Jpn. J. Infect. Dis., 65, 99-104, 2012

Original Article

Adverse Events following Immunization (AEFI) with the Novel Influenza A (H1N1) 2009 Vaccine: Findings from the National Registry of All Vaccine Recipients and AEFI and the Passive Surveillance System in South Korea

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(Received August 29, 2011. Accepted November 21, 2011)

SUMMARY: This study characterized the adverse events following immunization (AEFI) with the novel influenza A (H1N1) 2009 vaccine in Korea. Data on immunization and AEFI were collected between October 27, 2009 and March 15, 2010 through the national immunization registry and passive surveillance systems. The frequency of AEFI and serious adverse events (SAEs) were calculated according to age, sex, priority group, and vaccine type. In 13,758,527 vaccine recipients aged 6 months or older, 2,530 AEFI were reported (18.4 per 100,000 immunizations). The AEFI reporting rate was highest among people aged 10–19 years (29.6 per 100,000 immunizations) and was higher in female recipients than in male recipients (20.0 versus 16.7 per 100,000 immunizations). Most AEFIs were nonspecific systematic reactions that occurred within 24 h (77.4%) after vaccine administration. A total of 178 vaccine-related SAEs were identified, and vaccine-related mortalities were not reported. This study showed that the AEFI reporting rate after influenza A (H1N1) 2009 vaccinations was relatively high, especially in the younger population. Mild systemic reactions accounted for the majority of reported AEFI, and fatal SAEs were rare. This study also implied that passive surveillance might be an efficient safety monitoring system that can detect relatively rare AEFI.

INTRODUCTION

A national influenza A (H1N1) immunization program was conducted with great urgency in South Korea in 2009 after the identification of the first patient in Korea in May 2009. The safety of the mass vaccination program against influenza A (H1N1) 2009 has been of great public concern. A study has shown that the safety of the H1N1 vaccine was similar to that of the seasonal influenza vaccine and that their manufacturing processes were the same (1). Even though no serious adverse events (SAEs) related to the seasonal influenza vaccine have been reported in clinical trials, the government has monitored the safety of the H1N1 vaccine in order to rapidly detect any unexpected safety problems (2–4). In addition, an adjuvant vaccine was used to enhance the immunogenicity, and this caused concern about adverse events in South Korea. Clinical trials of the new vaccines against the novel influenza A (H1N1) 2009 virus did not have sufficient sample sizes or follow-up durations to identify rare adverse events (5,6). These trials were not big enough to provide information on rare adverse events, such as Guillain-Barré syndrome, which was reported in individuals vaccinated against the swine influenza that prevailed in 1976 (7).

The purpose of the present study was to investigate the characteristics of adverse events following immunization (AEFI) against influenza A (H1N1) 2009 through the national immunization registry system and the passive surveillance system.

MATERIALS AND METHODS

Background on the 2009 immunization campaign and the AEFI surveillance systems in South Korea: All influenza A (H1N1) 2009 vaccines that were administered during the nationwide immunization program in Korea were domestically produced starting in June 2009. They were monovalent, inactivated, and split-virus vaccines for injection use. The Korean government established a system to register all recipients of this new vaccine through the national immunization registration system. A nonadjuvant vaccine (hemagglutinin, 15 μg/0.5 mL)

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was administered to healthcare workers, preschool children aged 36 months to 6 years, elementary school children, middle and high school adolescents, and pregnant women. A half dose of the nonadjuvant vaccine (hemagglutinin, 7.5 μg/0.25 mL) was administered twice at 4 week intervals to infants aged 6 to 35 months. The MF59-adjuvanted vaccine (hemagglutinin, 3.75 μg/0.25 mL) was administered to people with chronic medical conditions, the elderly (aged 65 years or older), military personnel, and the rest of the general public. The immunization was conducted in an orderly fashion to each target group using a standard vaccine production and distribution schedule.

