Evaluation of the Protection Provided by Hepatitis B Vaccination in India

Jacob Puliyel, Pathik Naik, Ashish Puliyel, Kishore Agarwal, Vandana Lal, Nimmi Kansal, Devki Nandan, Vikas Tripathi, Prashant Tyagi, et al.

The Indian Journal of Pediatrics

ISSN 0019-5456
Volume 85
Number 7

Indian J Pediatr (2018) 85:510-516
DOI 10.1007/s12098-017-2601-0

Springer

The Indian Journal of Pediatrics (July 2018) 85(7):510–516
https://doi.org/10.1007/s12098-017-2601-0

ORIGINAL ARTICLE

Evaluation of the Protection Provided by Hepatitis B Vaccination in India

Jacob Puliyel[1] · Pathik Naik[2] · Ashish Puliyel[3] · Kishore Agarwal[4] · Vandana Lal[5] · Nimmi Kansal[5] · Devki Nandan[6] · Vikas Tripathi[7] · Prashant Tyagi[7] · Saroj K. Singh[8] · Rajeev Srivastava[9] · Utkarsh Sharma[10] · V. Sreenivas[11]

Received: 5 May 2017 / Accepted: 21 December 2017 / Published online: 10 January 2018

Abstract

Objective In India, Hepatitis B vaccination is recommended at 6 wk except for hospital-deliveries. The authors examined protection afforded by the birth dose.

Methods A case-control study was done. HBsAg and HBcAb were tested in 2671 children, 1 to 5 y and HBsAb was evaluated in a subset of 1413 children. Vaccination history was recorded. Cases were HBsAg carriers. In another analysis, children who got infected (HBsAg and/or HBcAb positive) were considered as cases. Exposed were the unvaccinated. In another analysis, exposed were those vaccinated without the birth dose.

Results The odds ratio (OR) for HBsAg positivity with birth vaccination was 0.35 (95% CI 0.19–0.66); while with vaccination at 6 wk was 0.29 (95%CI 0.14–0.61), both compared to unvaccinated. Birth vaccination has no added protection when compared to the unvaccinated. Unvaccinated children in index study had HBsAg positivity of 4.38%. The number needed to treat (NNT) to prevent one case of HBsAg positivity was 32.6 (95% CI, 20.9 to 73.6). The odds of getting HBV infection was 0.42 (CI 0.25–0.68) with birth dose and 0.49 (CI 0.30–0.82) without the birth dose compared to the unvaccinated. Protective antibody (HBsAb) was present in about 70% of the vaccinated. In the unimmunised, in the first 2 y HBsAb protection was present in 40%. The odds ratio (OR) for HBsAb in the fully vaccinated between 4 and 5 y was 1.4 (95%CI 0.9–2.18) compared to the unvaccinated.

Conclusions The present study lends support to the pragmatic approach of the Government to vaccinate babies born at home starting at 6 wk.

Keywords Immunization · Passive immunity · Hepatitis B surface antigen · Hepatitis B core antigen · Antibody to hepatitis B surface antigen · Antibody to hepatitis B core antigen

Introduction

Hepatitis B virus (HBV) can cause chronic hepatitis, liver cirrhosis and lead to hepato-cellular carcinoma (HCC) in susceptible persons. A systematic review and meta-analysis done by Batham et al. on prevalence of Hepatitis B in India showed that in non-tribal populations the prevalence was 2.4% (95% CI: 2.2%–2.7%) and among tribal populations it was 15.9% (CI: 11.4%–20.4%) [1]. Assuming that 4% are chronic carriers in India and extrapolating trends from Taiwan it was estimated

