# Approximate Iatrogenic Blood Loss in Medical Intensive Care Patients and the Causes of Anemia

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***Background****: Anemia is the most common hematologic problem worldwide especially in developing world. There are many causes of anemia in ICU patient such as gastrointestinal bleeding, anemia of chronic inflammation, trauma or surgery. Patient who were admitted in the ICU need to have a lot of blood tests related to their illness and for further treatment, however that can cause decrease of hematocrit or anemia.*
***Objective****: To identify the estimate volume of blood drawn from medical ICU patients and findout whether the volume of blood drawn effects the Hemoglobin/Hematocrit (Hb/Hct) or anemia and to identify the cause of anemia in ICU patient.*
***Material and Method:*** *This is an observation prospective cohort study collecting the volume of blood drawn from patients who were admitted to ICU Thammasat university hospital during 1st October 2007 through 31st March 2008.*
***Results****: This study found the mean volume of blood samples drawn from ICU patients is 77.8 ml. Sixty-eight percents of patients had a decrease Hb/Hct level during admission and around sixteen percent had anemia during admission. There is no statistically significant between the volume of blood drawn and the decrease of Hb/Hct.*
***Conclusion:*** *Decrease of Hb/Hct or anemia are common in ICU patient. This study showed that iatrogenic blood loss for laboratory investigation is one of the cause of anemia. We concluded that physician should order phlebotomy for necessary investigation for the most effective of diagnosis and treatment, but the less complication.*

***Keywords****: Anemia, Iron deficiency anemia, Iatrogenic anemia*

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Anemia is the most common hematologic problem worldwide especially in developing world. The incidence of anemia during 1889-1990 in Thailand were 86% in working male adult, 32% in childbearing age female, 45% in the elderly, 24.5-30% in pregnant women, and 57.4% in children. Iron deficiency is the most common cause of anemia. Moreover, some patient develops anemia after admitted in the hospital, especially patient in intensive care unit (ICU). More than 95% of ICU patient develop anemia after 3 days of admission[1]. There are many causes of anemia in ICU patient such as gastrointestinal bleeding, anemia of chronic inflammation, trauma or surgery[2]. Patient who were admitted in the ICU need to have a lot of blood tests related to their illness and for further treatment, however that can cause decrease of hematocrit or anemia[3-7]. To identify the causes of anemia can bring high cost healthcare and many medical problem especially in patient with medical illness such as severe ischemic heart disease and cerebrovascular disease[8]. Anemia may effect hemostasis by interfere platelet, endothelial cell and vascular function, so anemic patient will be easily bleeding than the one whose hemoglobin is normal[9]. Anemia in post-operative patients will cause more muscle weakness, fatigability, confusion, interference of cardiac function, and also delay wound healing and delay post-op recovery[10-12]. Anemia effects survival in post-operative coronary artery bypass graft patient[13].

Nowadays there were many blood investigations, which few investigations identified the volume of blood drawn. This study will collect the average volume of blood drawn, incidence, and the cause of anemia in ICU patient which will be beneficial for treatment of ICU patient in the future.

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## Objective

The main objective is to identify the estimate volume of blood drawn from ICU patients. The second

objective is to find out whether the volume of blood drawn effects the Hb/Hct or anemia and to identify the cause of anemia in ICU patient.

## Material and Method

This is an observation prospective cohort study collecting the volume of blood drawn from patients who were admitted to ICU Thammasat university hospital during 1st October 2007 through 31st March 2008.

Demographic data were collected and the change of Hb/Hct from baseline or incidences of anemia were also collected.

### *Inclusion and exclusion criteria*

All patients who were admitted in medical ICU Thammasat University Hospital from 1st October 2007 through 31st March 2008 were included in the study. Pediatric or surgical patients who were admitted to medical ICU and patients whose incomplete data collection were excluded.

All the patients will be treated by ICU doctors normally, including investigation for diagnosis the cause of anemia. The volumes of blood drawn from patients were record every times during their ICU admission until discharge from ICU or death. The volumes of blood, the changing of hemoglobin and hematocrit level, and the causes of anemia were collected and analysed.

### *Definition*

Anemia: Hb below 13 gm/dl in male or 12 gm/dl in women.

Anemia of chronic disease: anemia caused by chronic illness (longer than 1 week) and Serum iron < 60 mg/dl, Serum ferritin > 50 ng/ml[14-17].

Hemolytic anemia: anemia with the evidence of reticulocytosis and red cell morphology show agglutination, microspherocyte, polychromasia, fragmentation and in autoimmune hemolytic anemia with positive direct antiglobulin test.

Unexplained anemia: anemia without the cause identified by documented investigation.

