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Factors affecting the occurrence of otitis media with effusion in preschool and elementary school children: a comparative cross-sectional study

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ABSTRACT

Objective Identify the risk factors for otitis media with effusion (OME), especially laryngopharyngeal reflux (LPR), adenoid hypertrophy and allergic rhinitis, that could be used to develop prevention strategies in children.

Design A comparative cross-sectional study was conducted to make sure the adequacy of proportions of OME and non-OME cases in finding the related factors.

Setting History taking, ear/nose/throat (ENT) examination, and tympanometry were performed in preschool and elementary schools. Flexible fibreoptic nasopharyngolaryngoscopy was performed in a bronchoesophagology outpatient clinic in a tertiary referral hospital in Jakarta, Indonesia.

Participants Preschool and elementary children in East Jakarta, Indonesia were recruited for this study. A total of 2016 participants underwent history taking, ENT examination and tympanometry. The case group was 46 children with OME, and the control group was 46 children without OME. The number of subjects fulfilled the minimum sample size for two proportions comparison.

Main outcome measures A type B tympanogram indicated OME. A Reflux Finding Score of more than 7 indicated LPR. Adenoid hypertrophy was diagnosed using flexible fibreoptic nasopharyngolaryngoscopy. Allergic rhinitis was diagnosed using a questionnaire based on the International Study of Asthma and Allergies in Childhood phase III that has been validated for Indonesians.

Results The proportion of LPR in the OME group was significantly higher than in the non-OME group, at 78.3% and 52.2%. The probability of OME occurrence in patients with LPR was 3.3 times higher than in patients without LPR (OR 3.3; 95% CI 1.33 to 8.189; p=0.01). There was no significant relationship between adenoid hypertrophy and OME (p=0.211; 95% CI 0.71 to 3.97), and also between allergic rhinitis and OME (p=0.463; 95% CI 0.61 to 4.28).

Conclusion The probability of OME occurrence in patients with LPR was 3.3 times higher than in patients without LPR. LPR should be considered in patients with OME and vice versa.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Stratified random sampling, multistage random sampling and spatial random sampling were used for sample selection to represent the large population.
⇒ The control group was randomly chosen from patients without otitis media with effusion who were age and sex matched with the case group.
⇒ Flexible fibreoptic nasopharyngolaryngoscopy was performed blindly between the two groups to reduce examiner bias.
⇒ Allergic rhinitis was not diagnosed using gold-standard examination because of the risks in the school setting; therefore, the examination was conducted using validated International Study of Asthma and Allergies in Childhood phase III questionnaires.
⇒ The time relationship between risk factors and the outcomes could not be explained.

INTRODUCTION

Otitis media with effusion (OME) is a disease that is characterised by inflammation of the middle ear with fluid formation, without signs or symptoms of acute infection, and with intact tympanic membrane. This disease commonly occurs in children and can appear symptomless.[1] Diagnosis and management of OME are usually late and are associated with complications. OME is the most common cause of hearing loss in children in developing countries and can impair the child's behavioural and language development.[2]

OME is one of the most common childhood illnesses in the USA, with more than 2.2 million cases diagnosed yearly. It is estimated that 80% of children will have at least one episode of OME by the age of 10 years.[3] In the UK, it is estimated that 5% of children aged 5 years have persistent bilateral hearing impairment due to OME. Furthermore, OME is one of the most common reasons for referral to surgery in children in the UK.[4] The prevalence rate of OME is 15.5% in children in Upper Egypt; 17.89% in Kuala Lumpur, Malaysia; and 5.3% in Hong Kong for children aged 6–7 years old.[5–7]