✉ Jacob Puliyel
Puliyel@gmail.com

1 Department of Pediatrics, St Stephens Hospital, Delhi 110054, India
2 Department of Pediatrics, Pathik Children's Hospital, Surat, India
3 Consumer CAP HPI, London, UK
4 Department of Pediatrics, Sardarmal Khandaka Memorial Hospital, Hathoj, Jaipur, India
5 Department of Biochemistry, Dr Lal PathLabs, Rohini, Delhi, India
6 Department of Pediatrics, PGIMER, Dr. RML Hospital, New Delhi, India
7 Department of Pediatrics, Pt Madan Mohan Malaviya Hospital, Malaviya Nagar, Delhi, India
8 Department of Pediatrics, Nazareth Hospital, Allahabad, India
9 Department of Pediatrics, SGRRIM&S, SMI Hospital, Patel Nagar, Dehradun, India
10 Department of Pediatrics, Thiranker Mahhavir Medical College, Muradabad, India
11 Department of Biostatistics, All India Institute of Medical Science, Delhi, India

that 250,000 persons in India die of HCC each year [2]. However, projections from the ICMR Cancer Registry shows the incidence of HCC due to hepatitis B infection in India is about 5000 cases a year [3] accounting for 0.02% of the annual mortality of approximately 25 million. This is much lower than expected.

The risk of developing chronic HBV infection is inversely related to age of acquisition. The risk of chronic infection is 90% in children younger than 1 y; 30% for those 1–5 y and 2% for adults [4]. Mother-to-infant transmission is an important factor responsible for chronic HBV infections [5]. This form of perinatal transmission of HBV is believed to be responsible for a third of adult chronic carriers in India [6]. Vaccination at birth is done to prevent mother to child transmission and horizontal transmission from infected children to others [7]. Vaccination starting at 6 wk is thought to prevent only horizontal transmission [8].

A large percentage of births in India take place at home away from health-care institutions and so newborns cannot be reached easily, immediately after birth. For this reason the draft National Immunization Policy recommends a pragmatic HBV vaccination schedule wherein the vaccine is given at birth for institutional deliveries and at 6 wk to children born outside such health-care settings [9].

There is no clear data on how much of the HBV chronic carrier state is prevented by the two schedules. According to a systematic review by the Indian Medical Association there are no studies showing that the 'pragmatic schedule' was effective in reducing the chronic carrier rate in any country [10].

This study was undertaken to examine the efficacy of hepatitis B vaccination in those who were vaccinated at birth (within 48 h of delivery) and those who were vaccinated thereafter, using a case-control model. The secondary objective of the study was to look at hepatitis b surface antibody (HBsAb) levels in the vaccinated for serological response in the two schedules and among the unvaccinated as a marker of natural immunity.

Material and Methods

Data collection was done from November 2013 through July 2015. Children between the ages 1 and 5 y were invited to participate in the study if they were having blood taken for other investigations at the hospital or laboratory. Consent was taken from parents to collect an additional 2 ml of blood for Hepatitis B testing. Samples were obtained from participating centres in Delhi, Rajasthan, Uttar Pradesh, Uttarakhand, and Gujarat. The study protocol was approved by the Institute Ethics Committee of St. Stephens Hospital, Institutional Ethics Committee of Dr. Ram Manohar Lohia Hospital Delhi, and the Emmanuel Health Association Research Committee for centres without their own ethics committees. The study was funded by an ICMR grant which also covered costs for serological testing of the samples (Reference PCR/Virology/20–12/ECD-1).

Immunization status was inferred from patient held immunization cards, supplemented by history when required. Samples were collected in serum gel 4 ml vaccutainers, centrifuged and the serum was stored at minus 20° centigrade till testing. All the samples were tested for hepatitis B surface antigen (HBsAg) and antibody to hepatitis B core antigen (HBcAb). A subset was also tested for antibody to surface antigen (HBsAb). All the serological tests were done using ELISA method of immunoassay. GS HBsAg EIA 3.0, MONOLISA™ Anti-HBc EIA and MONOLISA™ Anti-HBs EIA by Bio-Rad© Laboratories was used for serological testing. The titre cut-off used for HBsAb was 10 IU/L, and for HBsAg and HBcAb it was 1 IU/l, as specified by the manufacturers of the testing kits. All the tests were done at Dr. Lal PathLabs -Rohini (National Reference Laboratory).

