

## Three vs Four Dose Schedule of Hepatitis-B Vaccine in HIV-infected Children

With respect to the recent publication by Jain, *et al.* [1] on the above topic, we seek the following clarifications:

Abstract mentions trial participants being fifty (25 per group) HIV-infected children aged 18 months - 12 years receiving ART for at least 6 months who had not received any prior dose of HBV vaccine, and were anti-HBs negative [1]. While in methods section it is mentioned as participants being seronegative for Hepatitis B virus (HBs antigen negative). Were participants anti-HBs antibody titre negative or HBsAg antigen negative? Or both antigen and antibody negative? Please clarify this confusion.

Regarding immunization status of participants, methods section mentions that immunization status was ascertained on the basis of previous immunization records [1]. Hepatitis B vaccination in immunization schedule of Delhi was introduced more than a decade ago [2]. So either participants were completely unvaccinated for all vaccines or vaccinated for all vaccines along with hepatitis B, depending on at what age they voluntarily stopped getting vaccines intentionally. So, no immunization record with no history of immunization too would have been a better proxy for unvaccinated subjects. How participants were left out for hepatitis B vaccine only? A previous randomized trial on similar topic [3] had subjects that were older, as routine hepatitis B vaccination had started just 1-2 years prior to the study.

Due to the convenience sampling, it is still unclear if double strength (20 µg) 4-dose schedule (0, 1, 2 and 6 months) is equally efficacious or superior to 3-dose schedule (0, 1 and 6 months), as the study was not powered to detect a difference unanswered thereby leaving this important question.

Baseline characteristics table shows mean age of groups I and II being 7 and 11 years, respectively [1]. It seems to differ significantly despite SNOSE technique and block randomization. Moreover, CONSORT flow chart shows 70 participants being eligible. While during enrollment, 40 (on summing up) were excluded.

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### REFERENCES

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2. Lahariya C, Subramanya BP, Sosler S. An assessment of hepatitis B vaccine introduction in India: Lessons for roll out and scale up of new vaccines in immunization programs. *Indian J Public*

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### AUTHORS' REPLY

We thank the readers for their interest in our work [1] and provide the following clarifications: Regarding the inclusion criteria of participants, we wish to clarify that HIV-infected children aged 18 months - 12 years who had been receiving ART for at least 6 months and who had not received any prior dose of HBV vaccine were eligible, provided they were seronegative (HBs antigen negative). Immunization status for hepatitis B was assessed by studying the immunization cards of the child as well as absence of anti-HBs antibodies. We had noticed that the immunization records of some of these children were incomplete due to reasons like relocation/ migration, or where the parents had succumbed to HIV. Hence, relying solely on immunization records and history, did not seem a robust method.

Although, hepatitis B vaccination had been introduced in several Indian states almost a decade ago, the coverage of hepatitis B vaccine was reported low with huge gaps in coverage of DPT3 and HBV3 persisting [2]. A survey from India [3], reported that in 2015-16, 45% of the children aged 12-59 months were not fully vaccinated against hepatitis B, and 20% children had not received even a single dose of hepatitis B vaccine. Some of the participants in our study had been born in remote rural areas and had later migrated to Delhi, and therefore had not received hepatitis B vaccine. Some of these children had also not received other vaccines; the missing vaccination doses were administered by us during their visits to the anti-retroviral clinic.

The disparity in ages of participants in both groups despite block randomization may have been due to the small sample size and because we did not perform stratified randomization [4]. We excluded 20 children out of 70 eligible children. The CONSORT diagram depicts that 20 children were excluded and also elucidates the reasons for exclusion [1].

We agree that the research question addressed remains unanswered. Finding even 50 children who had never received any dose of hepatitis B vaccine was very challenging for us, and hence a convenience sampling was done. This question may be answered by pooling similar data from other studies and performing a meta-analysis.

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