Iatrogenic Anemia in Covid-19 Patients Admitted to the Intensive Care Unit

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ABSTRACT

During intensive care unit (ICU) management of COVID-19, blood tests are often conducted for close monitoring of patients, a poor prognostic factor for survival, especially in hypoxemic patients. This study aimed to determine the degree of anemia and its effect on prognosis in ICU COVID-19 patients. This retrospective study included COVID-19 patients admitted to the ICU between 1 October 2020 and 1 May 2021. All the patients included were aged > 18 years and stayed in the ICU for ≥14 days. Patients aged <18 years, those with major bleeding, and those recovering from surgery were excluded. The total blood samples (mL) taken in the ICU were calculated. From among the 395 patients screened for inclusion, 112 patients were included in the study. Mean age of the patients was 71.3 ± 13.2 years (Male/Female: 1.8). Mean hemoglobin (Hb) at admission was 13.2 ± 1.8 g dL^{-1}. At the end of the ICU stay mean Hb was 9.74 ± 1.98 g dL^{-1}. During ICU stay, the mean reduction in Hb was 3.47 ± 2.11 g dL^{-1}. Age (p= 0.049), drawn blood volume per day (p= 0.001), and higher hemoglobin at admission (p= 0.001) were determined by multivariate analysis as independent risk factors for hemoglobin reduction. Hemoglobin reduction (OR: 1.34), and intubation status (OR: 57.50) were independent risk factors for mortality. Considering that most COVID-19 patients are admitted to the ICU due to acute respiratory failure (ARF), it is vital to maintain the Hb level as high as possible, so as to maintain oxygenation.

Keywords: Bleeding, Critical care, Dyspnea, Monitoring, Transfusion

INTRODUCTION

Since the start of the COVID-19 pandemic, there have been 328.532.929 confirmed cases of COVID-19; hundreds of thousands of them have been admitted to intensive care units (ICU), and 5.542.359 deaths have been reported as of 18 January 2022.[1] Age, obesity, respiratory failure, comorbidities, concomitant organ failure, and such biochemical markers as high D-dimer, elevated lactate dehydrogenase (LDH), C-reactive protein, selective troponin I, and hematological markers (e.g., lymphopenia) are associated with poor prognosis and mortality.[2] As such, for close monitoring of prognostic markers, preventing organ dysfunction, and monitoring blood oxygenation, an excessive amount of blood may have been collected in ICUs.

Iatrogenic anemia is a common but frequently overlooked condition in daily practice. The most common causes are excessive diagnostic blood sampling that outpaces the daily production capacity of bone marrow, gastrointestinal bleeding due to underlying disease or stress gastritis, surgical interventions, and a decrease in red blood cell (RBC) production.[3,4]

It causes worsening of symptoms, blood test abnormalities, unnecessary investigations to determine the cause of anemia, and an increase in RBC transfusions.[5]

Iatrogenic anemia is associated with such adverse outcomes as weaning failure, an increased re-intubation rate, myocardial infarction, and mortality.[6-8] Blood sampling and its consequences in ICUs have been previously studied.[4,9] The present study primarily aimed to determine the collected blood volume and the anemia development rate in COVID-19 patients admitted to the ICU. The secondary outcome was to determine factors affecting prognosis.

PATIENTS AND METHODS

Patients and Data Records

This retrospective study included COVID-19 patients admitted to the ICU between 1 October 2020 and 1 May 2021. From among 395 patients with a positive PCR test for SARS-CoV-2 virus or thorax radiography findings compatible with typical COVID-19 involvement, male and female patients aged > 18 years with ICU stay ≥ 14 days were included in the study. All the included patients had respiratory failure, required oxygen therapy, and/or had hemodynamic instability or multiple comorbidities. We defined acute respitory failure as " PO_2 > 50 mmHg or, PCO_2 > 50 mm Hg. Patients aged < 18 years, those with a history of major bleeding, patients with hematological malignities and post-operative patients were excluded. The remaining 112 patients that met the inclusion criteria constituted the study group.