The national AEFI management system is composed of the AEFI passive surveillance system, the AEFI rapid response system, and the AEFI investigation team. The AEFI rapid response system reviews the AEFI, which are reported through a web-based passive surveillance system, and determines causality between a SAE and the vaccine. If suspicious SAEs were reported, the AEFI Response Committee reviewed the results of the AEFI investigation and made a decision as to whether or not that lot of vaccine would be banned from the immunization program.

Study population: We obtained data from the Korean national AEFI surveillance system between October 27, 2009 and March 15, 2010. According to the national vaccination program, we could classify the study population into 7 priority groups: healthcare workers, students, infants and preschool children, pregnant women, persons with chronic medical conditions, elderly ($\geq$65 years old), and others (8). A SAE was defined as any adverse event that led to hospitalization. All reported SAEs were reviewed by the AEFI investigation team and then classified as a local or systemic reaction. A systemic reaction was further classified into 4 categories: neurologic, allergic, gastrointestinal, and nonspecific. The causal relationship with vaccine administration was assessed according to the World Health Organization causality assessment guidelines (9).

Statistical analysis: The frequencies of AEFI and SAEs were calculated according to age, sex, and priority group. The frequency and type of AEFI were further studied separately for the nonadjuvant and adjuvant vaccines. The reporting rate was estimated by dividing the number of adverse events by the number of vaccination recipients during the study period. In order to determine the denominators, we extracted data on the age group, sex, priority group, and vaccine type of recipients from the national immunization system during the study period. The numerators were the number of people who reported any type of AEFI because the presence and types of AEFI were reported without hierarchy and multiple types of AEFI could be reported for one person. Chi-square test and logistic regression analyses were used to compare the reported AEFI rates between the different characteristics. The SAS software package (version 9.2; SAS Institute, Cary, N.C., USA) was used for statistical analyses.

RESULTS

During the 5-month study period, 13,758,527 people received vaccinations, and 76.3% of them received the nonadjuvant vaccine. A total of 2,530 reports of AEFI were confirmed, thus making the overall AEFI reporting rate 18.4 per 100,000 immunizations (Table 1). The AEFI reporting rate was highest in the 10–19-year age group (29.6 per 100,000 immunizations). The AEFI reporting rate was higher in women than in men. Students had the highest AEFI reporting rate (27.1 per 100,000 immunizations) among the priority vaccination

Table 1. AEFI against influenza A (H1N1) 2009 in Korea by demographic characteristics and vaccine type

Characteristic	Total vaccine recipients No. (%)	Reported AEFI No. (%)	AEFI reporting rate per 100,000 immunization	*P*
Age (y)				
0.5–9	5,178,138 (37.6)	806 (31.9)	15.6	
10–19	4,633,254 (33.7)	1,372 (54.2)	29.6	
20–59	1,413,383 (10.3)	179 (7.1)	12.7	<0.0001
60–69	1,074,580 (7.8)	76 (3.0)	7.1	
≥70	1,459,172 (10.6)	97 (3.8)	6.6	
Sex				
Male	6,725,369 (48.9)	1,122 (44.3)	16.7	<0.0001
Female	7,033,158 (51.1)	1,408 (55.7)	20.0	
Priority group				
Healthcare workers	550,341 (4.0)	71 (2.8)	12.9	
Students	6,507,784 (47.3)	1,764 (69.7)	27.1	
Infants & preschool children	3,219,495 (23.4)	413 (16.3)	12.8	
Pregnant women	82,551 (0.6)	17 (0.7)	20.6	<0.0001
Persons with chronic medical conditions	963,097 (7.0)	133 (5.3)	13.8	
Elderly (≥65 years old)	1,926,194 (14.0)	98 (3.9)	5.1	
Others	509,065 (3.7)	34 (1.3)	6.7	
Type of vaccine				
Nonadjuvant	10,491,364 (76.3)	2,281 (90.1)	21.7	<0.0001
Adjuvant	3,267,163 (23.7)	249 (9.9)	7.6	
Total	13,758,527 (100)	2,530 (100)	18.4	

AEFI, adverse events following immunization.

