age distribution, residence, father's occupation, and education **(Table 1).**

Table (1): Baseline data among the research groups

	Group with onset of infection (n = 30)	**Group without onset of infection (n = 30)**	**Test of Sig.**	***P***
Sex				
- Male	12 (40%)	14 (46.67%)	X2 = 0.271	0.602
- Female	18 (60%)	16 (53.33%)		
Age (months)				
- Mean ± SD.	22.13 ± 3.1	20.9 ± 4.17	t = 1.299	0.199
- Median (IQR)	22.5 (20 - 24)	20 (18 - 24.75)		
- Range (Min-Max)	12 (17 - 29)	16 (13 - 29)		
Age distribution				
- 6 m – 2 y	24 (80%)	22 (73.33%)	X2 = 0.373	0.542
- 2 y – 5 y	6 (20%)	8 (26.67%)		
Residence				
- Urban	13 (43.33%)	12 (40%)	X2 = 0.069	0.793
- Rural	17 (56.67%)	18 (60%)		
Father's occupation				
- Don't work	10 (33.33%)	8 (26.67%)	X2 = 0.317	0.573
- Works	20 (66.67%)	22 (73.33%)		
Father's education				
- Educated	14 (46.67%)	13 (43.33%)	X2 = 0.067	0.795
- Non-educated	16 (53.33%)	17 (56.67%)		

SD: Standard Deviation, **χ2:** Chi-Square test, **t:** Independent T test, **IQR:** Interquartile Range, ***P***: P Value for comparing between the studied groups, P-value < 0.05: Significant; P-value > 0.05: Non-significant; P-value < 0.001: Highly significant

There was highly statistically significant variance (p= <0.001) among both groups regarding WBC **(Table 2).**

Table (2): Total white blood cell count (WBC) among the study groups

	Group with onset of infection (n = 30)	**Group without onset of infection (n = 30)**	**Test of Sig.**	***P***
WBC (cells/µL)				
- Mean ± SD.	18.47 ± 2.26	12.13 ± 1.5	t = 12.802	<0.001
- Median (IQR)	18.5 (17 - 20)	12 (11 - 13)		
- Range (Min-Max)	9 (13 - 22)	7 (8 - 15)		

There was highly statistically significant variation (p= <0.001) among both groups regarding LCP and LYM **(Table 3).**

Table (3): Lymphocyte count percentage (LCP) and Lymphocyte count (LYM) among the study groups

	Group with onset of infection (n = 30)	**Group without onset of infection (n = 30)**	**Test of Sig.**	***P***
LCP (%)				
- Mean ± SD.	36.07 ± 4.47	50.3 ± 6.12	t =-10.285	<0.001
- Median (IQR)	36 (33 - 39.75)	50 (45.5 - 54)		
- Range (Min-Max)	17 (28 - 45)	24 (39 - 63)		
LYM (cells/µL)			t = -6.675	<0.001

- Mean ± SD.	4388.6±1085.65	5987.4±736.52		
- Median (IQR)	4386 (3489.75-5177)	6054.5 (5501.75-6496.75)		
- Range (Min-Max)	4192 (2735-6927)	2797 (4587-7384)		

There was a statistically insignificant distinction between the groups regarding PLT and aggregation index **(Table 4).**

Table (4): Platelet count and function test results among the study groups

	Group with onset of infection (n = 30)	**Group without onset of infection (n = 30)**	**Test of Sig.**	***P***
PLT (cells/µL)			t = 2.023	0.48
- Mean ± SD.	375.4 ± 45.72	352.27 ± 42.79		
- Median (IQR)	378.5 (345.25 - 415)	346 (329 - 368.25)		
- Range (Min-Max)	190 (262 - 452)	193 (274 - 467)		
Aggregation Index			t = 2.116	0.39
- Mean ± SD.	0.92 ± 0.11	0.86 ± 0.11		
- Median (IQR)	0.9 (0.87 - 0.96)	0.88 (0.81 - 0.95)		
- Range (Min-Max)	0.5 (0.7 - 1.2)	0.44 (0.57 - 1.01)		

There was highly statistically significant variance (p= <.001) among both groups regarding ESR and CRP **(Table 5).**

Table (5): ESR and CRP results after 6-month follow-up among the study groups

	Group with onset of infection (n = 30)	**Group without onset of infection (n = 30)**	**Test of Sig.**	***P***
ESR			t = 9.917	<0.001
- Mean ± SD.	72.3 ± 8.8	52.7 ± 6.3		
- Median (IQR)	73 (67 - 76)	52.5 (48 - 57)		
- Range (Min-Max)	40 (52 - 92)	25 (43 - 68)		
CRP			t = 31.904	<0.001
- Mean ± SD.	45.03 ± 5.33	13.23 ± 1.17		
- Median (IQR)	46 (42 - 48.75)	14 (12.25 - 14)		
- Range (Min-Max)	22 (32 - 54)	5 (10 - 15)		

C-reactive protein demonstrated a significant positive association with WBCs and PLT, while C-reactive protein revealed a significant negative correlation with HCT **(Table 6).**

Table (6): Correlation between CRP and CBC.

