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Importation of travel-related infectious diseases is increasing in South Korea: An analysis of salmonellosis, shigellosis, malaria, and dengue surveillance data

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ABSTRACT

Background: International travel has an important role in transmission of emerging infectious diseases. We described the imported infectious diseases in Korea from 2003 to 2012, and to analyze association of travels with the change in the incidences.

Methods: We used National Notifiable Disease Surveillance System to investigate the incidence of salmonellosis, shigellosis, malaria, and dengue. Data from Korea Tourism Organization was used to describe the inbound and outbound travelers by their age group, gender, and purpose of travel. We assessed association between international travel and the incidence of the infectious diseases, and seasonal variability.

Results: Among 1849 imported cases, dengue comprised the largest number with 631 cases. The proportion of imported cases among total cases gradually increased from 4.1% in 2003 to 30.3% in 2012 ($P < 0.001$). There was a positive correlation between the number of travelers and the number of imported cases of shigellosis, dengue ($P < 0.001$), but not for malaria. Seasonal variability was observed for importation of salmonellosis, shigellosis and dengue fever ($P = 0.005$).

Conclusion: International travel was associated with the incidence of imported infectious diseases in Korea. Pre-travel consultation for international travelers planned to visit endemic area should be recommended strongly.

1. Introduction

International travel has an important role in transmission of emerging and re-emerging infectious diseases across the geographical areas [1]. The travel-associated transmission of diseases was anticipated during the past decades. Since 1980s, meningococcal epidemic was transmitted globally after the Hajj pilgrimage [2]. In the early 2000s, severe acute respiratory syndrome rapidly spread around the world because travelers infected with the virus traveled on airplane to distant countries [3]. Moreover, importation of measles cases along air travel had caused an outbreak of the disease, which was once eliminated from the United States [4].

In spite of the major health issue to both sending and receiving countries, importation of infectious diseases had been a problem that is ignored in countries with growing economies including South Korea. International travel in Korea is a growing industry with over 10 million outbound travelers travel every year in the 2000s [5]. Destinations are in every continent including country with poorly developed, as well as those with an advanced hygiene and public health infrastructure.

Recently in Korea, there has been a concern in increased number of imported infectious diseases, including emerging infectious diseases such dengue [6]. The increase in international travel may have an association with an increase in the number of imported infectious diseases. However, the incidence of imported infectious diseases has not been reflected in surveillance programs as they largely fail to capture comprehensive epidemiological data. In this study, we aimed to describe the imported infectious diseases in Korea from 2003 to 2012, and to analyze association of international travels with change in incidence.

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2. Methods

2.1. Data source and definition

We used National Notifiable Disease Surveillance System (NNDSS), which collects passively reported data on clinically-diagnosed and laboratory-confirmed cases of the 75 designated infectious diseases. The monthly number of inbound and outbound travelers by their age group, gender, purpose of travel (for inbound travelers), and destination (for outbound travelers) was obtained from the Korea Tourism Organization [7]. An imported case was defined as infection acquired outside Korea, based on the travel history of individual case-patient and incubation period of infectious diseases. An endemic case was defined as infection acquired inside Korea within incubation periods for respective infectious diseases.

2.2. Data analysis

We selected four infectious diseases that are potentially importable to South Korea: salmonellosis, shigellosis, malaria, and dengue. We assessed the association of imported infectious diseases cases and international travelers using Spearman rank correlation test. The relation between seasonal variability and the monthly incidence of imported infectious diseases was examined. We then assessed the monthly proportion of imported cases among total cases including endemic transmissions.

To explore the linear trend and seasonality from 2003 to 2012, we used linear regression time-series analysis. The total numbers of inbound and outbound travelers, age group, gender, purpose of visit (for inbound travelers), and destination (for outbound travelers) were assessed. Multivariable regression analysis was used to adjust for the time-trend effect and seasonality. All analyses were performed using SPSS (SPSS Inc., USA) and using the R 3.0.2 statistical software. Because all the data used in this study is anonymous and publically available, this study was exempted from ethical consideration.

