

# Frequency of Anemia in Critically Ill Patients Admitted to the Pediatric Intensive Care Unit

## Çocuk Yoğun Bakım Ünitesine Kabul Edilen Kritik Hastalarda Anemi Sıklığı

İ Kübra İRDAY<sup>1</sup>, İ Medine BATARGÜN<sup>2</sup>, İ Mehmet BAKLACI<sup>2</sup>, İ Mehmet BOZKURT<sup>2</sup>,  
İ Mehlika Çağan KÜTKÜT<sup>2</sup>, İ Mahmut ÖZCAN<sup>2</sup>, İ İlknur ARSLAN<sup>3</sup>

<sup>1</sup>Clinic of Pediatrics, University of Health Sciences Türkiye, Adana City Training and Research Hospital, Adana, Türkiye

<sup>2</sup>Clinic of Pediatrics, Health Sciences University, Adana Faculty of Medicine, Adana, Türkiye

<sup>3</sup>Clinic of Pediatric Intensive Care, University of Health Sciences Türkiye, Adana City Training and Research Hospital, Adana, Türkiye

### ABSTRACT

**Objective:** Although anemia is known to be common in patients admitted to and followed up in the pediatric intensive care unit (PICU), our knowledge regarding the pre-intensive care period is limited. This study was conducted to investigate the frequency of anemia in critically ill children admitted to the PICU.

**Material and Methods:** During the study period between 15 November 2023 and 15 March 2024, the sex, age, acute and/or chronic diseases, reason for admission, complete blood count, and C-reactive protein (CRP) results obtained within 24 hours before or at the time of admission of the patients admitted to the intensive care unit were recorded from the hospital computer management system.

**Results:** Total of n=292 patients were admitted to the intensive care unit. According to the exclusion criteria, n=87 patients were excluded from the study. Of the 205 patients included, 58.5% were male, with a mean age of 74.34±66.66 months. The incidence of anemia was found to be 59%. It was observed that 30.2% of anemia was normocytic, and 25.9% was microcytic. Normocytic anemia was the most common type in all age groups except for 7-24 months, in which microcytic anemia was more frequent. Anemia most frequently accompanied acute infections, hemato-oncologic diseases, and chronic illnesses, and was of the normocytic type. Red cell distribution width (RDW) was elevated in 65.4% of patients. In patients without anemia, RDW was normal, whereas in microcytic and normocytic anemia, it was high and associated with elevated CRP, acute infection, hemato-oncologic, and chronic diseases.

**Conclusion:** Anemia is a finding requiring specific evaluation according to the patient's age and health status. Since critically ill children have a low capacity to tolerate anemia, their blood count values should be monitored regularly during and after admission. Comprehensive studies are needed to investigate whether RDW may serve as a marker of inflammation in critically ill children.

**Keywords:** Anemia, critically ill child, pediatric intensive care, incidence

### ÖZ

**Giriş:** Aneminin çocuk yoğun bakıma kabul edilen ve takip edilen hastalarda sık olduğu bilinmesine karşın yoğun bakım öncesi dönem konusundaki bilgilerimiz kısıtlıdır. Bu çalışma çocuk yoğun bakım ünitesine (YBÜ) kabul edilen kritik hasta çocuklarda anemi sıklığını araştırmak amacıyla yapılmıştır.

**Gereç ve Yöntemler:** Çalışma aralığı olan 15 Kasım 2023 ve 15 Mart 2024 arasında YBÜ kabul edilen hastaların cinsiyeti, yaşı, akut ve/veya kronik hastalıkları, üniteye yatış nedeni, yatışından önceki 24 saat içerisinde veya yatış sırasında alınmış olan tam kan sayımı, C-reactive protein (CRP) sonuçları hastane bilgisayar yönetim sisteminden kayıt edilmiştir.