Table 2. Frequency and type of AEFI among recipients of nonadjuvant vaccine

Demographic characteristic	Vaccine recipient No.	People with local reaction No. (%)[1)]	People with systemic reaction, No. (%)[1)]				People with any AEFI No. (%)	Odds ratio	*P*
			Neurologic	Gastrointestinal	Allergic	Nonspecific			
Age (y)									
0.5–9	5,176,540	105 (13.0)	81 (10.0)	133 (16.5)	185 (22.9)	546 (67.8)	805 (35.3)	0.52	<0.0001
10–19	4,627,769	92 (6.7)	212 (15.5)	335 (24.4)	304 (22.2)	1,034 (75.4)	1,372 (60.1)	1.00	—
20–59	643,814	5 (5.0)	8 (8.0)	16 (16.0)	16 (16.0)	80 (80.0)	100 (4.4)	0.52	<0.0001
≥60	43,241	1 (25.0)	0 (0)	1 (25.0)	1 (25.0)	1 (25.0)	4 (0.2)	0.31	0.0139
Sex									
Male	5,305,540	101 (9.6)	130 (12.4)	213 (20.3)	213 (20.3)	765 (73.1)	1,047 (45.9)	1.00	—
Female	5,185,824	102 (8.3)	171 (13.9)	272 (22.0)	293 (23.7)	896 (72.6)	1,234 (54.1)	1.20	<0.0001
Total	10,491,364	203 (11.1)	301 (13.2)	485 (21.3)	506 (22.2)	1,661 (72.8)	2,281 (100)		

[1)]: Multiple responses were allowed, so the total row percentages will exceed 100.

Table 3. Frequency and type of AEFI among recipients of adjuvant vaccine

Demographic characteristic	Vaccine recipient No.	People with local reaction No. (%)[1)]	People with systemic reaction, No. (%)[1)]				People with any AEFI No. (%)	Odds ratio	*P*
			Neurologic	Gastrointestinal	Allergic	Nonspecific			
Age (y)									
20–59	769,569	12 (15.2)	7 (8.9)	9 (11.4)	23 (29.1)	48 (60.8)	79 (31.9)	1.54	0.0037
60–69	1,042,690	14 (19.2)	14 (19.2)	9 (12.3)	17 (23.3)	50 (68.5)	73 (29.4)	1.05	0.7262
≥70	1,447,821	5 (5.2)	13 (13.5)	19 (19.8)	24 (25.0)	71 (74.0)	96 (38.7)	1.00	—
Sex									
Male	1,415,331	10 (13.5)	7 (9.5)	10 (13.5)	23 (31.1)	46 (62.2)	74 (28.9)	1.00	—
Female	1,844,749	21 (12.1)	27 (15.5)	27 (15.5)	41 (23.6)	123 (70.7)	174 (71.1)	1.80	<0.0001
Total	3,260,080	31 (12.5)	34 (13.7)	37 (14.9)	64 (25.8)	169 (68.1)	248 (100)		

[1)]: Multiple responses were allowed, so the total row percentages will exceed 100.
This table excludes 1,598 subjects (male 827, female 771) aged 6 months–9 years and 5,485 subjects (male 3,671, female 1,814) aged 10–19 years, who were targeted for the nonadjuvant vaccine but received the adjuvant vaccine. Among them, one AEFI was reported.

groups (Table 1).

Among the 10,491,364 recipients of the nonadjuvant vaccine, 2,281 people reported some type of AEFI (21.7 per 100,000 immunizations). In all age groups, the majority of AEFI were nonspecific reactions, which were followed by allergic reactions and gastrointestinal symptoms. The AEFI reporting rate was the highest in the 10–19-year age group. The reporting rate was higher in women than in men, but the types of AEFI were similar between men and women (Table 2). There were 3,267,163 adjuvant vaccine recipients. However, 1,598 people from the group aged 6 months to 9 years and 5,485 people in the group aged 10 to 19 years were not included. They were vaccinated with the adjuvant vaccine even though they were targeted for the nonadjuvant vaccine. Among them, only one AEFI (nonspecific reaction) was reported. Among the adjuvant vaccine recipients, older age and female sex were associated with a higher AEFI reporting rate (Table 3).

