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Red blood cell distribution width and haemoglobin are associated with hospital admission in patients with acute allergic reactions

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ABSTRACT

Introduction: Red blood cell distribution width (RDW) is significantly associated with a variety of human disorders. This study aimed to investigate whether RDW value at admission may predict the need of hospitalisation in patients presenting to the emergency department (ED) with acute allergic reactions.

Materials and Methods: The study population consisted of adult patients (aged > 17) admitted to the ED for acute allergic reactions.

Results: One hundred and thirty-two subjects were included, 12 of whom (9%) required hospital admission for severity of symptoms. Patients who needed hospital admission displayed significantly lower values of haemoglobin and significantly higher values of RDW-coefficient of variation (RDW-CV). In multivariate analysis, haemoglobin and RDW-CV were found to be independent predictors of hospital admission. The area under the curve (AUC), sensitivity and specificity for predicting hospital admission were 0.72, 0.88 and 0.42 for haemoglobin and 0.73, 0.88 and 0.50 for RDW-CV, respectively. The combination of these tests (both positive) was characterised by 0.76 AUC, 0.83 sensitivity, 0.67 specificity, 0.96 negative predictive value and 0.30 positive predictive.

Discussion: The results of this study suggest that two common and inexpensive parameters such as haemoglobin and RDW are independent predictors of hospital admission in patients presenting to the ED with acute allergic reactions.

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Allergy; anaphylaxis; emergency medicine; RDW; haemoglobin

Introduction

Anaphylaxis, angioedema and urticaria are common allergic disorders, globally affecting 15–25% of the general population.[1] Although most urticarial reactions are self-limited and do not require specialist referral or hospital visit, they may occasionally associate with angioedema, or else be important symptoms of an anaphylactic episode which requires immediate medical treatment.[1] It is hence intuitive that the emergency department (ED) is the most frequent health care setting where severe allergic reaction are managed. It has been estimated that more than 30,000 anaphylactic reactions are treated in ED every year in the US, accounting for up to 200 deaths.[2]

After urgent ED management, the rate of patients needing hospitalisation for acute allergic reactions remains high, usually between 5 and 15%.[3] A large Australian retrospective study concluded that the combined rate of hospital admissions and deaths exhibited an incremental trend of approximately 3% per year for patients with angioedema, 6% per year for those with urticaria and as high as 9% per year for patients presenting with anaphylaxis.[4] Similar information was published in another US statewide administrative database study, wherein the hospitalisation rate for anaphylaxis was found to be increased by more than 4-fold in a 16-year period.[5] Interestingly, another and more recent retrospective study also showed that allergies to medications were one of the leading correlates of frequent ED usage along with unemployment, public insurance, mental health conditions and tobacco use.[6] It is hence reasonable to hypothesise that the identification of some rapid and economic screening tests would be effective for a more effective triage of patients with acute allergic reactions in the ED, thus decreasing overcrowding and reducing health care costs.

The red blood cell distribution width (RDW) is a simple and inexpensive measure of anisocytosis, which is calculated by dividing the standard deviation of the mean erythrocyte cell size by the mean corpuscular volume (MCV) of red blood cells, and is now automatically generated along with the complete blood cell count (CBC) by virtually all haematological analysers.[7] Reliable

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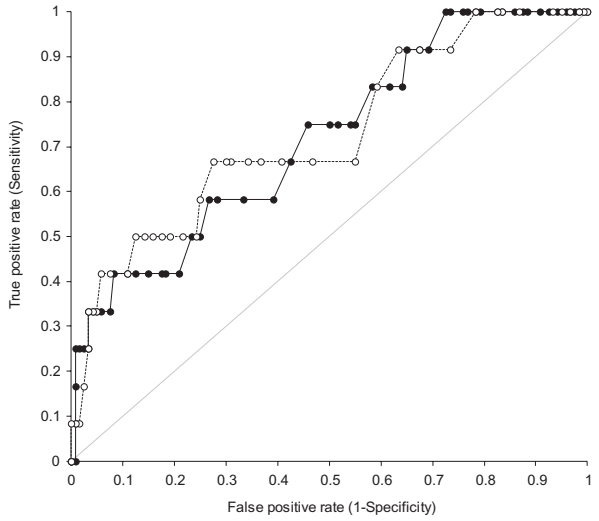

Figure 1. Receiver operating characteristics (ROC) curve analysis of haemoglobin (●) and red blood cell distribution width (RDW; ○) values for predicting hospital admission in patients admitted to the ED for severe allergic reactions.

evidence attests that an increased RDW value may be helpful for the diagnosis and prognostication of a number of acute and life-threatening diseases including acute myocardial infarction (AMI),[8] acute pancreatitis,[9] sepsis,[10] acute poisoning[11] and it also correlates with overall mortality in the general population.[12]

Therefore, the aim of this study was to investigate whether the measurement of RDW may help predict the need of hospitalisation in patients presenting to the ED with acute allergic reactions.

