Letter to Editor

Dear Editor-in-chief

We studied with great enthusiasm the valuable comments of Dr. Khosravi[1] *et al*, on our previously published article "Evaluation of Hepatitis B Infection Prevalence in Institutionalized Intellectually Disabled Children[2]". They had three major concerns with the methods and findings of our article. Below we have responded to their concerns.

Their first and major concern was the interesting finding of a higher frequency of HBV infection in children with a positive history of vaccination versus those with no such history and the authors stated "While there are studies in which the efficacy of neonatal HBV immunization has been proven. How the authors justify this finding?''.

Higher frequency of HBV infection in vaccinated individuals has not been previously reported, however the following observations have been reported in the literature:

A) There are reports on the lower response of patients with Down syndrome to hepatitis B vaccination (as low as 17-29%)[3]. Low responders are at a higher likelihood of infection in comparison with non-vaccinated individuals.

B) There are also reports on the shorter sustainability of HBsAb in vaccinated individuals with Down syndrome[4].

C) There are studies in which a higher frequency of vaccine escape mutations has been reported in vaccinated individuals.

It is mentioned in the article that this is probably due to the infection by mutant HBV strains which could be resistant to immune response and vaccine. Indeed, some researchers have reported coexistence of HBs Ag and HBs Ab in HBV infected patients especially who received vaccine before[5]. For example, in one study in 1998 it has been shown that HBs Ag mutations accumulate with higher frequency in vaccinated than unvaccinated children[6]. Again, another study in 2006 it has been shown that in chronic hepatitis B patients, the coexistence of HBs Ag and HBs Ab is associated with an increase of HBs antigen variability, suggesting a selection of HBV immune escape mutants during chronic carriage[7]. Also the researchers suggested that the consequences of this selection process with regard to vaccine efficacy, diagnosis, and clinical evolution remain partially unknown. Also in another study in 2007 it has been suggested that such HBs Ag-mutated HBV strains may not be fully sensitive to vaccine-induced HBs Ab with the potential risk of vaccine failure including contamination of presumably protected vaccinated individuals[8]. On the other hand, the detection of such non-protective HBs Ab may also lead to misdiagnose chronic HBV infection if detection of HBsAg is not carried out simultaneously.

Their second concern was that "the authors have not mentioned the sampling method of their study, which is the crucial factor of prevalence studies". We admit that in ideal situations a random sampling of centers would have been the best option but practically regarding the disabilities of these children, ethical and legal issues impose a major limitation for blood sampling from these children. We sampled from centers with the cooperation of the staff and consequently parents or guardians of the children. We intentionally selected one center from each geographical location of Tehran (east, west, north, south and center) to cover the differences in economic and cultural differences of families living in different districts of Tehran. We sampled every eligible child in selected centers who had permissions of their parents or guardians. No recent study has been conducted on these vulnerable children for HBV infection. Therefore, the results of this study can be considered as the most representative available study until further studies would be available.

The third concern of Dr. Khosravi et al., was that whether we enrolled children born before or after the national hepatitis B vaccination program as they quoted: "the time period in which the study was conducted has not been determined by the authors. Was it after or before distribution of a national vaccination program for hepatitis B?" We had mentioned in the article that all our participants were younger than 14 years. The reason for this age limitation in this study was based on internal roles of centers which held children younger than 14 years separates from older persons. Our study was performed during 2013-2014; therefore study

participants must have been born after 1999 which is well after the start of hepatitis B national vaccination program in Iran.

References

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