

Increased red cell distribution width levels in children with seasonal allergic conjunctivitis

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Received: 27 January 2017 / Accepted: 10 May 2017
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Abstract

Purpose Seasonal allergic conjunctivitis (SAC) is an inflammatory disease of the conjunctiva. Red cell distribution width (RDW) is a widely accepted inflammatory marker. We aimed to investigate whether RDW level is associated with the development of SAC in pediatric population.

Methods The present study consisted of 90 subjects (45 children with SAC and 45 age- and sex-matched healthy children). The demographic findings, complete blood count parameters including RDW and laboratory parameters, were evaluated.

Results The mean RDW levels were significantly higher in children with SAC compared to the control group (14.02 ± 0.82 vs. $13.26 \pm 0.64\%$, respectively, $p < 0.001$). In receiver operating characteristic analysis, the area under the curve for RDW for predicting SAC was 0.786, and a RDW value of 13.45 or higher predicted SAC with a sensitivity of 75.6% and specificity of 65%.

Conclusion Our study suggests that elevated RDW levels are significantly associated with SAC in pediatric population, which may imply a possible role of increased inflammatory status and oxidative stress in the pathogenesis of SAC.

Keywords Children · Inflammation · Red cell distribution width · Seasonal allergic conjunctivitis

Introduction

Allergic conjunctivitis (AC) is an inflammation of the conjunctiva secondary to an immune response caused by contact with an allergen at the bulbar or tarsal conjunctiva in a previously sensitized individual [1]. Seasonal allergic conjunctivitis (SAC) is the most frequent type of AC and clinically characterized by itching, redness, and tearing. SAC is associated with an accumulation of inflammatory cells in the conjunctiva [1], which imply a possible role of increased inflammatory response in the pathogenesis of SAC. On the other hand, higher levels of oxidative stress parameters are associated with the occurrence of SAC, which also suggests a possible role of oxidative stress in the pathogenesis of SAC [2].

Red cell distribution width (RDW) is widely accepted as a global prognostic marker in several cardiovascular and cerebrovascular diseases such as hypertension, heart failure, coronary artery diseases,

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and stroke [3, 4]. Elevated RDW level indicates the presence of elevated inflammatory status and high levels of oxidative stress [5, 6]. Oxidative stress directly damages erythrocytes and leads to shortened erythrocyte survival, resulting in elevated RDW [5]. Inflammatory response and oxidative stress play a pivotal role in various ophthalmic diseases as well [2, 7–9]. Both of them are telltale signs of AC. In a recent study, RDW has found to be an independent predictor of hospital admission in patients presenting to the emergency department with acute allergic reactions [10]. We have hypothesized that elevated RDW levels would be correlated with SAC. Hence, we aimed to investigate the association of RDW with SAC in pediatric population.

Materials and methods

Forty-five children with clinically diagnosed AC (SAC group) and 45 age and sex-matched healthy children (control group) were enrolled in this study. The patients were seen from May 2016 to July 2016 which is allergy season in our region, and all participants lived in the same region. AC was diagnosed based on past history, clinical symptoms such as ocular itching, redness, tearing, and slit-lamp examinations showing hyperemia, papillae of the palpebral conjunctiva, filamentous (mucous) discharge, or chemosis. Patients who had acute or chronic infection, inflammatory ocular, and systemic diseases (except allergic diseases as allergic rhinitis or asthma for study group) were excluded from the study. Patients who required any kind of medical or surgical treatment, and had vitamin B12 deficiency, iron deficiency, hematological disorders (hemolytic anemia, thalassemia), liver diseases, and malnutrition were also excluded.

Each patient underwent full ophthalmologic examination including best-corrected visual acuity, biomicroscopic anterior segment, and fundus examination. The complete blood cell parameters were determined at the time of the ophthalmic examination. The complete blood cell count parameters including RDW were studied by *ABX Pentra DF120/USA* biochemical analyzer. High-sensitivity C-reactive protein (hs-CRP), immunoglobulin E, and ferritin levels were measured by BN II System/Siemens/China.

This study was carried out with the Institutional Review Board/Ethics Committee approval. The research adhered to the tenets of the Declaration of Helsinki.

Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) for Windows (version 18.0, SPSS, Chicago, IL). Continuous variables are presented as mean $\pm$ standard deviation (SD) or percentages for normally distributed data or as median and interquartile range for non-normally distributed data. Comparison of continuous values between two groups was performed by means of independent samples *t* test. Categorical variables were compared by χ^2 test. The receiver operating characteristic (ROC) curve analysis was performed in order to determine the best cutoff value of RDW to predict SAC, and the sensitivity and specificity at that point were obtained. Two-tailed *p* value < 0.05 was considered statistically significant.

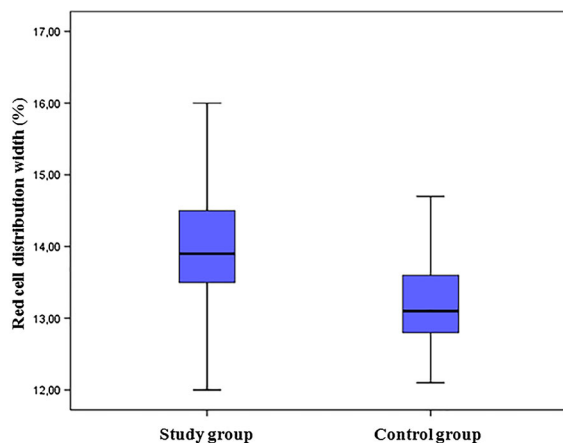
Results

In this study, patients ranged in age from 5.11 to 17.9 years. The baseline demographic and laboratory features of study subjects are shown in Table 1. The mean age was 11.22 ± 3.28 years for the SAC group and 12.26 ± 3.09 years for the control group. Thirty-one (68.9%) children were male in SAC group, and 29 (64.4%) were male in control group. There was no statistically significant difference between groups for age and gender ($p > 0.05$, both comparisons). The mean RDW levels were significantly higher in the SAC group compared to the control group (14.02 ± 0.82 vs. $13.26 \pm 0.64\%$, respectively, $p < 0.001$) (Fig. 1). The hs-CRP levels were also higher in the SAC group than control group ($3.38 [3.18–5.19]$ mg/L and $3.27 [3.17–3.45]$ mg/L, respectively, $p = 0.029$) in the control group. Median immunoglobulin E levels were 76.4 (25.6–366) IU/mL in the study group and 17.90 (17.90–21.05) IU/mL in the control group ($p = 0.008$). According to the ROC curve analysis, the optimal cutoff value of RDW to predict SAC was >13.45 , with 75.6% sensitivity and 65% specificity [area under the curve (AUC) 0.796, 95% CI 0.691–0.880] (Fig. 2).

Table 1 Comparison of demographic and laboratory parameters between groups

Parameters	SAC group <i>N</i> = 45	Control group <i>N</i> = 45	<i>p</i>
Age (years)	11.22 ± 3.28	12.26 ± 3.09	0.463
Gender (boy)	31 (68.9%)	29 (64.4%)	0.218
Red cell distribution width (%)	14.02 ± 0.82	13.26 ± 0.64	<0.001
Mean corpuscular volume (fL)	82.56 ± 4.57	84.05 ± 4.88	0.140
Hemoglobin (g/dL)	13.81 ± 1.08	13.96 ± 0.98	0.514
White blood cell count (10 ³ /μL)	7.82 ± 2.30	7.24 ± 1.87	0.193
Neutrophil count (10 ³ /μL)	3.95 ± 1.96	3.85 ± 1.35	0.777
Lymphocyte count (10 ³ /μL)	2.82 ± 0.95	2.63 ± 0.75	0.282
Neutrophil-to-lymphocyte ratio	1.60 ± 1.36	1.55 ± 0.65	0.798
Platelet count (10 ³ /μL)	306 ± 83	294 ± 73	0.463
Mean platelet volume (fL)	8.02 ± 0.81	8.12 ± 0.65	0.504
Ferritin (ng/mL)	30.7 ± 15.35	26.4 ± 13.47	0.358
High-sensitivity C-reactive protein (mg/L)	3.38 (3.18–5.19)	3.27 (3.17–3.45)	0.029
Total Immunoglobulin E (IU/mL)	76.4 (25.6–366)	17.90 (17.90–21.05)	0.008

