

IBERIAN STUDY OF AEROALLERGENS SENSITISATION IN ALLERGIC RHINITIS

C. Pereira (1), A. Valero (2), C. Loureiro (3), I. Dávila (4),
C. Martinez-Cócerca (5), C. Murio (6), P. Rico (7), R. Palomino (8)

SUMMARY

■ **Background:** Allergic rhinitis (AR) is a prevalent allergic disease in Iberian countries, but there are no recent epidemiological studies that characterize this pathology according to clinical classification and aeroallergens sensitisation. This is a clinical study, representative of each country

■ **Methods:** Descriptive, observational cross-sectional, population-based study carried-out in Portugal and Spain. 3397 consecutive patients (5 regions in Spain and 3 regions in Portugal) were selected for clinical observation and skin prick tests were carried out using the same panel of standardized aeroallergens.

■ **Results:** 3225 patients (aged 10-50 years old) completed the study (IC 95%, SE 15). Intermittent rhinitis makes up 36% of the entire sample. Of them, intermittent AR mild forms represented 82% in Spain and 92% in Portugal that is, 87% for Iberian countries. Persistent types of rhinitis showed exactly the same rate of severity in Portugal and Spain, 44% mild and 56% moderate/severe. Seasonal forms represent 37% while 63% were perennial. BA was present in 49% of AR patients. There were significant differences between aeroallergens according to the different regions considered. Mites and grass pollens are the most relevant aeroallergens in Spanish and Portuguese AR patients, while *Alternaria* showed higher positive rates among 10-20 year old patients.

■ **Conclusions:** This study characterizes the AR patients in Iberian countries according to the ARIA classification. No correlation was observed between this classification and the conventional (seasonal/perennial). Our results also characterize the allergic cutaneous pattern of aeroallergen sensitisation using the same panel of standardized allergens and show differences between the different regions analysed.

Key-words: Aeroallergens sensitisation - Allergic rhinitis - Skin Prick Test, Epidemiology - Portugal, Spain.

INTRODUCTION

Allergic rhinitis (AR) is one of the most prevalent allergic diseases in western countries, and several studies point towards an increase of this pathology (1-4). Recent studies show that rhinitis prevalence in the adult population of Portugal and Spain is relevant, 26.1% and 23% respectively (4, 5). In spite of the fact that it is frequently undervalued by patients or undiagnosed by non-specialists doctors there is an obvious health impact on quality of life with social and economic costs (6).

The conventional classification of AR as seasonal allergic rhinitis (SAR) and perennial allergic rhinitis (PAR) was insufficient to characterize patients, as extensively described in literature. For instan-

ce, there are regions with large and persistent pollen counts in central inland regions in Portugal and Spain, where patients have symptoms almost all year round. The current ARIA classification possibly may solve this problem and includes measurement of the frequency and duration of symptoms and severity scores from mild to moderate/severe¹. Recent studies have been published not only to compare and validate the ARIA document, but also to study the reality of AR in different countries (7).

The aeroallergen sensitisation prevalence in the general population is related to different factors. In each region, the sensitisation reflects the exposure to allergens and the influence of other environmental factors such as pollution (7-11).

The association to bronchial asthma (BA) is a common feature in AR patients, and has been extensively discussed (1). The non-diagnosis, the under treatment or inadequate control of symptoms in allergic patients could be the major points accounting for this association.

1. President of Iberian Chapter of SLAAI.

2. Spain Study Coordinator.

3. Portugal Study Coordinator.

4. Iberian Chapter of SLAAI Committee.

5. Vice-President SLAAI and Iberian Chapter Committee.

6. Medical Adviser Consultant (Almirall Prodesfarma).

7. Medical Department (ALK-Abelló, S.A.).

8. Gestió Organització Comunicació S.A, Barcelona (Spain).

The present study has several aims. The first one is to characterize AR patients in the two countries of the Iberian Peninsula (Portugal and Spain) that had been diagnosed by specialists in Allergology. Our purpose was that this study were representative of this European region that shares common aspects concerning genetic, social, geographic, and climate conditions, besides the natural life-style proximity. It is known that in AR the aeroallergen sensitisation with a same panel of allergen extracts is useful to clarify new strategies of diagnosis and adequate the management plan of treatment. This study could define what kind of AR patients are present in our countries, according to ARIA and conventional classification. Another objective of the study was to describe the characteristics of different types of AR related to sensitisation patterns, demography, severity of symptoms, disease self-awareness, and also the concomitant presence of BA. Defining specific regions related to socio-demographic and geographical conditions, in both countries, was considered very important for allergic epidemiological purposes.

The Iberian study was promoted by the Iberian Chapter of SLAAI that joins the two scientific Allergy and Clinical Immunology Societies (SPAIC and SEAIC). Despite the logistic and financial support from the sponsors of the study (Allmiral Prodesfarma and ALK-ABELLÓ, S.A.) the scientific committee has had full freedom to conduct the project.

METHODOLOGY

The study was descriptive, observational, cross-sectional, population-based and conducted in Portugal and Spain.

The aim of this epidemiological study was to evaluate the prevalence of allergic skin sensitisation to 20 aeroallergens in allergic rhinitis patients diagnosed by Allergists in the two involved countries. We also intended to characterize the AR of the selected population according to the ARIA classification (clinical and severity) and according to the old practice that divided the AR in seasonal and perennial.

Another objective of this study was to evaluate the prevalence and severity of bronchial asthma, according to GINA classification, in this AR population.

■ **Patients:** AR patients, both genders, between 10 and 50 years-old. Patients had to be living in Portugal or Spain for at least 2 years; if not, their previous residing location should be registered. All patients had been diagnosed of AR by Allergists Specialists according to clinical criteria and they had to have a previous positive skin prick test (SPT) to at least one aeroallergen.

