Hepatitis B immunization:
cost calculation in a community-based study in India

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Background and Aim: In India, approximately 65% of mothers deliver at home, and a community-based study evaluating the cost of vaccinating newborns with the first dose of hepatitis B vaccine within 48 hours has not been undertaken previously. This policy planning study was done to evaluate the costs of such immunization in India. **Methods:** All mothers delivering in the study area (population 65,000) over a 1-year period were tested for hepatitis B surface antigen (HBsAg; ELISA), and babies of positive mothers were vaccinated starting at birth. The cost of such selective vaccination was calculated. The cost of nursing time required for universal immunization was calculated from the data on nursing time required for vaccination in the selective vaccination program. The national cost of universal immunization without testing was calculated as well as cost-benefit and cost-utility in terms of cost per quality-adjusted life-year (QALY) saved. Sensitivity testing considering economies of scale was also factored in. **Results:** 1100 mothers delivered during the study period. 252 were primiparous. Nationwide universal vaccination would cost Rs 48,000 per QALY saved, which was double the per capita GNP of the country; discounted at 3% the cost was Rs 260,000. **Conclusions:** Universal immunization vaccination with hepatitis B vaccine is not cost-beneficial in India, since cost of every life-year gained with it will exceed India's per capita GNP. [*Indian J Gastroenterol* 2004;23:16-18]

Key words: Hepatitis B vaccination, universal immunization, universal vaccination

The World Health Organization has recommended universal immunization with hepatitis B (HB) vaccine.[1] There are no field studies on the actual cost of such a program in India. We undertook this community-based study to evaluate the cost of vaccinating babies with HB vaccine, starting at birth. We first determined the prevalence of hepatitis B surface antigen (HBsAg) in pregnant women in a community area. As it was not feasible to vaccinate all babies at birth, we vaccinated babies born to HBsAg-positive mothers to prevent vertical transmission from mother to child.

Methods

The community health project (St Stephens Community Health Project, Nandnagari, Delhi) and the hospital research committee of St Stephens Hospital approved the intervention. The study was done in a community health project area in Sangam Vihar on the outskirts of Delhi, covering a population of approximately 65,000. The project covered three community centers and had 60 community health workers (HW). A registered medical practitioner was recruited and trained as Research Assistant (RA). HWs in the community centers identified pregnant women, who were tested for HBsAg by the RA using ELISA (*Hepacard;* J Mitra, New Delhi; sensitivity 99%, specificity 100%, as per the manufacturer) around the 7th month of pregnancy; this time point was chosen to save costs since 7 months of gestation is considered the lower limit for viability of the newborn. The true prevalence of HBsAg among pregnant women who delivered during 1-year study period was calculated using the formula by Tu *et al.*[2] The HW informed the RA when a HBsAg-positive mother delivered, and the latter vaccinated the babies within 48 hours of delivery. The second and third doses were given at 6 and 10 weeks after birth, along with the Expanded Program of Immunization (EPI) vaccines, as per the guidelines of the Indian Academy of Pediatrics.[3]

Using the data from our project, we estimated the costs of selective vaccination and universal vaccination. The term 'selective vaccination' denotes testing mothers for HBsAg status and vaccinating babies born to HBsAg-positive mothers, and 'universal vaccination' denotes vaccination of all newborn babies, irrespective of their mothers' HBsAg status. We assumed the cost of single-dose vials of the vaccine, a disposable syringe and needle as Rs 70 each, based on actual costs to the project. We also did a sensitivity analysis assuming that economy of scale can bring down the vaccine cost to Rs 10 per dose. The costs of HBsAg test strip and of disposables used for testing were Rs 30 and Rs 10, respectively, per mother.

We calculated the cost-effectiveness in terms of cost per life-year gained. Investment in vaccination with hepatitis B prevents death from hepatocellular carcinoma (HCC) but many years later. The value of the initial investment (after adding compound interest at a standard bank rate of returns) at the time when the benefit arises, needs to be calculated. This is the process of

discounting for the opportunity cost of money and we have used the lowest rate of 3% for this purpose. Cost-utility was calculated as cost per quality-adjusted life-year (QALY) gained. Using the technique described by Tyagi *et al*,[4] the cost per QALY gained was compared with India's per capita gross national product (GNP).

Results

During the 1-year study period (December 1, 2001 to November 30, 2002), 1100 mothers delivered in the study area. Of these, 987 were tested for HBsAg prior to delivery; 22 mothers tested positive, with a point prevalence rate of 2.2%. The calculated true prevalence was 1.47%.