Record collection was through a custom built web-application hosted on large cloud-services vendor. An append-only data-structure (CouchDB) protected against inadvertent data-loss and allowed authors to ensure that individuals involved in reporting serology were blind to the immunization status of the children. Once a child's test results were available, the application parsed and extracted the results of each test directly from the lab's PDF report - avoiding any human-introduced transcription errors. The application, on demand, could produce a table-based, flattened view of the underlying (non-relational) database for Microsoft Excel. This extract was used for analysis at the conclusion of the study. That data, anonymized and garnished with slicers for easy analysis, is made available free online, for further analysis by interested researchers (http://bit.ly/hepbdata).

HBsAg positive children were considered as carriers. Those who got infection and cleared it having developed HBcAb and those who became carriers were considered together (HBcAb and/or HBsAg) as children who had got infected with hepatitis B. Completely immunized children were those who received at least 3 doses of hepatitis B vaccine, without regard for the birth dose. Birth dose was defined as hepatitis B vaccination within 48 h of delivery. Unvaccinated were those who received no immunization for hepatitis B. The two groups [children who got infected (HBcAb and/or HBsAg) and children who became carriers (HBsAg)] were each analysed as cases in two different analyses. Controls were the remaining children in the two analyses. Exposure was vaccinated status. Those who had received 3 doses of the vaccine were considered protected (unexposed). In another analysis only those vaccinated from birth were considered protected. For the secondary outcome HBsAb was examined in the fully vaccinated starting at birth, those fully vaccinated but not starting at birth and in the unvaccinated. HBsAb was

Table 1 Characteristics of the study population

Characteristics	Number of children	Percentage
Sex		
Males	1672	62.60
Females	999	37.40
Immunization status		
Completely vaccinated	1566	58.63
Completely vaccinated with birth dose	880	32.95
Completely vaccinated without birth dose	686	25.68
Unvaccinated	844	31.62

also analysed by age to look for waning immunity among the vaccinated and in the unvaccinated.

It was calculated that 94 cases needed to be recruited for this study. Assuming that the prevalence of Hepatitis B virus infection in unvaccinated children was 1% and assuming that it is 0.5% in those vaccinated at 6 wk, in a two sided test with 80% power, it was calculated that 4700 children each in the vaccinated at birth and vaccinated after 6 wk groups would need to be recruited. Those vaccinated at birth were assumed to have a 90% chance of being protected against Hepatitis B infection.

Statistical analysis was done using MedCalc Statistical Software version 14.8.1 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2014). Fisher's exact test and Pearson chi square test were used to compare proportion of children in the subgroups of interest. Chi square test for trend was used to assess age-wise positivity of HBsAb. Number needed to treat (NNT) was also calculated.

Results

The prevalence of Hepatitis B infection was higher than projected for sample size calculations. The study was concluded after 2671 children were recruited. In the case control model authors had recruited 116 cases of children infected with Hepatitis B (defined by presence of either HBcAb and/or HBsAg) and of these 69 were HBsAg positive chronic carriers. Table 1 gives the population characteristics. One thousand five hundred sixty six (58.63%) children had received complete vaccination whereas 844 (31.60%) were completely unvaccinated. The remaining was partially immunized. Of the study population 880 (32.95%) was fully immunized starting at birth and 686 (25.68%) were fully immunized but without the birth dose. One thousand four hundred thirteen were also tested for HBsAb out of whom 858 (60.72%) had protective levels.

Table 2 shows results of testing in those completely vaccinated with and without the birth dose. Odds of becoming HBsAg positive was 1.22 (95%CI 0.52–2.83) without birth dose compared to with birth dose. Protection rates (HBsAb) was also very similar (70.3 and 69.5% respectively). The study was however not powered for a head to head comparison between these two groups.

