



RESEARCH ARTICLE

Cutaneous vasculitis in children: A nationwide epidemiological study in Spain [version 1; referees: 2 approved]

Leyre Riancho-Zarrabeitia ¹, Ana Santurtún²

¹ Department of Rheumatology, Sierrallana Hospital , Torrelavega, 39300, Spain

²Department of Physiology and Pharmacology, Legal Medicine Unit, University of Cantabria, Santander, 39011, Spain

v1 First published: 21 Aug 2017, 6:1527 (doi: [10.12688/f1000research.12372.1](https://doi.org/10.12688/f1000research.12372.1))
 Latest published: 21 Aug 2017, 6:1527 (doi: [10.12688/f1000research.12372.1](https://doi.org/10.12688/f1000research.12372.1))

Abstract

Background: Cutaneous vasculitis (CV) are a complex group of conditions in children, of which IgA vasculitis (IgAV) is the most common. The objectives of the current study are to describe the incidence of CV in Spain and to analyze the temporal trend in the last 11 years, as well as its seasonal distribution.

Methods: Hospital discharges of patients aged 0-18 years with a diagnosis consistent with CV in Spain from 2005 to 2015 were collected from the Spanish National Institute of Statistics (INE) databases.

Results: A total of 7304 patients from January 2005 to December 2015 were included; 6991 patients (95%) had a diagnosis of IgAV. The yearly incidence in the whole group was 7.7 per 100,000. Mean age at diagnoses was 6±3 years and 52% were male. The highest rate of admissions was found in the 5-9 year-old group, followed by those with 0-4 years of age (15.7 and 9.0 admissions per 100,000, respectively). Admissions due to CV followed an annual cyclic pattern, with the highest number of daily admissions during fall and winter months and the lowest number in summer months. There was an overall downwards trend of the number of hospital admissions during the period of study, in both males and females (p=0.01).



Conclusions: We have estimated an incidence of a 7.7 cases per 100,000 CV in children in Spain. CV-related hospitalization rates have a marked seasonal pattern, with a peak in fall and winter and a nadir in summer months. Children between 5 and 9 years of age are most frequently affected. There is a decreasing trend in CV-related hospitalization, the causes of which should be further assessed.

Keywords

Cutaneous vasculitis, IgA vasculitis, Children

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Referee Status:  

	Invited Referees	
	1	2
version 1 published 21 Aug 2017	 report	 report

- 1 **Javier del Pino-Montes**, Salamanca University Hospital, Spain
- 2 **Robert Micheletti**, University of Pennsylvania, USA

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Corresponding author: Leyre Riancho-Zarrabeitia (leriancho@gmail.com)

Author roles: **Riancho-Zarrabeitia L:** Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Project Administration, Software, Validation, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; **Santurtún A:** Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Software, Supervision, Validation, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

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How to cite this article: Riancho-Zarrabeitia L and Santurtún A. **Cutaneous vasculitis in children: A nationwide epidemiological study in Spain [version 1; referees: 2 approved]** *F1000Research* 2017, **6**:1527 (doi: [10.12688/f1000research.12372.1](https://doi.org/10.12688/f1000research.12372.1))

First published: 21 Aug 2017, **6**:1527 (doi: [10.12688/f1000research.12372.1](https://doi.org/10.12688/f1000research.12372.1))

Introduction

Cutaneous vasculitis (CV) are a complex group of conditions in children. The most common are IgA vasculitis (IgAV) (formerly known as Schonlein-Henoch purpura, (SHP)), which represents more than half of the cases, followed by cutaneous small-vessel vasculitis (formerly known as hypersensitivity vasculitis). Other disorders, such as urticarial vasculitis or ANCA associated vasculitis are poorly represented in children¹. The global incidence is not known², while incidence of IgAV in children range from 3–26.7 per 100,000³. Symptoms vary from a cutaneous-limited disorder to a systemic disease, and the etiology is not fully understood. However in many cases, particularly in IgAV, an external trigger is frequently suspected; IgAV in children has been frequently associated with a preceding upper respiratory infection, but no specific pathogen has been identified. It has also been linked to antibiotics and other medications³. The reported seasonal pattern, with a fall-winter incidence peak, is consistent with the hypothesis of an infectious trigger³.

