Factors Contributing to Hospital Acquired Anemia among Critical Ill Patients

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Abstract

Background: Hospital acquired anemia (HAA) is one of the most common intensive care unit (ICU) acquired complications that associated with poor outcomes, increase morbidity and mortality for critically ill patients. Factors contribute to its development include profound loss of RBCs or insufficient RBCs production. **Aim of the study:** to assess factors contributing to HAA among critical ill patients. **Design:** A descriptive exploratory design was utilized. **Setting:** The study was carried in Beni –Suief university hospital inside the critical care units which include; general ICU, cardio care unit (CCU) and chest ICU. **Study subjects:** purposive sample of 75 newly admitted adult critically ill patients to the above mentioned sitting was included in the study. **Data collection tools**: Data were obtained through patients assessment tool, factors contributing to HAA and indicators of HAA tool. **Results:** reveals that, nearly one third of studied patients their age were more than or equal fifty years. As regard to gender, the results revealed that, more than half of them were males, nearly one third of anemic patients had HAA in the 5th day from admission to hospital. As well more than three quarter of anemic patients were under feeding and more than one third of them had sepsis, in addition to mean amount of blood loss for anemic patients exceed amount of blood loss for non anemic patients. **Conclusion:** More than half of studied patients developed HAA during their ICU stay. Even, non-anemic patients were subjected to a decline in their Hb level. As well as, there were statistically significant relation between nutrition deficiency, sepsis, blood loss in ICU and drugs increase RBCs loss factors and occurrence of HAA. Also there were insignificant relation between demographic characteristic of studied patients, their diagnosis on admission to hospital, hemodilution, drugs affect RBCs production and occurrence of HAA. **Recommendations:** Designing in-service training and educational program for nurses about blood conversation strategies especially prevention of blood loss associated invasive procedure and phlebotomy practice.

Key words: Factors, Hospital acquired anemia, Critically ill patients.

Introduction

Critically ill patients are characterized by the presence of actual or potential life threatening problems that occur after ICU admission such as venous thromboembolism, hospital acquired infections, medication errors, pressure ulcers, catheter-related infections, ventilator-associated pneumonia and HAA that result in considerable morbidity and mortality **(Asfour et al., 2016)**.

Hospital-acquired anemia (HAA) is anemia that is directly attributable to hospitalization. It is a reduction of hemoglobin (Hb) during hospitalization, as compared with the Hb on admission. Various studies have shown that among critically ill patients without anemia at the

time of admission, the prevalence of HAA was 74% with almost 95% of patients were demonstrating some level of anemia during their stay in ICU by 3 day, and 53% of patients still anemic 6 months after ICUs discharge (**Corwin & Napiltano, 2014).**

In critically ill patient, HAA results from two fundamental processes: a shortened RBC circulatory life span and diminished RBC production. Causes of shortened life span include RBCs destruction as hemolysis or RBCs loss as (phlebotomy losses, oozing at injury sites, invasive procedures, hematoma formation and gastrointestinal bleeding). Causes of diminished RBCs production as nutritional deficiencies (iron deficient, vitaminB12 and folate deficiency), erythropiotein (EPO) deficiency, drugs induced anemia and anemia of inflammation (**Astin & Puthucheary, 2014).**

Phlebotomy is the commonest procedure performed in health care settings. Diagnostic phlebotomy in the critically ill patients represents the most important factor in developing HAA and it is estimated that for every 100 ml of blood withdrawn, there is an associate decrease in Hb 0.7 g/dl and in hematocrit of 1.9%, even with a conservative measurement of blood loss of 100 ml/d from phlebotomy, the impact is significant, especially in the patient who is hospitalized for several weeks in ICU (**Morton & Fontaine, 2013).**

Another form of blood loss in ICU are blood loss associated with invasive procedure and gastrointestinal (GIT) bleeding, various studies have shown that about 90% of critically ill patients had bleeding associated with invasive procedure and GIT bleeding, 38% developed bleeding at the site of insertion of a vascular catheter, 16% associated with an endotracheal tube, 15% at a surgical site and 6% related to gastrointestinal bleeding (stress ulcer) (**Rawal, Kumar, Yadav & Singh, 2016).**

The RBCs loss also can be induced by certain drugs in the form of internal, external bleeding or subcutaneous hematoma formation. As Thrombolytic, NSAIDS and anticoagulants drugs are the most common drugs used in ICUs that have bleeding consequences. Exposing patients to further blood loss and then worsening to HAA (**Ferris, 2017).**

Also, HAA can also be attributed to decreased production of RBCs which can be caused by many factors, including reduced concentrations of EPO, toxic effects of medications, nutritional deficiencies of essential substrates (iron, vitamin B12, folate), Also, toxic effects of medications commonly used in the ICU can decrease bone marrow activity, including proton pump inhibitors, nephrotoxic drugs, corticosteroids, histamine-2blockers, and others (**Richards & Stapleton 2014).**

Hospital acquired anemia can be induced bysepsis and inflammation, because cytokines (IL-1, IL-6, TNF)which are known to be increased in sepsis and inflammatory processes during critical illness leading to inhibition of EPO release from the kidneys, decreased the responsiveness of the bone marrow to EPO. Also, hemodilution is important factor in developing HAA because the dilution of RBCs concentration resulting in a lower measured hemoglobin level and typically is the result of substantial fluid resuscitation during hospitalization (**Van et al., 2011) & (Jelkmann & `Jelkmann, 2013).**

