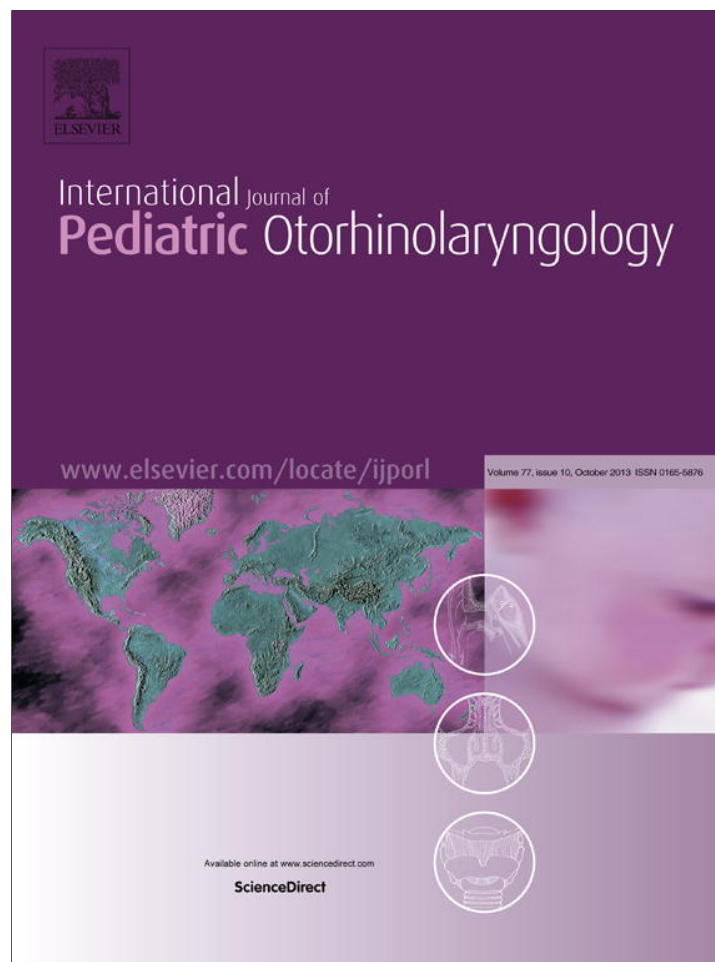


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Recurrent acute otitis media in infants: Analysis of risk factors



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ABSTRACT

Objective: Recurrence acute otitis media (RAOM) may cause a considerable morbidity and a great parental concern. The aim of this study was to analyze the risk factors that are likely to be responsible for RAOM in infants, and their impact on treatment failure.

Methods: A retrospective study on 340 infants with RAOM was conducted. Data were collected from hospital charts. A 10 days course of amoxicillin/clavulanate was used for treatment of recurrence, while surgical management in the form of adenoidectomy and/or myringotomy was reserved for patients with persistent disease. We analyzed various risk factors that may affect the prognosis of RAOM, including: age, prematurity, upper respiratory tract infections (URTI), duration of breastfeeding, use of pacifiers, parental smoking, seasonality, the presence of siblings (family size), gender, adenoid hypertrophy, allergy, and craniofacial abnormalities.

Results: Use of pacifiers, short duration of breastfeeding, older infantile age, winter season, URTI and presence of adenoid hypertrophy were identified as risk factors for RAOM. Treatment failure may be due to adenoid hypertrophy, short duration of breastfeeding and it is more common in older age infants. We did not find a significant association between RAOM and gender, prematurity, exposure to passive smoking, the presence of siblings, allergy, craniofacial abnormalities.

Conclusions: Factors that may cause recurrence of the disease in infant population are use of pacifiers, short duration of breastfeeding, older infantile age, winter season, upper respiratory tract infections and adenoid hypertrophy. Also, treatment failure may be caused by adenoid hypertrophy and short duration of breastfeeding. Good understanding of these factors may help to decrease the recurrence rate and to improve the treatment of the disease.

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1. Introduction

Acute otitis media (AOM) is one of the most common infections in children. It remains the leading cause of doctors' consultations by children and the most common reason for children to take antibiotics [1,2]. By the age of 2 years, 70% of all children have suffered at least one episode of AOM, and approximately 5–15% of children experience four or more episodes per year [3,4].