Unidentified-cause anemia: anemia without any investigation nor identified cause.

### *Severity of anemia[18]*

Severity of anemia is classified to mild, moderate, and severe according to Hb level.

| | | |
|---|---|---|
| Mild anemia | Hemoglobin (g/dl) > 10-12 | Hct > 30-36% |
| Moderate anemia | Hemoglobin 7-10 | Hct 21-30% |
| Severe | Hemoglobin < 7 | Hct < 21% |

### *Statistic analysis*

The clinical data was showed by descriptive statistic in the mean, standard deviation (SD) and percent. The correlations between volume of blood drawn and the change of hemoglobin/hematocrit level were analyzed by Pearson correlation with defined statistic significant when p-value below 0.05. Independent-sample t-test was used when compare not only between the patients with changing and non-changing hemoglobin level, but also in anemic and non-anemic patients. Independent-sample t-test was used for comparison of blood drawn between the group which Hb/Hct changed and unchanged, or anemia and non-anemia. The causes of and severity of anemia were presented in descriptive statistic.

## Results

The data were collected from 1st October 2007 through 31st March 2008. There were 102 patients who were admitted to ICU. Fifty-eight patients were excluded from analysis due to the exclusion criteria. The excluded patients were 9 pediatric and surgical patients, 30 patients received blood transfusion before admission, and 19 patients cannot complete the data. Finally there were 44 patients whose data were complete in this study.

Table 1 shows patient characteristics. The mean age was 62.9 years. There were 24 women (54.4%) and 20 men (45.5%). The mean hemoglobin on admission was 11.5 g/dl and the mean hematocrit was 34.2%. Mean duration of admission was 10 days. Twenty-seven has anemia on ICU admission (61.4%; 40.7% male and 59.3% female). By observation and record, the mean of total blood drawn volume for investigation was 77.8 ml and the mean volume drawn per day was 9.8 ml. There were 30 patients (68.2%) have hemoglobin/hematocrit decreased during admission. Within that group, 7 patients (15.9%) had anemia. Twenty-one patients received blood transfusion during admission (47.7%).

Static analysis by Pearson Correlation showed the correlation between the change in hemoglobin and hematocrit and expected predictors in Table 2. The initial hemoglobin/hematocrit is the factor effecting the changing of hemoglobin and hematocrit ($p = 0.001$). The mean volume of blood drawn, age, gender, and duration of admission were not correlated with the changing of hemoglobin and hematocrit.

When compared the phlebotomy volume per

in each patient group, the patients with decrease Hb/Hct have more phlebotomy volume than the gorup without decrease Hb/Hct but there was no statistically significant. The patient with anemia also have more phlebotomy volume than the gorup without anemia but there was no statistically significant. Those data shown in Table 3.

Table 4 and Fig. 1 shows the causes of anemia in the studied patients. The most common cause of anemia in this study is anemia of chronic disease. (11 patients, 32.4%) Chronic disease suspected to cause anemia are infection (9 patients) and cancer (2 patients). The second common causes of anemia is blood loss anemia. Other causes of anemia are iron deficiency anemia, dilutional, and anemia in chronic renal failure patients. Two patients have multifactorial causes of anemia and one patient has unexplained anemia. There were 7 patients whose anemia were not assess (20.6%). Table 5 shows severity of anemia in the patient who become anemia during admission, total 34 patients. Twenty-six patients (76.5%) have moderate anemia. Eight have mild anemia (23.5%), and there is no one with severe anemia.

**Table 1.** Patients characteristics (n = 44)

| | |
|---|---|
| Mean age (yrs) | 62.9 ± 16.8 |
| Gender | |
| Female | 24 (54.5%) |
| Male | 20 (45.5%) |
| Mean initial Hb level (g/dl) | 11.5 ± 2.3 |
| Mean initial Hct level (%) | 34.2 ± 6.8 |
| Total volume of blood drawn (ml) | 77.8 ± 59.2 |
| Mean blood drawn volume per day (ml) | 9.8 ± 5.5 |
| Mean admission duration (day) | 10 ± 8.9 |
| Patient with anemia on admission | 27 (61.4%) |
| Male | 11 (40.7%) |
| Female | 16 (59.3%) |
| Patient with anemia during admission | 7 (15.9%) |
| Patient with decrease Hb/Hct level | 30 (68.%) |
| Patient with transfusion (%) | 21 (47.7%) |
| Patient with anemia on admission | 19 (90.5%) |

## Discussion

In this study, we want to know phlebotomy volume in medical ICU patient. The result found average volume for investigation during hospitalization were 77.8 ml, leading to anemia during hospitalization for 15.9% which like study of Thavendiranathan P et al[19] (Table 6) Thavendiranathan P et al observe 381 medical patient during admission, he found the mean volume of phlebotomy was 74.6 ml and about sixteen percent (15.8%) had anemia. They found the correlation between phlebotomy volume and the decreasing of hemoglobin and hematocrit with statistical significant. One milliliter of phlebotomy related to the decrease of 0.007 g/dl hemoglobin and 0.019% hematocrit, however this study did not find a statistical significant of the correlation. This is possible due not only to a small population but also this study did not exclude other factors which can effect the hemoglobin and hematocrit level such as gastrointestinal bleeding or dialysis patient.