When compared to the unvaccinated, the odds of being an HBsAg carrier was 0.35 (95% CI 0.19–0.66) for those vaccinated at birth compared to 0.29 (95% CI 0.14–0.61) without the birth dose. Birth vaccination has no added protection compared to the unvaccinated. The odds of getting infected was 0.42 (95% CI 0. 26–0.68) and 0.49 (95% CI 0.30–0.82) and the odds of being HBsAb positive was also similar (Tables 3 and 4).

Table 5 shows the comparison between those fully vaccinated (3 doses irrespective of whether birth dose was received or not) and the unvaccinated. Protective antibodies (HBsAb) were present in 69.9% of the fully vaccinated and in 39.5% of the unimmunised. Table 6 shows HBsAb positivity (protective antibodies) increases with increasing doses of vaccination. 52.73% of children who received single dose of Hepatitis B vaccine had protective levels of HBsAb

Table 2 Serological markers of past infection (HBsAg and/or HBcAb) and protective antibody (HBsAb) in completely vaccinated babies with and without birth dose

	HBsAg	HBcAb	HBcAb and/or HBsAg	HBsAb
Birth dose and complete vaccination	14/880 (1.59%)	11/880	24/880 (2.72%)	331/471 (70.28%)
No birth dose but completely vaccinated	9/686 (1.31%)	14/686	22/686 (3.21%)	274/394 (69.54%)
Odds ratio	1.22 (95% CI 0.52–2.83)	0.61 (95% CI 0.27–1.35)	0.85 (95% CI 0.47–1.52)	1.04 (95% CI 0.77–1.39)

Table 3 Serological markers of past infection (HBsAg and/or HBcAb) and protective antibody (HBsAb) in completely vaccinated babies including birth dose compared to unvaccinated babies

	HBsAg	HBcAb	HBcAb and/or HBsAg	HBsAb
Birth dose and complete vaccination	14/880 (1.59%)	11/880	24/880 (2.72%)	331/471 (70.28%)
Unimmunized	37/844 (4.38%)	19/844	53/844 (6.28%)	146/370 (39.46%)
Odds ratio	0.35 (95% CI 0.19–0.66)	0.58 (95% CI 0.27–1.22)	0.42 (95% CI 0.26–0.61)	3.63 (95%CI 2.72–4.83)

compared to 84% with 4 doses. The trend was statistically significant ($p < 0.0001$).

Table 7 shows antibody titres in the unvaccinated with age. The highest levels were in the youngest tested and the lowest levels were in the oldest group. Forty five percent of the unvaccinated were naturally immune at 1 y of age. Between 4 and 5 y the odds of being protected with HBsAb was 1.4 (95%CI 0.9–2.18) in the vaccinated compared to the unvaccinated.

Discussion

The purpose of this study was to look primarily for the benefits if any, of giving the first dose of Hepatitis B vaccination at birth in India. The findings lend support for the pragmatic approach of the Government of India to vaccinate babies born at home at 6 wk. The carrier rate was not improved with birth dose.

The OR for HBsAg positivity with birth vaccination was 0.35 (95%CI 0.17–0.67); while with vaccination at 6 wk was 0.29 (95%CI 0.12–0.62) both compared to unvaccinated. This empirical evidence contradicts what the principle investigator and others have assumed about the need for the birth dose in India [11–14]. Unvaccinated children in present study had HBsAg positivity of 4.38%. The numbers needed to treat (NNT) to prevent 1 chronic carrier was 32.6 (95% CI, 20.9–73.6). The study done by Aggarwal et al. in children 5 to 10 y of age, found HBsAg positivity of 0.15% in immunized children and 0.17% in the unimmunized (p value 0.855) [15]. The authors of the present study found HBsAg positivity of 1.47% in the vaccinated between 1 and 5 y and 4.38% in the unvaccinated. These differences probably relate to the differences in the populations studied.