■ **Sample Size.** Clinical Epidemiologists from both countries defined the sample size in order to be representative. Eight geographical areas or regions were proposed, 5 regions in Spain and 3 in Portugal. The regions were defined according to geographical and environmental aspects. The sample size for each region was calculated considering: the estimated prevalence of the aeroallergen with lowest frequency expected (1%); the significance rate (95%); the acceptable standard error (1%); the referred population; the lost studied patients percentage (13). No correcting factor was included for any geographical region because all of them had more than the population required.

The following formula was used to establish the sample size for each region:

$$n = t^2 \times p(1-p) / d^2. n = 1.96^2 \times 0.01(1-0.01) / .01^2. n = 380,318 (381).$$

n = required sample value

t = significance rate (SD of 1.96)

p = prevalence to estimate

d = standard error of 1%

Considering 10% of lost studied patients, the final sample value for each region was 423 AR patients. In Spain it represented 2,115 patients (5 regions) and Portugal 1,269 patients (3 regions), and the total sample was 3,384 AR patients.

■ **Study Design.** The study was conducted from the end of October 2004 to the beginning of March 2005. Each Centre included AR patients consecutively (after clinical or controlled consultation). All the procedures were done in only one visit, except for patients who were taking medication that interfered with the SPT. In those patients a wash out time of 1 week was permitted.

■ **Researchers** provided the patients' informed consent which was voluntarily signed by all the participants. Approval was obtained from Ethics and Scientific Committees of corresponding national authorities, and by each Centre if applied.

Forty-eight centres were involved in Spain belonging to the 5 regions (North, Centre, Mediterranean, South, and Canary Islands); and 18 Centres were involved in Portugal in the 3 Regions (North, Centre, and South including Madeira Island). Balears and Azores Islands were not included due to logistical difficulties.

■ **Questionnaire.** The patients were submitted to a questionnaire including the following aspects:

- Social-demographic data (age, sex, nationality, location of birth, years of stable residence, previous place of residence).
- AR diagnosis (onset of the disease; ARIA classification; seasonal or perennial clinical symptoms).
- BA diagnosis (concomitant presence; GINA classification).

■ **Skin Prick Tests (SPTs).** 20 different standardized aeroallergens were selected for this study. The diagnostic tests were carried out with commercial extracts supplied by ALK-ABELLÓ, S.A (Madrid, Spain). The extracts used by the participants' centres were from the same batches. The selected panel of extracts represents the most relevant aeroallergens in this pathology from previous reports in Portugal and Spain. The allergens used were: Mites (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Lepidoglyphus destructor*, *Acarus siro*, *Glyciphagus domesticus*, *Tyrophagus putrescentiae* and *Blomia tropicalis*); Animal dander (cat and dog), Moulds (*Alternaria alternata*); Grasses (Mixture and *Cynodon dactylon*); Weeds (*Parietaria judaica*, *Artemisia vulgaris*, *Plantago lanceolata*, and *Salsola kali*); Trees (*Olea europaea*, *Platanus acerifolia*, *Betula pubescens*, and *Cupressus arizonica*), and controls (histamine and saline).

SPTs were performed according to international guidelines (12). The medium diameter of the wheal was measured and registered. A wheal > 3 mm above the negative control was considered positive.

■ **Data Analysis.** All the results were introduced on to the same database. In Spain, the researchers introduced the results directly on to a web site. In Portugal the results were registered on paper CRD and introduced later by the central data centre.

The statistical analysis was performed by an SPSS program. A descriptive analysis was made.

RESULTS

From a total estimated sample of 3,384 patients (Spain=2,115; Portugal=1,269), 3,397 patients were included (Spain=2,124; Portugal=1,273) and 3,225 patients (Spain=2,020; Portugal=1,205) were correctly studied. This represents 95.3% of the initial sample. All the regions had significant samples, except the Canary Islands in Spain.

According to sex, AR was more frequent in females than in males (53% vs. 47%). The mean age of the sample was 26.93 years (10-50 years). Considering age groups the following results were obtained: 10 to 20 years = 31%; 21 to 30 years = 34%; 31 to 40 years = 23%; 41 to 50 years = 12%. 98% of the sample had Portuguese or Spanish nationality.

Stable living area was present in 98% of the patients with AR in Portugal and Spain. Cutaneous tests were carried out during the first observation in 95% of total patients; in the remaining, a wash-out period of one week was needed.

The majority of the patients studied had AR with long lasting symptoms (<1 year=5%; 1-2 years= 17%; 2-5 years= 31%; 5-10 years= 31%; >10 years= 17%).

Intermittent rhinitis makes up 36% of the sample. The results according to ARIA severity of the disease are shown in Table 1. Mild forms represented the 82% of intermittent rhinitis 82% in Spain and 92% in Portugal, which renders 87% for Iberian countries. North and South regions in Spain showed the highest rates of moderate/severe intermittent rhinitis (25%) like the Southern area of Portugal.

Persistent type of rhinitis showed exactly the same rate of severity in Portugal and Spain, mild 44% and moderate/severe 56%. In Spain, The Canary Islands showed the highest value of moderate/severe rhinitis, 82%, followed by Mediterranean (58%), South (55%), North (55%) and Centre (45%). Portugal presented

Region	Mild Intermittent		Moderate/Severe Intermittent		Mild Persistent		Moderate/Severe Persistent		Unknown		
Spain	N	%	N	%	N	%	N	%	N	%	%
Canary Islands	32	18	2	1	27	15	119	66	0	0	0
Center	160	29	17	3	204	37	166	30	6	1	1
Mediterranean	118	26	20	4	130	29	180	40	3	1	1
North	89	23	29	8	113	30	137	36	12	3	3
South	110	24	36	8	139	30	171	38	0	0	0
Portugal	N	%	N	%	N	%	N	%	N	%	%
Center	235	57	7	2	68	17	90	22	10	2	2
North	179	45	4	1	94	24	101	25	19	5	5
South	86	22	31	8	114	29	163	41	4	1	1
Total	1.009	31	146	5	889	28	1.127	35	54	2	2

Table 1: Allergic Rhinitis results according to ARIA classification in different regions in Portugal and Spain.

similar values in the three regions: South (59%), Centre (57%) and North (52%).

