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ARTICLE

Risk Factors and Causative Organisms of Otitis Media in Children

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Abstract

Background: Otitis media (OM) is an important health problem among children. It is the one of the leading causes of bacterial infections and antibiotic prescriptions. **Patients and Methods:** Three hundred patients with OM [147 with acute suppurative otitis media (ASOM), 80 with secretory otitis media (SOM) and 73 with chronic suppurative otitis media (CSOM)] ranging in age from 3 months -12 years were investigated for possible risk factors of OM. Age- and sex- matched healthy children served as controls (n=300). Bacteriological examinations were completed for 178 patients (110 with ASOM and 68 with CSOM) with discharge from their ears. **Results**: Residence in rural areas, artificial feeding, low socioeconomic standard (SES), parental smoking, allergic rhinitis, adenoid hypertrophy, chronic tonsillitis, URTI, LRTI and introduction of foreign body (FB) into ears were major risk factors for the occurrence of OM (P<0.01). Unilateral infection was more significantly (P<0.001) found in ASOM and CSOM, while bilateral infection was more significantly found in SOM (P<0.01). Bacteriological examination showed that the prevailing bacteria in cases of ASOM were *S. pneumoniae* (24.8%), *Staph. aureus* (24.8%), *P. aeruginosa* (15.2%), *H. influenzae* (9.5%), and *S. pyogenes* (7.6%). On the other hand, the prevailing bacteria in CSOM were *Proteus mirabilis* (31%), *P. aeruginosa* (26.8%), *Klebsiella* species (14.1%), *Staph. aureus* (8.5%), and *E. coli* (5.6%). **Conclusion:** many risk factors have a role in the occurrence of OM in children and control of these factors may decrease the incidence of this disease. Many bacterial species (*S. pneumoniae* and *Staph. aureus* in ASOM and *Proteus mirabilis*, *P. aeruginosa* and *Klebsiella* in CSOM) are the causative organisms of this disease in our locality.

Key words: Risk factor, acute suppurative otitis media, chronic suppurative otitis media, secretory otitis media, causative bacteria of OM.

Abbreviations: ASOM: acute suppurative otitis media, CSOM: chronic suppurative otitis media, EAC: external auditory canal, ET: Eustachian tube, FB: foreign body, LRTI: Lower respiratory tract infection, ME: middle ear, OM: otitis media, NP: nasopharynx, SES: socioeconomic standard, SOM: secretory otitis media, URTI: upper respiratory tract infection, RTI: respiratory tract infection.

Introduction

OM is a major health problem and occurs with a high incidence and prevalence in both developed and developing countries (1,2). ASOM is a common childhood illness and can progress to CSOM (3). Although the use of antibiotics for treatment has reduced the number of acute complications, the number of chronic complications appears to be increasing (4). Understanding the epidemiology and microbiology of OM may facilitate development of strategies for primary prevention and better management of the disease (5).

Although many organisms may be responsible for development of ASOM, three organisms account for the majority of infections (6). However, there are variations in different localities of the world and the response of these isolates to antibiotics may vary in different sites (6,8). A wide range of organisms may be isolated from cases of CSOM. The increasing emergence of bacterial strains, which are resistant to known antimicrobial agents, is a significant cause of treatment failure (2,9). This study was performed to evaluate the risk factors of OM and to identify the causative bacterial agents in our locality.

Patients and Methods

Characteristics of Patients

The study included 300 patients with OM ranging in age from 3 months-12 years. They were selected from the ENT outpatient clinic, Menoufiya University Hospital. Patients were classified into three groups:

a) Group I: 147 patients with ASOM (110 with perforated tympanic membrane and 37 without perforation), b) Group II: 80 patients with SOM, c) Group III: 73 patients with CSOM (68 with discharging ears and 5 with dry ears).

In addition, 300 age and sex-matched healthy children, who never complained about ear troubles, served as controls. They were selected from the Ophthalmology and Dermatology clinics. Patients and controls were subjected to a full history taking and complete physical examination. Tympanometry (for children > 7 months) and audiometry (for children > 3 years) were performed as previously described (10). An informed consent was obtained from the parents of the children before enrollment in the study.

