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Factors contributing to nosocomial anemia in the critically ill patients

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Abstract
Background; *Nosocomial anemia in critically ill patients may be the result of a variety of causes including RBCs losses and insufficient RBCs production. Therefore, critical care nurses should prevent nosocomial anemia through identifying the risk factors group, minimizing the factors contributing to nosocomial anemia, using of blood conservation strategies in the ICU, and monitoring of oxygen status as well as hematological one.*
Aim of this study *was to identify factors contributing to nosocomial anemia in the critically ill patients.*
Methods; *three tools were used for data collection. Tool one "Factors contributing to nosocomial anemia assessment", tool two "Indicators of nosocomial anemia" and tool three "Estimation of blood loss volume tool".*
Results of the study; *more than three-quarters of the studied patients developed nosocomial anemia (76.9%) by the third day while the rest of them did not develop nosocomial anemia.*
Conclusion; *Critically ill patients were highly susceptible for exposure of multiple iatrogenic factors which can contribute to nosocomial anemia during ICU stay. The volume of blood withdrawn for laboratory tests and malnutrition are among the factors that contribute to nosocomial anemia in the critically ill patients.*
Keywords: *Nosocomial Anemia - Critically Ill Patients*

I. Introduction

Critical care nursing is defined according to the Canadian Association of Critical Care Nurses (CACCN) as that" specialty which exists to care for patients who are experiencing life-threatening health crises within a patient/family centered model of care". Critical care nursing is a specialty concerned with human responses to life threatening problems, as well as the prevention of health problems. Thus, nursing critically ill patients is considered a continuous and intensive process, which needs advanced technology [(1, 2)]. The goals of critical care must extend beyond patients survival and include shared, multidisciplinary collaboration to prevent and manage the long-term complications of critical care [(1, 2)]. The reduction of hospital-acquired complications is currently being targeted in patient safety initiatives. Hospital acquired complications all significantly impact patient safety causing morbidity, sometimes mortality and are costly to treat [(3)].

Critically ill patients are at a vulnerable period of their lives. Physiological, pathological, psychological and environmental stressors in intensive care units (ICUs) are increasing the risk of critically ill patients experiencing complications that occur after ICU admission. These include conditions such as venous thromboembolism, nosocomial infections, medication errors, falls, pressure ulcers, catheter-related infections, ventilator-associated pneumonia, and nosocomial anemia that result in considerable morbidity and mortality [(4,5)]. ***Nosocomial anemia*** is the actual reduction in the total number of circulating erythrocytes or a decrease in the quantity or quality of hemoglobin (Hb) induced by multiple iatrogenic factors in the health care settings. Values less than 12 g/dl in the male and 10.6 g/dl in the female are considered anemia in ICUs [(6)].

Most patients in intensive care units develop anemia because of blood losses, nutritional deficiencies, hemolysis, inflammation, or infection. After patients' admission to the hospital, especially in ICU more than 95% of ICU patients develop nosocomial anemia after 3 days of admission [(7, 8)]. *Salisbury et al 2011* suggest that nosocomial anemia may be yet one more potentially preventable complication associated with ICU stay [(4)]. Moreover, *Debellis 2007* reported that anemia is the most common hematologic problem especially in critically ill patients [(7)]. So, attention to nosocomial anemia is important because it can impact negatively upon patients [(4)]. The decrease in oxygen (O_2)–carrying capacity and plasma volume is considered the most significant risk associated with nosocomial anemia in critically ill patients. This decrease in O_2 –carrying capacity can result in tissue hypoxia, anaerobic metabolism, production of lactic acids, multi organ failure and death. Nosocomial anemia can be particularly problematic for patients with severe ischemic heart diseases or cerebrovascular diseases. Decreased blood viscosity which is associated with anemia can lead to increase in cardiac output, stroke volume, heart rate, and myocardial O_2 consumption. Compensatory mechanisms that increase O_2 delivery

(DaO_2) to vital tissues include improvement in the microcirculation and increases in the O_2 extraction (O_2 ER) ratio [9].

Nosocomial anemia also can affect platelet function and interactions between platelets and the vascular wall. Fewer platelets are available to adhere to sites of endothelial injury and prevent bleeding in patients with anemia compared with non-anemic patients. The ability to tolerate anemia depends on the circulatory status. Patients with an adequate circulatory volume can tolerate lower Hb concentrations than can hypovolemic patients. The impact of nosocomial anemia isn't only physiological oriented, but its impact will affect the patients' length of stay (LOS), need for blood transfusion exposing the patients to transfusion complications as well as increasing the cost [7, 10].

Several factors contribute to the decline in Hb concentration during ICU stay. In critical illness, nosocomial anemia results from two fundamental processes: Red blood cells (RBCs) loss caused by phlebotomy losses and invasive procedures and diminished RBCs production caused by nutritional deficiencies and blunted erythropoietin (EPO) response [3, 7, 11-14]. In addition, hemodilution has a significant role in the decrease of Hb concentration which is induced by increasing the plasma volume in critically ill patients and thus the development of nosocomial anemia. As well, multiple drugs used in ICUs may cause decreased bone activity (e.g., corticosteroids, antibiotics, select antifungal, and others) which in turn affect RBCs production [7].

Erythropoietin is a glycoprotein hormone that is mainly secreted by tissue cells in the interstitial peritubular areas of the renal cortex while lower EPO levels is synthesized in hypatocytes, macrophages, and liver kupffer's cells. Because EPO is mainly produced by the kidneys, renal insufficiency can decrease its concentration. Inappropriately low circulating concentrations of EPO, and diminished responsiveness of bone marrow precursor cells to EPO are included among the numerous factors that may contribute to the development of nosocomial anemia in critically ill patients[8].

Erythropoietin stimulates the bone marrow to produce RBCs thereby increase the O2-carrying capacity of the blood, promote red blood cell survival through protecting these cells from apoptosis, and to keep RBCs mass and Hb constant day by day, and hasten RBC recovery after hemorrhage. EPO is essential for erythropoiesis which is a slow-acting process. Following a rise in plasma EPO it takes 3–4 days before reticulocytosis becomes apparent. O2sensors exist at the level of organs as the kidneys. These O2-sensing mechanisms during acute anemia, triggers an increase in renal EPO production to restore Hb concentration while an early decrease in renal tissue oxygen partial pressure (PO2) occurs. Tissue O2 tension is thought to regulate EPO production via an O2-responsive transcription factor called hypoxia-inducible factor (HIF-1). Increased expression of hypoxia sensitive molecules, including HIF-1, occurs in acute anemia at a Hb threshold near 70 g / liter [13,14].