AR was also grouped according to the classic designation: 37% were SAR while 63 were PAR.

There was not agreement between the two AR classifications (intermittent/persistent and SAR/PAR). Only 43% of SAR had intermittent rhinitis (mild=38%, moderate/severe=5%), and 57% were classified into persistent (mild=25%, moderate/severe=31%). In PAR patients 32% had intermittent rhinitis (mild=28%, moderate/severe=4%), and 66% were classified into persistent (mild=29%, moderate/severe=37%).

BA was concomitantly observed in 49% of AR patients of Iberian countries with long lasting symptoms (<1 year=10%; 1-2 years= 23%; 2-5 years= 26%; 5-10 years= 25%; >10 years= 16%) as occurred in the allergic patients without asthma. According to GINA criteria they were classified into: 56% intermittent; 33% mild persistent; 10% moderate persistent; and only

1% severe persistent. BA was present in 16% of the patients with AR long lasting to 2 years symptoms, 28% in those with 2-5 years of disease, 35% in those with 5-10 years, and 21% in those patients with AR lasting more than 10 years.

Table 2 presents the SPTs results of the patients studied for each aeroallergen according to global sample and for each region and each country. *Dermatophagoides* species were the most frequent allergens in the global sample, followed by grass pollens. Mites were more related to AR in Portugal than in Spain, unlike pollen sensitizing. *Olea*, *Plantago*, *Salsola*, *Platanus* and *Cupressus* were more often positive in Spain. Parietaria allergy was higher in Portugal, as well as *Alternaria* sensitisation. There were obvious differences between the different regions considered.

There were no significant differences among sex, but there were relevant results in the age groups considered, Table 3. We stress the highest sensitizing rate

			Skin Prick Tests																				
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	
Spain	Canary Islands	N	155	154	69	70	58	78	94	65	66	8	32	16	16	33	15	14	8	8	4	5	
		%	86	86	38	39	32	43	52	36	37	4	18	9	18	8	8	4	4	2	3		
	Center	N	121	114	86	50	56	81	59	182	180	68	455	342	105	162	265	175	326	193	85	248	
		%	22	21	16	9	10	15	11	33	33	12	82	62	19	29	48	32	59	35	15	45	
	Mediterranean	N	263	256	106	90	75	115	103	125	112	56	160	108	103	56	80	79	164	98	20	64	
		%	58	57	24	20	17	25	23	28	25	12	35	24	23	12	18	18	36	22	4	14	
	North	N	295	295	189	174	162	192	173	118	124	26	196	116	34	58	84	42	95	66	37	58	
		%	78	78	50	46	43	51	46	31	33	7	52	31	9	15	22	11	25	17	10	15	
	South	N	236	227	142	96	131	140	115	140	134	56	268	209	67	116	175	132	286	128	62	74	
		%	52	50	31	21	29	31	25	31	29	12	59	46	15	25	38	29	63	28	14	16	
Subtotal Spain	N	1.070	1.046	592	480	482	608	544	630	616	214	1.111	791	325	425	619	442	879	493	208	449		
	%	53	52	29	24	24	30	27	31	30	11	55	39	16	21	31	22	44	24	10	22		
Portugal	Center	N	315	310	280	249	220	241	214	141	130	95	211	160	137	121	103	68	110	84	79	59	
		%	77	76	68	61	54	59	52	34	32	23	51	39	33	30	25	17	27	20	19	14	
	North	N	339	316	285	220	229	243	201	129	90	46	212	108	79	74	107	49	53	50	45	21	
		%	85	80	72	55	58	61	51	32	23	12	53	27	20	19	27	12	13	13	11	5	
	South	N	309	279	213	178	192	211	195	126	99	44	165	90	78	70	77	44	80	48	26	37	
		%	78	70	54	45	48	53	49	32	25	11	41	23	20	18	19	11	20	12	7	9	
Subtotal Portugal	N	963	905	778	647	641	695	610	396	319	185	588	358	294	265	287	161	243	182	150	117		
	%	80	75	65	54	53	58	51	33	26	15	49	30	24	22	24	13	20	15	12	10		
Total			N	2.033	1.951	1.370	1.127	1.123	1.301	1.154	1.026	935	399	1.699	1.149	619	690	906	603	1.122	675	358	566
			%	63	60	42	35	35	40	36	32	29	12	53	36	19	21	28	19	35	21	11	18

1 Dermatophagoides pteronissinus

2 Dermatophagoides farinae

3 Lepidoglyphus destructor

4 Acarus siro

5 Glyciphagus domesticus

6 Tyrophagus putrescentiae

7 Blomia tropicalis

8 Felis domesticus

9 Canis familiaris

10 Alternaria alternata

11 Gramineas Mix

12 Cynodon dactylon

13 Parietaria judaica

14 Artemisia vulgaris

15 Plantago lanceolata

16 Salsola kali

17 Olea europea

18 Platanus acerifolia

19 Betula pubescens

20 Cupressus arizonica

Table 2: Sin Prick Tests results to the different aeroallergens studied in Portugal and Spain.

