

C. S. ROSÁRIO¹, M. MURRIETA-AGUTTES², N. A. ROSARIO¹

Allergic rhinitis: impact on quality of life of adolescents

¹Department of Pediatrics, Federal University of Paraná, Curitiba (PR), Brazil

²Medical Affairs, Sanofi, Gentilly, France

KEY WORDS

Allergic rhinitis; quality of life; adolescents; rhinoconjunctivitis; allergy.

Corresponding author

Cristine Secco Rosário
Departamento de Pediatria
Universidade Federal do Paraná
Hospital de Clínicas da Universidade Federal do Paraná
Rua Padre Camargo 453
Alto da Glória, Curitiba (PR), Brazil
ORCID ID: 0000-0003-4457-3540
E-mail: cristinerosario@hotmail.com

Doi

10.23822/EurAnnACI.1764-1489.176

Summary

Adolescence is one of the most rapid phases of human development, in which biological maturity precedes psychosocial maturity. Rhinoconjunctivitis (ARC) is present in around 15% of 13-14-year-old children, which indicates a higher prevalence when compared with 6-7-year-old children (8.5%). During childhood (0-10 years) prevalence of allergic rhinitis (AR) is higher among males compared to females. Quite the reverse, during adolescence (11-17 years) females display higher prevalence of AR compared to males. However, when they reach adulthood (18-79 years), there is no difference in prevalence between genders. AR and ARC have significant physical and mental impacts on the QoL of adolescents and their parents. Apart from the adverse effects of first generation antihistamines, which include sedating effects, AR/ARC leads to school absences and poorer performance due to distraction, fatigue and irritability. The mobile technology facilitates an innovative investigatory approach to better and more precisely characterize allergy symptoms and their association with other allergic diseases. The success of treatment lies in the partnership between adolescents with AR and mobile technology, allowing them to have more information both on the disease and treatment. Adolescence is a special period in which AR is highly prevalent with some sex-dependent differences. There are also peculiarities on how AR affects QoL of adolescent patients.

IMPACT STATEMENT

AR and ARC have significant physical and mental impacts on the QoL of adolescents and their parents.

Introduction

The World Health Organization (WHO) describes adolescence as one of the most rapid phases of human development, in which biological maturity precedes psychosocial maturity. It is worth noting that the changes occurring in adolescence have health consequences not only in adolescence but also over the life-course, and therefore, explicit and specific attention in health policy programs should be paid during this period of life (1).

Objective

Chronic disease such as allergic rhinitis affects health related quality of life (HRQoL) of children going through the process of growth and development by substantially interrupting their daily activities. The symptoms of allergic rhinitis can cause sleep disturbance, fatigue, poor concentration, and limitations in daily activities. This review aims to evaluate the literature regarding the burden of allergic rhinitis (AR) and allergic rhinoconjunc-

tivitis (ARC) in adolescents (aged 10-19 years) and provide to healthcare professionals with an understanding of the impact of Allergic Rhinitis in adolescents.

Methods

Data source

The generic terms “rhinitis”, “adolescents” and “quality of life” have been screened using PubMed platform.

Data synthesis

Health Related Quality of Life (HRQoL)

A critical aspect in the management of respiratory allergy is its burden on patient’s health-related quality of life (HRQoL), defined as the impact of a disease and its treatment perceived by patients themselves (2).

Health-related quality of life (HRQoL) is an individual’s or a group’s perceived physical and mental health over time (3). It is usually assessed via multiple indicators of self-perceived health status and physical and emotional functioning. Together, these measures provide a comprehensive assessment of the burden of preventable diseases, injuries, and disabilities (4).

The use of questionnaires to assess HRQoL is today recommended by international guidelines and regulatory authorities for the evaluation of new drugs. Furthermore, the fundamental role of patient’s perspectives is underlined by the GRADE system, which represents the best option in defining the criteria for grading evidence and developing guidelines. The RHINASTHMA-Adolescents questionnaire is able to discriminate the disease severity level, it is sensitive for individual changes, and it is simple to administer, giving an immediate idea of the burden of the disease in patient’s everyday life (2). AR causes a global negative impact on the HRQL of children and teenagers, altering mostly the physical function, according to the perception of parents or guardians, and affects negatively the family group (5).