SAC seasonal allergic conjunctivitis

**Fig. 1** Comparison of RDW levels between the two groups

The incidence of SAC symptoms and clinical findings of study subjects are shown in Table 2. All the patients in the SAC group had itchy eyes. The most common symptom was itching followed by redness. The presence of hyperemia, papillae in the upper tarsal conjunctiva, eyelid edema was the common signs. The papillary reaction was severe in 27.7% (5 of 18 of eyes) in the SAC group. Twenty-six patients had allergic rhinitis, and four patients had asthma in SAC group. Forty-three of patients were emmetropic, and two patients had amblyopia in both groups. Spherical values were between −1.75 and +0.75 D in SAC

group, −2.75 and +1.0 D in control group. All astigmatism values were recorded in plus cylinder; cylindrical values were between +0.50 and +2.00 D in both groups.

Discussion

To the best of our knowledge, this is the first study that demonstrates RDW values in children with SAC and compares RDW levels with healthy ones. First, we have found that RDW levels are significantly higher in the SAC group. Second, RDW cutoff value >13.45 predicts SAC with a sensitivity of 75.6% and a specificity of 65% in our study population.

Allergic diseases are among the most common disorders in children, and ocular allergy represents one of the most common ocular conditions encountered in clinical practice [11, 12]. The prevalence of allergic diseases in children aged 6–14 years varies significantly from 0.3 to 20.5% and is gradually increasing [12–14]. This increase may be due to genetics, air pollution in urban areas, pets, and early childhood exposure. AC is differentiated into a spectrum from the benign SAC, perineal AC, and giant papillary conjunctivitis to the chronic, morbid, and potentially sight-threatening vernal keratoconjunctivitis, atopic keratoconjunctivitis, and contact blepharoconjunctivitis. The

Fig. 2 Receiver operator characteristic curve analysis of RDW level for the development of seasonal allergic conjunctivitis

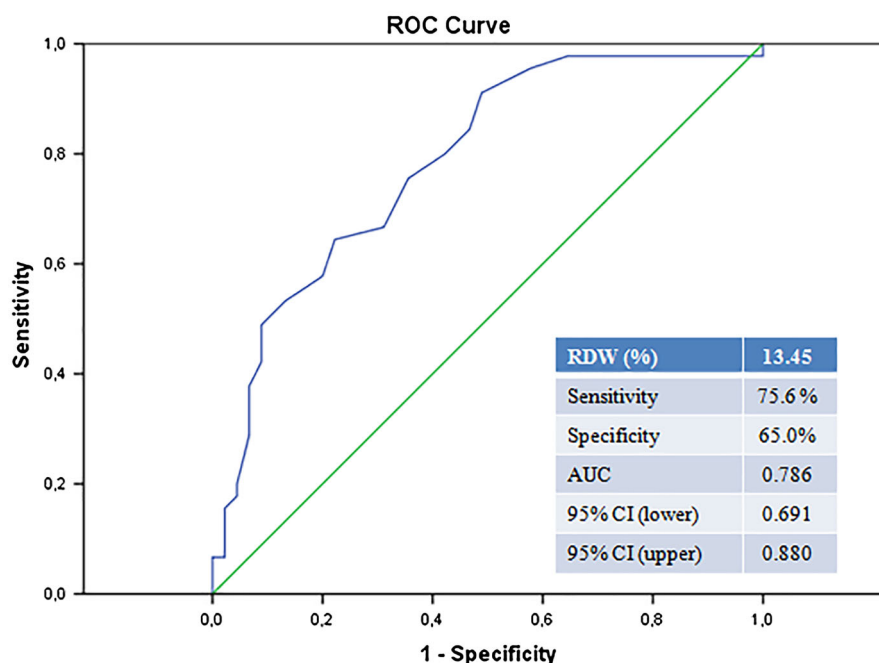


Table 2 Ophthalmic symptoms and signs of seasonal allergic conjunctivitis group

Variable	SAC group (n = 45)
Itching	45 (100%)
Redness	26 (57.8%)
Tearing	18 (40%)
Burning	8 (17.8%)
Pain	1 (2.2%)
Hyperemia	35 (77.7%)
Papillary reaction	18 (40%)
Eyelid edema	11 (24.4%)
Chemosis	3 (6.7%)
Lid eczema	2 (4.4%)
Filamentous discharge	1 (2.2%)

