

Persistence of anti-HBs and immunologic memory in children immunized with hepatitis B vaccine.

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Reviewer's comments		Author's response	
Date review assigned	21 December 2022	Date sent to author	28-Feb-23
Date review returned	22 January 2023	Date received from author	08-Mar-23
Reviewer name, affiliation, email, ORCID	Palash Chandra Banik Department of NCD, BUHS 0000-0003-2395-9049 palashcbanik@gmail.com		
Conflict of interest of the reviewer	None		
Please write Yes or No		Please write a response if the reviewer's comment is No. You must change the manuscript as per your response.	
1. Is the research question or study objective clearly defined in measurable terms?	Yes		
2. Is the abstract accurate, balanced and complete?	Yes		
3. Is the study design appropriate to answer the research question or achieve objective?	Yes		
4. Are the Methods described sufficiently to allow others to repeat it?	No	Methods are now described enough to allow others to repeat the study.	
5. Are the operational definitions and ascertainment of key variables given adequately?	No	Described the definition of key variables.	
6. Are the outcomes clearly defined?	No	Revised the results section.	
7. Are statistics used appropriately and described fully?	No	Given the separate sub section regarding statistical analysis.	
8. Do the Results address the research question or objective clearly?	No	Revised the results section.	
9. Are the tables and figures clear and appropriate to address the objective or research question?	No	Revised the tables.	
10. Does the Discussion cover the main points of the paper?	No	Revised the description focusing the major findings.	
11. Are the strengths and limitations addressed?	No	Described the strengths and limitations in Discussion section.	
12. Are the conclusions justified by the results?	No	Revised the Conclusion.	
13. Are the references up-to-date, and appropriate?	Yes		
14. Is the standard of written English acceptable for publication?	No	Improved the standard English writing.	
15. Descriptive comments to the authors (Divide it into MAJOR and MINOR points).		Respond and reflect it in your manuscript. If you refute, justify your argument using references.	
Major: Need substantial revision in the methods, results and discussion parts.			
1. Need explanation about inclusion of 6 and 11 year children.		1. As the study aimed to evaluate the persistence of antiHBs five and ten years after primary vaccination by EPI schedule, so this two groups were included who were vaccinated around 5 and 10 years back respectively.	
2. It was not clear whether the authors used any formula for sample size determination or not, if not then why only 100 sample size.		2. Please see the reply of the editor's comments.	
3. Need to mention the ethical approval permission for this study as you collect blood samples. Only		3. Described in the methods section and IRB clearance number was given.	

<p>written consent is not enough, need ascent from the guardians as they are minors.</p> <p>4. Authors mentioned “For those who were HBsAg negative and had declined level of antibodies (<10 mIU/ml), hepatitis B vaccine, genetically engineered recombinant DNA vaccine, Engerix B, manufactured by GlaxoSmithKline, 0.5 ml, intramuscular was given to test for an anamnestic reaction.” This is not the right procedure to measure this. Authors need to justify their choice of study design with reference(s).</p> <p>5. Tables 3 & 4: not clear why the authors analyzed the data for only 12 (group A) and 18 (group B) subjects instead of 50 in each group. Need explanation n in methods. Need footnote about GMT.</p> <p>Minor:</p> <p>6. Need professional English editing.</p> <p>7. The authors used a questionnaire but did not mention whether it was validated.</p> <p>8. Please mention who collected the interview data and blood samples. Did they receive any compensation for blood samples?</p> <p>9. Why do authors collect anthropometric data if these are not used?</p> <p>10. Authors should mention which statistical test was done for which condition.</p>		<p>4. Studies demonstrating anamnestic responses among those with low or undetectable anti-HBs levels following challenge with HB vaccine, together with the production of anti-HBs in circulating B-cells by spot ELISA, confirmed the presence of immune memory among vaccinees. Anamnestic anti-HBs responses all correlate close in kinetics and magnitude with proliferative T-cell responses. The accumulated data from studies assessed in this Review indicate that protection is dependent on immune memory, rather than declining anti-HBs responses and add additional weight to the European Consensus recommendations that following a complete course of vaccination, booster doses are unnecessary in immunocompetent persons. Reference: Banatvala JE, Damme PV. Hepatitis B vaccine – do we need boosters?. J Viral Hepat.2003; 10: 1–6. doi: 10.1046/j.1365-2893.2003.00400.x</p> <p>5. We have mentioned in manuscript in discussion part “One month after vaccination another sample was taken from 12 and 18 children in both groups. Others lost follow up”. Footnote given.</p> <p>6. We have modified manuscript.</p> <p>7. The questionnaire was not validated. However, the study protocol was approved by IRB.</p> <p>8. Mentioned in manuscript.</p> <p>9. Table 2 was added showing anthropometric data.</p> <p>10. We have added in statistical analysis part.</p>	
<p>Reviewer’s Recommendation (Tick mark on the open boxes to the right)</p>	a. Minor revision		
	b. Major revision	✓	
	c. Reject		

Editor’s comments	Author’s response
1. The manuscript needs a major revision . Please use the Admin checklist attached	Used the admin checklist and formatted the manuscript accordingly.
2. Revise to meet the criteria of a Brief article .	Revised the article into a “Brief Article”
3. It is not clear why a sex-specific analysis is needed. It is not mentioned in the objective, nor in the Introduction that there are sex differences.	As it was not mentioned in objective, we have omitted this data.
4. How was the sample size calculated? Has the calculated basic sample size been multiplied by 2	Sample size was calculated by using the formula (Sayed et al., 2011)

for sex strata? If no multiplier was used, splitting into male and female is not supportable.	$n = \frac{P1(100 - P1) + P2(100 - P2)}{(P1 - P2)^2 \times (Z\alpha + Z\beta)^2}$ <p>Here, n = Sample size P1 = proportion in one group (19 %) P2 = proportion in another group (52 %) Zα = 1.96 at 5% level Zβ = 0.85 at 80% power So, after calculation sample size of this study will be 30 children in each group. In the present study 50 children have been taken in each group.</p>
5. The analysis should be for 5 and 10 years, not for the sexes. Please revise all tables or change your text descriptions.	We have modified table and text descriptions as per your suggestion
6. Table 1 could be merged with table 2 having two broad headings: GMT and >=10 categories. Basically, these two provide the same information.	We have omitted table 1 as it showed sex difference data. Now table showing distribution of children in both groups according to Anti HBs titre.
7. Tables 3 and 4 could be merged to describe post-booster dose data.	We have done this.

Second round

Executive Editor's comments (10-April-23)	Author's response (13-May-23)
<p>Thanks for the revised version of the manuscript. The editorial office has formatted it for your further revision. The following points are yet to be addressed:</p> <ol style="list-style-type: none"> 1. The manuscript has plagiarized test (attached report), which must come down to 15% or less. 2. Reduce the word count to meet the criteria for a "Brief article". 3. Add email addresses of co-authors (marked as Yellow in the manuscript). 4. Add author contributions (marked as Yellow in the manuscript). 	<p>Please respond to all comments from the editor and reviewer(s). Indicate the line number(s) of the manuscript where the changes are done.</p> <ol style="list-style-type: none"> 1. I have thoroughly reviewed the manuscript and made the necessary corrections to reduce the plagiarism. 2. The word count has been reduced to meet the criteria for a "Brief article." 3. Email addresses of co-authors, marked in yellow, have been added to the manuscript. 4. Author contributions, have been included in accordance with the journal's rules.