Of the 1100 mothers, 252 were pregnant for the first time. Since HB carrier state is usually acquired in childhood[5] and carrier status is unlikely to change after the first pregnancy, only primiparous women, who constitute only about one in four mothers, need HBsAg testing in a selective vaccination program.

Using a simple module devised by Tandon *et al,*[6] considering the cost of 3 doses of the vaccine and the cost of testing, universal immunization is several-fold more expensive than selective vaccination (Table 1). However the cost of nursing time needs to be added.

Addition of cost of manpower

For implementing a 'selective vaccination' strategy in our study population of 65,000 with 1100 deliveries per year, around 20 HBsAg tests were needed every month. Also, the 22 infants born to HBsAg carriers in one year needed administration of 66 vaccine doses, including 22 first doses that necessitated house visits at short notice within 48 hours of delivery. This could easily be done by one HW, working half-time (alternate day). Assuming the cost in wages and travel as Rs 5000 per month, this would have cost Rs 60,000 per year. Adding this to the cost calculation in Table 1, the total cost of selective vaccination in our study population would have been Rs 74,700. If the cost of vaccine were Rs 10 per dose, the total cost would be only Rs 70,740. In this strategy, the 2nd and 3rd doses can be administered with routine DPT vaccination with no additional administration costs.

Of the 22 HB-positive mothers, 20 delivered at home. For purposes of our calculations we have assumed that all babies had to be given their first vaccination at home. In a country where 65% of mothers deliver at home (National Family Health Survey 2, 1998-99) health workers will be well advised to visit the homes of all mothers within 48 hours of delivery to ensure that every baby is covered.

For universal vaccination in our study population, administration of 1100 doses within 48 hours of birth would have been needed annually, necessitating 3-4 visits every day to homes where deliveries had taken place. This would have required one full-time worker and a half-time worker; at the rate of Rs 10,000 per person per month, the cost of their salaries and travel would amount to Rs 180,000 per year. Adding this to costs in Table 1, the total cost would have been Rs 4,176,000. If the cost of vaccine were Rs 10 per dose, the total cost would be Rs 219,600 per year.

National cost

For computing the national cost, we assumed vaccine cost as Rs 10 per dose in view of economy of scale. Twenty-five million births take place in India every year. Approximately 5000 people in India die from HCC due to HB each year.[8] Life expectancy in 2040 in India, when benefits of vaccination now will accrue, is expected to be 66 years.[9] It is assumed that HCC occurs around 45 years[9] and 21 years are saved for each case of HCC averted. Death is assumed to occur within 6 months of diagnosis of HCC and the quality of life is reckoned to be 0.2.[9] This suggests that 20.6 QALY are saved for each case of HCC averted.

Using these figures, the undiscounted cost per QALY saved was Rs 48,540 (Table 2). The per capita GNP of India is Rs 20,250. Hence, the cost per QALY saved with universal vaccination is more than double the GNP. After discounting, to account for the opportunity cost of money, at the rate of 3% for 45 years, the discounted cost per QALY was Rs 259,610.

The fertility rate in India according to the UNICEF is 3.2.[7] Assuming that each mother has 3 children on an average, a third of 1100 mothers, i.e., 367 mothers would have needed HBsAg testing in our study population.

Discussion

The carrier rate of HB in India has been reported previously as 3.7% in a hospital-based study of pregnant

Table 1: Cost calculations for selective and universal immunization

Item	Total cost (in rupees)
Testing primiparous women in community	252 x (30+10) = 10,080 (A)
Vaccinating babies of 22 HBsAg-positive mothers	22 x 70 x 3 = 4,620 (B)
Control of perinatal spread by selective vaccination	A + B = 14,700
Cost of universal vaccination	1100 x 70 x 3 = 231,000

Table 2: Cost-effectiveness and cost-utility of universal immunization

Total cost in project area	Rs 219,600
National cost	25 million x 219,600/1100 = approximately Rs 5000 million
Cost per life saved	5000 million/5000 = Rs 1,000,000
QALY saved per patient	20.8
Cost per QALY saved	1000,999/20.6 = 48540
Discounted cost per QALY*	Rs 262,120

*Discounting at the rate of 3% for 45 years

women in Delhi.[10] We have previously reported a prevalence rate of 1% in a similar study of 6910 pregnant women in Delhi.[11] In the present community-based study, we found the true prevalence to be 1.47%.

The best method to protect babies against HB carrier state is to introduce universal immunization at birth and to administer additional immunoglobulin to babies born to HB carrier mothers.[12] However, a study from Taiwan[13] suggested that universal immunization started at birth alone without immunoglobulin can bring down the carrier rate.