Demographic data, comorbidities, APACHE II score, type and duration of respiratory support, follow-up durations, and outcomes were retrospectively collected from computer-based patient records. Hemoglobin (Hb), hematocrit (Hct), and mean cell volume (MCV) levels at baseline, time of ICU admission, and at discharge were recorded. Transfusion data, use of central venous catheters, hemodialysis, and continuous renal replacement therapy (CRRT) were also recorded. The institutional ethics committee approved the study protocol (E1-21-1923).

ICU Blood Collection Routine

The total number of blood samples (mL) taken in the ICU (ml) was recorded. Routine ICU blood sampling practice was to draw blood from the central venous catheter in catheterized patients. First, 5 mL of blood was drawn and discarded. Then, a sufficient volume of blood was drawn for testing. Next, 10 mL of sodium chloride 0.9% was injected. Adequate blood was drawn via needle system (syringe or vacuum tube) from peripheral veins (antecubital veins or another site) in non-catheterized patients. All the hemogram, biochemistry, coagulation, blood gas, and blood culture tubes in the hospital system were enumerated. In total, approximately 3 mL of blood was collected into hemogram (pink tube), biochemistry (yellow or red), and coagulation tubes (blue), 2 mL was collected into blood gas tubes, and 10 mL was collected into blood culture tubes (BD Blood Collection Tubes, Belliver Industrial Estate, Plymouth, PL6, 7BP, UK).

Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows v.24.0 (IBM Corp., Armonk, NY). Descriptive statistics were used for patient characteristics, comorbidities, laboratory values, and treatment modalities. Descriptive statistics are shown as mean ± SD and median (interquartile range), according to whether continuous variables were normally distributed. The Kolmogorov-Smirnov test and Shapiro-Wilk tests, and histograms were used to determine the distribution of continuous variables. An independent samples t-test was used to determine the relationship between normally distributed continuous variables and categorical variables. The Mann-Whitney U test and t-test were used for determining the relationship between continuous variables and the chi-square test for categorical variables. Univariate regression analysis was used to detect factors associated with hemoglobin reduction, and mortality. For the multivariate analysis, possible factors identified in the univariate analysis were inserted into the logistic regression model to identify the individual factors affecting mortality. We used the Hosmer-Lemeshow goodness-of-fit test to evaluate the fit

Table1. Demographics data, and univariate analysis showing factors affecting mortality				
	Survivor (n= 46; 41.1%)	**Non- Survivor (n= 66; 58.9%)**	**Total (n= 112)**	**p**
Age (mean, SD)	69.1 ±14.9	73.0 ±11.9	71.4 ± 13.3	0.13
Sex (female)	20 (43.5)	20 (30.3)	40 (35.7)	0.15
Hypertension	22 (47.8)	38 (57.6)	60 (53.6)	0.31
Diabetes Mellitus	9 (19.6)	17 (25.8)	26 (23.2)	0.45
CHD	10 (21.7)	19 (28.8)	29 (25.9)	0.40
CHF	4 (8.7)	9 (13.6)	13 (11.6)	0.42
COPD	5 (10.9)	8 (12.1)	13 (11.6)	0.84
Dementia	6 (13.0)	5 (7.6)	11 (9.8)	0.35
CVD	3 (6.5)	3 (4.5)	6 (5.4)	0.69
Cancer	1 (2.2)	4 (6.1)	5 (4.5)	0.65
CRD	0 (0)	4 (6.1)	4 (3.6)	0.14
Apache II (median, IQR)	11.0 (8.0-13.0)	14.0 (11.0-17.0)	12.0 (10.0-16.0)	<0.001
Hemoglobin at admission g/dL (mean, SD)	13.2 ±1.9	13.2 ±1.8	13.2 ±1.8	0.99
Anemia at admission	14 (30.4)	26 (39.4)	40 (35.7)	0.33
Total sampling tubes (median, IQR)	131.5 (116.0-222.8)	156.0 (131.8-193.5)	150.5 (123.0-202.5)	0.19
Drawn volume per day (mL) (median, IQR)	22.6 (20.7-27.6)	29.5 (27.3-33.7)	27.9 (23.1-31.5)	<0.001
Total drawn volume (mL) (median, IQR)	509.5 (348.8-715.5)	607.5 (516.0-746.3)	575.0 (460.5-738.8)	0.02
Hemoglobin at discharge g/dL(mean, SD)	10.7 ±2.1	9.1 ±1.5	9.7 ±2.0	<0.001
Anemia at discharge	39 (84.8)	64 (97.0)	103 (92.0)	0.03
Hemoglobin reduction g/dL (mean, SD)	2.5 ±1.9	4.2 ±2.0	3.5 ±2.1	<0.001
Transfusion	9 (19.6)	23 (34.8)	32 (28.6)	0.08
Hemodialysis	3 (6.5)	21 (31.8)	24 (21.4)	0.001
CRRT	0 (0)	7 (10.6)	7 (6.3)	0.04
Entubation	21 (45.7)	65 (98.5)	86 (76.8)	<0.001
Length of stay (days) (median, IQR)	19.0 (15.0-32.0)	19.0 (16.0-25.0)	19.0 (16.0-26.8)	0.56