Sample Collection and Bacteriological Examination

Samples were carefully obtained from the discharging ears using small sterile swabs after cleaning the external auditory meatus with a sterile dressing on a probe. Children with history of antibiotic use in the last two weeks were excluded. Samples were cultured immediately onto plates of blood agar, MacConkey agar, and chocolate agar. The blood and MacConkey agar plates were incubated aerobically at 37°C while chocolate agar plates were incubated at 35-37°C in presence of 5-10% CO_2. In addition, direct films were prepared and examined after Gram staining. After 24-48 hours incubation, plates were examined and standard microbiological techniques were used for bacterial identification (11).

Statistical analysis

Data were collected, tabulated and statistically analyzed using a personal computer with a statistical package (Microstat software) where the Chi-square (c2) and Z tests were done at 5% level of significance.

Results

Risk factors of OM

The relation between OM and possible risk factors is demonstrated in tables 1-4

Table 1 shows that OM was more common in children who were: a) from rural versus urban areas (P<0.001); b) artificially- fed versus breast- fed children (P<0.001); c) children from very low SES versus those from higher standards (P<0.001); and d) children of smoking parents compared to those of non-smokers (P<0.01). Allergic rhinitis (P<0.001), adenoid hypertrophy (P<0.001), chronic tonsillitis (P<0.001), recurrent common colds (P<0.001) and LRTI (P<0.01) were significant risk factors. However, there was no significant association between OM and chronic sinusitis as shown in table (2). The presence of family history of OM, introduction of FB and antibiotic misuse were significant risk factors of OM (P<0.001, P<0.01 and P< 0.05 respectively). However, sniffing was not a significant factor (Table 3). Table 4 shows that unilateral infection was significantly higher in ASOM and CSOM, while bilateral infection was significantly more prevalent in SOM (P<0.001). ASOM occurred more significantly (P<0.001) among infants and preschool children while SOM and CSOM were higher in school-aged children. All

Table 1: Distribution of patients and controls according to sociodemographic factors

Baseline. Living in rural areas, artificial feeding, low SES, standard and smoking were significantly associated with occurrence of OM.

The studied variables		Patients (n=300)		Controls (n=300)		X2	P value
		No.	%	No.	%		
Age	Infants (< 1 Y.)	59	19.6	54	18.oo		
	Preschool (>1 Y-<6Ys.)	125	41.7	128	42.66	0.27	> 0.05
	School children (>6Ys.)	116	38.7	118	29.34		
Sex	Male	181	60.3	165	55.00	1.54	> 0.05
	Female	119	39.7	135	45.00		
Residence	Urban	56	18.3	90	30.0	9.86	< 0.001
	Rural	244	81.7	210	70.0		
Type of feeding	Breast*	100	33.3	210	70.0		
	Mixed	70	23.3	30	10.0	42.82	< 0.001
	Artificial	130	43.4	60	20.0	60.57	< 0.001
Socioeconomic standard (SES)	High*	36	12.0	57	19.0		
	Moderate	86	28.7	99	33.0	1.22	> 0.05
	Low	65	21.7	86	28.7	0.29	> 0.05
	Very low	113	37.6	58	19.3	17.26	< 0.001
Parent smoking	Non-smokers*	133	44.3	215	71.7		
	Smokers:	167	55.7	85	28.3	44.89	< 0.001
	Cigarette Smokers	141	47.0	67	22.3	44.39	< 0.001
	Gauza smokers	26	8.7	18	6.00	6.22	< 0.01
Smoking index	0*	143	47. 7	219	73.0		
	<10	17	5.7	14	4.7	3.07	> 0.05
	10-	28	9.3	17	5.7	10.58	< 0.001
	20-	28	9.3	12	4.0	12.88	< 0.001
	30-	26	8.7	12	4.0	9.10	< 0.001
	> 40	58	19.3	26	8.6	25.01	< 0.001

types of OM were significantly (P<0.001) more prevalent during winter as compared to other seasons of the year. Impairment of hearing was more commonly encountered in cases of SOM and CSOM compared to ASOM (P<0.001).