Comparing phlebotomy volume, both the group of patient with a decrement of hemoglobin and anemia had more phlebotomy volume than both the group who without a decrement of hemoglobin and

**Table 2.** Predictors of change in Hematocrit during hospitalization

| Variable | Correlation coefficient (r) | p-value |
|---|---|---|
| Mean volume of blood drawn per day | 0.042 | 0.790 |
| Age | -0.130 | 0.411 |
| Gender | 0.048 | 0.765 |
| Duration of admission | 0.061 | 0.676 |
| Initial Hct | 0.530 | 0.001 |

**Table 3.** Comparisons of phlebotomy volume and Hemoglobin/Hematocrit change

| Patient group | Volume of blood drawn per day (Mean ± SD; ml) | p-value |
|---|---|---|
| Patient with decrease Hb/Hct | 11.6 ± 6.5 | 0.322 |
| Patient without decrease Hb/Hct | 9.5 ± 5.1 | |
| Patient with anemia | 10.7 ± 5.9 | 0.967 |
| Patient without anemia | 10.6 ± 6.3 | |

**Table 4**. Causes of anemia in the patients (n =34)

| Cause of anemia | Number of patients, (%) |
|---|---|
| Blood loss | 4 (11.8) |
| Hemolysis | 1 (2.9) |
| Anemia of chronic disease | 11 (32.4) |
| Infection | 9 |
| Malignancy | 2 |
| Chronic kidney disease | 3 (8.8) |
| Iron deficiency anemia | 3 (8.8) |
| Dilutional anemia | 2 (5.9) |
| Multifactorial | 2 (5.9) |
| Not assess | 7 (20.6) |
| Unexplain | 1 (2.9) |

**Table 6.** Predictors of change in Hematocrit during hospitalization

| Variable | p-value (This Study) | p-value (Thavendiranathan P, et al ) |
|---|---|---|
| Volume of blood drawn (ml) | 0.790 | < 0.0001 |
| Age (yr.) | 0.411 | 0.0247 |
| Gender | 0.765 | 0.5432 |
| Duration of admission (day) | 0.676 | 0.0019 |
| Initial Hct (%) | 0.001 | < 0.0001 |

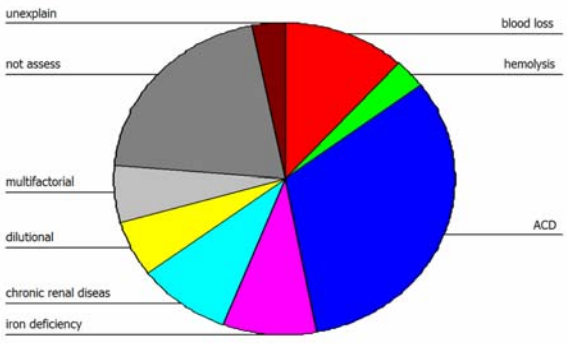


**Fig. 1** Causes of anemia in medical ICU patient

anemia respectively. The statistic analysis was significant.

This study reported the initial hemoglobin level of the patient was the factor which effected the decrement of hemoglobin. The higher the hemoglobin

**Table 5.** Severity of anemia in the patients who become anemic during admission

| Severity of anemia | No. of patient (%) |
|---|---|
| Mild | 8 (23.5) |
| Moderate | 26 (76.5) |
| Severe | 0 |

level the more decreasing the hemoglobin level with statistically significant. This result was also reported by Thavendiranathan P et al[19] (Table 6). The first explanations should be high hemoglobin patient had more red cell which trend to loss during investigating phlebotomy and another reason should be high hemoglobin patient from initial hemoconcentrate had a dilutional effect of hemoglobin after ICU admission combined with iatrogenic blood loss.

Looking into the effect of age of the patient and the decreasing of hemoglobin, we found the younger of the patient, the more decreasing of hemoglobin level but the statistically non-significant. Same as our result, Thavendiranathan P et al[19] suspected that the young patient has a chance to receive more volume due to doctor bias in awareness of fluid infusion (Table 6).

