International Journal of Pediatric Otorhinolaryngology 85 (2016) 136–140

Contents lists available at ScienceDirect

International Journal of Pediatric Otorhinolaryngology

journal homepage: www.elsevier.com/locate/ijporl

Information on co-morbidities collected by history is useful for assigning Otitis Media risk to children☆

Margaretha L. Casselbrant [a,*], Ellen M. Mandel [a,b], William J. Doyle [a]

[a] University of Pittsburgh School of Medicine, Department of Otolaryngology, Pittsburgh, PA, USA
[b] Division of Pediatric Otolaryngology, Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA, USA

ARTICLE INFO

Article history:
Received 20 January 2016
Received in revised form 25 March 2016
Accepted 27 March 2016
Available online 11 April 2016

Keywords:
Otitis Media
Risk factors
Children
Multivariate analysis

ABSTRACT

Objectives: Determine if a 2-Step multivariate analysis of historical symptom/sign data for comorbid diseases can abstract high-level constructs useful in assigning a child's "risk" for different Otitis Media expressions.

Methods: Seventeen items related to the symptom/sign expression of hypothesized Otitis Media comorbidities were collected by history on 141 3-year-old children. Using established criteria, the children were assigned to 1 of 3 groups: Control (no significant past Otitis Media, $n = 45$), Chronic Otitis Media with Effusion ($n = 45$) and Recurrent Acute Otitis Media ($n = 51$). Principal Component Analysis was used to identify factors representing the non-redundant shared information among related items and Discriminant Analysis operating on those factors was used to estimate the best predictor equation for pairwise group assignments.

Results: Six multivariate factors representing the assignable comorbidities of frequent colds, nasal allergy, gastroesophageal disease (specific and general), nasal congestion and asthma were identified and explained 81% of the variance in the 17 items. Discriminant Analysis showed that, for the Control-Chronic Otitis Media with Effusion comparison, a combination of 3 factors and, for the Control-Recurrent Acute Otitis Media comparison, a combination of 2 factors had assignment accuracies of 74% and 68%, respectively. For the contrast between the two disease expressions, a 2-factor combination had an assignment accuracy of 61%.

Conclusion: These results show that this analytic methodology can abstract high-level constructs, comorbidities, from low-level data, symptom/sign scores, support a linkage between certain comorbidities and Otitis Media risk and suggest that specific comorbidity combinations contain information relevant to assigning the risk for different Otitis Media expressions.

1. Introduction

Otitis Media (OM), inflammation of the middle ear (ME) mucosa, is very common in the pediatric population [1]. The onset of an OM episode is most often coincident with a viral upper respiratory tract infection (vURI) [2,3] and OM presentation can be symptomatic acute OM (AOM), or asymptomatic OM with effusion (OME). Usually, OM episodes are self-limited [4] but, in a subset of children, resolution is delayed for months to years, chronic OME (COME). Alternatively, some children are at high risk for frequently recurring AOM episodes (RAOM) [1]. Both COME and RAOM are difficult to manage, troublesome conditions and there is long-standing interest in developing intervention strategies that reduce their risks [5,6].

A large body of published work identified specific traits, behaviors, environments and conditions that increase an individual's risk for the different OM expressions [7]. For example, COME and, perhaps, RAOM risk is heritable [8,9], is increased by behaviors and environments that promote infection with upper-respiratory bacterial pathogens and viruses [10–12] and is higher in individuals with certain comorbid conditions such as craniofacial dysmorphologies, frequent viral upper respiratory infections (vURIs), nasal allergy and gastro-esophageal reflux (GER) [4,13–17]. These types of studies are needed to develop the database for

☆ Presented in part at the 18th International Symposium on Recent Advances in Otitis Media, June 7–11, 2015, National Harbor, MD.

* Corresponding author at: Children's Hospital of Pittsburgh of UPMC, ENT Department, Faculty Pavilion, 4401 Penn Avenue, Pittsburgh, PA 15224, USA. Tel.: +1 412 692 6213; fax: +1 412 692 6074.
E-mail address: Margaretha.Casselbrant@chp.edu (M.L. Casselbrant).

http://dx.doi.org/10.1016/j.ijporl.2016.03.040
0165-5876/

construction of individual risk profiles that allow a child to be identified as at high risk for OM and "in need" of close clinical observation for early OM diagnosis and management. Also, an individual's risk factors can be targeted for reduction by modifying the individual's behaviors, environments and conditions [5,10,13,15,18].

For those applications, it is important that the risk factor database be specific, complete and not contaminated by spurious associative factors. However, a review of the literature shows that some identified "risk factors" have poor reproducibility across studies while others are redundant expressions of a more inclusive, higher level construct. For example, there is a conceptual linkage among such diverse childhood OM "risk factors" as socioeconomic status, breastfeeding, day care attendance, pacifier use, home crowding and frequent upper respiratory infections, among others. There, socioeconomic status partially determines the probability that a child will be breastfed, exposed to crowded conditions, enrolled in daycare and use pacifiers. These considerations show that the previously identified "risk factors" can be hierarchically classified with the lowest level occupied by groups of related elements containing redundant information and successively higher levels occupied by broader constructs representing the shared information for each group of related items in the immediately lower level. In this typology, the lower level elements are reasonably referred to as "risk modifiers" and the higher level constructs as "risk factors".