The odds of getting infected (HBsAg and/or HBcAb) was similar with and without birth dose when they were compared to the unvaccinated. 6.28% of those unvaccinated had been infected compared to 2.72% vaccinated with birth dose and 3.21 without birth dose. NNT for preventing Hepatitis B infection was 28.2 (95% CI 18.2 to 62.2) with completely immunized including with birth dose and 32.5 (95% CI, 19.1 to 110.8) without birth dose.

A priori, sample size calculations were not performed to look for differences among the fully vaccinated, with and without the birth dose. The sample studied by authors had 880 children who were completely vaccinated starting at birth dose. Six hundred eighty six children were fully vaccinated but without the birth dose. Given the very small difference of Hepatitis B infection between groups (2.72% and 3.21% respectively), it appears (on retrospective analysis) that the study is not powered to look for such small differences.

However, according to INSAL, 4.7% of the population in India are carriers [16]. This is not very much higher than the HBsAg positive rate of 4.38 found among unvaccinated children in index study. Nayak et al. report that one-third of HBV carriers evolve from perinatal transmission [6]. This can be prevented by the birth dose. If it is assumed that 30% of the carrier rate of 4.7% is due to vertical transmission from mother to child (that will be prevented by vaccination starting at birth), then those without birth dose will have 1.7% carrier

Table 4 Serological markers of past infection (HBsAg and/or HBcAb) and protective antibody (HBsAb) in completely vaccinated babies without birth dose compared to unvaccinated babies

	HBsAg	HBcAb	HBcAb and/or HBsAg	HBsAb
No birth dose but completely vaccinated	9/686 (1.31%)	14/686	22/686 (3.21%)	274/394 (69.54%)
Unimmunized	37/844 (4.38%)	19/844	53/844 (6.28%)	146/370 (39.46%)
Odds ratio	0.29 (95%CI 0.14–0.61)	0.90 (95%CI 0.45–1.81)	0.49 (95%CI 0.30–0.83)	3.50 (95%CI 2.60–4.72)

Table 5 Serological markers of past infection (HBsAg and/or HBcAb) and protective antibody (HBsAb) in completely vaccinated babies and unvaccinated babies

	HBsAg	HBcAb	HBcAb and/or HBsAg	HBsAb
Completely immunized	23/1566 (1.47%)	25/1566	46/1566 (2.94%)	605/865 (69.94%)
Unimmunized	37/844 (4.38%)	19/844	53/844 (6.28%)	146/370 (39.46%)
Odds ratio	0.33 (95%CI 0.19–0.55)	0.70 (95%CI 0.39–1.29)	0.45 (95%CI 0.30–0.68)	3.57 (95%CI 2.77–4.60)

Table 6 Protective levels of HBsAb with increasing number of doses of vaccine

Number of doses received	Serology marker			
	HBsAb tested	HBsAb positive	Percentage positive	Odds ratio compared to unvaccinated
1	110	58	52.73	48.4 95% CI 26.9–87.3
2	68	49	72.06	112 95% CI 55.7–225.1
3	721	484	67.128	88.7 95% CI 54.8–143.4
4	144	121	84.02	228.4 95% CI 120.8–431.9
Trend significance	$P < 0.0001$			

rate. Assuming 100% efficacy against vertical transmission with the birth dose, the carrier rate due to vertical transmission will be zero with full vaccination starting from birth.

For type 1 error of 0.05 and power of 80%, a sample size of 569 in each group (fully vaccinated starting at birth *vs*. no protection against vertical spread at birth) is adequate. The sample size studied (880 fully vaccinated from birth and 686 fully vaccinated without birth dose) is adequate if assumptions are made based on these previous reports.

This was not a randomised control trial. Unvaccinated children usually belong to a different social class whose parents may be less literate, poorer and more likely to be exposed to unsterile needles and other sources of infection. The lower infection rate seen in this study among the vaccinated could be related both to the fact that immunization is protective and also to the fact that those immunised were less likely to get infected in the first place.

Protective antibody HBsAb was present in about 70% of those fully immunised and was not significantly improved by providing the birth dose. The protective levels waned rapidly from 82% in the first year to 47% by age 5 y.