Bacterial causative organisms

Bacterial cultures were performed for 110 patients with ASOM. Ten cultures showed no bacterial growth and five cases showed mixed cultures. On the other hand, all the 68 CSOM patients evaluated had positive cultures. Table 5 shows that *S. pneumoniae* and *Staph. aureus* were the most common isolates among cases of ASOM (24.7% and 23.8%) while *Proteus mirabilis* (31%) and *P. aeruginosa* (26.7%) were the most common isolates from CSOM cases. Table 6 shows that the rate of detection of *H. influenzae* was significantly (P<0.05) higher among infants and preschool children compared to school-aged children. On the other hand, *P. aeruginosa* was more significant (P<0.05) among school-aged children. However, there was no significant effect of age on other organisms.

Discussion

OM has long been recognized as a major health problem among children in Egypt (1) and other countries (4). Many

Table 2: Distribution of OM patients and controls according to allergic rhinitis, adenoid hypertrophy, and URTI

* Baseline; Allergic rhinitis, adenoid hypertrophy, chronic tonsillitis and sinusitis, recurrent flu and LRTI were significant risk factors of OM.

The studied variables		Patients (n=300) No.	%	Controls (n=300) No.	%	X^2	P value
Allergic rhinitis	Absent*	247	82.8	247	91.3		
	Present	53	17.7	26	8.7	9.85	< 0.001
Adenoid hypertrophy	Absent*	154	51.3	223	74.3		
	Present	146	48.7	77	25.7	33.00	< 0.001
Chronic tonsillitis	Absent*	154	47.0	198	78.2		
	Present	146	53.0	102	21.8	12.71	< 0.001
Chronic sinusitis	Absent*	276	92.0	279	93.0		
	Present	24	8.0	21	7.0	0.1	> 0.05
Recurrent common colds	Absent*	198	66.0	234	78.0		
	Present	102	34.0	66	22.0	10.13	< 0.001
LRTI	Absent*	213	71.0	238	79.3		
	Present	87	29.0	62	20.7	5.56	< 0.01

Table 3: Distribution of patients and controls in relation to family history of OM and some health behaviors.

* Baseline
- Introduction of FB, positive family history and antibiotic misuse were significant risk factors of OM.

The studied variables		Patients (n=300) No.	%	Controls (n=300) No.	%	X^2	P value
Sniffing	Absent*	261	78.0	268	89.3		
	Present	39	22.0	32	10.7	0.58	> 0.05
Introduction of F.B. to ear	Absent*	220	73.3	247	82.3		
	Present	80	26.7	53	17.7	6.53	< 0.01
Family history of O.M.	Absent*	202	67.3	257	85.7		
	Present	98	32.7	43	14.3	27.03	< 0.001
Antibiotic misuse	Absent*	263	87.9	279	93.0		
	Present	37	12.3	21	7.0	4.29	< 0.05

risk factors may affect the occurrence of this disease. In this study, children from rural areas were found to be at higher risk than those living in urban areas, a finding which was reported by Minja and Machemba (12). This result could be explained by differences in SES, medical care, sanitary conditions, and level of education. In this study, children from very low SES were more likely to develop OM compared to other social classes. In agreement with our finding, CSOM was reported to be associated with low SES (13). Many studies proposed that OM is a heritage of poverty and occurs more prominently among poor children (13). This may be attributed to crowding, suboptimal nutritional status, inadequate hygiene, relative insensitivity, and inattention to symptoms, limited access to health care services of high quality, and limited compliance with prescribed regimes (12,13).

This study demonstrated that OM was more common in

Table 4: Distribution of ASOM, SOM and CSOM patients according to laterality, age, gender, season and hearing impairment.

Bilaterality was more commonly associated with SOM, winter season was more; commonly associated with ASOM while hearing impairment was more commonly associated with CSOM.