Anemia has several adverse effects on the body including a decrease in intravascular volume that leading to increased cardiac output, heart rate, stroke volume and oxygen extraction. It is important to recognize that anemia is associated with increased morbidity and mortality in the ICU. Many studies have shown an association between anemia and adverse outcomes in critically ill patients. It can contribute to failure to liberate from

mechanical ventilation, demand ischemia, and death. It is crucial note that correction of anemia through blood transfusions orerythropoietic agents has also been shown to be harmful for patients **(Retter et al., 2013 and Docherty & Walash, 2017).**

Critical care nurses (CCN) has major role in prevention and treatment of this problem. Clinical judgment of nurses should be used to modify routine practice. The primary nursing principles for managing care include minimizing blood loss, maximizing oxygen delivery, attend to patients' nutritional status, assessing the nutritional status, calculating nutritional components requirements based on patient's condition, deciding the timing and the appropriate method for feeding & preventing of feeding method – related complications, and evaluating the response to nutritional support **(Richards & Stapleton, 2014 and Asfouret al., 2016).**

Also, CCN has critical role to avoid blood loss during invasive procedure such as placement of arterial and central venous catheters by assessing patient's hemodynamic status, reviewing drugs patients may be taking that inhibit the coagulation cascade to prevent and treat HAA in critically ill patients. Despite this impact of this anemia on critically ill patients **(Asfour etal., 2016).**

There are few studies related to this problem, .so that, this study will be conducted to identify factors contributing to HAA among critically ill patients.

Significance of the study

Attention to HAA is important because it can impact negatively on critical ill patient, it can lead to increase length of hospital stay, increase mortality rate, increase need for blood transfusion that associated with major complication and decrease in oxygen carrying capacity and

plasma volume that are the most significance risks associated with HAA in critically ill patients, this decrease in oxygen carrying capacity can result in tissue hypoxia, anaerobic metabolism, production of lactic acid and death **(Salisburyetal., 2011).**

Aim of the Study

This study aimed to:

Assess factors contributing to HAA among critically ill patients

Research question:

This study was conducted for answering the following question:

What are the factors contributing to HAA among critically ill patients?

Subject and Methods

Research Design: A descriptive explorative design was utilized for the conduction of this study.

Setting of the Study: This study was conducted in Beni –Suief university hospital inside the critical care units which include; general ICU, cardio care unit (CCU) and chest ICU

Subject:- A purposive sample of 75newly admitted adult critically ill patients to the above mentioned sitting was included in the study according to inclusion criteria.

Inclusion criteria:

Adult male and female patients. Hemoglobin level > (12) g/dl for males and > (10)g/dl for females at admission, compensated liver disease, compensated renal disease, cardiac patient, endocrine disorders, neurological disorders,

gastrointestinal disorders and respiratory disorders.

Exclusion criteria:

Patients with (bleeding disorders, postoperative, end stage renal insufficiency, autoimmune disease, end stage liver disease, malnourished patients before hospital admission and patients on chemotherapy) were excluded from study.

Data Collection tools

Data were collected using the following tools:

Tool 1: Patients' assessment sheet:

This tool used to assess studied patients on admission, it was developed by the investigator based on literature review **Smeltzer et al., (2014)**, it consisted of two parts:

Part (I): Patients' demographic data:

The investigator was assessed demographic characteristic of the studied patients as (age and gender).

Part (II): Patients' clinical data:

The investigator recorded laboratory investigation for studied patients from patients sheets on admission as (hemoglobin, hematocrit level, total leukocyte count, red blood cells), to determine the included patients in this study.

Tool 2: Factors contributing to hospital acquired anemia Assessment sheet:

This tool was used to assess factors contributing to HAA associated intervention, and it was consist of four sections:

Part (I) Nutritional and fluid balance-related Factors:

This part was developed by investigator after reviewed related literature **Skipper, (2012),** It consisted of two sections:

Section 1: Nutritional related factors:

- The actual and ideal caloric requirements were recorded and compared daily from admission by investigator after reviewing the dietitian to determine nutritional status of studied patients

- Actual calories consumed by the patients were calculated through identifying type and the amount of each oral, enteral or parenteral intake by investigator after that the dietition converted amount and type of food intake into calories and assessed nutritional status for studied patients according to their disease.

- The ideal caloric requirements needed for the patient were calculated by dietitian by using Harris and Benedict equation, it was adopted from**, Skipper 2012**, Basal energy expenditure (BEE): It differs according to sex.

- **BEE (men):** $66.47 + (13.75 \times weight\ in\ Kg) + (5.0 \times height\ in\ cm) - (6.76 \times age\ in\ yr.)$

- **BEE (women):** $65.51 + (9.56 \times weight\ in\ Kg) + (1.7 \times height\ in\ cm) - (4.68 \times age\ in\ yr.)$, then ideal and actual intake were recorded and assessed by dietitian

- **Scoring system**

- If the actual nutritional intake was equal the ideal nutritional requirements, it means that the patient was adequate feeding – give 1 degree.

- If the actual nutritional intake was less than the ideal nutritional requirements, it means that the patient was inadequate feeding – give zero degree.

- If the actual nutritional intake was exceed the ideal nutritional requirements, it means that the patient was over feeding – give 2 degrees.

Section 2: Fluid balance- related factors

The investigator recorded daily fluid intake and output for each subject patient from patient's sheet to assess patient's hydration status and calculate balance between intake and out put. If patients intake exceed output that contribute to HAA and this factor called hemodilution.

