Section A-Research paper

Quality of Life among Allergic Rhinitis Children

Mohammed Sanad Nagiub, Amira Abd Elbadea Hefny, Mohammed Mahmoud Romih

Pediatrics Department, Faculty of Medicine, Zagazig University, Egypt

Email: dramirahefny89@gmail.com

Abstract

Allergic rhinitis (AR) defined as an immunoglobulin E (IgE) mediated inflammation of nasal mucosa as a result of contact to aeroallergens causing nasal symptoms such as nasal congestion, watery rhinorrhea, nasal itching and sneezing are primarily observed in patients with AR then Snoring or mouth breathing due to nasal obstruction, cough, loss of taste or smell are secondary chronic symptoms of allergic rhinitis. This condition is common in pediatric patients which severely affects their quality of life due to sleep disturbance, irritability or sleepiness affecting emotional, physical, and social aspects of quality of life. Although AR is a very common disease, it is often underdiagnosed. The prevalence of AR is globally increasing. A report from the World Health Organization (WHO) indicates that 40% of the population suffers from one or more allergic diseases When referring to an individual's health, it is called health-related quality of life (HRQL), it is the impact of an illness and its therapy upon a patient, as perceived by the patient himself so, the goal of therapy should be to reduce impairments that patients consider important. AR in children results in a variety of problems that may impair HRQL, such as the need to rub the eyes and nose, blow nose repeatedly, carry tissues, and take medications, children may have a variety of other limitations than adults, For example, children may have problems at school because of a learning impairment or may be unable to participate in individual or family activities such as playing sports on grass, playing with pets, and camping trips that will probably elicit allergic symptoms. In addition, children may have emotional disturbance as a result of an inability to fully integrate with their peers and they may feel isolated, leading to frustration, sadness, and anger. The pediatric rhino conjunctivitis quality of life questionnaire (PRQLQ) has 23 items in 5 domains (nasal symptoms, ocular symptoms, other symptoms, practical problems, and activities) that children answer on the basis of the previous week. Validation of the instrument has shown that most children give reliable and accurate response

Keywords: Allergic rhinitis

Introduction

Allergic rhinitis (AR) defined as an immunoglobulin E (IgE) mediated inflammation of nasal mucosa as a result of contact to aeroallergens causing nasal symptoms such as nasal congestion, watery rhinorrhea, nasal itching and sneezing are primarily observed in patients with AR then Snoring or mouth breathing due to nasal obstruction, cough, loss of taste or smell are secondary chronic symptoms of allergic rhinitis. This condition is common in pediatric patients which severely affects their quality of life due to sleep disturbance, irritability or sleepiness affecting emotional, physical, and social aspects of quality of life **(1)**.

Epidemiology of Allergic Rhinitis

Although AR is a very common disease, it is often underdiagnosed. The prevalence of AR is globally increasing. A report from the World Health Organization (WHO) indicates that 40% of the population suffers from one or more allergic diseases. Allergic rhinitis is the most common type of chronic rhinitis, affecting 10 to 20% of the population**,** In adults, the prevalence of AR varies from 10% to 30%, while in children it is nearly 40% **(2)**.

In Egypt:

Due to variances in geography and aeroallergens, different countries have different prevalence rates of allergic rhinitis.While the prevalence of physician-diagnosed asthma in Cairo was 9.4%, the prevalence of Allergic rhinitis was 15.3% , **(2).**

Age:

Acquisition of sensitization to inhaled allergens occurs progressively throughout childhood and got to peak in adult life. Seasonal AR is a disease particularly of teenagers and young adults and appears to be less common in primary and pre school age children. At this age perennial rhinitis with the prominent symptom of nasal blockage is more common,] Specifically, it affects 13% to 21% of preschool children, 15% of school-age children and teenagers, and approximately 40% of young adults. **(3)**

Sex:

Although males and females share identical mechanisms of the immune system, it was found that females were more likely to have asthma, hay fever, allergic rhinitis, or chronic bronchitis than were males**, (4).**

Classification of Allergic Rhinitis

Old classification: AR has been categorized as seasonal (occurs during a specific season) or perennial (occurs throughout the year). Conversely, not all patients fit into this classification. For example, some allergic triggers, such as pollen, may be seasonal in chiller climates, but perennial in warmer climates, and patients with multiple "seasonal" allergies may have symptoms through most of the year **(5)**.

