

Role of Obesity in Otitis Media in Children

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Abstract The ongoing childhood obesity epidemic has garnered significant attention among healthcare providers due to its short- and long-term sequelae. Multiple diseases have been associated with obesity, not limited to hypertension, diabetes, and attention deficit hyperactivity disorder. Over the past decade, the relationships between obesity and otologic conditions have been investigated. In this setting, otitis media has remained the focus of research, representing one of the most common pediatric illnesses. Initial studies suggesting a relationship between the two conditions have been supported with epidemiological studies controlling for socioeconomic factors. The purpose of this article is to review our current understanding of the relationship between otitis media and obesity and to discuss the healthcare implications of this association. In addition, several identifiable factors associated with each condition are discussed, as are potential pathophysiologic mechanisms that may help to elucidate the complex and multifactorial relationship between the two disease entities.

Keywords Obesity · Otitis media · Pediatric · Epidemiology · Public health · Pathophysiology · Inflammatory markers · Immune system · Taste disturbance · Eustachian tube dysfunction · Gastroesophageal reflux disease

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Introduction

Childhood obesity remains a significant public health issue worldwide, with North American countries maintaining the greatest incidence per capita [1]. In the USA alone, an estimated 17 % of children are obese [2•, 3•, 4], and according to data from the National Health and Nutrition Examination Survey (NHANES), the prevalence of childhood obesity has increased steadily from 5 % in their 1976–1980 survey to 12.4 % in 2003–2006 [5].

Obesity is thought to have a multifactorial etiology, not limited to chronic caloric imbalance, genetic influence, and metabolic dysregulation [6–8]. It is characterized primarily by chronic systemic inflammation and has been associated with several comorbid disease processes, including cardiovascular sequelae, pulmonary disease, sleep-disordered breathing, and attention deficit hyperactivity disorder [6, 7•, 9••]. During infancy, it has been associated with gross motor delays and an increased incidence of hospital admissions [9••]. Early-onset obesity has also been associated with an increased severity of obesity later in life [7•, 10]. Due to the multitude of health consequences attributed to obesity and the preventable nature of this disease process, it remains a major focus of public health awareness. With this in mind, significant efforts have been made to identify relationships between common pediatric disease processes and the development of obesity in children. Recently, the relationships between obesity and several otolaryngologic diseases have been postulated. Due to the prevalence and public health burden, otologic pathology such as otitis media (OM) has been the rightful frontrunner in the majority of these research efforts [2••, 3•, 7•, 9••].

The importance of OM stems from the long-term consequences and the public health burden attributed to the disease. Sequelae of OM are primarily the result of conductive hearing loss, chronic inflammation, and the effects of long-term negative pressure on structures of the middle ear. These sequelae

include speech and language delays, chronic hearing loss, and erosive changes of the ossicular chain [2••, 11]. When considering the public health burden, OM is possibly the most significant single disease process in the pediatric population. Specifically, 70 % of American children experience at least one episode of acute otitis media (AOM) before their second birthday, and at 6 years of age, up to 40 % of children have had three episodes [7•, 12, 13]. Nearly all children have experienced at least one episode of AOM by the time they have reached school age, and approximately 20 % of children have a middle-ear effusion at any single point in time [14]. In the USA alone, approximately \$555 million in Medicaid expenditures annually were attributed to OM in children 14 years old and younger [14, 15]. Direct costs attributed to OM notwithstanding (including medical and surgical visits and procedures) indirect costs such as school absences and caregiver work absences also add tremendous financial burden [11, 14, 16]. Due to the sociologic and public health impacts of both childhood obesity and otitis media, we aim to review the current literature that discusses potential relationships between each disease process.

Childhood Obesity and Otitis Media

There is a substantial overlap between the established risk factors for both childhood obesity and otitis media. In addition to the inflammatory nature that characterizes each disease, both obesity and OM are associated with male gender and lower socioeconomic status, and possibly immune dysfunction. Independent of obesity, OM is also associated with prematurity, adenoid hypertrophy, prolonged bottle use during feeding, and a history of allergy [7•, 17, 18]. This overlap had long suggested a relationship between OM and obesity and has served as an impetus into several investigations over the past decade.

