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REVIEW ARTICLE

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Allergic rhinitis and dental caries: A systematic review

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Abstract
Objective: Dental caries is one of the most common chronic diseases affecting millions of people globally. Some studies revealed the presence of bidirectional relationship between allergic rhinitis (AR) and oral diseases, with each disease having a potential impact on the other. In this study we aimed to systematically review the literature and analyze the available evidence regarding whether AR contributes to the development of dental caries.
Methods: Three authors, members of the YO-IFOS rhinology study group, independently analyzed the data sources (Pubmed, the Cochrane Library, EMBASE, SciELO) for papers assessing the relationship between rhinitis and caries, in adult and pediatric patients.
Results: Eight studies met the inclusion criteria (87612 participants). Six studies were performed in children. A total of three studies found an association between AR and dental caries. Only two studies had adjusted the measure of effect for potentially confounding variables. Regarding the quality of the selected studies according to the NICE classification, the most observed methodological limitations detected were: (1) the cross-sectional design of the included studies which could have introduced a simultaneity bias, and (2) not clearly reporting the inclusion and exclusion criteria.
Conclusion: This systematic review can neither confirm nor deny the presence of an association between AR and caries. Despite the evidence is very scarce to conclude a relationship between AR and caries, the option for examining patients with repetitive caries by an otolaryngologist and those with AR by odontologist should be considered, as these examinations do not possess any risk for the patient.

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Introduction

Dental caries is the decay of teeth mediated by bacterial infection. It is one of the most common chronic diseases affecting millions of people globally.[1] It is mainly caused by the formation of bacterial biofilm (dental plaque) over teeth, that results in mineral loss from dental hard tissues.

Allergic rhinitis (AR) is the mucosal inflammation of the nasal epithelia, mediated by an allergic mechanism. It is also a common disease, with an increasing prevalence in recent decades.[2] The International Study of Asthma and Allergies in Childhood (ISAAC) reported that after 7 years of follow-up, the prevalence of allergic rhinitis increased in 83% of the included centers.[2]

Some studies revealed the presence of bidirectional relationship between AR and oral diseases, with each disease having a potential impact on the other.

On one hand, it has been suggested that oral pathogens can act as potential mitigators of allergic diseases,[3] though inconsistent findings are available in the literature. Growing up in a clean environment decreases the exposure to bacteria and thus contributes to a reduced immunity which increases the probability of suffering an allergic disease.[4]

On the other hand, several hypotheses suggest that AR leads to poor oral health. These hypotheses are supported by several facts. Firstly, AR complicates nasal breathing, making the patients breathe mainly through their mouth. Chronic mouth breathing causes the evaporation of saliva which is essential for controlling the temperature, humidity, and pH of the mouth.[5] It is well established that patients with significantly reduced saliva due to xerostomia or Sjögren's syndrome are highly susceptible to oral infections, dental caries, or periodontitis.[6] Secondly, saliva plays an important role in the oral immune defense, as it contains antimicrobial agents such as secretory IgA and lysozyme. Hyposialia or salivary hyposecretion diminishes the presence of these antimicrobial agents and hence contributes to dental caries formation. Thirdly, saliva is rich in ions that maintain the pH in the oral cavity near neutrality between 6.2 and 7.4, which is vital for the prevention of caries and teeth demineralization. Therefore, hyposialia could trigger the formation of dental caries.

Other studies on the association between AR and dental caries have reported completely different results, making it necessary to review this topic in a systematic way.

Accordingly, in this study, we aimed to systematically review the literature and analyze the available evidence regarding whether AR contributes to the development of dental caries.

Methods

The protocol of this review is registered in PROSPERO under the identification number: CRD4202126202. The study was carried out following the recommendations of A Measurement Tool to Assess Systematic Reviews (AMSTAR-2) guidelines.

Literature search—Inclusion and exclusion criteria

The criteria for including studies in this systematic review were based on the population, intervention, comparison, and outcome (PICOTS) framework.

