Hospital-Acquired Anemia

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Objective: *The incidence and etiologies of hospital-acquired anemia has not been well defined. A prospective study was conducted to determine the incidence and etiologies of hospital-acquired anemia developed in patients admitted in the medical ward of a tertiary care university hospital.*
Material and Method: *All non-anemic (hemoglobin (Hb) ≥ 13 g/dl in male, ≥ 12 g/dl in female) patients who were admitted to the general medical wards for at least 1 week, between March 2001 to October 2001, were included in the present study. Outcome of interest was anemia developed during hospital stay. The total volume of blood collected for investigations were recorded.*
Results: *Of the 98 evaluable patients, 64 (65.3%) developed anemia. Thirty-five percent of the patients had mild anemia (Hb > 10.0 g/dl) and 7% had severe anemia (Hb ≤ 8.0 g/dl). Anemia of chronic disease was the most common cause found in 57.4% of anemic patients. Mean total volume of blood collected for investigation was higher in the anemic compared with the non-anemic group (147.0 ml vs. 52.0 ml, $p < 0.05$). Total volume of investigational blood also correlated significantly with degree of anemia ($r = 0.638$, $p < 0.05$).*
Conclusion: *Anemia was a common complication occurring in almost two-thirds of patients admitted to the hospital. Even though anemia of chronic disease was the leading cause, investigational blood loss was also an important contributing factor.*

Keywords: *Anemia, Hospital-acquired, Anemia of chronic disease, Investigational blood loss*

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Anemia is a common manifestation of most systemic diseases. Patients with anemia are an every-day-life scenario faced by physicians in practice. However, few studies have been conducted to evaluate the anemia that develops during the hospital course. Iatrogenic or anemia of investigation had been previously coined by some researchers[1,2].

Previous studies on iatrogenic anemia, conducted mostly among patients admitted to intensive care units, found that investigational as well as non-investigational blood loss were the main contributing factors[3-7]. The effect of other etiologies as well as the incidence of the hospital-acquired anemia were not well defined. The purpose of the present study was to determine the incidence, causes and contributing factors of anemia developing in patients admitted to the general medical wards of a tertiary care university hospital.

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Material and Method

Unselected consecutive non-anemic patients (male; hemoglobin (Hb) ≥ 13 g/dl, female; Hb ≥ 12 g/dl) who were admitted to the general medical wards, from March 2001 to October 2001, at King Chulalongkorn Memorial Hospital were enrolled in the present study. To be eligible, the length of hospital stay had to be longer than 1 week. Patients with underlying hematologic diseases or malignancies were excluded. Hemoconcentration that caused spurious non-anemic state was also excluded. The outcome of interest were patients who developed a Hb level of less than 13 g/dl for males and 12 g/dl for females[8], during hospitalization. All patients were cared for by medical residents under supervision of the faculty. The selection of laboratory investigations performed depended on

medical residents in charge, were not directed by the investigators except Hb reassessment before hospital discharge in case of non-anemic patients. The study was approved by the institutional ethical committee. Written informed consent was obtained from all patients before they entered the study.

Anemias were classified by severity into 3 categories; mild (Hb > 10.0 g/dl), moderate (Hb = 8.1-10.0 g/dl) and severe (Hb ≤ 8.0 g/dl). Investigations for the causes of anemia included peripheral blood smear, reticulocyte count, stool occult blood, antiglobulin test, serum iron, total iron binding capacity (TIBC) and assessment of ferritin level. In each patient, not all the tests would be performed depending also on the physician in charge as mentioned above. Hemoconcentration that caused spurious non-anemic state was diagnosed based on clinical findings, urine specific gravity, blood urea nitrogen-creatinine ratio or uric acid. To ascertain non-anemic state, patients who did not show outcome of interest were reassessed of their Hb performed within 48 hours before hospital discharge. Any non-anemic patients who were not reassessed of their Hb level before hospital discharge would be excluded. Observation for blood volume collection in each patient was done day by day. Volume of blood was estimated from test tube before sending for laboratory test. The total volume of blood collected for investigations during the hospital course in each patient was recorded. Anemia of chronic disease (ACD) was diagnosed when, in the presence of illness which lasted longer than 1 week, the serum iron was < 60 mg/dl and the serum ferritin level was ≥ 50 ng/ml[9-12]. Hemolytic anemia was defined as anemia with reticulocytosis and consonant blood picture (e.g. high polychromasias, fragmentation, microspherocyte, red cell agglutination) and immune hemolytic anemia was an anemia with positive direct antiglobulin test[13,14].