● **Scoring system**

-If patients intake less than output this called in adequate hydration (hemoconcentration) – give zero degree.

-If patients intake equal output this called adequate hydration – give 1 degree.

-If patients intake exceed output this called hemodilution – give 2 degree.

Part (II): Drugs –related factors:

-This part was adapted from **Asfour et al., (2016)** and modified by the investigator after reviewed related literature **Ferris, (2017.**

-The investigator recorded daily prescribed medication to patients during ICU stay that affects RBCs production or increase RBCs loss such as: Thrombolytic therapy, Antiplatelet, NSAIDS, Specific antibiotic as (cephalosporines, quinolones), investigator recorded name, dose and frequency of previous drugs from patients sheet

● **Scoring system**

-If studied patients take any one from previous drugs, put yes ― was given one degree.

- Patient who didn't take, put no ―was given zero.

Part (III) blood loss –related factors (Estimation of blood loss volume):

This part was used to estimate blood loss volume during ICU stay that contribute to developing of HAA. It consisted of three sections:

Section 1: Sampling blood loss volume:

This tool was adopted from **Asfour et al., (2016),** its consisted of name of requested investigation, frequency, volume of blood needed, amount of blood withdrawn, volume of blood discard, site of blood withdrawn, number of trials each time of withdrawn, calculation of mean blood volume withdrawn per 24 hours assessed and recorded by investigator.

Section 2: Estimation of blood loss volume from puncture site (Invasive procedure):

It was estimated by using Gauze visual analogue scale (GVAS). It was adopted from **Algadiem et al., (2016)**, it consisted of three different sizes of commonly used gauze (10×10 cm, 30×30 cm, and 45×45 cm).The gauze was tested for their absorptive capacity, four patterns were selected for each gauze to construct the visual guide. Each pattern represented 25%, 50%, 75%, and 100% saturation. Different percentages of staining were photographed to create an analogue for the amount of blood absorbed by the gauze.

- **Scoring system**

o If gauze 10×10 cm was used to absorb blood, the percentage saturation of blood 25%this mean blood loss 3ml, percentage of saturation 50%this mean blood loss 6ml, percentage of saturation 75% this mean blood loss 6ml, percentage of saturation 100% this mean blood loss 12ml.

o If gauze 30×30 cm was used to absorb blood percentage saturation blood 25% this means blood loss 25 ml, if percentage of saturation was 50%this means blood loss 50ml, if percentage of saturation was 75% this means blood loss 75ml, if percentage of saturation was 100%this means blood loss 100 ml.

o If gauze 45×45 cm was used to absorb blood percentage saturation blood 25%this mean blood loss 40 ml, if percentage of saturation was 50% this means blood loss 80 ml, if percentage of saturation was 75% this means blood loss 120 ml, if percentage of saturation was 100%this means blood loss 160ml.

Section 4: Estimation of blood loss volume from gastrointestinal system:

This was developed by investigator after reviewing related literature. It was used to estimate volume of blood loss from gastrointestinal system (hematemesis or melena)**,** the investigator was assessed and recorded site of bleeding, frequency and associated factors for blood loss volume, The investigator researcher estimated volume of GIT bleeding by open nasogastric tube (in case of hematemesis) if connected to patient, from abdominal ultrasound if done or by oozing scale,

Oozing Scale: It was adopted from **Black, (2008).** The scale designed for measurement any leakage of blood to dressing or linen.

Scoring system

The investigator measured oozed area of blood with ruler 0 mark then classified oozing into four categories according to surface area soaked with blood:

-No oozing (dry dressing or linen).

- Mild oozing ($< 2cm^2$ in diameter dressing or linen soaked with blood).

- Moderate oozing ($2\leq 5cm2$ in diameter dressing or linensoaked with blood).

- Severe oozing ($5\leq 10$ cm2 in diameter dressing or linen soaked with blood).

Pilot study

A pilot study was conducted to test feasibility and applicability of the study tools used in this study. It was carried out on 10% of total study subjects (8).There was no modifications on tools were done after pilot study so that, the patients who included in the pilot study were included in the main study group**.**

Fieldwork

The purpose of the study was simply explained to the studied conscious patients who agreed to participate in the study prior to data collection. Data were collected in 7 months, from beginning of August 2017 to the end of February 2018.

- Data were collected by the investigator daily at morning and afternoon shifts in the previous mentioned settings, for newly admitted patient according to inclusion and exclusion criteria for seven days from admission for non anemic patients and daily from admission until patient become anemic during hospitalization course.

• During night shifts the investigator teach and ask helping from faculty nurse student at internship to observe blood loss and record amount of dietary intake for subject patient

• Assessment of patient demographic data, medical data, fluid balance, lab investigation and medications (Patient file) took about 15 minutes.

• Assessment of the hemodynamic parameters and estimation amount of blood loss done by investigator took about 20 minutes.

• Nutritional status of studied patients assessed by dietitian, investigator recorded amount and content of patients diet, then dietition convert it to calories and determined nutritional status of studied patients by Harris and Benedict equation according to their disease.

• Phlebotomy technique done by CCN and investigator estimate amount of blood loss during this procedure.

• Investigator measured hematoma size by putting the ruler's 0 at the firm edge of the hematoma and marked it then measured directly across to the opposite firm edge

• The investigator estimated blood loss associated invasive procedure by GVAS. The gauze wastested for their absorptive capacity, four patterns were selected for each gauze to construct the visual guide. Each pattern represented 25%, 50%, 75%, and 100% saturation. Different percentages of staining were photographed to create an analogue for the amount of blood absorbed by the gauze.