Participants: participants suffering from allergic rhinitis
Intervention: none
Comparison: two groups: patients with rhinitis and patients free from rhinitis
Outcomes: the presence of dental caries
Timing and **setting**: without limitation
Types of studies: Clinical trials, case series, and prospective and retrospective cohort study designs were included.

Exclusion criteria

Exclusion criteria consisted of the following: (1) studies carried out on syndromic patients; (2) duplicated publications; (3) studies with mixed outcomes on different dental disorders; and (4) case reports, theses, or meetings communications.

Search strategy

We undertook the search strategy following PRISMA guidelines. We searched the following databases until July 2021: PubMed (Medline), the Cochrane Library, EMBASE, and SciELO. We used a predefined search strategy, as described in Supplementary data 1. The abstracts of the retrieved papers were thoroughly reviewed by the three authors who were members of the YO-IFOS Rhinology Study Group (CCH, PRR, GMC). Abstracts potentially fulfilling the inclusion criteria were selected for full-text review. In case of discrepancies between the reviewers regarding the selection of the abstracts, the corresponding papers were included in the full-text review stage for final assessment. We also manually reviewed the references of all selected articles to identify any potentially missing publication.

The search strategy was carried out without any date, publication type, or language restrictions.

Study extraction, categorization, and analysis

Two authors (CCH and PRR) independently reviewed the articles that met the inclusion criteria and extracted the relevant data. Whenever a discrepancy arose, it was resolved by referring to a third reviewer (FGB).

Extracted variables encompassed: sample size, age, method used to diagnose dental caries and allergic rhinitis, measure of the association between allergic rhinitis and caries (odds ratio or risk ratio and their 95% CI), and the main outcome (dental carries).

Assessment of quality of included studies

Two authors (CCH and PRR) independently assessed the quality of included studies. The reviewers rated the level of evidence

and checked the risk of bias and the control of the measurement of association for confounding variables. Discrepancies were resolved by referring to a third reviewer (FGB).

The level of evidence was classified according to the Oxford Center for Evidence-Based Medicine Levels. The risk of bias was assessed according to the Quality Assessment of case series studies checklist from the National Institute for Health and Clinical Excellence (NICE).[7] We inspected the following items:

1 Was the case series collected from more than one center?
2 Is the hypothesis, aim, or objective of the study clearly described?
3 Are the inclusion and exclusion criteria clearly reported?
4 Are the reported outcomes clearly defined?
5 Was the data collected prospectively?
6 Is there an explicit statement about the consecutive recruitment of the patients?
7 Are the main findings of the study clearly described?
8 Are the outcomes stratified by confounding factors?

The control of confounding variables was assessed through a checklist developed for the purpose of this study. We examined whether the studies controlled for the presence of asthma, socioeconomic status, use of medication, diet, oral hygiene habits, use of fluoride supplements, and laryngopharyngeal reflux.

Statistical analysis

Data was analyzed using STATA for Macintosh v. 15.1 (StataCorp®). Statistical significance level was considered with a P-value < 0.05. Comparison tests were not possible in this study. The math used with STATA was mean sample size and mean age weighted for total sample, cases, and controls.

RESULTS

Search results

A flowchart of the search process is represented in Figure 1. The initial search resulted in 182 publications. After reviewing all titles and abstracts, 20 studies were selected for full text revision. Twelve publications were excluded for the

