# Related Factors of Anemia in Critically Ill Patients

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Anemia is common in critically ill patients; almost 95% of patients admitted to intensive care units (ICUs) have hemoglobin levels below normal. Several causes may explain this phenomenon as well as the tendency to transfuse patients without adequate cause: due to a lack of adherence to protocols, lack of supervision, incomplete transfusion request forms, or a lack of knowledge about the indications, risks, and costs of transfusions. Daily sampling to monitor the coagulation parameters and the acid–base balance can aggravate anemia as the main iatrogenic factor in its production.

anemia blood practice management medical

## 1. Introduction

Anemia is very common in critically ill patients [1]; almost 95% of patients admitted to intensive care units (ICU) have hemoglobin levels below normal [2]. The CRIT study, a prospective, multicenter, observational cohort study in the United States that included 4892 ICU patients, reported that almost two-thirds of these patients had hemoglobin concentrations below 12 g/dL [3]. Although the etiology of anemia in critical patients is due to many factors which generate admission to the ICU, such as trauma, surgery, and gastrointestinal bleeding, it is also possible to determine anemia in critical patients who do not bleed. The pathogenesis of anemia in a non-bleeding, critical patient involves a combination of causes, the most important of which are sepsis; losses due to phlebotomy and minor procedures; decreased production of endogenous erythropoietin (EPO), and red blood cells with increased EPO resistance; destruction of red blood cells and functional iron deficiency associated with the immune system. In addition to the presence of neocytolysis, a hypothetical explanation for the selective lysis of young red blood cells (RBCs) (neocytes) associated with decreased plasma levels of erythropoietin (EPO), a phenomenon observed under experimental conditions that take place whenever a rapid RBC mass reduction is required [4]. In a critical patient, there could be a similar pathophysiological behavior within the first days of admission; there may be significant hemodilution due to the alteration of the hydric compartments after an initial intensive fluid therapy, where a plasma Hb has decreased but the total Hb mass has not been altered, with differences greater than 2 g per 100 mL being found between a measurement and the corrected one (carbon monoxide test) [5][6][7]. Since 2010, blood donations have fallen by 6.6% despite an increase in the global population, all while there has been an increase in the consumption of albumin and immunoglobulins of 58% and 99.6%, respectively, since 2012. This has led to shortages in blood, blood components, and blood products in some countries [8][9][10]. Nevertheless, it has been estimated that 5–58% of transfusions performed may be unnecessary, either due to clinician error or

inaccurate transfusion volume [7]. Currently in Spain, after onco-hematology and emergency departments, intensive care services are one of the main consumers of blood components and blood products. The patient blood management (PBM) programs were developed to minimize unnecessary practices, reduce variabilities in clinical practice, decrease the rate of inappropriate and unnecessary transfusions, and promote the treatment of anemia as well as the correction of hemostasis, among others [11]. The inappropriate use of these limited resources is associated with increased respiratory distress, cardiac overload, iatrogenic infections, and hemolysis. This has led to longer hospital stays and complications derived from the transfusions themselves [12] as well as financial burdens and poor outcomes. In intensive care units (ICU), 40% of patients receive a transfusion of RBC concentrates during their stay at an average of 2–5 units [12][13]. Up to 30% of these patients with pre-transfusion Hb levels above 9 g/dL have been transfused without a clear indication [14], due to the characteristics of critical patients. The daily sampling of laboratories to control the coagulation parameters and the acid-base balance has resulted in weekly sampling between 340 and 660 mL of ICU patients, which can aggravate anemia as the main iatrogenic factor in its production [5][15]. In 1986, Burum referred to “vampire doctors” in his description of why iatrogenic anemia was the main factor that occurred in critical patients in the ICU [16][17] and how it could be improved with a PBM program.

## 2. Related Factors of Anemia in Critically Ill Patients

It was to estimate the association and importance of anemia and iatrogenic blood loss with related factors. The researchers results indicated that in a cohort of 142 subjects admitted to the ICU, 66.90% of them had anemia during their stay. Likewise, the rate of anemia increased the longer they remained in the ICU. In a recent study published by Warner et al. [18], in a cohort of 6901 adults hospitalized in the ICU, 41% had anemia before hospitalization, a value slightly lower than that obtained in the researchers study. However, as the researchers have commented previously, the longer they remained in the ICU, the more the prevalence of anemia increased.

One of the predominant medical indications in patients hospitalized in ICUs is the treatment and recovery of anemia. There is a paucity of data on recovery from anemia in patients hospitalized in ICUs. There have been studies that affirmed that more than 50% of survivors with anemia on discharge from the ICU had persistent anemia at 6 months [19]. One of the possible explanations for this phenomenon may be an inflammatory process mediated by C-reactive protein and interleukin-6 that could alter erythropoiesis [20].

Regarding the risk factors associated with the appearance of anemia, these included the presence of arterial and venous catheters, drains, the length of stay in the ICU, and, especially, the amount of blood volume extracted from the critical patient. the researchers results showed that the volume of the blood extracted daily (OR = 1.99, 95% CI: 1.03–3.82) from critical patients could be one of the main risk factors associated with the appearance of anemia. In addition, the risk was higher in patients admitted to the ICU as they are more closely observed and it is necessary to obtain blood samples for subsequent analysis, which may increase their vulnerability to anemia. In the researchers multivariate analysis, there was a clear relationship ($p$-value 0.038) between the volume of blood collected and the production of iatrogenic anemia. Considering the systematic review carried out by Whitehead et al. [21], the researchers results agreed, and the researchers likewise emphasized the use of blood conservation

systems to eliminate blood waste when drawing blood for analysis. The researchers results are in correlation with those established by Salisbury et al. [22], where an 18% risk increase for anemia was correlated to every 50 mL of blood drawn. While a healthy person can tolerate a loss of approximately 500 mL of blood in a donation, critical patients develop anemia at much lower loss volumes. The relationship (*p*-value 0.031) indicates the importance of the limit of collecting blood in the iatrogenic blood loss in daily procedures. The use of pediatric devices for collected blood is common in ICUs in order to minimize the impact of iatrogenic blood loss in critically ill patients. A total of 32.63% of the researchers patients developed anemia with the extraction of more than 60 mL. Currently, modern blood analyzers require around 100–200 microliters of blood for analysis while blood draws are performed with standard volume tubes ranging from 4 to 6 mL in volume. Several studies [5][15] have shown that weekly blood loss due to laboratory blood samples for coagulation control, the acid–base balance for the detection of iatrogenic infections, or for the monitoring of organ function varies from 340 to 660 mL in ICU patients. The appearance of anemia in these types of patients coincides with a series of deficiencies, such as decreased mobility [23][24], muscle weakness [25], and global cognitive impairment [26]. Therefore, appropriate treatment is essential to avoid these deficiencies.

When using standard volume tubes, more than 90% of the blood is discarded; therefore, the volume of blood collected could be reduced without reducing the number of diagnostic tests, which could improve outcomes for critical patients [27].

The researchers findings suggested the association and importance of iatrogenic blood loss and different factors in critically ill patients. There was a statistical significance in the onset of iatrogenic anemia due to the daily blood draws for laboratory monitoring, which could be improved with the implementation of PBM programs as well, as has been demonstrated in different studies [28][29][30]

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