3. Results

3.1. General surveillance

Over the 10-year period from 2003 through 2012, we identified 1849 imported cases of salmonellosis, shigellosis, malaria, and dengue (Table 1). Among those, dengue comprised the largest number of cases with 631, followed by shigellosis (n = 482) and malaria (n = 407). The proportion of imported cases was highest in dengue (100%), followed by shigellosis (15.7%) and salmonellosis (15.3%). Overall during the 10-year period, the proportion of imported cases among total cases gradually increased from 4.1% in 2003 to 30.3% in 2012 (Table 1, $P < 0.001$ for trend). The proportion generally increased for salmonellosis (from 8.0% in 2003 to 27.8% in 2012, $P < 0.001$ fore trend) and shigellosis (from 0.6% to 46.7%, $P < 0.001$ for trend), while the proportion was relatively constant for malaria (from 5.2% to 9.7%, $P = 0.019$ for trend).

3.2. Secular trend and seasonality

From 2003 to 2012, the number of inbound travelers showed linear increase, while the number of outbound travelers increased from 2003 to 2007, with a decline during 2008–2009, and a rebound increase after 2010 (Fig. 1). The secular or long-term trend was characterized by a gradual increase in number of cases of imported infectious diseases from 2003 through 2012, with occasional decreases and rebounds in 2005 and 2010–2013. A cyclical pattern of occurrences of imported infectious diseases at interval of about 3–6 months was noted, with malaria being the major pathogen in the early 2000s, while dengue and shigellosis being the major pathogens in the late 2000s.

Estimation with linear regression model showed the best fit data of salmonellosis ($P = 0.007$), shigellosis ($P < 0.001$), and dengue ($P < 0.001$), while there was no significant linear trend was observed in the data of malaria (Fig. 2). Pearson correlation showed a positive correlation between the number of outbound and inbound travelers and the number of imported cases of shigellosis, dengue, and the total number of imported infectious diseases (Table 2, $P < 0.001$).

When classified by months, the proportion of imported cases of salmonellosis and shigellosis increases during summer season (July–September); while nearly half of malaria cases reported during winter season (January–February) are imported cases (Fig. 3). Throughout the year, all reported cases of dengue were imported cases, with the peak incidence during summer season. Variable seasonality was observed in the occurrence of imported salmonellosis, shigellosis and dengue fever ($P = 0.005$).

The upper curve in Fig. 4 shows the monthly number outbound travelers. There was a remarkable seasonal pattern, clustering during summer (July–August) and winter (January). Apparently, there was also an increase in the number of imported cases of dengue, malaria and shigellosis, during the summer and winter season. The shape of lower curve, which indicates the number of inbound international travelers, however, was dissimilar to the shape of the imported infectious diseases curve. Spearman rank correlation showed a correlation between monthly occurrence of

Table 1
Surveillance of imported infectious diseases in South Korea, 2003–2012.

Years	Salmonellosis**		Shigellosis**		Malaria		Dengue**		Total**	
	No.*	(%)	No.*	(%)	No.*	(%)	No.*	(%)	No.*	(%)
2003	21/262	(8.0)	6/996	(0.6)	61/1164	(5.2)	13/13	(100.0)	101/2435	(4.1)
2004	24/217	(11.1)	23/489	(4.7)	38/858	(4.4)	19/19	(100.0)	104/1583	(6.6)
2005	29/197	(14.7)	44/293	(15.0)	46/1360	(3.4)	29/29	(100.0)	148/1879	(7.9)
2006	42/235	(17.9)	20/299	(6.7)	28/1974	(1.4)	37/37	(100.0)	127/2545	(5.0)
2007	28/262	(10.7)	42/136	(30.9)	33/2205	(1.5)	94/94	(100.0)	197/2697	(7.3)
2008	20/228	(8.8)	60/196	(30.6)	29/1025	(2.8)	51/51	(100.0)	160/1500	(10.7)
2009	20/197	(10.2)	35/183	(19.1)	21/1298	(1.6)	58/58	(100.0)	134/1736	(7.7)
2010	34/173	(19.7)	102/220	(46.4)	49/1682	(2.9)	115/115	(100.0)	300/2190	(13.7)
2011	59/188	(31.4)	108/172	(62.8)	48/795	(6.0)	66/66	(100.0)	281/1221	(23.0)
2012	52/187	(27.8)	42/90	(46.7)	54/555	(9.7)	149/149	(100.0)	297/981	(30.3)
Total	329/2146	(15.3)	482/3074	(15.7)	407/12,916	(3.2)	631/631	(100.0)	1849/18,767	(9.9)

*No. in imported cases/total cases (imported + endemic cases).
**$P < 0.001$ for trend.

