

Peer Review File

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**Reviewer A**

Comment1: SG cysts are an uncommon complication of intubation in the neonate presenting with stridor and potential airway obstruction.

The aetiology involves mucous retention cysts in the subglottis likely caused by tube trauma. Risk factors for development however are poorly understood and few large case series exist.

This paper attempts to define potential risk factors by comparing to a control group and is the first group to take this approach. The authors find a correlation with ETT suctioning. It is the first Australian data on this topic since the mid 1990's when both Bruce Benjamin (Sydney) and then Berkowitz (Melbourne) both published their series. Given publishing in AJO I would encourage citing these local similar studies and discussing results in context of these papers.

*Bauman NM, Benjamin B. Subglottic ductal cysts in the preterm infant: association with laryngeal intubation trauma. Ann Otol Rhinol Laryngol. 1995 Dec;104(12):963-8. doi: 10.1177/000348949510401209. PMID: 7492069.*

*Smith SP, Berkowitz RG, Phelan PD. Acquired subglottic cysts in infancy. Arch Otolaryngol Head Neck Surg. 1994 Sep;120(9):921-4. doi: 10.1001/archotol.1994.01880330011003. PMID: 8074818.*

*Reply1: These articles have been acknowledged and reference in the article. Lines 84 -98*

Comment2:

Discussion:

168 - typo -patient

Reply: Amended

Comment3:

225 - mean duration intubation 8.8 vs 4.8 days- is this not statistically different? How does this then correspond to the number of hour intubated? This is a confusing given the authors state no significant difference in hours intubated.

Neither fig 1 or table 1 are referenced within the paper

Reply3: These have now been appropriately reference within the paper.

Lines 107, and 196 respectively.

Comment4:

Given only 15 patients could the authors provide a table of cases for readers to be able to analysis the findings presented.

Reply4:

This can be included in the appendix

### **Reviewer B**

The authors have presented a concise summary of the clinical problem.

A minor point of clarification is sought from the authors: the main point of difference between control and cases was that there was for suctioning. The patients were intubated due to airway distress due to SGCs. Whilst in the discussion the authors have hypothesised that increase suctioning was required possibly due to higher amount of secretion, reflux and aspiration, they conclude that suctioning may lead to the "development of SGCs". In the discussion the relevance is an association but in the conclusion it is portrayed as a cause. Do the authors have enough evidence from this retrospective study with small numbers to make this conclusion

Comment5:

Reply5: Agreed. It would be more reasonable to conclude that an association may exist and this has been amended in the summary, as opposed to making such a strong conclusion. Line 342.

### **Editorial Comments**

#### **Abstract**

1. Please present all key results with precise data and their precisions (95% CI) in the abstract, instead of vague wording like similar,  $p < 0.05$ , etc.
2. It's advised to state year and dates rather than only describing the length of time periods. The statistical methods could also be briefly described here.

Reply 2: This has been updated as request. Line 44 and 108.

3. Please also include the details of the methodology: what variable of interest were collected?

Reply 3: Specific variables have been added on lines 138-141.

, including gestational age, weight, suction frequency, duration of intubation, number of re-intubations, and size of endotracheal tube.

### **Introduction**

4. Lines 100-101, “Furthermore, there has been an increase in the incidence of acquired SGCs”, would like to add the specific data or range here.

Reply 4: Additions references. Studies referenced on lines 77-80.

A study by Desanto et al. in 1970 had only one subglottic cyst in their case series of 238 laryngeal cysts (3). A study by Benjamin and Bauman in 1995 noted 78% of their patients had subglottic cysts, in their series of laryngeal cysts (4).

5. Lines 104-105, “there has been no definite association between the period of intubation and the risk of developing such a pathology”, please add the corresponding reference to back up the claim.

Reply 5: We have added the appropriate reference in the text. Lines 93, and added to the reference list.

6. The authors could add more comments about the symptoms of SGC, including simple noisy breathing to stridor, respiratory failure etc.