The studied parameters		ASOM (n=147) No.	%	SOM (n=80) No.	%	CSOM (n=73) No.	%	Total (n=300) No.	%	X^2	P value
Laterality	Bilateral	46	31.3	57	71.3	23	31.5	126	42.0	38.36	< 0.001
	Unilateral	101	68.7	23	28.8	50	68.5	174	58.0		
Age	Infants (0-1Y.)	49	33.3	6	7.5	4	5.5	59	19.7		
	Preschool (>1<6Ys.)	71	48.3	32	40.0	22	30.1	125	41.7	69.83	< 0.001
	School (>6Ys.)	27	18.4	42	52.5	47	64.4	116	38.7		
Sex	Males	83	56.5	49	61.3	49	67.1	181	60.3	2.35	> 0.05
	Females	64	43.5	31	38.8	24	32.9	119	39.7		
Season	Winter	58	45.7	30	37.5	15	20.6	103	34.3		
	Spring	34	26.8	26	32.5	20	27.4	80	26.7	17.54	< 0.001
	Summer	17	13.4	12	15.0	17	23.3	46	15.3		
	Autumn	18	14.5	12	15.0	21	28.8	71	23.7		
Hearing impairment		**ASOM (n=79) No.**	**%**	**SOM (n=110) No.**	**%**	**CSOM (n=82) No.**	**%**	**Total (n=271) No.**	**%**	**X^2**	**P value**
	Absent	42	53.2	5	4.6	4	4.9	51	18.8		
	Mild	32	40.5	52	47.3	46	56.1	130	48.0	100.59	< 0.001
	Moderate	5	6.3	50	45.5	27	32.9	82	30.3		
	Severe	0	0,0	3	2.7	5	6.1	8	3.0		

children of parents who smoke. Exposure to tobacco smoke was reported to be an important risk factor for OM (14,15). This finding may be due to the direct effect of irritants in tobacco smoke on the mucosa of the middle ear (ME) or Eustachian tube (ET), or indirectly due to the more frequent respiratory tract infections (RTI) among them or their smoking parents (14). Parental smoking was found to increase the effect of a positive family history of asthma on respiratory morbidity (15). Our study showed that artificial and mixed feeding were significant risk factors for occurrence of this disease. Malnutrition and bottle-feeding have been reported as significant risk factors (4). Cow or formula milk may contain allergic components, which result in alteration of the mucosa of ET and ME. Moreover, aspiration of fluid into ME may occur during bottle-feeding (6). On the other hand, breast-feeding has been suggested as an important factor in prevention of respiratory and gastrointestinal infections and OM (6,16). Breast milk contains immunological factors including immunoglobulins, leukocytes, complement, interferon and lysozyme (16).

Table 5: The isolated bacterial organisms in ASOM & CSOM patients

- Cultures were done for 110 patients with ASOM. Ten showed no bacterial growth while 5 cases showed mixed cultures. On the other hand, none of the 68 CSOM patients resulted in negative cultures and 3 had mixed cultures.
- The most common isolates were *S. pneumonia* and *Staph. aureus* in ASOM, and *Proteus mirabilis* and *P. aeruginosa* in CSOM.

The isolated organisms	ASOM (n= 105) No.	%	CSOM (n= 71) No.	%	Z value	P value
Gram-positive (85)	**69**	**65.7**	**16**	**22.5**	**5.6**	**< 0.001**
S. pneumoniae (26)	26	24.7	0	0.0	4.5	< 0.01
Staph. aureus (31)	25	23.8	6	8.5	2.6	< 0.05
S. pyogenes (8)	8	7.6	0	0.0	2.8	< 0.05
Diphtheroids (10)	6	5.7	4	5.6	0.0	> 0.05
Staph. epidermidis (10)	4	3.8	6	8.5	1.3	> 0.05
Gram-negative (91)	**36**	**34.3**	**55**	**77.5**	**5.6**	**< 0.001**
Proteus mirabilis (26)	4	3.8	22	31.0	5.0	< 0.01
P. aeruginosa (35)	16	15.2	19	26.8	1.8	> 0.05
Klebsiella (14)	4	3.8	10	14.1	2.5	< 0.05
E. coli (6)	2	1.9	4	5.6	1.4	> 0.05
H. influenzae (10)	10	9.5	0	0.0	2.7	< 0.05

Table 6: Distribution of isolated organisms according to age of the studied patients

Among infants, the most common bacterial organisms were *S. pneumonia*, *Staph. Aureus* and *S. pyogenes*.
Among preschool children, the most common bacterial organisms were *P. aeruginosa*, *Staph. aureus* and *S. pneumonia*
Among school children, the most common bacterial organisms were *P. aeruginosa, Proteus mirabilis* and *Staph. aureus*

