Long-term follow-up after recurrent otitis media and ventilation tube insertion: Hearing outcomes and middle-ear health at six years of age

Eman M.A. Alenezi [a,b,c,*], Monique Robinson [c], Robyn S.M. Choi [b,c], Tamara Veselinović [b,c], Peter C. Richmond [b,c,d], Robert H. Eikelboom [e,f,g,h], Christopher G. Brennan-Jones [b,c,d,e]

[a] Faculty of Allied Health Sciences, Kuwait University, Kuwait

[b] The University of Western Australia, Perth, Western Australia, Australia

[c] Telethon Kids Institute, The University of Western Australia, Perth, Western Australia, Australia

[d] Perth Children's Hospital, Perth, Western Australia, Australia

[e] Faculty of Health Sciences, Curtin University, Perth, Western Australia, Australia

[f] Ear Science Institute Australia, Subiaco, Western Australia, Australia

[g] Centre for Ear Sciences, The University of Western Australia, Nedlands, Western Australia, Australia

[h] Department of Speech Language Pathology and Audiology, University of Pretoria, South Africa

* Corresponding author. Telethon Kids Institute, The University of Western Australia, Perth Children's Hospital, 15 Hospital Avenue, Nedlands, Western Australia, 6009, Australia. Email: Eman.al-enezi@telethonkids.org.au

Abstract

Objectives: To investigate the long-term impact of recurrent otitis media (rOM) and ventilation tube insertion (VTI) in early childhood on hearing outcomes and middle-ear health three to five years later, in a prospective pregnancy cohort study.

Methods: Children were classified into rOM (n= 314), VTI (n= 94), and reference (n=1735) groups, according to their otitis media (OM) history in their first three years of life. Audiometry at frequencies 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz, and tympanometry were performed when children were approximately six years of age.

Results: A binary logistic regression incorporating a range of potential confounding variables showed that hearing outcomes and middle-ear health status in children who had early childhood rOM with or without undergoing VTI were not significantly different to those in the reference group. The only significant difference was found in the VTI group for both tympanometry (OR= 2.190; 95% CI= 1.123, 4.270) and audiometry outcomes at 4000 Hz (OR= 3.202; 95% CI 1.341, 6.717), in the left ear only. The median score of the better ear 4FA was 20 dB in children in all groups.

Conclusion: Children with rOM with or without undergoing VTI in the first three years of childhood had comparable hearing outcomes and middle-ear health status to those with no history of the disease, at around the age of six years. Although children who underwent VTI had an increased risk of abnormal middle-ear status and some elevation in hearing levels in their left ear only, their audiometry results were still within normal limits, indicating that the impact of VTI in early childhood is unlikely to have clinically significant adverse impact on later hearing outcomes.

Keywords: Ventilation tube insertion; Grommets; Tympanostomy tubes; Otitis media; Hearing Middle ear health

Abbreviations

OM- Otitis Media
AOM - Acute Otitis Media
rOM - Recurrent Otitis Media
VTI - Ventilation Tube Insertion
4FA- Four Frequency Average

1. Introduction

Otitis media (OM) is a common disease that mostly occurs during infancy and early childhood [1]. OM is generally classified into different types including acute otitis media (AOM), which is characterised by a number of symptoms (e.g. fever); and otitis media with effusion (OME), which is typically asymptomatic. A mutual characteristic of AOM and OME is the presence of effusion in the middle-ear cavity, which is considered to be the main cause of OM-related hearing loss [2]. Hearing loss is a common and significant complication of OM, with hearing levels usually ranging from 15 to 40 dB in the affected ear [2, 3]. Although spontaneous recovery from OM can occur within three months [4, 5], it has a high rate of recurrence [6]. Therefore, some children may retain the effusion for extended periods including subsequent hearing loss, which can adversely affect their development [5, 7-11]. Untreated, persistent OM can also progress to significant extracranial (e.g. tympanic membrane perforation) and intracranial (e.g. meningitis) complications [12]. For those reasons, it is imperative to receive appropriate treatment and management for OM.

