

Peer Review File

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Reviewer A

Thanks for your paper, I agree although there are many studies which show that allergic rhinitis is associated with sleep disorder, larger and better studies need to be done.

I am concerned however with a few methodological issues.

Comment 1

Firstly, you have chosen 410 of 1165 and suggested all these should have or could have been allergic based on having allergic symptoms and were testing - does this bias the results?

Response: The entire selection of patients is biased towards those who have allergy symptoms. The objective of the paper was to determine the relationship between allergic rhinitis and sleep disordered breathing through an objective parameter, being IgE testing. However, patients only undergo IgE testing if there is presence of allergy symptoms. While it would be ideal to have a subset of pediatric patients without allergy symptoms who have had IgE testing for comparison, this would have to be performed prospectively with patient recruitment, which is outside the scope of this study.

This limitation has been included in the discussion as “The studied population were also children undergoing tonsil/adenoid/turbinate surgery, which reduces the translatability of results to the general population. As pediatric patients without allergy symptoms are unlikely to have IgE testing, this negative control group would need to be recruited through a prospective study.”

Comment 2

You state “Patients were excluded from the study if they did not have symptoms and/or examination findings of allergic rhinitis” this implies ALL study participants should have had allergy.

Should this be reworded? if patients were NOT tested for allergy then they were excluded.

Response: The implication that all study participants should have had allergy is correct. This has been included in the remainder of that statement, which reads “Patients were excluded from the study if they did not have symptoms and/or examination findings of allergic rhinitis, **if they did not have allergy testing performed**, and if there was no pre-operative clinical notes available.

Comment 3

I am also very concerned about your statistical analysis - for multiple measures you need to do the Bonferroni test.

The Bonferroni test is a statistical test used to reduce the instance of a false positive. In particular, Bonferroni designed an adjustment to prevent data from incorrectly appearing to be statistically significant.

Looking at your table of multiple variables the 'Sleep Symptoms in General' (this is a grouped category not defined in methods) has 168 of 175 Vs 180 of 200 – even if this was slightly statistically significant, can you infer any clinical value or significance especially when NONE of the individual symptoms were even close to being significant.

Response: The Bonferroni test was considered for the multivariate statistical analyses, but a decision was made against its use after weighing the reduction of false positives against the risk of false negatives. Overall, the study preferred the reduction of false negatives as the large sample size reduces the risk of false positives. While individual symptoms may not have been statistically significant, it is possible that a difference existed when accounting for any symptom. As this difference would not have been significant if the Bonferroni correction was applied, this has been mentioned in the methods as “Due to the large sample size, small groups for multiple hypothesis testing, and preference for reducing false negatives, the Bonferroni correction was not applied to multiple hypothesis testing”, and the discussion as “in fact, sleep symptoms in general were more prevalent in the sIgE negative group, while snoring was more prevalent in the tIgE negative group. These results may confer false positives due to multiple hypothesis testing, but this is countered by the large sample size used in this study.”

Comment 4

Also - Examination findings showed patients had significantly smaller adenoids in the sIgE positive group ($p=0.003$) - the statistic may have been significant but how can 21 nil or small in the Positive group VS 23 in the Negative group BE clinically relevant?

Response: The sample size for the IgE positive group ($n=200$) is larger than the IgE negative group ($n=175$), so the comparison of nil / small adenoids is 10.7% to 13.3%, respectively. Obstructing adenoids were lower in the IgE positive group (56.2 vs 67.9%), but moderate adenoids were seen to be more prevalent in this group. Although the trends are not homogenous, the overall trend supports the conclusion and therefore this sentence has been left in the paper.

Comment 5

Another issue you have to acknowledge in your discussions is the well documented high Incidence of false negative RAST tests in children, which can be as high as 50%.

In a systematic review of SPT negative tests in patients WITH allergy symptoms 25% had Specific IgE detected on nasal brushings showing local allergy as opposed to 3% if there were no symptoms. If all your patients had allergy symptoms, then there is a HIGH change that many of the negative tests are false negatives.

Response: This has been mentioned in the text, and in fact the conclusion states “this can be explained by the relatively poor sensitivity and specificity of IgE testing for allergic rhinitis signs and symptoms, which ranged from 32.6% to 66.3% and 21.4% to 61.3% respectively.” However, we have highlighted this more clearly in the limitations section as “the poor sensitivity and specificity of IgE testing limits the ability to detect a correlation between allergic rhinitis and SDB. As skin prick testing has been shown to be more sensitive to serum IgE testing (23-25), this would have improved the methodology.”

Comment 6

Ages divided into two groups of four years or younger and five years or older – THEN what happen to patients aged 4-5 e.g., 4years and 6 months? division needs to be greater or equal to 5 and under 5.

Response: This has been amended to reflect the age ranges of less than five years old, and five years or older. The tables and all in-text references of these age ranges have been changed accordingly.

Comment 7

I think you would be better off looking at the whole cohort including patients with NO symptoms of allergy to get a better understanding of any difference.

Response: Agreed, however as mentioned previously, patients only undergo IgE testing if there is presence of allergy symptoms. While it would be ideal to have a subset of pediatric patients without allergy symptoms who have had IgE testing for comparison, this would have to be performed prospectively with patient recruitment, which is outside the scope of this study.

This limitation has been included in the discussion as “The studied population were also children undergoing tonsil/adenoid/turbinate surgery, which reduces the translatability of results to the general population. As pediatric patients without allergy symptoms are unlikely to have IgE testing, this negative control group would need to be recruited through a prospective study.”

Comment 8

When your results are so discordant with the literature it may point to your methodology rather than you finding novel results. There have been a few studies larger than this

recently published e.g., Sherrey J., Biggs S., Dorrian J., et al Allergic disease, sleep problems, and psychological distress in children recruited from the general community. *Ann. Allergy Asthma Immunol.* 2022;129(3):366-372

This study looked at 1449 Australian children.

Please try and address these or incorporate them in your discussion

Response: The fact that the findings of this paper do not agree with some of the published literature has been mentioned in the text, and this study has been added to that section of the discussion, which now reads “A meta-analysis and systematic review (12) of twenty-seven observational studies up to 2019, including both adult and paediatric patients, found allergic rhinitis patients had significantly worse sleep latency, efficiency, daytime sleepiness, morning headaches, restless sleep, SDB and OSA, though the general standard of studies included was judged to be low or very low. A recent, large-scale observational study in children from the general community found an association between allergic disease and psychological distress that was mediated through sleep problems (Sherrey 2022).”

Reviewer B

This is a large retrospective study looking for association between sleep disordered breathing and allergic rhinitis.

It reported that there was no correlation between IgE-positive allergic rhinitis and sleep disordered breathing. Only a small proportion of the patients had skin prick testing.

This would have been strengthened if patients had skin prick testing rather than IgE testing but it adds to the literature give in it's negative association.

Response: A comment on skin-prick testing has been included in the limitations section, which reads “the poor sensitivity and specificity of IgE testing limits the ability to detect a correlation between allergic rhinitis and SDB. As skin prick testing has been shown to be more sensitive to serum IgE testing (23-25), this would have improved the methodology.