Ethical considerations

The ethical research considerations in this study included the following:

1-The research approval of protocol was obtained from scientific research ethical committee in faculty of nursing at Ain shams University before starting the study.

2– The investigator clarified the objective and aim of the study to the patients included in the study.

3 - The investigator assured maintaining anonymity and confidentiality of the subject data.

4– Patients were informed that they allowed choosing to participate or not in the study and that they had the right to withdraw from the study at my time without giving any reasons.

5- Oral 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).

6- Ethics, values, culture and beliefs were respected.

7- An approval was obtained from the director of Beni-Suef university hospital and director of General, cardio care unit and chest ICU unit to conduct the study.

Result

Table (1): Demographic characteristics of studied patients (n=75).

Items	No.	%
Age		
18 -< 30	15	20.1%
30- < 40	17	22.6%
40 -< 50	18	24%
≥ 50	25	33.3%
Mean±SD42±13.4		
Gender		
Male	38	50.6 %
Female	37	49.4%

Table (1) reveals that, 33.3% of studied patients their age ≥ 50 with a mean age of 42±13.4. As regard to gender, the results revealed that the 50.6% of them were males.
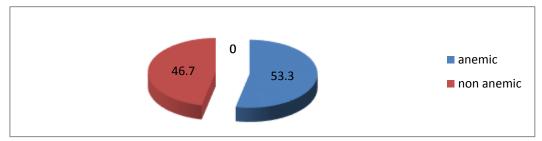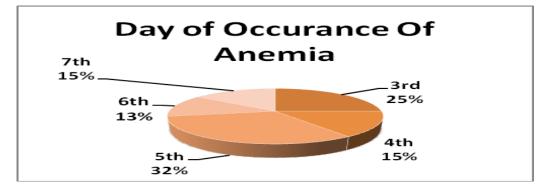

Figure (1): Frequency distribution of the total studied patients according to incidence of hospital acquired anemia (n =75).

Figure (1) illustrated that, 53.3% of the studied patients had hospital acquired anaemia, while 47.7% of them not had hospital acquired anemia.

Figure (2): Frequency and percentage distribution of the studied anemic patients according to day of occurrence of anemia (n=40).

Figure (2): showed that, 32.5%of anemic patient had anemia in the 5th day from admission to hospital, while 25% of them had anemia in the 3rd day, 15% of them had anemia in the 4th and 7th day, as well 12.5% of them had anemia in the 6th day from admission.

Table (2): Frequancy and percentage of studied patients regarding factors contributing to HAA

Factors	Anemic =40		non anemic =35	
	No	**%**	**No**	**%**
Nutrition				
Inadequate feeding	33	82.5%	18	51.4%
Adequate feeding	7	17.5%	17	48.2%
Drug increase red blood cells loss (N= 27)				
Non steroidal anti inflammatory drugs	6	31.6%	3	37.5
Thrombolytic and anticoagulant drugs	13	68.4%	5	62.5%
Fluid balance				
Inadequate hydration	13	32.5%	11	31.4%
Adequate hydration	14	35%	19	54.2%
Hemodilution	13	32.5%	5	14.2%
Drug affect red blood cells production (N = 24)				
Proton pump	8	53.3%	7	77.7%
Nephrotoxic drugs	5	33.3%	2	22.3%
Others	2	13.3%	0	0%
Sepsis and presence of infection				
Yes	14	35%	5	14.2%
No	26	46.4%	30	53.6%

Table (2) this table represents that, 82.5%of anemic patients had inadequate feeding as well72.5 %of them were on enteral feeding, also 35% of them had sepsis and 70.3% of anemic patients took drugs increased red blood cells loss.

Table (3): Distribution of studied patients regarding their the mean score of blood loss (n= 75).

Items	Anemic =40		Non anemic =35	
	Mean	**SD**	**Mean**	**SD**
Phlebotomy blood loss	153.2	±73.4	83.9	37.1
blood loss associated invasive procedure	71.3	123.4	11.1	8.4
blood loss from gastrointestinal tract	287	149.6	50	7

Table (3) this table reveals that, the mean score of blood loss volume from phlebotomy at anemic patients were 153.2 while in non anemic were 83.9. The table also illustrate that the mean of blood loss volume from invasive procedure in anemic patients were 71.3 while 11.1 in non anemic patient. The mean score of blood loss from gastrointestinal tract were 287 in anemic patient while in non anemic patient were 50 ml.

Table (4): Relation between factors contributing to hospital acquired anemia in studied patients and occurrence of hospital acquired anemia (n=75).

Factors	Anemic =40		Non anemic=35		Test	
	No	%	No	%	X^2	P-value
Nutrition related factor						
Adequate feeding	33	64.7%	18	35.3%		
Inadequate adequate feeding	7	29.1%	17	70.9%	8.2	**0.004****
Fluid balance						
Inadequate hydration	13	54.1%	11	45.9%		
Adequate hydration	14	42.4%	19	57.6%	4.1	0.12
Hemodilution	13	72.2%	5	27.8%		
Drug affect red blood cells production						
Yes	15	62.5%	9	37.5%		
No	25	49%	26	51%	1.1	0.27
Drug increase red blood cellsloss						
Yes	19	70.3%	8	29.7%		
No	21	43.7%	27	56.3%	4.9	0.02*
Sepsis						
Yes	14	73.6%	5	26.4%	4.2	0.03*
No	26	46.4%	30	53.6%		

In significant p > 0.05 Significant* P value < 0.05 Highly significant ** P

Table (4) reveals that there were highly statistically significant relation between inadequate feeding and occurrence of hospital acquired anemia at p value (0.004), also this table illustrated that there were significant relation between drugs increased blood loss, sepsis and occurrence of hospital acquired anemia at P values (0.02, 0.03) respectively.