Because EPO production depends on the tissue PO2, EPO expression is also activated when the arterial PO2 declines or when the O2 affinity of the blood increases. EPO binds to EPO receptors on erythroid progenitor cells. In response to EPO, these progenitor cells further differentiate into burst-forming unit erythroid cells and colony- forming unit erythroid cells. These cells then differentiate into erythroid precursors and proerthroblasts, followed by differentiation to erythroblasts and reticulocytes, and eventually to mature erythrocytes [13,14].

So the blunted EPO response during critical illness could result from inhibition of the EPO gene by inflammatory cytokines. The cytokines interleukin-1 and TNFa directly inhibit EPO expression. These inflammatory mediators decrease erythropoiesis, leaving patients unable to secrete the level of EPO necessary to increase RBCs production. Even if EPO is secreted, TNFa, interferon gamma, and interleukin 1 inhibit erythrocyte proliferation, causing these patients to become anemic. These inflammatory mediators can also impair iron availability for EPO through increased uptake and retention of iron within cells of the RES [8].

Patients' safety is the cornerstone of high-quality health care. The most critical contribution of nursing to patient safety is the ability to predict, prevent harm through coordinating and integrating the multiple aspects of quality within the care directly provided by nursing and across the care delivered by others in the setting. According to the Institute of Medicine report "*To Err Is Human",* so developing quality improvement projects, adopting evidence-based standards of practice, and implementing system-wide interventions is crucial [15].

Prevention of the hospital acquired complications is an important element to ensure patient safety. ***Critical care nurses*** are advocates for patients' safety, so nurses have an important role to prevent such complications such as nosocomial anemia. Critical care nurses have a major role in preventing nosocomial anemia through identifying the risk patient groups, assessing risk factors contributing to nosocomial anemia, monitoring of O_2 status as well as hematological ones; minimizing blood loss through excessive blood sampling; and using of blood conservation strategies in ICUs [6,16,17]. Patients nutritional status through revising policies, procedures, and feeding protocols related to nutritional support practices, developing and implementing nutrition assessment sheet, evaluating the adequacy of nutritional support, and reasons impeding adequate delivery [13,18, 19].

Also critical care nurses have a role in developing skills in delivering and monitoring tolerance to drugs such as EPO and new intravenous iron preparations, reviewing drugs that patients may be taking with the intention of inhibiting the coagulation cascade [7, 16]. Although many studies [7, 11- 14, 17] discussing nosocomial anemia in critical illness concerning the etiology, consequences, and management have been carried out, there are no national studies that have been conducted to identify factors contributing to nosocomial anemia in critically ill patients. Therefore, this study is conducted to identify factors contributing to nosocomial anemia in critically ill patients.

Aim of the study; is to identify factors contributing to nosocomial anemia in critically ill patients.
Study question: What are the factors that contribute to nosocomial anemia in critically ill patients?

II. Materials and method

Materials

Research design: A correlational descriptive design was used in this study to identify factors contributing to nosocomial anemia in critically ill patients.

Setting: This study was carried out at the ICUs of the Alexandria Main University Hospital, namely; Casualty care unit (unit I is the known name and General intensive care unit (unit III). Both units receive patients in the acute stage of illness with a variety of disorders. Patients admitted to these units directly from ER or transferred from other hospital departments.

Subjects: A convenient sample of 65 newly admitted adult critically ill patients to the above mentioned settings during a 4 months period were included in the study with exclusion criteria: Hb <11 g /dl for adult males, Hb <10.6 g /dl for adult females, Hct <36% for adults, patients with bleeding abnormalities, patients who are postoperative, patients with renal insufficiency, patients with autoimmune diseases and patients on chemotherapy were excluded from the study. Because Erythropoietin is mainly produced by the kidneys, renal insufficiency can decrease its concentration leading to non-acquired anemia but pathological one.

Tools Three tools were developed by the researchers after reviewing the relevant literature [6, 8, 12, 14, 18,19-26] except tool two part (1) which was developed by *Keene et al* [21] and adopted by the researchers.

Tool one: Factors contributing to nosocomial anemia assessment tool. This tool was developed by the researchers to observe non -blood loss associated interventions. It consists of two parts:
Part (I): Nutritional –related factors. It includes actual nutritional intake and the ideal nutritional requirements needed for each patient (Kcal/day) [19, 20].
Part (II): Drug –related factors. It includes prescribed medications during the ICU stay such as thrombolytic, antiplatelet, PPI, NSAIDs, nephrotoxics drugs [8, 14]. The response format is measured using scale of Yes (present), No (not present).

Tool two: Indicators of nosocomial anemia. This tool was used to monitor critically ill patients' indicators of nosocomial anemia. It consists of three parts:
Part (I): Therapeutic intervention severity score (TISS). This part was developed by *Keene et al* [21] and adopted by the researchers. Items are summed to assess the severity of illness for critically ill patients with higher scores reflecting deterioration of patients' condition and vice versa. It consists of four items; 4 point intervention such as patients on controlled ventilation, 3 point intervention such as patients with chest tube, 2 point intervention such as patients with central venous catheter, 1 point intervention such as patients who need tracheostomy care. It is scored according to the number of points related to each item if Yes and it is scored zero if No.
Part (II): Hemodynamic parameters. Part (II) was developed by the researcher after reviewing the relevant literature [6].This part is used to assess the change in hemodynamic parameters values at different times during insertion of invasive lines. It includes patients' hemodynamic parameters such as heart rate, temperature, mean arterial pressure, and central venous pressure.
Part (III): laboratory investigations data. Part (III) was developed by the researchers after reviewing the relevant literature [12, 22].This is used to monitor nutritional status, the development of nosocomial anemia, occurrence of infection and includes patient's hemoglobin level, serum hematocrit level, serum erythropoietin level, serum transferrin, serum pre-albumin, total protein, renal function tests, PT, APTT, INR, WBCs count.

In addition to demographic data such as sex, age and name of the ICU and clinical data in relation to nosocomial anemia such as admission medical diagnosis, co-morbidities, admission hemoglobin and hematocrit level, LOS, APACHE II score, the highest total leukocytes count and corresponding temperature value.

Tool three: Estimation of blood loss volume tool. This tool was developed by the researchers and is used to calculate the amount of blood lost.

Part (I): blood loss associated interventions. Observational checklists were developed by the researchers after reviewing the relevant literature [23, 24] and include pre-procedural assessment, procedure performance, and post-procedural care including documentation regarding withdrawing of blood sampling (venous, arterial, or indwelling catheters) and the insertion of the invasive lines such as CVC, arterial line, chest tube. Interventions are measured using a dictomous scale of done and not done.