			Skin Prick Test																			
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Total Spain and Portugal	10 - 20y	N	730	687	507	422	423	468	408	323	271	172	511	339	150	173	261	146	286	159	99	120
		%	36	35	37	37	38	36	35	31	29	43	30	30	24	25	29	24	26	24	28	21
	21 - 30y	N	699	689	474	383	373	454	405	369	331	120	564	383	212	239	309	223	396	243	119	194
		%	34	35	35	34	33	35	35	36	35	30	33	33	34	35	34	37	35	36	33	34
	31 - 40y	N	435	411	283	223	232	259	225	238	216	76	418	275	158	177	207	147	279	166	84	150
		%	21	21	21	20	21	20	20	23	23	19	25	24	26	26	23	24	25	25	24	27
	51 - 50y	N	168	163	105	98	94	119	115	96	116	31	204	150	99	99	128	87	160	106	55	101
		%	8	8	8	9	8	9	10	9	12	8	12	13	16	14	14	14	14	16	15	18

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17 Olea europea

18 Platanus acerifolia

19 Betula pubescens

20 Cupressus arizonica

Table 3: Skin Prick Tests in Portugal and Spain in allergic rhinitis patients according age to groups.

to *Alternaria* among AR patients aged 10-20 years. In the group aged 21-30 and 31-40 years-old there was no predominant sensitisation rates among the chosen allergens. In the oldest sample patients (41-50 years) the prevalence of pollen was higher than the prevalence mites sensitisation.

Table 4 (A, B, C) presents the aeroallergen sensitisation in AR patients according to the ARIA classification. The results did not allow recognition of any specific aeroallergen as responsible for a particular type of AR (intermittent or persistent) or severity of the allergic disease.

In patients that had concomitant presence of BA there was not also an allergic sensitisation pattern correlated with a particular aeroallergen. Both mites and pollens are able to induce sensitisation and clinical manifestations of rhinitis and asthma, Table 5.

DISCUSSION

This observational study with a large sample is aimed to characterize AR in this area of Southern Europe following the same methodology and is representative of the two countries. Diagnosis of the allergic disease by specialists in Allergy reduces the error factors of other studies carried out by telephone contacts or questionnaires. Epidemiological studies performed both in Spain and Portugal had shown the prevalence of AR in the general population, but failed to describe, exactly, which were the rates of the different patterns of clinical expression, and the severity according to ARIA guidelines.

Epidemiological studies in Portugal made by questionnaires showed 48% of patients with intermittent forms of rhinitis ranging from 16-95 years-old (4). In the present study the value is slightly lower, 45%, in

			Pruebas realizadas																				
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	
España	Canarias	Intermitente Leve	N	26	26	14	10	10	15	20	14	13	1	9	4	3	10	2	4	3	3	2	1
		%	17	17	20	14	17	19	21	22	20	13	28	25	19	30	13	29	38	38	50	20	
		Intermitente Moderada / Grave	N	1	1	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0
		%	1	1	0	0	0	0	0	2	2	0	0	0	0	0	0	0	0	0	0	0	
		Persistente Leve	N	24	24	9	12	9	10	14	10	11	1	3	1	3	6	3	1	0	0	0	0
		%	15	16	13	17	16	13	15	15	17	13	9	6	19	18	20	7	0	0	0	0	
	Centro	Persistente Moderada / Grave	N	104	103	46	48	39	53	60	40	41	6	20	11	10	17	10	9	5	5	2	4
		%	67	67	67	69	67	68	64	62	62	75	63	69	63	52	67	64	63	63	50	80	
		Intermitente Leve	N	25	33	34	14	18	25	19	49	51	25	127	95	31	43	76	66	100	56	29	76
		%	21	29	40	28	32	31	32	27	29	37	28	28	30	27	29	38	31	30	35	31	
		Intermitente Moderada / Grave	N	7	6	5	5	4	4	2	7	7	1	14	12	5	4	9	6	8	5	5	8
		%	6	5	6	10	7	5	3	4	4	1	3	4	5	3	3	3	2	3	6	3	
	Mediterráneo	Persistente Leve	N	50	45	27	15	19	31	22	69	64	22	170	120	37	65	93	56	112	71	28	86
		%	42	40	31	30	34	39	37	39	36	33	38	36	35	41	35	33	35	38	34	35	
		Persistente Moderada / Grave	N	37	29	20	16	15	20	16	54	54	19	138	110	32	47	84	44	102	57	21	75
		%	31	26	23	32	27	25	27	30	31	28	31	33	30	30	32	26	32	30	25	31	
		Intermitente Leve	N	60	55	23	17	16	27	20	33	26	18	35	22	18	14	21	20	47	19	2	13
		%	23	22	22	19	22	24	20	26	23	32	22	20	17	25	26	25	29	20	10	20	
	Norte	Intermitente Moderada / Grave	N	9	9	4	4	4	5	6	7	8	3	8	5	7	5	3	6	8	7	0	5
		%	3	4	4	4	5	4	6	6	7	5	5	5	7	9	4	8	5	7	0	8	
		Persistente Leve	N	74	74	29	29	22	32	30	37	33	16	54	32	34	21	23	24	47	34	9	24
		%	28	29	28	33	30	28	29	30	29	29	34	30	33	38	29	30	29	35	45	38	
		Persistente Moderada / Grave	N	117	115	49	39	32	50	46	48	45	19	63	49	44	16	33	29	62	37	9	22
		%	45	45	47	44	43	44	45	38	40	34	39	45	43	29	41	37	38	38	45	34	
	Sur	Intermitente Leve	N	60	62	44	40	37	46	38	28	28	5	47	32	6	13	22	8	28	18	9	13
		%	21	22	16	14	13	16	13	10	10	2	17	11	2	5	8	3	10	6	3	5	
		Intermitente Moderada / Grave	N	22	23	14	15	12	13	15	9	7	0	13	9	1	5	4	2	9	5	4	7
		%	8	8	8	9	8	7	9	8	6	0	7	8	3	9	5	5	9	8	11	12	
		Persistente Leve	N	90	93	62	54	51	57	51	36	39	9	55	32	12	20	29	12	26	19	11	15
		%	32	33	34	32	33	31	31	32	32	35	29	28	36	35	35	29	27	29	30	26	
Subtotal España	Persistente Moderada / Grave	N	111	107	61	58	55	67	60	40	47	12	77	41	14	19	28	20	32	24	13	23	
	%	39	38	34	35	35	37	37	35	39	46	40	36	42	33	34	48	34	36	35	40		
	Intermitente Leve	N	60	62	41	26	37	39	38	38	34	10	68	48	16	30	50	35	70	34	16	16	
	%	25	26	17	11	16	17	16	16	14	4	29	20	7	13	21	15	30	14	7	7		
	Intermitente Moderada / Grave	N	20	22	8	8	8	12	11	10	11	4	15	13	4	8	12	7	21	8	6	4	
	%	8	10	6	8	6	9	10	7	8	7	6	6	7	7	5	7	6	10	5	5		
Subtotal España	Persistente Leve	N	77	68	45	31	40	44	29	47	46	24	84	65	24	41	58	43	93	43	23	26	
	%	33	30	32	32	31	31	25	34	34	43	31	31	36	35	33	33	33	34	37	35		
	Persistente Moderada / Grave	N	79	75	48	31	46	45	37	45	43	18	101	83	23	37	55	47	102	43	17	28	
	%	33	33	34	32	35	32	32	32	32	32	38	40	34	32	31	36	36	34	27	38		
	Intermitente Leve	N	231	238	156	107	118	152	135	162	152	59	286	201	74	110	171	133	248	130	58	119	
	%	22	23	27	23	25	26	25	26	25	28	26	26	23	26	28	30	28	27	28	27		
Subtotal España	Intermitente Moderada / Grave	N	59	61	31	32	26	34	34	34	34	8	50	39	17	22	28	21	46	25	15	24	
	%	6	6	5	7	6	6	6	5	6	4	5	5	5	5	5	5	5	5	7	5		
	Persistente Leve	N	315	304	172	141	141	174	146	199	193	72	366	250	110	153	206	136	278	167	71	151	
	%	30	29	30	30	30	29	27	32	32	34	33	32	34	36	33	31	32	34	34	34		
	Persistente Moderada / Grave	N	448	429	224	192	187	235	219	227	230	74	399	294	123	136	210	149	303	166	62	152	
	%	43	42	38	41	39	39	41	36	38	35	36	38	38	32	34	34	34	35	34	30	34	