Table (5): Relation between the estimated amount of blood loss for studied patients and occurrence of hospital acquired anemia (n=75).

Items	Anemic =40		Non anemic =35		T	P
	Mean	SD	Mean	SD		
Phlebotomy blood loss	153.2	±73.4	83.9	37.1	5.4	0.00001**
blood loss associated invasive procedure	71.3	123.4	11.1	8.4	2.8	0.0002**
blood loss from gastrointestinal tract	287	149.6	50	7	2	0.04*

Significant* P value < 0.05 Highly significant ** P value <0.001

Table (5) showed that, there were highly significant relation between blood loss from phlebotomy & blood loss associated invasive procedure and hospital acquired anemia in which p value (0.00001&0.0002) respectively, also this table represents there were significant relation between blood loss from gastrointestinal tract and hospital acquired anemia P (0.04).

Discussion

Part I: Demographic characteristic of studied patients: The current study showed that As regards the age of patients under the present study, the present study showed that, nearly one third of studied patients their age ≥ 50 years with a mean age of 42 ± 13.4. This finding is consistent with what was reported by *Peter et al., (2013)* who conducted study about, incidence of HAA, and found that, one third of studied patients their aged >55 years, this finding is contradicted with by*Choi et al. (2013),* who conducted study about, Clinical Impact of Hospital-Acquired Anemia in Association with Acute Kidney Injury and Chronic Kidney Disease in Patients with Acute Myocardial Infarction and reported that, more than three quarter of studied patients their age >55 years with a mean age in the total study population was 61.3 ± 12.4 years.

This result could be due to most of critically ill patients were old age due to critical illness and chronic disease affect old age more than young age.

Related to gender**,** the present study results showed that, more than half of the studied patients were males. This finding is consistent with what was reported by*Asfour et al. (2016),* who conducted study about HAA and its contributing factor in the critically ill patients and who stated that more than half of the studied patients were males. And contradicted with

Tiwari & Rance, (2014) who conducted study about Hospital-Acquired Anemia Secondary to Phlebotomy in Elderly Patients and found that more than half studied patients were females.

Concerning incidence of HAA in this study, the present study results indicated that, more than half of the studied patients were experience deterioration of hemoglobin level and developed some degree of anemia. This deterioration in hemoglobin level was due to exposure of studied anemic patients to multible factors that contribute to HAA during ICU stay. This finding is supported by *Choi et al. (2013),* who found, that more than half the patients with normal Hb level at admission developed anemia during hospitalization, and with *Koch et al., (2013)*who stated that, among 188, 447 hospitalizations, nearly three quarter of studied patients have HAA, this finding is contradicted with *Tiwari & Rance, (2014)*who stated that less than half of studied patients have HAA.

According to day of occurrence of HAA, this study finding showed that, more than one quarter of studied anemic patients had HAA in 5th day of admission, followed by 3rd day of admission, while minority of studied anemic patients had HAA in 4th, 6th& 7th day of admission to ICU.

This result in the same line with**,** *Wong & Intragumtornchai, (2006),* who conducted study about hospital acquired anemia at King Chulalongkorn Memorial Hospital in Thailand and stated that. The median time to develop HAA was the fifth day of admission.

This result was contradicted with *Hayden et al. (2012),* who conducted study about, Anemia in critical illness; insight into etiology, consequences, and management in Washington and found that**.** Anemia is highly prevalent in critically illpatients and all studied anemic patients

become anemic by day 8 from admission to ICU.

As well with **Mcevoy & Shander, (2013),** who conducted study about. Anemia, bleeding, and blood transfusion in the intensive care unit: Causes, risks, costs and new strategies in New York, and reported that, high percentage of patients become anemic during a stay ICU, more than three quarter of studied patients had HAA at 3 day of admission to ICU and all studied anemic patients have HAA at 8 day of admission to ICU.

Part II: Factors contributing to HAA. The findings of the current study related to the factors that decreased RBCs production

Revealed that, regarding to **nutritional requirements,** the majority of studied critically ill patients received a much lesser caloric intake than their daily requirements along their ICU stay. more than three quarter of the studied anemic patients had inadequate feeding, while more than half of non anemic studied patients had inadequate feeding,

This could be attributed to many reason as; barriers to provide sufficient nutritional requirements were related to a number of factors: patients (gastrointestinal) related factors, nurses related factors, diagnostic and therapeutic purposes. The present study shows that GIT related factors followed by nurses' related factors were the most frequent reasons for barriers. This finding goes in the same line with, **Cahill, et al. (2010**), who conducted study about. Nutrition therapy in the critical care setting: What is ―best achievable practice? An international multicenter observational study*)* and described the nutrition practices in ICU in a prospective, observational study and found that most of patients received inadequate amounts of nutritional requirements, feeding practices in ICU

failed to provide critically ill patients and related this finding to the poor adherence to guidelines recommendations.

This finding disagreement with **Kan et al. (2003)** who conducted a study to assess nutritional status of patients in ICU and calculated their caloric requirements to identify the adequacy of caloric delivery during ICU stay and they stated that a higher percentage of patients were fed appropriately and the rest of patients were over fed and less percentage were under fed.

