

# Low Compliance with National Guidelines for Preventing Transmission of Group 1 Nationally Notifiable Infectious Diseases in Korea

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**Purpose:** This study was performed to evaluate the compliance with, and adequacy of, the Korean national guidelines which had been recommended until 2011 for isolation of patients with group 1 nationally notifiable infectious diseases (NNIDs), namely cholera, typhoid fever, paratyphoid fever, shigellosis, and enterohemorrhagic *Escherichia coli* (EHEC) infection. **Materials and Methods:** We evaluated the clinical and microbiological characteristics of confirmed cases of group 1 NNIDs and compliance with the guidelines in 20 Korean hospitals nationwide in 2000-2010. We also compared the Korean guidelines with international guidelines. **Results:** Among 528 confirmed cases (8 cases of cholera, 232 of typhoid fever, 81 of paratyphoid fever, 175 of shigellosis, and 32 EHEC infections), strict compliance with the Korean guideline was achieved in only 2.6% to 50.0%, depending on the disease. While the Korean guidelines recommend isolation of all patients with group 1 NNIDs, international guidelines recommend selective patient isolation and screening for fecal shedding, depending on the type of disease and patient status. **Conclusion:** Compliance with the previous national guidelines for group 1 NNIDs in Korea was generally very low. Further studies are needed to evaluate whether compliance was improved after implementation of the new guideline in 2012.

**Key Words:** Communicable disease control, guideline adherence, patient isolation, cholera, typhoid fever, shigellosis

## INTRODUCTION

Food-borne diseases are mostly acquired by ingestion of water and food contaminated with pathogenic microorganisms. However, infections also occur through

person-to-person transmission, especially among members of the same household or in crowded places where hygiene is often compromised, such as day care centers and nursing homes. In these conditions, transmission can sometimes cause large outbreaks in the community and even in hospital settings.<sup>1-3</sup> Successful prevention of spreading of infectious diarrhea in the community depends largely on adequate control measures such as rapid and accurate microbiological diagnosis among the populations at risk, reporting of specific communicable diseases to the appropriate public health authorities, adequate follow-up strategies to monitor fecal shedding after treatment in groups at risk, patient isolation and preventative education.<sup>4</sup>

Cholera, typhoid fever, paratyphoid fever, shigellosis, and enterohemorrhagic *Escherichia coli* (EHEC) infections have been classified as group 1 nationally notifiable infectious diseases (NNIDs) in Korea. To prevent spreading of group 1 NNIDs in the community and in hospitals, the national guidelines have recommended that all patients with these diseases should be hospitalized under enteric precautions until screening for fecal shedding becomes negative 2 or 3 times consecutively after finishing antibiotic therapy until 2011.<sup>5</sup> International guidelines for these communicable diseases also recommend adequate patient isolation, adopting enteric precautions and regular screening for fecal shedding in some situations.<sup>6,7</sup> This study was performed to characterize the clinical and microbiological features of group 1 NNIDs in Korea and evaluate compliance with the Korean guideline for control and isolation of patients with group 1 NNIDs. A more realistic isolation policy for Korea was suggested by comparing the Korean national guidelines with international guidelines.

## MATERIALS AND METHODS

Infectious disease specialists retrospectively reviewed the medical records of confirmed cases of group 1 NNIDs, diagnosed in 20 Korean hospitals nationwide, from 2000 to 2010. Cases of cholera were limited only to instances in which *Vibrio cholerae* O1 or O139 was isolated in clinical specimens. Data on demographic characteristics, clinical information, and microbiological and epidemiological findings were collected. Clinically or serologically diagnosed cases were excluded as were cases of non-typhoid salmonellosis.

Three aspects of compliance with the 2011 Korean national guidelines were assessed:<sup>5</sup> 1) isolation of patients

with group 1 NNIDs and asymptomatic carrier in hospitals using enteric precautions; 2) regular screening for fecal shedding; and 3) maintaining patient and carrier isolation until microbiological confirmation of negative conversion after finishing antibiotic treatment. Isolation methods for patients and carriers were considered adequate when they occupied single rooms or were admitted in cohorts. Based on the 2011 Korean national guidelines,<sup>5</sup> microbiological confirmation of negative conversion involved two consecutive negative cultures of stool specimens taken 24 hours apart and at least 48 hours after finishing antibiotic therapy for cholera, shigellosis, and EHEC infections.<sup>5</sup> For typhoid fever and paratyphoid fever, three consecutive negative stool cultures were required.

