Author's response to reviews

Title: Evaluation of Immune Response to Hepatitis B Vaccine in Health Care Workers at a Tertiary Care Hospital in Pakistan: An observational prospective study

Authors:

Mohammad Zeeshan (dr.zeeshan@adeels.net)
Kausar Jabeen (kausar.jabeen@aku.edu)
Anita N Akbar (anitanaushir@yahoo.com)
Ailia W Ali (ailia.ali@hotmail.com)
Saadia Z Farooqui (saadia.farooqui@gmail.com)
Vikram Mehraj (vikram.mehraj@aku.edu)
Afia Zafar (afia.zafar@aku.edu)

Version: 4 Date: 5 July 2007

Author's response to reviews: see over
21-06-2007

To,
Anita Makri
Assistant Editor,
BMC-Series Journals.

Dear Anita

Thanks for your communication. We appreciate the comments of the reviewers. As per their advice we have addressed the issue and made changes in the manuscript accordingly. Details as given below:

1st Reviewer’s report:

- **In this study, anti-HBc was not included. Without the result of anti-HBc, their findings were hard to interpret. Please provide the results of anti-HBc, at least in the 60 subjects who were negative for either HBsAg or anti-HBs.**

  Response:

  The major limitation of this study is the inability to evaluate the hepatitis B core antibody (antiHBc) in our study population due to low budget and limited resources. Therefore there is a possibility that reduced immune response to HBV vaccine was due to occult hepatitis B infection. We agree that a non responder rate of 14% might be an over estimate in our study population; however in a resource limited setting our results are providing a baseline for future epidemiological studies in this area. Moreover our finding matched with the studies conducted in other countries. (Discussion Page # 8--- line #6)

- **The history of HB vaccination of study subjects should be provided or discussed. Vaccine may loss their anti-HBs long term after HB vaccination without nature booster**

  Response:

  HCWs included in this study were previously not vaccinated and the antibody response was measured after 6-8 weeks of last dose of HBV vaccine. HCWs with prior HBV vaccination were excluded from the study. (material & method Page # 5 ... line # 10)

- **Please perform multivariate analysis to adjust the interaction between age and sex. In general, gentlemen (doctors) should be older than ladies (nurses) in hospitals.**

  Response:

  Multivariate analysis was done. (Table # 3)
** Please identify manufacturer of the MEIA kits for anti-HBs. If Abbott kits were used, the concentration of anti-HBs higher than 1000 IU/ml was recorded as “>1000 IU/ml”. How can you calculate the mean of anti-HBs concentration? 

Response:

Information regarding the kit used for anti-HBs quantification is added in manuscript. (Material and methods- page # 5...line # 5).

As far as mean antibody titer is concerned, it was a statistical error. For that reason table 3 and table 4 (of last manuscript) and the description in the discussion have not been included in the revised manuscript.

** 2nd Reviewer report:**

- **Page 6, Material & Methods: Which HBV vaccine was used, Plasma derived or Recombinant vaccine? Which vaccination schedule was followed, rapid vaccination schedule (0, 1, 2 months) or standard vaccination schedule (0, 1, 6 months)? What was the dose of vaccine given? Standard 20 microgram, less or more. What was the route of vaccine administration, subcutaneous or intramuscular? What was the site of vaccination, deltoid or gluteal? (Deltoid site vaccination always induces better antibody response). What was the brand name of the vaccine and the address of its manufacturer.**

Response:

Details of the vaccine are added in the manuscript.

(Material & methods page # 5 … line # 5 to 8)

- **Page 7, Results: Were the non responders (14%) tested for antiHBc to exclude occult HBV infection. Recently 17.2% of HBsAg negative, HBV DNA negative blood donors from Pakistan are reported antiHBc positive, suggesting high prevalence of occult HBV infection among healthy population (Bhattiet.al.Transfusion.2007;47:74-79)**

Response:

The major limitation of this study is the inability to evaluate the hepatitis B core antibody (antiHBc) in our study population due to low budget and limited resources. Therefore there is a possibility that reduced immune response to HBV vaccine was due to occult hepatitis B infection. We agree that a non responser rate of 14% might be an over estimate in our study population; however in a resource limited setting our results are providing a baseline for future epidemiological studies in this area. Moreover our finding matched with the studies conducted in other countries. (Discussion Page # 8--- line # 6)
• **Page 7 Results & Table 2:** Higher frequency of non responders among both sexes should be compared in different age groups to rule out the impact of age on the response.

Response:

Multivariate analysis was done which shows the age and gender as an independent risk factor. (Table # 3)

• **Page 7, Results & Table 4:** Difference in antibody titers should be compared in different age groups among both sexes to rule out the impact of age.

Response:

Table 4 is deleted.

• **Page 4, last line:** The prevalence of HBV positivity in Pakistan is mentioned as 3-4% but the reference 17 cited to this effect is from India, pertaining to “Evaluation of immunogenicity and reactogenicity of recombinant DNA hepatitis B vaccine produced in India. Hussain et.al. World J.Gastroentrol.2005

Response:

New reference for the prevalence of HBV positivity in Pakistani population is given. at reference # 17.

• **Page 2, Abstract, Background, line 5:** Replace the word knows with “known”. **Page 2, Abstract, Results, line 3:** Delete word “About”. **Page 2, Abstract, Results, line 7:** Age group 25-49 should be “35-49”. **Page 2, Abstract, Conclusion, line 5:** Replace the word carrier with career.

Response:

All the grammatical and spelling errors have been rectified according to the reviewer’s suggestions.

• **References are not as per style of BMC Infectious Diseases. The references should be cited in text with in [Square brackets] and should be listed as: Authors. Title. Journal. Year; Volume: Page from-to**

Response:

All the references in the text are placed in the square brackets and listed in the recommended sequence.
3rd Reviewer report:

- **Complete details on the used HBV vaccine**
- **Complete details on the test kit used for anti-HBs detection**

  **Response:**
  
  The details of the above two have already been given.

- **Rates of seroconversion (i.e. values comprised between 1 and 10 mIU) and relative distributions by age and sex.**

  **Response:**
  
  Information has given in figure 1 and table 2

**New additions:**

- Figure 1 (Descriptive Characteristics of study participants) and table 3 (Multivariate comparison of non-responders with normal responders) is included in the revised manuscript.
- Vikram Mehraj (VM) is also included in the author’s list. He had contributed in statistical analysis and also contributed in manuscript writing.

**Formatting changes:**

Copy-editing: copy editing is done.
Ethics: not required
Competing interests: section of competing interest is included in the revised manuscript.
Author’s contribution: author’s contribution is also included at the end of the revised manuscript.

Looking forward for your positive response.

Thanks and kind regards

Dr. Mohammad Zeeshan

Department of Pathology and Microbiology
Aga Khan University