The aims of our study are to describe the incidence of CV in Spain and to analyze the temporal trend of CV in the last 11 years, as well as its seasonal distribution.

Methods

Hospital discharges with a diagnosis consistent with CV (International Classification of Diseases ICD-9 codes hypersensitivity angiitis (446.2) and allergic purpura, including SHP (287.0)) in Spain from January 2005 to December 2015 were collected from the Spanish National Institute of Statistics (INE) databases.

We calculated the overall average incidence of admission per 100,000 inhabitants during the 11 years in children (from 0 to 18 years). Moreover, we calculated the annual rate of admission in children, and for the temporary trend calculations, a Kendall's tau correlation coefficient. Monthly admission rates were compared with Krustal-Wallis test. Statistical analysis were performed with R v2.3.

Results

A total of 7304 patients from 0 to 18 years of age were discharged from January 2005 to December 2015 with a diagnosis of CV. 6991 patients (95%) had a diagnosis of IgAV and 313 had hypersensitivity angiitis. The yearly incidence in the whole group was 7.7 per 100,000. Mean age at diagnosis was 6 ± 3 years and 52% were male, with a male to female ratio of 1.02:1. The highest rate of admissions was found in the 5–9 year-old group, followed by those aged 0–4 years (15.7 and 9.0 admissions per 100,000, respectively) (Figure 1).

Admissions due to CV followed an annual cyclic pattern (Figure 2), with the highest number of daily admissions during fall and winter months and the lowest number in summer months. This pattern was consistent over the 11 years of study, with a 3-fold increase in the number of daily admissions in October compared with August ($p < 0.001$; Figure 3).

The annual analysis showed a downwards trend of the number of hospital admissions during the 11-year period of study, in both men and women ($p = 0.01$; Figure 4).

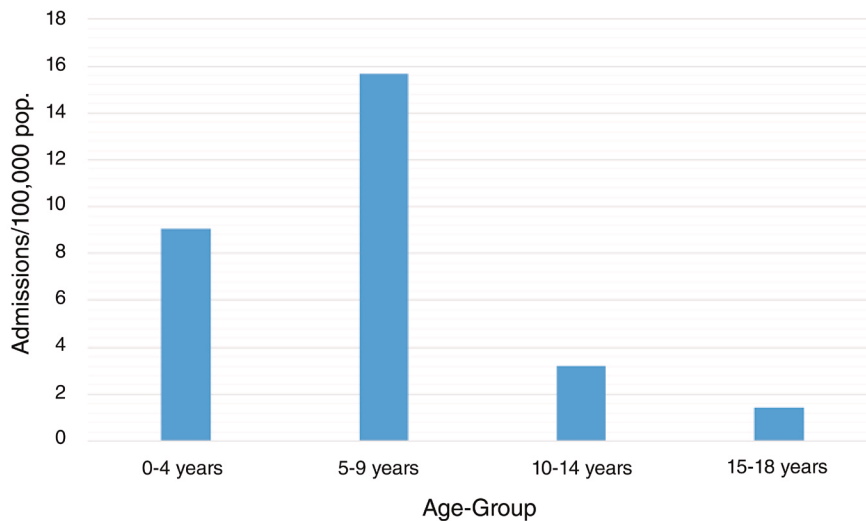


Figure 1. Incidence of cutaneous vasculitis across age groups between January 2005 and December 2015. The highest incidence occurred in children 5–9 years of age.

