Peer Review File

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Reviewer A

The pathogenesis of IgA vasculitis remains unclear, and I believe this paper is very interesting and important. On the other hand, it contains several problems with the methods of the study as indicated below.

Major comments

1) This article uses the diagnostic name "HSP", which was changed to "IgA vasculitis" in the 2012 CHCC (Chapel Hill Consensus Conference) vasculitis revision.
Is there any reason why the authors use the diagnostic name "HSP"? If not, I think it is better to use the diagnostic name “IgA vasculitis”.
Reply: I have modified our text as advised (the entire article).

2) Since this study is a comparison with a healthy control group, is the study design a case-control study?
Were healthy controls recruited at the same time as IgA vasculitis patients? Also, was there any bias in the season in which they were recruited? Please describe in the text.
Reply: I have modified our text as advised (see Page 2, line 36-37).

3) The healthy group had to perform blood tests that were not required. How was consent obtained from patients and their families?
Reply: I have modified our text as advised (see Page 2, line 38-39).

4) How many patients with IgA vasculitis had renal biopsy, skin biopsy or gastrointestinal endoscopic intestinal biopsy, respectively? Please describe if the authors know.
Reply: I have modified our text as advised (see Page 10, line 297-299).

Minor comments

1) Page 4, L115
What are the "Chinese Society of Pediatric Rheumatology diagnostic criteria"? Please indicate any references or books cited.
Reply: I have modified our text as advised (see Page 4, line 122).

2) Page 4, L119-Page 5, L123
Please provide a flowchart diagram including the number of patients to be excluded and the inclusion/exclusion criteria until the final number of eligible patients is determined.
Reply: I have modified our text as advised (see Page 16, line 483).

3) Page 5, L142

How was the streptococcal infection diagnosed? Did you have a positive rapid test or culture test, or did you measure ASK/ASO? Indicate in the Methods section.
Reply: I have modified our text as advised (see Page 5, line 150).

4) Page 5, L151-
The authors classify the patients into three groups according to their vitamin D levels, where does this classification appear in the paper? The analysis seems to be based on the vitamin D value as it is, as a variable.
Reply: I have delete this content in our text as it seems a little redundant (see Page 5, line 155).

5) Table2
It is disconcerting that the third and subsequent rows are a breakdown of 605 HSP patients, yet 400 healthy children are included in the same row.
The authors should either separate the table or change the type of lines to make it easier to view.
Reply: I have modified our text as advised (see Page 15, line 457).

6) Table2,3
Put the unit (ng/mL) in the cell for "Levels of 25-hydroxyvitamin D3".
Reply: I have modified our text as advised (see Page 15, line 457and 464).

7) Table3
What is the "F" to the left of the P value?
The authors used the Tukey test, a parametric method, but were the population variances for each group equal?
Reply: I have modified our text as advised (see table 3).

8) Figure1
The authors should align the typeface in the cell.
It might be better to include in the figure description, "Patients are duplicates."
Reply: I have modified our text as advised (see Page 16, line 481 and Page 17, line 492).

Finally, although not related to the text, I have the impression that the number of HSP admissions within the observation period is very high. Do HSP patients tend to congregate at the authors' facility? Or is this a common number of HSP patients in general hospitals in China?
Reply: Our hospital is a children's specialized and a tertiary hospital, Pediatric rheumatology and immunology department is the key department. HSP patients tend to congregate at the our facility.

Reviewer B

1) First, in the title “a retrospective observational study” is not an accurate description of the clinical research design of this study, which should be a comparative study. The authors also need to indicate the comparisons of VD3 levels across different subgroups pf HSP.

Reply: I have modified our text as advised (see Page 1, line 2).

2) Second, the abstract needs substantial revisions. The background did not indicate the knowledge gaps on VD3 in HSP and what the clinical significance of this research focus is.
Reply: I have revised our text as advised, see Page 1, line 30-34.
The methods need to describe the inclusion of subjects, whether and how the case and control groups were matched, assessment of clinical factors and subtypes of HSP, and the measurements of serum VD3.
Reply: I have revised our text as advised, see Page 2, line 37-41.
The results need to describe the clinical characteristics of the two groups and the baseline comparability of the case and control groups.
Reply: I have revised our text as advised, see Page 2, line 52-53.
Please quantify the findings by reporting the VD3 levels of different groups and the accurate P values for their comparisons
Reply: I have revised our text as advised, see Page 2, line 54-56.
The conclusion needs comments for the clinical implications of the findings.
Reply: I have revised our text as advised, see Page 2, line 61-63.

3) Third, the introduction needs to have a detailed review on the small-scale studies on VD3 in HSP, analyze their limitations and knowledge gaps, and clearly indicate the clinical significance of this research focus. The authors need to have some hypotheses on the VD3 levels in different subtypes of HSP.
Reply: I have revised our text as advised, see Page 4, line 115-116.