Unpaired T test was computed to determine the significant difference of the mean values of investigational blood volume between the anemic and non-anemic group. The relationship between volume of investigational blood loss and degree of anemia and length of hospital stay were determined by Pearson correlation (r). P-value of < 0.05 was considered as statistical significance.

Results

One hundred and eighteen patients were recruited. Twenty patients were excluded; 18 because Hb values within 48 hours before discharge to confirm non-anemic state were not performed and the remainder had the final diagnosis of malignancies. Ninety-eight patients, comprised of 55 males and 43 females, were analyzed. Demographic data for the patients is shown in Table 1.

Of the 98 evaluable patients, 64 (65.3%) developed anemia during hospital course. Thirty-four patients had mild, 23 had moderate and 7, severe anemia (Table 2). The mean amount of Hb reduction was 3.65 ± 1.9 g/dl. The median time to develop anemia was the fifth day of admission.

Causes of hospital-acquired anemia are shown in Table III. The total number of analyzed patients was 47 as iron studies were not performed in 17 patients. Anemia of chronic disease was the most frequent diagnosis in each anemic severity found in 57.4% of the patients. Iron studies and ferritin level in ACD and non-ACD patients are shown in Table 4. No patients had ferritin lower than 50 ng/ml (lowest ferritin 89 ng/ml). Twelve patients had overt blood loss; 8 patients with gastrointestinal bleeding, 3 surgical bleeding and 1 subcutaneous hematoma from heparin overdose.

Table 1. Demographic data of 98 patients

	Male (n = 55)		Female (n = 43)	
	Mean ± SD	Range	Mean ± SD	Range
Age (year)	54.2±20.0	16-96	55.8±18.2	17-89
Length of hospital stay (day)	21.1±16.3	7-84	23.1±24.1	7-157
Hb value on admission (g/dl)	14.4±1.0	13.0-17.2	13.0±0.8	12.0-15.5
Type of associated diseases		n (%)		n (%)
Infection		24 (43.6)		11 (25.5)
Stroke		8 (14.5)		7 (16.2)
Heart disease		6 (10.9)		8 (18.6)
Obstructive airway disease		5 (9.0)		-
Systemic lupus erythematosus		-		3 (6.9)
Miscellaneous		12 (21.8)		14 (32.5)

Table 2. Severity of anemia

Severity of anemia	n	Lowest Hb (g/dl)	Amount of Hb reduction (g/dl)
Mild	34	11.2±0.7*	2.4±1.2*
Moderate	23	9.0±0.6*	4.6±1.5*
Severe	7	6.7±1.6*	5.9±1.9*

* Mean value ± SD

Table 3. Causes of anemia

Causes	Mild (n = 23)		Moderate (n = 19)		Severe (n = 5)		Total (n = 47)	
	n*	%	n*	%	n*	%	n*	%
Anemia of chronic disease	11	47.8	14	73.7	2	40.0	27	57.4
Overt blood loss	2	8.7	8	42.1	2	40.0	12	25.5
Hemolysis	1	4.3	2	10.5	2	40.0	5	10.6
Hemodilution	4	17.4	3	15.8	-	-	7	14.8
Undetermined	9	39.1	2	10.5	-	-	11	23.4

* One patient may have several causes

Table 4. Iron studies of ACD and Non-ACD

	ACD	Non-ACD
Serum iron (mg/dl)	35.9±12.6*	102.8±38.9*
TIBC (mg/dl)	259.0±73.2*	290.9±79.4*
Transferrin saturation	14.5±6.3*	38.3±17.1*
Serum ferritin (ng/dl)	422.5±422.9*	782.1±650.3*

***** Mean value ± SD

Table 5. Severity of anemia, length of hospital stay and quantity of investigational blood loss