Table 7 Protective levels of HBsAb in the fully vaccinated with increasing age

Age	Serology marker			
	HBsAb positive	Total	Percentage	Odds ratio compared to unvaccinated
<1 y	211	256	82.42	9.2 95% CI 6.1–14
1 y to 2 y	142	199	71.36	3.8 95% CI 2.6–5.5
2 y to 3 y	108	146	73.97	4.9 95% CI 2.9–6.7
3 y to 4 y	61	104	58.65	2.2 95%CI 1.4–3.4
4 y to 5 y	44	93	47.31	1.4 95% CI 0.9–2.18
Trend significance	$P < 0.0001$			

Protective levels of HBsAb were present in 39.46% of completely unvaccinated. The numbers with protective levels of antibody in the unvaccinated was higher in the early years of life and gradually declined with advancing age. Protection in the second year was 44.9% and at age 5 it was 28.9%. Aggarwal et al. who studied children older than 5 y, this antibody was found in 28% of unimmunised at 6 y of age and in 16% at the age of 10 [15]. The protective HBsAb in unvaccinated babies could be due to active immunity developed in these babies after getting infected. However this seems unlikely because most of them were HBcAb negative. Also, if this were active immunity after exposure to natural infections, the numbers are likely to increase with age with more opportunities for exposure. This is not what was seen in this study nor was it the case in the study by Aggarwal et al. [15].

The large numbers of unvaccinated children with protective levels of antibodies (HBsAb) observed in index study and the study by Aggarwal could reflect natural, passively acquired immunity from their mothers which wanes slowly over the years**.** Even so, the persistence of this passively acquired antibody beyond the age of 9 mo is surprising.

There are very few studies that have looked at HBsAb levels in unvaccinated mothers who could transmit it passively to their babies. In a study in Arunachal Pradesh, 40.0% of the unvaccinated had HBsAb above 10 mIU/ml [17]. Asim studied HBsAg negative, first-time blood-donors and found 20% had previous natural infection and had developed HBcAb [18]. Of these 62% had protective levels of HBsAb levels above 10 IU/L and of them 68% had very high HBsAb levels between 100 and 500 IU/L. Studies by Waaijenborg and colleagues looking at measles immunity have shown that the unimmunised population of mothers have higher titres of antibodies and they pass these higher titres to their babies and the duration of the passive protection to the babies is dependent on the antibody titres in the mothers [19]. Mothers in highly immunized communities have lower antibody levels as vaccine induces lower antibody levels than does natural infection and the antibody levels of vaccinated cohorts are no longer boosted by exposure to wild-type infection.

The fact that a good number of unvaccinated babies had high levels of antibody, suggests it could be protecting some babies early in life, at the time when they are vulnerable to developing chronic hepatitis [4].

Among the vaccinated, protection decreased with age and the odds of having protective antibodies in children over 4 y was 1.4 (95%CI 0.9–2.18) compared to the unvaccinated children.

Conclusions

This study lends support for the Government of India programme of vaccinating babies born outside of institutional health care facilities at 6 wk. Those vaccinated starting at 6 wk had the same benefits as those vaccinated from birth, when both were compared to the unvaccinated.

Contributions This multicenter study was conceived by JP and designed originally by JP, PN, AP KA and VS. AP developed the computer architecture for data monitoring and VS helped with the statistical analysis. PN was responsible for study in Surat; DN, VT, PT, JP were responsible for study in Delhi centres; SKS and US for UP; RS for Uttarakhand. VL and NK were responsible for testing and interpretation of the test data.

The first draft was written by PN and it was finalised with critical inputs from each of the authors. AP was responsible for the write up on the computer programme used and he overlooks the data availability and will ensure it is available openly with no conditions attached.

Each author has seen the final draft, takes responsibility for its contents and signed the copyright transfer forms. JP will be the guarantor for the study report.

Compliance with Ethical Standards

Conflict of Interest None.

Source of Funding Indian Council of Medical Research, Delhi.