**Bulgular:** 15 Kasım 2023 ve 15 Mart 2024 arasında yoğun bakım ünitesine toplam n=292 hasta yatışı olmuştur. Çalışma dışı bırakma kriterlerine göre n=87 hasta çalışma dışı bırakılmıştır. Çalışmaya dahil edilen 205 hastanın %58,5'i erkek, yaş ortalaması: 74,34±66,66 ay'dır. Anemi insidansı %59 bulunmuştur. Aneminin %30,2 normositik, %25,9 mikrositik olduğu görülmüştür. Normositik anemi 7-24 ay hariç tüm yaş gruplarında en sık görülen anemi şeklidir. Yedi-24 ay arasında mikrositik anemi daha fazla görülmüştür. Anemi en sık akut enfeksiyon, hematoonkolojik hastalık ve kronik hastalıklara eşlik etmektedir ve normositik tiptedir. Hastaların %65,4'ünde kırmızı kan hücrelerinin (RDW) yüksek olduğu gözlenmiştir. Anemi saptanmayan hastalarda RDW normal iken mikrositik ve normositik anemi, CRP yüksekliği, akut enfeksiyon, hematoonkolojik hastalıklar ve kronik hastalıklar ile ilişkili ve yüksek bulunmuştur.

**Address for Correspondence:** İlknur Arslan MD, Clinic of Pediatric Intensive Care, University of Health Sciences Türkiye, Adana City Training and Research Hospital, Adana, Türkiye

**E-mail:** ilknurtolunay@gmail.com **ORCID ID:** orcid.org/0000-0002-3454-8483

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ÖZ

**Sonuç:** Anemi hastanın yaş ve sağlık durumuna göre özel değerlendirme gerektiren bir belirtidir. Kritik hasta çocukların anemiyi tolere etme kapasitesinin düşük olması nedeniyle hastaların kan sayımı değerleri kabul sırasında ve sonrasında düzenli olarak takip edilmelidir. Kritik hasta çocuklarda RDW'nin enflamasyon göstergesi olabileceği konusunda geniş katımlı çalışmalara ihtiyaç vardır.

**Anahtar Kelimeler:** Anemi, kritik çocuk hasta, çocuk yoğun bakım, sıklık

## INTRODUCTION

Anemia is defined as a decrease in hemoglobin (HGB), hematocrit levels, and erythrocyte count below two standard deviations according to age and sex (1,2). Anemia is a common and serious problem in the pediatric intensive care unit (PICU) (3). It is known that one-third of critically ill children hospitalized in the PICU for at least two days are anemic at admission, and 40% develop anemia during their stay (4). In critically ill children, chronic anemia, acute or chronic blood loss, underlying diseases, bone marrow-suppressing treatments, and insufficient erythropoietin response contribute to anemia development. In these patients, anemia reduces the oxygen-carrying capacity of the blood and causes tissue and organ failure. Critically ill children with low baseline HGB levels have been shown to require multiple transfusions, prolonged intensive care stay, and more inotropes, invasive mechanical ventilation and extracorporeal therapy (5,6). Although anemia is common in critically ill patients, it is an important finding often overlooked in daily medical practice. The balance between avoiding unnecessary transfusions and tolerating anemia depends on understanding the complex etiology of anemia. Using HGB levels in transfusion decisions is the most common practice. The TAXI and TRIPICU guidelines provide transfusion recommendations based on HGB levels. However, in different clinical conditions such as sepsis, shock, congenital heart disease, and trauma, these guidelines emphasize that the patient's clinical findings should also be considered when deciding whether to monitor anemia or increase HGB levels (7,8). Although anemia is known to be frequent in patients admitted to and followed up in the intensive care unit, information regarding the pre-intensive care period is limited. The aim of this study was to investigate the frequency of anemia in critically ill children admitted to the PICU.

## MATERIALS and METHODS

The study was conducted within the framework of the Basic Competency Course, which aimed to provide fourth-year students of Adana Faculty of Medicine during the 2023-2024 academic year with instruction on the planning, execution, and completion of a research project, in collaboration with the student researchers. During the study period between 15 November 2023 and 15 March 2024, the student researchers made regular visits to the intensive care unit. The sex, age, acute and/or chronic diseases, reason for admission to the unit, and complete blood count and C-reactive protein (CRP)

results obtained within the 24 hours before admission or at the time of admission were recorded from the hospital computer management system.

### Inclusion of Patients in the Study

Patients followed for more than 48 hours in the PICU, aged between 1 and 216 months, whose admission data and blood test results were available, were classified into seven groups according to their reason for admission:

**Infection:** Acute infectious diseases such as encephalitis, acute lower respiratory tract infection, hepatitis, sepsis.

**Hemato-oncological Diseases:** Hematological diseases such as leukemia, hemophagocytic syndrome, and solid tumors.

**Chronic Diseases:** Chronic cardiac, renal, respiratory, and rheumatologic diseases.

**Bleeding/trauma:** Patients with acute blood loss such as from traffic accidents or trauma, who were not operated on and did not receive transfusion.

