

Review report

BSMMUJ-17.3 – 74632

Serum thyroid autoantibodies in malignant thyroid nodules

Awal TR *et al.* (drawal80026@gmail.com)

REVIEW COMMENTS	AUTHOR RESPONSE
<p>[Note: Please write the responses to each point here mentioning line number(s). You must change the manuscript as per your response.]</p>	
<h3>A. Mechanical review</h3>	
Date sent to author: 13-Apr-23	Date: 11-Jul-23
1. Abstracts should be having background, methods, results, and conclusion sub-headings. Please keep acronyms spelled out if used once in the abstract. If used more than once in the abstract, mention the acronym in parenthesis in the first mention.	Background, methods, results, and conclusion sub-headings are added in abstracts. Acronyms were revised.
2. Add a section on "highlights" before the abstract. Please note that this section should be no more than five bullet points relating to the strengths and limitations of this study specifically to the methods, not the results of the study.	"Highlights" has been added before abstract.
3. Reduce the volume of "acknowledgements" section. Currently it is more than 400 words.	The volume of "acknowledgements" section has been reduced.
4. Use recent references only.	Only recent references have been used.
<h3>B. Technical review</h3>	
ROUND 1	
Handling Editor's name: Ferdous Hakim	
ORCID: 0000-0003-2376-3978	
Date sent to author: 26-May-23	Date: 11-Jul-23
1. In an earlier submission, it was indicated that this manuscript emerged from the thesis work of the first author. Therefore, please follow the editor's instructions on keeping the number of authors to six. Otherwise, the student's contribution will deemed to be inadequate.	Editor's instructions have been followed on keeping the number of authors to six.
2. Please insert the word counts in the title page	Word counts are added in the title page.
3. The submitted version shows that two bullets are on background information, and two bullets are on methods. Revise the highlights following the author's	The highlights have been revised following the author's instructions in the Journal that this section are related to the strengths and limitations of this study.

REVIEW COMMENTS	AUTHOR RESPONSE [Note: Please write the responses to each point here mentioning line number(s). You must change the manuscript as per your response.]
instructions in the Journal that this section should relate to the strengths and limitations of this study.	
4. The introduction has been segmented into paragraphs based on themes (page 4, lines 72–91).	Introduction has been revised (page 4, lines 72–91).
5. Was the recruitment of the patients consecutive? Purposive sampling needs to have a justification for its use. (Page 5, line 101)	Yes, it was consecutive.
6. Page number not inserted though line number was. I have inserted the page number.	Page number has been inserted.
7. Consent – was it informed written consent? Please clarify. (Page 5, lines 101–102).	Consent was informed in written. (Page 5, lines 101–102).
8. ‘Student’s <i>t</i> -Tests’ is the correct write-up, please correct (page 5, line 118).	The correct write- up of ‘Student’s <i>t</i> -Tests’ has been corrected (Page 5, line 118).
9. <i>P</i> is the recommended symbol for probability (page 5, line 121).	<i>P</i> is used as the recommended symbol for probability (Page 5, line 121).
10. Please elaborate on acronyms at the first instance and use the acronyms for the subsequent iterations throughout the manuscript. (e.g., page 5, line 125)	Acronyms has been elaborated at the first instance and the acronyms were used for the subsequent iterations throughout the manuscript. (Page 5, line 125)
11. Please revise the language and check the grammar. e. g. ‘Table II shows’ – a table cannot show anything. (Page 6, line 135).	Language and grammar have been revised accordingly.
12. The first paragraph of the discussion section should reflect the summary of the findings of the study without citing results in numbers. Please revise accordingly.	The first paragraph of the discussion section has been revised accordingly.
13. In the limitations, the author mentions that sample might not be representative of the whole population. I do not think that the authors claim such, so how can it be a limitation? Is the result representative of the study hospital (i.e., internal validity of results)?	The limitations have been revised.
14. The write-up on the author’s contribution needs alignment with ICMJE guidelines and the Journal’s recommendations.	The write-up on the author’s contribution has been revised with the alignment of ICMJE guidelines and the Journal’s recommendations.
15. Tables need to be independently readable/ understandable. (e.g., ‘ns’ is not required, but the P cut-off must be mentioned in the footnote)	Tables have been prepared independently readable/ understandable. (e.g., ‘ns’ was omitted, but the P cut-off were mentioned in the footnote)
16. A journal style of table formatting is needed. Please use single digits after decimals for citing results throughout the tables except for P, where actual value can be cited.	A journal style of table is formatted
17. Table I: age, and sex distribution by benign or malignancy is shown. Is the title reflect aligned with this? (Page 11)	In table 1, title has been revised.
18. Table II: overuse of acronyms, as ample space is available for writing the full name of tests. The unit of the test results is not mentioned. What does the superscripted symbol after every P denote? (Page 12)	Table II: Full test name are mentioned. Symbol has been superscripted after every <i>P</i> denoted significance (page 12).
19. Table III: please insert details on how the multivariate logistic regression model was run and the P cut-off that was used. (Page 13)	Table III: The multivariate logistic regression model is shown in result section. (Page 13).
20. Figure 1: please detail the calculations of the sensitivity analysis in the footnote of the Figure.	The details of the calculations of the sensitivity analysis were described in the footnote of the Figure.
Handling Editor’s recommendation: Revision required	
Reviewer’s name: Hussein Adil Abid	
ORCID: 0000-0002-5226-816X	
Date assigned: 19-Mar-24	