References

1. Batham A, Narula D, Toteja T, Sreenivas V, Puliyel JM. Sytematic review and meta-analysis of prevalence of hepatitis B in India. Indian Pediatr. 2007;44:663–74.
2. Puliyel JM. Policy analysis of the use of hepatitis B, Hemophilius influenzae type B, Steptococcus pneumoniae-conjugate and rotavirus vaccines in the national immunization schedules. Health Econ. 2004;13:1147.
3. Dhir V, Mohandas KM. Epidemiology of digestive tract cancers in India IV. Gall bladder and pancreas. Indian J Gastroenterol. 1999;18:24–8.
4. Jensen MK, Balistreri WF. Viral hepatitis. In: Kliegman RM, Stanton B, Geme JS, Schor NF, Behrman RE, editors. Nelson Textbook of Pediatrics, 20th ed. New Delhi: Elsevier Science Health Science; 2015.
5. Shah U, Kelly D, Chang MH, et al. Management of chronic hepatitis B in children. J Pediatr Gastroenterol Nutr. 2009;48:399–404.
6. Nayak NC, Panda SK, Zuckerman AJ, Bhan MK, Guha DK. Dynamics and impact of perinatal transmission of hepatitis B virus in North India. J Med Virol. 1987;21:137–45.
7. Lee C, Gong Y, Brok J, Boxall EH, Gluud C. Hepatitis B immunisation for newborn infants of hepatitis B surface antigen-positive mothers. Cochrane Database Syst Rev. 2006;2:CD004790.
8. Marion SA, Tomm Pastore M, Pi DW, Mathias RG. Long-term follow-up of hepatitis B vaccine in infants of carrier mothers. Am J Epidemiol. 1994;140:734–46.
9. Ministry of Health and Family Welfare I. Immunizatio_UIP. wwwmohfwnicin [Internet]. Available at: http://www.mohfw.nic.in/WriteReadData/l892s/Immunization_UIP.pdf. Accessed on 5th May 2017.
10. Puliyel JM, Rastogi P, Mathew JL. Hepatitis B in India: systematic review & report of the 'IMA sub-committee on immunization'. Indian J Med Res. 2008;127:494–7.
11. Geeta MG, Riyaz A. Prevention of mother to child transmission of hepatitis B infection. Indian Pediatr. 2013;50:189–92.
12. Gupta I, Sehgal A, Sehgal R, Ganguly NK. Vertical transmission of hepatitis B in north India. J Hygiene, Epidemiol Microbiol Immunol. 1992;36:263–7.
13. Puri P. Tackling the hepatitis B disease burden in India. J Clin Exp Hepatol. 2014;4:312–9.

14. Abass F, Thomas RD, Rajkumar A, Gupta N, Puliyel JM. Controlling perinatally acquired hepatitis B. Indian J Pediatr. 2001;68:365.
15. Aggarwal R, Babu JJ, Hemalatha R, Reddy AV, Sharma D, Kumar T. Effect of inclusion of hepatitis B vaccine in childhood immunization program in India: a retrospective cohort study. Indian Pediatr. 2014;51:875–9.
16. Indian Association for Study of the Liver (INASL). Hepatitis B in India; therapeutic options and prevention strategies – Consensus statement. Indian J Gastroenterol. 2000;19:C54–66.
17. Borkakoty B, Mahanta J, Biswas D. HBV vaccination in hyperendemic remote tribal areas in India. Vaccine. 2007;25:8347–9.
18. Asim M, Ali R, Khan LA, Husain SA, Singla R, Kar P. Significance of anti-HBc screening of blood donors and its association with occult hepatitis B virus infection: implications for blood transfusion. Indian J Med Res. 2010;132:312–7.
19. Waaijenborg S, Hahne SJ, Mollema L, et al. Waning of maternal antibodies against measles, mumps, rubella, and varicella in communities with contrasting vaccination coverage. J Infect Dis. 2013;208:10–6.