Results

Prevalence of allergic rhinitis in adolescence

The ISAAC (The International Study of Asthma and Allergies in Childhood) Phase III study has analyzed the prevalence and severity of current symptoms of asthma, rhinoconjunctivitis and eczema in the main regions of the world in approximately 1,200,000 children. The results of the epidemiological survey showed that rhinoconjunctivitis was present in around 15% of 13-14-year-old children, which indicates a higher prevalence when compared with 6-7-year-old children (8.5%) (6).

Allergic rhinitis (AR) in children has some peculiarities. Even though nasal congestion is the main symptom in adolescents (7) halitosis deserves special attention due to the social impact that it can have in their lives.

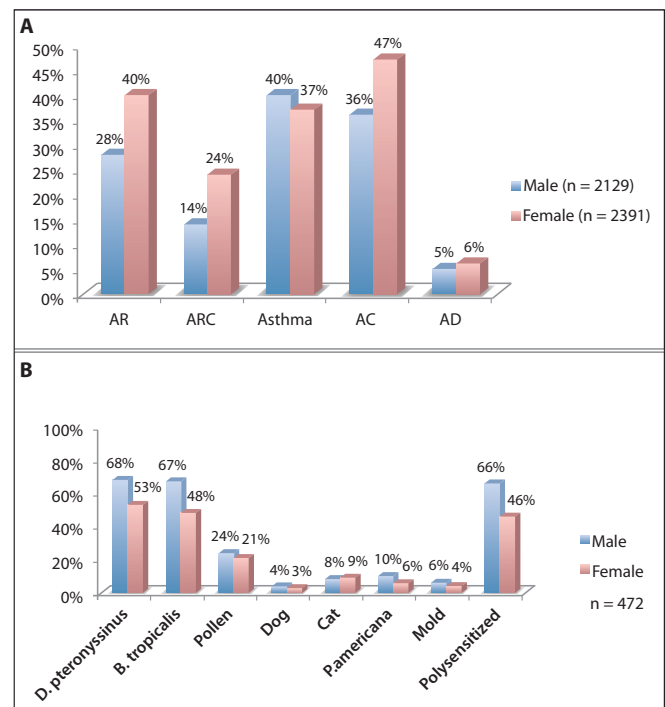
Comorbidities may facilitate the diagnosis of AR, such as asthma, eczema, pollen-food syndrome, sleep disorders and hearing impairment. Other conditions may lead to non-allergic non-infectious rhinitis diagnosis: esophageal reflux, hormonal dysfunction, exposure to irritants or specific drugs (8).

Sex differences in allergy

During childhood (0-10 years) prevalence of AR is higher among males compared to females. On the contrary, during adolescence (11-17 years) females display higher prevalence of AR compared to their male counterparts. However, when they reach adulthood (18-79 years), there is no difference in prevalence between genders. The same pattern occurs, even more pronounced, for prevalence of coexisting AR and asthma (9). Allergic rhinitis in obese teenage girls may be a risk factor for wheezing (10).

A recent analysis performed in 4,500 children aged 13-14 years has shown that females not only have a higher prevalence of AR compared to males, but also of allergic rhinoconjunctivitis (ARC), asthma, allergic conjunctivitis (AC) and atopic dermatitis (AD) (**figure 1 A**). Interestingly, there is an opposite allergic sensitization pattern with respect to gender, with more allergic

Figure 1 - (A) Prevalence of allergic diseases according to gender (n = 4,520). (B) Allergic sensitization pattern according to gender (n = 472).



AR: allergic rhinitis; ARC: allergic rhinoconjunctivitis; AC: allergic conjunctivitis; AD: atopic dermatitis. Adapted from reference 11 with permission.

sensitization in boys than in girls (**figure 1 B**). Moreover, it has also been observed that monosensitization is more frequent in females, while polysensitization is more common in males (11).

Approaching the patient

Effect of allergic rhinitis on Health Related Quality of Life (HRQoL)
AR and ARC have significant physical and mental impacts on the HRQoL of adolescents (12). Apart from the adverse effects of most antihistamines, which include sedating effects, AR/ARC leads to school absences and poorer performance due to distraction, fatigue and irritability. AR/ARC often produce embarrassment feelings which results in a poor interaction by peers, thus leading to isolation and low self-esteem. In addition, it also has a negative impact on the parents HRQoL, who frequently become anxious, overprotective and sometimes results on absenteeism.

