Jpn. J. Infect. Dis., 66, 290-294, 2013

Original Article

Epidemiological Features and Surveillance Performance of Measles in the Republic of Korea, 2002–2011

Young June Choe[1]*, Young-Joon Park[1], Hye Suk Eom[1],
Eun Seong Kim[1], Geun-Ryang Bae[1], and Jong-Koo Lee[2,3]

[1]*Division of Vaccine Preventable Disease Control and National Immunization Program, Korea Centers for Disease Control and Prevention, Osong;*
[2]*Department of Health Policy and Management and Department of Family Medicine, Seoul National University College of Medicine; and*
[3]*Policy and Development, Seoul National University Hospital, Seoul, Republic of Korea*

(Received November 9, 2012. Accepted April 10, 2013)

SUMMARY: Measles was declared eliminated from the Republic of Korea in 2006; however, recently the number of reported cases has been gradually increasing. To address this issue, we summarized the measles surveillance data collected during 2002–2011, and aimed to evaluate the performance of the current surveillance system in Korea. We analyzed data from the national surveillance system to describe the occurrence of measles. Surveillance indicators proposed by the World Health Organization were used to evaluate the performance of the current measles surveillance system. Between 2002 and 2005, a gradual decrease in confirmed cases of measles was noted, whereas cyclical increases were noted from 2006 to 2011. Since 2006, confirmed cases of measles were more likely to be identified by laboratory methods. In general, the incidence of confirmed case was less than one per million in Korea; however, this figure increased in 2002 (1.3/million), 2007 (4.0), and 2010 (2.3). Most cases were occurred in the age groups 0–23 months and 12–17 years. Laboratory testing was performed in most suspected cases; however, the proportion of discarded cases was low. Overall, more than half of the reported cases experienced an onset of symptoms from April to June. The incidence of measles is relatively low in Korea, and the laboratory surveillance may have helped in identifying under-diagnosed cases within the country. It remains important to continuously assess the surveillance data to improve the surveillance performance.

INTRODUCTION

Surveillance is one of the most important public health measures for the control and elimination of measles, and it provides information that allows identification of trends in the incidence of measles and facilitates rapid detection of outbreaks. Therefore, routine monitoring of measles is critical to the control or elimination of measles and for guiding decisions regarding appropriate public health policies.

Till date, countries and regions that have attempted to eliminate measles are facing unexpected outbreaks and importation-related cases of the infection (1,2). The change in epidemiological features following a reduction in the incidence of measles should be considered when operating a traditional surveillance system (3). However, little is known regarding the basic epidemiological characteristics in countries that have successfully eliminated measles outbreaks. Therefore, comprehensive descriptions of epidemiological features and evaluation of surveillance outcomes would aid in the improvement of measles surveillance systems.

In the Republic of Korea, following the implementation of the 5 Year National Measles Elimination Program, which included supplementary immunization programs, measles was declared eliminated from the country in 2006 (4). Since then, immunization against measles has been strengthened by the administration of two vaccine-doses at 12–15 months and 4–6 years of age by both private and public health sectors. However, the disease is still common throughout the world, including neighboring countries in the Western Pacific Region of the World Health Organization (WHO) (5). Therefore, comprehensive surveillance data, including epidemiological features, can provide guidance to public health policies at the national level to promote preventative measures designed to control and eliminate the occurrence of measles. In this study, we used the 2002–2011 measles surveillance data to identify and describe basic epidemiological features of measles and to evaluate the performance of the current surveillance system in Korea.

MATERIALS AND METHODS

Background: In Korea, a routine measles surveillance program was established in 1995 and involved passive reporting of clinically diagnosed cases. Following a nationwide measles outbreak, case-based surveillance with laboratory confirmation was introduced in 2001, in

*Corresponding author: Mailing address: Division of VPD Control and NIP, Korea Centers for Disease Control and Prevention, Osong Health Technology Administration Complex, 187 Osongsaengmyeong2(i)-ro, Gangoe-myon, Cheongwon-gun, Chungcheongbuk-do, 363-951, Korea. Tel: 82-43-719-7348, Fax: 82-43-719-7379, E-mail: choeyj@yahoo.com

which patients with fever, measles-like rash, and either cough, coryza, or conjunctivitis was reported as a suspected case of measles. Since then, the collection of serum and throat swab specimens from suspected cases was emphasized. Subsequently, in 2006, an active laboratory-based surveillance program was established, which involved sentinel laboratories that received and tested serum samples for measles-specific IgM to directly notify the Korea Centers for Disease Control and Prevention (KCDC).