We compared the Korean guidelines with two major international guidelines for control and isolation of patients with group 1 NNIDs: the guidelines of the American Public Health Association in the United States<sup>6</sup> and of the Public Health Laboratory Service in the United Kingdom.<sup>7</sup> This study was approved by the Institutional Review Board of Seoul National University Bundang Hospital.

## RESULTS

Of the 20 participating hospitals, 15 were tertiary care teaching hospitals and 5 community-based secondary care general hospitals. All had their own microbiology laboratories, and the etiologic microorganisms were identified in each institute. The locations of participating hospitals were: 5 in Seoul, 1 in Busan, 1 in Daegu, 2 in Incheon, 1 in Gwangju, 5 in Gyeonggi, 2 in Gangwon, 1 in Chonbuk, 1 in Gyeongbuk, and 1 in Gyeongnam.

During the study period, 528 cases of group 1 NNIDs were microbiologically confirmed in the 20 hospitals; 8 cases of cholera, 232 of typhoid fever, 81 of paratyphoid fever, 175 of shigellosis, and 32 of EHEC infections (Table 1). Of the 175 cases of shigellosis, 98 were caused by *Shigella flexneri*, 58 by *S. sonnei*, 6 by *S. dysenteriae*, 5 by *S. boydii*, and 8 by unidentified *Shigella* species. 75.0% and 43.2% of the cases of cholera and paratyphoid fever were imported from Southeast Asian countries and the Indian subcontinent respectively, and 15.9%, 20.6% and 0% of the typhoid fever, shigellosis, and EHEC infection, respectively, developed in travelers returning from abroad. EHEC infections mainly developed in children under 10 years of age whereas the other group 1 NNIDs developed in diverse age groups. Fever, ab-

**Table 1.** Clinical and Microbiological Characteristics of Group 1 Nationally Notifiable Infectious Diseases Developed during 2000 through 2010 in 20 Korean Hospitals

	Cholera (n=8)	Typhoid fever (n=232)	Paratyphoid fever (n=81)	Shigellosis (n=175)	EHEC (n=32)
Female, n (%)	4 (50.0)	107 (46.1)	33 (40.7)	102 (58.3)	14 (43.8)
Age, median (range), yrs	42 (10-70)	39 (0-94)	34 (0-76)	45 (1-87)	3 (0-72)
0-9 (n)	0	23	12	28	24
10-19 (n)	1	31	4	16	5
20-29 (n)	1	33	15	21	0
30-39 (n)	1	30	14	17	0
40-49 (n)	1	48	17	12	0
50-59 (n)	1	28	9	15	2
60-69 (n)	2	30	8	35	0
≥70 (n)	1	9	2	31	1
Imported cases, n (%)	6 (75.0)	37 (15.9)	35 (43.2)	36 (20.6)	0
Major symptoms, n (%)					
Abdominal pain	6 (75.0)	84 (36.2)	19 (23.5)	90 (51.4)	15 (46.9)
Chill	0	107 (46.1)	43 (53.1)	32 (18.3)	0
Diarrhea	7 (87.5)	107 (46.1)	47 (58.0)	159 (90.9)	26 (81.3)
Fever	2 (25.0)	208 (89.7)	71 (87.7)	106 (60.6)	15 (46.9)
Headache	1 (12.5)	79 (34.1)	23 (28.4)	22 (12.6)	23 (71.9)
Nausea	0	43 (18.5)	43 (53.1)	27 (15.4)	2 (6.3)
Vomiting	1 (12.5)	37 (15.9)	11 (13.6)	39 (22.3)	13 (40.6)
Weakness	0	41 (50.6)	11 (13.6)	25 (14.3)	3 (9.4)
Specimen yielding initial positive cultures, n (%)					
Stool	8 (100.0)	11 (4.7)	14 (17.3)	162 (92.6)	32 (100.0)
Blood	0	203 (87.5)	65 (80.2)	3 (1.7)	0
Urine	0	2 (0.8)	0	5 (2.9)	0
Others	0	7 (3.0)	1 (1.2)	3 (1.7)	0
Stool and blood	0	7 (3.0)	1 (1.2)	2 (1.1)	0
Stool and urine	0	2 (0.8)	0	0	0
Antibiotic treatment, n (%)					
Yes	7 (87.5)	216 (93.1)	76 (93.8)	157 (89.7)	19 (59.4)
No	1 (12.5)	0	3 (3.7)	11 (6.3)	13 (40.6)
Unknown	0	16 (6.9)	2 (2.5)	7 (4.0)	0
Follow up of stool cultures after initial positive culture, n (%)					
Done	7 (87.5)	175 (75.4)	63 (77.8)	133 (76.0)	28 (87.5)
Not done	1 (12.5)	57 (24.6)	18 (22.2)	42 (24.0)	4 (12.5)
Duration of fecal shedding after initial positive culture, n					
<3 d	1	8	2	5	1
3-5 d	0	3	4	5	2
6-7 d	0	2	1	4	2
8-14 d			1	8	2
15-21 d		1		2	
22-28 d				1	
In-hospital mortality, n (%)	0	3 (1.3)	0	2 (1.1)	1 (3.1)

