

**ANEMIA AND ANYSOCYTOSIS IN THE EMERGENCY DEPARTMENT:  
A CROSS-SECTIONAL INVESTIGATION**

## ANEMIA I ANIZOCITOZA U HITNOJ SLUŽBI: STUDIJA PRESEKA

Giuseppe Lippi<sup>1</sup>, Silvia Pipitone<sup>1</sup>, Valentina Campana<sup>2</sup>, Gianfranco Cervellin<sup>2</sup><sup>1</sup>Unità Operativa Diagnostica Ematochimica, Dipartimento di Patologia e Medicina di Laboratorio,  
Azienda Ospedaliero, Universitaria di Parma, Italy<sup>2</sup>Unità Operativa Pronto Soccorso e Medicina d'Urgenza, Azienda Ospedaliero, Universitaria di Parma, Italy**Summary**

**Background:** Anemia is a public healthcare problem, which is associated with increased morbidity and mortality. Some studies assessed the frequency of anemia in pediatric emergency departments (EDs), but no such information is available in adult patients admitted to the ED.

**Methods:** The study population consisted of adult patients admitted to the ED of the Academic Hospital of Parma during the year 2010 with the five most frequent acute pathologies (i.e., acute myocardial infarction, AMI), renal colics, pneumonia, pancreatitis and major trauma). Hospital records were extracted from informatics database according to ICD-9 code and related terms. Routine hematological testing was performed on the entire population with identical instrumentation.

**Results:** The study population consisted of 462 ED patients (cases; 262 renal colics, 62 pneumonia, 51 acute pancreatitis, 46 AMI and 41 major trauma) and 429 healthy blood donors (controls). The median hemoglobin value was significantly lower in all patients than in controls (137 versus 151 g/L;  $p < 0.01$ ), whereas the median RDW value was significantly higher (13.7 versus 13.4%;  $p < 0.01$ ). The frequency of anemia and anysocytosis was higher in patients than in controls (anemia: 23 versus 4%,  $p < 0.01$ ; anysocytosis: 25 versus 16%;  $p = 0.03$ ). Hemoglobin values of all subclasses

**Kratak sadržaj**

**Uvod:** Anemija predstavlja problem javnog zdravstva i povezana je s porastom morbiditeta i mortaliteta. Neke studije istražile su učestalost anemije u pedijatrijskim hitnim službama, ali takve informacije nisu dostupne za odrasle pacijente primljene na odeljenja za hitnu pomoć.

**Metode:** Ispitivanu populaciju činili su odrasli pacijenti primljeni na odeljenje hitne pomoći Akademske bolnice u Parmi tokom 2010. godine s jednom od pet najčešćih patologija (akutni infarkt miokarda, AIM), bubrežne kolike, pneumonija, pankreatitis i teške povrede). Bolnički podaci preuzeti su iz informatičke baze podataka u skladu sa šifrom ICD-9 i srodnim terminima. Rutinsko hematološko testiranje izvršeno je na čitavoj populaciji pomoću identičnog instrumenta.

**Rezultati:** Populaciju u ovoj studiji činilo je 462 pacijenata sa odeljenja za hitnu pomoć (slučajevi; 262 bubrežne kolike, 62 pneumonija, 51 akutni pankreatitis, 46 AIM i 41 teške povrede) i 429 zdravih davalaca krvi (kontrola). Srednja vrednost hemoglobina bila je značajno niža kod svih pacijenata u odnosu na kontrolne subjekte (137 prema 151 g/L;  $p < 0,01$ ), dok je srednja vrednost eritrocita bila značajno viša (13,7 prema 13,4%;  $p < 0,01$ ). Učestalost anemije i anizocitoze bila je veća kod pacijenata nego kod kontrolnih subjekata (anemija: 23 prema 4%,  $p < 0,01$ ; anizocitoza: 25 prema 16%,  $p = 0,03$ ). Vrednosti hemoglobina u svim potklasama

Address for correspondence:

Prof. Giuseppe Lippi  
U.O. Diagnostica Ematochimica,  
Azienda Ospedaliero-Universitaria di Parma,  
Via Gramsci, 14,  
43126 – Parma, Italy  
Tel. 0039-0521-703050  
Fax. 0039-0521-703791  
e-mail: glippi@ao.pr.it, ulippi@tin.it

of patients were significantly lower than those of the controls, while those of RDW were significantly increased in patients with AMI, pancreatitis and pneumonia.

**Conclusions:** We found a high prevalence of anemia and anisocytosis in a population of ED patients, whose identification may be vital for appropriate therapy and subsequent management.