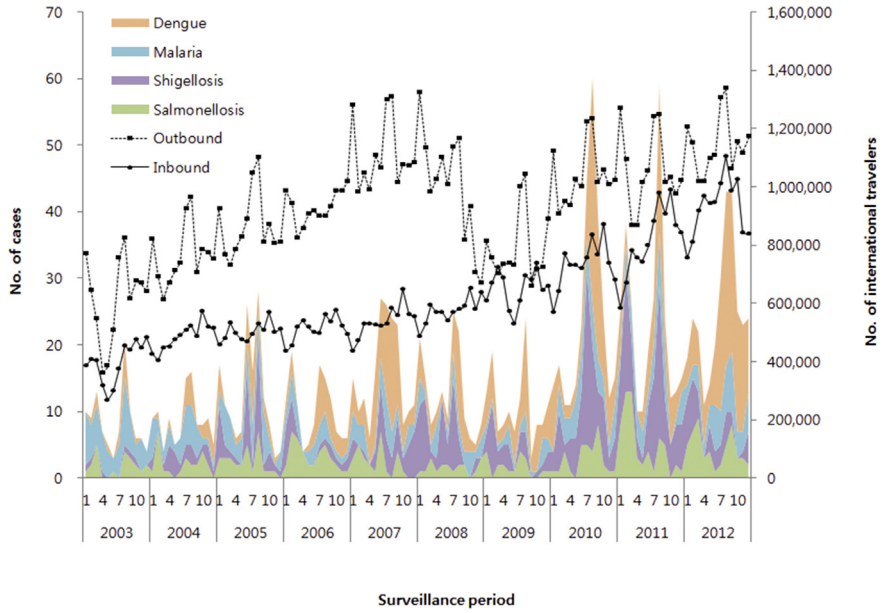

Fig. 1. Secular trend of imported infectious disease cases and the number of international travelers in South Korea, by months and surveillance years 2003–2012.