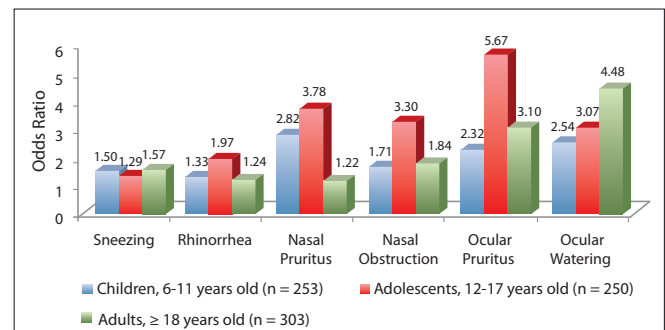
Illness comprehension by adolescents, particularly as they get older, influences their HRQoL and may be an important target for intervention aimed at improving their psychological well-being (13).

Despite the impact of AR on HRQoL of both adults and children, it is interesting how symptom perception differs in children, adolescents and older patients. A study performed on 806 French patients suffering from moderate-to-severe persistent ARC showed that the symptoms with highest impact on adolescents were nasal pruritus, nasal obstruction and ocular pruritus as evaluated by the rhinoconjunctivitis quality of life questionnaire (RQLQ) (**figure 2**) (14).

Few years ago, Juniper *et al.* already emphasized that the impairment of HRQoL in adolescents may not be the same as in adults and proposed a specifically designed questionnaire for adolescents with rhinoconjunctivitis (14). They propose that this questionnaire should include both physical and emotional functions, items that are important to adolescents with ARC. It should be short and include summary scores for each domain being amenable to statistical analysis and being responsive to clinically important changes.

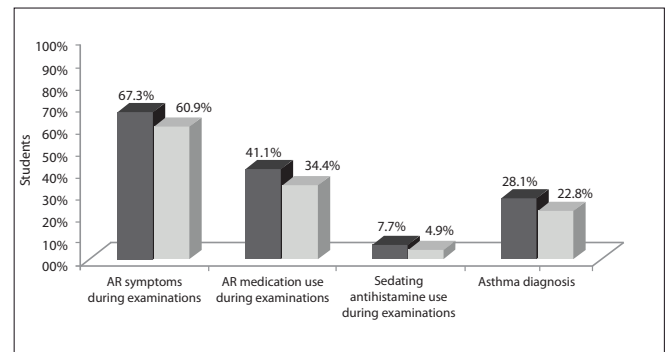
A case-control analysis involving 1,834 students has shown that seasonal allergic rhinitis is associated with a detrimental effect on exam scores in teenagers (15). This study distinguished between cases (consisting on students who dropped 1 or more their grades) and controls (students whose grades were either unchanged or improved). Data reported that cases were significantly more likely to have been diagnosed with asthma, to have had AR symptoms during exams and to have taken AR medication or sedating antihistamines compared to controls (**figure 3**). When measuring quality of life, data are collected directly from the patients, which somewhat differ from those obtained with the conventional measurement used in clinical practice. Instruments for measuring quality of life can be subdivided into generic and specific tools. The generic tools measure multi-di-

Figure 2 - Impact of symptoms on the RQLQ score.



Odds ratio [95% CI]. Adapted from reference 13 with permission.

Figure 3 - Association between allergic rhinitis and detrimental effect on examination in teenagers.



Black bars: case students; grey bars: control students; OR: odds ratio; adapted from reference 15.

mensions in different health conditions whereas specific tools are focus on measuring particular aspect of a certain disease. **Table I** illustrates available questionnaires to assess HRQoL in adolescents.

Treatment burden impact of AR and ARC

A study with the primary aim of validating a health-related QoL assessment in adolescents with rhinoconjunctivitis, asthma or both, has also reported on treatment aspects of these conditions, and found that a high proportion of adolescents are bothered by having to take medications and by experiencing bothersome medication adverse effects (AEs). The new QoL assessment tool proposed in this study, RHINASTHMA-Adolescents questionnaire, is comprised of 20 questions. The results of this survey revealed that the items with the greatest impact in HRQoL of adolescent patients were the following: feeling uncomfortable (81.4%), having a stuffy nose (68.2%), feeling

Table I - Available questionnaires to assess HRQoL in adolescents.