Laboratory methods: Measles-specific antibodies were evaluated at two different levels, i.e., local public health laboratories and Environment and Division of Respiratory Viruses of the KCDC using an identical method with an enzyme-linked immunosorbent assay for IgM and IgG (EIA; Siemens Healthcare Diagnostics Inc., Erlangen, Germany). Blood specimens were obtained ≤72 h after the onset of rash from suspected cases, and for those who were negative for IgM, a second blood specimen was collected for confirmation. Throat swab samples were frozen at −70°C until shipment for testing using reverse transcription polymerase chain reaction (RT-PCR) and virus isolation. RT-PCR was used to amplify 450 base pairs coding for the -COOH terminus of the N gene, and all sequences that were amplified were analyzed to prevent laboratory cross-contamination.

Data collection and analysis: We analyzed data collected by the KCDC from 2002 to 2011 to evaluate the performance of measles surveillance in Korea. Suspected measles cases were stratified using WHO criteria which included the following: (i) clinically-compatible, defined as a case that meets the clinical case definition (fever, rash, and either cough, coryza, or conjunctivitis) and for which no adequate blood specimen was obtained; (ii) epidemiologically-linked, defined as a case that meets the clinical case definition and was linked to a laboratory-confirmed case; and (iii) laboratory-confirmed, defined as a case that meets the clinical case definition and was laboratory-confirmed (serum measles-specific IgM or virological confirmation) (6). The incidence of cases of measles was calculated on the basis of the 2005 population statistics obtained from Statistics Korea (7).

Subsequently, we analyzed the surveillance data and case reports to evaluate the performance of the surveillance system. The transmission source was identified using in-depth epidemiological investigation data. A cluster-related case was defined as a patient with measles who had contact with another patient with measles during 7–18 days before the onset of the rash (i.e., epidemiological-linkage, according to the WHO definition). An importation-related case was defined as a patient with measles who was outside of Korea for 7–18 days before the onset of rash, cases with virological evidence of importation, or cases that had contact with another importation-related case. The cases that were not cluster-related or importation-related were classified as cases with an ''unknown-source of transmission''.

To determine the performance of measles surveillance in South Korea, we selected the following five performance indicators proposed by the WHO (6): (i) the proportion of discarded cases per 100,000 people; (ii) the proportion of cases adequately investigated within 48 h of the report; (iii) the proportion of laboratory test performed in reported cases, (iv) the proportion of cases with an adequate blood specimen (collected within 28 days onset of rash), and (v) the proportion of specimens with results given within 7 days of receipt. Data from virological surveillance conducted by the KCDC during the surveillance period were used. To evaluate performance indicators, the analysis only considered data from 2007 onward because data for previous surveillance years were not collected. We defined a timely reporting of measles as an interval within 7 days from diagnosis to reporting the case to the KCDC. To reduce the risk of bias, cluster-related cases, which may have had a greater opportunity for early identification because of active surveillance measures, were excluded from this subgroup analysis.

Ethical approval: Ethical approval is not required by our institution for investigations of surveillance data.

RESULTS

During the surveillance period, 1,506 suspected case of measles were reported to the KCDC, of which 510 were assessed as clinically-compatible, epidemiologically-linked, or laboratory-confirmed cases. There were no significant differences in demographics among those with clinically-compatible, epidemiologically-linked, or laboratory-confirmed measles, and all were treated as a single group of confirmed case of measles.

Between 2002 and 2005, a gradual decrease in confirmed cases of measles was observed, whereas cyclical increases were noted from 2006 to 2011 (Fig. 1). Since 2006, confirmed cases of measles were more likely to be identified by laboratory methods. Only a minority of epidemiologically-linked cases were identified in 2006 and 2010. During the surveillance period, the incidence of confirmed cases were generally less than one per million; however, this incidence rate exceeded in 2002 (1.3/million), 2007 (4.0), and 2010 (2.3) (line-graph in Fig. 1).