Part (II): blood loss volume estimation. It includes three sections as follows:

a) **Estimation of sampling blood loss volume:** It consists of name of requested investigation, frequency, amount of blood withdrawn, site of blood withdrawal , number of trials each time of withdrawal, calculation of the mean blood volumes drawn per 24 hours[6, 18], …….etc.
b) **Estimation of blood loss volume during the insertion of invasive lines:** It consists of name of inserted invasive line, frequency, amount of blood lost [25, 26].
c) **Hematoma measurement:** It includes the hematoma size and the degree of hematoma which is categorized as minor and major [25, 26].

Method

An approval from the research ethical committee in the Faculty of Nursing was obtained to conduct the study. An official letter from the faculty of nursing was delivered to the hospital authorities in the Main University Hospital and approval to conduct this study was obtained after providing explanation of the aim of the study. The study tools were developed after reviewing the related literature except tool two part (I) was adopted from *Keene et al*. The tools were submitted to a Jury of 7 experts in Clinical Pathology, Critical Care Nursing, and Anesthesia to assess clarity and content validity of the tools and all necessary modifications were done. The modifications included removing unnecessary steps which were not related to nosocomial anemia from the observational checklists and re-clustering the laboratory tests.

A written informed consent was obtained from each conscious adult patient or from responsible person who is the first relative and the medical attorney (if unconscious patient). It included the aim of the study, potential benefits, risks and discomforts from participation. The anonymity, confidentiality and privacy of responses, voluntary participation and right to withdraw from the study were emphasized to subjects. A pilot study was carried out on five patients in order to assess the clarity and applicability of the tools, and all necessary modifications were done. Appropriate modifications were done prior to data collection of the study. Reliability of the tools was measured using Cronbach Alpha reliability, the reliability coefficients were (r = 0.788) which was acceptable. The researchers collected data personally during approximately four months starting from April 2012 to August 2012.

Data collection:

Newly admitted patients were enrolled in the study according to the previously mentioned exclusion criteria, then patients' characteristics such as age, sex and the name of ICU, in addition to patients' clinical data such as admission medical diagnosis, co-morbidities, admission Hb and Hct level, APACHE II score, total leukocytes count and corresponding temperature value were recorded upon the admission using tool two.

Measurement of hemodynamic parameters: Heart rate (beats/ min), Respiratory rate (cycles/ min) were counted; mean arterial pressure (mmHg) was calculated. Central venous pressure (cmH_2o) and temperature (°C) were measured and recorded using tool two part II. HR, RR, MAP, CVP, and temperature values were measured and recorded using part II of the tool for four times except CVP at T2, T3, and T4 (if inserted):

Time one (T1): the immediate time before the insertion of any invasive maneuver.
Time two (T2): the time after the insertion of the invasive maneuver with two hours.
Time three (T3): the time after the insertion of the invasive maneuver with four hours.
Time four (T4): the time after the insertion of the invasive maneuver with six hours.

The performance of withdrawing blood samples (venous, arterial, or indwelling catheters) which were done by nurses and the insertion of the invasive lines such as CVC, arterial line, and chest tube (which were done by physicians) were assessed and recorded by the researchers using observational checklists on admission and each time repeated using tool three part (I) in which interventions were measured using a dictomous scale of done and not done. Intern nurses were trained as research assistant to observe nurses' practices during night shifts.

Blood loss volume during the insertion of invasive lines was estimated using tool three part (II) through weighing of a dry linen pad-saver which is placed under the appropriate area at the insertional site then weighing it after the insertion has been completed. The researchers converted grams of saturated weight into

milliliters of blood loss to be easy to estimate blood loss in ml (based on the advice of statistician to be easy for estimation) for data analyses through weighing of an empty standard-sized tube, which is used for collecting a blood specimen then re-weighing it with two milliliters of blood. The difference between two weights equals weight of two milliliters of blood then calculation of one milliliter of blood weight.

Calculation of total blood volume withdrawn, needed, and discarded was done daily considering the number of trials for each laboratory test using tool three part II. Palpating the borders of hematoma firstly before measuring hematoma size by using two-dimensional ruler with $1cm^2$ precision was done through measuring the size of blood accumulation under the skin in two dimensions (length and width).

The ruler's 0 mark was placed at the firm edge of the hematoma and marked and then measured directly across to the opposite firm edge. The second dimension was measured in the same manner as the first dimension then according to the size of the hematoma, ;(that is by measuring its linear dimensions with a ruler. Either hematoma is two-dimensional (length x width) or a circle (diameter x diameter) or an oval (maximum diameter x maximum diameter perpendicular to the first measurement) then the researcher recorded it as minor < 5 cm or major > 5 cm using tool three part II.

Laboratory investigations data (patient's hemoglobin level, serum hematocrit level, serum erythropoietin level, serum transferrin, serum pre-albumin, total protein, renal function tests, PT, APTT, INR, WBCs count.), intake and output were recorded in an assessment sheet by the researcher on a daily basis using tool two part (III) from admission until the occurrence of nosocomial anemia for monitoring of nosocomial anemia indicators or until the discharge in the non-anemic patients. Laboratory investigations especially hemoglobin and hematocrit levels were recorded three times on 3 consecutive days after the development of nosocomial anemia for confirmation of the presence of nosocomial anemia.

TISS score data was collected at the same time each day by the researcher using tool two part I then sum of points of interventions was calculated and classified according to the four degrees of severity Class IV : ≥ 40 points, Class III : 20 - 39 points, Class II : 10 -19 points, and Class I : □ 10 points. Drug related factors were recorded regularly using tool one part (II). Name, dose, and frequency of certain medications prescribed to the patient was recorded using scale of Yes (present), No (not present).

Using tool one part I the actual and ideal caloric requirements were recorded and compared daily from admission until anemia occurred in the "***Nutritional requirements sheet***" or until the discharge in the non-anemic patients. Actual calories consumed by the patient were calculated through identifying type and the amount of each enteral or parenteral intake then calculating the calories included. The ideal caloric requirements needed for the patient were calculated using Harris and Benedict equation.

Basal energy expenditure (BEE): It differs according to sex.

BEE (men): 66.47+ (13.75xweight in Kg) + (5.0xheight in cm) – (6.76xage in yr.)

BEE (women): 65.51+ (9.56xweight in Kg) + (1.7xheight in cm) – (4.68xage in yr.)