**Keywords:** anemia, RDW, hemoglobin, emergency department, emergency room

## Introduction

Anemia is a public healthcare problem, displaying an estimated prevalence of ~25% worldwide but also notable differences, with a gradual increase from 9%, 25.7% and 42.8% of the population in countries in the high-, medium- and low-development categories, respectively (1). Anemia is typically defined as a decreased value of circulating red blood cells (RBCs) or hemoglobin concentration. The most widely used anemia thresholds, as currently established by the World Health Organization (WHO) are <120 g/L in women and <130 g/L in men, regardless of the presence of nutritional deficiencies (1, 2).

Anemia has recently been included among one of the ten most important causes that contribute to the global burden of diseases by the WHO, especially in elderly and female populations. Several lines of evidence also attest that this condition is independently associated with morbidity and mortality in the general population, especially in subjects with chronic diseases where its prevalence is reportedly higher (3, 4).

Although some previous studies have investigated the frequency of anemia in urban pediatric emergency departments (5, 6), there is, to the best of our knowledge, no reliable information in the current scientific literature about the frequency of anemia and anisocytosis in adult patients admitted to the emergency room. Therefore, we planned a cross-sectional study aimed at investigating the values of both hemoglobin and red blood cell distribution width (RDW) in a population of adult patients admitted to the ED with acute conditions.

## Materials and Methods

The study population consisted of adult patients admitted to the ED of the Academic Hospital of Parma during the year 2010, with the five most frequent acute pathologies (i.e., acute myocardial infarction, renal colics, pneumonia, acute pancreatitis and major trauma, which altogether represent over 60% of ED admissions). The ED of the Academic Hospital of Parma is a large urban ED, with nearly 90,000 accesses per year, which serves a hospital with 1250 beds and specialized wards including adult and pediatric intensive care units, cardiology as well

pacijenata bile su značajno niže nego kod kontrolnih subjekata, dok su vrednosti eritrocita bile značajno povišene kod pacijenata sa AMI, pankreatitisom i pneumonijom.

**Zaključak:** Utvrdili smo da postoji visoka prevalenca anemije i anizocitoze u populaciji pacijenata u hitnoj službi, čija identifikacija može biti presudna za odgovarajuće lečenje i potonji tretman.

**Ključne reči:** anemija, eritrociti, hemoglobin, hitna služba, urgentni centar

as coronary care, cardiac intensive care and cardiovascular surgery units. The Academic Hospital of Parma is classified as a level 2 Trauma Center, and the vast majority of major traumas from three Provinces (Parma, Piacenza and Reggio Emilia) are centralized in our hospital. All hospital records were extracted from the informatics database according to diagnostic criteria universally accepted for pathology (i.e., ICD-9 code and related diagnostic terms), whereas trauma cases included those with an Injury Severity Score (ISS) of 15 or higher. The final number of patients for each pathology (i.e., 25%) was selected by means of a program of randomization in order to maintain the highest possible degree of match and homogeneity of age and gender across the entire study population. The reference population (i.e., »controls«) consisted of healthy blood donors who were referred for regular blood donation to our hospital over the same study period. Routine hematological testing was performed on the entire study population by using identical laboratory instrumentation, i.e., Sysmex XE-2100 (Sysmex Inc, Mundelein IL, USA). The quality of test results was assured throughout the study period by means of internal quality control (IQC) and participation in an External Quality Assessment Scheme (EQAS). Data were finally presented as median and interquartile range (IQR) or proportion. The significance of differences between groups was assessed by the Kruskal-Wallis test (for continuous variables) and chi-squared test (for categorical variables). Statistical analysis was performed with Analyse-it for Microsoft Excel (Analyse-it Software Ltd, Leeds, UK).