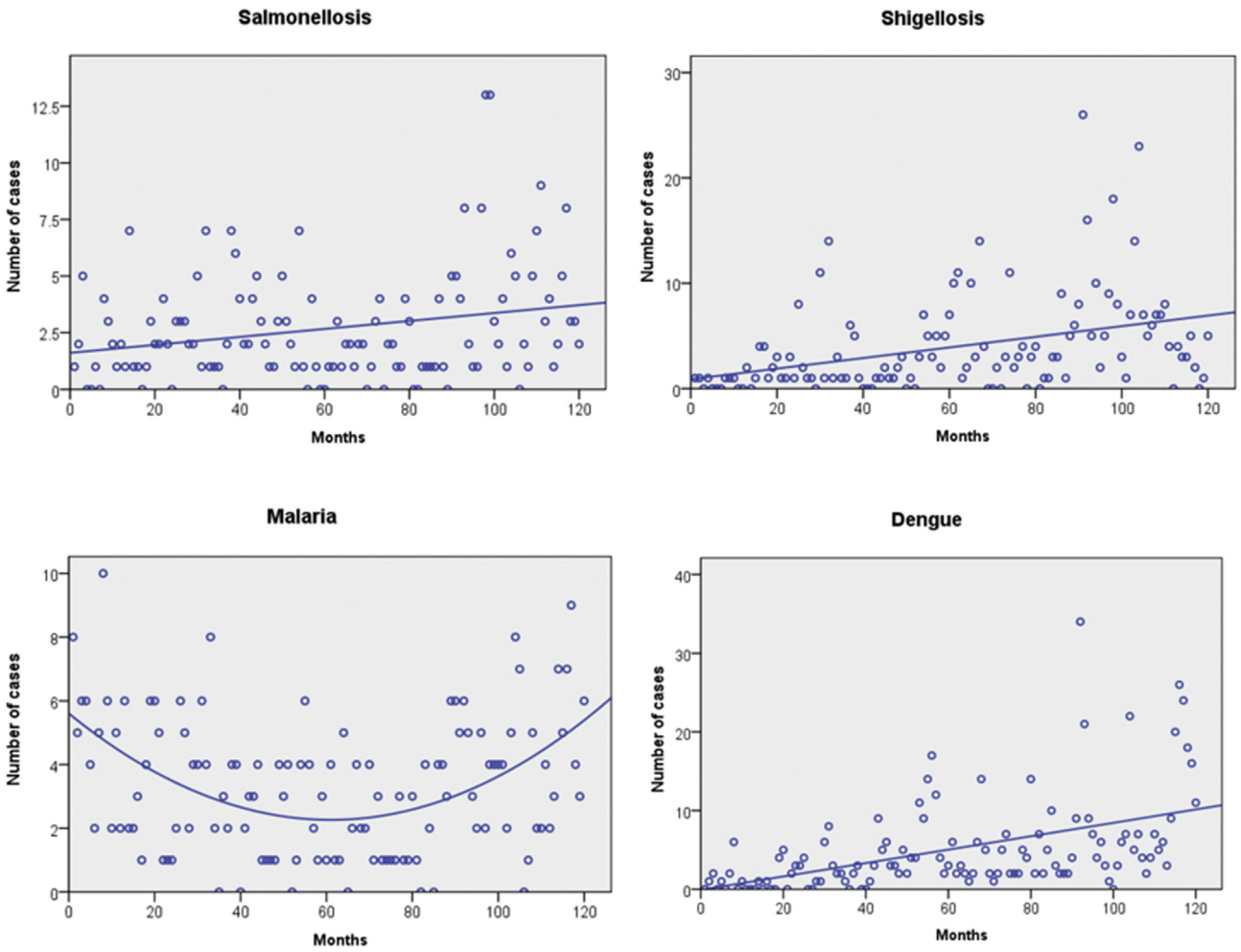

Fig. 2. Regression analysis of trend for imported infectious diseases, by months 2003–2012, South Korea. *Estimated trend equation were: salmonellosis, $y_t = 1.615 + 0.018t$ ($P = 0.007$); shigellosis, $y_t = 0.893 + 0.050t$ ($P < 0.001$); malaria, $y_t = 5.604–0.109t + 0.001t^2$ (F statistic = 14.699); and dengue, $y_t = -0.079 + 0.085t$ ($P < 0.001$).

Table 2
Correlation coefficients for imported infectious diseases and time, number of inbound and outbound travelers, South Korea 2003–2012.

Imported diseases*	Yearly secular trend		Monthly seasonal trend		Inbound travelers		Outbound travelers	
	r	*P*	rho	*P*	r	*P*	r	*P*
Salmonellosis	0.272	0.003	−0.269	0.003	0.242	0.008	0.226	0.013
Shigellosis	0.387	<0.001	0.164	0.073	0.328	<0.001	0.515	<0.001
Malaria	−0.012	0.898	−0.052	0.576	0.119	0.195	0.104	0.258
Dengue	0.482	<0.001	0.163	0.075	0.562	<0.001	0.604	<0.001
Total	0.501	<0.001	−0.121	0.188	0.54	<0.001	0.638	<0.001

*Pearson correlation was used for yearly secular trend, inbound travelers, and outbound travelers; Spearman rank correlation was used for monthly seasonal trend.