The isolated organisms	Infants (n= 35) No.	%	Preschool (n=75) No.	%	School (n= 66) No.	%	Z value	P value
Gram-positive (85)	**22**	**62.9**	**40**	**53.3**	**23**	**34.8**	**8.50**	**< 0.01**
S. pneumoniae (26)	8	22.9	11	14.7	7	10.6	2.70	> 0.05
Staph. aureus (31)	8	22.9	13	17.3	10	15.2	0.94	> 0.05
S. pyogenes (8)	2	5.7	4	5.3	2	9.1	0.57	> 0.05
Diphtheroids (10)	3	8.8	5	6.7	2	3.0	1.55	> 0.05
Staph. epidermidis (10)	1	2.9	7	9.3	2	3.0	3.25	> 0.05
Gram-negative (91)	**13**	**37.1**	**35**	**46.7**	**43**	**65.1**	**8.50**	**< 0.01**
Proteus mirabilis (26)	3	8.6	8	10.7	15	22.7	5.30	> 0.05
P. aeruginosa (35)	2	5.7	14	18.7	19	28.8	7.70	< 0.05
Klebsiella (14)	2	5.7	6	8.0	6	9.1	0.36	> 0.05
E. coli (6)	1	2.9	3	4.0	2	3.0	0.14	> 0.05
H. influenzae (10)	5	14.3	4	5.3	1	1.5	6.99	< 0.05

Allergic rhinitis is the most common chronic allergic disorder in children (17). A role of allergic rhinitis in occurrence of OM was detected in this study in agreement with other investigators (18), However, no role was documented by others (19). Children with allergies may have stronger inflammatory reaction in the ME mucosa or in the nasopharynx (NP) which prolongs the infection process and leads to treatment failure (20). Moreover, this effect may be attributed to abnormal ciliary function, mucosal edema or hypersecretion (18).

This study showed that adenoid hypertrophy, URTI (chronic tonsillitis and recurrent common colds) and LRTI (bronchitis and pneumonia) might be risk factors for OM, a finding that was reported in other studies (21). More than 60% of episodes of symptomatic URTI among young children were complicated by ASOM (22). Moreover, carriage of multiple types of *S. pneumoniae* and *H. influenzae* was associated with increased risk for OM (2). It has been reported that ASOM occurs mostly after URTI by pathogenic bacteria that colonize the NP (22). Respiratory bacterial pathogens ascend the ET from the NP to the ME, causing inflammation (23). OM and sinusitis share common features and the same risk factors (24). Both paranasal sinuses and ME acquire respiratory pathogens from the NP (24). Initial viral infection may affect the mucosa of the ME making it less resistant to organisms that are normally present in the NP allowing bacterial overgrowth (22). The co-morbidity between ear infections and these diseases may be attributed to a common infectious predisposition, which may be genetic or environmental in origin (25). Infected hypertrophied tonsil or adenoid and chronically inflamed sinus could act as a septic focus predisposing to OM (26).

Introduction of FB may break the skin and allow secondary infection to occur (27). Our results showed that introduction of FB to the ear and antibiotic misuse could be risk factors for OM. Misuse of antibiotics by parents for treatment of many childhood ailments including ME infections is widespread in Egypt because antibiotics are available over the counter in this country. Moreover, the low compliance to treatment regimes leads to emergence of resistant strains of the commonly used antibiotics leading to treatment failure (28).

In this study, A**S**OM was more prevalent among infants and preschool children while CSOM was more common in school children, a finding that was previously reported (29). The high incidence of ASOM among infants could be attributed to poor immunity, active growth of their lymphoid tissue and the short wide horizontal ET helping to spread infections (22). On the other hand, the increased frequency of CSOM among school-aged groups may be due to accumulation of new cases every year with increasing age. However, OM was a common health problem among all age groups (30).

OM was more common among males than females (1). This may be a reflection of the overall male predominance of childhood infections due to anatomic, behavioral, and socioeconomic differences between males and females (31). The role of sex hormones in the regulation of the immune system may also be a contributing factor (31). Interestingly, ASOM and SOM were higher during winter, a finding, which correlates with the incidence of URTI. However, seasonal variation was not evident in CSOM as chronicity depends on other factors rather than the season (1).

An association between hearing impairment and OM was reported (32). Our findings showed that hearing impairment was more significantly associated with SOM and CSOM than with ASOM, which has been reported to have little or no long-term harmful effect on hearing (32). On the other hand, SOM (10,20) and CSOM (33) result in a significant hearing impairment. Hearing loss was reported in about 50% of cases of CSOM (13).