The 2006 outbreak occurred in a preschool in Incheon, in which 15 cases were confirmed out of 152 exposed children. The second outbreak occurred during 2007, when multiple transmission chains of measles were mainly identified in hospital settings. Among 180 cases confirmed as measles, 81 (45%) were acquired via nosocomial transmission in 6 hospitals, mainly located in Seoul and the surrounding metropolitan area. A school outbreak in Incheon that occurred in 2010, involved 127 suspected cases out of 878 exposed students, which mostly affected inadequately vaccinated students. In 2011, Gyeongnam province reported multiple transmissions of measles in hospitals and preschools, resulting in 32 confirmed cases of measles.

Approximately two-thirds of the confirmed measles cases occurred in children <59 months old, 37% were female, and half were cluster-related (Table 1). In 2010, an outbreak occurred in an all-male junior high school, which affected 108 students; however, these students contributed to the disproportion in sex and age groups. More than 90% of cases during 2002–2004 had an unknown source of transmission; however, the source of transmission is identified in recent cases.

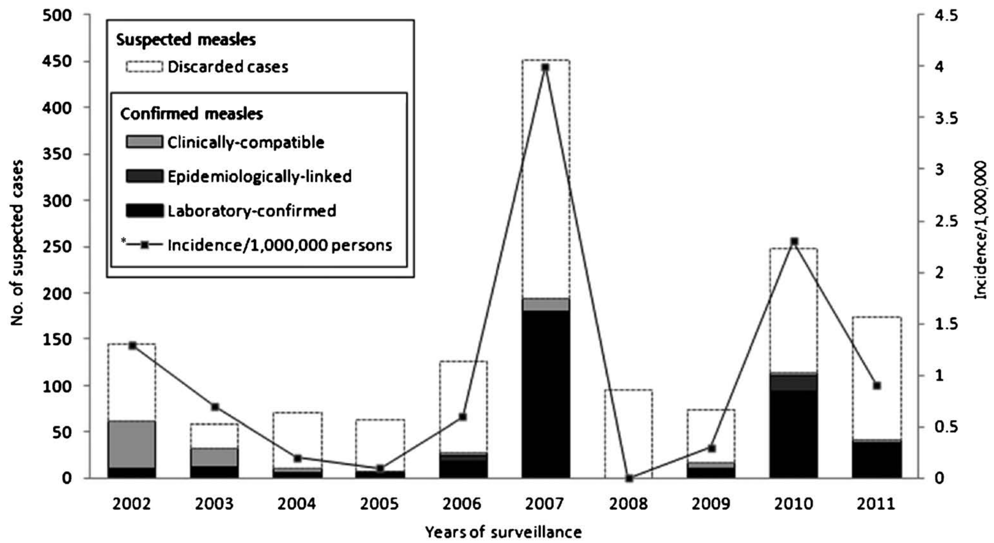

Fig. 1. Summary of measles surveillance results, Republic of Korea, 2002–2011.
*Crude incidence per 1,000,000 inhabitants.

Table 1. Demographic and epidemiologic characteristics of confirmed measles cases, by surveillance year, Republic of Korea, 2002–2011

Characteristic	Year of surveillance										Total No. (%)
	2002 No. (%)	2003 No. (%)	2004 No. (%)	2005 No. (%)	2006 No. (%)	2007 No. (%)	2008 No. (%)	2009 No. (%)	2010 No. (%)	2011 No. (%)	
Confirmed measles	62	33	11	7	28	194	2	17	114	42	510
Sex											
M	42 (68)	17 (52)	4 (36)	5 (71)	10 (36)	101 (52)	1 (50)	10 (59)	104 (91)	26 (62)	320 (63)
F	20 (32)	16 (48)	7 (64)	2 (29)	18 (64)	93 (48)	1 (50)	7 (41)	10 (9)	16 (38)	190 (37)
Age group											
< 12 mo	16 (26)	4 (12)	5 (45)	0 (0)	3 (11)	77 (40)	0 (0)	2 (12)	2 (2)	11 (26)	120 (24)
12–23 mo	20 (32)	9 (27)	3 (27)	2 (29)	5 (18)	68 (35)	0 (0)	5 (29)	10 (9)	10 (24)	132 (26)
24–59 mo	8 (13)	6 (18)	2 (18)	1 (14)	15 (54)	26 (13)	0 (0)	2 (12)	5 (4)	6 (14)	71 (14)
6–11 yr	7 (11)	9 (27)	1 (9)	2 (29)	2 (7)	5 (3)	1 (50)	3 (18)	0 (0)	4 (10)	34 (7)
12–17 yr	5 (8)	2 (6)	0 (0)	1 (14)	2 (7)	2 (1)	1 (50)	1 (6)	94 (82)	1 (2)	109 (21)
18–49 yr	6 (10)	3 (9)	0 (0)	1 (14)	1 (4)	16 (8)	0 (0)	4 (24)	3 (3)	10 (24)	44 (9)
Source of transmission											
Cluster-related	0 (0)	0 (0)	0 (0)	0 (0)	22 (79)	92 (47)	0 (0)	0 (0)	108 (95)	24 (57)	246 (48)
Importation-related	1 (2)	2 (6)	1 (9)	1 (14)	4 (14)	2 (1)	1 (50)	1 (6)	1 (1)	10 (24)	24 (5)
Unknown-source	61 (98)	31 (94)	10 (91)	6 (86)	2 (7)	100 (52)	1 (50)	16 (94)	5 (4)	8 (19)	240 (47)