SAC seasonal allergic conjunctivitis

most common form of ocular allergy is SAC, accounting for 90% of cases. The most prevalent allergens in SAC are grass, tree, and weed pollen and outdoor molds [3, 12–14]. In this study only SAC patients were evaluated. The acute or subacute symptoms of SAC fluctuate with temporal exposure to the offending airborne environmental antigens, which are typically tree pollens in early spring, grasses in May through July [11].

Comorbidity of AC and rhinitis is well known. Allergic conjunctivitis, frequently associated with allergic rhinitis, is the most common form of ocular allergy known as allergic rhinoconjunctivitis. The percentage of undiagnosed AC in patients presenting with rhinitis may range from 25 to 60%. When considering patients with rhinitis, asthma, and other atopic condition, this incidence increases to 40–80% [8]. In our study rhinitis in 26 patients (57.8%) and asthma in four patients (9.3%) have accompanied SAC in study group.

The allergic stimulus, such as pollen in SAC, interacts first with the corneal and conjunctival epithelial cells [15]. The pathophysiology predominantly involves immunoglobulin E-related mast-cell activation, with release of histamine and other mediators contributing to the propagation of the response by calling in other immune cells and further inflammation [2]. Conjunctival epithelial and especially goblet cell responses to chronic inflammatory mediators including those produced in ocular allergy [15]. SAC is a type 1 hypersensitivity reaction induced by airborne allergens. The immediate hypersensitivity associated with this disease is characterized by allergen-mediated cross-linking of immunoglobulin E on mast cells, leading to degranulation and release of mediators, such as histamine, tryptase, interleukin-1

and IL-8, cytokines, epidermal growth factor, and platelet-activating factors. Activated T cells and inflammatory cytokines damage goblet cells and conjunctival epithelial cells [3]. These mediators stimulate nerve endings, dilate blood vessels, and recruit inflammatory cells to the reaction site, causing clinical symptoms such as itching, erythema, and palpebral and conjunctival edema. The late phase of this disease is associated with an accumulation of inflammatory cells in the conjunctiva [16–19]. SAC patients typically present bilaterally with itching, lacrimation, burning, vasodilation, and chemosis; however, it can be asymmetrical. Patients consider ocular itching the most disruptive symptom of AC and also complain of a concomitant foreign body sensation, blurring, and photophobia if there is corneal involvement. Rubbing the eyes augments the intensity and duration of itching, chemosis, and hyperemia [12]. In our study all the patients had itching in SAC group.

Previous studies have constantly demonstrated that RDW is independently associated with cardiovascular prognosis, and elevated RDW levels predict poor clinical outcomes [20]. Because of the potential role of inflammation and oxidative stress in the development of SAC, mediators reflecting both processes, such as RDW, might be involved SAC. Thus, in this study, we investigated whether RDW levels are associated with the development of SAC in child population. Consequently, we have demonstrated a positive correlation between RDW and SAC.

Neutrophil-to-lymphocyte ratio (NLR) could also be an important measure of systemic inflammation as RDW. NLR can be used as an indicator of inflammation in allergic rhinitis or asthmatic children [21, 22]. But in our study, there was no significant difference between groups in terms of NLR.

Our study had several limitations. First, it was a single-center, cross-sectional, and retrospective design. Second, we assessed a relatively small number of subjects. Third, we could not have the skin prick test data of all patients.

In conclusion, RDW levels are significantly associated with SAC in pediatric population. We suggest that increased RDW levels may be an indicator of an increased inflammatory activity in children with SAC. Further investigations and controlled studies carried out on larger groups are needed to investigate the possible role of RDW levels in children with AC.

Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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