CHD: Coronary Heart Disease, CHF: Chronic Heart Failure, COPD: Chronic Obstructive Lung Disease, CVD: Cerebrovascular Disease, CRD: Chronic Renal Disease, CRRT: Continious Renal Replacement Therapy, SD: Standart deviation, IQR: Interquartile Range

of the logistic regression model. We used a multiple linear regression model to identify independent factors affecting hemoglobin reduction. The fitness of the model was tested using appropriate residual and goodness-of-fit tests. A 5% type-I error level was used to infer statistical significance.

RESULTS

Out of a total of 395 patients, 134 were hospitalized in ICU for more than 14 days, and we included 112 of them who met the criteria. Mean age of the 112 included patients was 71.3 ± 13.2 years (M/F: 1.8). The median length of ICU stay was 19 d (range: 14-58 d). In total, 66 (58.6%) of the patients died while in the ICU.

At the time of ICU admission, 14 (30.4%) of survivors and 26 (39.4%) of non-survivors were anemic (according to the World Health Organization definition of Hb < 13 g dL^{-1} in males and < 12 g dL^{-1} in females).[10] The mean reduction in Hb during ICU stay was 3.47 ± 2.11 g dL^{-1}. Patient demographics, blood sampling data, and factors related to mortality are summarized in Table 1. After determination of factors affecting mortality with univariate analysis; age, sex, APACHE-II, hemoglobin reduction, intubation, and hemodialysis were put into the logistic regression model to identify the independent factors associated with death. It showed that hemoglobin reduction and the presence of intubation increased the risk of death (OR: 1.34; OR: 57.50, respectively) (Table 2).

In total, 70.269 mL of blood was drawn into 18.734 sample tubes. A median of 575 mL (range: 265-1720 mL) of blood was collected during the ICU stay. During a total of 2545 hospitalization days,

Table 2. Multivariate analysis showing factors affecting mortality			
Risk Factor	**p value**	**OR**	**95% Confidence Interval**
Hemoglobin reduction*	0.04	1.34	1.02-1.77
Intubation	< 0.001	57.50	6.64-497.82
Hemodialysis	0.09	3.50	0.83-14.71

Model: Age, Sex, APACHE-II, Hemoglobin reduction, Intubation, Hemodialysis
** For each unit increment*

a mean of 27.6 mL of blood was collected into 7.4 sampling tubes per patient day. Biochemistry tests were the most common reason (8276 tubes) for blood collection, followed by blood gases (n= 3639 tubes), complete blood count (CBC) (n= 2898 tubes), coagulation (n= 2665 tubes), and blood culture (n= 1256 tubes). In addition, 91 (81%) of the patients had a central catheter, and 9265 mL of extra blood (the initial 5 mL that was discarded) was collected during 1710 catheterized days in total.