Several studies have been performed to identify the risk factors for OME. Craniofacial dysmorphology, adenoid hypertrophy, respiratory tract infections, obstruction of the nasopharynx and allergies have been suggested as risk factors for OME.[8] Other risk factors for OME are gender, race, environment, climatic conditions, humidity, a crowded home, socioeconomic status, breastfeeding duration, kindergarten nursery, passive smoking and gastro-oesophageal reflux.[9] However, the risk factors for OME reported in several studies remain controversial.[10] A systematic review by Lechien *et al* concluded that the association between laryngopharyngeal reflux (LPR) and OME was unclear.[11] Several studies have reported on the association between adenoid hypertrophy and OME.[12 13] However, a study by Durgut and Dikici concluded that adenoid size and location were not associated with hearing thresholds and the duration of OME.[14] Several studies found an association between allergic rhinitis and OME in children in subtropical countries[15–17]; however, there are several differences in the main sensitisers in allergic patients living in tropical urban environments and subtropical areas.[18]

Based on the high prevalence of OME and the problems that this disease can cause in children, it is important to identify the risk factors for OME. This study aimed to determine whether LPR, allergic rhinitis and adenoid hypertrophy are risk factors for OME. We hope that the results improve the prevention of OME in children, medical services for communities in general and the management of OME.

MATERIALS AND METHODS

This comparative cross-sectional study was conducted in an educational unit of preschool and elementary children in East Jakarta district, Indonesia. The inclusion criteria for the OME group included preschool and elementary children in East Jakarta, willingness to participate in the study, and diagnosis with OME based on history, ear/nose/throat (ENT) examination, otoscopy, and tympanometry. The inclusion criteria for the non-OME group included preschool and elementary children in East Jakarta, willingness to participate in the study and no diagnosed OME. The exclusion criteria included uncooperative patients, upper respiratory tract infections, and congenital defects, such as palatoschisis, laryngomalacia, and other neuromuscular disorders.

A total of 2016 preschool and elementary school children in the district were chosen from the population using stratified random sampling, multistage random sampling and spatial random sampling. The children underwent history taking, ENT examination and tympanometry. The tympanometer used in this study was the Intercoustics Impedance Audiometer AT-235. A type B tympanogram indicated OME. Using the exclusion and inclusion criteria, 46 children with OME were selected for the case group; 46 children were randomly chosen for the control group using stratified random sampling from patients without OME age and sex matched with the case group. Both groups were treated equally regarding history taking, questionnaire completion, ENT examination and examination using a flexible fibreoptic nasopharyngolaryngoscope. For questionnaire completion, participants were asked to fill out questionnaires with their parents' or teachers' help regarding allergic rhinitis based on the International Study of Asthma and Allergies in Childhood (ISAAC) phase III and LPR based on the Reflux Symptoms Index (RSI). The ISAAC questionnaire has been validated in Indonesia with 90% sensitivity, 83.58% specificity, 68.2% positive predictive value and 95.73% negative predictive value.[19] Flexible fibreoptic nasopharyngolaryngoscopy, which evaluates adenoid hypertrophy and LPR using the Reflux Finding Score (RFS), was performed in the bronchoesophagology outpatient clinic at the Otorhinolaryngology-Head and Neck Surgery Department, Faculty of Medicine, Universitas Indonesia (FMUI)–Cipto Mangunkusumo Hospital, Jakarta, Indonesia. Endoscopy was performed blindly between the two groups by one staff member of the Endoscopic Broncho-Esophagology Division FMUI. The adenoids were evaluated based on the percentage of adenoid tissue that caused blockage of the posterior choana (choanal obstruction ratio) into four grades: grade I, adenoid tissue obstructs 0%–25% of the posterior choana; grade II, adenoid tissue obstructs 26%–50% of the posterior choana; grade III, adenoid tissue obstructs 51%–75% of the posterior choana; and grade IV, adenoid tissue obstructs 76%–100% of the posterior choana. Patients were considered to have adenoid hypertrophy if the choanal obstruction ratio was >50% (grades III and IV). Patients were considered to have LPR if the total RFS was >7.