Therefore, allergic rhinitis is now classified according to: symptom duration (intermittent or persistent) and severity (mild, moderate or severe)

- **According to symptom duration** Intermittent symptoms occur less than four days per week or for less than four consecutive weeks while in persistent allergic rhinitis symptoms are present more than four days per week or for more than four consecutive weeks**((6)**.
- **According to severity :** thy are classified into mild cases, characterized by normal sleep, no impairment of daily leisure, or sport activities, normal work or school and no troublesome symptoms and moderate or severe cases, characterized by one or more of the following: abnormal sleep, impairment of daily leisure, or sport activities, abnormal work or school and troublesome symptoms**((6)**.

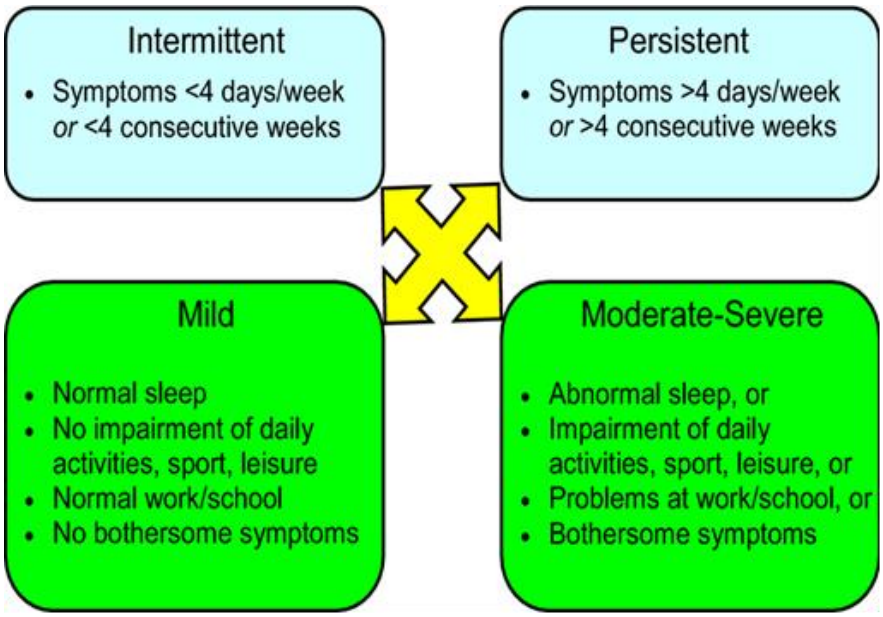

Figure 1: *Classification of allergic rhinitis according to symptoms duration and severity*.

Morbidity and mortality

Compared with other medical conditions, AR may not seem as serious as other medical diseases. However, the burden and expenditures are significant since AR lowers patients' quality of life, degrades their sleep and cognitive performance, and makes them irritable and exhausted. Additionally linked to poorer performance at school, especially during the peak pollen season. It is a frequent cause of visits to general practitioners' offices. **(6)**.

Allergic rhinitis is also associated with the subsequent development of asthma or lower airway disease. Children with allergic rhinitis and asthma had an increased prevalence of bronchial hyperresponsiveness to allergens in comparison with children with nonallergic rhinitis. The link between rhinitis and asthma has been highlighted in a World Health Organization report, Allergic rhinitis and its impact on asthma (ARIA), approximately 30% of patients with rhinitis develop asthma and up to 80% of patients with perennial asthma have rhinitis **(6)**.