Patients with anemia at ICU admission had a significantly smaller reduction in Hb (2.52 ± 1.44 g dL^{-1}) than those that were not anemic at ICU admission (3.99 ± 2.24 g dL^{-1}) ($p< 0.001$, $r= 0.43$). More blood was drawn from intubated patients than non-intubated patients, resulting in a greater reduction in the Hb level (463 mL [2 g dL^{-1}] versus 677 mL [3.9 g dL^{-1}], respectively) ($p< 0.001$). Furthermore, 7 patients that received CRRT and 24 patients that received hemodialysis had higher mean Hb reductions than the non-CCRT and non-hemodialysis patients (CRRT/non-CRRT: 4.1/3.4 g dL^{-1}; hemodialysis/non-hemodialysis: 4.3/3.2 g dL^{-1}). APACHE-2 score was positively correlated with drawn blood volume per day ($p= 0.01$, $r= 0.26$) but not with Hb reduction ($p= 0.26$). Previously diagnosed diseases were not associated with either the daily amount of blood taken or the decrease in Hb. Multivariate linear regression analysis created to identify independent factors influencing hemoglobin reduction. Age (B: 0.03), drawn blood volume per day (B: 0.13), and hemoglobin at admission (B: 0.60) increased the hemoglobin reduction independently. Results of univariate and multivariate analysis showing factors associated with Hb reduction were depicted in Table 3, and Table 4, respectively.

DISCUSSION

In the present study, ICU care resulted in excessive blood collection, and anemia developed in most of the patients. Although 35.7% of the patients were anemic at ICU admission, 91.2% were anemic at the end of their ICU stay. The mean reduction in Hb was 3.47 ± 2.11 g dL^{-1}, the median volume of blood drawn per collection was 27.9 mL d^{-1} (range: 16.4-45.0 mL d^{-1}), and the median total volume of blood collected per patient was 575 mL (range: 265-1720 mL). Beverina et al. similarly studied COVID-19 patients and reported that whereas 41.7% (10/24) of patients were anemic at ICU admission, 100% were anemic at discharge.[11] In their study median ICU stay was longer (29 days), and total iatrogenic blood loss was higher (719 mL) than in the present study, but iatrogenic blood loss per d (21.7 mL) was lower. In addition, Chornenki et al.[9] reported median blood loss of 25 mL d^{-1} and 213 mL in total in a comprehensive study conducted before the COVID-19 pandemic. Although the present study and these 2 earlier studies differ in design and patient groups, all 3 observed that ICU blood collection is associated with anemia.

Iatrogenic anemia caused by ICU admission is a well-known and common condition that is associated with increased morbidity and mortality.[12-14] Iatrogenic anemia during ICU stay has 2 causes: reduced RBC production; increased RBC loss. Reduced RBC production in the ICU is due to bone marrow suppression caused by infection, inflammation, a low erythropoietin level, medications, and decreased iron absorption in the intestines.[15,16] The causes of increased RBC loss include bleeding, invasive procedures, and blood collection for laboratory testing.[17,18] Although it seems unimportant because small amounts of blood were drawn for testing, numerous articles showed that many