After an uncomplicated attack of AOM, the child may face the problem of recurrent episodes of AOM. If at least 3 episodes occur in 6 months, then the patient is said to experience recurrent acute otitis media (RAOM) [1,3]. Factors that may be responsible for recurrence of the disease include: an increase in using pacifiers, a decrease in duration of breastfeeding, upper respiratory tract infection (URTI), winter season, presence of obstructive adenoid, young age, prematurity, parental smoking, the presence of

siblings (family size), allergy, and craniofacial abnormalities [1,3,5–8].

Recurrent AOM may cause a considerable morbidity and a great parental concern with each attack. The disease may also cause long-term middle ear damage, endangering hearing. Furthermore, it can cause major complications such as mastoiditis and facial paralysis [9], thus reliable epidemiological data on etiology and management of AOM are important to make well-informed health policy decisions [2].

The aim of this study was to analyze the risk factors that are likely to be responsible for recurrent episodes of AOM in infants, and their impact on treatment failure.

2. Methods

A retrospective study was conducted. The data were acquired from patients' files of 666 AOM patients below the age of 2 years presented to the outpatient clinic of the Pediatric Otorhinology Unit of Cairo University Hospital during the period from May 2011 to April 2012.

Only 400 cases were documented to have RAOM, we excluded 60 infants who have had the following criteria: infants who had

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previous chronic otitis media with effusion, infants of episodes less than 3 in 6 months, or who underwent tympanostomy tubes insertion, and infants who did not continue the follow up period for at least 6 months. Only 340 infants who fulfilled the study criteria were included in this work.

Data were collected from hospital charts. Medical history has been fulfilled by the parents including; number of attacks and their duration, symptoms of disease, previous medical treatment, family history of allergic rhinitis, and parental smoking.

Diagnosis was based on otoscopy (congested and/or bulging eardrum, or otorrhea) and presence of acute signs of infection (fever, pain, irritability), according to the guidelines of the Dutch College of General Practitioners [10]. Examination also included search for any possible risk factors as obstructive adenoid, allergy and any possible craniofacial abnormalities as cleft palate either overt or submucous type.

All infants were treated with antibiotics. A 10 days course of amoxicillin/clavulanate 90 mg/kg per day has been conducted [11]. The clinical outcome was evaluated after treatment, and every 4 weeks using otoscopy, tympanometry to detect middle ear effusion complicating the otitis media, and X-ray for detection of adenoid hypertrophy.

The antibiotic course has been repeated on recurrence of AOM, while surgical management in the form of adenoidectomy and/or myringotomy was reserved for patients with persistent disease despite antibiotic treatment.

We analyzed various risk factors that may affect the prognosis of RAOM, including: age, prematurity, URTI, the duration of breast-feeding, use of pacifiers, parental smoking, seasonality, the presence of siblings (family size), gender, presence of obstructive adenoid obliterating the choana, allergy, craniofacial abnormalities.

According to Monobe et al. [12], early recurrence was considered if the symptoms and signs of AOM reappeared within 1 month after an initial improvement. Treatment failure was considered when there was persistence or worsening of symptoms and signs of acute infection for up to 1 week following the initial treatment. And RAOM was defined as having three episodes or more within a period of 6 months.

2.1. Statistical analysis

Data was summarized using mean or median and standard deviation or percentiles for quantitative variables and frequency and percentage for qualitative variables. Comparison between groups was done using independent sample t test for quantitative variables, Chi square test or Fissure exact test for qualitative variables. Multivariate analysis was used for prediction of binary outcomes through logistic binary regression model. It had shown predictors of probability of treatment failure among the risk factors. Omnibus tests of model coefficients were done and X^2 , p value, and R^2 were detected. p values equal to or less than 0.05 were considered statistically significant.

All collected questionnaires were revised for completeness and consistency. Pre-coded data was entered on the computer using "Microsoft Office Excel Software" program (2010) for windows. Data was then transferred to the Statistical Package of Social Science Software program, version 15 (SPSS) to be statistically analyzed.

3. Results

Three hundred and forty infants with RAOM were enrolled in this study, data in hospital files were reviewed with special attention to the predisposing factors that may be responsible for recurrence of the disease (Table 1), number of episodes of AOM, treatment failure, and early recurrence.

Table 1
Descriptive statistics.