In this study, negative cultures were found among 10 of the 110 patients tested with ASOM (9.1%). Sterile ME fluid after appropriate cultures was detected in 4% (24) and 12% (35) of cases. Negative cultures may be due to presence of other organisms (e.g. viruses, mycoplasma and chlamydia) or anaerobic bacteria. In this study, *S. pneumoniae* was found to be the most prevalent organism in ASOM followed by *Staph. aureus* as reported by others (9). The importance of these organisms in ASOM was previously reported by Cheng, *et al* (36), but *Staph. aureus* was considered a contaminant from the external auditory canal (EAC) (34). However, the role of this organism as a potential causative agent in ME infection could not be excluded (36) because obtaining the specimen by swabs was found as good as the aspiration technique (37).

Our data showed that *H. influenzae* formed 9.5% of isolates, a finding similar to that reported by Cheng, *et al* (36). However, Canter (38) showed that it was the second most important pathogen in ASOM and interestingly, this organism was more significantly isolated from infants and preschool children compared to school children, indicating

that the proportion of *H. influenzae* declines with increasing age. Leibovitz, *et al* (39) showed that bilateral ASOM was frequent and that *H. influenzae* was more frequently involved in the etiology of bilateral as compared to unilateral ASOM. On the other hand, *S. pyogenes* constituted 7.6% of our isolates although higher results were reported by others (9). A major role for *S. pneumoniae* and *H. influenzae* was demonstrated by other investigators (24). Therefore, empiric therapy for ASOM should include an agent with activity against beta-lactamase-positive *H. influenzae* and *S. pneumoniae* (2,3,8). However, it is of great importance to select patients who will benefit from the use of antibiotics to minimize the frequency of bacterial resistance (40).

In this study, there was a high incidence of *P. aeruginosa* (15.2%) and Gram-negative enteric bacteria (9.5%). In ASOM, *P. aeruginosa* was the most commonly isolated organism (36) followed by Gram- negative enteric bacilli (9) and methicillin-resistant *S. aureus* (MRSA) (41). The high rate of isolation of *Staph aureus, P. aeruginosa* and Gram- negative enteric bacteria in our study may be explained by entry of these organisms from the outside with FB introduction which was found as a significant risk factor for OM. Diphtheroids and *Staph. epidermidis* constituted 5.7% and 3.8% of the total isolates respectively. Higher figures were reported by Cheng, *et al* (36), and were attributed to possible contamination from the EAC. However, Bluestone and Klein (42) indicated a pathogenic role of these organisms under certain conditions.

In this study, Gram- negative bacterial isolates were more significantly isolated from CSOM compared to ASOM patients. This finding agrees with previous studies and can be explained by presence of lysozymes, which are strongly active against Gram- positive bacteria in ear exudates in CSOM (5,43). *Proteus mirabilis* and *P. aeruginosa* accounted for a significant proportion of our isolates in CSOM (31% and 26.7% respectively) as previously reported (43). *Proteus* was the most prevalent organism (44,45); *Pseudomonas* was the second isolate (46,47); and *Klebsiella* was the third isolate (48). However, other investigators found that the most common organism was *Staph. aureus* (46,48) or *P. aeruginosa* (45). In another study, *S. aureus* and *Proteus spp*. were the predominant pathogens of CSOM (30). In this study, *E. coli* accounted for 5.6% of isolates. Proctor (44) and Gray (47) reported 8.1% and 7% respectively. However, higher (46) and lower (44) results were found.

In conclusion, many risk factors (especially artificial feeding, low SES, exposure to smoking, allergic rhinitis, adenoid hypertrophy, chronic tonsillitis, URTI and LRTI) may predispose to occurrence of OM in children. Control of these factors may decrease the occurrence of this disease. The major causative organisms of ASOM include *S. pneumoniae*, *Staph. aureus*, *P. aeruginosa, H. influenzae* and *S. pyogenes*. On the other hand, the major causative organisms of CSOM include *Proteus mirabilis*, *P. aeruginosa*, *Klebsiella* species, *Staph. aureus* and *E. coli*.

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