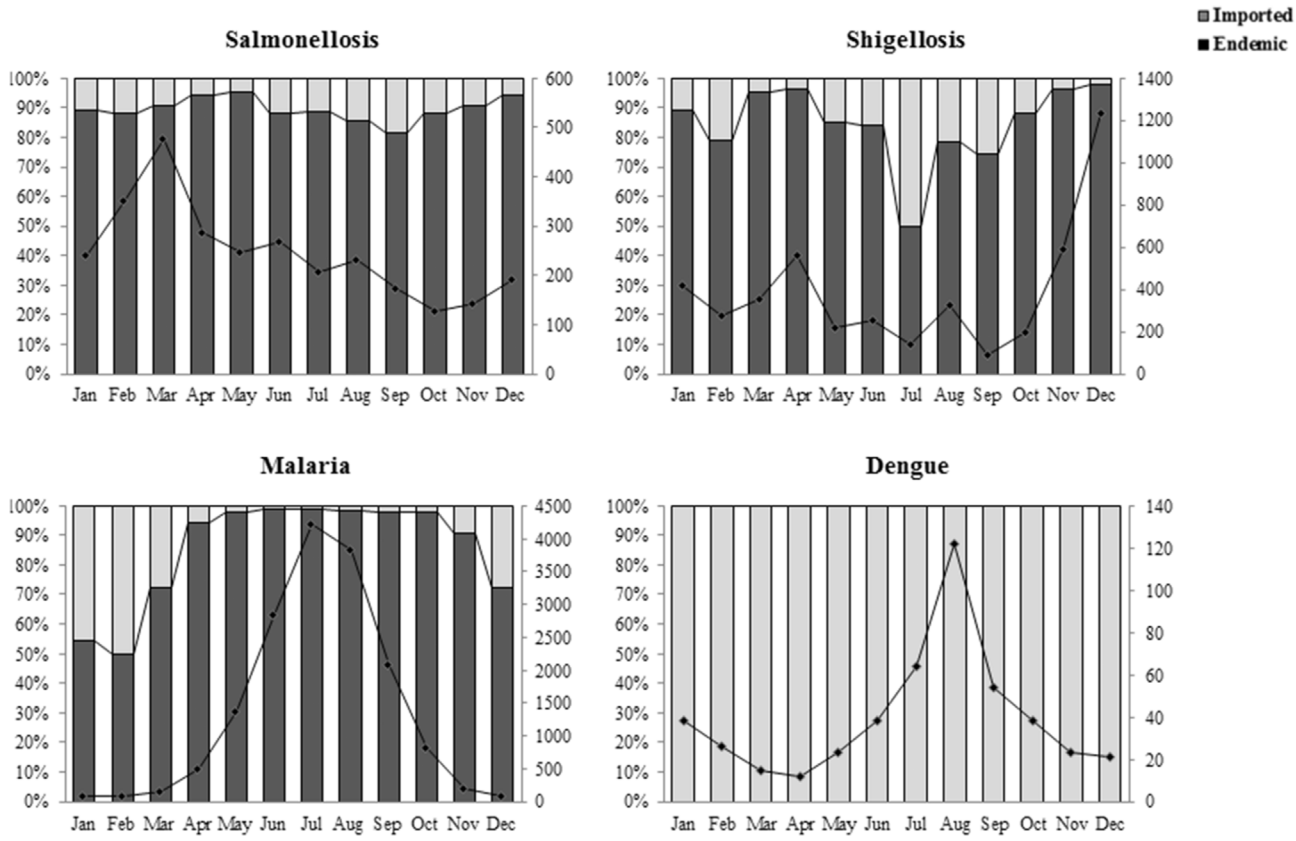

Fig. 3. Proportion of cases with imported infectious diseases by month, South Korea, 2003–2012. * Dark bar, proportion of endemic cases; light bar, proportion of imported cases; line graph, number of total cases; left axis, percentage; right axis, number of cases.

imported salmonellosis cases (−0.269, $P = 0.003$).

Linear regression time-series analysis revealed the potential association as follows: salmonellosis with the proportion of travelers aged 20s; shigellosis with the total number of inbound travelers and the proportion of travelers on purpose of tourism (Table 3). There was no association with given variables in related to inbound travels with the decreasing trend of malaria or increasing trend of dengue.

4. Discussion

In the past decade from 2003 through 2012, the increased number of international travelers was associated with an increase in the number of imported infectious diseases in Korea. We measured the overall incidence of importable infectious disease in Korea, which was found to range between 0.46 (cholera) and 35.60 (malaria) cases per 100,000 population per year. Although the incidence of endemic transmission decreased during the surveillance period, we observed a gradual increase in the proportion and absolute number of imported cases. Our findings are consistent with the pattern described in other countries with increased international travel volume, resulting in the emergence or reemergence of once disappeared infectious pathogens. There have been concerns about possible exchange of infectious diseases between continents mainly produced by the increased volume of international travels [8]. From 1997 through 2006, data on travel-related dengue analyzed by GeoSentinel Surveillance Network suggested an overall annual incidence from 50 to 159 cases per 1000 ill returned travelers [9]. A study conducted in Spain reported the incidence of imported cases of malaria from 2.4 cases per 100,000 in 1989 to 3.5 cases in 2005 [10]. During late 2000s, there was nearly 600% increase in the number of travelers returning from Africa to Romania and an associated increase in the number of imported malaria cases has been recently recognized [11]. In the United States with high immunization coverage, imported cases of measles represent an important continuing source of transmission [4].

