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Prevalence and time trends of symptoms of allergic rhinitis and rhinoconjunctivitis in Spanish children: Global Asthma Network (GAN) study

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Abstract
Introduction: The time trends of the prevalence of rhinitis, rhinoconjunctivitis and nasal allergy previously described in the ISAAC (International Study of Asthma and Allergies in Childhood) in 2002 are unknown; or if the geographical or age differences in Spain persist.
Objective: To describe the prevalence of rhinitis, rhinoconjunctivitis and nasal allergy in different Spanish geographical areas and compare them with those of the ISAAC.
Methods: Cross-sectional study of the prevalence of rhinitis, rhinoconjunctivitis and nasal allergy, carried out in 2016-2019 on 19943 adolescents aged 13-14 years and 17215 schoolchildren aged 6-7 years from six Spanish areas (Cartagena, Bilbao, Cantabria, La Coruña, Pamplona, and Salamanca), through a questionnaire based on the Global Asthma Network (GAN) protocol.

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Results: The prevalences of recent rhinitis and rhinoconjunctivitis (last 12 months), and nasal allergy/hay fever were 35.1%, 17.6%, and 14.6% in the adolescents and 20%, 8.5%, and 8.9% in the schoolchildren, respectively, with rhinoconjunctivitis in adolescents varying from 20.9% in Bilbao to 13.4% in Cartagena; and in schoolchildren, from 9.8% in La Coruña to 6.4% in Pamplona. These prevalences of rhinoconjunctivitis and nasal allergy in adolescents were higher than those described in the ISAAC (16.3% and 13%) and similar in schoolchildren to the ISAAC (9% and 9.4%).
Conclusions: There has been a stabilisation of rhinitis, rhinoconjunctivitis and nasal allergy in schoolchildren that slows the previous upward trend of ISAAC; and a slight non-significant increase in rhinoconjunctivitis and nasal allergy in adolescents. The variability found in adolescents would require local research to be better understood.

Introduction

Allergic diseases in children and adolescents are a global public health problem, which involve considerable morbidity and geographical variations, as has been shown in the data published by the "International Study of Asthma and Allergies in Childhood" (ISAAC) (1992–2012).[1-4] Whilst the prevalence of asthma, allergic rhinitis and atopic dermatitis symptoms increased at a worrying level in some centres, in other centres with already high prevalence they remained stable. The ISAAC study has offered a huge amount of epidemiological data, including the prevalence of rhinitis and allergic rhinoconjunctivitis and their risk and protective factors, from a large number of centres and countries worldwide and has demonstrated the importance of climate variations,[5,6] environmental pollution,[7] Mediterranean diet[8-10] and obesity in allergic diseases.[11] In recent years, the "Global Asthma Network" (GAN) has been set up with the aim of updating the prevalence of allergic diseases and their associated factors,[12-14] with its first global estimation of asthma having already been published. These show the presence of wheezing in one of every 10 adolescents and schoolchildren,[15] as well as the Spanish asthma data which confirm an increase in adolescents (15.3%) and a stabilisation in Spanish schoolchildren (10.4%) with respect to ISAAC-III 2002–2003 (10.6% and 9.9%, respectively).[16-18]

Despite rhinitis and allergic conjunctivitis being among the conditions that most frequently affect the paediatric population and which have a major clinical, economic and quality-of-life impact, epidemiological research about them is scant. The first data from the GAN network suggest that the worldwide prevalence of allergic rhinoconjunctivitis symptoms has stabilised with a slight decrease in the upward trend previously shown in the ISAAC study.[19] In Spain, the latest prevalence data available in adolescents and schoolchildren correspond to ISAAC-III and are 31.2% and 17.1% for allergic rhinitis symptoms and 16.7% and 8.3% for allergic rhinoconjunctivitis in the past year, respectively.[1,20,21] At present, the evolution of rhinitis and allergic rhinoconjunctivitis symptoms is not known. Also, not known is whether, as with bronchial asthma, a stabilisation of their prevalence in schoolchildren and an increase among adolescents has occurred, or if geographical differences exist within our country.

The GAN study in Spain consists of six centres: Murcia, Bilbao, Cantabria, La Coruña, Pamplona and Salamanca. The aim of the present study is to describe the prevalence of rhinitis and allergic rhinoconjunctivitis symptoms in those Spanish centres and compare the prevalence of those centres that took part in phase III of ISAAC (2002–2003) with those of the GAN study (2016–2019).

