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ORIGINAL ARTICLE

Factors Related to Completed Status and Seropositivity of Hepatitis A Immunization Among Children Aged 1—3 Years and 6—8 Years in South Korea

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Abstract
This study was designed to identify factors associated with hepatitis A immunization status and seropositivity in Korean children. In-person interviews, reviewing their vaccination cards and testing hepatitis A antibody were conducted with 389 children aged 1-3 years and 544 children aged 6-8 years. In all age groups, earlier birth order was the only significant factor in children receiving either single or both doses of the vaccination. And completion of the second dose of vaccination was a prerequisite for increased seropositivity. Additionally, household income had a positive impact on seropositivity only in children aged 6-8 years. Our findings suggest that presence of an economic barrier is the underlying cause of the decreased hepatitis A vaccination services in Korea. Therefore, hepatitis A vaccine should be included in the essential National Immunization Program.

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1. Introduction

Vaccine-preventable diseases are still a public health burden worldwide [1], and this could be largely attributed to the prevailing suboptimal vaccination rate [2]. The number of patients infected with the hepatitis A virus (HAV) has increased dramatically from 1398 in 2001 to 38,811 persons in 2010 [3,4].

Since the hepatitis A vaccine was introduced in Korea in 1997, the anti-HAV seroprevalence rate in children under the age of 10 years has increased from 33.4% in 2005 to 69.9% in 2009 [5]. Results of two studies have confirmed that 50.6% of children have received the hepatitis A immunization [6], and 42.3% have received the first dose whereas only 24.7% have received both doses of the vaccination [7], indicating that there are significant barriers in accessing immunization services. Yun et al conducted a study to investigate the seroprevalence and vaccination rates in Korea [6]. However, the results of the study were inconclusive owing to sampling limitations. In this study, participants were selected from a hospital (participants ranged from children under the age of 10 years to elderly persons older than 80 years of age). Immunization status and seropositivity of hepatitis A vaccine and its related factors among Korean toddlers older than 5 years of age has not yet been studied.

Therefore, we analyzed a population-based sample of children aged 1−3 years and 6−8 years from a metropolitan city and a province in Korea to investigate factors related to the status and seropositivity of hepatitis A immunization status.

2. Materials and Methods

2.1. Participants

The study population included 392 children aged 1−3 years and 550 children aged 6−8 years living in a metropolitan city (Daejeon) and three counties (Nonsan, Geumsan, and Gyeryong) in the Chungnam Province of Korea. We excluded nine children due to refusal to collect a blood sample ($n = 3$), no vaccination record ($n = 5$), or a partially completed interview ($n = 1$). A face-to-face interview with 933 caregivers was conducted between July 2010 and February 2011.

2.2. Questionnaire and outcome measures

We developed a questionnaire that included several factors such as low family income [8,9], low level of parental education [8,10], young age of parents [10], birth order of the child [11,12], and region [6].

We retrospectively assessed the dates of administering a first and a second dose of hepatitis A vaccine by reviewing written records from vaccination cards, based on the immunization schedule of the Korean Centers for Disease Control and Prevention [13]. Completed status of immunization was defined as whether children received both first and second dose of the vaccine.

The anti-HAV immunoglobulin G test was conducted by a chemiluminescent microparticle immunoassay (ARCHITECT; Abbott Laboratories, Abbott Park, IL, USA). Assay protocols, cutoffs, and interpretations were carried out according to the manufacturers' instructions. Seropositivity was defined as S/CO (relative light units of sample/relative light units of calibrator) > 1.

2.3. Analysis

Hepatitis A immunization status in the 933 participants and seropositivity in the 542 immunized participants were assessed by age group (1−3 years and 6−8 years) using the Chi-square test. Odds ratio (OR) and 95% confidence interval (CI) were calculated by multiple logistic regression analyses. The models were constructed to include all independent variables for which the p value calculated from the Chi-square test was less than 0.10. All statistical analyses were conducted with SPSS version 20 software (SPSS Inc., Chicago, IL, USA).

2.4. Ethical considerations

Informed consents were given for children and their caregivers who participated voluntarily in this study. The purpose of the study was explained to them. Names of the participants were not registered in the questionnaires. An ethical approval was obtained from the Institutional Review Board at Konyang University, Korea.

3. Results

3.1. Factors affecting hepatitis A immunization status

Factors playing a significant role in hepatitis A immunization status are shown in Table 1. Immunization status of both first and second doses was significantly higher for children aged 1−3 years who had an earlier birth order ($p < 0.001$), fewer siblings ($p = 0.019$), and lived in the city ($p = 0.025$). Immunization rates of both first and second doses were significantly higher for children aged 6−8 years who had an earlier birth order ($p < 0.001$), fewer siblings ($p = 0.037$), and higher monthly household income ($p = 0.044$).