**Epilepsy and Mental-Motor Retardation:** Epileptic diseases accompanied by antiepileptic drug use and mental-motor retardation.

**Metabolic Diseases:** Metabolic conditions such as organic acidemia, maple syrup urine disease, acute gastroenteritis, diabetic ketoacidosis.

**Postoperative/post-arrest:** Postoperative patients who underwent elective surgeries such as gastrostomy placement, scoliosis, kyphosis operations, and patients with a history of out-of-hospital cardiac arrest.

To determine normal values for HGB, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean MCH, red cell distribution width (RDW), leukocyte, and platelet counts according to age group and sex, the Turkish Society of Hematology Complete Blood Count Guide was used (9). CRP values above 5 mg/L were considered elevated.

### Exclusion criteria for the patients:

- Patients followed in the PICU for less than 48 hours,
- Patients whose blood results could not be obtained due to clotting or insufficient sample,
- Patients admitted to the unit after surgical intervention for acute blood loss,
- Patients admitted to the unit after receiving a blood transfusion in the inpatient ward or emergency department,
- Patients transferred to the ward but readmitted to the PICU within 24 hours for any reason.

Ethical approval for the study was obtained from the University of Health Sciences Türkiye, Adana City Training

and Research Hospital Clinical Research Ethics Committee (decision no: 2938, date: 09.11.2023).

Families of the patients included in the study were informed about the study and informed consent was obtained.

### Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS 20.0; Chicago, IL) software. Following distribution analysis, continuous variables were presented as mean  $\pm$  standard deviation (minimum-maximum), while categorical data were expressed as numbers and percentages. For the analysis of two different categorical variables, contingency tables and the Pearson chi-square test were applied. A *p* value  $<0.05$  was considered statistically significant.

## RESULTS

During the study period between 15 November 2023 and 15 March 2024, a total of *n*=292 patients were admitted to the intensive care unit. According to the exclusion criteria, *n*=87 patients were excluded from the study. Among the 205 patients included in the study, 58.5% (120/205) were male, and the mean age was  $74.34 \pm 66.66$  months.

The incidence of anemia among patients admitted to the PICU was 59%, and it was observed that 30.2% of the anemia cases were normocytic and 25.9% were microcytic. No significant difference was found between patients with and without anemia in terms of sex and reason for admission. A significant relationship was identified between age groups and types of anemia. Normocytic anemia was the most common type of anemia in all age groups except for the 7-24-month group. Microcytic anemia was more frequently observed in the 7-24-month age group. The age of patients without anemia was higher than that of patients with anemia. Anemia was most frequently accompanied by acute infections, hemato-oncological diseases, and chronic diseases, and was of the normocytic type (Tables 1 and 2).

The CRP level was elevated in 50.8% of patients, and no relationship was found between CRP and anemia. It was observed that 65.4% of the patients had elevated RDW. While RDW was normal in patients without anemia, it was found to be elevated in patients with microcytic and normocytic anemia. Although not statistically significant, RDW was found to be elevated in patients most frequently admitted to the intensive care unit and diagnosed with normocytic anemia. In the 7-24-month group, RDW elevation accompanied microcytic anemia, whereas in the 0-6-month and 25-72-month groups, RDW elevation accompanied normocytic anemia.