Multiplying by the stress factors such as peritonitis multiplied by 1.4, trauma multiplied by 1.4, and sepsis multiplied by 1.8 and multiplying by the activity factors such as confined to bed multiplied by 1.2, out of bed multiplied by 1.3.

Statistical Analysis:

The raw data were coded and transformed into coding sheets. The results were checked. Then, the data were entered into SPSS system files (SPSS package version 18) using personal computer. Output drafts were checked against the revised coded data for typing and spelling mistakes. Finally, analysis and interpretation of data were conducted. The following statistical measures were used: Descriptive statistics including frequency, distribution, mean, and standard deviation were used to describe different characteristics. Kolmogorov – Smirnov test was used to examine the normality of data distribution. Univariate analyses including: t-test and Mann Whitney test were used to test the significance of results of quantitative variables. Moreover, Chi-Square test, Monte Carlo test and Fisher's Exact test were used to test the significance of results of qualitative variables. Linear correlation was conducted between different variables using Pearson correlation coefficient and Spearman Rho correlation coefficient. The significance of the results was at the 5% level of significance.

III. Results

Regarding ***patients' age***, 31% of the studied patients were less than 30 years old and 21% of them are between 40 to less than 50 years old and regarding ***sex***, more than half of the studied patients in this study (55.4%) were males. As regard ***patient care unit***, the majority of studied patients 83.1% were admitted to casualty care unit (unit I). Regarding ***their admission medical diagnoses***, It reveals that 38.5%of the patients had poisoning conditions, and 24.6% of them had respiratory disorders Distribution of studied patients according to their characteristics are presented in table (1)

Table (1) Distribution of studied patients according to their characteristics

Characteristics		Patients (n=65)	
		N	%
Age	less than 30	20	30.8
	30-	15	23.1
	40-	14	21.5
	50-≤60	16	24.6
Sex	Male	36	55.4
	Female	29	44.6
Unit	ICU unit I	54	83.1
	ICU unit III	11	16.9
Diagnoses	Cardiovascular disorders	8	12.3
	Respiratory disorders	16	24.6
	Neurological disorders	8	12.3
	Endocrine/metabolic disorders	8	12.3
	Poisoning	25	38.5

Table (2) shows patients distribution according to the ***occurrence/ outcomes of nosocomial anemia*** "nosocomial anemia, mortality rate, length of ICU stay and need for blood transfusion". It can be noted that 76.9% of patients have developed nosocomial anemia. Thirty patients died during the study and the mortality rate is 86.7% (of 30 patients who died in the ICU) of patients who developed nosocomial anemia. More than half of patients (60.0%) had a length of ICU stay between 5 to less than 10 days. Only 12.3% of patients who developed nosocomial anemia received blood transfusion.

Table (2): Distribution of the studied patients according to the *occurrence/* outcomes of nosocomial anemia

Outcomes		**Patients (n=65)**	
		N	**%**
Nosocomial anemia		50	76.9
Mortality rate	*Anemic (n=50)*	26	86.7
	Non-anemic (n=15)	4	13.3
	Total (n=65)	30	46.2
Length of ICU stay	*<5 days*	15	23.1
	5-10	39	60.0
	>10	11	16.9
Need for blood transfusion		8	12.3

Table (3) represents ***the onset day of nosocomial anemia and the day of discharge*** among the studied patients. It can be seen that 40% of anemic patients have developed nosocomial anemia on the third day followed by the second day 22%. It can be noted also that 22% of the studied patients have developed nosocomial anemia over the period from the 5th day to the 11th day. After 5 days or more from ICU stay most of those anemic patients 90% have been discharged. However, 60% of non-anemic patients have been discharged on the 4th day.

Table (3): Distribution of the studied patients according to the onset day of nosocomial anemia and the day of discharge on different days of ICU stay.

Studied patients		**Days**									
		Onset of nosocomial anemia					**Discharge from ICU**				
		Day 1	**Day 2**	**Day 3**	**Day 4**	**Day 5 0r more**	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 5 0r more**
Anemic (n=50)	**N**	0	11	20	8	11	0	0	0	5	45
	%	0.0	22.0	40.0	16.0	22.0	0.0	0.0	0.0	10.0	90.0
Non-anemic (n=15)	**N**						0	0	1	9	5
	%						0.0	0.0	6.7	60	33.3

Table (4) shows the change in hemoglobin level (g/dl) among the non-anemic patients. This table explains that even patients who did not develop anemia, their hemoglobin level was decreased while they are in the ICU. It can be observed from this table that 40% of those non-anemic patients were having a decrease in the hemoglobin level with 2-3 g/dl while 13.3% of patients' their hemoglobin level decreased for less than 1g/dl.

Table (4): Distribution of non-anemic patients according to the change in hemoglobin level (g /dl)

Change in hemoglobin level (g/dl)	Patients (n=15)	
	N	%
1	2	13.3
1-2	3	20.0
2-3	6	40.0
3	4	26.7

Table (5) illustrates the frequency distribution of the studied patients according to factors contributing to nosocomial anemia. Concerning factors contributing to increase RBCs loss; sampling blood loss, insertional blood loss and drugs that might contribute to increase RBCs loss. As regard sampling blood loss, it can be noted that most of patients who had sampling blood loss from 20 to less than 50 were got nosocomial anemia. There is a statistical significant positive correlation between the sampling blood loss volume and the occurrence of nosocomial anemia R=0.355, P=0.004*. Regarding insertional blood loss, most of patients 62.5% who experienced no insertional blood loss were developed nosocomial anemia. There is no statistically significant correlation between the insertional blood loss and the occurrence of nosocomial anemia r=-0.013, p=0.931.

The majority of patients who lost blood while the insertions of different invasive lines were developed nosocomial anemia as the insertional blood volume loss was 67.6% (10 ml), 95% (10 20 ml) and (100% ≥ 20 ml) respectively , however, the correlation between the insertional blood loss and the occurrence of nosocomial anemia although was not statistically significant as in table 8. It can be noted from this table that related to drugs, 80%, 77.8% respectively of patients who consumed NSAIDs and anticoagulants were developed nosocomial anemia. There was no significant association between the occurrence of nosocomial anemia and the consumption of NSAIDs as FEP=1.0.