REVIEW COMMENTS	AUTHOR RESPONSE [Note: Please write the responses to each point here mentioning line number(s). You must change the manuscript as per your response.]
Date submitted: 31-Mar-24	
Do you have any conflict of interest with the author/s? No	
Comments sent to author (Date: 27-May-24)	Date: 11-Jul-24
1. The abstract provides a good overview of the study, including the background, methods, results, and conclusion.	Abstract has been written according to reviewer's comment.
2. Include the sample size (n=104) in the methods section of the abstract.	Sample size (n=104) has been included in the methods section.
3. Provide the full form of abbreviations (FNAC, BSMMU) when first mentioned.	The full form of the mentioned abbreviation has been provided.
4. The conclusion could be more specific, highlighting the potential utility of thyroid autoantibodies as predictive markers for thyroid malignancy.	The conclusion has been revised accordingly.
5. The introduction provides relevant background information and justifies the study's importance.	Introduction has been prepared to justify the study's importance.
6. Consider adding more recent references to strengthen the rationale and highlight the knowledge gap addressed by this study.	More recent references have been added.
7. Clearly state the study's objectives or hypotheses at the end of the introduction.	Study's objectives were stated at the end of the introduction.
8. The study design, setting, and duration are clearly described.	The study design, setting, and duration are prepared to describe clearly.
9. The inclusion and exclusion criteria for participant selection are well-defined.	The inclusion and exclusion criteria for participant selection were prepared according to that.
10. Provide more details on the FNAC procedure and the criteria used for classifying nodules as malignant or benign.	The FNAC procedure and the criteria used for classifying nodules as malignant or benign were provided.
11. Specify the method used for measuring thyroid autoantibodies (e.g., ELISA, chemiluminescence) and provide information on the assay's sensitivity, specificity, and reference ranges.	The method for measuring thyroid autoantibodies (immunoassay) were specified and reference range were provided.
12. Describe the sample size calculation and justify the chosen number of participants.	According to the given formula, the sample size for each group was 52 (each group). Total sample size was 104.
13. Mention any efforts made to minimize potential biases (e.g., blinding of investigators).	Unanswered.
14. The results are presented clearly and concisely, with appropriate statistical analysis.	The results have been prepared to clearly present the statistical analysis.
15. Table I: Provide the actual numbers and percentages for each age group in addition to the mean±SD.	The actual number and percentage have been provided for each age group in addition to mean±SD.
16. Figure 1: Improve the resolution of the image and ensure that the percentages add up to 100% for each group.	The resolution of the image is made improved.
17. Tables II and III: Clarify the cutoff values used to define "normal" and "elevated" levels of TgAb and TPOAb.	Cutoff values have been clarified.
18. Table IV: Provide the 95% confidence intervals for the odds ratios.	The information has been provided.
19. Consider presenting the sensitivity, specificity, PPV, and NPV of thyroid autoantibodies for predicting malignancy in a separate table or figure.	Presenting the sensitivity, specificity, PPV, and NPV of thyroid autoantibodies for predicting malignancy in a separate table or figure has been provided.
20. The discussion effectively interprets the study's findings and compares them with previous literature.	The discussion has been made accordingly.
21. Elaborate on the potential mechanisms underlying the association between thyroid autoantibodies and malignancy.	The potential mechanisms underlying the association between thyroid autoantibodies and malignancy are elaborated.