Children with OM are initially managed by a period of watchful waiting or medically treated with antibiotics [13]. Surgical treatment, such as ventilation tube insertion (VTI), is also indicated in cases who are unresponsive to medical treatment. This surgery is carried out to ventilate the middle-ear cavity, which can in turn, improve hearing [14]. VTI was found to be effective in accelerating the clearing of effusion and decreasing the period of its existence in the middle-ear cavity by 32% in the first year [15, 16], resulting in different degrees of improvement in hearing during that period [15-17]

A few studies have monitored children for extended periods to investigate long-term hearing outcomes of a VTI intervention. Some of those studies found that worse hearing outcomes and tympanic membrane abnormalities are generally more common in children who underwent VTI [18-20], whereas others showed no significant differences in long-term hearing outcomes compared to children who did not receive VTI [21, 22]. Hong, et al. [19] and Johnston, et al. [23] have also reported that although children who underwent VTI had significantly elevated hearing levels in the long term, their hearing was within normal limits, while Rosenfeld, et al. [24] and Schilder [25] noted that this impact on hearing is not of clinical significance. The long-term impact of VTI on hearing outcomes is still unclear due to limitations of previous studies, including small sample size [18, 19, 22], lack of control for potential confounding variables [19, 20], age differences between groups [19], and/or lack of observation [21] or reference group [18, 19]. Due to potential long-term risks of post-insertion complications, including tympanic membrane abnormalities, that may have an impact on long-term hearing outcomes and middle-ear health for children undergoing VTI, studies that address the limitations existing in the previous literature are required.

The present study aimed to investigate the impact of recurrent OM (rOM) with and without undergoing VTI within the first three years of childhood on hearing outcomes and middle-ear health status three to five years post-treatment, with consideration of a wide range of potential confounding factors, in a well-characterised Australian-based pregnancy cohort.

2. Methods

2.1. Participants

Participants included in the current analysis were from the Raine Study, a longitudinal pregnancy cohort study that was established between May 1989 and November 1991, in Western Australia. The Raine Study included 2,900 eligible 16-to-20-weeks pregnant women (Gen1) from King Edward Memorial Hospital (KEMH) and other private clinics in Western Australia and 2,868 live-born children (Gen2) [26]. The Raine Study Gen2 participants were followed-up prospectively and comprehensively during their childhood and were regularly seen at different stages in their lives to assess different areas including middle-ear health and hearing.

Only children who completed their tympanometry and pure-tone audiometry assessments at Gen2-5 year follow-up, who also had available information on OM history and VTI in the first three years of life, as well as the confounding variables listed in Table 1, were included in the present analysis. These children were classified intro three groups according to their OM-related history in the first three years of life based on parents' answers to the questions 'Has your child had ever had (in his/her life) otitis media (middle ear infection)? If yes, how many times?', as well as the information related to undergoing VTI during that period as coded using the International Classification of Disease – 9th Revision (ICD-9). The first group included those with early history of rOM (defined in this paper as having three or more episodes of OM in the first three years of life) without undergoing VTI (rOM group), the second group were those who underwent VTI as a surgical treatment for rOM (VTI group), while the last group was the reference group, which included children with no history of rOM (i.e. none or less than three episodes of OM in the first three years of childhood) in the same cohort.

2.2. Hearing and middle-ear health assessments

Pure-tone audiometry and tympanometry were performed using Grason-Stadler (GSI) at Gen2-5 year follow-up, when children were approximately six years of age [27]. Testing was carried out according to the Guidelines for Screening for Hearing Impairment and Middle-Ear Disorders [28]. Testing level of hearing thresholds for both ears were obtained at 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz to a minimum intensity of 20 dB.

Contraindications for tympanometry included: inflammation of the ear canal or tympanic membrane, wax occlusion, or presence of a foreign body. Tympanometry was also not performed in 54 children due to having ventilation tubes in situ at assessment time and were therefore not included in the analysis. These contraindications were identified through otoscopic examination, prior to performing tympanometry and audiometry. Testing was conducted by a child health nurse trained by a registered audiologist. Children with pre-identified sensorineural hearing loss were not audiometrically tested.

2.3. Ethical considerations

The human ethics committees at both KEMH and Princess Margaret Hospital in Perth, Western Australia approved participation in the Raine Study and follow-up of the participants. Written informed consent was obtained from parents of children participating in the Raine Study before participation and each of the follow-ups. When children turned 18 years of age, they were asked to provide written informed consent for the continued use of their data. The Raine Study Executive Committee has approved the research proposal of the current analysis and has, therefore, approved the release of the results.