Severity of anemia	Length of hospital stay (day)	Investigational blood loss (ml)
Mild	19.9±14.5*	92.3±48.3*
Moderate	34.4±30.5*	204.5±132.0*
Severe	40.1±13.1*	224.0±114.6*

* Mean value ± SD

Five patients with positive direct antiglobulin tests (anti IgG) and agglutinations on blood smear were diagnosed with immune hemolysis. Two of the five patients with hemolysis were caused by prolonged usage of intravenous cloxacillin, 1 had systemic lupus erythematosus and the remaining 2 had hemolysis of unknown cause. In the authors' observation, 7 patients had anemia within 5 days after admission. Anemia from hemodilution was diagnosed in seven patients as no blood loss or hemolysis was detected and all were hydrated with intravenous fluid from 2500 ml/day to 5000 ml/day. Five of these patients also fitted the ACD criteria. It was noted that ACD was also found in 75%, 20% and 71% of the patients with overt blood loss, hemolysis and hemodilution respectively. Eleven patients with undetermined anemia comprised of 9 mild and 2 moderate anemias. There were 7 patients with positive for stool occult blood solely which could not be considered firmly to be the cause of anemia. The remaining 4 had unknown causes after completing the anemic work up. These patients had very mild anemia and follow up of their Hb was the chosen intervention.

Mean total volume of blood collected for investigation in 64 anemic patients was 147.0 ml (range 28-545 ml) which was significantly higher than 52.0 ml (range 5-114 ml) of the 34 non-anemic patients ($p < 0.05$). Amount of investigational blood loss correlated significantly with amount of Hb reduction ($r = 0.638$, $p < 0.05$) and length of hospital stay ($r = 0.583$, $p < 0.05$) (Table 5).

Discussion

The present study revealed the incidence of hospital-acquired anemia was 65.3%. Most anemic patients had mild to moderate severity; however, 10.9% of anemias had Hb value ≤ 8 g/dl. Anemia of chronic disease was the most common contributing factor. In addition, the severity of anemia correlated directly with

volume of investigational blood and length of hospital stay. Consistent with the present results, von Ahsen et al found that 71 of 96 patients (73.9%) in intensive care units suffered from anemia acquired during treatment[3]. However, many patients in their study were already admitted with subnormal Hb value. The authors found no other previous studies reporting the incidence of hospital-acquired anemia.

The present study found ACD as the most common etiology of hospital-acquired anemia that underlie other causes of anemia. The suppression of the bone marrow response related to chronic infectious and inflammatory diseases was also found by von Ahsen et al[3]. Similar to the present study, they found diminished iron availability by low transferrin saturation (< 20%) in at least 50% of intensive care unit patients[3].

Correlation between total volume of investigational blood, degree of anemia and hospital length in the present study may imply that higher volume of investigational blood loss causes more anemia and longer hospital stay causes more investigational blood loss. Although the mean total volume of investigational blood (147 ml) seems unlikely to be the main cause, it is certainly one of the contributing causes. Tarpey et al found an average investigational blood loss of 336 ml in intensive care patients[4]. They also found a correlation between diagnostic blood volume and length of hospital stay, similar to the present results. Three other previous studies of iatrogenic anemia also reported iatrogenic blood loss for diagnostic purposes as a major determinant of anemia in critically ill patients[5-7]. In contrast to the others, von Ahsen et al found that blood samples drawn for laboratory analysis, together with blood discarded during the sampling procedure, contributed less than one third to the estimated total blood loss. They suggested that the major proportion of blood loss in intensive care units may result from occult gastrointestinal bleeding, minor intensive care unit procedures and blood loss associated with renal replacement therapy[3]. However, these sources of blood consumption were difficult to measure.

Hemodilution is the suspected cause of anemia in patients with no obvious causes, especially in acute anemia developed shortly after admission. However, the incidence of hemodilution varied with the type of patients studied and is difficult to prove definitely.

King Chulalongkorn Memorial Hospital is a 1,550-bed university hospital. It is one of the pivotal centers for medical residency training programs of the country and most patients are referral cases with complicated medical problems. The data depicted in the present study should therefore be generalized to institutes of similar level.

