Author's response to reviews

Title: Hepatitis B and C: Prevalence and social factors associated with seropositivity among children in Karachi, Pakistan

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Author's response to reviews:

29 May, 2006
Dear Sir,
We have made changes keeping in view comments made by the two reviewers. However, we are willing to make further changes if need arises to improve the manuscript.
Yours sincerely,
Dr Wasim Jafri
Pietro Luigi Lopalco

Dear Reviewer: Thank you for your comments regarding our manuscript.

1) Multivariate analysis was only done for Hepatitis B virus. There was nothing of statistically significance among risk factors pertaining to HCV as was shown previously in the Table 2. We agree it would be better to give multivariate analysis for HBV in a separate table. In the revised manuscript it is given as Table 2 while univariate analysis for HCV has been given in Table 3.

2) Association between piercing and HBV/HCV infection was documented but not mentioned previously as it did not achieve statistical significance. It is now given for both HBV and HCV in Table 1 and 3.

3) A Table has been inserted reporting ALL findings in univariate analysis (percentages, OR where available and p value) different than that one for multivariate model. However, only some risk factors in the HBV achieved a level of significance while no risk factor was of significance value in HCV.

Discussion

Re: "HBV in children is often associated to vertical transmission"
Vertical transmission follows but it is not very common in Pakistan which an area with intermediate Endemicity of HBV. Reference pertaining to the vertical transmission in our population has been added to the Introduction part page 3, lines 10-14.

Re: "In this paper both diseases seem to be linked basically to an improper use of syringes"

There is ample evidence for the same as suggested in the previous studies, one such study is that by Khan et al, published in Bulletin of the World Health Organization, 2000; 78(8): 956-963.

"Non-sterile syringes and needles were the source of HCV and HBV infections in a peri urban community of Karachi, Pakistan. Patients who received more injections were more likely to be infected with HCV".

Furthermore, in figure 2 there is an evidence for higher infection rate in males >13 yrs. Is it significant? How
It was not significant. It is probably a cohort effect. It is observed that with an increase in age the prevalence of HBV and HCV tends to increase as one is exposed to more of the risk factors such as unsterilized and inappropriate therapeutic injections etc. Horizontal transmission for HBV is probably more important a cause for this effect of higher HBV infection in boys. It is less likely to be related to sexual behavior.

Minor Essential Revisions

1) In the paragraph Methods>Data Management and Analysis Plan the multivariate analysis isn't mentioned. It has been mentioned now.

2) Figure 1 is redundant. Consider skip it. Figure 1 has been deleted.

Maria Chironna

Dear Reviewer: Thank you for your comments regarding our manuscript.

1. This is a cross sectional study aimed at the evaluation of seroprevalence of HBsAg+ and of anti-HCV in children from Karachi and assessment of risk factors associated with seropositivity. This study extended over the period of May 2003- August 2004 and has been included in the methodology page 4 and lines 19.

2. Potential risk factors were evaluated by comparing seropositive and seronegative for HBsAG and anti-HCV antibody among children. We have added information about this aspect in the methodology section (Study design), page 5, lines 3-4.

3. We agree that the seronegativity for HBsAg is not indicative of susceptibility to HBV infection. Some children could have been infected by HBV and recovered. This could affect the strength of association between a HBV infection and the potential risk factors. Data on the prevalence of anti-HBc which is indicative of exposure to HBV in this population is not available. However, we have a placed reference for another study in this regard (page 3, line 4).

4. Figures 1 - 3 has been deleted as suggested. Figures 1, 2 and 3 reported prevalence rates.

5. The number of headings has been reduced in the Methods section as suggested into:
   i. Study design and setting,
   ii. Data collection and serology,
   iii. Cases and controls,
   iv. Data management and analysis and
   v. Ethical issues

6. Some parts of the Methods section (comprising Multivariate analysis) have been shortened.

7. "Therapeutic injections with the use of new needles and syringes represent a risk for hepatitis B and C infections".

This highlights the alarming problem being faced by the community at large of the used syringes being washed, packaged and resold in Pakistan; Ahmad K. Lancet 2004; 364:1843-1844.

Also, as shown in the Table 1, HBV was positive with and without use new needle ad syringe among children and it was statistically significant. Similarly, in Table 2, half of the HCV positive did not use sterile needle and syringe.


"Non-sterile syringes and needles were the source of HCV and HBV infections in a peri urban community of Karachi, Pakistan. Patients who received more injections were more likely to be infected with HCV".
8. We considered dental procedures, presence of HBsAg carriers and/or HCV chronically infected subjects among family members, death of a family member due to liver disease and hospitalization, as risk factors for hepatitis B and C infection. However, as none of these factors attained a level of statistical significance they were not mentioned earlier. They have now been included in the Univariable analysis Table 1 and 2 and commented upon in the discussion on page 13 and lines 10-13.

9. We found a positive correlation with the number of injections in case of HBV; increased OR with increasing number of injections? This has been included in the Table 1.

10. Did you verify that none of the study was vaccinated against hepatitis B?

We ascertained whether children received vaccination or not. Generally, it includes Diphtheria, Tetanus, Pertussis (DTP3), oral Polio and measles vaccination. Vaccination for HBV as part of Global Alliance for Vaccines and Immunization (GAVI) only became available in Pakistan from 2004.

11. Analyses have been substantially revised and reconsidered on the basis of these considerations.

12. What is the vaccination policy against hepatitis B in Pakistan?

The vaccination policy against hepatitis B that is being implemented in Pakistan follows International recommendation that three doses of HB vaccine starting soon after birth and completing at 6 months. This is followed by 2 booster doses over the years completing at 5 years of age. In children, born to HBV positive mothers immediate vaccination for HBV is given with anti-hepatitis B virus immunoglobulins.