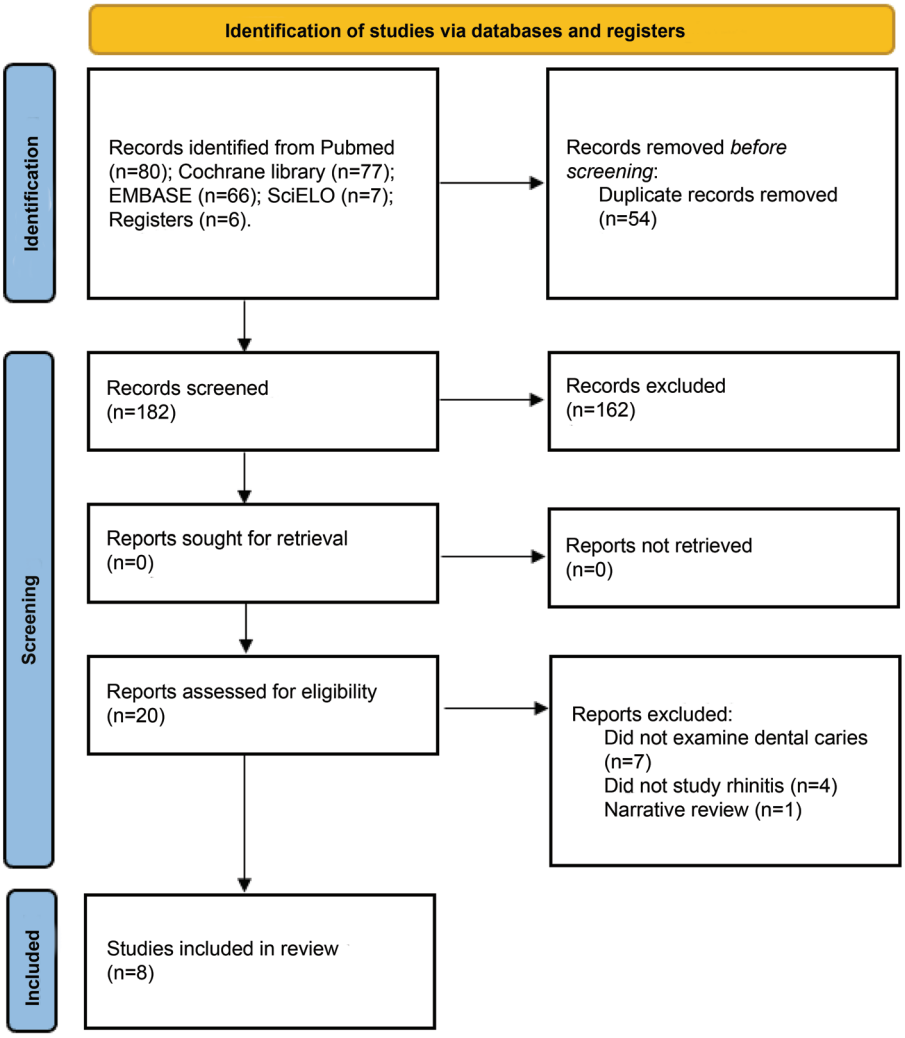

Figure 1 PRISMA flowchart.[20]

following reasons: 7 did not examine dental caries,[8-14] 4 did not study rhinitis,[15-18] and 1 was a narrative review.[19]

Eight studies met the inclusion criteria.[21-28] They involved a total of 87,612 participants: 11569 with allergic rhinitis, 17,888 with dental caries, 54,251 without allergic rhinitis, and 3904 free from dental caries. All eligible studies were of cross-sectional design, with the exception of Ho et al., who performed a retrospective cohort study. The mean age adjusted by sample size was 18.02 years for the entire study participants. The lowest and the maximum mean ages were 4.5[26] and 20 years,[21] respectively. Six studies were performed in children.[12,22-26] Three studies did not report the mean age of the included participants.[12,25,27] The mean age of the participants in the remaining studies was 8.42 years in AR children and 8.39 years in children without AR.