Material and Methods

This is a cross-sectional study that follows the methodology detailed in the specific manual for all GAN centres.[12] This study is based on gathering information through standardised questionnaires that have been previously validated from a general sample that is estimated at 3000 participants in each age group (13–14 years and 6–7 years), which would enable to distinguish the prevalence of asthma that differ by 3% or more with a power of 90% and a 99% confidence level.[13,14]

The field work was carried out during the 2016–2019 school years, depending on the participating centres. Each principal researcher contacted the corresponding regional Education Department to obtain authorisation for the study in the primary and secondary schools selected and subsequently contacted the school heads, teachers and parents to explain the nature of the study. Pupils who were in second and third years of secondary school education (13–14 years) or in first and second years of primary school education (6–7 years) were selected from both public and private schools. A calendar of visits to the primary and secondary schools was charted out to supervise and advise on the handing out and collection of the written self-administered questionnaires for adolescents and the questionnaires for primary schoolchildren aged 6–7 years, which were filled in by their parents.

The fundamental instrument was the validated questionnaire, which included sections referring to allergic rhinitis symptoms, the seriousness of those symptoms and risk and/or protective factors. The questionnaire was translated from English to Spanish and back-translated from Spanish to English, as per the ISAAC method, to ensure that the sense of the items was not lost.[22,23] Each participating centre followed the recommendations of the GAN study operating manual in relation to the selection of participating schools,

the inclusion criteria, the specific variables and their coding. Sample sizes of at least 1000 and preferably 3000 were sought for each age group.[12]

The presence of recent allergic rhinitis in the past year was defined as a positive answer to the question: "In the past 12 months, have you (has this child) had a problem with sneezing, or a runny, or blocked nose when you (he/she) did not have a cold or the flu?" For recent rhinoconjunctivitis, the presence of recent allergic rhinitis was established by a positive answer to "In the past 12 months, has your (this child's) nose problem been accompanied by itchy-watery eyes?" The variable of serious rhinoconjunctivitis had to comply with the presence of recent rhinoconjunctivitis and a positive answer of "a lot" to the question "In the past 12 months, how much did your (this child's) nose problem interfere with your (his/her) daily activities?" In the case of the presence of hay fever or nasal allergy, it was necessary to answer yes to the question "Have you (Has this child) ever had nasal allergy, including hay fever or rhinitis?"

The questionnaires were anonymised and read in the coordinating centre of Cartagena (Murcia) using a scanner (Fujitsu fi-7700) with OMR Remark Office© V10 mark recognition software (Gravic Inc. Malvern, PA, USA). A descriptive analysis of the variables was performed and subsequently a comparison was made using the chi-square test to calculate the possible differences found by sex among the participating centres. The prevalence was calculated with their 95% confidence intervals (95%CI) and were compared for each age group with those described in the centres that participated in the ISAAC study using the chi-square test. The statistical significance threshold was set at $p \leq 0.05$. The STATA version 17 (College Station, TX, USA) software package was used for the said analysis.

The GAN study was approved in the national coordinating centre by the Ethics Committee for Clinical Research of the University Clinical Hospital "Virgen de la Arrixaca" in Murcia and subsequently validated and approved in each participating centre. Prior informed consent was obtained from the parents in the case of adolescents.

Results

The GAN study was carried out in six Spanish centres with a total sample size of 19,943 adolescents aged 13–14 years and 17,215 schoolchildren aged 6–7 years. One hundred and eighty-four secondary schools with adolescents and 323 primary schools with schoolchildren aged 6–7 years participated (Table 1). The participation rate was higher in adolescents, 81.3% (58.8%–95%), than in schoolchildren, 62.6% (55.2%–73.7%). This finding was similar to the rest of the GAN centres from other countries because the questionnaires of schoolchildren were completed by their parents at their homes.

Prevalence results

The prevalence obtained by means of the written questionnaire is given in Tables 2 and 3. The total prevalence of recent rhinitis and allergic rhinoconjunctivitis symptoms were 35.1% and 17.6% in adolescents, and 20% and 8.5% in the schoolchildren. For adolescents, the range was from 42.2% for recent rhinitis in La Coruña and 20.9% for recent rhinoconjunctivitis in Bilbao, to 25% and 13.4% in Cartagena, respectively. With respect to schoolchildren, there was less variation, with La Coruña having 23.8% for rhinitis and

Table 1 Characteristics of the participating GAN centres.