3. Analysis

The characteristics of the study population were summarised using descriptive statistics. In this study, tympanometry recordings of low compliance of 0-0.1 mmho (i.e. type B), or negative pressure of -100 decapascals or more (i.e. type C) were indicative of abnormal middle-ear health status, while a lowest response level of 25 dB or greater was considered to be an elevated hearing level. A binary logistic regression was used to assess the impact of the categorical predictor variable of rOM and VTI on middle-ear health status (normal versus abnormal) and hearing outcomes (normal versus elevated) at child level, using tympanometry findings and the four frequency average (4FA) of 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz, in the better ear. Median score and interquartile range (IQR) were calculated for the better ear 4FA for the VTI, rOM, and reference groups. Ear-specific analysis was also performed using the binary logistic regression to assess the impact of rOM and VTI on hearing outcomes at individual frequencies and middle-ear health status and in the left and right ears, independently.

Estimates of the effect were presented as odds ratios (ORs) along with 95% confidence intervals (95% CIs). A number of confounding variables have been suggested to have an impact on OM recurrency in previous work involving the Raine Study participants [9, 10, 29], and were therefore incorporated in the regression analyses. A p-value < 0.05 was used to indicate statistical significance. The analysis was conducted using the Statistical Package for Social Sciences (SPSS) software version 28.0.

4. Results

4.1. Participants

Of the 2868 children recruited in the study, 2143 had information related to OM and VTI in their first three years of life, including 94 in the VTI group, 314 in the rOM group, and 1735 in the reference group (Table 1). At the Gen2-5 year follow-up, 1124, 1090, and 1093 children had tympanometry results from the better, left, and right ears, respectively, in addition to data for the confounding variables listed in Table 1 and were therefore included in the analysis. This includes 3.7% in the VTI group, 16.1% in the rOM group, and 80.2% in the reference group. In terms of hearing outcomes,1191 and 1192 children had results from the right and left ears, respectively, while 1195 had results from the better ear, in addition to data on the confounding variables, and were included in the analysis. This includes 4.2% in the VTI group, 16.0% in the rOM group, and 79.8% in the reference group. When tympanometry or audiometry results are only available in one ear of a participant, that ear was considered to be the better ear. Only one participant in the VTI group spoke a language other than English at home and two were from non-Caucasian mothers (Table 1). As such, the ‘language most spoken at home’ and ‘maternal ethnicity’ variables were not included as confounding variables in all binary regression analyses of this paper.

Table 1. Frequency distribution of the potential covariates between reference, rOM, and VTI groups

Covariates	***n (%)***	***n (%)***	***n (%)***	***Total n=2143***
Sex				
Male	881 (50.8)	161 (51.3)	56 (59.6)	1098
Female	854 (49.2)	153 (48.7)	38 (40.4)	1045
Language most spoken at home§				
English	1599 (92.2)	300 (95.5)	90 (95.7)	1989
Other	102(5.9)	9 (2.9)	1 (1.1)	112
Maternal Ethnicity§				
Caucasian	1501 (86.5)	300 (95.5)	89 (94.7)	1890
Other	200 (11.5)	9 (2.9)	2 (2.1)	211
Low household income at age three years (<$27,000)†				
No	955 (55.0)	189 (60.2)	43 (45.7)	1187
Yes	712 (41.1)	115 (36.6)	39 (41.5)	866
Maternal Education				
< Year 12	980 (56.5)	175 (55.7)	51 (54.3)	1206
≥ Year 12	715 (41.2)	134 (42.7)	40 (42.6)	889
Passive Smoking exposure 0 to 3 years				
No	945 (54.5)	179 (57.0)	46 (48.9)	1170
Yes	788 (45.4)	134 (42.8)	48 (51.1)	970
Parity				
No older siblings	852 (49.1)	124 (39.5)	41 (43.6)	1017
One or more older siblings	849 (48.9)	185 (58.9)	50 (53.2)	1084
Pre-term birth (<37 weeks)				
No	1574 (90.7)	289 (92.0)	85 (90.4)	1948
Yes	126 (7.3)	20 (6.4)	6 (6.4)	152
Breastfeeding Stopped < 1 year				
No	299 (17.2)	53 (16.9)	17 (18.1)	369
Yes	1316 (75.9)	237 (75.5)	73 (77.7)	1626
Low birth weight (<2500 g)				
No	1589 (92.1)	295 (93.9)	84 (89.4)	1977
Yes	137 (7.9)	19 (6.1)	10 (10.6)	166
***Alcohol consumption* in *pregnancy* (at 34 weeks)**				
Never	970 (55.9)	158 (50.3)	43 (45.7)	1171
Once a week or more	605 (34.9)	126 (40.1)	40 (42.6)	771
Day care Attendance 0 to 3 years				
No	872 (50.3)	120 (38.2)	29 (30.9)	1021
Yes	853 (49.4)	194 (61.8)	65 (69.1)	1112
Smoking during pregnancy				
No	1287 (74.2)	239 (76.1)	65 (69.1)	1591
Yes	414 (23.9)	70 (22.3)	26 (27.7)	510