Confirmed cases were noted in both children and adolescents with the highest incidences in the age groups 0–23 months and 12–17 years. Those aged between 6 and 11 years had the lowest proportion of laboratory confirmed cases (44%), followed by those aged 24–59 months (63%) and 12–23 months (76%). Overall, more than half of the cases (66%) were reported to experience an onset of symptoms from April to June (Fig. 2).

Table 2 shows the analytical results of selected surveillance performance indicators from 2007 to 2011. During the surveillance period, less than one case per 100,000 people was discarded. The proportion of adequately investigated cases increased from 29% in 2007 to 73% in 2011. Across all surveillance years, laboratory tests were performed in most suspected cases and more than 80% had their blood specimens tested, the results of which were given in a timely manner (Table 2). Among the isolated viruses, D5 was identified in 2003, 2004, and 2007; H1 was identified in 2006, 2007, 2009, and 2010; and D9 was identified in 2011. After excluding cluster-related cases, which may have been more likely to be identified earlier because of active surveillance measures, recently identified cases were more likely to be notified faster compared with cases of early 2000's.

DISCUSSION

In Korea, from 2002 to 2011, the national estimated incidence of measles was low (0–4.0 per 1,000,000 people). These data suggested that although the incidence was low, measles remained a potential threat to public health in Korea and that the occurrence of outbreaks may pose reintroduction of endemic transmission of the virus. There was no significant change in the overall age-specific annual incidence, although there were spikes in 2006, 2007, 2010, and 2011, due to cluster-related cases. The increase in incidence was mainly a

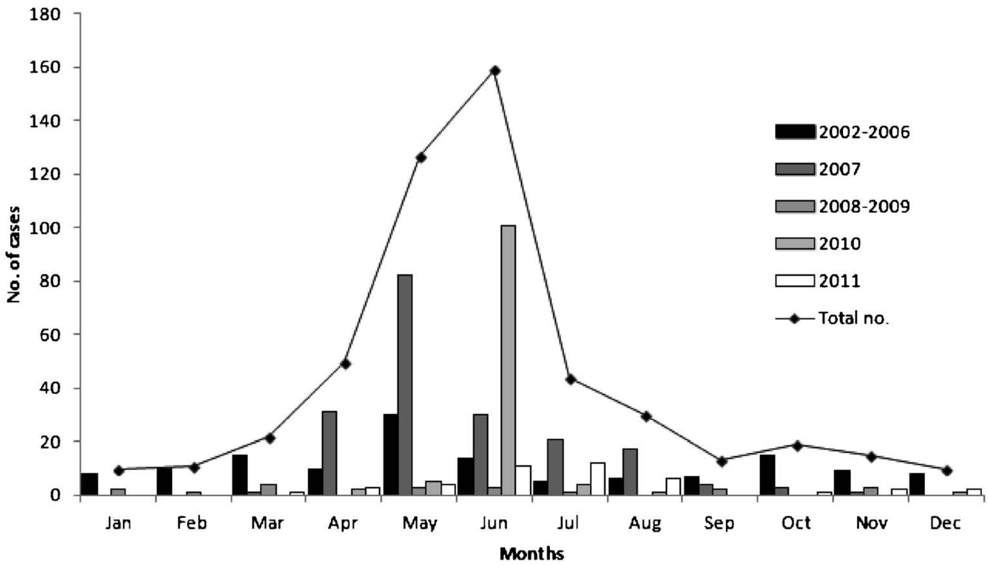

Fig. 2. Reported measles cases by month of disease onset and transmission status, Republic of Korea, 2002–2011.