GAN Centre	Population type	Participating schools n	Study population n	Sample size n	Participation (% pupils)
Bilbao					
6–7 years	Urban	52	4902	2707	55.2
13–14 years		33	3711	3379	91.1
Cantabria					
6–7 years	Urban	75	5052	2841	56.2
13–14 years		47	5664	4382	77.3
Cartagena					
6–7 years	Urban	61	5342	3509	65.7
13–14 years		26	4657	3437	73.8
La Coruña					
6–7 years	Urban	48	4796	3407	71
13–14 years		26	3760	3462	92.1
Pamplona					
6–7 years	Urban	36	4163	2363	56.8
13–14 years		21	3056	1798	58.8
Salamanca					
6–7 years	Mixed	51	3242	2388	73.7
13–14 years		31	3668	3485	95.0
Total					
6–7 years		323	27,497	17,215	62.6
13–14 years		184	24,516	19,943	81.3

Table 2 Prevalence (%) of rhinitis symptoms in children.

Centre	Sample size	Rhinitis ever	Recent rhinitis	Recent rhinitis and itching	Recent rhinocon-junctivitis	Recent rhinoconjunctivitis and daily activity limited					Nasal allergy/ Hay fever ever	Physician-diagnosed nasal allergy/Hay fever
						Never	On occasions	Quite often	Very often	NA		
Bilbao	2707	682 (25.2)	556 (20.5)	321 (11.9)	239 (8.8)	79 (33.1)	113 (47.3)	24 (10.0)	15 (6.3)	8 (3.4)	239 (8.8)	181 (6.7)
Cantabria	2841	760 (26.8)	574 (20.2)	326 (11.5)	243 (8.6)	101 (41.6)	100 (41.2)	26 (10.7)	12 (4.9)	4 (1.7)	246 (8.7)	190 (6.7)
Cartagena	3509	758 (21.6)	595 (17.0)	351 (10.0)	268 (7.6)	77 (28.7)	132 (49.3)	38 (14.2)	13 (4.9)	8 (3.0)	233 (6.6)	145 (4.1)
La Coruña	3407	1000 (29.4)	810 (23.8)	443 (13.0)	334 (9.8)	106 (31.7)	161 (48.2)	50 (15.0)	12 (3.6)	5 (1.5)	391 (11.5)	310 (9.1)
Pamplona	2363	513 (21.7)	414 (17.5)	218 (9.2)	152 (6.4)	38 (25.0)	83 (54.6)	25 (16.5)	4 (2.6)	2 (1.3)	163 (6.9)	119 (5.0)
Salamanca	2388	609 (25.5)	492 (20.6)	257 (10.8)	224 (9.4)	82 (36.6)	107 (47.8)	25 (11.2)	6 (2.7)	4 (1.8)	261 (10.9)	198 (8.3)
Total	17,215	4322 (25.1)	3441 (20.0)	1916 (11.1)	1460 (8.5)	483 (33.1)	696 (47.7)	188 (12.9)	62 (4.3)	31 (2.1)	1533 (8.9)	1143 (6.6)

Written GAN questionnaire in schoolchildren aged 6–7 years.
*Prevalence expressed in absolute numbers and percentage in brackets. NA: no data available; GAN: Global Asthma Network.

Table 3 Prevalence (%) of rhinitis symptoms in adolescents.

Centre	Sample size	Rhinitis ever	Recent rhinitis	Recent rhinitis and itching	Recent rhinocon-junctivitis	Recent rhinoconjunctivitis and daily activity limited					Nasal allergy/ Hay fever ever	Physician-diagnosed nasal allergy/ Hay fever
						Never	On occasions	Quite often	Very often	NA		
Bilbao	3379	1628 (48.2)	1303 (38.6)	688 (20.4)	705 (20.9)	301 (42.7)	265 (37.6)	95 (13.5)	39 (5.5)	5 (0.7)	526 (15.6)	378 (11.2)
Cantabria	4382	1861 (42.5)	1436 (32.8)	689 (15.7)	697 (15.9)	283 (40.6)	282 (40.5)	93 (13.3)	34 (4.9)	5 (0.7)	586 (13.4)	424 (9.7)
Cartagena	3437	1191 (34.7)	860 (25.0)	443 (12.9)	460 (13.4)	193 (42.0)	200 (43.5)	47 (10.2)	14 (3.0)	6 (1.3)	322 (9.4)	227 (6.6)
La Coruña	3462	1791 (51.7)	1462 (42.2)	664 (19.2)	689 (19.9)	301 (43.7)	286 (41.5)	68 (9.9)	30 (4.4)	4 (0.6)	540 (15.6)	408 (11.8)
Pamplona	1798	821 (45.7)	644 (35.8)	327 (18.2)	313 (17.4)	129 (41.2)	140 (44.7)	31 (9.9)	12 (3.8)	1 (0.3)	210 (11.7)	149 (8.3)
Salamanca	3485	1539 (44.2)	1291 (37.0)	675 (19.4)	643 (18.5)	251 (39.0)	271 (42.2)	75 (11.7)	38 (5.9)	8 (1.2)	718 (20.6)	489 (14.0)
Total	19,943	8831 (44.3)	6996 (35.1)	3486 (17.5)	3507 (17.6)	1458 (41.6)	1444 (41.2)	409 (11.7)	167 (4.8)	29 (0.8)	2902 (14.6)	2075 (10.4)

Written GAN questionnaire in adolescents aged 13–14 years.
*Prevalence expressed in absolute numbers and percentage in brackets. NA: no data available; GAN: Global Asthma Network.