In one of the first cross-sectional studies to evaluate the influence of obesity on the development of OM, Kim and colleagues compared BMI, triglyceride concentrations, and total cholesterol concentrations in children with and without otitis media with effusion (OME). They demonstrated an association between OME and both total serum cholesterol and increased BMI in children [8]. In 2011, the same group assessed 140 children undergoing ventilation tube placement for an association with obesity. These children were compared to control patients who underwent surgery for non-ear related diseases. The prevalence of obesity was significantly higher in the patients undergoing ventilation tube placement, and the authors concluded that pediatric obesity might have an effect on the development of OME [7•]. Although each of those studies played an important role in the early investigation into the association between OM and obesity, the authors did not

control for socioeconomic factors that might have influenced study outcomes.

A subsequent prospective cohort study performed in a single school in the Canadian province of Nova Scotia was reported in 2011. The authors used a population-based survey in combination with an administrative national health dataset to evaluate patient weight status (BMI) and healthcare utilization for suppurative OM. In that study of fifth grade students, childhood obesity was identified as a significant risk factor for OM when controlling for potential confounders. Additionally, obese children were more likely to have repeated OM and have higher healthcare costs than their non-obese counterparts [2••]. Also in 2011, a separate investigation performed at the University of Minnesota by Nelson and colleagues evaluated data gathered from a prospective cohort of more than 500 children from 1991 to 1996. In that report, the authors demonstrated a significantly increased risk of obesity in infants undergoing tympanostomy tube treatment for OM when controlling for maternal prenatal smoking, maternal education, family income, and birth weight [17].

Additional investigations into dietary patterns in patients with otitis media have also been performed, with the goal being to evaluate the association between OM, dietary behaviors, and body weight. In a study performed by the College of Agriculture and Natural Resources at the University of Connecticut, a significant association was demonstrated between children with dietary intakes composed of excessive adiposity (and a greater affinity for foods high in fat and sugar) and a greater BMI percentile. A similar relationship was demonstrated between the same diet preferences and OM, confirming an association between high OM exposure and increased adiposity in the preschool population studied [19••].

In a recent investigation published in 2013, the relationship between acute middle ear disease and obesity was evaluated in school-age children in the USA. This study relied on a cross-sectional analysis of the Medical Expenditure Panel Survey (MEPS), in which a national sample of approximately 42.1 million children was evaluated. In this report, the authors demonstrated a statistically significant increase in the incidence of AOM in the presence of obesity. Specifically, AOM was demonstrated with an annualized incidence of 7.0 % in the obese population, in contrast to 4.6 % in the non-obese population. This difference represents an increase of 1.0 million cases of AOM annually due to obesity alone [9••].

Obesity and Inflammatory Markers

Kim et al. examined middle ear fluid of more than 200 children to identify potential differences in humoral and innate immunity between obese and non-obese patients. When considering humoral immunity and bacterial cultures, the authors were unable to identify a significant difference between obese

and non-obese patients. However, when examining innate immunity in the middle ear, the authors discovered that toll-like receptor-mediated expression of messenger RNA for several cytokines—in particular, interleukin-6, interleukin-10, and tumor necrosis factor alpha—was actually lower in obese patients than in non-obese patients. Because obesity is regarded as a low-grade systemic inflammatory state, one would assume that the results from their experiment were inconsistent. However, the authors reasoned that the decreased pattern recognition receptor-mediated cytokine expression in the middle ear reflected a local dysfunction of the innate immune response in the middle ear in obese patients [3•]. This idea of local immune dysfunction facilitating bacterial persistence in the middle ear in OME patients was furthered by a recent study performed by Lee et al. The authors examined the middle ear fluid in 68 pediatric patients and identified a significantly lower level of toll-like receptor 9 (a common pattern recognition receptor in the innate immune response) in patients who had confirmed bacterial pathogens. Although not statistically significant, they found that several inflammatory cytokines—such as IL-12, TNF-alpha, and IL-6—tended to decrease in patients with increasing identification of bacteria [20]. Although the study by Lee and colleagues did not stratify patients based on the presence of obesity, their results along with those from Kim et al. suggest that the middle ear milieu in obese pediatric patients predisposes them to OME.

Obesity and Taste Dysfunction

Adult patients with OME have demonstrated higher taste thresholds on the affected side of the tongue—ipsilateral to the site of OME—with the use of electrogustometry [21]. Electrogustometry involves passing anodal current through the tongue mucosa in order to stimulate taste receptors and subsequently measure taste thresholds through patient perception. Taste sensation on the anterior two thirds of the tongue is mediated by the chorda tympani nerve. The chorda tympani is a branch of the facial nerve and travels through the middle ear on its way to innervate the tongue. Although sweet, salty, and bitter tastes are regarded as being detectable by electrogustometry, some researchers question its ability to detect sour taste; chemical testing seems to be more appropriate for sour testing [1, 22]. Nevertheless, recent studies evaluating non-sour tastes have demonstrated findings that merit mention. In one study from South Korea, electrogustometry and chemical taste testing were performed on a pediatric population. The investigators demonstrated a significantly higher BMI in patients with OME than in non-OME controls. They also demonstrated higher taste thresholds for salty and sweet foods in patients with OME. The authors hypothesized that this taste dysfunction influenced OME patients to ingest more food/liquids in order to attain the same intensity of taste as their non-