Regarding **hemodilutional factors**. **In accordance with current study findings,** This finding indicated that, more than one quarter of anemic patients had fluid over load (hemodilutional), while minority of non anemic patients had hemodilution, this explain that less than half of studied patients had hemodilution, this finding is contradicted with **Philbert et al., (2013),** who conducted study to assess blood volume in critically ill patients on Thirty-six patients admitted to the ICU were enrolled and blood volume analysis performed on up to three consecutive days, and found that more than half of the studied population had the hypervolemic state (hemodilution) and had some level of anemia.

Regarding to **drugs affect RBCs production.** The present study findings showed that, more than two third of the studied anemic patients took this drugs, while less than one quarter of non anemic studied patients took this drugs, but the majority of studied patient took this drugs, Proton pump inhibitors (PPI) drugs considered the most drugs was taken by anemic patients (more than two quarter of anemic patients were taken proton pump inhibitor), and more than three quarter of non anemic patients were taken PPI, followed by nephrotoxic drugs (nearly one third of studied patients were took nephrotoxic drugs) had HAA,

This finding could be attributed to many reasons as; policy of general ICU in study setting indicated that any admitted patients must take prophylactic PPI against stress peptic ulcer and prophylactic antibiotic against hospital acquired infection, result of this study stated that no significant relation between this drugs and HAA. This might 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.

This finding goes in the same line with *Asfour et al. (2016)* who stated that majority of studied patients taken drugs affect RBCs production. As well, with *Mcevoy & Shander, (2013)* who conducted study about. Anemia, bleeding, and blood transfusion in ICU: Causes, risks, costs and new strategies, and reported that bone marrow suppression can occur as a complication of drugs that are often given in ICU setting as nephrotoxic and PPI drugs.

Regarding to **Sepsis related factors**, The results of the current study indicated that less than half of studied patients had infection, and more than two third of them had HAA.

This finding could be attributed to many reasons as; lack of sufficient knowledge regarding applying of good infection control program and importance of maintaining aseptic technique during invasive procedure as tracheal suctioning, insertion of CVC or chest tube, unavailability of supplies and equipment, increased work load and lacking of close nursing supervision, excessive antibiotic usage that increase chance for antibiotic resistant and lacking of isolation protocol.

This finding is in agreement with *Asfour et al. (2016)*who stated that infection occurred to one fifth of the

studied critically ill patients and all of them have developed HAA.

As well, *Wong & Intragumtornchai, (2006)* who reported that, inflammation was the most common contributing factor of HAA, and more than half of studied patients had HAA due to infection and inflammation this secondary to suppression of bone marrow.

Factors increased RBCs loss

Regarding to **drugs increased blood loss,** the present study findings showed that**,** more than half of anemic patients were taken drugs that increase RBCs loss as NSAIDs, thrombolytic and anticoagulant drugs. **This finding could be attributed to many reasons;** limited knowledge of health care providers about adverse effects and precausions should be taken to avoid adverse effects of these drugs as reviewing coagulation profile during administration from other side some coagulation profile that needed to follow up these adverse effects and dose for some of this drugs not available in hospital and expensive for patient.

This finding is consistent with *Meron et al., (2012),* who studied the predictors of HAA and its prognostic significance in coronary care units and suggested that up to more than half of patients admitted with normal Hb values developed HAA due to antiplatelet and anticoagulant therapy. As well, *Parker, (2012),* who conducted study about. etiology and significance of thrombocytopenia in critically ill patients, and concluded that, drug-induced thrombocytopenia (antipletlete) as heparin develops in about only one quarter of ICU patients and develop complication from it as bleeding.

Regarding to **blood loss in ICU**, based on the results of the current study, it

was found that, blood loss considered important and essential factor to development HAA, from forms of blood loss in ICU that assessed and evaluated by the current study (phlebotomy blood loss (sampling), blood loss associated invasive procedure (insertional), and blood loss from gastrointestinal tract (GIT) as hematemesis and melena).

Regarding to **phlebotomy blood loss in ICU,** this study revealed that, the mean volume of blood withdrawn for laboratory tests was much more than the required volume which resulted in iatrogenic blood loss. Additionally, indicating that the increase in sampling blood loss is associated with an increase in the risk for HAA.

This finding could be attributed to many reasons; phlebotomy procedure performed by CCN in this study setting, blood loss through phlebotomy considered most important form of blood loss due to (nurses related factors or physician related factors) . From nurses related factor a slack of knowledge of CCN about the exact required volume for each investigation that lead to the volume of blood withdrawn for laboratory tests was much more than the required volume that cause discard amount of blood and blood loss. In addition to technique of phlebotomy is not applied correctly as use of large collection tubes, lack of reporting of the daily cumulative blood loss, majority of nurses prefer withdrawing blood sample from femoral artery that result hematoma formation and nurses malpractices related to the collected sample which lead to repeating sample withdrawal, physician related factor as unnecessary investigation order.

Phlebotomy is a major factor for developing of HAA in CCN, this result is similar to the study of *Salisbury et al. (2011),* who conducted study about diagnostic blood loss from phlebotomy and HAA during acute myocardial infarction on

17 676 cardiac patients from57hospitals, who found that for every 50 mL of blood collected majority of studied patients had moderate to severe HAA.As well with *Tosiri, Kanitsap & Kanitsap, (2010).***who conducted study about** Approximate iatrogenic blood loss in medical intensive care patients and the causes of anemia and stated that iatrogenic blood loss is common in ICU patients and is considered a factor contributing to HAA. This result is disagree with *Thomas et al., (2009),* who conducted prospective cohort study about anemia and blood transfusion practices in the critically ill and concluded that sampling blood loss did not pose a serious problem and did not influence the rate of HAA.