9.8% for recent rhinoconjunctivitis in the upper limit, and Cartagena with 17% for recent rhinitis and Pamplona with 6.4% for recent rhinoconjunctivitis in the lower limit. In this age group, only Cartagena and Pamplona had recent rhinitis prevalence below 20%. On the other hand, the prevalence of nasal allergy (including hay fever or rhinitis) on occasions was relatively high, with 14.6% in adolescents and 8.9% in schoolchildren.

Regarding the seriousness of allergic rhinoconjunctivitis, 4.8% of adolescents were afflicted (0.8% of the studied population) and 4.3% of schoolchildren (0.3% of the studied population) indicated that the rhinoconjunctivitis symptoms interfered in their daily activities to a great extent.

Comparison of the prevalence between ISAAC-III and GAN

A comparison of the prevalence of rhinitis symptoms in the past year from the ISAAC-III (2002–2003) and GAN (2016–2019)

Table 4 Comparison of the prevalence of allergic rhinitis symptoms in schoolchildren aged 6–7 years and adolescents aged 13–14 years in the ISAAC-III study versus the GAN study. *Written questionnaire.

		Schoolchildren aged 6–7 years			Adolescents aged 13–14 years		
		ISAAC-III	GAN		ISAAC-III	GAN	
Variable	Centre	Prevalence % (95%CI) n	Prevalence % (95%CI) n	Comparison p	Prevalence % (95%CI) n	Prevalence % (95%CI) n	Comparison p
Recent rhinitis	Bilbao	20.1 (18.7-21.6) 613	20.5 (19.0-22.1) 556	0.865	26.9 (25.3-28.6) 775	38.6 (36.9-40.2) 1303	<0.001
	Cantabria	NA	20.2 (18.7-21.7) 574	NA	44.0 (41.8-46.4) 799	32.8 (31.4-34.2) 1436	<0.001
	Cartagena	17.1 (15.7-18.6) 467	17.0 (15.7-18.2) 595	0.966	31.4 (29.7-33.2) 898	25.0 (23.6-26.5) 860	0.003
	La Coruña	24.7 (23.2-26.3) 745	23.8 (22.4-25.2) 810	0.679	37.0 (35.2-38.7) 1102	42.2 (40.6-43.9) 1462	0.008
	Pamplona	17.1 (15.8-18.5) 544	17.5 (16.0-19.1) 414	0.871	39.4 (37.7-41.2) 1156	35.8 (33.6-38.1) 644	0.132
	Salamanca	NA	20.6 (19.0-22.3) 492	NA	NA	37.0 (35.4-38.7) 1291	NA
	Total	19.8 (19.1-20.5) 2369	20.0 (19.4-20.6) 3441	0.851	35.1 (34.3-35.9) 4730	35.1 (34.4-35.7) 6996	1.0
Recent rhinoconjunctivitis	Bilbao	9.1 (8.1-10.2) 278	8.8 (7.8-10.0) 239	0.905	14.3 (13.0-15.6) 412	20.9 (19.5-22.3) 705	0.006
	Cantabria	NA	8.6 (7.6-9.6) 243	NA	11.9 (10.4-13.4) 215	15.9 (14.8-17.0) 697	0.150
	Cartagena	8.8 (7.8-9.9) 240	7.6 (6.8-8.6) 268	0.622	16.8 (15.4-18.2) 480	13.4 (12.3-14.6) 460	0.146
	La Coruña	11.0 (9.9-12.2) 333	9.8 (8.8-10.9) 334	0.612	19.9 (18.5-21.4) 593	19.9 (18.6-21.3) 689	1.0
	Pamplona	7.0 (6.1-7.9) 222	6.4 (5.5-7.5) 152	0.820	16.7 (15.3-18.1) 489	17.4 (15.7-19.2) 313	0.797
	Salamanca	NA	9.4 (8.2-10.6) 224	NA	NA	18.5 (17.2-19.8) 643	NA
	Total	9.0 (8.5-9.5) 1073	8.5 (8.1-8.9) 1460	0.659	16.3 (15.6-16.9) 2189	17.6 (17.1-18.1) 3507	0.205
Nasal allergy/ Hay fever ever	Bilbao	8.9 (7.9-9.9) 270	8.8 (7.8-10.0) 239	0.968	15.7 (14.4-17.1) 453	15.6 (14.4-16.8) 526	0.966
	Cantabria	NA	8.7 (7.7-9.8) 246	NA	16.5 (14.9-18.3) 300	13.4 (12.4-14.4) 586	0.061
	Cartagena	7.9 (6.9-9.0) 216	6.6 (5.8-7.5) 233	0.595	11.3 (10.1-12.5) 322	9.4 (8.4-10.4) 322	0.429

(Continued)

Table 4 Continued.