Among the 317 SAEs reported, 178 cases were determined to be related to the vaccine. However, there were no deaths or miscarriages among the 178 vaccination-related SAEs (Fig. 1). Of the reported 178 SAEs that were proven to be related to the vaccine, 177 were systemic reactions (Table 4) and 1 was a local reaction (cellulitis). The neurologic reactions included 2 cases of Guillain-Barré syndrome. The first case was that of a 16-year-old boy who had an onset time of 27 h after the vaccination. The other case was that of a 35-year-old man who had an onset time of 3 days after the vaccination. There was also a case of acute disseminated encephalomyelitis (11-year-old girl with an onset time of 5 days after the vaccination), a case of acute transverse myelitis, a case of Bicker-staff brainstem encephalitis, 3 cases of facial palsy, a case of myopathy, and 66 cases of nonspecific peripheral neuropathy. Among the 178 vaccine-related SAEs reported, there were 18 cases of allergic reactions, such as anaphylaxis (n = 5), anaphylactoid reactions (n = 10), urticaria (n = 2), and allergic purpura (n = 1). All 5 gastrointestinal reactions consisted of nausea. In the 139 SAEs that were determined not to be related to the vaccination, 12 deaths and 8 miscarriages were included. The causes of death were intracerebral hemorrhage (3 male recipients and 3 female recipients; median onset time, 48 h), cardiac disorder (4 male recipients and 1 female recipient; median onset time, 7 h), and enterorrhagia (1 male recipient; onset time, 4 h). Autopsies were conducted for only 5 cases of death. Among the 8 miscarriages, 1 case (24-year-old mother; onset time, 4 days; autopsy done) was related to intrauterine growth retardation, and another case (37-year-old mother; onset time, 3 days; autopsy not done) was assumed to be related to chorioamnionitis. The other 6 cases of miscarriage were of unknown causes because no autopsy was done. The mean ± SD age and median onset time were 56 ± 21.7 years and 7 h (interquartile range, 6–168) for 5 cardiac disorders; 21.3 ± 29.8 years and 48 h for 6 brain disorders; and 1 year