This typology cannot be generated using the analytic methodology commonly used to identify OM "risk factors". Specifically, most past studies used a two-step analysis consisting of an initial set of univariate Control-disease comparisons for a set of hypothesized "risk factors" followed by a multivariate selection procedure operating on set members identified as being "significant" [14,19–23]. Because the set of hypothesized risk factors likely contains subsets of mutually correlated elements, the first step will identify as significant all elements in those subsets whose shared information construct predicts OM risk. The second step simply selects from each predictive subset the member with the highest accuracy assignment. However, the identified subset member is not a risk factor but rather an exemplar for a class of variables whose shared information is the risk factor. Consistent identification of that same member across studies requires that it is included in the set of hypothesized factors and has the highest group assignment accuracy among all other subset members.

The present study introduces an alternative statistical methodology that is expectedly capable of abstracting the higher level constructs (risk factors) from a set of lower level risk modifiers. The procedure requires two procedural steps and a third step to test efficiency. First, a multivariate data reduction procedure is used to extract the shared information contained in a set of hypothetical risk modifiers for representation as a smaller number of independent "factors". Then, the set of extracted factors is analyzed using a comparative multivariate procedure to identify those that discriminate between groups defined by disease state. Finally, the efficiency of the analytic methodology for identifying risk factors is quantified as measures of assignment accuracy for the identified risk factor combinations. Here, this analytic procedure was used to determine if constructs representing the non-redundant information contained in a symptom/sign set for comorbid diseases collected by history is useful in assigning a child's "risk" for different OM expressions.

2. Material and methods

The study is a multivariate analysis of the cross-sectional, historical data for 3-year-old children relating to the symptoms/signs of those comorbidities suspected to increase OM risk for purposes of identifying information-rich constructs that impact the risk for the different OM expressions. The data were abstracted from a standard history questionnaire completed by parents at the time of enrolling their 3-year-old child into either of two parallel longitudinal studies. The enrollment criteria for these studies were similar with the exception that, while the first study enrolled 3-year-old children in each of the three OM expression groups to describe maturational changes in Eustachian tube anatomy and function [24], the second enrolled 3- to 7-year-old children in the COME group to determine if Eustachian tube function tests are predictive of disease recurrence after tympanostomy tubes became dysfunctional [25]. Those studies were approved by the University of Pittsburgh Institutional Review Board with enrollment between 2007 and 2011.

The information collected by questionnaire included: general demographics for the child and family; socio-economic measures for the household; OM and other disease histories for the extended family; typical OM "risk factors" for the child, sibs and parents, and the child's history of the typical symptom/sign presentations for comorbid conditions associated with OM. Based on an ENT examination done at entry and a review of the parent-provided OM history supplemented by information available in the child's medical charts, each child was assigned to one of three groups: Control, COME and RAOM [26]. Briefly, children were classified as: (1) Controls if they had not had tympanostomy tubes or satisfied the criteria for a positive history of COME or RAOM; (2) RAOM if they had three or more episodes of symptomatic OM in one year or five or more episodes by study entry with at least two AOM episodes or tympanostomy tubes inserted for RAOM within the year prior to enrollment irrespective of whether or not they also had OME episodes; and (3) COME if they had three or more consecutive months of middle ear effusion if bilateral, six consecutive months of effusion if unilateral or three or more episodes of OM lasting for at least two months with at least one episode of OME or tympanostomy tube insertion in the year prior to entry and had not met the criteria for RAOM. Children were excluded if presenting with craniofacial anomalies, syndromes predisposing to OM, significant orthodontic treatment, cholesteatoma or ear surgery other than tympanostomy tube insertion.

2.1. Data analyses

The data analyzed were limited to the 17 symptom/sign items listed in Table 2 and representing the expression of presumed OM-related comorbid diseases for the enrolled children who were 3-years-old at entry. Parents responded to these items by recording a positive, scored as 1, or negative, scored as 0, history for the item in their child. These data were analyzed in three steps.

First, because the 17 items contained redundant information, a variable reduction procedure called Principal Component Analysis (PCA) with varimax rotation was done. There, a minimum 80% total explained variance cut-off was used to limit the number of factors to be considered and, for each factor, a minimum item loading

Table 1
Sex, race and age distribution of children by group, number (%).

	Variable	Group		
		Control	COME	RAOM
Total	Number	45	45	51
Sex	Males	23 (51)	24 (53)	26 (51)
Race	Black	12 (27)	8 (18)	8 (16)
	White	27 (60)	33 (73)	37 (73)
	Other	6 (13)	4 (9)	6 (12)
Age (yrs)	Average	3.52	3.53	3.4
	Standard deviation	0.34	0.33	0.31