		Schoolchildren aged 6-7 years			Adolescents aged 13-14 years		
		ISAAC-III	GAN		ISAAC-III	GAN	
Variable	Centre	Prevalence % (95%CI) n	Prevalence % (95%CI) n	Comparison p	Prevalence % (95%CI) n	Prevalence % (95%CI) n	Comparison p
	La Coruña	12.6 (11.5-13.9) 381	11.5 (10.4-12.6) 391	0.639	15.4 (14.2-16.8) 460	15.6 (14.4-16.8) 540	0.931
	Pamplona	8.2 (7.3-9.2) 261	6.9 (5.9-8.0) 163	0.625	7.4 (6.5-8.4) 218	11.7 (10.2-13.3) 210	0.130
	Salamanca	NA	10.9 (9.7-12.3) 261	NA	NA	20.6 (19.3-22.0) 718	NA
	Total	9.4 (8.9-10.0) 1128	8.9 (8.5-9.3) 1533	0.658	13.0 (12.5-13.6) 1753	14.6 (14.1-15.0) 2902	0.127

*Prevalence expressed in percentage, confidence interval 95% CI in brackets and absolute number. NA: no data available; GAN: Global Asthma Network; ISAAC: International Study of Asthma and Allergies in Childhood.

studies is presented in Table 4. A stabilisation of the total prevalence of recent rhinitis was observed in adolescents (35.1% ISAAC-III versus 35.1% GAN) and schoolchildren (19.8% ISAAC-III versus 20% GAN). However, in adolescents there was variability among the participating centres: whilst Bilbao and La Coruña presented a statistically significant increase, Cantabria, Cartagena and Pamplona showed lower prevalence. For schoolchildren, similar prevalence was shown for recent rhinitis in all the centres that participated in both studies.

For recent rhinoconjunctivitis, a slight increase, albeit non-significant, in the total prevalence in adolescents (16.3% ISAAC-III versus 17.6% GAN) and a stabilisation in schoolchildren (9% ISAAC-III versus 8.5% GAN) was observed. Major variability was also detected in adolescents, with centres such as Bilbao and Cantabria having increased rhinoconjunctivitis prevalence, Cartagena with a lower prevalence and La Coruña and Pamplona showing no significant changes. In the case of schoolchildren, changes in the prevalence of rhinoconjunctivitis were not found in each centre between the two studies.

When the presence of nasal allergy (including hay fever or rhinitis) ever was compared between the two studies, a non-significant increase in its prevalence was observed in adolescents (13% ISAAC-III versus 14.6% GAN) and a stabilisation in schoolchildren (9.4% ISAAC-III versus 8.9% GAN). There was also variability between centres in adolescents: Cantabria presented a lower prevalence of nasal allergy in the GAN study, an increase in Pamplona and no change in Bilbao, Cartagena and La Coruña. Salamanca, the only centre that had not participated in ISAAC-III, contributed the highest prevalence of nasal allergy (20.6%).

Comparison of prevalence between sexes

With regard to the differences according to sex (Table 5), it was observed that the prevalence of recent rhinitis and rhinoconjunctivitis was higher in female adolescents in five of the GAN centres, whilst in schoolchildren the opposite was true, with the males having a higher prevalence of rhinoconjunctivitis in all the centres. This difference was greater in some of the GAN centres in comparison with the ISAAC-III study in the case of the prevalence of recent rhinoconjunctivitis.

Discussion

The results described and the comparisons between ISAAC-III and GAN show a stabilisation in the total prevalence of recent rhinitis and allergic rhinoconjunctivitis in schoolchildren, as well as a stabilisation of recent allergic rhinitis and a slight non-significant increase in rhinoconjunctivitis in adolescents. The increasing trend of rhinoconjunctivitis in both age groups previously shown in the ISAAC study throughout its different phases carried out from 1993 to 2003 in Spain[20,21,24] is not globally confirmed in our study, suggesting a stabilisation in schoolchildren (8.5%) and a slight increase in adolescents (17.6%). The same data were observed when the presence of nasal allergy was analysed (hay fever or allergy rhinitis) ever, with a stabilisation in schoolchildren and a slight non-significant increase in adolescents.