Some percentages do not add up to 100% due to missing data.† Australian Dollar in 1993-1995. § covariate not included in the analyses.

4.2. Middle-ear health status

An abnormal middle-ear status in the better ear was found in 4.8%, 2.79%, and 2.97% of children in the VTI, rOM and reference groups, respectively. A binary logistic regression model incorporating a wide range of potential confounding variables showed increased odds of abnormal middle-ear health status in the better ear in rOM group (OR= 1.216; 95% CI= 0.787, 1.878) and VTI group (OR= 1.823; 95% CI= 0.863, 3.850), compared to the reference group. These results, however, were not statistically significant (Table 2).

Similarly, per-ear analysis showed increased odds of abnormal middle-ear health status in the left and right ears in both rOM and VTI groups compared to the reference group (Table 2). This increase was statistically significant in VTI group in the left ear only (p= 0.021). This result indicated that children in the VTI group were 2.19 times more likely to have abnormal middle-ear status in that ear (95% CI= 1.123,4.270) compared to the reference group.

Table 2. Binary logistic regression analyses comparing the middle-ear status of VTI and rOM groups to reference group at Gen2-5 year follow-up.

	OR	**S.E.**	**95% CI**		**p-value**
Type B or C tympanogram (Better ear)					
rOM group	1.216	0.222	0.787	1.878	0.378
VTI group	1.823	0.381	0.863	3.850	0.115
Type B or C tympanogram (Right ear)					
rOM group	1.058	0.204	0.709	1.579	0.782
VTI group	1.421	0.370	0.689	2.934	0.342
Type B or C tympanogram (Left ear)					
rOM group	1.318	0.193	0.903	1.923	0.153
VTI group	2.190	0.341	1.123	4.270	**0.021***

Covariates listed in Table 1, except for 'language most spoken at home' and 'maternal ethnicity', were incorporated in the model. Asterisk and bold indicates a statistical significance. OR, odds ratio; S.E., standard error; 95% CI: 95% confidence interval.

4.3. Hearing outcomes

Elevated hearing levels were generally uncommon in all groups but were found to be more frequent in children in the VTI group than in the rOM and reference groups. For instance, elevated 4FA in the better ear was found in 8.0% of children in the VTI group compared to 2.62% and 3.16% of children in the rOM and reference groups, respectively. The binary logistic regression model showed increased odds of elevated 4FA in the better ear in children in the VTI but not the rOM group (OR= 2.912; 95% CI= 0.962, 8.819) compared to the reference group. However, the difference was not statistically significant (Table 3). The median score of the better ear 4FA was 20 dB (IQR= 1.25 dB) in all children, indicating that hearing levels were within the normal limits for most of the children in VTI, rOM, and reference groups.

Per-ear analysis showed no significant impact of early childhood recurrent OM with or without undergoing VTI on hearing outcomes across all the frequencies in the right ear compared to the reference group (Table 3). Similar results were found in the left ear except for one statistically significant result at 4000 Hz in the VTI group only. This result indicated that children in the VTI group were 3.202 times (95% CI= 1.341, 7.646; p= 0.009) more likely to have elevated hearing levels at 4000 Hz, compared to the reference group (Table 3).