Regarding to **blood loss associated invasive** procedure**,** critically ill patient need invasive monitoring and insertion of excessive invasive procedures. From types of invasive procedures that frequently required in ICU (central venous catheter, urinary catheter, venous or arterial catheter, tracheostomy tube, endotracheal tube, cardiac sheathe).

This study represent that, the majority of blood loss for anemic patients associated invasive procedures was from cardiac sheathe, followed by blood loss associated CVC, followed by blood loss associated chest tube, while less amount of blood loss associated with venous cannula, endotracheal tube and tracheostomy tube .

This finding could be attributed to many reasons; These invasive procedures inserted without good assessment of coagulation cascade for patients or inserted falsely that lead to accidently complication from insertion as hemothorax from mal insertion of CVC or rupture urethra from insertion of urinary catheter for old male prostatic enlargement without taking history or physical examination, in addition to blood loss during removal of this invasive procedure as cardiac catheter sheathe without making good compression

that lead to hematoma formation and blood loss, finally routine care for this procedures not followed correctly as leaving open clamp without close it as CVC or cardiac sheathe, all these considered reasons for blood loss associated invasive procedures.

This study is in the same line with *Low, Harrington & Stoltzfus (1995),* who conducted study about, the effect of arterial lines on blood-drawing practices and costs in ICU and concluded that, more than one third of studied patients in ICU had blood loss from central venous catheter versus peripheral access.

As well, with *Mumtaz et al., (2001),* 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.

Related to blood loss associated GIT, the finding of the current study showed that, the mean volume of blood loss associated GIT exceed for anemic patients more than mean volume of blood loss associated GIT for non anemic patients.

This finding could be attributed to many reasons; One cause of GIT bleeding in this study was stress ulcer mainly due to coagulopathy and over dose from anticoagulant therapy without precaution and minority of causes of stress ulcer in this study was not taken prophylactic PUP as PPI this cause is not common due to majority of patients took prophylactic PPI in the current study setting.

This study is in the same line with *Richards, & Stapleton, (2014)*who stated that, in one prospective study, 10 % of all patients admitted to the ICU developed bleeding, (is the most common site, accounting for more than one quarter of all

significant bleeding in the ICU was from (GIT).

This study contradicted with**,** *Hayden et al., (2012),* who conducted study about anemia secondary to critical illness and reported that, the impaired mucosal integrity of (GI) tract is a source of on-going occult blood loss clinically important bleeding from stress gastritis occurs in minority of ICU patients, with the main risk factors were being mechanical ventilation, nutritional deficiencies, acute renal failure, and prophylactic or therapeutic anticoagulation.

Part III: Relation between different variable of the study

Relation between demographic characteristics of studied patients and occurrence of HAA:

Although this study stated that HAA occure in old age more than young age, this study reported that there were not significant relation between demographic characteristic of studied patients (age & gender) and occurrence of HAA.

This finding agrees with *Asfour et al., (2016),* who concluded that there were not significant relation between demographic characteristic of studied patients (age & gender) and occurrence of HAA.

This finding was contradicted with *Adam et al. (2012),* who stated that, HAA have relation between several common risk factors including old age, female sex, and the presence of chronic renal disease, as well *Meron et al. (2012),* who concluded that, there were relation between old age and occurrence of HAA.

More over with what was reported by **Peter, et al. (2013)** who found that, more than half of studied patients their aged

>55 years became anemic during hospitalization, compared to less than half of studied non patients their aged ≤50 years has a high incidence and is more common in older female patients than young age and male patients). Also, with, **Choi, et al. (2013)**, who found that, Patients who developed HAA were older than those who did not.

Relation between factors contributing to HAA in studied patients and occurrence of HAA

Factors affect RBCs production

Regarding to **nutritional factor**. This study revealed that, there was significant relation between inadequate feeding and occurrence of HAA. This finding is in line with *Rodriguez et al. (2001)*, who conducted study in titled. Nutritional deficiencies and blunted erythropoietin response as cause of the anemia of critical illness, identified some of the potential causes of ineffective erythropoiesis in a cohort long term ICU patients in USA and found that nutritional deficiencies is a correctable cause of HAA. Furthermore, nutritional deficiencies can lead to diminished RBCs production and iron therapy is an essential part of the management of HAA,

This results was contradicted with *Walsh and Saleh, (2006),* who conducted study about, Anemia during critical illness, and emphasized, that the relation between nutritional deficiencies and HAA is unknown. As well with *Von Ahsen et al. (1999),* who observed that, the significance of folic acid deficiency and vitamin B12 deficiency as a factor contributing to ICU-acquired anemia remains uncertain.

Concering **Hemodilutional factor**, the current study finding showed that, there was not significant relation between hemodilution and occurrence of HAA. This finding supported by *Philbert et al. (2013)*

who reported that by using the Pearson correlation coefficient, no consistent or significant linear relationships were observed between net fluid balance and changes in blood volumes and Hb level

This result was contradicted with *Monnet et al. (2013)*, Lactate and venoarterial carbon dioxide difference/ arterial-venous oxygen difference ratio, but not central venous oxygen saturation, predict increase in oxygen consumption in fluid responders and seems that the administration of 500 ml of fluids may acutely decrease the Hb concentration by about 1 g/dl, or administration of large amounts of intravenous fluids may cause iatrogenic hemodilution at times, even a paradoxical decrease in DO2. The associated decrease in Hb values to below the acceptable transfusion, this reflect that there were significant relation between hemodilution and anemia.