On the other hand, great variability was observed for rhinitis and rhinoconjunctivitis in adolescents in each GAN centre and some differences among the prevalence of recent allergic rhinitis and nasal allergy (hay fever) in both age groups (35.1% versus 14.6% in adolescents and 20% versus 8.9% in schoolchildren, respectively), which were already seen in all phases of the ISAAC study. These data, together with the presence of physician-diagnosed nasal allergy (10.4% in adolescents and 6.6% in schoolchildren), require greater local research to be understood and for preventive health strategies to be established. It is possible

Table 5 Comparison of the prevalence of rhinitis symptoms by sex in schoolchildren aged 6-7 years and in adolescents aged 13-14 years in the ISAAC-III study versus the GAN* study. Written questionnaire.

	Recent rhinitis				Recent rhinoconjunctivitis				Nasal allergy/Hay fever ever			
	ISAAC-III		GAN		ISAAC-III		GAN		ISAAC III		GAN	
Centre	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male
Bilbao												
6-7 years	17.7 (15.8-19.7)	22.7 (20.5-24.9)	19.5 (17.4-21.7)	21.5 (19.4-23.8)	7.5 (6.2-8.9)	10.9 (9.3-12.6)	7.5 (6.1-9.0)	10.2 (8.7-12.0)	7.5 (6.2-8.9)	10.4 (8.9-12.1)	7.3 (6.0-8.9)	10.4 (8.8-12.1)
13-14 years	28.8 (26.6-31.2)	24.7 (22.4-27.0)	41.7 (39.3-44.2)	36.0 (33.6-38.4)	15.9 (14.0-17.8)	12.6 (10.9-14.5)	24.2 (22.1-26.4)	17.6 (15.8-19.5)	15.2 (13.4-17.1)	16.3 (14.3-18.3)	16.2 (14.4-18.1)	15.4 (13.7-17.3)
Cantabria												
6-7 years	NA	NA	18.5 (16.5-20.7)	21.9 (19.8-24.2)	NA	NA	7.0 (5.7-8.5)	10.1 (8.6-11.8)	NA	NA	7.1 (5.8-8.5)	10.4 (8.8-12.1)
13-14 years	48.7 (45.4-52.0)	39.2 (36.0-42.5)	38.1 (36.1-40.2)	26.8 (24.9-28.8)	13.0 (10.9-15.4)	10.6 (8.7-12.8)	19.5 (17.8-21.2)	12.1 (10.7-13.5)	17.2 (14.9-19.8)	15.8 (13.5-18.4)	14.0 (12.6-15.6)	12.8 (11.4-14.3)
Cartagena												
6-7 years	15.5 (13.7-17.6)	18.8 (16.8-21.0)	14.8 (13.2-16.6)	19.1 (17.2-21.0)	8.4 (7.0-10.0)	9.3 (7.8-10.9)	7.1 (5.9-8.4)	8.2 (6.9-9.5)	7.6 (6.2-9.1)	8.3 (6.9-9.9)	5.7 (4.6-6.8)	7.6 (6.4-8.9)
13-14 years	36.0 (33.5-38.5)	26.9 (24.6-29.3)	27.8 (25.8-30.0)	22.2 (20.2-24.3)	19.0 (17.0-21.1)	14.6 (12.8-16.5)	15.8 (14.2-17.6)	10.9 (9.4-12.5)	11.3 (9.7-13.0)	11.3 (9.7-13.1)	10.2 (8.8-11.7)	8.5 (7.2-9.9)
La Coruña												
6-7 years	21.0 (19.0-23.2)	28.5 (26.2-30.9)	21.4 (19.5-23.5)	26.1 (24.1-28.3)	9.5 (8.1-11.1)	12.6 (11.0-14.4)	9.4 (8.0-10.9)	10.2 (8.8-11.8)	11.8 (10.2-13.5)	13.5 (11.8-15.4)	10.1 (8.7-11.6)	12.7 (11.2-14.4)
13-14 years	39.5 (36.9-42.1)	34.6 (32.3-37.1)	45.4 (43.0-47.8)	39.1 (36.8-41.5)	22.0 (19.8-24.2)	18.0 (16.1-20.0)	22.3 (20.3-24.3)	17.5 (15.8-19.4)	15.6 (13.7-17.5)	15.3 (13.5-17.2)	15.2 (13.5-17.0)	16.2 (14.5-18.0)
Pamplona												
6-7 years	15.5 (13.7-17.4)	18.8 (16.9-20.8)	17.5 (15.4-19.8)	17.5 (15.4-19.8)	6.5 (5.4-7.9)	7.4 (6.2-8.8)	6.1 (4.8-7.7)	6.7 (5.4-8.3)	7.3 (6.1-8.7)	9.1 (7.8-10.7)	6.8 (5.4-8.5)	7.0 (5.6-8.5)
13-14 years	42.2 (39.5-44.8)	37.0 (34.6-39.5)	34.8 (31.8-37.9)	37.0 (33.7-40.4)	19.2 (17.1-21.4)	14.5 (12.8-16.3)	16.5 (14.2-19.0)	18.4 (15.9-21.2)	7.1 (5.8-8.6)	7.8 (6.5-9.2)	12.3 (10.3-14.5)	11.0 (8.9-13.3)
Salamanca												
6-7 years	NA	NA	18.9 (16.7-21.3)	22.4 (20.0-24.9)	NA	NA	8.3 (6.8-10.0)	10.5 (8.8-12.4)	NA	NA	9.5 (7.9-11.3)	12.4 (10.6-14.4)
13-14 years	NA	NA	41.1 (38.7-43.4)	32.7 (30.5-35.0)	NA	NA	22.6 (20.7-24.6)	14.0 (12.4-15.7)	NA	NA	21.9 (20.0-23.9)	19.5 (17.6-21.5)