The sample size was calculated based on the formula for comparing the proportions of the two groups. Assuming a type 1 error of 0.05, 80% power, 95% confidence level, 64% proportion of LPR in patients with OME and 25% proportion of LPR in patients without OME, a sample size of 46 cases and 46 controls was required.

All statistical tests were performed using the SPSS software V.26 (IBM Corporation). Data processing was performed using bivariate analysis to determine the relationship between independent and dependent variables. Afterwards, determinant factors for OME and other contributing factors were processed using multivariate logistic regression analysis.

Patient and public involvement

None.

RESULTS

The largest age group of patients with OME in this study was 5–7 years old (45.7%), while the smallest group was aged 11–13 years old (13%). The largest gender group for OME was male (52.2%). In this study, 26 children (56.5%) with OME had adenoid hypertrophy based on

Table 1 Sociodemographic and clinical characteristics of the patients

Risk factors		Case		Control	
		n	%	n	%
Sex					
Male		24	52.2	24	52.2
Female		22	47.8	22	47.8
Age group (years)					
5–7		21	45.7	21	45.7
8–10		19	41.3	19	41.3
11–13		6	13	6	13
Adenoid hypertrophy					
Adenoid hypertrophy (+)	>50%–75%	16	34.8	15	32.6
	>75%–100%	10	21.7	4	8.7
	Subtotal	26	56.5	19	41.3
Adenoid hypertrophy (–)	0%–25%	3	6.5	2	4.3
	>25%–50%	17	37	25	54.3
	Subtotal	20	43.5	27	58.6
Total		46	100	46	100
Allergic rhinitis					
Allergic rhinitis (+)		13	28.3	9	19.6
Allergic rhinitis (–)		33	71.7	37	80.4
Total		46	100	46	100
LPR					
LPR (+)	RFS 8–13	20	43.5	15	32.6
	RFS 14–19	16	34.8	9	19.6
	RFS 20–26	0	0	0	0
	Subtotal	36	78.3	24	52.2
LPR (–)		10	21.7	22	47.8
Total		46	100	46	100

LPR, laryngopharyngeal reflux; RFS, Reflux Finding Score.

nasopharyngeal examination. Moreover, 13 children (28.3%) with OME had allergic rhinitis as a risk factor. In the OME group, 36 out of 46 children (78.3%) had LPR. Complete data are presented in table 1.

In the OME group, 15 children (32.6%) complained of ear fullness, and hearing impairment was found in 17 children (37%). Complaints of sneezing, runny nose and nasal blockage in the OME group were reported in 19 children (41.3%); however, only in 13 children (28.3%) had persistent complaints for more than 12 months. The most common complaint in the OME group with adenoid hypertrophy was breathing through the mouth, which was reported in 17 children (37%). The RSI questionnaire was used to calculate the severity of LPR symptoms. The number of children with an RSI score above 13 was 13 (28.3%) in the OME group.

In table 2, after bivariate analysis, a significant relationship was observed between OME and LPR (p=0.016). According to the logistic regression test, the probability of OME occurrence in patients with LPR was 3.3 times higher than in patients without LPR (OR 3.3; 95% CI 1.33 to 8.189; p=0.01). Furthermore, no significant relationship was observed between OME and adenoid hypertrophy (p=0.211) or allergic rhinitis (p=0.463). Multivariate analysis was performed by inserting variables that had p<0.25 in the bivariate analysis. Adjusted OR was obtained using a multiple regression logistic test, while

Table 2 Relationship between otitis media with effusion and risk factors

Variable	P value	cOR (95% CI)	AdjOR (95% CI)
LPR	0.016	3.30 (1.30 to 8.19)	3.30 (1.33 to 8.19)
Adenoid hypertrophy	0.211	1.85 (0.81 to 4.23)	1.69 (0.71 to 3.97)
Allergic rhinitis	0.463	1.62 (0.61 to 4.28)	–

AdjOR, adjusted OR; cOR, crude OR; LPR, laryngopharyngeal reflux.

crude OR was obtained using a simple regression logistic test.