Regarding factors contributing to decrease RBCs production; nutritional deficiencies, presence of infection (impaired EPO) and drugs that might contribute to decrease RBCs production. It can be seen that regarding to nutritional deficiencies, all patients (76.9%) who developed nosocomial anemia were underfed. However, there is no statistically significant correlation between nutritional deficiencies and nosocomial anemia. Related to the development of infection, all patients who developed infection (100%) were developed nosocomial anemia and **there is no significant association between the occurrence of infection and nosocomial anemia FEP=0.182.**

It can be seen from this table that related to drugs, 71.1%, 84.4%, 73.3% respectively of patients who consumed nephrotoxics, PPI and miscellaneous drugs were developed nosocomial anemia. There was no significant association between the occurrence of nosocomial anemia and the consumption of drugs regarding nephrotoxics, proton pump inhibitors, NSAIDs and miscellaneous drugs FEP=0.12, X2=1.972, P=0.16, FEP=1.0 and FEP=0.317 respectively.

Table (5) Frequency distribution of the studied patients according to factors contributing to nosocomial anemia

Factors				Occurrence of nosocomial anemia		Total N=65	Significance
				Yes N=50	No N=15		
Increase RBCs loss	Sampling blood loss volume (ml)	10 20	N	2	8	10	r 0.355 p 0.004*
			%	20	80	100	
		20 30	N	19	4	23	
			%	82.6	17.4	100	
		30 40	N	14	1	15	
			%	93.3	6.7	100	
		40 50	N	5	1	6	
			%	83.3	16.7	100	
		≥ 50	N	10	1	11	
			%	90.9	9.1	100	
	Insertional blood loss volume (ml)	No loss	N	5	3	8	r=-0.013 p=0.931
			%	62.5	37.5	100	
		10	N	23	11	34	
			%	67.6	32.4	100	
		10 20	N	19	1	20	
			%	95	5	100	
		≥ 20	N	3	0	3	
			%	100	0	100	

	Drugs that may affect RBCs loss	NSAIDs	N	4	1	5	^{FE}P=1.0
			%	80	20	100	
		Anticoagulants	N	28	8	36	
			%	77.8	22.2	100	
Decrease RBCs production	**Nutritional deficiencies**	Underfed □ 80%	N	50	15	65	**r 0.16**
			%	76.9	23.1	100	**p -0.176**
		Adequate fed 80-110%	N	0	0	0	**r 0.075**
			%	0	0	0	**p -0.222**
		Over fed ≥110	N	0	0	0	**r 0.068**
			%	0	0	0	**p 0.228**
	Presence of infection	Yes	N	8	0	8	**FEP=0.182**
			%	100	0	100	
		No	N	42	15	57	
			%	73.7	26.3	100	
	Drugs that may affect RBCs production	Nephrotoxics	N	32	13	45	^{FE}P=0.12
			%	71.1	28.9	100	
		Proton pump inhibitors	N	27	5	32	X^2=1.972
			%	84.4	15.6	100	P=0.16
		Miscellaneous	N	22	8	30	^{FE}P=0.317
			%	73.3	26.7	100	

X^2: Chi-Square test ^{FE}P: Fisher's Exact test
r: Spearman Rho correlation coefficient*significant at P□ 0.05

Table (6) shows the relationship between patents' diagnosis and the occurrence of nosocomial anemia. It can be noted that 66.7%, 71.4% of patients with cardiovascular and respiratory disorders have developed nosocomial anemia respectively. It can be observed from this table that 83.3% of patients who suffered neurological, endocrine/ metabolic and poisoning disorders have developed nosocomial anemia. Moreover, none of the patients included in this study were admitted to the target ICUs with infectious, gastrointestinal, renal or musculoskeletal disorders. There was a statistically significant association between anemic and non anemic patients regarding respiratory, neurological, endocrine and poisoning disorders X^2=4.88 P=0.027*, X^2=6.06 P=0.014*, X^2=6.06 P=0.014*, X^2=19.05 P<0.0001* respectively.

Table (6): Relationship between the studied patients' diagnosis and the occurrence of nosocomial anemia

Diagnosis	**Occurrence of nosocomial anemia**				**Significance**
	Anemia (N=50)		**No anemia (N=15)**		
	N	%	N	%	
Cardiovascular disorder	8	66.7	4	33.3	X^2=3.47 P=0.062
Respiratory disorder	15	71.4	6	28.6	X^2=4.88 P=0.027*
Neurological disorder	10	83.3	2	16.7	X^2=6.06 P=0.014*
Endocrine/ metabolic disorder	10	83.3	2	16.7	X^2=6.06 P=0.014*
Poisoning	25	83.3	5	16.7	X^2=19.05 P<0.0001*

X^2: Chi-Square test *significant at P □ 0.05

Table (7) describes the mean sampling blood volume needed for each blood test (therapeutic) and the mean blood volume discarded (iatrogenic) among the studied patients. It can be seen that the highest mean of iatrogenic blood loss was related to blood gases analysis 11.5ml ±6.1 and coagulation test was the least contributor to sampling blood loss volume 3.1ml±2.1. Hematology and chemistry also contributed in sampling blood loss volume 6.1 ml ±2.8, 4.9 ml ±3.0 respectively. From this table, it can be noted that there is a statistically significant difference between therapeutic blood loss and iatrogenic blood loss regarding chemistry, hematology, coagulation and blood gas analysis tests Z=8.729, P<0.0001*, t=3.536, P=0.0006*, Z=5.167, P<0.0001*, Z=2.839, P=0.005* respectively.

Laboratory test	**Sampling blood loss volume**		**Test of significance**
	Therapeutic blood loss (VN X F)	**Iatrogenic blood loss (VD)**	
Chemistry	**11.4±5.2**	**4.9±3.0**	**Z=8.729**
Mean ±SD %	**24.3±5.5**		**P<0.0001***
Hematology	**8.1±3.6**	**6.1±2.8**	**t=3.536**

Mean ±SD %	**26.9±17.8**		**P=0.0006***
Coagulation	**5.5±3.1**	**3.1±2.1**	**Z=5.167**
Mean ±SD %	**12.6±4.9**		**P<0.0001***
Blood gas analysis	**8.7±5.1**	**11.5±6.1**	**Z=2.839**
Mean ±SD %	**40.7±9.5**		**P=0.005***
Total (ml) / ICU stay	**67.2±30.4**		

Z: Mann Whitney test t: t-test VN: volume needed F: frequency VD: volume discarded

IV. Discussion

Admission to ICU represents a considerable crisis for patients and family members [(2)]. Multiple stressors in ICU make a burden on critically ill patients exposing them to hospital acquired complications. Nosocomial anemia may be yet one more potentially preventable complication associated with ICU stay which impact negatively upon the patients [(4)]. *Corwin et al (2004)* [(27)] stated that nosocomial anemia is common in critically ill patients and is seen early in their ICU course. They added that by forty eight hours after ICU admission, almost seventy percent of patients admitted to the ICU had a baseline hemoglobin level of twelve g/dl, and half of these patients had a level of ten g/dl. Moreover, *Vernon and pfeifer (2003)* [(17)] stated that critical care nurses play a crucial role in reducing nosocomial anemia in ICUs, subsequently decrease the need for blood transfusions in critically ill patients. So, critical care nurses must be aware of the risk factors that can contribute to nosocomial anemia in critically ill patients. Therefore, this study was conducted to identify nosocomial anemia in critically ill patients and its contributing factors.