## DISCUSSION

Critically ill children are at high risk of anemia during and after their stay in intensive care. It is known that 33% of patients admitted to the PICU have anemia at the time of admission, 41% develop anemia during hospitalization, and 74% require transfusion. Patients requiring transfusion are known to be younger, to have higher PRISM mortality scores, and to have lower HGB values at the time of admission (4,10,11). In this study, the frequency of anemia among patients admitted to the PICU was found to be 59%. Although normocytic anemia was the most common type detected, there was a significant relationship between age and MCV. Accordingly, microcytic anemia was more frequent in the 7-24-month group, while normocytic anemia was more common in the 0-6-month and 25-72-month groups. The frequency of anemia decreased with increasing age. Nutritional deficiencies may be the cause of this result. It has been reported previously that 9% of intensive care patients have iron deficiency, and 2% have vitamin B12 and folate deficiency (12). Nevertheless, our knowledge regarding the relationship between nutritional anemia and critical illness in critically ill children remains limited. Anemia in patients admitted to the intensive care unit is multifactorial, and etiological investigations should be performed before transfusion and managed appropriately. In children, an MCV value within the normal range for age indicates normocytic anemia. A high reticulocyte level in the presence of anemia is usually associated with hemolysis. In contrast, a normal or low reticulocyte level despite the presence of anemia indicates bone marrow insufficiency and is commonly seen in critically ill patients. Acute blood loss, early stage of acute hemolysis, acute inflammatory diseases, malignancy, renal, rheumatologic, and other chronic diseases, heart failure, chronic lung disease, ulcerative colitis, Crohn's disease, and celiac disease are causes of normocytic anemia with normal reticulocyte counts (13,14). In our patients, normocytic anemia is frequently observed in association with acute infections, hemato-oncological diseases, and chronic diseases. This result is expected in critically ill patients. In children, especially during infections accompanied by inflammation, decreased erythropoiesis, abnormal iron metabolism, and reduced erythropoietin production and response lead to a reduction in HGB levels. This condition is associated with suppression of iron metabolism due to increased hepcidin as a defensive response of immune cells. In addition, bone marrow suppression caused by infectious agents, administered treatments, and accompanying hemolytic processes contribute to the development of anemia (15,16). However, unlike previous studies, in our patients, RDW

Table 1. Anemia situation of patients according to sex, age groups and admission reason						
	Non-anemic patients *n=84 (41%)		Anemic patients n=121 (59%)		Total n=205 (%)	p
		Microcytic n=53 (25.9%)	Normocytic n=62 (30.2%)	Macrocytic n=6 (2.9%)		
<b>Sex</b>						
Female	35 (17)	17 (8.3)	30 (14.6)	3 (1.5)	85 (41.5)	0.343
Male	49 (24)	36 (17.6)	32 (15.6)	3 (1.5)	120 (58.5)	
<b>Age groups</b>						
1-6	10 (4.9)	11 (5.4)	18 (8.8)	-	39 (19.0)	<0.001
7-24	9 (4.4)	21 (10.2)	6 (2.9)	1 (0.5)	37 (18.0)	
25-72	19 (9.2)	9 (4.4)	11 (5.4)	1 (0.5)	40 (19.5)	
73-144	22 (10.7)	11(5.4)	12 (5.8)	1 (0.5)	46 (22.5)	
145-216	24 (11.8)	1 (0.5)	15 (7.3)	3 (1.5)	43 (21.0)	
<b>Admission reason</b>						
Acute infections	27 (13.2)	18 (8.8)	23 (11.0)	1 (0.5)	69 (33.6)	0.047
HOD**	14 (6.8)	7 (3.4)	10 (4.9)	2 (1.0)	33 (16.1)	
Chronic disease	13 (6.4)	8 (3.9)	11 (5.4)	-	32 (15.6)	
Bleeding/trauma	5 (2.5)	3 (1.5)	9 (4.4)	1 (0.5)	18 (8.8)	
Epilepsy, MMR**	4 (1.9)	3 (1.5)	5 (2.5)	1 (0.5)	13 (6.4)	
Metabolic disease	14 (6.8)	8 (3.9)	2 (1.0)	1 (0.5)	25 (12.2)	
Postop, postarest	7 (3.4)	6 (2.9)	2 (1.0)	-	15 (7.3)	

n\*: Number, HOD\*\*: Hematooncologic disease, MMR\*\*\*: Mental motor retardation

Table 2. RDW levels of patients according to anemia situation, admission reason, age groups and CRP				
	Normal RDW n*=71 (34.6%)	Elevated RDW n=134 (65.4%)	Total n=205 (100%)	p
<b>Anemia</b>				
Non-enemic	46 (22.5)	38 (18.5)	84 (41.0)	<0.001
Mikrocytic anemia	4 (1.9)	49 (24.0)	53 (25.9)	
Normocyticanemia	19 (9.2)	43 (21.0)	62 (30.2)	
Macrocytic anemia	2 (1.0)	4 (1.9)	6 (2.9)	
<b>Admission reason</b>				
Acute infections	23 (11)	46 (22.5)	69 (33.6)	0.142
HOD**	11 (5.4)	22 (10.7)	33 (16.1)	
Chronic disease	6 (2.9)	26 (12.7)	32 (15.6)	
Bleeding/trauma	9 (4.4)	9 (4.4)	18 (8.8)	
Epilepsy, MMR***	5 (2.5)	8 (3.9)	13 (6.4)	
Metabolic disease	11 (5.4)	14 (6.8)	25 (12.2)	
Postop, postarest	6 (2.9)	9 (4.4)	15 (7.3)	
<b>Age groups</b>				
0-6	8 (3.9)	31 (15.1)	39 (19.0)	0.008
7-24	7 (3.4)	30 (14.6)	37 (18.0)	
25-72	15 (7.3)	25 (12.2)	40 (19.5)	
73-144	19 (9.2)	27 (13.3)	46 (22.5)	
145-216	22 (10.7)	21 (10.2)	43 (21.0)	
<b>CRP</b>				
Normal	46 (22.5)	55 (26.7)	101 (49.2)	0.001
Elevated	25 (12.1)	79 (38.7)	104 (50.8)	