- | | | | |
|----------------------------------|----------------------------|------------------------|------------------------|
| 1 Dermatophagoides pteronissinus | 6 Tyrophagus putrescentiae | 11 Gramineas Mix | 16 Salvia kali |
| 2 Dermatophagoides farinae | 7 Blomia tropicalis | 12 Cynodon dactylon | 17 Olea europea |
| 3 Lepidoglyphus destructor | 8 Felis domesticus | 13 Parietaria judaica | 18 Platanus acerifolia |
| 4 Acarus siro | 9 Canis familiaris | 14 Artemisia vulgaris | 19 Betula pubescens |
| 5 Glyciphagus domesticus | 10 Alternaria alternata | 15 Plantago lanceolata | 20 Cupressus arizonica |

Table 4A: Skin Prick Tests results in Spain in allergic rhinitis patients according to ARIA.

patients aged 10-50 years old. In Spain there were lower values of intermittent AR patients, 28.8%, and patients with persistent forms showed higher levels of severity. The Canary Islands showed the highest value of moderate/severe persistent form (66%) from all the regions analysed.

A multicentre study performed in Europe (including Spanish patients) describes a higher prevalence of intermittent forms, 71%, compared to persistent types (7). These results, confirmed by medical observation, coincided with those obtained by telephone interview. In the present study with a large and representative sample, the intermittent forms for the Iberian countries equals 36% of AR patients aged 10-50 years. As other studies had shown, there was not concordance between ARIA and conventional classification

(Intermittent=36% vs. SAR=41%), and they are not interchangeable (7, 14).

Determination of the cutaneous sensitisation using the same biologically standardized aeroallergen panel allows for the comparison of the results between regions and between the two countries. We would like to have tested same specific pollens correlated to relevant aeropallinology counts in both countries (15, 16). However we decided only to select standardized allergenic extracts with known biological potency in order to minimize errors.

Polisensitisation was common, involving both mites and pollens. Considering the global sample mites were the more frequent aeroallergen in the Iberian countries.