Risk factors of allergic rhinitis:

Allergic rhinitis is a multifactorial disease with genetic as well as environmental factors influencing disease development **(6)**.

a. **Genetics and familial history:**

Allergic diseases such as asthma and rhinitis have closely related phenotypes and often occur with atopy. They show strong familial and intra-individual clustering, suggesting overlapping disease aetiology. However, some genetic polymorphisms have been associated with rhinitis alone **(7).**

b. Early-life risk factors:

Sensitization to allergens may occur in early life . Conditions like prematurity, low birth weight, growth retardation, hormones during pregnancy and perinatal asphyxia were all inconstantly related to the risk of developing allergic diseases or rhinitis**,** The influence of early childhood exposure to infections , animals and secondary tobacco smoke on the development of atopy and AR is still unknown **(8)**.

c. Ethnic groups:

The prevalence of Asthma and AR have been demonstrated by Spergel J.M with lower rates in many English-language and Western European countries and with concomitant higher rates in the developing world Africa, Latin America, and parts of Asia**,.** Also migrants from developing to industrialized countries seem to be at higher risk of allergy and asthma development, **(9).**

d. Allergen exposure:

Allergens are foreign bodies (protein or polysaccharides) that induce type I hypersensitivity reactions through eliciting Th2 immune responses, which culminate in IgE production and allergy, **(10).**

Exposure to environmental allergens is the most extensively studied potential risk factor for sensitization and manifestation of atopy. From a number of cross-sectional studies performed in children and in adults, it has become obvious that there is a close association between allergen exposure, particularly in the domestic environment, and sensitization to that specific allergen. Longitudinal studies like the MAS study in Germany have clearly demonstrated that during the first years of life there is a dose–response relationship between indoor allergen exposure to dust mite and cat allergens and the risk of sensitization to mites and cats, respectively, **(11).**

Aeroallergens are very often implicated in allergic rhinitis and asthma They are usually classified as indoor (principally house dust mites, pets, insects or from plant origin e.g. ficus), outdoor (pollens and molds) or occupational chemical agents (fumes and acids), **(12).**

Due to climatic conditions there are regional differences between allergens. It is therefore of importance for physicians to determine the allergens of their region, **(6)**.

Air pollution and increasing prevalence of allergic rhinitis

Air pollutants affect the prevalence of allergy. Many potentially hazardous substances are released into the air in increasing quantities each year. Approximately 25% of atmospheric aerosols are biogenic in origin, and they consist of pollen, plant fragments, mold spores, bacteria, crystalline proteins, animal epithelia, and

other particles. Unlike inorganic particles, bio aerosols are characterized by their aerodynamic diameters, which are different from crude physical diameters ***(13)***.

Studies have shown an association between high levels of air pollution and an increased risk of allergic sensitization and prevalence of rhinitis**.** The increase in atmospheric pollutant (NO2, SO2, PM10, etc.) levels could explain the current increase in the prevalence of AR **(14).**

Pathophysiology:

The nasal mucosa is in direct contact with the external environment; and it is exposed constantly to air pollutants, pathogenic viruses, bacteria, fungal spores, and allergens derived from pollens, house dust mites, and animal dander. Thus, the nose protects the lower airways from the harmful effects of the inspired air in addition to warming and filtering the inspired air, **(15)**.

Allergic rhinitis is characterized by a two phases of allergic reaction: an initial sensitization phase where allergen exposure results in IgE formation as well as induction of the humoral response, and subsequent clinical disease after repeated antigen exposure The clinical allergic reaction can also be further subdivided into early- and late-phase responses: the early or immediate response-phase occurs within minutes after allergen exposure while the late phase-response starts 4-8h after allergen exposure **(16).**

1.Sensitization phase:

During the sensitization process, Antigen-Presenting Cells (Macrophages and Dendritic Cells) capture and process the allergen to present it to the T Cells (T CD4+ type 2 [Th2]) through the Major Histocompatibility Complex type II (MHC II). (Th2) cells then release IL-3, IL-4, IL-5, and IL13 which allow B cell differentiation into plasma cells (PC). These cells are responsible for the IgE production **(16).**

2. Clinical allergic reaction: subdivided into

a. Early-phase response: This phase is mediated by mast cells and basophils. Cross-linking of IgE with an allergen result in rapid (5 mins) release of a variety of mediators from these two cells types, including histamine, prostaglandins, kininogens and proteases (tryptase, chymase) and TNF-α This occurs 5 mins after allergen exposure. These mediators are responsible for some of the common symptoms associated with allergic rhinitis such as rhinorrhea **(16).**