Association between AR and dental caries

The results of included studies are summarized in Table 1. A total of three studies found an association between AR and dental caries.[21-23]

Two of the 6 studies carried out in children, found a significant association between dental caries and AR.[22,23] Bakhshaee et al.[22] used the DMFT index (decayed, missing, and filled teeth) to ascertain the presence of caries. They did not find any significant association between AR and dental caries in the global DMFT, but found an association between the missing and filled teeth. Chuang et al. determined the incidence of dental caries development per year, and found a statistically significant association between AR and dental caries. Regarding the other three studies that did not find an association between AR and dental caries, these studies applied different dental caries diagnoses criteria; Wongkamhaeng et al. applied the DMFT index,[24] Herrström et al. used the number of dental fillings or amalgams,[12] while Tanaka et al.[25] and Vazquez-Nava et al. determined the amount of caries.[26]

Two studies were performed in adults.[21,27] Ho et al. carried out a longitudinal study of 5-year follow-up period, and found a statistically significant association between AR and caries.[21] Kim et al., using the DMFT index, did not find any significant association with self-reported AR.[27]

Quality of included studies

The quality of the included studies is summarized in Table 2. According to the NICE classification, the study by Ho et al. obtained the highest quality score. The most observed methodological limitations detected in the selected studies were: (1) the cross-sectional design of the included studies which could have introduced a simultaneity bias, and (2) not clearly reporting the inclusion and exclusion criteria.

Only two studies (Ho et al. 2019 and Chuang et al. 2018) adjusted the measure of effect for potentially confounding variables. Ho et al. controlled the effect of asthma, socioeconomic status, and the presence of laryngopharyngeal reflux, while Chuang et al. controlled the presence of asthma and medication intake. Table 3 summarizes the list of confounding factors that were considered in each of the eight included studies.

DISCUSSION

To the best of our knowledge, this is the first systematic review about the association of AR and dental caries. The investigated problem is recent as more than half of included studies were published in the latest 10 years. AR was suggested to be associated with several oral diseases such as periapical lesions, periodontitis, or pulpitis.[14] However, this review focused on the formation of dental caries exclusively in order to allow comparison of findings from different studies.

Only three out of eight included studies reported a statistically significant association between AR and caries. Regarding the mechanism behind the possible relationship between dental caries and AR, it is noteworthy mentioning the oral bacteria hypothesis. *Mutans streptococci* (MS), a group of cariogenic bacteria, are involved in the initiation of dental caries.[29] Wongkamhaeng et al. found an increased number of mutant Streptococci in children with AR compared to controls.[24] They attributed it to the fact that those children are mouth breathers. However, in relation to mouth-breathing hypothesis, Lee et al. in their study, which involved 1831 children,[15] did not find any association between mouth breathing and caries, which does not coincide with the hypothesis of AR causing cavities through a mouth-breathing mechanism. Another possible hypothesis is the low salivary flow rate. Medications may play a role in hyposalivation. At present, more than 500 drugs cause xerostomia or salivary hypofunction as an adverse effect.[30] Exposure to antihistamines was suggested to contribute to a lower salivary flow rate.[31] However, Wongkamhaeng et al. did not find any association between AR and salivary flow rate.[24]

Most studies failed to control for confounding factors. Caries development can be provoked by several factors,[32,33] including salivary flow rate, low quality of salivary buffer capacity, high levels of cariogenic bacteria, insufficient fluoride exposure, frequent consumption of sugar, toothbrushing, medication intake, and/or possibly mouth breathing. Therefore, to identify the potential determinant of dental caries, the measure of association should be controlled for all these confounding factors. The association of some of these confounding factors with AR and dental caries is discussed below.

Asthma has been related to dental caries,[34] as well as to AR.[35] Therefore, asthma might act as a confounding factor in the association between AR and dental caries. Only two included studies had been controlled for asthma using subgroup and logistic regression analysis.[21,23]

Socioeconomic status is known to be associated with asthma, AR and teeth care. Therefore, it might act as a confounding factor in the association between AR and dental care. AR is more prevalent in high-income individuals, while teeth disease is more frequent in individuals with low income.[28]

As Chuang et al. pointed out,[23] dental caries affects almost every child (93.34% of their study population), and thus a large sample size is required in order to detect differences between AR-exposed and unexposed groups. If we define a 1% difference in the caries prevalence between groups, a common variance of 5%, with an alpha (type-I error) of 0.05 and 80% statistical power, the minimum

Table 1 Description of the included studies.