Patients and methods

The study population consisted of adult patients (i.e. aged 17 years or older) admitted to the ED of the University Hospital of Parma (Italy) for acute allergic reactions in the year 2013, who had their blood collected for complete blood cell count (CBC) assessment. The facility is a 1250-bed teaching general hospital, serving a population of approximately 435,000 inhabitants. Information about ED admission was identified from the electronic hospital database using a double extraction key, i.e. ICD-9 codes 999, 995, 716, 708, 477 and 287 (including all the 4th and 5th digits), as well as verbal 'strings', i.e. 'allergy', 'anaphylaxis', 'urticaria', 'angioedema', 'shock'. Patients admitted to the ED for allergic rhinitis, asthma and chronic urticaria were excluded, thus limiting the analysis to cases of acute urticaria, acute angioedema, urticaria–angioedema and anaphylaxis. The CBC was always performed upon patient admission and before treatment using the same haematological analyser (Sysmex XE-2100; Dasit SpA, Cornaredo, Italy).[13] In the local institution, hospitalisation of subjects with acute allergic reactions is established by the emergency physician in charge of the patient, according to clinical judgement.

Since the Kolmogorov–Smirnov normality test revealed non-normal distribution of the parameters, results were finally reported as median and interquartile range (IQR). The statistical analysis was based on Wilcoxon–Mann–Whitney test (for continues variables), Pearson's χ^2 statistics with Yates' correction (for categorical variables), univariate and multivariate regression analysis, receiver operating characteristics (ROC) curve analysis (Analyse-it Software Ltd, Leeds, UK) and calculation of the relative risk (RR) and 95% confidence interval (95% CI) (MedCalc Version 12.3.0, MedCalc Software, Mariakerke, Belgium). The statistical significance was set at $p < 0.05$ for a desired statistical power of 0.8. The study was carried out in accord with the Declaration of Helsinki, under the terms of relevant local legislation (see Figure 1).

Results

The final study population consisted of 132 patients presenting to the local ED for acute allergic reactions, 12 of whom (9%) required urgent hospital admission for severity of allergic symptoms, cardiorespiratory failure, or need of cardiorespiratory/resuscitative interventions. Patients requiring hospital admission were older, whereas no significant difference was found in sex distribution, frequency of anaphylaxis and MCV values (Table 1). Patients who needed hospital admission displayed significantly lower values of haemoglobin and significantly higher values of RDW-coefficient of variation (RDW-CV) (Table 1). In univariate analysis, hospital admission was found to be significantly associated with age ($r = 0.235$; $p = 0.01$), haemoglobin ($r = 0.287$; $p = 0.001$) and RDW-CV ($r = 0.325$; $p < 0.001$), where no significant association was observed with sex ($r = 0.089$; $p = 0.313$) and MCV ($r = 0.05$; $p = 0.577$). In the following multivariate analysis, in which hospital admission was entered as dependent variable

Table 1. Demographical and haematological data in patients admitted to the ED for severe allergic reactions.

	Hospital admission		
	No	Yes	*p*
n	120	12	
Age	41 (31–60)	72 (50–80)	0.003
Sex (Women/Men)	72/48	9/3	0.480
Anaphylaxis	23 (19%)	3 (25%)	0.917
Haemoglobin (g/L)	139 (132–152)	131 (110–138)	<0.001
MCV (fL)	87.6 (85.5–90.4)	87.6 (84.3–90.7)	0.289
RDW-CV (%)	13.3 (12.8–14.0)	14.5 (13.2–15.9)	<0.001

Notes. MCV, mean corpuscular volume; RDW-CV, red blood cell distribution width-coefficient of variation.