Reply 6:

Lines 86-89. Subglottic cysts are almost always an acquired pathology with formation thought to result from mucosal tissue damage and obstruction of mucous glands. Congenital subglottic cysts are an exceedingly rare (5). Symptoms can range from mild cough to hoarseness, stridor and respiratory distress.

### **Methods**

7. The exact dates (including the month and year) should also be reported in the Methods. Also, the criteria of selection need to be exposed clearly of the two groups. For example, congenital SGCs were excluded.

Reply 7: Exact dates have been included and exclusion criteria added.

8. Could the authors describe the reason why the patients in the control groups also receive MLB?

Reply 8: Controls group had other reasons for MLB. These included ruling out airway pathology. Including subglottic cysts, laryngeal cleft and tracheomalacia. Lines 130-131.

9. The authors should describe the diagnostic methods of SGC used in this study in a bit more detail in the methods section.

Further details are required regarding the collected data in the Methods.

Reply 9: The addition of surgical technique, and who performed the procedures Lines 143-162

10. How was the recurrence or re-intubation determined?

Reply 10: Re-intubation was recorded from ICU records.

11. Please describe the investigators who collect the data. Always the same doctor? What is the level of experience?

Reply 11: Lines 135 - 136. The data was collected by a single senior ENT registrar.  
Lines 152 – 153

12. Since the authors analyze the obstruction grade of SGC, please describe the degree of airway obstruction by Cotton-Myer classification in the Methods.

Reply 12: Lines 159 – 162. This has been amended in the text. Myer-Cotton classification was used to grade the level of airway obstruction.

13. Please indicate when surgery or conservative treatment is required. Also, would suggest reporting the kinds of endoscopic managements (i.e. CO2 LASER, marsupialization with cold instruments etc.).

Reply 13. All procedure were completed using a cold steel technique. Lines 161-162

14. Is there any missing data issue? The authors should include the steps for addressing missing or incomplete data in the Methods section. If there was no missing data. Please also state it in the text.

Reply 14. No necessary data was missing. Lines 135-136

15. For better reporting, it's recommended to add some subheadings for each paragraph of the Methods sections. The authors could refer to the items of the STROBE checklist.

Reply 15: completed

## **Results**

16. The continuous variables should be described in the way of mean (SD) or median (IQR/range) in Table 1. The sample size in the two groups should be mentioned again in the table.

Reply 16: updated in Table 1.

17. provide the associated parameters of measurement uncertainty as appropriate (e.g., confidence intervals) and avoid providing only the results of statistical hypothesis tests (e.g., P values). This applies to the results from lines 166-189.

Reply 17: Completed

18. The authors only compared the gestation of the two groups. This is not enough. It's suggested to share more detailed demographic and clinical background of the case and control groups, such as sex, birth weight etc. This will be very helpful for reducing potential confounders.

Reply 18: 178 – 179, table page 18.

19. What about the patient outcomes after receiving treatments?

Reply 19: Lines 191-192, 220-221.

## **Other comments**

20. Line 55, “We aimed to determine the risk factors in patients with subglottic cysts”. After reading the manuscript carefully, we note the authors compared the difference of characteristics of intubation between groups. It cannot be called “the risk factors of SGC” without multivariable analyses, nor can it be called “independent risk factor” in line 267.

Reply 20: Changes in text. Lines 97 and 292.

21. Please kindly revise the form of P-value in the report according to our latest Author Instruction below:

The description of the P-value should be in uppercase italic format, i.e., “P”.

If  $P < 0.001$ , please report “ $P < 0.001$ ” to avoid reporting unnecessarily excessive precision.

If  $0.001 \leq P < 0.01$ , please report the specific P-value to 3 decimal places, e.g., “ $P = 0.001$ ”, “ $P = 0.009$ ”;

If  $P \geq 0.01$ , please report the specific P-value to 2 decimal places, e.g., “ $P = 0.01$ ”, “ $P = 0.06$ ”, “ $P = 0.10$ ”, “ $P = 0.90$ ”;

Do not round P-values, do not report “not significant” simply when the data is greater than an arbitrary value, and do not report only vague bounds, such as  $P < 0.05$ , as described above, but report the exact P-value.

Reply 21: Completed