		Frequency (N = 340)	Percentage
Age	3–6 months	113	33.2
	6–24 months	227	66.8
Sex	Males	210	61.8
	Females	130	38.2
URTI		219	64.4
Breastfeeding	<3 months	80	23.5
	>3 months	260	76.5
Parental smoking		87	25.6
Use of Pacifier		73	21.5
Seasonality	Winter	218	64.1
	Others	122	35.9
Prematurity		62	18.2
Presence of siblings		213	62.6
Obstructive adenoid		58	17.1
Allergy		152	44.7
Craniofacial abnormalities		14	4.1

The age of the studied patients was ranged from 3 to 24 months. They were divided into two age groups, 3–6 months (113 infants = 33.2%) and 6–24 months (227 infants = 66.8%). The study included 210 males (61.8%) and 130 females (38.2%). Out of the 340 infants with RAOM, URTI was detected in 219 infants (64.4%). Infants' breastfed less than three months were 80 (23.5%), while infants' breastfed more than three months were 260 (76.5%). Parental smoking was discovered in 87 infants (25.6%). 73 infants (21.5%) were users of pacifier. 218 infants (64.1%) presented during winter season, while 122 (35.9%) presented in other seasons. Premature infants (less than 37 weeks) were 62 (18.2%). 213 infants (62.6%) belonged to families with more than one sibling. 58 infants (17.1%) presented with obstructive adenoid, and 152 infants (44.7%) showed positive family history of allergic rhinitis. Regarding the craniofacial abnormalities, overt cleft palate was detected in 6 infants (1.8%), and submucous cleft palate in 8 infants (2.3%).

All infants received medical treatment, 221 infants (65%) showed early recurrence of AOM, 91 patients (26.8%) showed treatment failure and they necessitated surgical intervention in the form of myringotomy and/or adenoidectomy. Seven patients with obstructive adenoidal hypertrophy had undergone adenoidectomy only, as they did not develop treatment failure.

There were 1777 episodes of AOM among the 340 infants during the follow up period, with a range of 3 to 10 and a mean of 5.23 episodes per patient. The relations between risk factors and the number of episodes of RAOM were studied (Fig. 1).

RAOM was proved to have statistical significant relationships with age, URTI, breastfeeding, use of pacifier, and obstructive adenoidal hypertrophy (with p value <0.001, =0.001, 0.005, 0.005, 0.001 respectively). Recurrence tended to be more in infants more than 6 months of age (mean \pm SD = 5.6 \pm 1.7) than in younger group (mean \pm SD = 4.6 \pm 1.3), more in infants presented with URTI (mean \pm SD = 5.8 \pm 1.8) than in others without URTI (mean \pm SD = 5.1 \pm 1.6). Also, the recurrence was more in infants with breastfed less than 3 months (mean \pm SD = 5.7 \pm 1.9) than in infants with breastfed more than 3 months (mean \pm SD = 5.1 \pm 1.6). Infants using pacifiers showed a high recurrence rate (mean \pm SD = 5.8 \pm 1.8) relative to infants who did not use pacifiers (mean \pm SD = 5.1 \pm 1.6). Infants with obstructive adenoid developed high recurrence (mean \pm SD = 6.5 \pm 1.9) in relation to infants without adenoid hypertrophy (mean \pm SD = 5.0 \pm 1.5).

The relationship between seasonality and RAOM was statistically significant (p value = 0.03), with more tendency for recurrence in winter season (mean \pm SD = 5.4 \pm 1.7) than in other seasons (mean \pm SD = 5.1 \pm 1.6).

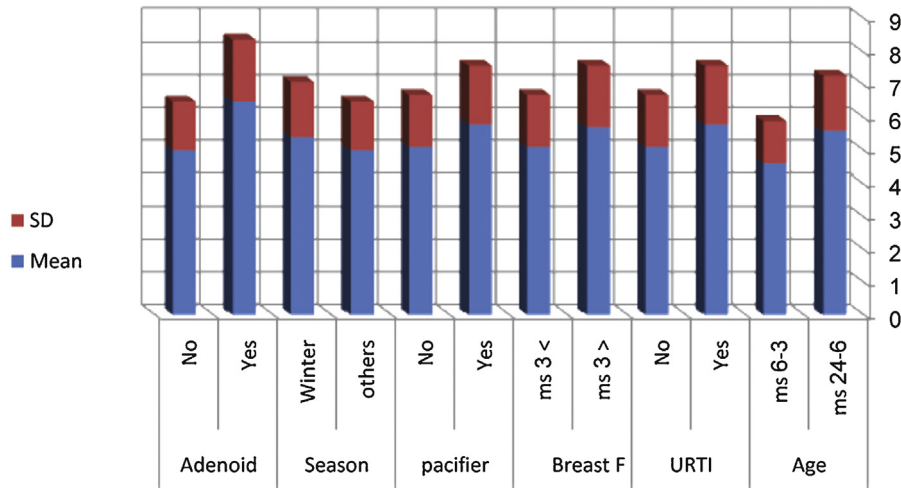


Fig. 1. Mean and standard deviation of number of AOM attacks with different significant risk factors; Breast F = breastfeeding, URTI = upper respiratory tract infection.