Author	Year	Description
Cui W <i>et al.</i> (16)	2013	Trends in adolescent HRQOL were assessed by using cross-sectional data from the 2001–2010 National Health and Nutrition Examination Survey. Adolescents' self-rated health and reported mental health declined significantly, especially among those in low-income families, but their physical health and activity limitation did not change.
Kim JH <i>et al.</i> (17)	2014	QOL-KCAR assessment tool comprising 10 questions was developed to assess the practical difficulties experienced in daily activities of Korean children with allergic rhinitis.
Juniper EF <i>et al.</i> (18)	1998	The Paediatric Rhinoconjunctivitis Quality of Life Questionnaire (PRQLQ) measures the quality of life impairments important to children with SAR. Children provide reliable and accurate responses, the measurement properties are strong.
Petersen DK <i>et al.</i> (19)	2008	The 15D instrument and the RQLQ instrument were capable of differentiating RC patients across different disease severities.
CDC (20)	2000	Medical Outcomes Study Short Forms (SF-12 and SF-36), the Sickness Impact Profile, and the Quality of Well-Being Scale.

limited in their social life (73.2%), being stressed by their parents (73.8%), breathing with difficulty (71.3%), having a runny nose (63.4%), being bothered by having to take drugs (81.9%) and the medication side effects (54.3%) (21).

Another study which surveyed parents of adolescents to assess the patient perceived burden of seasonal ARC revealed that the most important criteria for allergy medications were effectiveness, ease of use, consistency of relief, fewer AEs, rapid response and providing freedom to do more. In addition, the survey showed that the criteria that would make it easier for children to comply with medication were: convenient dosing schedule, fewer AEs, ease of use and better taste (22). Pediatric formulations of oral antihistamines and intranasal corticosteroids are available and significantly improve SAR symptoms in children and adolescents (23). Immunotherapy tablets (SLIT) can also improve HRQoL in adolescents with AR and conjunctivitis as observed in a recent two pooled double-blind placebo-controlled trials performed on 395 adolescents with house dust mite (HDM) allergic rhinitis. It can be observed a parallel increase in HDM-specific IgG4 in the active patient group after 4 weeks of treatment (24).

Perspectives

Things are changing, we are living a digital era, and treatment must be person-centered with the use of real-world evidence. In this context, ARIA (Allergic Rhinitis and its Impact on Asthma) has evolved from a guideline using the best evidence-based approach to develop care pathways suited to real-life using mobile

technology in AR and asthma multimorbidity. These include a novel phenotypic characterization of the patients, confirmation of the impact of AR on work productivity and treatment patterns in real life (23). Also, mobile technology MASK (Mobile Airways Sentinel network) allows every adolescent to search and be up to date on allergic diseases.

There is some understanding of the challenges faced by adolescents with asthma, but not so much with other allergic conditions. More studies are necessary, paying particular attention to the effects of allergic co-morbidities (24, 25).

Conclusions

It can be concluded that adolescence is a special period in which AR is highly prevalent with some sex-dependent differences. There are also peculiarities on how AR affects HRQoL of adolescent patients specifically. Considering the recent advances in the field, digital aid is the future. The success of treatment lies in the partnership between adolescents with AR and mobile technology, allowing them to have more information both on the disease and treatment.

Conflict of interests

NAR reports personal fees from Sanofi, Mylan, AstraZeneca, Chiesi, Abbott, Mantecorp and Abbvie outside the submitted paper. MM-A is Manager Medical Affairs: Sanofi, Gentilly-France. CSR is sub-investigator in clinical trials for Sanofi, AstraZeneca and FioCruz.