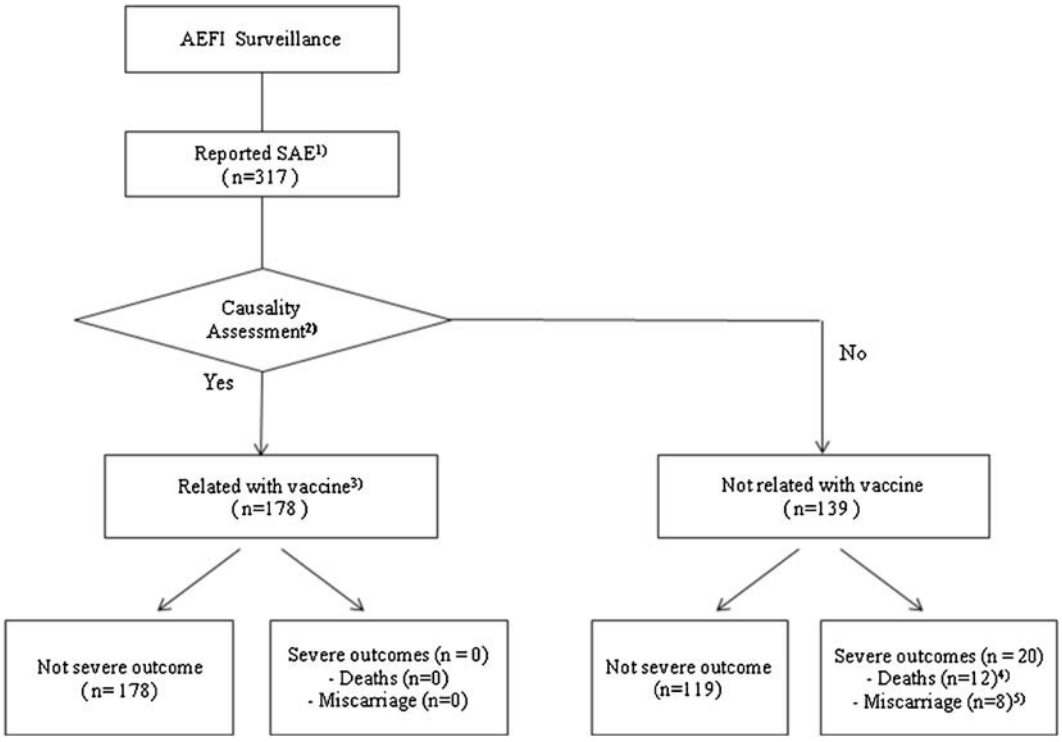

Fig. 1. Flow of identification and classification of serious adverse events (SAEs). 1) SAEs are defined as any adverse events that lead to hospitalization, including life-threatening experience or residual disability. 2) Causality assessed according to the WHO guidelines. 3) Types of SAE are described in Table 4. 4) Causes of death were 5 cardiac disorders (4 males/1 female), 6 brain disorders (3 males/3 females), and 1 enterorrhagia (1 male). 5) Causes of miscarriages were 1 chorioamnionitis, 1 intrauterine growth retardation, and 6 unknown causes.

Table 4. Serious adverse event reported through the AEFI surveillance system, Korea 2009

Type of SAE[1)]	No. of SAEs			Age (y) Mean ± SD	Onset time in hours Median [interquartile range]
	Total	Male/Female	Nonadjuvant/Adjuvant vaccine		
Local reaction (n = 1)					
Cellulitis	1	1/0	1/0	8	13
Systemic reaction					
Neurologic (n = 75)					
Guillain-Barré syndrom	2	2/0	2/0	25.5 ± 9.5	49.5 [27–72]
Acute disseminated encephalomyelitis	1	0/1	1/0	11	120
Acute transverse myelitis	1	1/0	1/0	7	144
Bicker-staff brainstem encephalitis	1	1/0	1/0	15	360
Facial palsy	3	1/2	3/0	15	48 [25–120]
Myopathy	1	1/0	1/0	16	7
Nonspecific peripheral neuropathy	66	30/36	66/0	12.9 ± 2.7	7 [1–27]
Allergic (n = 18)					
Anaphylaxis	5	2/3	5/0	14.4 ± 1.7	3
Analphylactoid reaction	10	2/8	10/0	13.0 ± 2.4	3.5 [1–24]
Urticaria	2	0/2	2/0	11.5 ± 0.7	11 [6–16]
Allergic purpular	1	0/1	1/0	9	96
Gastrointestinal (n = 8)					
Gastroenteropathy	8	3/5	8/0	12.3 ± 4.0	2.5 [1–13.5]
Nonspecific (n = 76)					
Myalgia	14	6/8	14/0	11.9 ± 2.2	16 [4–48]
Headache	22	7/15	22/0	13.5 ± 3.0	5 [3–28]
Lethargy	16	9/7	15/1	13.9 ± 7.8	13 [1–27]
Fever	16	5/11	16/0	10.5 ± 4.8	4 [1–26.5]
Dizziness	8	2/6	8/0	13.0 ± 3.4	6.5 [2–23]
Total	178	73/105	177/1	14.4 ± 11.1	6 [1–28]

[1)]: SAEs are defined as any adverse events that lead to hospitalization including life-threatening experience or residual disability.
SAE, serious adverse event.

and 4 h for enterorrhagia, respectively. For the miscarriages, the onset time was 72 h for chorioamnionitis, 96 h for intrauterine growth restriction, and a median of 108 h (interquartile range, 33–288 h) in 6 cases with unknown causes.