Multiple logistic regression analysis (Table 2) revealed that only being first in the birth order was a contributing factor for higher immunization status (children aged 1−3 years: OR = 2.5, 95% CI = 1.2−5.0; children aged 6−8 years: OR = 5.2, 95% CI = 2.3−11.7).

Table 1. Completed status of hepatitis A immunization by characteristics of children and their caregivers

	Children aged 1−3 years (389 participants)			Children aged 6−8 years (544 participants)		
Predictors	*N*	%	*p*	*N*	%	*p*
Child's factor						
Gender						
Male	80/200	40.0	0.090	137/271	50.6	0.797
Female	105/189	31.7		135/273	49.5	
Birth order						
First	85/168	50.6	<0.001	156/240	65.0	<0.001
Second	47/167	28.1		100/246	40.7	
Third or more	8/54	14.8		16/58	27.6	
Number of siblings						
None	44/107	41.1	0.019	38/68	55.9	0.037
One	82/214	38.3		182/347	52.4	
Two or more	14/68	20.6		52/129	40.3	
Caregiver's factor						
Monthly household income (KRW)						
<2,000	36/97	37.1	0.044	36/79	45.6	0.044
2,000−2,999	52/133	39.1		53/121	43.8	
3,000−3,999	33/104	31.7		95/187	50.8	
≥4,000	19/55	34.5		88/157	56.1	
Age (y)						
20−29	31/78	39.7	0.537	7/16	43.8	0.705
30−39	101/289	34.9		212/416	51.0	
≥40	8/22	36.4		53/112	47.3	
Region						
Rural	41/167	24.6	0.025	118/210	56.2	0.104
Urban	87/222	39.2		161/334	48.2	
Educational attainment (y)						
≤12	23/73	31.5	0.084	59/126	46.8	0.291
≥13	125/316	39.6		217/418	51.9	

KRW = South Korean Won.

3.2. Factors affecting seropositivity of hepatitis A immunization

Seropositivity in immunized children based on the predictor variables is shown in Table 3. Seropositivity was significantly higher for children who had been administered two doses of the vaccine: 82.4% in children aged 1−3 years receiving only first dose and 99.3% in children receiving both doses ($p < 0.001$), and 82.2%

Table 2. ORs and 95% CIs of receiving both the first dose and second dose of hepatitis A immunization

Predictors	Children aged 1−3 years	Children aged 6−8 years
Birth order		
First	2.5 (1.2−5.0)	5.2 (2.3−11.7)
Second	1.1 (0.5−2.5)	2.3 (1.0−5.1)
Third or more	1.0	1.0
Monthly household income (KRW)		
<2,000	—	1.0
2,000−2,999	—	1.1 (0.4−2.7)
3,000−3,999	—	1.3 (0.6−2.9)
≥4,000	—	2.2 (0.9−5.6)
Region		
Rural	1.0	1.0
Urban	0.9 (0.5−1.8)	1.5 (0.8−2.7)
Educational attainment		
≤12	1.0	—
≥13	1.2 (0.7−2.1)	—

CI = confidence interval; KRW = South Korean Won; OR = odds ratio.

Table 3. Seropositivity in children receiving hepatitis A immunization by characteristics of children and caregivers

	Children aged 1−3 years (225 participants)			Children aged 6−8 years (317 participants)		
Predictors	*N*	%	*p*	*N*	%	*p*
Child's factor						
Gender						
Male	112/120	93.3	0.782	149/158	94.3	0.153
Female	97/105	92.4		155/159	97.5	
Birth order						
First	110/118	93.2	0.902	168/173	97.1	0.482
Second	80/86	93.0		116/123	94.3	
Third or more	19/21	90.5		20/21	95.2	
Number of siblings						
None	61/69	88.4	0.199	41/44	93.2	0.914
One	121/127	95.3		204/210	97.1	
Two or more	27/29	93.1		59/63	93.7	
Immunization doses						
One	70/85	82.4	<0.001	37/45	82.2	<0.001
Two	139/140	99.3		267/272	98.2	
Caregiver's factor						
Monthly household income (KRW)						
<2,000	52/56	92.9	0.966	38/41	92.7	0.047
2,000−2,999	70/75	93.3		60/64	93.8	
3,000−3,999	59/64	92.2		109/114	95.6	
≥4000	28/30	93.3		97/98	99.0	
Age (y)						
20−29	43/45	95.6	0.207	10/11	90.9	0.271
30−39	156/168	92.9		234/241	97.1	
≥40	10/12	83.3		60/65	92.3	
Region						
Rural	28/31	90.3	0.549	81/84	96.4	0.775
Urban	181/194	93.3		223/233	95.7	
Educational attainment (y)						
≤12	84/88	95.5	0.230	106/113	93.8	0.162
≥13	125/137	91.2		198/204	97.1	

KRW = South Korean Won.

in children aged 6−8 years receiving only first dose and 98.2% in children receiving both doses ($p < 0.001$). We observed a significant positive relationship between monthly household income and seropositivity in children aged 6−8 years ($p = 0.047$).