*Prevalence expressed in percentage and confidence interval 95%CI in brackets. NA: no data available; GAN: Global Asthma Network; ISAAC: International Study of Asthma and Allergies in Childhood.

that, among the factors responsible for this, apart from the geographical and climatic factors, there are also differences in the access to diagnostic tests in the primary care setting or in referral to specialised hospital services. This could contribute to an underdiagnosis of allergic rhinitis, as the data shown would seem to suggest.

Our study provides information on the local evolution of rhinitis, rhinoconjunctivitis and nasal allergy in Spain, with a trend similar to that of the evolution of asthma in the recently published Spanish GAN study.[16] The Spanish study also confirmed an increase in asthma in adolescents and a stabilisation in schoolchildren. In the data referring to recent rhinitis and rhinoconjunctivitis and the presence of nasal allergy in each centre, there were no appreciable geographical variations between adolescents in coastal areas and inland areas, although there was a lower prevalence in Cartagena (25%, 13.4% and 9.4%, respectively) compared to the rest of the participating GAN centres (35.1%, 17.6% and 14.6%, respectively) and lower than in the ISAAC-III study.[20] These differences can be explained by the fact that it is the only Mediterranean representative in the study and that it was related to the climate difference and the hours of exposure to the sun as protective factors.[6] In schoolchildren, the centres of Cartagena and Pamplona stand out with lower prevalence than the rest of the GAN centres along the northern coast (Bilbao, Cantabria and La Coruña) and inland such as Salamanca. The GAN study on the evolution of asthma did not show clearly appreciable geographical variations either, although those areas that presented high prevalence in ISAAC continued to have high figures for asthma in the GAN study in adolescents, whilst in schoolchildren a geographical coast–inland pattern was observed.[16]

The first data from 25 countries in the GAN study (which includes only three Spanish centres that participated in both the ISAAC and GAN studies) refer to the prevalence of rhinoconjunctivitis, severe symptoms and hay fever in adolescents (13.3%, 0.8% and 15.2%, respectively) and in schoolchildren (7.7%, 0.6% and 11.1%, respectively), with a slight decrease in rhinoconjunctivitis, albeit not significant, in the 15 years separating ISAAC-III and GAN both in adolescents (−1.32% each 10 years) as well as in schoolchildren (−0.44% each 10 years). However, large variations existed in the trends observed among countries and among centres within each country so it is difficult to draw conclusions, although it is suggested that rhinoconjunctivitis may not increase further in schoolchildren, as is the case of the most complete data shown from six centres in Spain.[19,25,26] With regard to the severity of the rhinoconjunctivitis, the results of our study are within the mean of the rest of the GAN centres in the world: approximately 5% of adolescents suffering from it had sufficiently serious symptoms so as to significantly interfere in their daily activities.

Comparison with other studies

In other studies performed in youngsters in Finland, it was shown that since 2000 there has been a deceleration in allergic rhinitis (10.7% in 2017), which could stabilise from 2020.[27] In Poland, after monitoring 7- to 10-year-old children from 1993 to 2014, an increase in the prevalence of allergic rhinitis was observed until 2007 (15.9%) and stabilisation with a slight decrease in 2014 (13.9%).[28] In the United States, the data from the National Health Survey detected a decrease in hay fever and respiratory allergy in the period 1997–2018 from 17.5% to 14.7% in people under the age of 18 years, with a prevalence of only hay fever described in 2018 at 7.2% reaching a peak of 10.5% in adolescents.[29] Other countries, such as Turkey, showed an increased prevalence of physician-diagnosed allergic rhinitis in schoolchildren aged 6–14 years from 1994 to 2014.[30] It is likely that the stabilisation of rhinitis and rhinoconjunctivitis in many geographical areas and countries, including the data from our study, could indicate that the maximum potential has been reached with regard to all those persons predisposed already suffering it, and this would explain the upward trends in other countries in which certain protective factors have also stopped acting and that other risk factors prevail more.