Table 3. Factors associated with Hb reduction

		Mean Hb reduction (g dL⁻¹)	p
Age*			0.60
Sex	Female	2.76 ± 2.06	0.01
	Male	3.86 ± 2.05	
HT	Present	3.53 ± 2.15	0.72
	Absent	3.39 ± 2.08	
DM	Present	3.47 ± 1.85	1.0
	Absent	3.47 ± 2.19	
CHD	Present	3.26 ± 2.20	0.55
	Absent	3.54 ± 2.08	
CHF	Present	2.39 ± 1.89	0.05
	Absent	3.61 ± 2.11	
COPD	Present	3.31 ± 2.08	0.78
	Absent	3.49 ± 2.12	
Dementia	Present	2.53 ± 2.00	0.12
	Absent	3.57 ± 2.11	
CVD	Present	4.33 ± 1.80	0.30
	Absent	3.42 ± 2.12	
Cancer	Present	2.62 ± 2.28	0.36
	Absent	3.50 ± 2.10	
CRD	Present	3.90 ± 2.05	0.68
	Absent	3.45 ± 2.12	
Apache II*			0.26
Hb at ICU admission			<0.001 (r= 0.51)
Anemic at ICU admission			<0.001
	Present	2.52 ± 1.44	
	Absent	3.99 ± 2.24	
Total number of sampling tubes			0.001 (r= 0.32)
Volume per day			<0.001 (r= 0.40)
Total volume collected			<0.001 (r= 0.38)
Hb reduction			
Transfusion	Present	4.12 ± 2.27	0.04
	Absent	3.20 ± 2.00	
HD	Present	4.35 ± 3.80	0.02
	Absent	3.22 ± 2.12	
CRRT	Present	4.13 ± 1.58	0.39
	Absent	3.42 ± 2.14	
Intubation	Present	3.90 ± 1.92	<0.001
	Absent	2.02 ± 2.09	
Length of hospital stay*			0.02 (r= 0.21)
	Exitus		<0.001
	Present	4.15 ± 1.99	
	Absent	2.48 ±1.89	

HT: Hypertension; COPD: chronic obstructive lung disease; CVD: cerebrovascular disease; CRD: chronic renal disease; HFNO: high flow nasal oxygen; NIV: non-invasive ventilation; HD: hemodialysis.
** Correlation checked*
r: Correlation coefficient

patients suffer from iatrogenic anemia and related complications after discharge.

In the present study, patients who were not anemic at admission had a greater decrease in hemoglobin than those who were anemic at admission. Multivariate analysis showed that, age, drawn volume per day, and hemoglobin at admission were independently associated with hemoglobin reduction. Age is a well-known nonmodifiable risk factor for mortality for COVID-19[19] and other diseases.[20,21] Physicians' tendency to follow patients at high risk due to advanced age more closely may explain the association of advanced age with decreased hemoglobin in our study. It is not surprising that patients with higher baseline hemoglobin, and higher drawn volume per day experience greater hemoglobin reduction. In contrast, none of the observed comorbidities were associated with excessive blood collection or Hb reduction. Although the majority of patients have underlying diseases that will cause low (chronic renal disease) or high (chronic obstructive pulmonary disease) Hb levels, absence of relationship between the presence of comorbidity and Hb reduction thought us excessive blood collection and Hb reduction are associated with the severity of COVID-19 rather than with a patient's previous medical history. Araya et al.[22] noted that severe COVID-19 patients developed anemia more often than moderate cases. Similarly, a recent study reported that anemia at ICU admission was associated with severe disease and that severe patients were more likely to develop anemia.[23] These findings suggest that the severity of COVID-19 is a risk factor for iatrogenic anemia and vice versa.

Anemia is associated with poor outcomes, including mortality. Corwin et al.[12] reported that a low Hb level is associated with increases in the need for RBC transfusion, ICU stay, and mortality. Although they noted that the baseline Hb level is not directly related to the length of ICU stay or mortality, they reported that a Hb < 9 g dL^{-1} was a predictor of longer ICU stay and increased mortality. A similar study on post-hospital outcomes of anemia showed that anemia at discharge was significantly associated with 90-d mortality and that the severity of anemia was correlated with time to death. The present findings also show that Hb reduction (OR: 1.34) is associated with an increase in mortality risk.