Table 2. Selected performance indicators of measles surveillance in the Republic of Korea, 2007–2011

Parameter, no. (%)	Year of surveillance					Total No. (%)
	2007 No. (%)	2008 No. (%)	2009 No. (%)	2010 No. (%)	2011 No. (%)	
Suspected case	451	96	74	248	174	1,043
Discarded case/100,000 population	0.5	0.2	0.1	0.3	0.3	0.2
Case with adequate investigation	131 (29)	48 (50)	36 (49)	154 (62)	127 (73)	496 (48)
Laboratory test performed in reported case	421 (93)	83 (86)	65 (88)	211 (85)	163 (94)	943 (90)
Case with adequate blood specimen	382 (85)	81 (84)	63 (85)	210 (85)	147 (84)	883 (85)
Specimen with result within 7 days of receipt	421 (93)	82 (85)	63 (85)	207 (83)	160 (92)	933 (89)

result of the occurrence of measles outbreaks.

Among 15 preschoolers who were affected in the 2006 outbreak, 14 had an inadequate vaccination status, and measles affected 100% of children with no vaccination history (8). Among 180 confirmed cases of measles in the 2007 outbreak, 81 (45%) had originated from nosocomial transmissions in 6 hospitals, mainly located in Seoul and the surrounding metropolitan area (9). More importantly, 124 (69%) cases had no history of measles, mumps, and rubella vaccination. Molecular analysis of measles viruses from 11 cases diagnosed during the 2011 outbreak in Gyeongnam Province revealed the same D9 genotype, which was the first to be discovered in the country and was prevalent in neighboring Asian countries (10,11).

In addition, we determined that although the performance indicators for laboratory surveillance were acceptable in Korea, less than one cases per 100,000 people was recorded, which was lower than expected. This finding may implicate inadequate sensitivity of the current surveillance system. Indeed, these results were similar to those of other low-incidence countries (12,13). In countries with a low incidence of measles, diagnosis and reporting of suspected cases remains a challenge (14,15). Therefore, laboratory confirmation has been emphasized to improve the measles surveillance system. However, our findings suggested that even with significant attempts to confirm samples by laboratory measures in Korea, the overall sensitivity was lower than expected.

A proper diagnosis of suspected cases tends to be more difficult because recently trained physicians are less likely to encounter patients with measles during their training periods. However, measles should be considered when encountering a patient with fever and rash. The current Korean measles surveillance system defines a suspected case as an illness characterized by the presence of morbilliform rash, fever $>38.0°C$, and either cough, coryza, or conjunctivitis. However, we suspect that this original case definition is less sensitive to identify all cases of measles present in the country. Therefore, a more sensitive measles definition is required to better identify suspected cases within the country.

There were 3 measles virus genotypes introduced in Korea throughout the surveillance period. The change in the predominant genotype from D5 to H1 during the mid-2000s resulted in an increased incidence of mesles cases. In China, genotype H1 was predominant during 1991–2008 (16) and was also in the early 2000s in Japan (17). Further investigations comparing full genome sequences will be required to explore the association between viruses circulating between neighboring countries.

Our findings had several potential limitations. First, because surveillance data are subject to under-reporting and misdiagnosis, not every case of measles was reported to the KCDC, and some that were reported were reclassified. Second, because we did not obtain the immunization status for the majority of suspected cases, our data should be carefully interpreted. Third, small number of suspected measles cases in our surveillance data made it difficult to readily extrapolate our findings to other countries.

Despite these limitations, we believe that the present surveillance data may aid in elucidating the epidemiology of measles in a low-incidence setting. Moreover, our findings will add to the baseline data for future strategies to contain measles outbreaks in Korea. By making our surveillance data publicly available, we aimed to compare our surveillance data with those of other countries in the hope that this may lead to better understanding of the trend of measles spread in countries with a low-incidence of the virus. Recently, some countries have provided their national surveillance data; however, most were from countries with mid- or high-incidence rates of measles. In addition, differences in obtaining data from other countries should be taken into account.