Comparison of prevalence of rhinoconjunctivitis between sexes

Our results also confirm the sex differences in the prevalence of rhinitis and allergic rhinoconjunctivitis: schoolboys and female adolescents are the most affected, as was the case in ISAAC-III, and in accordance with the asthma symptoms.[16] This finding also agrees with other GAN centres where the trend in the prevalence of rhinitis and rhinoconjunctivitis change from primary school age to adolescence, when it is prevalent in females; whilst males are the most affected at primary school age.[25,26] These sex differences are not clear enough, but it is postulated that oestrogens and progesterone would increase the inflammation of the airways mediated by TH2 and would interact with the allergy.[31,32]

Limitations and strengths of the study

Despite the broad representability of the paediatric population studied to avoid selection bias, the fact that some ISAAC centres did not participate in GAN may limit the time trend data. Other limitations are those inherent in a cross-sectional study, that is, it does not enable a cause-effect relationship to be established and the use of questionnaires may cause memory bias in parents, although by limiting the questions to the past year, this bias is minimised. With regard to the diagnosis of rhinitis and allergic rhinoconjunctivitis by means of questionnaires of compatible symptoms (and not by physician diagnosis), massive epidemiological studies cannot implement any better system to compare cities and countries, although this limitation must be taken into consideration.

Conclusions

In short, the Spanish GAN study confirms the stabilisation of rhinitis, allergic rhinoconjunctivitis and nasal allergy in schoolchildren that slows the upward trend shown in ISAAC with a slight non-significant increase in rhinoconjunctivitis and nasal allergy in adolescents, similar to those found for asthma. The variability found in adolescents in each GAN

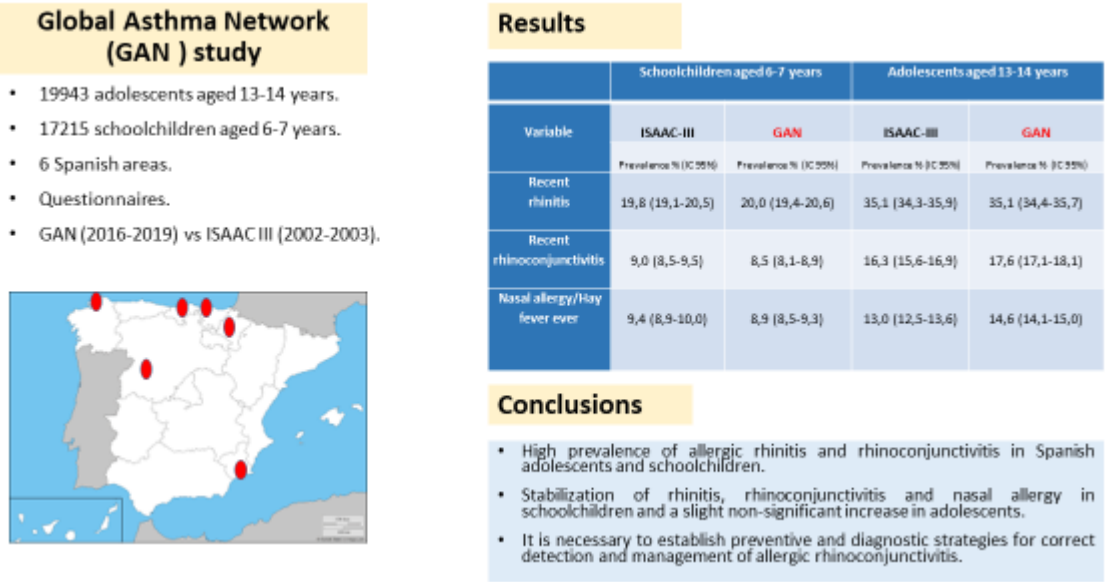

Figure 1. Prevalence and time trends of symptoms of allergic rhinitis and rhinoconjunctivitis in Spanish children.

centre warrants further study to improve understanding. The results of the present study indicate the need to establish similar preventive and diagnostic strategies throughout the country to correctly detect and manage allergic rhino conjunctivitis (Figure 1).

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