DISCUSSION

This study showed an overall AEFI reporting rate of 18.4 per 100,000 immunizations. This was higher than the rates reported in China (10.0 per 100,000 doses) or in the USA (8.2 per 100,000 doses) but lower than the rate in Denmark (179 per 100,000 immunizations) (1,10). In addition, this rate was much higher than the adverse event reporting rates after vaccinations against the seasonal trivalent influenza of the years 2007–2008 (0.79 adverse events per 100,000 immunizations) and 2008–2009 (0.74 adverse events per 100,000 immunizations) in Korea. This study showed a relatively high rate of AEFI reports, even though underreporting is a known limitation of the passive surveillance system (5). The most plausible explanations for the high reporting rate are the high public awareness and the enhanced efforts to increase the reporting of AEFI due to a number of endeavors, such as the distribution of vaccine information statements or media outreach. In addition, even though the influenza (H1N1) 2009 vaccine was licensed in a similar way as the seasonal influenza vaccine, the public perceived it as a new vaccine. There is a known tendency for an increase in the rates of reporting adverse events after immunizations with newly licensed vaccines (1,11).

The AEFI reporting rate among children and adolescents (6 months to 9 years and 10 to 19 years of age, respectively) was very high. The risk assessment reports stated that the novel influenza A (H1N1) 2009 vaccination might be associated with a higher frequency of fatal outcomes than the seasonal trivalent influenza in the younger age group (12), which therefore increased the rate of voluntary immunizations among this population. As a result, infants and children made up the majority of all recipients of the vaccine, and their vaccination coverage rate was fairly high (8). Moreover, parents and teachers were more likely to report potential AEFI. Students were double-checked at home and at school for any of the symptoms and signs. Some students were hospitalized with only anxiety reactions, hyperventilation syndrome, or mild nonspecific symptoms. These hospitalizations might have contributed to the higher AEFI reporting rate among children and adolescents.

It was recommended that individuals aged 65 years or older were immunized with adjuvant vaccine in order to enhance the immunologic reactions. Among the adjuvant vaccine recipients, older age groups reported relatively fewer AEFI. This finding is consistent with a previous study (13). In the literature, AEFI was more frequently reported in adjuvant vaccine recipients than in nonadjuvant vaccine recipients (10,14). However, we could not properly compare the AEFI rates between the vaccine types because the adjuvant and nonadjuvant vaccines were targeted to different priority groups. The Strategic Advisory Group of Experts advised that any licensed pandemic vaccine can be used to protect pregnant women regardless of the type of vaccine without specific contraindications (12,15). In the present study, we identified 82,551 pregnant recipients and 17 AEFI (7 systemic reactions, 7 neurologic reactions, 2 gastrointestinal reactions, and 1 local reaction) among them; there were no SAEs associated with the vaccination.

Most of the reported AEFI were nonspecific reactions, such as headache, fever, and myalgia, regardless of the recipient's age and vaccine type. These results are similar to a clinical study that was conducted in Italy (16) but differ from the results of other studies (1,3,16,17). The onset of AEFI was reported to usually occur within 24 h after the vaccination in this study, which is consistent with the findings of studies following pandemic monovalent or seasonal trivalent vaccines (18). SAEs, which are defined as hospitalizations after vaccinations, accounted for 7% of all AEFI and 0.0001% of the total vaccine recipients. The majority of SAEs were not fatal. However, people tended to be admitted to the hospital even with mild nonspecific symptoms. Among the neurologic SAEs, nonspecific peripheral neuropathy was the most common type, with a rate of 0.5 per 100,000 immunizations. However, it was difficult to diagnose certain neurologic diseases, such as vaccine-related peripheral neuritis. These diseases had different clinical aspects than the Guillain-Barré syndrome and showed improvement within 2 or 3 days in most cases. Their prognoses were benign. Guillain-Barré syndrome is a critical issue in aspects of vaccine vigilance that are relevant to the safety of vaccinations, even though its causal relationship with the influenza vaccination is still controversial (19,20). The reporting rate of the syndrome is known to be 0.8 to 1.9 per 1,000,000 vaccinations (7). In this study, 2 cases of Guillain-Barré syndrome were identified by the passive surveillance system with the nonadjuvant vaccine, and they met the Brighton Collaboration Criteria Level 2 or 3 (21).