			Skin Prick Test																				
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	
Portugal	Center	Intermittent Mild	N	159	157	144	120	111	123	107	67	56	44	129	98	83	74	65	45	68	45	47	34
		%	52	52	53	50	52	53	52	50	44	49	63	64	62	65	65	69	63	56	63	62	
		Intermittent Moderate /	N	5	4	3	3	3	3	3	1	1	1	3	3	1	2	2	1	3	2	1	2
		%	2	1	1	1	1	1	1	1	1	1	1	1	1	2	2	2	3	2	1	4	
		Persistent Mild	N	62	62	55	51	40	45	43	25	27	22	26	24	19	13	16	7	12	15	11	6
		%	20	21	20	21	19	19	21	19	21	25	13	16	14	11	16	11	11	19	15	11	
	North	Intermittent Moderate /	N	81	78	70	67	58	62	53	42	43	22	46	29	30	25	17	12	25	19	16	13
		%	26	26	26	28	27	27	26	31	34	25	23	19	23	22	17	18	23	23	21	24	
		Intermittent Mild	N	153	145	132	94	105	117	97	56	38	15	82	36	26	26	42	17	23	19	17	9
		%	48	48	49	45	49	51	51	46	45	33	40	34	34	36	41	35	44	38	39	45	
		Intermittent Moderate /	N	3	3	3	3	3	3	3	1	2	2	2	1	0	2	1	2	0	0	0	0
		%	1	1	1	1	1	1	2	1	2	4	1	1	0	3	1	4	0	0	0	0	
	South	Persistent Mild	N	78	71	61	53	49	53	46	30	17	11	59	30	20	18	27	12	8	12	11	6
		%	24	24	23	26	23	23	24	24	20	24	29	28	26	25	26	25	15	24	25	30	
		Persistent Moderate /	N	88	80	72	57	59	58	45	36	28	17	62	39	31	26	33	17	21	19	16	5
		%	27	27	27	28	27	25	24	29	33	38	30	37	40	36	32	35	40	38	36	25	
		Intermittent Mild	N	64	52	39	33	30	33	36	26	21	10	28	15	10	13	10	7	22	6	3	6
		%	21	19	18	19	16	16	19	21	21	23	17	13	19	13	16	28	13	12	16		
	Intermittent Moderate /	N	23	22	16	13	13	16	15	7	10	6	14	14	7	10	10	6	3	9	3	6	
	%	8	8	8	7	7	8	8	6	10	14	9	16	9	14	13	14	4	19	12	16		
	Persistent Mild	N	94	92	73	65	70	71	65	36	27	11	39	23	21	16	26	9	18	10	5	12	
	%	31	33	35	37	37	34	34	29	27	25	24	26	27	23	34	20	23	21	19	32		
	Persistent Moderate /	N	125	111	83	65	77	88	77	56	41	17	83	38	40	31	22	36	23	15	13		
	%	41	40	39	37	41	42	40	45	41	39	51	42	51	44	40	50	46	48	58	35		
Subtotal Portugal	Intermittent Mild	N	376	354	315	247	246	273	240	149	115	69	239	149	119	113	117	69	113	70	67	49	
	%	40	40	42	40	40	41	41	39	37	39	42	43	41	44	42	44	47	39	46	44		
	Intermittent Moderate /	N	31	29	22	19	19	22	21	9	13	9	19	18	8	14	13	9	6	11	4	8	
	%	3	3	3	3	3	3	4	2	4	5	3	5	3	5	5	6	3	6	3	7		
	Persistent Mild	N	234	225	189	169	159	169	154	91	71	44	124	77	60	47	69	28	38	37	27	24	
	%	25	26	25	27	26	25	26	24	23	25	22	22	21	18	25	18	16	21	19	21		
	Persistent Moderate /	N	294	269	225	189	194	208	175	134	112	56	191	106	101	82	81	51	82	61	47	31	
	%	31	31	30	30	31	31	30	35	36	31	33	30	35	32	29	32	34	34	32	28		

1 Dermatophagoides pteronissinus

2 Dermatophagoides farinae

3 Lepidoglyphus destructor

4 Acarus siro

5 Glyciphagus domesticus

6 Tyrophagus putrescentiae

7 Blomia tropicalis

8 Felis domesticus

9 Canis familiaris

10 Alternaria alternata

11 Gramineas Mix

12 Cynodon dactylon

13 Parietaria judaica

14 Artemisia vulgaris

15 Plantago lanceolata

16 Salsola kali

17 Olea europea

18 Platanus acerifolia

19 Betula pubescens

20 Cupressus arizonica

Table 4B: Skin Prick Tests results in Portugal in allergic rhinitis patients according to ARIA.

			Skin Prick Test																			
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Total Spain and Portugal	Intermittent Mild	N	607	592	471	354	364	425	375	311	267	128	525	350	193	223	288	202	361	200	125	168
		%	31	31	35	32	33	34	33	31	29	33	31	31	32	33	32	34	32	30	36	30
	Intermittent Moderate /	N	90	90	53	51	47	56	55	43	47	17	69	57	25	36	41	30	52	36	19	32
		%	5	5	4	5	4	4	5	4	5	4	4	5	4	5	5	5	5	5	5	6
	Persistent Mild	N	549	529	361	310	300	343	300	290	264	116	490	327	170	200	275	164	316	204	98	175
		%	28	28	27	28	27	27	27	29	29	30	29	29	28	30	31	28	28	31	28	31
	Persistent Moderate /	N	742	698	449	381	381	443	394	361	342	130	590	400	224	218	291	200	385	227	109	183
		%	37	37	34	35	35	35	35	36	37	33	35	35	37	32	33	34	35	34	31	33

1 Dermatophagoides pteronissinus

2 Dermatophagoides farinae

3 Lepidoglyphus destructor

4 Acarus siro

5 Glyciphagus domesticus

6 Tyrophagus putrescentiae

7 Blomia tropicalis

8 Felis domesticus

9 Canis familiaris

10 Alternaria alternata

11 Gramineas Mix

12 Cynodon dactylon

13 Parietaria judaica

14 Artemisia vulgaris

15 Plantago lanceolata

16 Salsola kali

17 Olea europea

18 Platanus acerifolia

19 Betula pubescens

20 Cupressus arizonica

Table 4C: Skin Prick Tests results in Portugal and Spain in allergic rhinitis patients according to ARIA.

Grass pollen was the second aeroallergen in Iberian countries. We stress the higher value in Central and Southern regions of Spain, 82% and 59% respectively. In Portugal we observed a decrease from north to south, where the temperature is high and usually enjoys dry spring seasons.

Others species of allergenic pollens produced lower values of sensitisation. *Parietaria judaica* was responsible for higher values in Mediterranean regions in Spain (23%) and in Central areas of Portugal (33%). Sensitisation to pollen weeds of *Artemisia vulgaris*, *Plantago lanceolata* and *Salsola kali* were more frequent to sensitisation in Central and Southern regions of Spain and in Central Portugal. We stress the similar climate conditions of these Spanish regions and the inland central area of Portugal, with large, hot and dry spring seasons.

1 <i>Dermatophagoides pteronissinus</i>	6 <i>Tyrophagus putrescentiae</i>	11 Gramineae Mix	16 <i>Salsola kali</i>
2 <i>Dermatophagoides farinae</i>	7 <i>Blomia tropicalis</i>	12 <i>Cynodon dactylon</i>	17 <i>Olea europea</i>
3 <i>Lepidoglyphus destructor</i>	8 <i>Felis domesticus</i>	13 <i>Parietaria judica</i>	18 <i>Platanus acerifolia</i>
4 <i>Acarus siro</i>	9 <i>Canis familiaris</i>	14 <i>Artemisia vulgaris</i>	19 <i>Betula pubescens</i>
5 <i>Glyciphagus domesticus</i>	10 <i>Alternaria alternata</i>	15 <i>Plantago lanceolata</i>	20 <i>Cucumis zucchini</i>

Table 5: Skin Prick Tests results in allergic rhinitis patients and concomitant presence of bronchial asthma.