Within 15 minutes, the mast cells secrete a new set of inflammatory mediators which are products of the metabolism of arachidonic acid, including prostaglandin D2 and the cystenil leukotrienes C4, D4 and E4; platelet-activating factor is also produced: cystenil leukotrienes, and bradykinin, cause blood vessels to dilate and stimulate the mucosal glands leading to mucosal edema, watery rhinorrhea and subsequent nasal congestion **(16).**

These mediators also cause sensory neural stimulation. Sensory nerves stimulation leads to the release of neurotransmitter which in turn produces itching and sneezing. The neurotransmitters released include the sensory neuropeptides, substance P, neurokinin A, and calcitonin gene-related peptide (CGRP) **(16).**

b. Late-phase response : The late phase response that may occur 4 - 6 hours after allergen exposure is characterized by the recruitment of inflammatory cells, (eosinophils, basophils, macrophages and T cells), as a result of endothelial cell activation in postcapillary venules by the inflammatory mediators released during the early phase which in turn promote the expression of vascular cell adhesion molecule-1 and E-selectin facilitating the adhesion of circulating leukocytes to the endothelial cells. Chemoattractants such as the chemokines and IL-5 promote further cell migration which then become activated and release additional inflammatory mediators resulting in increased symptoms usually associated with nasal congestion, **(17).**

Accumulation of mast cells, Th2 cells, basophils and eosinophils has been found in the airway epithelium. **(18).**

Complications of Allergic Rhinitis

AR in children can have numerous complications that have a major impairment on the child and the family **(19).**

- ***Physical complications including:***

Chronic rhinosinusitis which is characterized by nasal congestion or discharge persisting for longer than 3 months. Chronic rhinosinusitis may also demonstrate nasal polyps due to chronic inflammation of paranasal sinus mucosa. Nasal polyps are usually benign and bilateral. Its incidence in the general population is approximately 4% and more common in males **(20)**.

Adenoid hypertrophy is another complication; Sensitization to allergens in AR can alter immunological parameters of the adenoids, resulting in hypertrophy **(21)**.

Allergic asthma: AR and Asthma are linked epidemiologically, pathologically, physiologically and therapeutically and can be considered as a manifestation of a single inflammatory airway syndrome, In the past, allergic rhinitis was considered to be a disorder localized to the nose and nasal passages, but current evidence indicates that it may represent a component of systemic airway disease involving the entire respiratory tract, **(22).**

There are a number of physiological, functional and immunological relationships between the upper (nose, nasal cavity, paranasal sinuses, pharynx and larynx) and lower (trachea, bronchial tubes, bronchioles and lungs) respiratory tracts. For example, both tracts contain a ciliated epithelium consisting of goblet cells that secrete mucous, which serves to filter the incoming air and protect structures within the airways. Furthermore, the submucosa of both the upper and lower airways includes a collection of blood vessels, mucous glands, supporting cells, nerves and inflammatory cells. Evidence has shown that allergen provocation of the upper airways not only leads to a local inflammatory response, but also to inflammatory processes in the lower airways, and this is supported by the fact that rhinitis and asthma frequently coexist. Therefore, allergic rhinitis and asthma appear to represent a combined airway inflammatory disease, and this needs to be considered to ensure the optimal assessment and management of patients with allergic rhinitis **(22).**

Eustachian tube dysfunction also complicates AR and affects 10 to 40% of AR patients. Some other associated complications include otitis media with effusion, persistent cough, and eosinophilic esophagitis **(24)**.

- ***Mental and cognitive complications:***

AR results in: Irritability, depression, impairment of sleep and limitation of activities at school as well as home for children. also fatigue and impairment of cognition and memory in children which significantly affect the learning process and therefore significantly affect the quality of life for patients with AR **(25)**.