Conclusion

Hospital-acquired anemia is a common complication occurring in almost two-thirds of general medical patients. Half of these anemias caused only abnormal laboratory manifestations and the other half mediated to clinical problems. Anemia of chronic disease was the leading cause. Hemodilution should be kept in mind, especially in patients who developed mild anemia shortly after admission. Investigational blood loss was also one of the important contributing factors. Therefore, clinicians should take consideration in drawing blood for investigations in any patients admitted to the hospital.

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ภาวะโลหิตจางที่เกิดในโรงพยาบาล

พีระพล วอง, ธานินทร์ อินทรกำธรชัย

วัตถุประสงค์*: ในปัจจุบันอุบัติการณ์ และสาเหตุของภาวะโลหิตจางที่เกิดขึ้นในโรงพยาบาลยังไม่มีการรวบรวมไว้ชัดเจน จึงได้ดำเนินการวิจัยเพื่อหาข้อมูลดังกล่าวในผู้ป่วยอายุรกรรมที่เข้ารักษาตัวในโรงพยาบาลมหาวิทยาลัยระดับตติยภูมิ*

วัสดุและวิธีการ*: รวบรวมผู้ป่วยอายุรกรรมที่รับไว้รักษาในโรงพยาบาล ซึ่งไม่มีภาวะโลหิตจางแรกรับ (เพศชายมีค่าฮีโมโกลบินมากกว่าหรือเท่ากับ 13 กรัมต่อเดซิลิตร เพศหญิง 12 กรัมต่อเดซิลิตร) ช่วงเดือนมีนาคม ถึงตุลาคม พ.ศ.2544 โดยผู้ป่วยต้องอยู่รักษาในโรงพยาบาลไม่น้อยกว่า 1 สัปดาห์ หาอุบัติการณ์ของภาวะโลหิตจางที่เกิดขึ้นในโรงพยาบาล ตรวจค้นหาสาเหตุของภาวะโลหิตจางที่เกิดขึ้น บันทึกปริมาณเลือดที่ใช้เพื่อส่งตรวจทางห้องปฏิบัติการทั้งหมดขณะอยู่ในโรงพยาบาล*

ผลการศึกษา*: พบภาวะโลหิตจาง 64 คน ในผู้ป่วย 98 คน (ร้อยละ 65.3) ภาวะโลหิตจางที่เกิดขึ้นร้อยละ 35 เป็นชนิดรุนแรงน้อย (ฮีโมโกลบินมากกว่า 10 กรัมต่อเดซิลิตร) ร้อยละ 7 เป็นชนิดรุนแรงมาก (ฮีโมโกลบินน้อยกว่า หรือเท่ากับ 8 กรัมต่อเดซิลิตร) ภาวะโลหิตจางที่เกิดจากโรคเรื้อรัง (anemia of chronic disease) เป็นสาเหตุร่วมที่พบบ่อยที่สุดของภาวะโลหิตจางที่เกิดในโรงพยาบาล พบร้อยละ 57.4 ของผู้ป่วยที่เกิดภาวะโลหิตจาง ปริมาณเลือดเฉลี่ยที่ใช้ส่งตรวจทางห้องปฏิบัติการในกลุ่มที่เกิดภาวะโลหิตจางมีปริมาณมากกว่าในกลุ่มที่ไม่เกิดภาวะโลหิตจางอย่างมีนัยสำคัญทางสถิติ (147.0 มิลลิลิตร และ 52.0 มิลลิลิตร ตามลำดับ, $p < 0.05$) และมีความสัมพันธ์ไปในทางเดียวกันอย่างมีนัยสำคัญทางสถิติกับความรุนแรงของภาวะโลหิตจางที่เกิดขึ้น ($r = 0.638$, $p < 0.05$)*

สรุป*: ภาวะโลหิตจางเป็นภาวะแทรกซ้อนที่พบได้บ่อยถึงสองในสามของผู้ป่วยที่รักษาตัวในโรงพยาบาล แม้ว่าภาวะโลหิตจางจากโรคเรื้อรังจะเป็นสาเหตุร่วมที่พบบ่อยที่สุด การเสียเลือดจากการส่งตรวจทางห้องปฏิบัติการก็เป็นสาเหตุร่วมที่สำคัญเช่นกัน*