4) Fourth, in the methodology of the main text, please describe the clinical research design and sample size estimation procedures of this study, as well as the measurements of serum VD3 levels. In statistics, most of the comparative analyses are univariate analyses, which is potentially problematic and may generate misleading findings. Please indicate whether and how the case and control groups were matched. I suggest the authors to first test the comparability of different subgroups, and do multiple regression analysis to exclude the confounding effects of other variables. Please ensure $P<0.05$ is two-sided.
Reply: It's too difficult to perform the above project.

Reviewer C

1. Please check if there's a reference missing here since you've mentioned "a previous study".

435 pathogenesis of renal injury in IgA vasculitis. The mechanisms of pathogenesis are
436 unclear; however, a previous study speculated that the reduced synthesis of
437 1,25-dihydroxyvitamin D3 leads to the release of downstream inflammatory
438 mediators (IL-8 and TNF-α), which in turn causes the inflammatory destruction of the

Reply: I have modified it as requested (see Page 9, Line 270).

2. Please check Table 1-2 footnotes and revise.

Table 1 Comparison of age and sex between the IgA vasculitis and healthy control groups

Characteristic	IgA vasculitis patients	Healthy children	P
Sex, no. (%)			
Male	319 (52.7)	222 (55.5)	0.388
Female	286 (55.5)	178 (44.5)	0.388
Age (years)	7.23±2.63	7.33±2.26	0.513

IgA vasculitis, Henoch-Schönlein purpura.

Reply: I have modified it as requested (see table 1 and table 2).

3. How were those data presented in your Table 2? Please define them either inside the table or in table footnote.

Table 2 Comparison of vitamin D3 levels between IgA vasculitis and healthy children , and comparison of vitamin D3 levels within IgA vasculitis

Grouping	Levels of 25-hydroxyvitamin D3(ng/mL)	P
IgA vasculitis patients [605]	15.47±6.58	0.00
Healthy children [400]	22.48±6.24	
Renal involvement [110]	12.99±4.92	0.00
No renal involvement [495]	16.02±6.78	
Streptococcal infection [165]	14.20±6.06	0.004
No streptococcal infection [440]	15.93±6.71	
Gastrointestinal symptoms [231]	14.43±6.33	0.002
No gastrointestinal symptoms [372]	16.10±6.59	
Joints involved [244]	15.27±6.88	0.565

Reply: I have modified it as requested (see table 2).

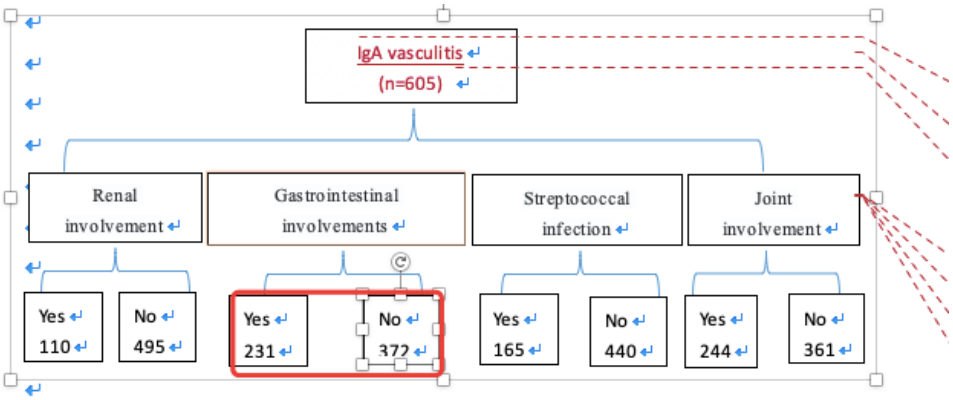
4. Likewise, please define these data either inside table 3 or in table footnote.

Table 3 Comparison of vitamin D3 levels in patients with IgA vasculitis with different onset seasons

Onset season	Number of cases	Levels of 25-hydroxyvitamin D3	F value	P
Spring	125 (20.66%)	13.374*	5.807	0.000
Summer	109 (18.17%)	17.625		
Autumn	181 (29.92%)	16.740		
Winter	190 (31.40%)	14.393*		

Reply: I have modified it as requested (see table 3).

5. Please check the numbers “231” and “372”, they do not add up to 605.



Reply: I have modified it as requested.

6. Please also check and revise Figure 2 legends.

Figure 2 The classification of 605 patients based on the presence of renal involvement, gastrointestinal involvement, streptococcal infection and joint involvement. **IgA vasculitis**, Henoch-Schönlein purpura.Patients are duplicates.

Reply: I have modified it as requested.