In the case of pollen trees, *Olea europaea*, *Platanus acerifolia*, *Betula pubescens* and *Cupressus arizonica* showed the same pattern of sensitisation in the two Iberian countries.

In Spain sensitisation to pollens also seems to have increased in AR patients in the last 10 years, in agreement with recent reports (15, 16). *Cupressus* presents an enormous increase of sensitisation in Iberian countries in recent years, in accordance with the reported in others areas of southern Europe (18, 21).

Sensitisation to cat and dog dander were similar, 32% and 29% respectively. In Spain there were no differences between positive SPT to both domestic animals, but in Portugal sensitisation to cat was higher than sensitisation to dog dander. Spain also presented an important increase in the last 10 years (15), but further studies analysing social habits and co-living presence of animals are needed to respond to those results.

Alternaria was the only mould that was studied in this population. We stress a significant increase in sensitisation rates in the last 10 years, ranging from 5% to 11% in Spain (15). This aeroallergen was responsible for the highest rate of positive SPT among AR patients aged 10-20 years old. Therefore, as the majority of the patients are polysensitised, these results point towards the necessity of monitoring this allergen in the future.

A great number of allergic asthmatic patients simultaneously present symptoms of rhinitis (22). The evaluation of bronchial reactivity in AR patients should be done even in those that do not report symptoms of BA (23). In our study 49% of AR patients also had BA. Both in Portugal and Spain there was not a specific aeroallergen that could be related to a major risk of asthma.

In this observational study, representative of Iberian countries, we defined and classified the AR patients aged 10-50 years old according the current classification of symptoms and according to severity levels. Recently, the need of a common paneuropean standard battery of skin tests has been suggested (24).

We believe that the present study is important within an European context because we have both characterized this pathology and evaluated the pattern of aeroallergen sensitisation using the same battery of standardized allergen extracts in a significant area of Southern Europe. We also stress the presence of BA in almost half our patients, apparently independent of a specific allergen sensitisation.

Our results were able to demonstrate that ARIA classification defines patients differently from the traditional seasonal/perennial clinical classification

Researchers involved:

Portugal. North: Graça Castel Branco, Josefina Cernadas, Carmen Botelho, Helena Falcão, Leonor Cunha, Daniela Malheiro, Paula Alendouro, Eliza Mariño, Arminda Guilherme, José Ferreira, Isabel Rosmaninho. **Center:** Celso Chieira, Ana Todo Bom, Graça Loureiro, Emília Faria, Luisa Geraldès, Alexandra Santos, Celso Pereira, Carlos Loureiro, Ana Moreti, Miguel Capão Filipe, Isabel Carrapatoso. **South:** Paula Leiria Pinto, Sara Prates, Manuel Barbosa, Elisa Pedro, Manuel Branco Ferreira, Amélia Spínola, Mário Morais Almeida, Elza Tomáz, Cristina Arede, Filipe Inácio, Vinhas Sousa, Irina Didenko, Luísa Lopes, Graça Sampaio, Felicidade Dias, Carlos Nunes, Susel Ladeira, Beatriz Tavares, Rita Câmara, Susana Oliveira.

Spain. Mediterranean: Albert Roger Reig- Coordinator, Alex Roger Reig, Alfonso Olivé Pérez, Ángel Julio Huertas Amorós, Antonio Valero Santiago, César Alias Tuduri, Javier Montoro Lacomba, José María Negro Álvarez, José Ramón Lavín Alonso, Josep Maria Roger Barri, Juan Antonio Pagán Alemán, Lluís Marqués Amat, M^a Dolores Martos Clahorro, M^a Teresa Dordal i Culla, Mercè Corominas Sánchez, Miguel Ángel Baltasar Drago, Miguel Ángel Díaz Palacios, Pol Pau, Ramon Leonart Belfill, Ramon Serra Juanpere, Rosa M^a Martínez López, Santiago Aparicio Español, Silvia Lara Alcón, Teresa Abós Mir. **South:** Julio Delgado Romero-Coordinator, Alfonso Del Cuvillo Bernal, Ana María Navarro Pulido, Carmen Moreno Escobosa, Dr. Porcel Carreño, Dra. Alvarado Arenas, Dr. Jiménez Timón, Esperanza Sanz Romero, Francisco Burgos Gómez, Francisco Javier Hernández Arbeiza, Francisco Moreno Benítez, Jesús Miguel García Menaya, José Amat López, José Carlos Orta Cuevas, José Luis Justicia Ruano, Laureano Fernández-Távora Fernández, M. Angeles Gonzalo Garijo, M^a Angeles Lara Jiménez, M^a Carmen Moya Quesada, M^a Cesárea Sánchez Hernández, M^a Sergia Cruz Granados, Remedios Pérez Calderón, Susana Duran Macarro. **Canary Islands:** Inmaculada Sánchez Machín- Coordinator, Juan Antonio García Marrero, Ruperto González Pérez, Anselmo Sánchez Palacios, Fernando de la Torre Morín, Fernando Schamann Medina, Javier Figueroa Ribero, José Carlos Robaina, Paloma Poza Guedes; **North:** Eduardo Fernández Ibáñez-Coordinator, Alejandro Joral Badas, Alicia Suárez Rodríguez, Beatriz Valeiro Pérez, Elena Ordoqui, Encarnación Antón Casas, Eulalia Camino Rodríguez, Gonzalo Bernaola Hortigüela, Isabel Jiménez Gómez, José Antonio Navarro, José Carlos García Ortiz, José Fernando Filgueira Iglesias, José Francisco Garmendia, Juan Jerez Domínguez, María Teresa Soto Mera, Marta Orta, Noemí Saiz Cordero, Sofía Alonso Juaristi, Teófilo Lobera. **Center:** Javier Domínguez Ortega- Coordinator, Alicia Alonso Gómez, Ana Alonso Llamazares, Ana Rosado Ingelmo, Angel Moral de Gregorio, Belén Añibarro, Carlos Senent Sánchez, Carmen Panizo Gravo, Concepción Vila Albelda, Consuelo Martínez Cócera, Elena Laffond Yges, Eloísa González Mancebo, Esther Moreno Rodilla, Ignacio Dávila González, M^a Dolores Herrero Gil, M^a Luisa González Gutiérrez, María del Mar Moro Moro, María Isabel Esteban, María Teresa Gracia Bara, Marta Chamorro, Marta López San Martín, Mercedes Martínez San Ireneo, Miguel Angel Tejedor Alonso, Nieves Cabañes Higuero, Rosa M^a Blanco González, Sara Acero Sainz, Tomás Chivato.