On the other hand, the relationships between RAOM and gender, prematurity, exposure to parental smoking, the presence of siblings (family size), allergy, craniofacial abnormalities, were statistically insignificant (p value > 0.05).

The relationships between early recurrence and each of the studied factors were proven to be statistically insignificant (p value > 0.05).

Treatment failure (Fig. 2) was found in 88% of infants with obstructive adenoid, compared to 20.9% of infants without adenoid hypertrophy, producing a highly significant relationship between treatment failure and adenoidal hypertrophy (p value < 0.001).

A significant statistical relation was reported between age and treatment failure, 30.8% of infants between 6 and 24 months of age developed failure of treatment compared to 18.6% of infants below 6 months of age (p value = 0.02).

Treatment failure was seen more in infants with breastfed less than three months (36.3%) compared to infants with breastfed more than three months (23.8%), the relationship was statistically significant (p value = 0.03).

The relationships between treatment failure and URTI, sex, parental smoking, use of pacifier, seasonality, prematurity, family

size, and craniofacial abnormalities were statistically insignificant (p value > 0.05).

Application of the logistic regression model revealed that short duration of breastfeeding and presence of adenoid hypertrophy represented significant risk factors for the treatment failure of RAOM (p value = 0.006, $p < 0.001$ respectively).

Based on these analyses, odds ratios (ORs) for the probability of treatment failure were calculated as: 2.265 for period of breastfeeding, and 4.632 for obstructive adenoid.

4. Discussion

The burden of RAOM for the health care system and the society in general is significant. It causes a considerable morbidity and great parental concern with each attack [13]. It may also cause long-term middle ear damage, and if not properly treated, can cause significant hearing loss, which may potentially result in speech, language, and cognitive skills impairment [2]. Furthermore, it can cause major complications such as mastoiditis and facial paralysis [9].

In addition to morbidity, complications and adverse developmental effects, RAOM episodes entail considerable financial

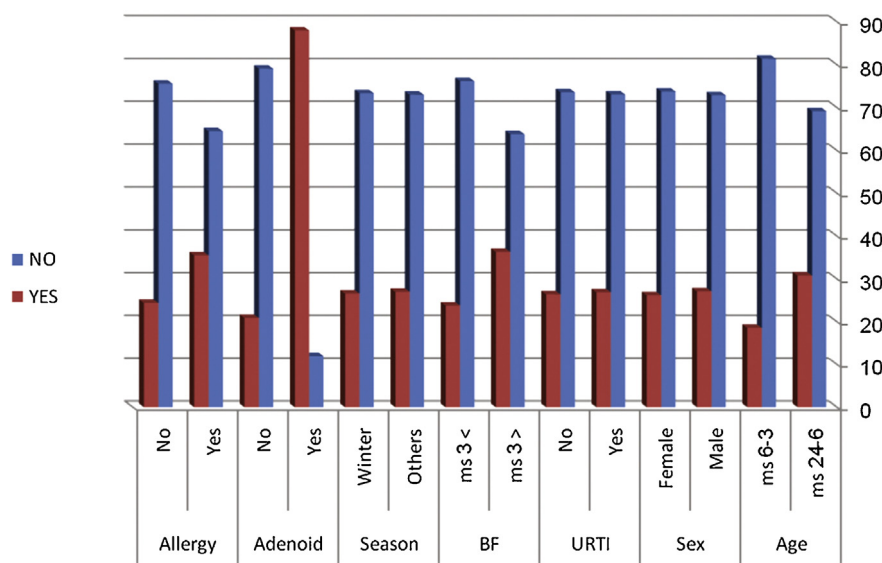


Fig. 2. Association between treatment failure of RAOM and some risk factors; BF = breastfeeding, ms = months; URTI = upper respiratory tract infection; Yes = treatment failure; No = no treatment failure.

burden in the form of medical visits, medication use, and parental time taken off from work [8]. The number of visits for otitis media in US increased from 9.5 to 24.5 million between 1975 and 1990 [2]. Furthermore, RAOM is among the most ordinary causes for children to be anesthetized for myringotomy and/or adenoidectomy [13]. Thus reliable epidemiological data on etiology and burden of RAOM are important to make well-informed health policy decisions [2].