Despite the current study indicates that ***less than one quarter of the studied patients didn't develop nosocomial anemia***, those patients were exposed to a decrement in the hemoglobin level during their ICU stay. This deterioration in hemoglobin level was due to the patients' exposure to the factors that contribute to nosocomial anemia during ICU stay, but it didn't reach the degree of anemia as those patients were admitted with a higher hemoglobin level than the other patients therefore, the initial hemoglobin is considered a protective factor against the occurrence of nosocomial anemia.

In addition, the present study reveals that ***more than three-quarters of the studied patients developed nosocomial anemia***. This is supported by *Debellis (2007)* [(7)] who found that the majority of the critically ill patients had got nosocomial anemia within three days after ICU admission. *Thomas et al (2009)* [(28)] examined the occurrence of nosocomial anemia in a prospective cohort study and found that the hemoglobin level of the studied critically ill patients dropped with ICU stay resulting in the development of nosocomial anemia for about three-quarters of those patients.

Moreover, this study indicates that ***the majority of studied patients have developed nosocomial anemia during their ICU stay by the third day***. This could be due to studied critically ill patients were exposed to multiple iatrogenic factors (diagnostic/therapeutic interventions) during their ICU stay; which induced a decrease in the quantity and quality of the circulating hemoglobin. Consequently, these made them at a higher risk for the development of nosocomial anemia. This finding is supported by *Corwin et al (2004)* [(27)] who stated that nosocomial anemia is very common in the critically ill in which most patients in ICU have a hemoglobin level below normal by the third day of ICU stay. As well, *Nguyen et al (2003)* [(29)] who have found that the hemoglobin concentrations among non-bleeding ICU patients who did not receive red cell transfusions decreased by the first three days and continued to decrease thereafter. Another study done by *Walsh and Saleh (2006)* [(30)] stated that critical illness frequently results in nosocomial anemia, which is developed within the first few days after ICU admission.

Nosocomial anemia is considered a frequent complication experienced by critically ill patients. There are two main factors that contribute to nosocomial anemia in critically ill patients: RBCs loss and insufficient production of RBCs. Loss of RBCs can be therapeutic in the form of sampling, insertional blood loss and drugs associated with bleeding complications and situational one. Decrease RBCs production can be caused by nutritional deficiencies, erythropoietin impairment and drugs that may suppress bone marrow activity [(28)].

Increase RBCs loss

Chemistry laboratory tests such as renal function tests, liver function tests and serum electrolytes. These tests require withdrawing between1-4 mls of blood from either a vein or an artery. They are usually performed on admission to the ICU and on a daily basis which are repeated more often if abnormal laboratory results are found or for assessment of certain therapy). Hematology laboratory tests include Hb concentration, red cell count, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, hematocrit (Hct), red cell distribution width, white cell count, WBCs differential, reticulocytes counts and platelet count. These blood tests involve taking approximately 3-4 mls of blood. A full blood count

is usually done on admission and then daily. If blood transfusions are required or there is an abnormal values then will be done more frequently [31].

Coagulation Studies include prothrombin time (PT), activated partial thromboplastin time (APTT), and INR to evaluate the clotting status of blood. Blood clotting is a complex process that can be affected by a number of critical illnesses. Regular coagulation studies are required especially when patients are receiving anticoagulant drugs. These tests require around 2-3 mls of blood from a vein or an artery and are done on admission and then daily unless the coagulation status is abnormal. Blood cultures may also be done if an infection is suspected, to identify types of microorganisms and to monitor the progress of antibiotic treatment. Ten to twenty mls of blood must be collected from a vein under sterile conditions then placed into specific specimen bottles and sent to the laboratory [31].

The findings of the current study regarding RBCs loss reveal that the volume of blood withdrawn for laboratory tests was much more than the required volume which resulted in iatrogenic blood loss. Additionally, the findings of this study show a statistically significant positive correlation between sampling blood loss volume and the development of nosocomial anemia indicating that the increase in sampling blood loss is associated with an increase in the risk for nosocomial anemia. This increase in ***sampling blood loss*** volume may be due to lack of knowledge of critical care nurses about the exact required volume for each investigation, unnecessary investigation orders, use of large collection tubes, lack of reporting of the daily cumulative blood loss and nurses malpractices related to the collected sample which lead to repeating sample withdrawal. However, blood volume amounts are determined by the specific sample tube and it is worth further investigation to determine if the total volume collected is necessary for analysis purposes.

Phlebotomy is a major determinant of nosocomial anemia in critical illness and it is a significant source of blood loss in which critically ill patients lose a significant volume of blood through blood sampling during their ICU stay and this could account for a higher percentage of the total blood transfused in the ICU [30, 31]. As well, this result is similar to Tosiri et al (2010) [10] who found that iatrogenic blood loss is common in ICU patients and is considered a factor contributing to nosocomial anemia. Vincent et al (2002) [32] reported in a prospective observational study conducted in western European ICUs that blood loss through blood sampling is considerable and the severity of patients' illness had accounted for association in the number of blood draws per day resulting in a higher total loss of blood than patients of lower acuity. In this respect Chant et al (2006) [33] conducted a retrospective chart review of consecutive patients admitted to a general ICU. The results of the latter studies are similar to the current study findings regarding mean daily phlebotomy volume and the number of draws per day. In a large study of Salisbury et al (2011) conducted on 17 676 cardiac patients from 57 hospitals, researchers found that for every 50 mL of blood collected, the risk of moderate to severe hospital-acquired anemia increased 18% [4]. On the contrary, Wisser et al (2003) [12] and Thomas et al (2009) [28] concluded that sampling blood loss did not pose a serious problem and did not influence the rate of nosocomial anemia. In this study, the minority of the patients had a major hematoma and half of the rest of patients had minor hematoma and the other half had both (minor and major). Patients with both minor and major hematomas developed nosocomial anemia more than those with major only or minor only. In line with this finding of the current study several studies suggested that hematoma formation is a common complication after insertion of most invasive lines and withdrawing blood sample especially arterial puncture [23, 34-40].