In the present study, we aimed to identify and describe basic epidemiological features of measles cases and to evaluate the performance of the current surveillance system in Korea. Our review of measles epidemiology in Korea indicated that the incidence was low and that laboratory surveillance may have helped in identifying under-diagnosed cases from the country. However, it remains important to continuously asses the performance of a surveillance system to identify more cases in a timely manner. The epidemiological features of measles described in this study may provide guidance for the future public health measures in Korea and its neighboring countries.

Conflict of interest None to declare.

REFERENCES

1. Muscat, M., Christiansen, A.H., Böttiger, B.E., et al. (2008): A cluster of measles cases in Denmark following importation, January and February 2008. Euro Surveill., 13(9): pii = 8050.
2. Parker, A.A., Staggs, W., Dayan, G.H., et al. (2006): Implications of a 2005 measles outbreak in Indiana for sustained elimination of measles in the United States. N. Engl. J. Med., 355, 447–455.
3. Guris, D., Harpaz, R., Redd, S.B., et al. (2004): Measles surveillance in the United States: an overview. J. Infect. Dis., 189 (Suppl. 1), S177–184.
4. Centers for Diseases Control and Prevention (2007): Elimination of measles—South Korea, 2001–2006. Morbid. Mortal. Wkly. Rep., 56, 304–307.
5. Sniadack, D.H., Mendoza-Aldana, J., Jee, Y., et al. (2011): Progress and challenges for measles elimination by 2012 in the Western Pacific Region. J. Infect. Dis., 204 (Suppl. 1), S439–446.
6. World Health Organization (2003): WHO-Recommended Standards for Surveillance of Selected Vaccine-Preventable Diseases. WHO/V&B/03.01. WHO, Geneva, Switzerland.
7. Statistics Korea. Korean Statistical Information Service: Online at <http://kostat.go.kr/portal/english/index.action>. Accessed 7 August 2012.
8. So, J.S., Go, U.Y., Lee, D.H., et al. (2008): Epidemiological investigation of a measles outbreak in a preschool in Incheon, Korea, 2006. J. Prev. Med. Public Health, 41, 153–158.
9. Choi, W.S., Sniadack, D.H., Jee, Y., et al. (2007): Outbreak of measles in the Republic of Korea, 2007: importance of nosocomial transmission. J. Infect. Dis., 204 (Suppl. 1), S483–490.
10. Pattamadilok, S., Incomserb, P., Primsirikunawut, A., et al. (2012): Genetic characterization of measles viruses that circulated in Thailand from 1998 to 2008. J. Med. Virol., 84, 804–813.
11. Aoki, Y., Mizuta, K., Suto, A., et al. (2009): Importation of the evolving measles virus genotype D9 to Yamagata, Japan from Thailand in 2009. Jpn. J. Infect. Dis., 62, 481–482.
12. Tikhonova, N.T., Bichurina, M.A., Gerasimova, A.G., et al. (2011): Enhanced surveillance for measles in low-incidence territories of the Russian Federation: defining a rate for suspected case investigation. Epidemiol. Infect., 139, 239–246.
13. Papania, M.J. and Strebel, P.M. (2005): Measles surveillance: the importance of finding the tip of the iceberg. Lancet, 365, 100–101.
14. van Isterdael, C.E., van Essen, G.A., Kuyvenhoven, M.M., et al. (2004): Measles incidence estimations based on the notification by general practitioners were suboptimal. J. Clin. Epidemiol., 57, 633–637.
15. Jayamaha, J., Binns, P.L., Fennell, M., et al. (2012): Laboratory diagnosis, molecular characteristics, epidemiological and clinical features of an outbreak of measles in a low incidence population in Australia. J. Clin. Virol., 54, 168–173.
16. Zhang, Y., Xu, S., Wang, H., et al. (2012): Single endemic genotype of measles virus continuously circulating in China for at least 16 years. PLoS One, 7, e34401.
17. Nagai, M., Xin, J.Y., Yoshida, N., et al. (2009): Modified adult measles in outbreaks in Japan, 2007–2008. J. Med. Virol., 81, 1094–1101.