Author (Year)	Design / Level of evidence	Cohort (sample size)	Sex (M, F)	Age (years). Mean ± SD (range)	Diagnosis of oral health	Variable	Result	Diagnosis of rhinitis	Main finding
Kim and Lee (2019)	Cross-sectional Level 4	Allergic rhinitis (486)	37.04% M; 62.96% F	NR ± NR (30-NR)	Medical records review	DMFT index	6.88 ± 0.26	Questionnaire	- No SSD between groups in DMFT (P = 0.138). - Less periodontitis in allergic rhinitis patients (P < 0.001) - More caries in patients with asthma (p=0.028)
		Controls (3243)	42.98% M; 57.02% F			DMFT index	7.26 ± 0.13		
Ho (2019)	Retrospective cohort study Level 4	Allergic rhinitis (7884)	41.18% M; 58.82% F	20 ± NA (NA)	Medical records review	Incidence of caries in a 5-year period	79.7%	Medical records review	- SSD (P < 0.001) between AR and non-AR in the incidence of caries. - No SSD for asthma.
		Controls (43,555)	45.12% M; 54.88% F			Incidence of caries in a 5-year period	69.1%		
Chuang et al. (2018)	Cross-sectional study (9-year period) Level 4	Allergic Rhinitis (2719)	60.10% M; 39.90% F	9 ± NA (NA)	Medical records review	Caries (mean incidence/year)	1.03 ± NR	Medical records review	- Allergic rhinitis is associated with an increased incidence of caries, but less severe (P < 0.001) - Asthma is not associated with an increased incidence of caries (P = 0.873)
		Controls (6319)	49.64% M; 50.35% F	9 ± NA (NA)		Caries (mean incidence/year)	0.89 ± NR		
Bakhshaee et al. (2017)	Cross-sectional Level 4	Suspected allergic rhinitis (77)	54.5% M; 45.5 F	5.23 ± 0.83 (5-7)	Dentist examination	DMFT index	5.13 ± 3.7	Physical examination and questionnaire.	- No SSD in DMFT (P = 0,07) - SSD in missing (p=0.01) and filling teeth (P = 0.02) - OR of poor oral health 1.21 (1.05-1.35)
		Controls (219)	47.5% M; 52.5 F	5.35 ± 0.78 (5-7)		DMFT index	4.23 ± 3.3		
Wongkamhaeng et al. (2014)	Cross-sectional Level 4	Confirmed allergic rhinitis (40)	62.5% M; 37.5% F	8 ± NR (6- 13)	Dentist examination	Combined DMFT/ DMFT index	3.0 ± NR	Specialist examination: Prick test	- No SSD in caries (P = 0.20). - No SSD in salivary flow rate (P = 0.10) - SSD in mutant Streptococci (P = 0.01; OR=2.23)
						Salivary flow rate (ml/min)	0.50 ± NR		
						Mutant Streptococci: prevalence (%) and CFU/ml.	57.5%; 11×10^5		

		Controls (40)	40% M; 60% F	9 ± NR (NR)		Combined DMFT/ DMFT index	4.0 ± NR		
						Salivary flow rate (ml/min)	0.76 ± NR		
						Mutant Streptococci: prevalence (%) and CFU/ml.	5%; 3 × 10^5		
Vázquez-Nava et al. (2008)	Cross-sectional Level 4	Allergic rhinitis (334)	50.2% M; 49.8 F	4.5 ± 0.5 (4-5)	2 dentist examinations	DMFT index	1.02 ± 2.37	Questionnaire and physical examination	- No SSD between children with and without allergic rhinitis in caries prevalence (P = 0.321)
		Controls (826)				DMFT index	NR ± NR		
Tanaka et al. (2008)	Cross-sectional Level 4	At least 1 decayed or filled teeth (17,888)	49.39% M; 50.61% F	NR ± NR (6-15)	Dentist examination	Rhinitis prevalence	7.4%	Questionnaire	- An inverse association between dental caries and the prevalence of allergic rhinoconjunctivitis was apparent only in children with a positive parental allergic history (OR: 0.84 [95% CI: 0.72, 0.99])
		No decayed or filled teeth (3904)				Rhinitis prevalence	8.4%		
Herrström and Högstedt (1994)	Cross-sectional Level 4	Allergic rhinitis (29)	62.07% M; 37.93% F	NR ± NR (13-15)	Medical records review	Number of dental amalgams	1.36 ± NR	Questionnaire	- No SSD were found between allergic rhinitis and no allergic rhinitis in number of dental amalgams (P = 0.90) and dental fillings (P = 0.54)
						Number of dental fillings	2.46 ± NR		
		Controls (49)	NR			Number of dental amalgams	1.40 ± NR		
						Number of dental fillings	2.94 ± NR		