In the past, food and water borne infectious disease such as

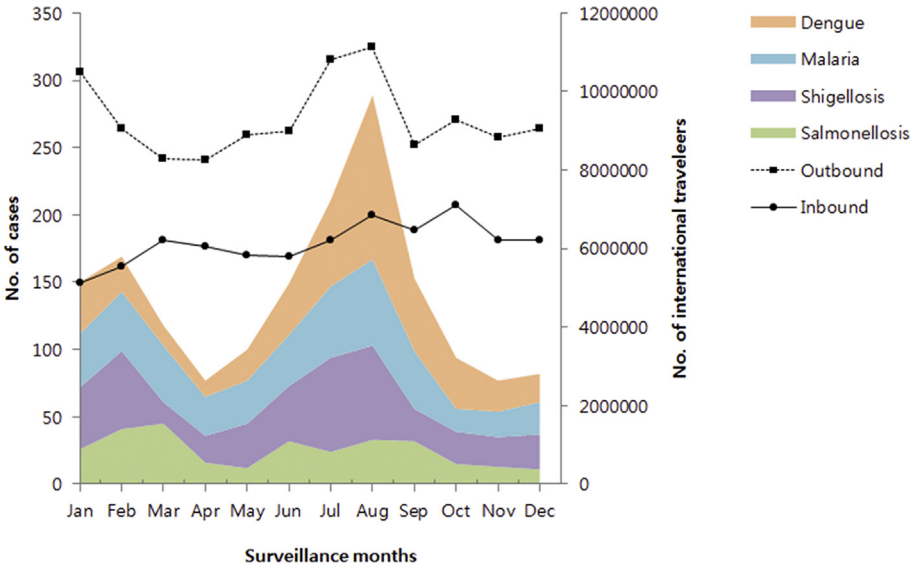

Fig. 4. Seasonal trend of number of cases with imported infectious diseases and number of international travelers, South Korea, 2003–2012.

Table 3
Linear regression time-series analysis on salmonellosis, shigellosis, malaria, and dengue, in association with the inbound travel-related parameters, South Korea 2003–2012.

Parameters	Salmonellosis		Shigellosis		Malaria		Dengue	
	Estimate (B)	SE	Estimate (B)	SE	Estimate (B)	SE	Estimate (B)	SE
Total no. of inbound travelers	4.708E-6	2.993E-6	2.420E-5*	8.472E-6	5.314E-6	3.667E-6	2.640E-5	9.369E-6
Male	7.563	12.196	12.259	34.517	17.083	14.939	13.917	38.172
On purpose of tourism	−11.636	6.487	−52.965*	18.360	1.878	7.946	−64.843	20.304
Age at 20s	18.883*	8.996	35.047	25.463	21.181	11.020	4.650	28.159

*$P < 0.05$.

cholera and typhoid fever were mainly recognized importable infectious diseases in non-endemic countries; while recently, vector borne disease such as dengue, malaria are increasingly recognized as diseases that crosses borders [12,13].

Cholera, typhoid fever, paratyphoid fever, and shigellosis had been recognized as endemic diseases in Korea since 1950s; malaria, which once was disappeared in 1980s, has reemerged since 1990s mainly in the northern border of the country; and dengue has never been considered endemic in Korea.

Much of the current understanding of importation of infectious diseases had relied more on common sense and experience rather than evidence-based scientific data. We used National Notifiable Disease Surveillance System (NNDSS), which started to collect data on cases reported as cholera, typhoid fever, paratyphoid fever and shigellosis since 1954; malaria since 1963; and dengue since 2000. The surveillance and control of internationally transmissible infectious diseases had relied more on common sense and experience rather than evidence-based scientific data. Moreover, important in protection of persons from contracting imported infectious disease and prevention from generating secondary transmission.

We also found that there was seasonal variation in the peak incidence of imported infectious diseases, which was similar to the reports presented by other authors. A study performed in Japan reported that 60% of imported cases of dengue occurred during July to October, the summer holiday season in Japan [14]. In the Netherlands, hepatitis A was mainly imported from other countries by children returning from summer holiday [15]. In the United Kingdom the number of imported childhood malaria cases peaked usually holiday seasons from July through September [16]. Moreover, Swedish data on dengue importation demonstrated a peak number of cases during holiday season in January [17].