All infants in this study were treated with antibiotics. A 10 days course of amoxicillin/clavulanate 90 mg/kg per day has been conducted [11]. On the other hand, some authors in Europe and the US do not recommend the use of antimicrobial agents for AOM, as it has been reported that most cases of AOM improve without use of antimicrobial agents and also, in the Netherland it has been proposed that antimicrobial agents are unnecessary in at least 90% of cases, and that patients should be observed for 3–4 days without antimicrobial agent administration [14].

AOM is an infectious disease that is influenced by various environmental factors [13]. Otitis-prone children often have a defective or immature antibody response specially a reduced level of immunoglobulin G2 (IgG2) [15]. Risk factors for RAOM have widely been studied and several investigators identified many risk factors for RAOM as young age, short duration of breastfeeding, male gender, URTI, use of pacifiers, exposure to passive smoking, seasonality, the presence of siblings (family size), prematurity, presence of obstructive adenoid and allergy [1,3,5–7].

Inflammatory process in the middle ear and Eustachian tube (ET) in the first 6 months of life is a risk factor for RAOM. Alternatively, an early attack may reflect an innate predisposition (physiological or anatomic) for middle ear disease, in which the early affection is a marker for underlying predisposing factor [3,16]. In their study on 8900 children, Teele et al. [3] found that infants between 6 and 11 months of age were at the greatest risk for AOM and the recurrence rate was also higher in those who had their first attack before the age of 18 months. In contrast, Sipila et al. [17] examined the number of episodes of AOM in young children with a mean age of 25 months and they concluded that the most important risk factor was group nursing, whilst prolonged breastfeeding increased protection against AOM during the first year of life. In our study, we found that the age is a highly significant risk factor for recurrence of AOM ($p < 0.001$), infants between 6 and 24 months of age were associated with a high incidence of RAOM (mean \pm SD = 5.6 ± 1.7) compared with infants less than six months of age (mean \pm SD = 4.6 ± 1.3). This may be attributed to the fact that most infants below the age of 6 months are usually breastfed that has a protective function due to its immunoglobulin contents.

In this study, we found a highly significant relationship between URTI and RAOM as frequency of recurrent episodes of AOM was found more among infants presented with URTI (mean \pm SD = 5.8 ± 1.8) than those who did not have URTI (mean \pm SD = 5.1 ± 1.6). Similar findings have been found in the study conducted by Koivunen et al. [18] that is revealed an estimated risk of AOM in children with URTI ranges between 26% and 43%. It was reported that AOM is usually preceded by a viral upper respiratory tract infection causing impairment of the mucociliary function of the ET, which permits the bacterial infection to proceed into the middle ear [13].

Bottle-feeding increases the incidence of RAOM compared to breastfeeding, a meta-analysis of risk factors for AOM showed that breast-feeding for at least 3 months reduces the risk of AOM [5]. Breastfeeding has been significantly associated with decreasing the risk of AOM during the first 3 years of life and RAOM during the first year of life [3]. Many hypotheses have been suggested to provide reasons for this effect: the presence of immunological and non-immunological antiviral and antibacterial factors in the breast

milk, allergy to cow milk or formula milk with resulting changes in the upper respiratory tract mucous membrane, difference in development of facial musculature between breast-fed and bottle-fed children, or difference in position between breastfeeding and bottle feeding [16].

In the present study, similar results have been documented. The period of breast feeding has had a statistically significant impact on RAOM. We found that infants who were breastfed for less than three months were associated with an increased incidence of developing RAOM (mean \pm SD = 5.7 ± 1.9) compared with infants who were breastfed for more than three months (mean \pm SD = 5.1 ± 1.6) ($p = 0.005$). Also, Teele et al. [3] and Duffy et al. [19] found that short duration of breastfeeding, i.e. less than 3 months, increases the risk for AOM. On the other hand, in a retrospective cohort study of 106 nursing infants, Harsten et al. [20] have found no significant difference in the number of otologic visits among children that were exclusively breastfed, breastfed with supplementary feeding and bottle-fed only. However, Daly et al. [7] showed that breastfeeding decreases the risk of AOM during the first 6 months of life, although the association of exclusive breastfeeding and RAOM was not as statistically significant as it is on respiratory and gastrointestinal infections.