Our study found the cost-to-benefit ratio of universal immunization was high. This is because the mortality rate among HB carriers is quite low in India and the benefit in terms of lives saved is therefore small. We used mortality data in India as projected by the ICMR.[8] Further, since the benefits of HB vaccine program will accrue nearly 45 years later,[9] the benefits need to be discounted. We used a discount rate of only 3%; a higher discount rate would in fact show universal vaccination to be even less cost-beneficial. We assumed that the vaccine yields 100% protection. The cost analysis will be even more unfavorable if imperfect vaccine efficacy is taken into account.

Considering the vaccine cost as Rs 10 per dose and ignoring the costs for administration of the vaccine, the cost of each QALY saved would be twice the per capita GNP. We have previously shown that the discounted cost of vaccine and its delivery must be below Rs 5.20 per dose for universal immunization to be cost-beneficial in India.[4]

Selective immunization can protect newborns of carrier mothers from vertical transmission, but does not prevent horizontal acquisition of infection by unvaccinated children. In the absence of data on how many lives are saved by selective immunization, we could not calculate the cost of selective immunization per life saved or per QALY saved.

Our data show that the largest component of cost of universal vaccination is that of delivery of first dose. This has led to suggestions that vaccine be given with the current EPI vaccines. Aggarwal and Naik[14,15] suggested that delayed vaccine would be effective. Nayak *et al*[10] stated that one-third of chronic HB carriers acquired infection by perinatal spread and the remaining acquired infection in early childhood, as is the pattern in Africa. This emphasizes the need for immunization at birth to prevent mother-to-child transmission.

In conclusion, our study suggests that universal HB immunization is not cost-beneficial in India since the discounted cost of saving each QALY with this strategy is about ten times the per capita GNP.

References

1. Hoofangle JH. Towards universal vaccination against hepatitis B. *N Engl J Med* 1989;321:1333-4.

2. Tu XM, Litvak E, Pagan M. Issues in human immunodeficiency virus (HIV) screening programs. *Am J Epidemiol* 1992;136:244-55.

3. Committee on Immunization of IAP. *Hepatitis B vaccine.* IAP Guidebook on Immunization. Indian Academy of Pediatrics: Mumbai. 2001.

4. Tyagi V, Saroj K, Sawhney A, Vikas T, Puliyel JM. Using gross national product to calculate acceptable immunization costs. *Pharmacoeconomics* 2003;21:497-9.

5. Stevens CE. Immunoprophylaxis of hepatitis B viral infection. *Semin Pediatr Infect Dis* 1999;2:135.

6. Tandon BN, Irshad M, Mathur RH, GP Rao MN. Prevalence of HBsAg and anti HBs in children and strategy suggested for immunization in India. *Indian J Med Res* 1991;93:337-9.

7. UNICEF. The Progress of Nations 1999. New York: United Nations Publications. 1999: p. 34-5.

8. Dhir V, Mohandas KM. Epidemiology of digestive tract cancers in India III – Liver. *Indian J Gastroenterol* 1998;17:100-3.

9. Miller MA, Kane M. Routine hepatitis B immunization in India. Cost effectiveness assessment. *Indian J Pediatr* 2000;67:299-300.

10. Nayak NC, Panda SK, Zuckerman AJ, Guha DK. Diagnosis and impact of perinatal transmission of hepatitis B virus in North India. *J Med Virol* 1987;21:137-45.

11. Abass F, Thomas RD, Rajkumar A, Gupta N, Puliyel JM. Controlling perinatally acquired hepatitis B. *Indian J Pediatr* 2001;68:365.

12. Beasley RP, Hwang LY. Postnatal infectivity of hepatitis B surface antigen carrier mothers. *J Infect Dis* 1983;147:185-90.

13. Chang MH, Chen CJ, Lai MS, Hsu HM, Wu TC, Kong MS, *et al*. Universal hepatitis B vaccination in Taiwan and incidence of hepatocellular carcinoma. *N Engl J Med* 1997;336:1855-9.

14. Aggarwal R, Naik SR. *Cost efficacy and evaluation of inclusion of hepatitis B vaccine in Expanded Programme of Immunization in India. In:* Sarin SK, Singal AK, Eds. Hepatitis B in India: Problems and Precautions. Delhi: CBC Publishers. 1996: p. 206-16.

15. Aggarwal R, Naik SR. Prevention of hepatitis B infection: the appropriate strategy for India. *Natl Med J India* 1994;7:216-20.