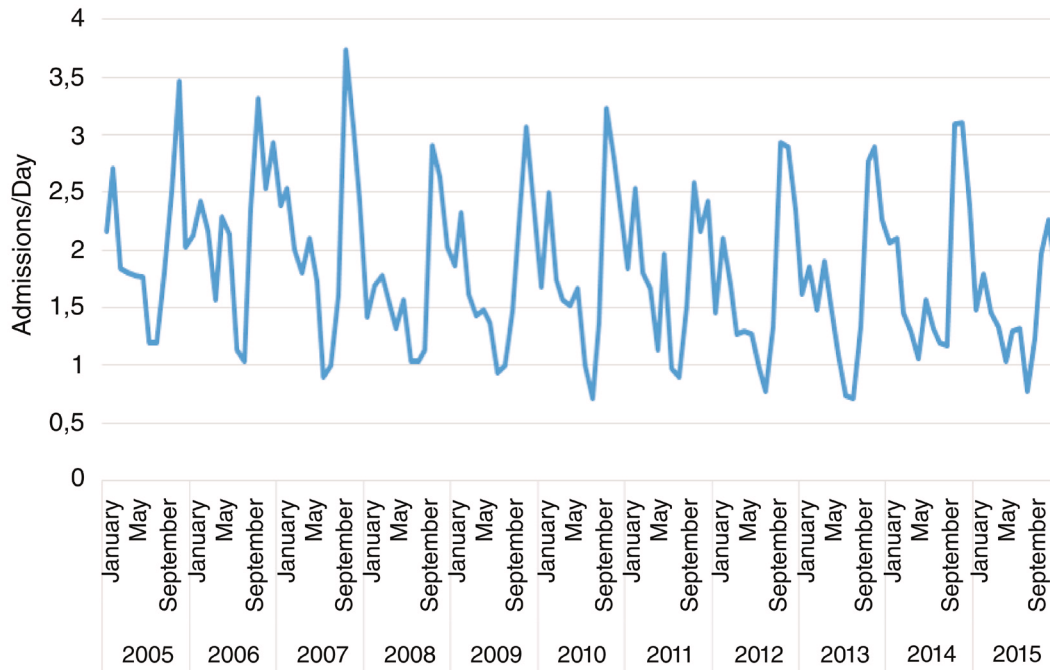


Figure 2. Monthly incidence of cutaneous vasculitis during the period of study (January 2005–December 2015). A cyclic pattern was revealed, with a peak during fall and winters months and a nadir in summer.

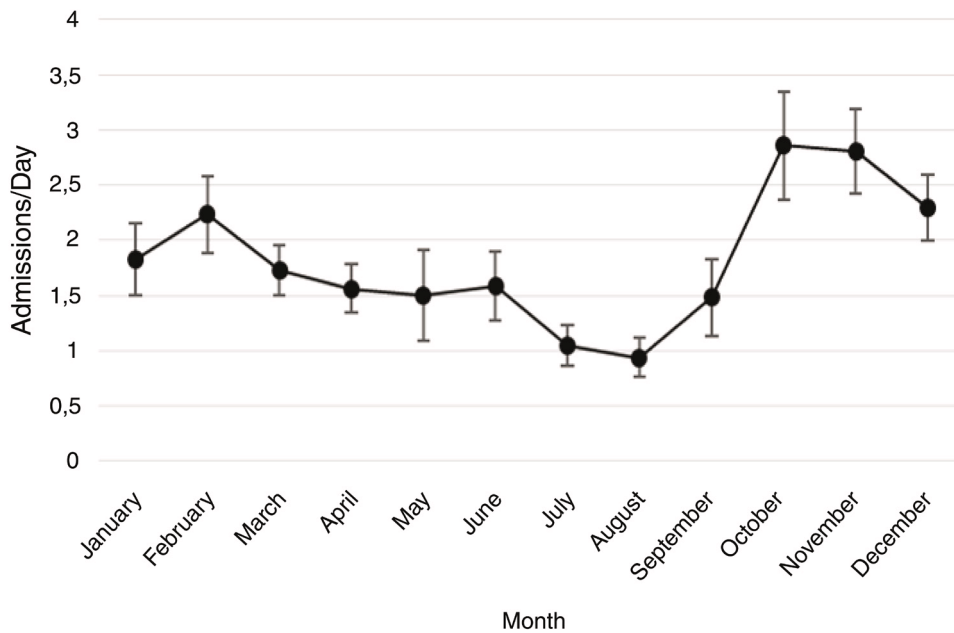


Figure 3. Average (mean and standard deviation) monthly incidence of cutaneous vasculitis during the period of study (January 2005–December 2015). The combined analysis confirms the seasonal pattern throughout the period of study.