Our study did not directly observe the efficacy of the influenza A (H1N1) 2009 vaccine in Korea. A previous clinical trial reported excellent immunogenic results for it. Although the immunogenicity was moderately different between children, adolescents, and younger (18–64 years) and older (65 years or older) adults, seroprotection and seroconversion rates were significantly greater than the criteria set by the E.U. Committee for Medicinal Products for Human Use and the US Food and Drug Administration for all age groups (17,22). Another case-control study reported that the influenza A (H1N1) 2009 vaccine was substantially protective against pandemic influenza in Korea during the 2009–2010 season. The overall vaccine efficacy was estimated at 73.4% with a 95% confidence interval of 49.1–86.1% (23). Taken together, these previous studies and our current findings support that the influenza A (H1N1) 2009 monovalent vaccine was safe and efficient.

The goal of this study was to determine the AEFI and safety of the novel influenza A (H1N1) 2009 vaccine by analyzing data from the passive surveillance system and the national immunization registry system of South Korea. These systems include the entire Korean population who were vaccinated. However, we could not establish a causal relationship due to the limitations of the passive surveillance system. Another limitation is that

we could not properly compare AEFI between the adjuvant and nonadjuvant vaccines because they were recommended for different vaccination priority groups. In addition, we were unable to compare the AEFI reporting rate between influenza A (H1N1) 2009 and previous seasonal influenza vaccinations because the national immunization registry system for the seasonal influenza vaccination was started only very recently.

This study found that the AEFI reporting rate after influenza A (H1N1) 2009 vaccination was relatively high, especially in the younger population. Mild systemic reactions accounted for the majority of reported AEFI, and fatal SAEs were rare. In addition, this study implied that a passive surveillance system may be an efficient and fast safety monitoring system for mass vaccination programs because it can detect relatively rare AEFI.

Acknowledgments This study was reviewed and approved by the Institutional Review Board at Severance Hospital, Yonsei University Health System, Seoul, Korea.

We wish to thank Moranhee Kim, administrative assistant, who provided information on the AEFI data and Dong-Wook Kim who helped with the extraction of data from the Immunization Registry System.

Conflict of interest None to declare.