Quality of Life of Allergic Rhinitis Children

When referring to an individual's health, it is called health-related quality of life (HRQL), it is the impact of an illness and its therapy upon a patient, as perceived by the patient himself so, the goal of therapy should be to reduce impairments that patients consider important. Unlike many other disorders whose treatment may be centered on preventing death or future morbidity, the goal of treatment of allergic rhinitis (AR) is to improve a patient's well-being, or quality of life (QoL) **(19).**

AR in children results in a variety of problems that may impair HRQL, such as the need to rub the eyes and nose, blow nose repeatedly, carry tissues, and take medications, children may have a variety of other limitations than adults, For example, children may have problems at school because of a learning impairment or may be unable to participate in individual or family activities such as playing sports on grass, playing with pets, and camping trips that will probably elicit allergic symptoms. In addition, children may have emotional disturbance as a result of an inability to fully integrate with their peers and they may feel isolated, leading to frustration, sadness, and anger. **(19).**

"Comorbid disorders often associated with rhinitis, including asthma, sinusitis, otitis media, and frequent respiratory infections, can further compromise QoL. Pharmacologic treatments can have both positive and negative effects on QoL. Agents that have troublesome adverse effects such as sedation can have a negative impact on QoL in patients of all ages with rhinitis" **(19).**

Allergic Rhinitis Quality of Life Questionnaire (QoLQ)

The pediatric rhino conjunctivitis quality of life questionnaire (PRQLQ) has 23 items in 5 domains (nasal symptoms, ocular symptoms, other symptoms, practical problems, and activities) that children answer on the basis of the previous week. Validation of the instrument has shown that most children give reliable and accurate response. It has a time specification of the previous week so children were asked to recall their experiences during this period, because this is the maximum length of time over which younger children can recall their experiences with any degree of accuracy. The questionnaire was developed to measure the problems that patients with allergic rhinitis experience in their day-today lives. **(26)**.

Symptoms scoring of AR:

The following scale can be used for each symptom scoring: 0 = no symptom, 1 = mild (symptom was of short duration and not annoying), 2 = moderate (symptom was frequently annoying but did not interfere with normal daily activity or sleep), or 3 = severe (symptom interfered with normal daily activity or sleep). The total nasal symptom score (TNSS) is the sum of the scores for the individual symptoms. TNSS values (0–12) are categorized as mild (0–4), moderate (5–8), and severe (9–12) **(26).**

q**Prognosis of Allergic Rhinitis**

"The belief is that the prevalence of allergic rhinitis peaks in adolescence and gradually decreases with advancing age. In a longitudinal study, at the time of the 23-year follow up, 54.9% of patients showed improvement in symptoms with 41.6% of those being symptom-free. Patients who had an onset of symptoms at a younger age were more likely to show improvement. The severity of AR can vary over time and depends on a variety of factors such as location and season" **(27).**

References

1. Komnos, I. D., Michali, M. C., Asimakopoulos, A. D., Basiari, L. V., & Kastanioudakis, I. G. (2019). The Effect of Allergic Rhinitis on Quality of Life in Patients Suffering from the Disease: A Case Control Study. International Journal of Otolaryngology and Head & Neck Surgery, 8(4), 121-131.
2. Roxbury, C. R., Qiu, M., Shargorodsky, J., & Lin, S. Y. (2018). Association between allergic rhinitis and poor sleep parameters in US adults. Paper presented at the International forum of allergy & rhinology.
3. Dziekanski M, Marcelino T. Quality of life in pediatric patients with allergic rhinitis treated at the Medical Clinic of Integrated Education – Unisul.
4. Pleis J.R., Ward B. and Lucas J.W, Nathan RA., Meltzer E.O and Derebery J (2008) The prevalence of nasal symptoms attributed to allergies in the United States: findings from the burden of rhinitis in an American survey. Allergy Asthma Proc 29. (6): 600-608.Summary Health Statistics for U.S. Adults: National Health Interview Survey,. Vital Health Stat 10 249. 1-86.
5. Lee, P. & Mace, S. (2009). An approach to allergic rhinitis. Allergy Rounds, 1, 1.
6. Brozek, J. L., Bousquet, J., Baena-Cagnani, C. E., Bonini, S., Canonica, G. W., Casale, T. B., ... & Schuenemann, H. J. (2010). Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 revision. J Allergy clin immunol, 126(3), 466-76.
7. Kurz T, Altmueller J, Strauch K, Ruschendorf F, Heinzmann A and Moffatt MF (2005) A genome-wide screen on the genetics of atopy in a multiethnic European population reveals a major atopy locus on chromosome 3q21.3. Allergy. ;60(2):192-9.
8. Hagerhed-Engman L, Bornehag CG, Sundell J, et al., (2006): Day-care attendance and increased risk for respiratory and allergic symptoms in preschool age. Allergy; 61(4):447-53.
9. Tedeschi A, Barcella M, Bo GA and Miadonna A (2003) Onset of allergy and asthma symptoms in extra European immigrants to Milan, Italy: possible role of environmental factors. Clin Exp Allergy. Apr;33(4):449-54.
10. Schaible B, Schaffer K and Taylor CT (2010) Hypoxia, innate immunity and infection in the lung. Respiratory Physiology & Neurobiology 174: 235–243.
11. Ownby D., Johnson Cand Peterson E (2002) Exposure to dogs and cats in the first year of life and risk of allergic sensitization at 6–7 years of age. JAMA ; 288:963-972.