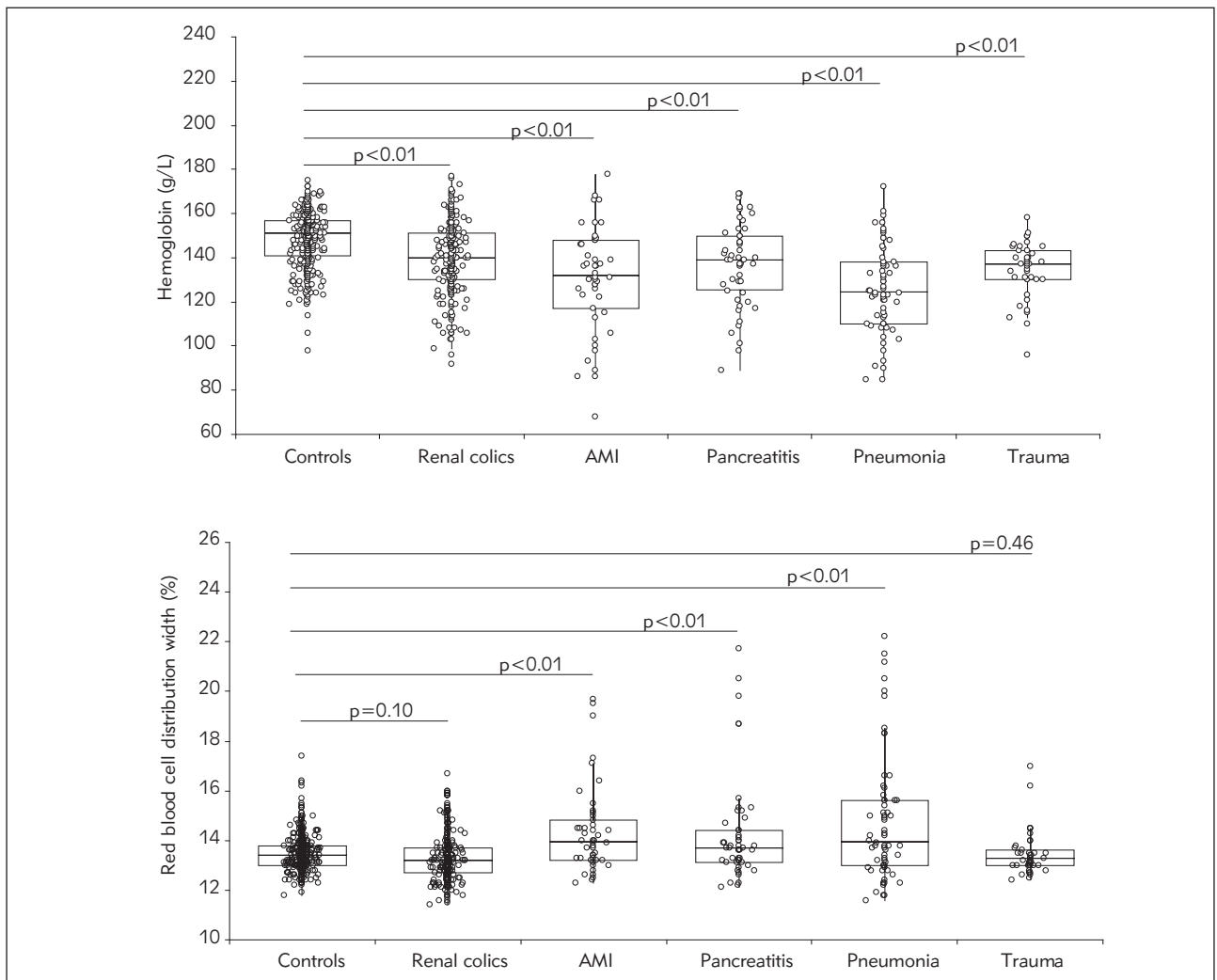
## Results

The final study population consisted of 462 patients admitted to the ED (i.e., cases; 262 renal colics, 62 pneumonia, 51 acute pancreatitis, 46 AMI and 41 major trauma) and 429 healthy blood donors (i.e., controls). No statistically significant difference was observed for gender and age distribution between healthy controls and cases, except for age between patients with pancreatitis and healthy controls (Table 1). The median hemoglobin value in all patients (137 g/L; IQR, 126–148 g/L) was significantly lower than in healthy controls (151 g/L; IQR, 141–157 g/L;  $p < 0.01$ ), whereas the median value of

**Table I** Main demographic and hematological data of the study population.

	Healthy controls	Renal colics	AMI	Pancreatitis	Pneumonia	Trauma
n	429	262	46	51	62	41
Age (years)	48 (32–64)	48 (30–66)	47 (38–56)	56‡ (42–70)	46 (31–61)	44 (26–62)
Gender (M/F)	241/188	134/128	29/17	24/27	33/29	16/25
Hemoglobin						
- Values (g/L)	151 (141–157)	140‡ (130–151)	132‡ (117–148)	139‡ (126–150)	124‡ (110–138)	137‡ (130–158)
- Anemia	8%	24%‡	41%‡	35%‡	60%‡	22%‡
RDW						
- Values (%)	13.4 (13.0–13.8)	13.2 (12.7–13.7)	14.0‡ (13.2–14.8)	13.7‡ (13.1–14.4)	14.0‡ (13.0–15.6)	13.3 (13.0–17.0)
- Anisocytosis	16%	17%	43%‡	31%‡	48%‡	15%

AMI, acute myocardial infarction; RDW, red blood cell distribution width. †  $p < 0.05$ ; ‡  $p < 0.01$  for differences versus healthy controls.