EHEC, enterohemorrhagic *Escherichia coli*.

dominal pain, and diarrhea were the most frequently observed symptoms of these diseases. Follow-up stool cultures were made at least once in 75.4-87.5% of the confirmed cases of group 1 NNIDs. While the period of fecal shedding is relatively short in most of cases of cholera, typhoid fever, and paratyphoid fever, cases with longer periods of fecal shedding was more frequent in shigellosis and EHEC infections. In-hospital deaths involving Group 1 NNIDs were rare.

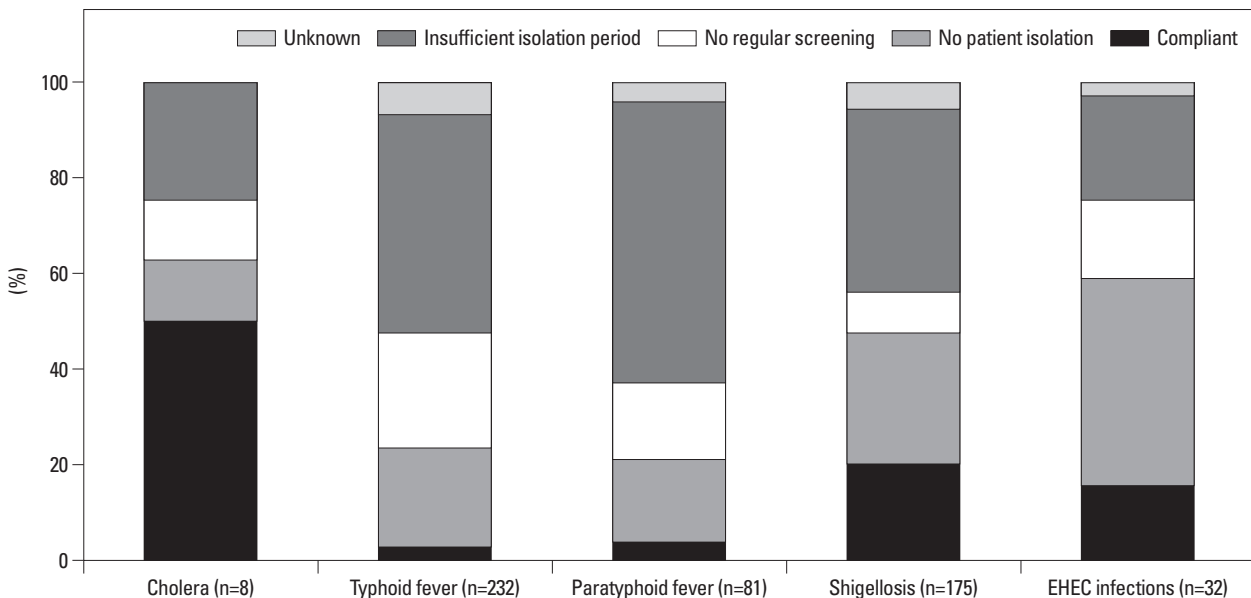
Compliance with the Korean national guidelines for patients with group 1 NNIDs was generally low (2.6-50.0%), especially in cases of typhoid fever and paratyphoid fever (Fig. 1). The most common type of non-compliance was failure to maintain patient isolation until microbiological confirmation of negative conversion. Moreover, substantial numbers (12.5-43.8%) of patients were not hospitalized in single rooms or in cohorts.