Table 3. Binary logistic regression analyses comparing the elevation in long-term hearing outcomes of VTI and rOM groups to reference group at Gen2 5-year follow-up
Covariates listed in Table 1, except for 'language most spoken at home' and 'maternal ethnicity', were incorporated

	OR	S.E.	95% CI		p-value
4FA – better ear					
rOM	0.851	0.498	0.321	2.256	0.745
VTI	2.912	0.565	0.962	8.819	0.059
500 Hz – Right ear					
rOM	0.913	0.165	0.661	1.261	0.582
VTI	0.845	0.296	0.474	1.509	0.570
1000 Hz – Right ear					
rOM	0.735	0.225	0.473	1.142	0.171
VTI	0.996	0.381	0.472	2.101	0.991
2000 Hz – Right ear					
rOM	1.316	0.390	0.613	2.824	0.482
VTI	2.475	0.564	0.820	7.472	0.108
4000 Hz – Right ear					
rOM	1.017	0.361	0.501	2.064	0.962
VTI	1.575	0.549	0.537	4.621	0.408
500 Hz – Left ear					
rOM	0.955	0.164	0.693	1.317	0.780
VTI	0.805	0.296	0.451	1.437	0.463
1000 Hz – Left ear					
rOM	0.816	0.281	0.471	1.414	0.468
VTI	1.502	0.428	0.649	3.474	0.342
2000 Hz – Left ear					
rOM	1.331	0.438	0.564	3.142	0.514
VTI	1.514	0.760	0.341	6.717	0.585
4000 Hz – Left ear					
rOM	0.955	0.377	0.456	1.999	0.902
VTI	3.202	0.444	1.341	7.646	**0.009***

in the model. Asterisk and bold indicates a statistical significance. OR, odds ratio; S.E., standard error; 95% CI: 95% confidence interval; 4FA: four frequency (500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz) average.

5. Discussion

The present study set out to assess the long-term impact of early childhood rOM and VTI on middle-ear health status and hearing outcomes. Overall, this study showed that children who had a history of rOM with or without undergoing VTI in the first three years had no clinically

significant differences in hearing outcomes three to five years post-treatment compared to children with no early history of the disease. However, in one ear only, there was an increase in the likelihood of having abnormal middle-ear health status and elevated hearing levels at one frequency for children who underwent VTI, but not in those who had rOM but were not surgically treated in the first three years of life. Previous studies have shown a potential elevation in hearing outcomes in the long-term as a result of undergoing VTI. For instance, the prospective cohort study by Stenstrom et al. [18] showed that 38 children with chronic OM who underwent VTI between 2.5 to 7 years of age had up to 8.1 dB loss in mean hearing levels when followed-up 6-to-10 years, and were at higher risks of elevated pure-tone average than 27 children in the medical treatment group. A retrospective study by Hong, et al. [19] also showed that 23 children with OM who were medically treated had significantly better hearing levels compared to 66 children who underwent VTI five year post intervention, however both had average hearing thresholds below 20 dB, which is consistent with the findings of the present study. Similar to our study, Johnston et al. [23] looked at the impact of persistent OM and VTI in early childhood on hearing outcomes at six years of age. They found that hearing levels were significantly higher in 281 children who were randomised to early or late VTI in the first three years of life compared to 200 children in the non-trial group. In addition, 178 children who received VTI in all groups had more abnormal tympanic membranes compared to 303 children who did not receive VTI in this study. However, despite having worse hearing levels in children who were randomised to VTI, the difference in their hearing levels were not likely to be clinically significant as they were also within normal limits in this study. A birth cohort study by de Beer, et al. [20] that provided a longer follow-up found significantly elevated hearing levels in 51 children who underwent VTI than in those who did not, and found that a hearing loss of 5 to 10 dB persisted until early

adulthood. The authors also reported that the 132 children with a history of OM who did not undergo VTI also had significantly elevated hearing levels compared to 174 reference group. However, in this study we found no difference between two similar groups in the present study.

In addition to elevated hearing levels, some studies have highlighted the long-term risks of developing tympanic membrane abnormalities following VTI surgery in early childhood. In the follow-up study by Hong et al. [19], up to 88.6% of children who underwent VTI had tympanic membrane abnormalities based on an otoscopic examination, compared to 8.7% in medically treated children. Similarly, Stenstrom et al. [18] reported that whilst 81% of children who underwent VTI surgery had tympanic membrane abnormalities, only 19% of those with OM not receiving surgery had evidence of tympanic membrane abnormalities. A 15-year follow-up of a controlled trial that examined the impact of unilateral VTI in 46 children found fewer normal tympanic membranes in operated ears (30%) compared to non-operated ears (54%), however, hearing and tympanometry results did not differ between the operated and non-operated ears [22]. According to Stenstrom et al. [18] VTI was found to be the only risk factor for developing tympanic membrane abnormalities in their study, while de Beer et al. [20] noted that tympanic membrane abnormalities were the mediating factor between VTI and hearing loss. The present study did not specifically investigate the adverse impact of VTI in appearance and the physical condition of the tympanic membrane, rather it looked at VTI impact on middle-ear health status as assessed using tympanometry. Our results showed that abnormal middle-ear status was more common in children who underwent VTI in early childhood compared to non-surgically managed children with rOM, which supports the previous reports related to the long-term impact of VTI on the physical abnormalities in tympanic membrane. These findings may suggest a long-