DISCUSSION

We found that the prevalence of OME was higher in young children (5–7 years old) compared with older children (11–13 years old). Our results are similar to a study by Humaid *et al* in which OME was significantly higher in young children (6–7 years old) compared with older children (8–12 years old).[20] In various studies, higher incidence of OME was commonly associated with the younger age group.[4 5 21] The youngest patients in our study were 5 years old because our study was conducted on an education unit that included preschool and elementary school children. In Indonesia, children usually enrol in kindergarten or preschool at 4 or 5 years old.[22] In addition, children under 5 years old cannot reliably or accurately self-report health outcomes. To communicate their health or illness, children must be able to focus, discriminate response options, recall health experiences, and understand the basic notions of illness and health.[23] This should be considered because our study used a questionnaire to assess allergic rhinitis.

Several studies have reported a higher risk of OME incidence in children with allergic rhinitis.[5 15–17] The correlation between allergic rhinitis and OME may be caused by Eustachian tube (ET) obstruction due to local hypersensitivity caused by the allergens. In addition, supporting the United Airway Concept, the middle ear mucosa has a similar allergy mediator and is as capable as the rest of the upper respiratory tract of responding to allergens.[24 25] In our study, there was no significant difference in allergic rhinitis in the OME and non-OME groups. This is probably due to the different methods of diagnosing allergic rhinitis. In our study, allergic rhinitis was diagnosed based on the ISAAC phase III questionnaire. Previous studies using questionnaires have been conducted to assess the association between allergic rhinitis and OME in children.[16 26] Diagnosing allergic rhinitis ideally involves a skin prick test; however, it is unsafe to perform skin prick tests in school, and it is technically difficult to bring the children to the hospital to perform the skin prick test.

The ISAAC questionnaire is a standardised questionnaire from worldwide ISAAC multicentre studies used to assess disease frequency, prevalence and severity.[27] It has been validated in Indonesia with high sensitivity, specificity, positive predictive value and negative predictive value.[19] In several studies, the ISAAC questionnaire was reported to have a high specificity for identifying patients with allergic rhinitis. Validation of the ISAAC questionnaire in Switzerland showed a high positive predictive value and specificity ranging from 77.5% to 97.6%.[27] Validation of the ISAAC questionnaire in Korea reported moderate sensitivity (57.5%) and specificity (58.4%), with a high negative predictive value (70.6%).[28] The ISAAC questionnaire was reported to have 73% sensitivity and 98% specificity in Congo.[29] In addition, the ISAAC questionnaire uses uncomplicated medical terminology and ordinary language to avoid incorrect answers and refusal to answer questions.[19] The advantages of using screening tools are that they have low cost, are non-invasive, provide rapid results and are easy to administer.[30] Parents and teachers could assist the patients with filling out the questionnaire in our study because the ISAAC questionnaire requires perceived and visible symptoms in the patients, such as sneezing, itchy/watery eyes, and runny and blocked nose.

Adenoid hypertrophy is the most common cause of tubal dysfunction in the paediatric population.[31] The effects of adenoid hypertrophy on the development of OME are obstruction of the ET with mass effect, accumulation of secretions, disruption of nasopharyngeal ventilation, oedema caused by inflammation and allergic mediator release from adenoid mast cells.[32] In our study, even though there was no significant difference between adenoid hypertrophy and OME, there was a clinically important difference. The difference was seen in 71.4% of patients with grade IV adenoid hypertrophy in the OME group. In grade IV adenoid hypertrophy, the adenoid covers almost all of the tubal opening, which leads to total choanal obstruction and causes ET obstruction and ventilation dysfunction.[33] Abdel Tawab and Tabook[12] reported a highly significant relationship between grade IV adenoid hypertrophy and type B tympanometry. Furthermore, they reported the correlation between grade IV adenoid hypertrophy and middle ear effusion viscosity.[12] Another study by Nwosu *et al*[13] found that a higher grade of adenoid size was associated with an increased incidence of OME.[13] In addition to adenoid size, the correlation between the adenoids and OME may be caused by microbial reservoirs for ascending infection to the middle ear.[34]