It should be noted that the above relationship, especially among food and water borne infectious diseases such as cholera and typhoid fever, may vary by different countries and factors such as hygiene and population density. Improvement in hygiene during the past decades in Korea potentially has contributed in overall reduction of disease burden. In contrast, the high density of population in Korea may account for the secondary transmissions of imported cases, which may facilitate reaching threshold density.

There is one concern as to whether an increased incidence in imported dengue since 2001 has been attributed to improved diagnostics and awareness. It has been argued that the recent spread and increase of dengue in subtropical countries probably have resulted from international travels [6,18]. There had been no documentation of Dengue endemicity in Korea. From 2006 to 2010, among 290 case-patients of Dengue had a history of international travel [6]. Destination were: Philippines (34.1%) contributed the largest number of cases, followed by visitors to Indonesia, India, Thailand, Vietnam, Cambodia, Laos, Malaysia, Myanmar, Bangladesh, China, East Timor, Maldives, Palau, Sri Lanka, Brazil, and Nigeria. In Korea, the surveillance system of dengue was established in 2001 and clinical diagnostic criteria have not been changed since then; therefore, we could hardly attribute such an increase to the changed diagnostic criteria since 2001. However, we do speculate whether surveillance awareness in primary healthcare physicians is one of the major contributions.

The importation of diseases that are transmissible from human to human may pose an outbreak endemically. In 2010–2011, importation of Shigellosis has caused an outbreak, that started from the travelers [20]. The destinations were mainly Asian countries, in

particular, India (21.7%), Cambodia (19.8%), Philippines (17.9%), and Vietnam (9.0%). It is of concern that transmissible disease should be monitored thoroughly not only from the airport or seaport, but throughout the duration of transmissible in suspected returning travelers.

Our findings have several potential limitations. First, the data we used was from administrative data, and thus we did not have access to laboratory information or patient's travel histories. Identification of subtypes of shigellosis, malaria, and dengue are essential in both clinical settings as well as in public health, because prevention and control measures vary according to the different subtypes of such diseases. Moreover, identification of travel history in individual case-patient may provide baseline data on quarantine measures in Korea. Second, several correlates were not controlled in this study, and the exact temporal sequence with adjustment for relevant factors should be addressed. The outbreak of infectious diseases in exporting country may potentially affect the number of imported infection to Korea, which has not been accounted in our study. Thirdly, because we did not have precise case definitions in six different infectious diseases, the quality of these data are limited. The NNDSS data lack specific definition and diagnostic criteria for cases of the six infectious diseases reported to the government; and our results should therefore be interpreted cautiously.

Despite these limitations, our observation in Korea may provide national and international baseline data for interpreting an association between international travel and incident cases of imported infectious disease in a country with rapidly-growing travel industry. It is evident that the volume of air traffic can be associated with not only infectious pathogens, but can harbor multidrug resistant organism, as have demonstrated from India [19]. The reports on international spread of diseases including antibiotic resistant bacteria are growing, and it is important to know the global patterns of transmission from public health stand point. Although the ecological design of this study limit the strength of the evidence, the design is appropriate for assessing the impact of volume of traffic and the transmission of infection. Nevertheless, our results indicate that the decision to make importable infectious disease notifiable in Korea was warranted and that increased vigilance focused on these new surveillance data is needed.

In conclusion, there was an increase in the number of incident cases of imported infectious diseases between 2003 and 2012, potentially related to the increased number of international travel in Korea. It remains important to assess the quantitative and qualitative impact of imported infectious disease and possibility of secondary endemic transmission of pathogens in order to protect both travelers and non-travelers in the changed social environment. We recommend continuing surveillance regarding the importable infectious diseases, and strengthening individual case assessment through implementing active investigation system to prevent the potential transmission to secondary cases.

Author statement

Young-June Choe has contributed to designing and conducting study, and writing the article. Seung-Ah Choe has contributed in analyzing and interpreting of data. Sung-Il Cho has contributed to designing and oversight of the study.

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None.

Conflict of interest

No authors declare conflicts of interest.

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