The multiple logistic regression analysis (Table 4) revealed that administration of two doses of the hepatitis A vaccine was a contributing factor for seropositivity (children aged 1−3 years: OR = 139.0, 95% CI = 19.4−993.7; children aged 6−8 years: OR = 59.2, 95% CI = 8.1−432.7). A positive relationship was observed between monthly household income and seropositivity in children aged 6−8 years [2000−<3000 South Korean Won (KRW) group:

Table 4. ORs and 95% CIs of seropositivity in children receiving hepatitis A immunization

Predictors	Children aged 1−3 years	Children aged 6−8 years
Immunization doses		
One	1.0	1.0
Two	139.0 (19.4−993.7)	59.2 (8.1−432.7)
Monthly household income (KRW)		
<2,000	—	1.0
2,000−2,999	—	3.8 (1.4−10.2)
3,000−3,999	—	5.3 (2.1−13.9)
≥4,000	—	4.7 (1.0−21.5)

CI = confidence interval; KRW = South Korean Won; OR = odds ratio.

OR = 3.8, 95% CI = 1.4−10.2; 3000−<4000 KRW group: OR = 5.3, 95% CI = 2.1−13.9; ≥4000 KRW group: OR = 4.7, 95% CI = 1.0−21.5].

4. Discussion

Because of growing concerns about hepatitis A in Korea, the Korean Ministry of Health and Welfare changed the classification of hepatitis A in 2011 into a first-class communicable disease, a category that includes foodborne diseases or waterborne diseases with the possibility of rapid transmission and the need for urgent countermeasures [14]. Hepatitis A immunization is the most effective measure to curtail this disease and was introduced in 1997. However, hepatitis A vaccination is not part of the National Immunization Program (NIP) in South Korea; thus, patients must pay to receive the vaccination, which probably serves as a barrier to access the service [15].

This study has for the first time provided results of hepatitis A immunization status and seropositivity in children in Korea. Our findings illustrate that earlier birth order was a contributing factor for hepatitis A immunization rates. This result was consistent with other studies that late birth order in the family has a negative effect on complete vaccination status [12,16]. However, this result was inconsistent with that of another study [17] in which low hepatitis A vaccination coverage in Korea was significantly related to economic status, rural area, and a mother's employment status.

Because the hepatitis A vaccine was not included in the essential NIP in Korea, caregivers whose children wish to receive the vaccination must pay for the service [18], and this seems to decrease the number of patients who avail this service. Therefore, there have been several arguments that HAV vaccination must be included in the NIP [19]. The number of people receiving two doses of the hepatitis A vaccine in Korea has been estimated at 41.6% based on the number of hepatitis A vaccines sold between 1998 and 2006 [20] and 24.7% based on a 2005 population-based survey [7]. Unfortunately, our study was not designed to provide hepatitis vaccination rates. Nevertheless, we hypothesize that a larger number of children implies higher vaccination costs for caregivers and these costs are likely to be a powerful contributing factor to the significant decrease in patients accessing hepatitis A vaccination services in these larger families in Korea. In addition, because in Korea it is not mandatory to maintain hepatitis A vaccination records by either the caregivers or health-care providers, it is impractical to get the complete vaccination status of the population. The latter problem is compounded by the fact that the vaccinations are administered in a private clinic whose records are not easily accessible.

Our findings illustrate that the number of immunization doses and household income are predictors of hepatitis A seropositivity. Our findings demonstrated that the location of residence (rural/urban) has no impact on seropositivity, which is inconsistent with the results of a previous study [6] that showed that children living in rural areas have higher seropositive rates compared with those living in the city.

In this study, seropositivity was considered to be an indicator of the effects of hepatitis A vaccination. In 2006, HAV seroprevalence was reported to be 55.6% in children aged 1−4 years and 47.2% in those aged 5−9 years [21]. More than 90% of children aged 1 year or more and adults had protective titers of the antibody 4 weeks after administering one dose of the vaccination [22] and anti-HAV persists for at least 10−12 years after vaccination in 5−6-year-old children [23]. Thus, a second dose of the vaccination 2−8 years after the single primary dose shows an excellent booster response [24−26].

Our findings are based only on analysis of data derived from children living in restricted areas in Korea and are not representative of the national estimate of hepatitis A vaccination coverage. Previous studies have demonstrated that the vaccination records can be incomplete [27], and because written records of vaccination for our analysis are not available, the accuracy of the assessment of the immunization's completeness is decreased. Because of excluding children without the written vaccination records, children with disadvantaged caregivers were possibly excluded. This bias is likely to result in an underestimation of the impact of the observed predictor variables on hepatitis A immunization rates and seropositivity.

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