This hematoma formation may be related to nurses' practices while withdrawing blood sampling (arterial/venous) such as applying pressure on the puncture site for a period less than required leading to oozing of blood in subcutaneous tissues, most of the nurses withdrew blood samples from femoral artery exposing patients to the risk of hematoma formation, multiple trials to puncture skin related to wrong angle of needle, withdrew more than one time from the same puncture site to obtain the required amount of blood for investigations, and nearly all nurses did not assess the puncture site for hematoma formation neither pre nor post procedure. Also, nurses didn't apply a continuous firm pressure and didn't apply an ice pack if the bleeding persisted.

There was a linear relationship between CVC insertional complications and failed attempts at catheterization exposing patients to bleeding complications [38]. As regards to ***insertional blood loss,*** the present study illustrates that central venous catheters and peripheral lines were the most common inserted invasive lines. Despite the current study findings which reveal that there was an associated blood loss with the insertion of these invasive lines, there is no statistically significant correlation between the insertional blood loss and the development of nosocomial anemia. In other words, both anemic and non-anemic patients have experienced insertional blood loss. Central venous catheters accounted for the highest insertional blood loss volume. This associated blood loss may be related to physicians neither assessing the coagulopathic state nor the insertional site for presence of hematoma or hemorrhage. Also, blood loss occurring during CVC insertion can be related to two folds; the need for confirmation of the correct placement of the catheter and therefore needed more blood to be withdrawn and unsuccessful insertion attempts which were mostly performed by the junior staff. This

finding is in line with *Mumtaz et al (2001)* [35] who studied the factors predictive of bleeding complications after central venous catheterization in a retrospective analysis of all central venous catheters placed over a two years period and found that the incidence of bleeding complications was defined as being significant, while the present study reveals that bleeding complications were associated with superficial oozing, non-expanding hematoma and bleeding at the suture site.

Although peripheral lines were considered the most common inserted invasive lines among the studied patients, they were the least one associated with blood loss volume. This result may be due to that most of ICU patients have already at least one inserted upon ICU admission. Additionally, critical care nurses exploited blood lost during insertion of the peripheral line through using this amount of blood for the required laboratory tests. Yet, this practice can minimize the amount of blood loss. Blood loss during intravascular cannulation escape into the subcutaneous tissues, so such blood loss can be estimated through hematoma measurement. This may be an explanation for the small amount of blood loss associated with peripheral line insertion. In this regard, several studies supported that blood loss associated with peripheral line insertion is mainly in the form of hematoma formation [24, 41,42].

The RBCs loss can be induced by certain ***drugs*** in the form of internal, external bleeding or subcutaneous hematoma formation. Thrombolytics, NSAIDS and anticoagulants are the most common drugs used in ICUs that have bleeding consequences. The present study reports that anticoagulants were administered to most of the studied patients while NSAIDS were administered to a small percentage of the studied sample and none of the subjects have taken thrombolytics. Drugs such as anticoagulants and NSAIDS are commonly encountered in patients admitted to ICU which can affect the coagulopathic state of the critically ill patients exposing patients to further blood loss and then worsening to nosocomial anemia [8]. However, the present study shows that there is no statistically significant association between patients taking these drugs and those who have not taken regarding the development of nosocomial anemia. This may be related to the small percent of the studied patients and bleeding complications associated with consumption of such drugs need longer periods of time to occur.

On the other hand, *Meron˜ o et al (2012)* [44] studied the predictors of nosocomial anemia and its prognostic significance in coronary care units and suggested that up to more than half of patients admitted with normal hemoglobin values developed nosocomial anemia due to antiplatelet and anticoagulant therapy. In this regard, there were studies concerning the factors that contribute to nosocomial anemia, but they didn't refer to drugs as a factor contributing to RBCs loss. They only mentioned that the use of anticoagulants was considered a risk factor for blood loss leading to nosocomial anemia [7, 14, 30,8].

Additionally, critically ill patients are also at risk for episodes of acute ***situational blood loss***, not only as a result of surgery but also in association with acute gastrointestinal bleeding as a consequence of stress ulcer [45]. The current study emphasizes that critically ill patients experienced non acute episodes of blood loss while undergoing minor procedures. The interpretation of this exclusion is due to the impossibility of estimating the volume of blood lost during major surgeries, or acute gastrointestinal bleeding.

Decrease RBCs production The profound metabolic response to critical illness is mediated by complex interactions between the nervous, endocrine, immune, and hematopoietic systems [8, 46]. The stress response to critical illness leads to increase in their energy requirement with accelerated protein catabolism and ultimately alterations of their immune and gastrointestinal systems. It is characterized by release of certain mediators which potentiate the secretion of proinflammatory cytokines such asinterleukin-1, interleukin-6, interleukin-8, tumor necrotic factor alpha (TNFa). The cytokines interleukin-1 and TNFa directly inhibit EPO expression. These inflammatory mediators decrease erythropoiesis, leaving patients unable to secrete the level of EPO necessary to increase RBCs production. Even if EPO is secreted, TNFa, interferon gamma, and interleukin 1 inhibit erythrocyte proliferation, causing these patients to become anemic.

The findings of the current study regarding decrease RBCs production reveal that related to ***nutritional requirements,*** all studied critically ill patients received a much lesser caloric intake than their daily requirements along their ICU length of stay. As a result, the current study reports that there is no statistically significant correlation between nutritional deficiency and the development of nosocomial anemia. Underfeeding may be due to the barriers of enteral nutrition which have occurred over the patients ICU stay as revealed by this present study. Even when enteral feeding meets the patients' daily caloric requirements regarding quantity; it doesn't meet these requirements regarding quality. Barriers to provide sufficient nutritional requirements were related to a number of factors: gastrointestinal factors, nurses related factors, diagnostic purposes, and therapeutic purposes. The present study shows that gastrointestinal related factors followed by nurses' related factors were the most frequent reasons for barriers. Barriers due to diagnostic and therapeutic related factors were the lowest frequent reason. This may be explained by lack of regular, and continuing educational and training programs to all healthcare team members involved in providing care to the critically ill patients, the absence of dietitian in ICU, lack of collaboration with members of the healthcare team to evaluate the adequacy

of nutritional support, the need for increase in critical care nurses' awareness regard assessing the nutritional status, deciding the timing and the appropriate method for feeding, the ideal constitutions of enteral feeding formulas, calculating the ideal nutritional requirements and detecting complications associated with enteral nutrition.