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References

1. Bousquet J., van Cauwemberge P., Khaltaev N. - ARIA Workshop Group. World Health Organization. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol* 2001;108 (suppl 5):S147-S334.
2. Ciprandi G., Vizzaccaro A., Cirrilo I., Crimi P., Canonica G.-W. - Increase of asthma and allergic rhinitis prevalence in young Italian men. *Int Arch Allergy Immunol* 1996;111: 278-283.
3. Arnedo-Pena A., Garcia Marcos L., Hernandez G. - Time trends and geographical variations in the prevalence of symptoms of allergic rhinitis in 6-7-year-old children from eight areas of Spain according to the ISAAC. *An Pediatr (Barc)*. 2005;62(3):229-36.
4. Morais-Almeida M., Loureiro C., Todo-Bom A. *et al.* - Avaliação da prevalência e caracterização da rinite em utentes dos cuidados de saúde primários de Portugal continental.-Estudo ARPA. *Rev. Port. Imunoalergologia* 2005;13:69-80.
5. Bauchau V., Durham S.-R. - Prevalence and rate of diagnosis of allergic rhinitis in Europe. *Eur Resp J* 2004;24:758-64.
6. Crystal-Peters J., Crown W.-H., Goetzel R.-Z., Schutt D.-C. - The cost of productivity losses associated with allergic rhinitis. *Am J Manage Care* 2000;6:373-8.
7. Bauchau V., Durham S.-R. - Epidemiological characterization of the intermittent and persistent types of allergic rhinitis. *Allergy* 2005;60:350-3.
8. Loureiro G., Rabaça M.-A., Blanco B. *et al.* - Urban versus rural environment--any differences in aeroallergens sensitization in an allergic population of Cova da Beira, Portugal? *Allerg Immunol (Paris)*. 2005;37(5):187-93.
9. D'Amato G., Spiekma F. Th M., Liccardi G. *et al.* - EAACI Position Paper: Pollen-related allergy in Europe. *Allergy* 1998;53:567-578.
10. D'Amato G., Liccardi G. - Pollen-related allergy in the European Mediterranean area. *Clin Exp Allergy* 1994;24:210-219.
11. von Mutius E. - The environmental predictors of allergic disease. *J Allergy Clin Immunol* 2000;105:9-19.
12. A caracterização do risco. - Risco relativo e odds ratio como medidas do grau de associação entre factores e doença. Ed. ACP Ramalheira, S Massano Cardoso. Almedina, Coimbra. 1995.
13. Dreborg S., Frew A. - EAACI Position Paper: Allergen standardization and skin tests. *Allergy* 1993;48(S14):1-82.
14. Demoly P., Allaert F.-A., Lecaesble M., Bousquet J., Pragma. - Validation of the classification of ARIA (allergic rhinitis and its impact on asthma). *Allergy* 2003;58:672-5.
15. Alergologica. - Factores Epidemiológicos clínicos y socioeconómicos de las enfermedades alérgicas en España. Ed. SEAIC, Abelló SA. Nilo Industria Gráfica. Madrid. 1995.
16. Subiza Garrido Lestache J. - Allergenic pollens in Spain. *Allergol Immunopathol (Madr)*. 2004;32:121-4.
17. Fernández-Caldas E., Lockey R.-F. - *Blomia tropicalis*, a mite whose time has come. *Allergy* 2004;59:1161-4.
18. D'Amato G., Spiekma F.-T., Liccardi G. *et al.* - Pollen related allergy in Europe. *Allergy* 1998;53:567-78.
19. D'Amato G., Liccardi G., D'Amato M., Cazzola M. - The role of outdoor air pollution and climatic changes on the rising trends in respiratory allergy. *Respire Med* 2001;95:606-611.
20. Sanchez Mesa J.-Á., Brandão R., Lopes L., Galan C. - Correlation between pollen counts and symptoms in two different areas of the Iberian Peninsula: Cordoba (Spain) and Evora (Portugal). *J Investig Allergol Clin Immunol*. 2005;15(2):112-6.
21. Sposato B., Mannino F., Terzano C. - Significant increase of incidence of cypress pollen allergy in the city of Rome. *Recenti Prog Med* 2001;92:541.
22. Muñoz-López F. - Rhinitis as a precursor for asthma. *Allergol et Immunopathol* 2003;31:297-9.
23. Valdesoiro L., Bosque M., Marco M.-T., Asensio O., Antón J., Larramona H. - Rinitis alérgica e hiperreactividade bronquial. *Allergol et Immunopathol* 2004;32:340-3.
24. Heinzerling L., Frew A.-J., Bindslev-Jensen C. *et al.* - Standard skin prick testing and sensitisation to inhalant allergens across Europe - a survey from the GA²LEN network. *Allergy* 2005;60:1287-1300.