whereas age, haemoglobin and RDW-CV were entered as independent variables, haemoglobin (beta coefficient, –0.032; $p = 0.026$) and RDW-CV (beta coefficient, 0.052; $p = 0.019$) values were found to be independent predictors of hospital admission. The resulting areas under the curve (AUCs) for predicting hospital admission were 0.72 (95% CI, 0.56–0.87; $p = 0.003$) for haemoglobin and 0.73 (95% CI, 0.56–0.89; $p = 0.003$) for RDW-CV, respectively. A haemoglobin value < 120 g/L displayed 0.88 sensitivity, 0.42 specificity, 0.94 negative predictive value (NPV) and 0.25 positive predictive value (PPV) for predicting hospital admission, whereas a RDW-CV value > 14.7% displayed 0.88 sensitivity, 0.50 specificity, 0.95 NPV and 0.29 PPV for predicting hospital admission. Accordingly, the RRs for hospital admission of patients with values of haemoglobin < 120 g/L and RDW-CV > 14.7% were 5.7 (95% CI, 1.9–16.7; $p = 0.002$) and 3.5 (95% CI, 1.7–7.2; $p < 0.001$), respectively. Interestingly, the combination of haemoglobin and RDW-CV values (both test positive) displayed a greater diagnostic performance than either test alone, exhibiting 0.76 (95% CI, 0.61–0.91; $p < 0.0001$) AUC, 0.83 sensitivity, 0.67 specificity, 0.96 NPV and 0.30 PPV value for predicting hospital admission.

Discussion

Acute allergic reactions are important causes of ED admission, with a worldwide frequency exhibiting a constant increase over time.[3–6] The impact on ED organisation is hence substantial, since both triage and urgent medical treatment of patients with acute allergic reactions in overcrowded EDs may overwhelm the ability to provide care within a reasonable time, thus possibly leading to patient dissatisfaction and poorer quality of care.[14] Laboratory tests should now be regarded as an essential part of the clinical decision-making. Indeed, the availability of easy, rapid, inexpensive and reliable analyses to help identifying the clinical severity of acute conditions treated in the ED, thus including acute allergic reactions, would contribute to optimise the use of resources, reduce cost, but may also help to improve patient management and clinical outcomes.[15]

Although there is universal agreement that the rate of escalation or resolution of symptoms in patients with acute allergic reactions is virtually unpredictable,[16] recent evidence attests that some laboratory biomarkers may provide valuable information. A recent study demonstrated that the measurement of baseline serum tryptase may predict the worsening of an allergic reaction into severe anaphylaxis with 90% probability.[17] It was also recently found that the concentration of cardiospecific troponin I is increased in patients admitted to the ED with acute allergic reactions, and an increased concentration of this biomarker is significantly associated with severity and systemic involvement.[18]

The results of our study suggest that two common and very inexpensive parameters such as haemoglobin and RDW are independent predictors of hospital admission in patients presenting to the ED with acute allergic reactions. It is noteworthy that the combination of both parameters allowed to identify patients who could be discharged with 76% diagnostic accuracy and 0.96 NPV. The evidence that low haemoglobin values may predict the severity of an acute allergic reaction is not really unexpected. More than 60 years ago, West et al. reported that haemoglobin accumulates in lung and heart tissues during anaphylaxis,[19] which may hence explain the observed decrease of its blood concentration as well as the need of hospitalisation due to the more severe respiratory and cardiac involvement in patients with lower haemoglobin values. At variance with these findings, the worse clinical outcome of allergic patients with increased RDW values has not been earlier described to the best of our knowledge. Indeed, a higher degree of anisocytosis reflects a number of biological and metabolic derangements.[7] It is hence reasonable that patients presenting to the ED with acute allergic reactions and increased RDW values may be more vulnerable to deterioration of the clinical picture, ultimately leading to the need of hospitalisation. More specifically, anysocytosis has been associated with enhanced oxidative stress, inflammation, dyslipidaemia and poor nutritional status, all factors that alone or in combination may contribute to worsen the clinical outcome of patients with cardiovascular disorders.[20, 21]

Current evidence suggests that there are very few effective approaches for prevention of allergic diseases,[22] so that a timely diagnosis remains a mainstay for management of this condition. Indeed, this study has some limitations including the fact that additional studies are needed to confirm these findings in larger patient populations and that sample size of 12 brings risk of types 1 and 2 statistical error. Nevertheless, our preliminary results suggest that two common and very inexpensive parameters such as haemoglobin and RDW may help stratify the risk of hospital admission in patients presenting to the ED with acute allergic reactions.

This work represents an advance in biomedical science because it shows that combining haemoglobin and RDW may be a promising approach for screening acute allergic reaction in the ED.

Disclosure statement

No conflict of interest reported.

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