Epidemiologic Impact of the New Guidelines for the Diagnosis of Acute Rheumatic Fever

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Objectives To estimate the incidence of acute rheumatic fever (ARF) in a metropolitan area of Northern Italy and study how the introduction of the 2015 revised Jones criteria affects the epidemiology in a region with moderate to high incidence of ARF.

Study design The incidence of ARF in children 5-14 years old living in the Province of Turin was estimated using low-risk criteria in a 10-year period (group A patients). The proportion of patients fulfilling only high-risk (HR) criteria (group B patients) was also calculated both prospectively (from July 2015 through December 2016) and retrospectively (from January 2007 through June 2015).

Results One hundred thirty-five group A patients were identified for an annual incidence of 3.2-9.6 out of 100 000 children. The use of HR criteria identified an additional 28 patients (group B), resulting in a 20.7% increase in the incidence of ARF. Age, sex annual incidence, and seasonal distribution pattern were comparable between group A and group B patients.

Conclusions HR criteria should be used for the diagnosis ARF in our region. The application of these criteria led to a 20% increase in patients with the diagnosis of ARF. The characteristics of patients fulfilling only HR criteria are similar to the remaining patients, suggesting that these criteria are sensitive and specific. (J Pediatr 2018;■■:■■-■■).

See editorials, p ■■ and p ■■

Acute rheumatic fever (ARF) is an autoimmune, multisystem complication of group A streptococcal infection. ARF remains a serious worldwide healthcare problem, despite its progressive decline in developed countries.1

The incidence of ARF in the 5-14 years age group varies greatly in different geographic areas, with the highest incidence in the Middle East, Asia, Eastern Europe, and Australia (10-350 out of 100 000 per year)2 and lowest incidence (0.5-3 out of 100 000 per year) in the US and Western Europe.3

The Jones criteria, used for the diagnosis of ARF since 1944, were modified in 1992,4 and recently in 2015 (Table 1).5 According to this revision, a single set of diagnostic criteria is no longer sufficient in all geographic regions. A distinction between moderate to high-risk (HR) and low-risk (LR) populations (incidence cut-off <2 out of 100 000 per year) has been set to avoid underdiagnoses of ARF in HR populations and overdiagnosis in LR populations. Specifically, the diagnostic criteria resemble previous versions in LR populations (except for subclinical carditis, which is now included as major criterion), whereas in HR populations polyarthritis or monoarthritis are included among the major criteria. Consequently, the knowledge of the incidence of ARF is a mandatory requirement for the application of the new diagnostic criteria in each country.

The precise incidence of ARF in Southern Europe is largely unknown. Breda et al reported an annual incidence of 2.3-5.6 out of 100 000 in a region of Central Italy, just above the threshold value.6 We performed an observational study to calculate the incidence of ARF in the last 10 years in a Province of Northern Italy and to outline the increase in the number of ARF cases using the new diagnostic criteria for HR populations.

Methods

To calculate the incidence of ARF, we included all patients with rheumatic fever, diagnosed according the classic (now LR) criteria, who were referred to the Regina
Margherita Children’s Hospital (Turin, Italy) in a 10-year period between 2007 and 2016 (group A patients). This is the only pediatric hospital in the Province of Turin, a territory in the Northwest of Italy, with 2 291 719 inhabitants in 2016 (203 869 between 5 and 14 years of age). In this province, there are another 10 pediatric wards in regional hospitals, but almost every patient with suspected or proven ARF is referred to our hospital for cardiology evaluation or rheumatologic follow-up (>95% of patients according to a targeted audit). Clinical, laboratory, microbiological, and demographic data of the study population were retrieved from medical records by 2 independent researchers. All patients underwent cardiological assessment with 2-dimensional Doppler echocardiography.

Patients who lived outside the Province of Turin or patients younger than 5 years or older than 14 years were excluded from the analysis.

Table I. 2015 revised Jones criteria

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<tr>
<th>Major criteria</th>
<th>Minor criteria</th>
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<tr>
<td>1. Carditis</td>
<td>1. Polyarthalgia</td>
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<tr>
<td>2. Arthritis</td>
<td>2. Fever (≥38.5°C)</td>
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<td>3. Chorea</td>
<td>3. ESR ≥ 60 mm/h and/or CRP ≥ 3.0 mg/dL</td>
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<tr>
<td>4. Polyarthalgia</td>
<td>4. Prolonged PR interval after accounting for age variability</td>
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<tr>
<td>5. Erythema marginatum</td>
<td>5. CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.</td>
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For all patient populations with evidence of preceding Group A streptococcal infection. Diagnosis of initial ARF: 2 major manifestations or 1 major plus 2 minor manifestations.

Overall, 135 group A patients satisfied the 2015 diagnostic criteria for LR regions (13.5 ± 3.7 patients/year) for an incidence of 3.2-9.6/100 000 in individual years, thus, persistently above the threshold of 2 out of 100 000/year (Figure 1). The mean age at diagnosis was 9.0 ± 2.1 years; 57.8% were male.

The diagnosis of ARF showed a typical seasonal distribution pattern. Patients without chorea were more frequently diagnosed in the spring (53.2% between March and May), and 41.9% of the 43 with chorea were diagnosed during the summer (June-August) (Figure 2).

Group B was composed of 28 patients. Two were diagnosed after July 2015, and 26 identified retrospectively. The use of HR criteria led to a 20.7% increase in the diagnosis of ARF in the entire study period (11.7% from July 2015). Demographic and clinical data of group A and B patients are shown in Table II.

Among group B patients, 53.6% had polyarthalgia, 21.4% monoarthralgia, and 25% both polyarthralgia and monoarthralgia. The concomitant Jones criteria used for the diagnosis of each group B patient is shown in Figure 3 (available at www.jpeds.com).

Group B patients had a sex distribution similar to group A patients (male 64.3% vs 57.8%, respectively; P = .67). The mean age did not differ significantly between group B and group A patients (8.3 ± 1.9 vs 9.0 ± 2.1 years, P = .09).

The proportion of group B patients varied over the years (19.9% ± 16.3%, mean ± SD). In general, there was concomitant higher incidence of group B patients in years with a higher incidence of group A patients.

The seasonal distribution of group B patients mirrored that of group A patients without chorea, with 60.7% of diagnoses occurring in the spring (Figure 2).
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