REFERENCES

1. Vellozzi, C., Broder, K.R., Haber, P., et al. (2010): Adverse events following influenza A (H1N1) 2009 monovalent vaccines reported to the Vaccine Adverse Event Reporting System, United States, October 1, 2009–January 31, 2010. Vaccine, 28, 7248–7255.
2. Greenberg, M.E., Lai, M.H., Hartel, G.F., et al. (2009): Response to a monovalent 2009 influenza A (H1N1) vaccine. N. Engl. J. Med., 361, 2405–2413.
3. Clark, T.W., Pareek, M., Hoschler, K., et al. (2009): Trial of 2009 influenza A (H1N1) monovalent MF59-adjuvanted vaccine. N. Engl. J. Med., 361, 2424–2435.
4. Zhu, F., Wang, H., Fang, H., et al. (2009): A novel influenza A (H1N1) vaccine in various age groups. N. Engl. J. Med., 361, 2414–2423.
5. Varricchio, F., Iskander, J., Destefano, F., et al. (2004): Understanding vaccine safety information from the Vaccine Adverse Event Reporting System. Pediatr. Infect. Dis. J., 23, 287–294.
6. Vellozzi, C., Burwen, D.R., Dobardzic, A., et al. (2009): Safety of trivalent inactivated influenza vaccines in adults: background for pandemic influenza vaccine safety monitoring. Vaccine, 27, 2114–2120.
7. Haber, P., DeStefano, F., Angulo, F.J., et al. (2004): Guillain-Barré syndrome following influenza vaccination. JAMA, 292, 2478–2481.
8. Kwon, Y., Cho, H., Lee, Y., et al. (2010): Relationship between intention of novel influenza A (H1N1) vaccination and vaccination coverage rate. Vaccine, 29, 161–165.
9. Collet, J.-P., MacDonald, N., Cashman, N., et al. (2000): Monitoring signals for vaccine safety the assessment of individual adverse event reports by an expert advisory committee. Bull. World Health Organ., 78, 178–185.
10. Folkenberg, M., Callréus, T., Svanström, H., et al. (2011): Spontaneous reporting of adverse events following immunisation against pandemic influenza in Denmark November 2009-March 2010. Vaccine, 29, 1180–1184.
11. Mayet, A., Ligier, C., Gache, K., et al. (2011): Adverse events following pandemic influenza vaccine Pandemrix® reported in the French military forces—2009–2010. Vaccine, 29, 2576–2581.
12. Chlibek, R., Anca, I., Andr, F., et al. (2010): Central European Vaccination Advisory Group (CEVAG) guidance statement on recommendations for 2009 pandemic influenza A (H1N1) vaccination. Vaccine, 28, 3758–3766.
13. Carvajal, A., Ortega, P.G., Sinz, M., et al. (2011): Adverse events associated with pandemic influenza vaccines: comparison of the results of a follow-up study with those coming from spontaneous reporting. Vaccine, 29, 519–522.
14. Pellegrini, M., Nicolay, U., Lindert, K., et al. (2009): MF59-adjuvanted versus non-adjuvanted influenza vaccines: integrated analysis from a large safety database. Vaccine, 27, 6959–6965.
15. World Health Organization (2009): Strategic Advisory Group of Experts on Immunization—report of the extraordinary meeting on the influenza A (H1N1) 2009 pandemic, 7 July 2009. Wkly. Epidemiol. Rec., 84, 301–304.
16. Parretta, E., Ianniello, B., Ferrazin, F., et al. (2011): Italian post-marketing surveillance for adverse event reports after MF59-adjuvanted H1N1v vaccination. Vaccine, 29, 3708–3713.
17. Cheong, H.J., Song, J.Y., Heo, J.Y., et al. (2011): Immunogenicity and safety of influenza A (H1N1) 2009 monovalent inactivated split vaccine in Korea. Vaccine, 29, 523–527.
18. Centers for Disease, Control and Prevention (2009): Safety of influenza A (H1N1) 2009 monovalent vaccines—United States, October 1–November 24, 2009. Morb. Mortal. Wkly. Rep., 58, 1351–1356.
19. Lasky, T., Terracciano, G.J., Magder, L., et al. (1998): The Guillain-Barré syndrome and the 1992–1993 and 1993–1994 influenza vaccines. N. Engl. J. Med., 339, 1797–1802.
20. Burwen, D.R., Ball, R., Bryan, W., et al. (2010): Evaluation of Guillain-Barré syndrome among recipients of influenza vaccine in 2000 and 2001. Am. J. Prev. Med., 39, 296–304.
21. Choe, Y.J., Cho, H., Bae, G.R., et al. (2011): Guillain-Barré syndrome following receipt of influenza A (H1N1) 2009 monovalent vaccine in Korea with an emphasis on Brighton Collaboration case definition. Vaccine, 29, 2066–2070.
22. Oh, C., Lee, J., Kang, J., et al. (2010): Safety and immunogenicity of an inactivated split-virus influenza A/H1N1 vaccine in healthy children from 6 months to <18 years of age: a prospective, open-label, multi-center trial. Vaccine, 28, 5857–5863.
23. Song, J.Y., Cheong, H.J., Heo, J.Y., et al. (2011): Effectiveness of the pandemic influenza A/H1N1 2009 monovalent vaccine in Korea. Vaccine, 29, 1395–1398.