AR: Allergic rhinitis; CFU: Colony forming unit; DMFT: Decayed, missing, and filled teeth (in uppercase for permanent teeth and lowercase for primary dentition); NA: Not applicable; NR: Not reported; OR: odds ratio; SSD: (Statistically significant differences

Table 2 Assessment of the risk of bias.

	1) Was the case series collected in more than one center?	2) Is the hypothesis/aim/ objective of the study clearly described?	3) Are the inclusion and exclusion criteria clearly reported?	4) Is there a clear definition of the outcomes reported?	5) Were data collected prospectively?	6) Is there an explicit statement regarding whether patients were recruited consecutively?	7) Are the main findings of the study clearly described?	8) Are outcomes stratified?
Kim and Lee (2019)	Yes	Yes	No	Yes	No	NA	Yes	Yes
Ho et al. (2019)	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Chuang et al. (2018)	Yes	Yes	Yes	Yes	No	NA	Yes	Yes
Bakhshaee et al. (2017)	Yes	Yes	No	Yes	No	NA	Yes	No
Wongkamhaeng et al. (2014)	No	No	No	Yes	No	NA	Yes	No
Vázquez-Nava et al. (2008)	Yes	Yes	No	Yes	No	NA	Yes	Yes
Tanaka et al. (2008)	Yes	Yes	Yes	Yes	No	NA	No	Yes
Herrström and Högstedt (1994)	No	Yes	Yes	Yes	No	NA	Yes	No

NA: Not applicable

Table 3 Control of confounding factors: Highlighted if authors performed a statistical analysis to control confounding factors.

Author	Asthma	Socioeconomic status	Medication	Diet	Oral hygiene habits	Fluoride supplements	LPR reflux	Final score (%)
Kim and Lee (2019)	Yes	Yes	No	No	Yes	No	No	42.86%
Ho et al. (2019)	Yes	Yes	No	No	No	No	Yes	42.86%
Chuang et al. (2018)	Yes	No	Yes	No	No	No	No	28.57%
Bakhshaee et al. (2017)	No	Yes	No	No	Yes	Yes	No	42.86%
Wongkamhaeng et al. (2014)	No	No	Yes	Yes	Yes	Yes	No	57.14%
Vázquez-Nava et al. (2008)	No	Yes	No	Yes	Yes	No	No	42.86%
Tanaka et al. (2008)	Yes	No	No	Yes	No	No	No	28.57%
Herrström and Högstedt (1994)	Yes	No	No	No	No	No	No	14.29%

LPR: Laryngopharyngeal reflux

sample size to detect a significant association should be at least 788 participants. Therefore, the sample size of three reviewed studies was relatively small in order to detect the association between AR and dental caries.[12,22,24]