term adverse impact of undergoing VTI in early childhood. However, it is also possible that less favourable hearing and middle-ear health outcomes in the VTI group found in this study might be due to a more severe history of OM and conseuqtently, worse hearing and middle-ear health status of children in this group, which might have indicated the need for surgery.
It should be noted that elevated hearing levels in a single frequency, and abnormal middle-ear status in the VTI group found in this study was statistically significant in one ear only. The reason for this unilateral VTI impact is unclear, but it is possible that this was a systematic error, or that children in the VTI group had worse left ears than right ears in this specific population. Further investigation of this matter was hindered by the lack of clinical reports and the reliance on parental reports to obtain information related to early OM history, which is a limitation of the present study.

Despite these findings, this paper showed that 4FA in the better ear was within normal limits in the VTI, rOM, and reference groups. This finding is consistent with the previous results of Hong et al. [19] and Johnston et al. [23] who found that although elevated hearing levels were found in children who underwent VTI surgery, they, as well as children who received medical treatment for OM, had hearing levels within normal limits in the long-term. A review by Schilder [25] also found that hearing levels of children with persistent OM, with or without undergoing VTI, and those with no history of the disease were comparable in the long-term and that VTI-subsequent tympanic membrane abnormalities resulted in an average hearing loss of less than 5 dB. All these findings are in line with clinical guidelines for VTI [30] and indicate that children who underwent VTI surgery in their childhood can be at a higher risk of having slightly elevated hearing levels which appeared to be small and is unlikely to be of a clinical significance. In

addition to the potential risks associated with the insertion of ventilation tubes, previous reviews have shown that VTI benefits tend to be of a short-term lasting for approximately 12 months, before showing no difference to those non-surgically treated [15-17], while other studies have shown no differences between outcomes of children undergoing prompt and delayed VTI surgery [31-34].

6. Strengths and limitations

The large sample size of children enrolled is a major strength of the present study. Those children have been prospectively followed-up for research purposes. The number of children in the VTI group who were eligible for inclusion in the analyses (i.e. have complete sets of data), however, was small. This was one of the limitations of the present study that may affect the generalisability of its findings. The comprehensive follow-up of children enrolled in the study allowed for the availability of important information collected before, at, and after birth which were controlled as covariates in the present analysis. This has potentially helped in the investigation of the relationship between rOM, with or without undergoing VTI, and middle-ear health status and hearing outcomes in the long-term, more reliably. However, this was an observational study and the control of confounding variables might not be complete due to the lack of information regarding other medical complications (e.g., craniofacial abnormalities) that are known risk factors for OM. Furthermore, due to testing eligibility criteria, the findings of the study may not be applicable to children with sensorineural hearing loss or those with ventilation tubes in-situ. This study was also limited by the lack of ear-specific information or timing regarding the insertion of ventilation tubes so that the VTI group might have included children who received VTI bilaterally as well as those who received it unilaterally. Another limitation of

the study was the lack of information on actual hearing thresholds of children as the lowest intensity level tested was 20 dB, which was considered as the normal response level in this study. Finally, since we relied on the OM-related information provided in the parental reports, ear-specific information and information related to the severity and the specific types of OM were not available. Identifying children with rOM based on these parental self-reports could have some concerns related to the reliability of the information, which is another limitation of this study.

7. Conclusion

Our findings and those of previous studies indicate that VTI may be associated with some risks related to hearing and middle-ear health in the long-term that are likely to be clinically insignificant as the mean hearing levels were found to be within normal limits. Although limitations of this study prevent assertive conclusions regarding the long-term impact of rOM and VTI, its findings, in addition to previous reports, indicate that despite the widespread use of ventilation tubes, there is some potential adverse impact associated with the surgery in the long-term, including elevated hearing levels and middle-ear health abnormalities, that needs to be considered and balanced with the potential benefits of the procedures.

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