	CRP	
	r	P value
WBCs	+.827*	0.001*
PLT	+.962*	0.011*
HCT	-.681*	0.032

P value < 0.05: statistically significant, r: Pearson correlation

ESR showed significant positive correlation with WBCs and PLT, while ESR showed significant negative correlation with HCT **(Table 7).**

Table (7): Correlation between ESR and CBC.

	CRP	
	r	P value
WBCs	+.912*	0.009*
PLT	+.863*	0.015*
HCT	-.456*	0.026

P value < 0.05: statistically significant, r: Pearson correlation

Discussion

Severe acute malnutrition (SAM) significantly contributes to the death rate of children under the age of five. It accounts for approximately fifty percent of deaths in kids under the age of five, with a mortality rate that varies from ten percent to forty percent in cases requiring hospitalization **(1).**

A significant cause of mortality in these cases is overwhelming illnesses for which they cannot generate an appropriate immune response. Because there is a lack of microbiological research in this case and the cases are highly prone to bacterial infection, they are given wide-spectrum antibiotics as a last resort until the test results are obtained, which may not be readily available in many cases. The complete blood count is a simple and cost-effective test commonly performed and used. It provides data regarding the constituents of a patient's blood **(9).**

Lymphocytes and neutrophils, white blood cells, are the primary cells used by the immune system in response to an infection. The origin determines the predominant type of white blood cell, stage of infection, and immune response of the case, which the nutritional state can also influence **[5].**

Both groups had statistically insignificant variance regarding sex, age, age distribution, residence, father's occupation, and father's education.

Bedha et al. [9] aimed to associate SAM in kids with hematological disorders in adulthood. The authors reported no significance regarding age and sex among the studied groups.

There was a highly statistically significant distinction (p = <0.001) between the two groups regarding WBC.

Our results are supported by **Isezuo et al. [10],** who demonstrated statistical significance among the study groups regarding WBCS (P value 0.001).

Bedha et al. [9] also demonstrated that there was a statistically significant distinction among the studied groups regarding white blood cells (P value 0.013).

There was highly statistically significant variance (p = <.001) among both groups regarding LCP and LYM.

Our results were supported by **Isezuo et al. [10],** who demonstrated statistical significance among the studied groups regarding lymphocyte count (P-value 0.001).

The groups had no statistically significant difference according to platelet count (PLT) and aggregation index.

Our findings did not align with **Khan et al. [11],** who showed that forty-eight percent of the kids with severe acute malnutrition exhibited pancytopenia and twenty-eight percent had bicytopenia. Additionally, they showed that thrombocytopenia was observed in sixty-six percent of kids, a low lymphocyte count was observed in twenty-

two percent of kids, and a low absolute neutrophil count was observed in twenty-five percent.

Thakur et al. [12] found that kids with severe acute malnutrition had lower mean hematocrit and red cell indices and higher average total leukocyte and platelet counts. Conversely, our investigation indicated an elevated total leukocyte count but a platelet count within the normal range.

There was a significant and highly statistically significant variation ($p < .001$) among the two groups regarding ESR and CRP.

Our findings matched the findings of **Kheir & Gebreel [13**], who discovered that malnourished kids can produce CRP in response to an infectious event, and the magnitude of this reaction is greater in those with severe infections. The high cost of alternative inflammatory indicators prevents their use in low-resource settings for clinical and routine applications. As a result, CRP is a practical marker for diagnosing infection in children with SAM because of its simple measurement and affordability.

The C-reactive protein had a significant positive association with white blood cells and platelets, but demonstrated a significant negative association with hematocrit. The erythrocyte sedimentation rate had a strong positive correlation with white blood cells and platelets, whereas it demonstrated a significant negative association with hematocrit.

Conclusion

Regarding our results, we can conclude that there is a positive correlation between inflammatory markers, including ESR, CRP, and serum ferritin, and CBC indices, including WBC and platelets, while for HCT, there is a negative correlation between it and the inflammatory markers in severely malnourished children.

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