Related to **drugs affect RBCs production**, the present study indicated that, there was no significant relation between drugs affect RBCs production and occurrence of HAA. This might be due to 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.

This results goes in the same line with *Asfour et al. (2016)* who stated that, there was no significant relation between this drugs and occurrence of HAA, and contradicted with *Schick and Besa, (2016),* who stated that, most common acquired causes of hemolysis during hospitalization include Toxic chemicals, infections (inflammatory process) and drugs that has significant association for occurrence of acquired hemolytic anemia in hospital (The most common drugs associated with this, are penicillin and its derivatives, cephalosporins, cefotetan, ceftriaxone, methyldopa, b-lactamase inhibitors).

Concering Sepsis related factors, the finding of this study concluded that, there was significant relation between sepsis and occurrence of HAA, this result consistent with *Meron et al. (2012),* who reported that, by analyzing different variable as predictors of HAA they found that, anemic patients had elevated serum CRP value (c-reactive protein) more than non anemic patients and there was highly significant association between patients with high serum CRP level and occurrence of HAA, this explains inflammatory process considered important variable of HAA.

Factors increased RBCs loss

Related to association between **drugs increased blood loss and development of HAA**, the current study showed that, there was significant relation between drugs increased blood loss and occurrence of HAA, this finding consistents with *McEvoy & Shander, (2013),* who found that, patients are those on medications such as aspirin, warfarin, clopidogrel, and other anticoagulants agents more risk for development of anemia in ICU due to inhibition of coagulation cascade.

Regarding **relation blood loss factors and development of HAA,** this study results revealed that, there were significant relation between blood loss factor and occurrence of HAA.

Phlebotomy blood loss, This finding consistents with **Wong & Intragumtornchai, (2006),** who concluded that, correlation between total volume of investigational blood and degree of anemia may imply that higher volume of investigational blood loss causes more anemia and and in consistent with **von***Ahsen et al. (1999),* who found that association between blood samples drawn for laboratory analysis, together with blood discarded during the sampling procedure is

not contributed to development of anemia. As well, with *Wisser et al* **(2003),** who conducted study about, Blood loss from laboratory tests in German, and concluded that, sampling blood loss did not pose a serious problem and did not influence the rate of nosocomial anemia.

More over with *peter et, al.* **(2013),** who reported that, more aggressive strategies such as reducing the frequency of blood draws and expanding the use of smaller volume tubes for other laboratory panels may be helpful in reducing the incidence of HAA during hospitalization.

Invasive procedures associated blood loss, this finding goes in same line with***Richards & Stapleton, (2014):***who stated that, association between the volume of blood loss associated invasive procedures as patients who have intravascular line to facilitate access for phlebotomy and develop anemia in ICU can be very significant but varies depending on the type of procedure

Conclusion

More than half of studied patients developed HAA during their ICU stay, nearly one third of anemic patients developed this anemia by fifth day from admission to ICU. As well more than three quarter of anemic patients were under feeding, majority of them were enteral feeding, more than one third of them had sepsis and more than one quarter of them had hemodilutional factor, in addition to mean amount of blood loss for anemic patients exceed amount of blood loss for non anemic patients. Moreover, there was statistically significant relation between nutrition deficiency, sepsis, blood loss in ICU and drugs increased RBCs loss factors and occurrence of HAA. Also there were insignificant relation between demographic characteristic of studied patients, their diagnosis on admission to hospital,

hemodilution, drugs affect RBCs production and occurrence of HAA.

Recommendation

Recommendations regarding clinical practice:

- Provide adequate nutritional support considering the quantity and quality of requirements according to patient's condition and availability of dietitian inside critical care unit.

- Encourage collaboration between nurses and pharmacists to increase nurses' awareness regarding drugs' side effects especially hematological side effects.

Recommendations regarding education:

- Provide continuous in- service educational programs and scientific courses for CCN to revise, acquire and develop knowledge and performance regarding to risk factors, etiology and preventive measures of HAA as:

  ➢ Blood conversation strategies specially prevention of blood loss associated invasive procedure and phlebotomy practice as minimal volume required per laboratory test.

  ➢ Standard procedure for venous and arterial blood sampling to minimize arterial and venous puncture complications

  ➢ Best practice of nasogastric tube feeding and provide knowledge about common drugs associated hematological problem.

  ➢ Importance of document intake and output accurately considering amount of blood loss as part of fluid balance chart.

Recommendations regarding administration:

- Unit protocols and policy regarding infection control program should be developed and reviewed regularly as updates and new evidence for best practice are constantly emerging and ICU nurses should be educated on updated protocols.

- Develop a quality improvement project, standards, or policies to prevent hospital acquired blood loss, including hematological assessment as a part in nursing flow sheet.

Recommendations regarding research:

- Consider further studies about HAA, its prevention and management in different areas such as: Develop standards for blood conservation strategies and standards for nutrition requirement for critically ill patients are highly recommended to maintain optimal health for such group of patients.

- The study should be replicated on large sample and in different hospitals setting in order to generalize the results.

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Factors Contributing to Hospital Acquired Anemia among Critical Ill Patients

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