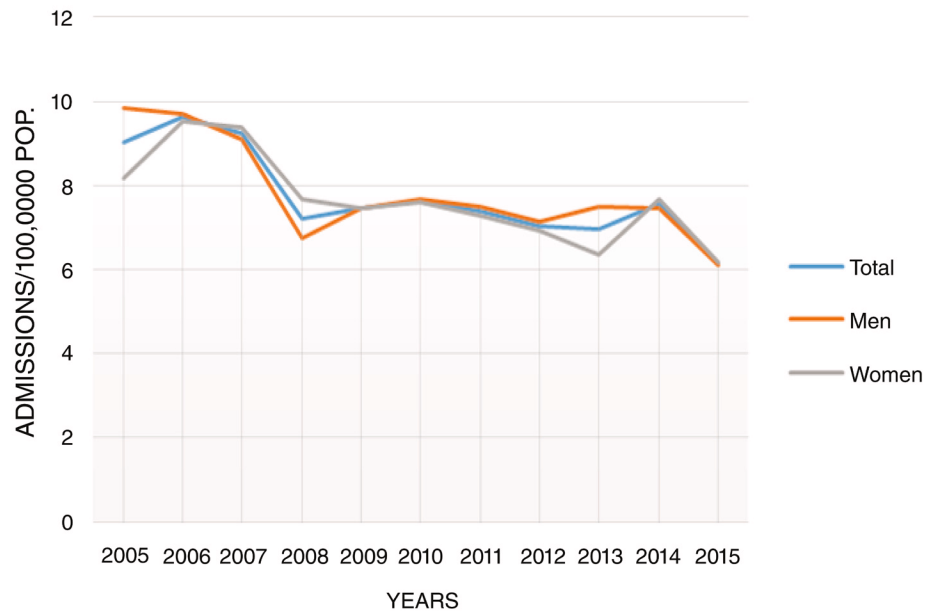


Figure 4. Average annual incidence of cutaneous vasculitis during the study period (January 2005–December 2015). A downwards trend in the overall incidence during the period of study was observed.

Discussion

This is the first population-based study of CV among children in Spain. We report the incidence rate of admissions of children with CV, defined as IgAV and hypersensitivity angitis, over 11 years.

We estimate a yearly incidence of 7.7 cases per 100,000. Data on incidences rate on CV are scarce, while previous series on IgAV have reported incidences that range from 6.1 in the Dutch population⁴ to 20.4 in the United Kingdom⁵. Most published series report incidences between 10 and 20 cases per 100,000, with some discrepancies probably due to the heterogeneity of the criteria used and also by the source of identification of cases (those based exclusively in hospital discharge data fail to identify children not referred to the hospital). The incidence we report in Spanish children keeps in line with previous literature, being in the lower part of the range. Our estimates are based on hospitalized cases, which might somewhat underestimate true incidence. However, we feel our estimated incidence should be close to the true incidence, as most cases are attended to at a hospital, at least in western countries. This idea is supported by a US study reporting that only 10% of children with IgAV were reported exclusively by primary care physicians⁶ and by a UK study showing that only 3% of IgAV cases were reported by general practitioners⁵.

IgAV mainly affects children between 3 and 12 years of age³, with a mean age of 5–6 years in most paediatric series^{6–8}. A slightly

male predominance has been reported, with a male to female ratio of up to 1.8:1^{5–7}, while others reported that cases were equally distributed⁸, or even a subtle female predominance⁹. In our case, we found a mean age of 6 years with no differences in sex distribution.

We found a remarkable seasonal variation in the frequency of CV. This is in line with other studies showing that IgAV has a seasonal distribution, with a peak during fall and winter and a nadir during summer months^{3,10}. This keeps in line with a commonly reported upper respiratory infection preceding the onset of the purpura, and a possible infectious trigger for the disease. Moreover, this increase during fall-winter time could also be related with atmospheric circulation patterns, as recently suggested for Kawasaki disease¹¹.