12. Marogna M, Massolo A, Berra D, Zanon P, Chiodini E and Canonica GW (2006) The type of sensitizing allergen can affect the evolution of respiratory allergy. Allergy.;61(10):1209-15.

13. Simons FE (2004) Advances in H1-antihistamines. N Engl J Med 351: 2203- 2217.

14. Kim H, Bernstein JA. Air pollution and allergic disease. Curr Allergy Asthma Rep. 2009; 9:128–133.

15. Eccles R (2008) Anatomy and Physiology of the Nose and Control of Nasal Airflow. Middleton's Allergy 7th Edition. Philadelphia: Mosby: 702-711.

16. Rosenwasser LJ (2011) Understanding of the Pathophysiology of Allergic Rhinitis. Immunol Allergy Clin N Am 31: 433-439.

17. Jeffery P and Haahtela T (2006) Allergic rhinitis and asthma: inflammation in a one-airway condition. BMC Pulm Med 6: S5.

18. Howarth PH, Salagean M and Dokic D (2000) Allergic rhinitis: not purely a histamine-related disease. Allergy 55: 7-16.

19. Meltzer, Eli O. (2006). Allergic rhinitis: managing the pediatric spectrum. In Allergy and asthma proceedings (Vol. 27, No. 1, pp. 2-8). OceanSide Publications, Inc.

20. Skoner, D. P. (2001). Allergic rhinitis: definition, epidemiology, pathophysiology, detection, and diagnosis. Journal of allergy and clinical immunology, 108(1), S2-S8.

21. Solomon, C. G. (2015). Lisa M. Wheatley, MD, MPH, and Alkis Togias, MD. N Engl J Med, 372, 456-463.

22. Bourdin A, Gras D, Vachier I and Chanez P (2009) Upper airway 1: Allergic rhinitis and asthma: united disease through epithelial cells. Thorax, 64:999-1004.

23. Yáñez, A., & Rodrigo, G. J. (2002). Intranasal corticosteroids versus topical H1 receptor antagonists for the treatment of allergic rhinitis: a systematic review with meta-analysis. Annals of Allergy, Asthma & Immunology, 89(5), 479-484.

24. Yáñez, A., & Rodrigo, G. J. (2002). Intranasal corticosteroids versus topical H1 receptor antagonists for the treatment of allergic rhinitis: a systematic review with meta-analysis. Annals of Allergy, Asthma & Immunology, 89(5), 479-484.

25. Jauregui I, Mullol J, Davila I, Ferrer M, Bartra J, del Cuvillo A, Montoro J, Sastre J and Valero A (2009) Allergic rhinitis and school performance. J Investig Allergol Clin Immunol;19 Suppl 1:32-9.

26. Juniper, E. F., Thompson, A. K., Ferrie, P. J., & Roberts, J. N. (2000). Development and validation of the mini Rhinoconjunctivitis Quality of Life Questionnaire. Clinical and experimental allergy: journal of the British Society for Allergy and Clinical Immunology, 30(1), 132-140.

27. Durham, S. R., Emminger, W., Kapp, A., Colombo, G., de Monchy, J. G., Rak, S., Scadding, G.K., Andersen, J.S., Riis, B., & Dahl, R. (2010). Long-term clinical efficacy in grass pollen–induced rhinoconjunctivitis after treatment with SQ-standardized grass allergy immunotherapy tablet. Journal of allergy and clinical immunology, 125(1), 131-138. e137.