Table 4. Multivariate analysis showing factors affecting hemoglobin reduction

Variable	Unstandardized Coefficients		p value
	B	Std. Error	
Age	0.03	0.01	0.049
Drawn volume by day	0.13	0.03	0.001
Hemoglobin at admission	0.60	0.09	0.001

Dependent Variable: Hemoglobin reduction (mg/dl)

The prevention of anemia is as crucial as treating critically ill patients.[24] Frequent blood sampling for blood gas analysis, biochemistry, or cultures can exacerbate anemia and cause poor outcomes.[24,25] Several approaches have been proposed to minimize iatrogenic blood loss, including use of small sampling tubes[26], closed blood conservation devices[27], point of care testing[28], and artificial intelligence techniques.[29] Beverina et al.[11] proposed use of low-volume sampling to reduce iatrogenic anemia in COVID-19 patients. Considering the tendency for doctors to order many laboratory tests, so as to avoid frequent examinations of COVID-19 patients, we think that strategies for reducing blood loss are essential for COVID-19 patient care. In addition to all these, we should not forget that interventions such as hemodialysis and CRRT, which we cannot modify, can cause intense blood loss and iatrogenic anemia.

The present study has some limitations, including a retrospective design, and the lack of baseline Hb levels and evaluation of a history of anemia in all patients. In addition, blood loss from the time of hospital admission to ICU admission wasn't calculated. Although there was a blood sampling protocol in the ICU, some differences in the volume of blood collected may have occurred. In contrast, the study's strengths include a large patient population, inclusion of both intubated and non-intubated patients, and collection of real-life data.

Conclusion

Anemia due to excessive blood sampling remains a significant problem in ICUs and is associated with poor outcomes. Considering that most COVID-19 patients are admitted to the ICU due to ARF, hemodynamic instability, and shock, it is vital to keep Hb level within normal range to maintain oxygenation. Clinicians should be encouraged to use low-volume blood sample strategies, including infrequent blood sampling, frequent physical examination, and use of low-volume blood tubes. Additional prospective studies comparing low-volume blood sampling strategies to traditional methods are needed to delineate the relationship between ICU blood collection and anemia.

REFERENCES

1. World Health Organization Coronavirus (COVID-19) Dashboard. https://covid19.who.int (Access date: 18/01/2022).
2. Gallo Marin B, Aghagoli G, Lavine K, et al. Predictors of COVID-19 severity: A literature review. Rev Med Virol 31: 1-10, 2021.
3. Hayden SJ, Albert TJ, Watkins TR, Swenson ER. Anemia in critical illness: insights into etiology, consequences, and management. Am J Respir Crit Care Med. 185: 1049-1057, 2012.
4. Vincent JL, Baron J-F, Reinhart K, et al. Anemia and blood transfusion in critically ill patients. JAMA 288: 1499-507, 2002.
5. Corwin HL, Parsonnet KC, Gettinger A. RBC transfusion in the ICU: is there a reason? Chest 108: 767-771, 1995.
6. Khamiees M, Raju P, DeGirolamo A et al. Predictors of extubation outcome in patients who have successfully completed a spontaneous breathing trial. Chest 120: 1262-1270, 2001
7. Thygesen K, Alpert JS, White H, Joint E. ACC/AHA/WHF Task Force for the Redefinition of Myocardial Infarction. Universal definition of myocardial infarction. Eur Heart J 28: 2525-2538, 2007.
8. Carson JL, Noveck H, Berlin JA, Gould SA. Mortality and morbidity in patients with very low postoperative Hb levels who decline blood transfusion. Transfusion 42: 812-818, 2002.