Our annual analysis showed a downwards trend of the number of hospital admissions during the period of study. A similar trend has been reported previously. Okubo *et al.*⁶ found a significant decreasing trend, with a total annual hospitalization rate of 2.45 per 100,000 children in 2003, falling to 1.89 per 100,000 children in 2012. This decrease could indicate a tendency to treat patients with IgAV in outpatient clinics, but also could reflect a real decrease in the incidence of the disease.

In summary, we have estimated an incidence of a 7.7 cases per 100,000 CV in children in Spain. CV-related hospitalization rates have a marked seasonal pattern, with a peak in fall and winter and a

nadir in summer months. Children between 5 to 9 years of age are most frequently affected. There is a decreasing trend in CV-related hospitalization, the cause of which should be further assessed.

Data availability

Data were downloaded freely from the Spanish National Institute of Statistics (INE) databases: <http://www.ine.es/prodyscr/microdatos.htm>.

Competing interests

No competing interests were disclosed.

Grant information

The author(s) declared that no grants were involved in supporting this work.

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Current Referee Status:  

Version 1

Referee Report 20 July 2018

doi:10.5256/f1000research.13398.r35432



Robert Micheletti

Department of Dermatology and Department of Medicine, University of Pennsylvania, Philadelphia, PA, USA

The manuscript is an interesting epidemiologic study of the incidence of cutaneous vasculitis in children. In particular, the observation of seasonality of the condition, as well as the estimation of the overall incidence and the declining incidence over time, are informative.

I do have some questions / criticisms that could perhaps be addressed in the discussion / limitations to make this a stronger paper:

- One limitation is the diagnosis codes used (hypersensitivity angitis and Henoch-Schonlein purpura). Are these the only codes? The best codes? It seems worth mentioning the limitations of identifying cases in this manner, since not all cases of interest may be identified. If you are not accurately including other types of cutaneous vasculitis with the "hypersensitivity angitis" code, perhaps this is just a study of IgA vasculitis alone and should be described in that manner?
- The authors argue that their estimate of hospitalized patients is representative of the true incidence of disease based on studies that primary care and general practitioners only handle a subsegment of cases. The inference is that most patients, therefore, end up at the hospital. I don't find this argument particularly persuasive? What about outpatient dermatology? Rheumatology? It is rare for me to manage IgA vasculitis in the hospital, whereas I have many outpatients with the disease. This limitation should be acknowledged (as the authors do), but probably I would eliminate the arguments related to most patients being hospitalized, etc.
- Additionally, the authors may wish to comment on the changing definition / criteria for IgA vasculitis. Since the Chapel Hill Consensus Conference nomenclature were revised in 2012 (in the middle of the years analyzed in this study), it is worth considering whether case definition affected frequency of diagnosis. Historically, children with palpable purpura were just called Henoch-Schonlein purpura without much effort to determine the presence of IgA, etc. It's possible in recent years some of these patients were classified as having other diagnoses.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

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Are the conclusions drawn adequately supported by the results?

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Competing Interests: No competing interests were disclosed.

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Referee Report 19 September 2017

doi:[10.5256/f1000research.13398.r25207](https://doi.org/10.5256/f1000research.13398.r25207)



Javier del Pino-Montes

Rheumatology Department, IBSAL, Salamanca University Hospital, Salamanca, Spain

This is an interesting study about the epidemiological data of cutaneous vasculitis in children in Spain. There is little information on this topic. It is common to find data from hospitals or registries but the value of this paper is that the data comes from all over Spain. It would be interesting to know if there are geographical differences,

Minor revision:

In the results section and Figure 4, children are analyzed by gender as men and women. Being a pediatric population, it is more consistent to use males and females

I recommend to accept the paper after minor revisions

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Are sufficient details of methods and analysis provided to allow replication by others?

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If applicable, is the statistical analysis and its interpretation appropriate?

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Are the conclusions drawn adequately supported by the results?

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Competing Interests: No competing interests were disclosed.

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