Usage of pacifier may increase the risk of RAOM. Niemela et al. [21] in a sample of 938 children, demonstrated that those used pacifiers had a greater risk of developing four or more episodes of AOM than those who did not use them. Similar finding has been found in our study, in which infants that used pacifiers had a greater risk of RAOM (mean \pm SD = 5.8 ± 1.8) more than those who did not use them (mean \pm SD = 5.1 ± 1.6). The relationship had been proven to be statistically a highly significant one.

Many authors have observed that the incidence of AOM was highest during the fall and winter months and lowest in the summer months. It was proven that a child born in the fall has a higher risk of RAOM, possibly because these children spent their vulnerable early months of life during the peak months of exposure to winter respiratory pathogens. Even regardless of climate, otitis media is more frequent in the winter months, presumably due to crowding in schools and in large group daycare centers during the URTI season [7,16]. Henderson et al. [22] confirmed the chronologic proximity of otitis media to URTI in daycare setting regardless of the time of the year. In contrast, Teele et al. [3] and Paradise et al. [23] did not find a statistically significant association between the occurrence of AOM and seasonality. In our study, we found a significant positive association between winter season and the recurrent episodes of AOM (mean \pm SD = 5.4 ± 1.7) compared to other seasons (mean \pm SD = 5.1 ± 1.6) ($p = 0.03$).

This study showed a statistically highly significant relation between adenoid hypertrophy and recurrent episodes of AOM, as infants presented with adenoid hypertrophy had greater rate of AOM (mean \pm SD = 6.5 ± 1.9) in relation to infants who did not have adenoid hypertrophy (mean \pm SD = 5.0 ± 1.5). Adenoid may act as a bacterial reservoir that increases the incidence of recurrent episodes of AOM, Brook et al. [24] studied qualitative and quantitative microbiology of adenoid tissue and they found that the number of potential pathogens was higher in adenoid of children with RAOM, recurrent adenotonsillitis and obstructive adenoid hypertrophy than in the controls. The presence of adenoid hypertrophy with or without infection may be an important factor in the occurrence of RAOM because of the close relationship between these lymphoid tissues with the ET, adenoid hypertrophy may block the tube and colonization of the adenoids with upper airway pathogens may be the main source of infection to the middle ear [25]. However, Koivunen et al. [26] detected that adenoidectomy alone or associated with ventilation tube placement does not play a role in the prophylaxis against RAOM in children younger than 2 year.

We did not find a significant association between RAOM and gender, prematurity, exposure to passive smoking, the presence of

siblings (family size), allergy, craniofacial abnormalities. Some authors found that there is a higher incidence of AOM in males and parental smoking may be a predisposing factor for recurrence of AOM during the first year of life, while, a family history of allergies or asthma are not significantly associated with an increased risk of RAOM [3,7].

The impact of the chosen factors on early recurrence, and treatment failure was studied in order to give prognostic indicators in cases of AOM. In this study, the relationships between early recurrence and each of the studied factors were proven to be statistically not significant. While, treatment failure was reported in 88% of infants with obstructive adenoid, 30.8% of infants between 6 and 24 months of age, and 36.3% in infants breastfed less than three months with a highly significant relationship between treatment failure and adenoid hypertrophy ($p < 0.001$), and significant statistical relations with age and duration of breastfeeding ($p = 0.02$, 0.03 respectively). The relationships between treatment failure and URTI, sex, parental smoking, use of pacifier, seasonality, prematurity, family size, and craniofacial abnormalities were statistically insignificant.

Application of the logistic regression model revealed that short duration of breastfeeding and presence of adenoid hypertrophy represented significant risk factors for the treatment failure of RAOM ($p = 0.006$, $p < 0.001$ respectively).

Careful study of the related risk factors for RAOM, and their impact on treatment failure and early recurrence is recommended for better understanding of the disease process. This will help a good planning for screening programs and provide helpful prognostic indicators in order to achieve better preventive measures that can reduce AOM among infants.

It is worth mentioning that our study was based mainly on investigating the relation between RAOM and their risk factors from the clinical point of view, however a bacteriologic and an immunological correlates should be considered in further studies.

5. Conclusion

RAOM is a considerable health problem that needs a special concern due to its morbidity and financial burden. Some factors have an impact on recurrence of AOM in infant population. Use of pacifiers, short duration of breastfeeding, older infantile age, winter season, URTI and presence of adenoid hypertrophy were identified as risk factors for RAOM. Treatment failure may be due to the presence of adenoid hypertrophy, short duration of breastfeeding and it is more common in older age infants.

Conflict of interest

The authors declare that they have no conflict of interest.

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