9. Jackson Chornenki NL, James TE, Barty R, et al. Blood loss from laboratory testing, anemia, and red blood cell transfusion in the intensive care unit: a retrospective study. Transfusion 60: 256-261, 2020.
10. WHO. Haemoglobin concentrations for the diagnosis of anemia and assessment of severity. Vitamin and Mineral Nutrition Information System. Geneva, World Health Organization,2011(WHO/NMH/NHD/MNM/11.1)(http://www.who.int/vmnis/indicators/haemoglobin. pdf (Access date: 18/01/2022).
11. Beverina I, Borotto E, Novelli C, et al. Iatrogenic anaemia and transfusion thresholds in ICU patients with COVID-19 disease at a tertiary care hospital. Transfus Apher Sci 60: 103068, 2021.
12. Corwin HL, Gettinger A, Pearl RG, et al. The CRIT Study: anemia and blood transfusion in the critically ill-current clinical practice in the United States. Crit Care Med 32: 39-52, 2004.
13. Gerth A, Hatch R, Young J, Watkinson P. Changes in health-related quality of life after discharge from an intensive care unit: a systematic review. Anaesthesia 74: 100-108, 2019.
14. Warner MA, Kor DJ, Frank RD, et al. Anemia in critically ill patients with acute respiratory distress syndrome and posthospitalization physical outcomes. J. Intensive Care Med. 36: 557-565, 2021.
15. DeAngelo AJ, Bell DG, Quinn MW, et al. Erythropoietin response in critically ill mechanically ventilated patients: a prospective observational study. Crit Care 9: 1-5, 2005.
16. Litton E, Lim J. Iron metabolism: an emerging therapeutic target in critical illness. Annual Update in Intensive Care and Emergency Medicine, 573-584, 2019.
17. Bodley T, Chan M, Levi O, et al. Patient harm associated with serial phlebotomy and blood waste in the intensive care unit: A retrospective cohort study. PloS One 16: e0243782, 2021
18. Van der Laan S, Billah T, Chi C, et al. Anaemia among intensive care unit survivors and association with days alive and at home: an observational study. Anaesthesia 76: 1352-1357, 2021.
19. Grasselli G, Greco M, Zanella A, et al. Risk factors associated with mortality among patients with COVID-19 in intensive care units in Lombardy, Italy. JAMA Intern Med 180: 1345-1355, 2020.
20. Dhingra R, Vasan RS. Age as a risk factor. Med Clin 96: 87-91, 2012.
21. De Winter C, Bastiaanse L, Hilgenkamp T, et al. Cardiovascular risk factors (diabetes, hypertension, hypercholesterolemia and metabolic syndrome) in older people with intellectual disability: results of the HA-ID study. Res Dev Disabil 33: 1722-31, 2012.
22. Araya S, Wordofa M, Mamo MA, et al. The Magnitude of Hematological Abnormalities Among COVID-19 Patients in Addis Ababa, Ethiopia. J Multidiscip Healthc 14: 545, 2021.
23. Tao Z, Xu J, Chen W, et al. Anemia is associated with severe illness in COVID-19: a retrospective cohort study. J Med Virol. 93: 1478-88, 2021.
24. Whitehead NS, Williams LO, Meleth S, et al. Interventions to prevent iatrogenic anemia: a Laboratory Medicine Best Practices systematic review. Crit Care 23: 1-11, 2019.
25. Baron D, Franchini M, Goobie S, et al. Patient blood management during the COVID–19 pandemic: a narrative review. Anaesthesia 75: 1105-1113, 2020.
26. Dolman HS, Evans K, Zimmerman LH, et al. Impact of minimizing diagnostic blood loss in the critically ill. Surgery 158: 1083-1088, 2015.
27. Mukhopadhyay A, See K, Chan Y et al. Effect of a blood conservation device in patients with preserved admission haemoglobin in the intensive care unit. Anaesth Intensive Care 39: 426-430, 2011.
28. Mahieu L, Marien A, De Dooy J et al. Implementation of a multi-parameter Point-of-Care-blood test analyzer reduces central laboratory testing and need for blood transfusions in very low birth weight infants. Clin Chim Acta 413: 325-330, 2012.
29. Cismondi F, Celi LA, Fialho AS, et al. Reducing unnecessary lab testing in the ICU with artificial intelligence. Int J Med Inform 82: 345-358, 2013.

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