n\*: Number, HOD\*\*: Hematooncologic disease, MMR\*\*\*: Mental motor retardation, CRP: C-reactive protein, RDW: Red cell distribution width

elevation accompanied normocytic anemia. In children with low MCV and high RDW, iron deficiency is the first condition to be considered. When the cut-off value for RDW is accepted as 16.7% and for MCV as 72 FL, it has been shown that evaluating RDW and MCV together provides 70% sensitivity and 82.95% specificity for the diagnosis of iron deficiency (17). However, in critically ill children, these parameters vary due to infection and inflammation. For example, in iron deficiency anemia, ferritin is typically low, but during infection, ferritin may increase as an acute phase reactant in 25% of patients, masking iron deficiency (14,18). RDW indicates the extent to which the volume of each erythrocyte deviates from the mean erythrocyte volume. Although it has long been used as a parameter to determine the etiology of anemia, recent studies have suggested that RDW and the HGB/RDW ratio are useful in predicting mortality in critically ill patients and determining prognosis in cancer patients (19,20). Among patients with normal RDW levels, 22.5% had normal CRP levels, while 38.7% of patients with elevated RDW had elevated CRP levels. RDW was found to be elevated in normocytic anemias, in the age groups where normocytic anemia was common, and in diseases frequently admitted to intensive care. These results support that RDW may serve as an indicator of inflammation in critically ill children. Comprehensive large-scale studies are needed on this subject.

### Study Limitation

Anemia was chosen as the study topic because it is frequently encountered in general pediatric practice. However, since the researchers' familiarity with the subject was limited, and their attention and perception were intended to focus more on the research process rather than the subject itself, the aim of the study was restricted to investigating the causes and frequency of anemia, while clinical course and mortality were not included. No additional tests or blood samples were taken for the purpose of this study. The results obtained during hospitalization were recorded. Therefore, etiological investigations, iron parameters, ferritin, and nutritional indicators remained incomplete. Since anemia is a multifactorial condition, it would be appropriate to plan comprehensive prospective studies in the future.

### CONCLUSION

Anemia is a clinical finding that requires specific evaluation according to the patient's age and health status. Due to the low tolerance capacity for anemia in critically ill children and the negative impact of anemia on mortality and morbidity, complete blood count parameters of patients should be regularly monitored at the time of PICU admission and thereafter. The underlying cause of anemia should be identified, and it should be treated appropriately in accordance with clinical guidelines. Comprehensive studies with wide participation should be planned to determine the

role of parameters such as ferritin and RDW, which serve as practical indicators in daily medical practice, in identifying the causes of anemia in critically ill patients.

### Ethics

**Ethics Committee Approval:** Ethical approval for the study was obtained from the University of Health Sciences Türkiye, Adana City Training and Research Hospital Clinical Research Ethics Committee (decision no: 2938, date: 09.11.2023).

**Informed Consent:** Families of the patients included in the study were informed about the study and informed consent was obtained.

### Footnotes

### Authorship Contributions

Surgical and Medical Practices: K.İ., İ.A., Concept: K.İ., İ.A., M.B., M.Ba., M.Bo., M.Ç.K., M.Ö., Design: İ.A., M.Ba., M.Bo., M.Ç.K., M.Ö., Data Collection or Processing: K.İ., İ.A., M.B., M.Ba., M.Bo., M.Ç.K., M.Ö., Analysis or Interpretation: K.İ., İ.A., M.B., M.Ba., M.Ç.K., M.Ö., Literature Search: İ.A., M.Bo., M.Ç.K., M.Ö., Writing: K.İ., İ.A., M.B., M.Ba., M.Bo., M.Ç.K., M.Ö.

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