From the past study[20], anemia in ICU patient were caused by multiple problem such as blood loss, hemolysis, decrease erythropoiesis, or erythropoietin deficiency. In this study, the most frequent identified causes of anemia were anemia of chronic disease. Mostly from anemia of chronic inflammation due to infection leading to impair erythropoiesis[21]. Unidentified causes of anemia is a the second large group, it may be due to the doctor ignoring mild dergree of anemia in this group.

In CRIT study[22], the study in 4,892 intensive unit patients found 44% of the patient was transfused during ICU admission. ABC study in 1,136 intensive care unit patients found the prevalence of transfusion during ICU admission was 37%[23]. The prevalence of ICU transfusion in this study was higher as 47.7%. We considered blood transfusion as a factor leading to other complication of hospitalized patients.

## Conclusion

Our study and the past studies can remind doctor and nurse about the important of anemia in hospitalized patients. Physician should order phlebotomy for necessary investigation for the most

effective of diagnosis and treatment, but the less complication. Transfusion should be limiting when indicated only.

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## ปริมาณเลือดที่แพทย์ใช้ในการตรวจทางห้องปฏิบัติการของผู้ป่วยในหอผู้ป่วยวิกฤตอายุรกรรม และสาเหตุของภาวะโลหิตจาง

**ปิติมา โตศิริ, นงลักษณ์ คณิตทรัพย์, อภิชาติ คณิตทรัพย์**

***ภูมิหลัง**: ภาวะโลหิตจางเป็นปัญหาทางโลหิตวิทยาที่พบบ่อยที่สุดในเวชปฏิบัติโดยมีผู้ป่วยจำนวนหนึ่งที่เกิดภาวะโลหิตจางระหว่างเข้ารับการรักษา โดยเฉพาะผู้ป่วยในหอผู้ป่วยวิกฤตอายุรกรรมสาเหตุของภาวะโลหิตจางในผู้ป่วยวิกฤตเกิดจากหลายสาเหตุ เช่น ภาวะเลือดออกในทางเดินอาหาร ภาวะโลหิตจางจากโรคเรื้อรัง การตรวจเลือดหรือสาเหตุอื่นๆ*

***วัตถุประสงค์**: เพื่อศึกษาปริมาณเลือดที่ใช้ในการตรวจรักษาของผู้ป่วยที่เข้ารับการรักษาในหอผู้ป่วยวิกฤตอายุรกรรม และศึกษาความสัมพันธ์ ของปริมาณเลือดที่ใช้ในการตรวจทางห้องปฏิบัติการของผู้ป่วยวิกฤตอายุรกรรม กับการลดลงของค่า Hb/Hct และการเกิดภาวะโลหิตจาง*

***วัสดุและวิธีการ**: เป็นการศึกษาแบบรวบรวมข้อมูลไปข้างหน้า (prospective study) ในผู้ป่วยอายุรกรรมที่เข้ารับการรักษาในหอผู้ป่วยวิกฤตอายุรกรรมโรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ ตั้งแต่วันที่ 1 ตุลาคม พ.ศ. 2549 ถึงวันที่ 31 มีนาคม พ.ศ. 2550*

***ผลการศึกษา**: การศึกษานี้พบว่าปริมาณเลือดที่ใช้ในการตรวจทางห้องปฏิบัติการของผู้ป่วยวิกฤตอายุรกรรมมีค่าเฉลี่ย 77.8 ml ซึ่งพบว่าร้อยละ 68.2 ของผู้ป่วยมีการลดลงของค่า Hb/Hct ระหว่างนอนโรงพยาบาล และร้อยละ 15.9 ของผู้ป่วยเกิดภาวะโลหิตจางระหว่างนอนโรงพยาบาลแม้ว่าจากการศึกษาความสัมพันธ์ ระหว่างปริมาณเลือดเฉลี่ยที่ใช้ตรวจทางห้องปฏิบัติการกับการลดลงของค่า Hb/Hct และการเกิดภาวะโลหิตจางจะไม่มีนัยสำคัญทางสถิติ*

***สรุป**: ภาวะโลหิตจางและการลดลงของค่า hemoglobin/hematocrit พบบ่อยในผู้ป่วยวิกฤตอายุรกรรม โดยสาเหตุของภาวะโลหิตจางมีหลายสาเหตุ ซึ่งการตรวจเลือดทางห้องปฏิบัติการมีความสำคัญต่อการลดลงของค่า hemoglobin/hematocrit และการเกิดภาวะโลหิตจางจากผลดังกล่าวการลดการตรวจเลือดทาง ห้องปฏิบัติการที่ไม่จำเป็นสามารถลดการเกิดภาวะโลหิตจางในโรงพยาบาลได้*