OME counterparts. Although the sensation of taste has a compensation mechanism with the glossopharyngeal nerve, the authors proposed that this compensatory mechanism may not be fully developed in children. Thus, the OME patients take in more calories and are at increased risk for developing obesity [23•]. Additionally, a histological research has shown increasing degrees of fibrosis of the perineurium of the chorda tympani nerve as otitis media progresses. This suggests that the inflammation in the middle ear results in progressive chorda tympani nerve dysfunction and may represent a mechanism for altered taste sensations in the OME group [24].

Obesity and Eustachian Tube Dysfunction

Several potential mechanisms have been proposed to explain the link between otitis media and obesity. Obesity causes abnormal adipose deposition in various tissues throughout the body, including the Eustachian tube (ET). The Ostmann fat pad is located inferomedial to the Eustachian tube. In some obese patients, it increases in size and can make it more difficult for the Eustachian tube to open completely when the tensor veli palatini contracts. This structural dysfunction can predispose obese patients to developing middle ear effusions [25, 26].

Obesity and Gastroesophageal Reflux Disease

Gastroesophageal reflux disease (GERD) is a relatively common occurrence in obese patients [27]. Increased intragastric pressure, decreased lower esophageal sphincter tone, and increased frequency of lower esophageal sphincter relaxation episodes are potential mechanisms to explain this association [28]. In these patients, gastric reflux reaches the nasopharynx and affects the ET. The subsequent inflammatory process contributes to ET dysfunction and middle ear inflammation. This phenomenon has been elucidated by several researchers including Crapko et al., who showed that pepsin was found in the middle ear space in 60 % of children with OME [29]. Additional research by O'Reilly et al. verified the presence of pepsin at a significantly higher rate in OME patients than in non-OME patients. Their analysis also demonstrated that pepsin in the middle ear served as an independent risk factor for developing OM. With increased inflammation, there was a shift towards more mucin-producing cells, which in turn caused the effusion to develop [30]. Although these studies have shown an association between obesity and OM, a recent systematic review by Miura et al. did not show uniform results. Of the 242 studies they examined, 15 studies met their inclusion criteria. Their results demonstrated a potentially higher prevalence of GERD in children with OME.

Although pepsin in the middle ear was higher in these patients, the range of pepsin was quite variable. And lastly, the available data they reviewed did not warrant anti-reflux therapy for otitis media in the obese pediatric population [31]. Additional research is being actively performed to provide more consistent results regarding the role of GERD in OM in the setting of obesity.

Conclusion

Obesity and otitis media are significant public health concerns. National campaigns designed to combat the current epidemic of childhood obesity are currently underway. Likewise, pediatric, otolaryngologic, and infectious disease guidelines are regularly updated and distributed to assist practitioners in diagnosing and treating OM. By means of healthcare visits, cumulative costs, and resource allocation, both OM and obesity individually produce enormous burden on the healthcare system as a whole. With obesity being a potential independent risk factor for OM, the combined public health implications of this association are enormous.

Over the past decade, a link between obesity and OM has been established. Current pathophysiologic studies have allowed us to better understand the etiology of these disease processes, with increasing evidence suggesting a multifactorial phenomenon. Systemic inflammation, local immune alteration, taste disturbance, ET dysfunction, and GERD all appear to play a role contributing to this complex relationship. Specifically, similar immunologic and inflammatory characteristics of each disease suggest a potential association. In addition, taste disturbance secondary to chorda tympani dysfunction has been postulated as a potential consequence of chronic ear disease, as well as the inciting factor for dietary changes that may lead to obesity and subsequently perpetuate OM. Together with the proposed relationship between OM, GERD, and obesity, these potential mechanisms can serve as the foundation for future avenues of investigation.

Ultimately, our increased awareness of the role of obesity in otitis media in children will help us to better treat and prevent each condition, thereby dramatically reducing the burden on both society and the healthcare system.

Compliance with Ethics Guidelines

Conflict of Interest Sameer Ahmed, Ellis Arjmand, and Douglas Sidell declare no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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