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Letter to Editor

Intrafamilial spread of hepatitis B virus: some comments

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We read with interest the recent paper about intrafamilial spreading of hepatitis B virus (HBV) by Mansour-Ghanaei et al [1]. Useful information have been presented. But, some clarification on a few small points may be helpful to the readers.

Authors have mentioned that "The present survey indicates that there is a significant difference in the prevalence of Hepatitis B in the general population and family members of Hepatitis B patients and this is an evidence for horizontal transmission of HBV in household contacts". I did not understand two issues: 1. Why general population? There was any sampling neither in cases nor in controls from general population. 2. Why horizontal transmission? Such transmission between family members can be due to common routes like mother and grandmother. I recommend them to assess this issue considering mother or grandmother as index case and compare such condition with other conditions when other cases have been considered as index case. This analysis may help us for discriminating between vertical and horizontal transmission. Do they evaluate all family members of an index case or they have only examined available cases with consent form? I am not sure about selection bias and they did not explain this issue in details. If, we were aware from this information, maybe available data could show is the route of transmission horizontal or vertical, specifically by comparing mothers with other family members. More precisely, network analysis could be a better choice for evaluating mechanism of intrafamilial spreading of HBV.

Moreover, there are two more comments about statistical analysis: 1. Because the sample size is high and interestingly, there is no missing data as tables show. So, the expected values of the crosstabs seem to be sufficient and there is no need for Fisher Exact test. They could simply use Pearson chi-square instead of Fisher Exact correction method. 2. *P*-value in Table 3 shows that they have compared all risk factors in all four mentioned groups at once. As expected, number of subgroups will increase to 24 instead of a 2*2 table with four cells and the chance of significant association will dramatically decrease. It is recommended to consider each risk factor separately in four groups.

There are some points about sampling: 1. One issue is about selecting controls from attendants of non gastrointestinal patients. We underestimate the odds of HBsAg positivity by such sampling. Maybe, neighborhood samples can be considered as more appropriate control group here specifically for comparability in view of the horizontal transmission between cases and controls.

2. Authors mentioned that systematic random sampling method has been hired. However, we need the sampling frame which is not available in such sampling. 3. Controls were selected from persons without "other liver diseases". By

such exaggerated restriction in selecting controls, we again underestimate odds of HBV infection in controls. Therefore, OR of HBV infection will be overestimated in cases in comparison with controls. It seems that only not being positive for HBsAg in controls or their families is sufficient. 4. "The participants who did not continue their cooperation were excluded from the survey". It is necessary to know that when we exclude some of cases, we should consider them once as positive and once again as negative cases and do sensitivity analysis. 5. Nurse and barber [2] are among competing risks of HBsAg positivity for family history of HBV infection. As Table 1 shows, these risks are zero in case group but considerable (35 persons) in controls. So, it is another reason that the selected control group is not a suitable group because of lack of comparability. 6. Another basic issue in selecting controls is representativeness which is less important than comparability. However, it is also not considered sufficiently in this study. Authors explained that "only 1 (0.2%) of control group was HBs Ag positive". It shows that their sampling is neither representative of cases who refer to a clinic/hospital nor general population. Our previous meta-analysis on prevalence of HBV in general population of Iran shows that percentage of HBS Ag positive cases in general population is 2.5% [3]. Surly, in clinic/hospital based population this is higher.

Authors have stated that "after taking consent of the participants, 5 ml blood samples were taken". Consent form should be taken before every action at the beginning of the study. Here, before taking history even about demographics. In Table 1, about "Vaccine titer after vaccination" in control group, it is recommended that like case group, these numbers (percentages) should be considered in 145 cases that had history of HBV vaccination and not in all controls. Another misunderstanding for me is the sentence about "The mean age of the index cases group was 46.5 ± 15.1 years old, from them 102 patients (65.4%) were male and 138 (88.5%) were married". This information is not consistent with Table 1.

Disclosure of conflict of interest

None.

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