References

1. World Health Organization. Adolescent development. Available at: https://www.who.int/maternal_child_adolescent/topics/adolescence/development/en/. Last access date: 03/17/2020.
2. La Grutta S, Landi M, Braido F, *et al.* RHINASTHMA-Adolescents: a new quality of life tool for patients with respiratory allergy. *Pediatr Allergy Immunol* 2014;25:450-5.
3. Chipper H, Clinch J, Olweny CLM. Quality of life studies: definitions and conceptual issues. In: Spilker B. (ed). *Quality of Life and Pharmacoeconomics in Clinical Trials*. Philadelphia: Lippincott-Raven Press, 1990;pp. 11-23.
4. Yin S, Njai R, Barker L, Siegel PZ, Liao Y. Summarizing health-related quality of life (HRQOL): development and testing of a one-factor model. *Popul Health Metr* 2016;14:22.
5. Silva CHM, Silva TE, Morales NMO, Fernandes KP, Pinto RMC. Quality of life in children and adolescents with allergic rhinitis. *Braz J Otorhinolaryngol* 2009;75(5):642-9.
6. Mallol J, Crane J, von Mutius E, Odhiambo J, Keil U, Stewart A, ISAAC Phase Three Study Group. The International Study of Asthma and Allergies in Childhood (ISAAC) phase three: a global synthesis. *Allergol Immunopathol (Madr)* 2013;41(2):73-85.
7. Blaiss MS, Hammerby E, Robinson S, Kennedy-Martin T, Buchs S. The burden of allergic rhinitis and allergic rhinoconjunctivitis on adolescents: a literature review. *Ann Allergy Asthma Immunol* 2018;121(1):43-52.
8. Zicari AM, De Castro G, Leonardi L, Duse M. Update on rhinitis and rhinosinusitis. *Pediatr Allergy Immunol* 2020;31(Suppl 24):32-3.
9. Frohlich M, Pinart Gilberga M, Keller T, *et al.* Is there a sex-shift in prevalence of allergic rhinitis and comorbid asthma from childhood to adulthood? A meta-analysis. *Clin Transl Allergy* 2017;7:44.
10. Kalm-Stephens P, Nordvall L, Janson C, Neuman Å, Malinovskychi A, Alving K. Different baseline characteristics are associated with incident wheeze in female and male adolescents. *Acta Paediatr* 2020;109(11):2324-31.
11. Rosario CS. Fatores associados à conjuntivite alérgica em adolescentes de Curitiba, Paraná. [Dissertação] 2018. Available at: <https://hdl.handle.net/1884/65989>.
12. James P, Caballero MR. Illness perception of adolescents with allergic conditions under specialist care. *Pediatr Allergy Immunol* 2020;31:197-202.
13. Devillier P, Bousquet PJ, Grassin-Delyle S, *et al.* Comparison of outcome measures in allergic rhinitis in children, adolescents and adults. *Pediatr Allergy Immunol* 2016;27(4):375-81.
14. Juniper EF, Guyatt GH, Dolovich J. Assessment of quality of life in adolescents with allergic rhinoconjunctivitis: development and testing of a questionnaire for clinical trials. *J Allergy Clin Immunol* 1994;93(2):413-23.
15. Walker S, Khan-Wasti S, Fletcher M, Cullinan P, Harris J, Sheikh A. Seasonal allergic rhinitis is associated with a detrimental effect on examination performance in United Kingdom teenagers: case-control study. *J Allergy Clin Immunol* 2007;120(2):381-7.
16. Cui W, Zack MM. Trends in health-related quality of life among adolescents in the United States, 2001-2010. *Prev Chronic Dis* 2013;10:E111.
17. Kim JH, Ahn YM, Kim HJ, *et al.* Development of a questionnaire for the assessment of quality of life in Korean children with allergic rhinitis. *Allergy Asthma Immunol Res* 2014;6(6):541-7.
18. Juniper EF, Howland WC, Roberts NB, Thompson AK, King DR. Measuring quality of life in children with rhinoconjunctivitis. *J Allergy Clin Immunol* 1998;101(2 Pt 1):163-70.
19. Petersen KD, Kronborg C, Gyrd-Hansen D, Dahl R, Larsen JN, Løwenstein H. Quality of life in rhinoconjunctivitis assessed with generic and disease-specific questionnaires. *Allergy* 2008;63(3):284-91.
20. Centers for Disease Control and Prevention. *Measuring Healthy Days*. Atlanta, Georgia: CDC, November 2000.
21. Meltzer EO, Farrar JR, Sennett C. Findings from an online survey assessing the burden and management of seasonal allergic rhinoconjunctivitis in US patients. *J Allergy Clin Immunol Pract* 2017;5(3):779-89.
22. Bousquet J, Arnavielhe S, Bedbrook A, *et al.* MASK 2017: ARIA digitally-enabled, integrated, person-centred care for rhinitis and asthma multimorbidity using real-world-evidence. *Clin Transl Allergy* 2018;8(1):45.
23. Meltzer EO, Scheinmann P, Rosado Pinto JE, *et al.* Safety and efficacy of oral fexofenadine in children with seasonal allergic rhinitis – a pooled analysis of three studies. *Pediatr Allergy Immunol* 2004;15:253-60.
24. Matsuoka T, Bernstein DI, Masuyama K, *et al.* Pooled efficacy and safety data for house dust mite sublingual immunotherapy tablets in adolescents. *Pediatr Allergy Immunol* 2017;28:661-67.
25. Vazquez-Ortiz M, Angier E, Blumchen K, *et al.* Understanding the challenges faced by adolescents and young adults with allergic conditions: A systematic review. *Allergy* 2020;75(8):1850-80.