Several studies correlate LPR with OME by identifying pepsin in middle ear effusions.[12 35–39] Correlation between LPR and OME may be caused by excessive vagal reactivity and direct noxious exposure of the middle ear mucosa to gastric acid contents, causing swelling, ciliary dyskinesia, mucus hypersecretion and stimulation of inflammatory mediator secretion that leads to ET dysfunction.[40] The structure of the ET in children is not yet fully developed, with a horizontal position that enables gastric contents to enter the middle ear.[39] According to our study, children diagnosed with LPR have a threefold higher risk of suffering OME than children without LPR.

The prevalence of LPR in children is high, with approximately one in five children likely having reflux disease.[41] Furthermore, the prevalence of OME is high in children, and 80% of children will have at least one episode of OME by the age of 10 years.[3] However, OME is easily missed in children because it is often asymptomatic.[8] Persistent OME leads to tympanic membrane damage and permanent hearing loss, affecting socialisation and communication. Hearing loss in children can cause delayed language development and learning problems that lead to behavioural disorders and poor school performance.[1 2 8] From our study, it is important to assess

OME in children with LPR to prevent undetected cases of OME and further complications due to untreated OME. In addition, it is important to assess LPR in children with OME to make its treatment more effective by addressing one of its risk factors.

The ideal design to study risk factors for disease is a case–control study. However, our study could not explain the time relationship between exposure (LPR, allergic rhinitis, adenoid hypertrophy) and the outcome (OME) as a case–control study because the risk factors and the outcomes were measured at the same time. This becomes one of our limitations. However, our cross-sectional study used two groups (case and control) based on the dependent variable so that, from the beginning of the study, it was known which group would develop OME, and the risk factors between the case and control groups could be compared. The control group was randomly chosen from patients without OME age and sex matched with the case group so that other risk factors could be eliminated. The second limitation of our study was that we only used a questionnaire to assess allergic rhinitis. However, the results were valid due to the high specificity, sensitivity and applicability of the questionnaire in our subject group. In addition, our study assessed a large number of participants, with a total of 2016 children. Although 46 patients were assessed to have OME, it fulfilled our study's minimum sample size (46 patients for each group). Our study participants were more significant than previous studies. Previous studies by Karyanta *et al* and Górecka-Tuteja *et al* assessed 28 patients with LPR.[40 42] A study by Galić and Klančnik assessed a total of 65 patients.[43] A study by Sharifian *et al* assessed 37 children as a case group and 52 children as a control group.[44] Moreover, our study used a 95% CI with a relatively narrow of range results, so it had adequate power.

CONCLUSION

This study reported a significant difference in the incidence of LPR in children with OME and without OME. The proportion of LPR in the OME group (case group) was higher than in the non-OME (control) group, at 78.3% and 52.2%, respectively. According to the results, it can be concluded that children with LPR have a 3.3-fold increased risk of OME than children without LPR. The correlation between other risk factors (allergic rhinitis and adenoid hypertrophy) and OME in children was clinically significant even though there was no statistically significant difference.

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Contributors RDR, ST and SMH designed the study. RDR, ST, DAN and SMH performed the study. RDR, ST, DAN and MM analysed the data. RDR, ST and DAN drafted the manuscript. SMH and MM contributed to drafts and critical revision for intellectual content. RDR acted as a guarantor of the study. All authors approved the final manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Parental/guardian consent obtained.

Ethics approval This study involves human participants and was approved by the Committee of Medical Research Ethics of the Faculty of Medicine, Universitas Indonesia, with regard to the protection of human rights and welfare in medical research with ethical number 109/PT02.FK/ETIK. The participants and their parents provided verbal and written informed consent before study participation.

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Data availability statement All data relevant to the study are included in the article or uploaded as supplemental information.

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