The medication used to treat AR may contribute to the occurrence of dental caries. Inhalation of corticosteroids was associated with an increase in the incidence of dental caries and periodontitis.[36] Corticosteroids induce a change in oral pH and modify local deposition of steroids in the oral cavity which consequently affect the oral mucosa.[36] Exposure to AR medication was only considered in two studies,[21,23] yet the corresponding data was not adequately managed. Both studies found an increased risk of dental caries in patients on topical nasal medication. However, this observation could reflect the severity of AR instead of the effect of the exposure to AR medication. Previous studies suggested a dose-response association between AR severity and dental illness.[8] Chuang et al. found a significant association between dental caries and the use of first- and second-generation antihistamines, b2-agonist, and topical nasal drugs.[23] Anti-allergic drugs were suggested to affect the salivary flow rate, which might explain the association between exposure to those drugs and the development of dental caries.[31] However, Kiykim et al. did not find any evidence of poorer oral health (DMFT, total teeth decay and fillings, gingival inflammation, dental plaque) in children receiving immunotherapy to treat AR as compared to healthy controls.[13]

The use of fluoride supplements, which prevent dental caries formation, might also act as a confounding factor. In fact, Bakhshaee et al. found that the exposure to fluoride is higher in children with AR than those free from AR.[22] However, the increased odds of allergic rhinitis in these children could also be related to socioeconomic status, as it facilitates odontological treatments. As socioeconomic status is also related to allergic rhinitis, fluoride treatment may act as confounding factor, being related to the exposure (AR) and the outcome (dental carries).

Some reports suggested that patients may develop allergy to the materials used in dental repair. Herrström et al. studied the prevalence of AR, dermatitis, and asthma according to the presence or absence of dental amalgams or dental fillings.[12] They found that the prevalence of AR and dermatitis is similar between patients with and without dental amalgams or dental fillings; however, the prevalence of asthma was lower in patients with amalgam restoration.

Several other potentially confounding variables should be also considered, such as diet, oral hygiene habits, and laryngopharyngeal reflux.[37,38] Another major methodological concern is the method used to diagnose AR or caries. AR should ideally have been diagnosed by a specialist (otolaryngologist, allergist, or pediatrician). However, the presence of AR was ascertained through self-reporting in more than half of the reviewed studies.[12,22,25-27] AR was adequately determined in three studies; Wongkamhaeng et al.,[24] who did not find a significant association, performed prick test analysis, and Chuang et al.,[23] and Ho et al.,[21] who reported a significant association between dental caries and AR, reviewed the patients' medical records.

Studies were homogeneous regarding the diagnosis of dental caries. All studies had referred to a dentist; however, they differed in the way of reporting the information on dental carries diagnosis. Three studies used the DMFT index.[22,24,27] A visual oral examination without radiography, is likely to underestimate the prevalence of dental caries, especially that of approximal and occlusal caries.[39]

The cross-sectional design of the majority of studies included in this review is also a concern. Cross-sectional studies suffer from simultaneity bias and are unable to determine a causal inference. Therefore, using this design, it cannot be established which of AR and dental caries occurs first.

Currently, clinical guidelines on caries, such as the American guidelines,[33] do not recommend screening or treatment of AR. Otolaryngology guidelines, such as the Spanish position paper on nasal obstruction,[40] also do not encompass the systematic examination of caries in patients suffering from AR. Our review of the literature does not provide evidence to support a formal recommendation of AR or dental care screening. Nonetheless, as the association between AR and dental caries could not be ruled out and certain hypotheses justify the association, we recommend the inclusion of AR or dental care screening in the otolaryngology respiratory medicine guidelines, respectively, as an option for clinicians.

As the conclusions drawn from a systematic review depend on the quality of the included studies, the main limitation of this review is the low quality of the available evidence. This is not a criticism to the effort made by the authors of included studies as it is almost impossible to control for all the potential confounding factors. The number of studies eligible for this review, especially those undertaken in adults, is low. And finally, the studies carried out in children had mixed permanent, decidual, and mixed dentition.

Conclusions

This systematic review can neither confirm nor deny the association between AR and caries. Despite the evidence is very scarce to conclude a relationship between AR and caries, the option for examining patients with repetitive caries by an otolaryngologist and those with AR by odontologist should be considered, as these examinations do not suppose any risk for the patient.

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