In the same line with this study, *Cahill et al (2010)* [46] described the nutrition practices in intensive care units in a prospective, observational study and found that most of patients received inadequate amounts of nutritional requirements and related this finding to the poor adherence to guidelines recommendations. These findings also are congruent with *Umali et al (2005)* [47] who compared the computed nutrient requirements of critically ill geriatric patients with their actual intake within the first three days after admission to ICU and determined the percentage of patients who achieved adequate intake. This survey reported discrepancies between prescribed intake and actual delivery of calories for patients in the ICU. As well, they agreed with this present study regarding the reasons that interrupt the continuity of feeding. *Binnekade et al (2005)* [48] evaluated the ICU daily feeding practices and compared the actual energy and protein intake with the ideal one and they found that feeding practices in ICU failed to provide critically ill patients with adequate nutrition.

This finding is also in line with *Rodriguez et al (2001)* [13] who identified some of the potential causes of ineffective erythropoiesis in a cohort long term ICU patients and found that nutritional deficiencies is a correctable cause of nosocomial anemia. Furthermore, nutritional deficiencies can lead to diminished RBCs production and iron therapy is an essential part of the management of nosocomial anemia [14]. This finding is similar to, *Kim et al (2010)* [49] who found in a descriptive study conducted to identify the adequacy of enteral feeding, and the reason and prevalence of under-nutrition that most patients were under fed and the most frequent reason for the feeding interruption was related to intubation/extubation then gastrointestinal bleeding.

This result opposes to *Kan et al (2003)* [50] who conducted a study to assess nutritional status of patients in a multidisciplinary ICU and calculated their caloric requirements to identify the adequacy of caloric delivery during ICU stay and they concluded that a higher percentage of patients were fed appropriately and the rest of patients were over fed and less percentage were under fed. Moreover, *Walsh and Saleh (2006)* [30] reviewed that the relation between nutritional deficiencies and anemia is unknown.

Because inflammatory mediators are released in response to several conditions including ***infection***, they are believed to play a major role in erythropoietin impairment [38, 52]. This is in line with the findings of the present study in which infection occurred to one fifth of the studied critically ill patients and all of them have developed nosocomial anemia.

Bone marrow is responsible for RBCs production. So, it is essential that critical care nurses study the hematological system, common complications and factors may affect bone marrow activity [53]. Multiple ***drugs*** used in the ICU may cause decreased bone activity. Drugs that can affect the RBCs production are nephrotoxics, proton pump inhibitor and others drugs such as antibiotics drugs. The current study states that most of the studied patients were on nephrotoxics followed by proton pump inhibitor and last, miscellaneous drugs. Most of those patients have developed nosocomial anemia, but there was no statistically significant association. This may be due to that the studied patients stayed for a short term period of ICU stay and drugs' side effects may need a longer time to impact the bone marrow. Despite researches on nosocomial anemia however up till now drugs as a factor contributing to the development of nosocomial anemia, was not studied. Several drugs used in the ICU may cause decreased bone activity (e.g., corticosteroids, antibiotics, select antifungal, histamine H_2 blockers, and others) and thus, suppress the normal renal erythropoietin secretion [7, 14]. Although many researchers [28, 30 ,52, 54-56] studied nosocomial anemia and its different etiologies, these researches didn't report that drugs can be a factor contributing to nosocomial anemia.

From the ongoing discussion, it can be noted that, applying patient safety practices is considered a nursing priority for critically ill patients to prevent ICU -acquired complications. Nosocomial anemia is one of the most prevalent acquired complications in ICUs and is associated with poor patients' outcomes. Two main factors in critically ill patients can contribute to nosocomial anemia: RBCs loss and insufficient production of RBCs. Therefore, Critical care nurses have a major role in preventing and managing nosocomial anemia through identifying factors contributing to nosocomial anemia.

V. Conclusion:

Nosocomial anemia is one of the most common ICU acquired complications, so the present study highlights factors contributing to nosocomial anemia in critically ill patients. Based on the results of this study, it can be concluded that: More than three- quarters of patients developed nosocomial anemia during their ICU stay. Most of them have developed nosocomial anemia by the third day of ICU stay. Even, non-anemic patients were subjected to a decrement in their hemoglobin level. Critically ill patients were highly susceptible for exposure of multiple iatrogenic factors which can contribute to nosocomial anemia during ICU stay. Regarding ***increase RBCs loss factors,*** the volume of blood withdrawn for laboratory tests was much more than the required volume which resulted in iatrogenic blood loss. In addition, central venous catheters and peripheral

lines were the most common inserted invasive lines associated with blood loss. Moreover, anticoagulants which can potentiate RBCs loss were administered to most of the studied patients. Regarding ***decrease RBCs production factors,*** it can be concluded that all critically ill patients were underfed during their ICU stay while a small percent of them developed infection which can potentiate erythropoietin impairment and the majority consumed drugs that can cause bone marrow depression.

VI. Recommendations:

Upon completion of this study, the following can be suggested:

Recommendations regarding clinical practice: Schedule and cluster the required laboratory tests. Provide adequate nutritional support considering the quantity and quality of requirements.

Encourage collaboration between nurses and pharmacists to increase nurses' awareness regarding drugs' side effects especially hematological side effects. Document intake and output accurately considering amount of blood loss. Use the correct technique for venipuncture/arterial puncture considering implementation of blood saving bundle

Recommendations regarding education: Assess nursing readiness to prevent occurrence of nosocomial anemia by applying clinical reasoning skills (using case studies). Provide scientific courses that increase critical care nurses' knowledge regarding to risk factors, etiology, preventive measures of nosocomial anemia. Develop educational program to educate critical care nurses minimal volume required per laboratory test. Apply training programs for critical care nurses on the standard procedure [(56)] for arterial blood sampling to minimize arterial puncture complications, reduce frequency of ABG samples, draw minimal blood volume as possible (as 2-3 mL of arterial blood should be obtained,) and use the noninvasive monitoring techniques (pulse oximetry and capnography) instead.

Recommendations regarding administration: Develop a quality improvement project, standards, or policies to prevent nosocomial blood loss. Include hematological assessment as a part in nursing flow sheet.

Recommendations regarding research: Consider further researches about nosocomial anemia, its prevention and management in different areas such as: Develop standards for blood conservation strategies and identify the relationship between malnutrition and nosocomial anemia. Replicate this study on a larger sample size for generalization of results.

Limitations of the study:

- This study was conducted in two ICUs only from one geographical area, therefore the results cannot be generalized, and the sample size does not represent all population.
- The inability to detect erythropoietin impairment as erythropoietin level is not requested in the routine investigations. Also, pre-albumin, total protein and serum transferrin.

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