**Figure 1** Distribution of hemoglobin and red blood cell distribution width (RDW) in patients admitted to the emergency department with renal colics, acute myocardial infarction (AMI), acute pancreatitis, pneumonia and trauma, as compared with a population of healthy blood donors. The boxes designate the median values and the interquartile ranges (IQRs).

RDW was significantly higher in all patients (13.7%; IQR, 13.1–14.1%) than in controls (13.4%; IQR, 13.0–13.8%;  $p < 0.01$ ). The frequency of anemia established according to the WHO criteria (i.e.,  $< 120$  g/L in women and  $< 130$  g/L in men) (1), as well as of anisocytosis (i.e.,  $RDW > 14.0\%$ ) (7), was also remarkably higher in patient cases than in controls (anemia: 23 versus 4%,  $p < 0.01$ ; anisocytosis: 25 versus 16%;  $p = 0.03$ ). As regards specific pathologies, the hemoglobin values of patient cases were always significantly lower than those of the control population, while those of RDW were significantly increased in patients with AMI, pancreatitis and pneumonia (Table I and Figure 1). Similarly, the frequency of anemia was always greater in the five patient subgroups than in the control population, whereas the frequency of anisocytosis was higher in patients with AMI, pancreatitis and pneumonia, but not in those with renal colics and trauma (Table I).

## Discussion

Anemia is a major healthcare problem for the substantial clinical and economical implications that it carries (8). In acute coronary syndromes (ACS), including AMI, anemia is associated with a worse prognosis, in terms of cardiovascular death, recurrent MI, or recurrent ischemia (9). If maintained beyond the hospital phase, persistent or worsening anemia is associated with increased mortality or heart failure (10). Typically, anemia is associated with older age and comorbidities, such as diabetes, renal failure and malignancy, which may contribute to worsening the prognosis. In ACS, baseline hemoglobin was also shown to be an independent predictor of risk of bleeding, both for procedure-related and non-procedure-related hemorrhages (11). The presence of anemia should also raise special attention for antithrombotic therapy. Red blood cell transfusions should be given only if strictly indicated, since blood replacement therapy is associated with an increased mortality, at least in non ST-elevation (NSTEMI)-ACS patients. It has hence been suggested that transfusions should be avoided when the hematocrit value is  $\geq 25\%$  and anemia is globally well tolerated by the patient (12). Although anemia in trauma patients is commonplace and may reflect the bleeding associated with multiple injuries,

we provide here the first evidence of a major burden of anemia in patients with renal colics, pneumonia or acute pancreatitis, even if reliable pathophysiological explanations are lacking for these findings, at least during the early phases of the diseases. It is noteworthy, however, that since repeated blood collection is associated with changes in hemoglobin and hematocrit levels in patients admitted to an internal medicine service and can further contribute to worsening the degree of anemia (13), the results of this study provide a reliable basis to define the hematological status of patients upon ED admission, establish a timely treatment and avoid subsequent and preventable diagnostic phlebotomies.

According to our findings, it is surprising that, to the best of our knowledge, no reliable information is available on the prevalence of anemia and anisocytosis in patients admitted to the ED, considering that the identification of anemic subjects may be vital for establishing an appropriate therapy and for subsequent outpatient management. The results of this cross-sectional study clearly attest that anemia is commonplace in patients admitted to a large European urban ED with the more frequent morbidities, with an overall frequency of 23% and a greater prevalence in patients with pneumonia and AMI. This frequency is nearly 6-fold higher than that in a presumably healthy control population and nearly two-fold higher than that reported by Kristinsson et al. in an urban pediatric ED (14). Unfortunately, the lack of previous studies on this topic in adults makes any comparison virtually impossible, but provides a rational basis for planning further investigations on the same issue, especially in medium- and low-development countries where the frequency of anemia in the general population is higher. Another important finding of this study is the increased frequency of anisocytosis in patients with AMI, pancreatitis and pneumonia. Given the established role of RDW in predicting all-cause, non-cardiac and cardiac mortality (7), its assessment might be helpful in the ED, to gather useful diagnostic and prognostic information.

## Conflict of Interest Statement

The authors stated that there are no conflicts of interest regarding the publication of this article.

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*Received: January 8, 2013*

*Accepted: February 2, 2013*