REVIEW COMMENTS	AUTHOR RESPONSE [Note: Please write the responses to each point here mentioning line number(s). You must change the manuscript as per your response.]
22. Discuss the clinical implications of using thyroid autoantibodies as predictive markers and how they could complement existing diagnostic methods like FNAC.	The clinical implications of using thyroid autoantibodies as predictive markers and how they could complement existing diagnostic methods like FNAC has been discussed.
23. Address the study's limitations more comprehensively, such as the single-center design, lack of long-term follow-up, and potential selection bias.	The study's limitations are more comprehensively addressed.
24. Suggest future research directions based on the study's findings and limitations.	The future research directions have been suggested.
25. The conclusion is concise and aligns with the study's results.	The conclusion has been prepared accordingly.
26. Consider emphasizing the potential role of thyroid autoantibodies in risk stratification and decision-making for patients with thyroid nodules.	The potential role of thyroid autoantibodies in risk stratification and decision-making for patients with thyroid nodules has been emphasized.
27. The references are relevant and up-to-date.	The references are relevantly prepared.
28. Ensure that all references are formatted consistently and adhere to the journal's guidelines.	All references are formatted consistently and adhere to the journal's guidelines.
Reviewer's Recommendation: Resubmit	
ROUND 2	
Handling Editor's name: Ferdous Hakim	
ORCID: 0000-0003-2376-3978	
Date sent to author: 14-Jul-23	Date: 17-Jul-24
1. The inclusion and exclusion criteria for participant selection were absent. Please include this.	The inclusion and exclusion criteria for participant selection has been added.
2. Sample size calculation and justification for the chosen number of participants were not found in the revised manuscript although it was shown in the reply.	Sample size calculation and justification for the chosen number of participants are added.
3. Table 2: if 95% confidence interval is shown, then showing <i>P</i> is redundant.	<i>P</i> has been removed.
4. The references should be up-to-date. Some of the references date back to 2004–2008. Please consider recent articles if it suits better.	The references have been prepared to make up-to-date with the best possible way.
5. The following reference was suggested at page 6 and line number 131. It has not been included in the manuscript. The authors did not mention the reason for non-inclusion in the reply.	Reference has been included at page 6 and line number 131. It was mistakenly removed.
6. Can you specify where in Reference No. 10 the cut-offs used in this study (page 5, line 128) have been mentioned? I could not find the cut-off values for TgAb and TPOAb mentioned in the article (>40 IU/mL and >35 IU/mL respectively). The full text of the article is appended below for your ease of work.	The cut-off values for TgAb and TPOAb mentioned in the article (>40 IU/mL and >35 IU/mL respectively) have been specified by giving the references.
Handling Editor's recommendation: Revision required	
ROUND 3	
Handling Editor's name: Ferdous Hakim	
ORCID: 0000-0003-2376-3978	
Date sent to author: 16-Jul-23	Date: 17-Jul-24
1. Please submit the responses in the reply template.	The responses have been submitted in the reply template.
2. In the methods section the write-up for sample size calculation needs to be concise. You can follow the style of the below article cited by you in the manuscript.	In the methods section the write-up for sample size calculation were made concise.

REVIEW COMMENTS	AUTHOR RESPONSE
3. Dash R, Mohapatra A, Manjunathswamy BS. Anti-thyroid peroxidase antibody in vitiligo: a prevalence study. J Thyroid Res. 2015;2015:192736. doi: 10.1155/2015/192736.	[Note: Please write the responses to each point here mentioning line number(s). You must change the manuscript as per your response.]
4. Reference number 18 has an error in DOI.	Reference number 18 has been corrected.
5. The following reference is not included in the reference list. It was parked on page 7 as a footnote by me and is remaining there still. Please include it in the reference list of the manuscript.	The mentioned reference has been included in the reference list.
6. Baratloo A, Hosseini M, Negida A, El Ashal G. Part 1: Simple Definition and Calculation of Accuracy, Sensitivity and Specificity. Emerg (Tehran). 2015 Spring;3(2):48-9.	
Handling Editor's recommendation: Revision required	
Executive Editor's name: M Mostafa Zaman	
ORCID: 0000-0002-1736-1342	
Comments sent to author (Date: 17-Jul-24)	Date: 17-Jul-24
1. The issue of >40 vs >=40 and >35 vs >=35 persists. This has to be corrected in the texts and tables.	The issue has been corrected in the texts and tables.
Executive Editor's decision: Revision required	

C. Editorial decision	Date: 5-Aug-24
Final editorial decision: Accepted	