Several differences were observed between the Korean guidelines and the two major international guidelines for control and prevention of these communicable diseases (Table 2).<sup>5-7</sup> The most distinctive feature of the international guidelines was that patient isolation and screening for fecal shedding were applied selectively depending on the type of disease, severity of illness, and patient characteristics such as age, ability to maintain general hygiene, and occupation. The Korean guidelines were much stricter in that all group 1 NNID patients were to be hospitalized until confirmation of negative conversion of fecal shedding.

## DISCUSSION

The Korean government has designated several communicable diseases, including five major food-borne or water-borne diseases - cholera, typhoid fever, paratyphoid fever, shigellosis, and EHEC infections - as NNIDs since 1957.<sup>5</sup> The government also strictly controls by law the handling of infected patients and carriers, because these communicable diseases can spread rapidly in the community and cause large outbreaks that have a substantial social impact. We retrospectively collected clinical and microbiological data on 528 cases of group 1 NNIDs for over 10 years. A total of 8396 cases including clinically suspicious cases were reported to the public health authority during that period.<sup>8</sup> The cases enrolled in this study were only 6.3% of all the cases developed nationwide. However, our data reflect general situation in Korea because we collected only microbiologically confirmed cases and excluded suspected cases. The medical records were also reviewed carefully by infectious diseases specialists in each hospital, and we did not depend only on data reported to the public health authorities, which can easily lack information on compliance with guidelines on isolation of patients and follow-up microbiological tests.

While a considerable proportion of cholera and paratyphoid fever cases in this study were imported from abroad, most of the cases of typhoid fever, shigellosis, and EHEC infections originated domestically as sporadic cases or epi-



**Fig. 1.** Compliance and types of non-compliance with the Korean national guidelines for preventing transmission of group 1 nationally notifiable infectious diseases (NNIDs) in Korea. The Korean national guidelines had recommended until 2011 that all patients with group 1 NNIDs be admitted to hospital under enteric precautions until fecal shedding was negative 2 or 3 times consecutively after ending antibiotic therapy. EHEC, enterohemorrhagic *Escherichia coli*.

**Table 2.** Comparison of the Korean Guidelines for Preventing Transmission of Group 1 Nationally Notifiable Infectious Diseases with International Guidelines

	Korean guidelines	APHA guidelines	PHLS guidelines
<b>Cholera</b>			
Admission	Mandatory	In severe cases	Recommended
Screening for fecal shedding	Mandatory	No recommendation	Usually not necessary
Duration of isolation	2 consecutive (-) stool cultures after ending antibiotics	No recommendation	48 hrs after first normal stool
Duration of work restriction	2 consecutive (-) stool cultures after ending antibiotics	No recommendation	No recommendation
<b>Typhoid/paratyphoid fever</b>			
Admission	Mandatory	During acute illness	Recommended
Screening for fecal shedding	Mandatory	Necessary	Depending on risk group (A-D)*
Duration of isolation	3 consecutive (-) stool culture after ending antibiotics	No recommendation	3-6 consecutive (-) stool culture in 3 wks after ending antibiotics
Duration of work restriction	3 consecutive (-) stool culture after ending antibiotics	3 consecutive (-) stool culture in 1 m after onset	No recommendation
<b>Shigellosis</b>			
Admission	Mandatory	During acute illness	Recommended
Screening for fecal shedding	Mandatory	For high risk groups <sup>†</sup>	According to <i>Shigella</i> species
Duration of isolation	2 consecutive (-) stool culture after ending antibiotics	No recommendation	<i>S. sonnei</i> : 48 hrs after first normal stool Other <i>Shigella</i> : 2 (-) stool culture for groups (A-D)*
Duration of work restriction	2 consecutive (-) stool culture after ending antibiotics	2 consecutive (-) stool cultures after ending antibiotics	No recommendation
<b>EHEC infection</b>			
Admission	Mandatory	During acute illness	Recommended
Screening for fecal shedding	Mandatory	For high risk groups <sup>†</sup>	According to risk group (A-D)*
Duration of isolation	2 consecutive (-) stool culture after ending antibiotics	No recommendation	48 hrs after first normal stool 2 (-) stool culture for group (A-D)*
Duration of work restriction	2 consecutive (-) stool culture after ending antibiotics	2 consecutive (-) stool cultures after ending antibiotics	No recommendation

APHA, American Public Health Association; PHLS, Public Health Laboratory Service; EHEC, enterohemorrhagic *Escherichia coli*.

\*A, any person of doubtful personal hygiene; B, children attending pre-school or nursery; C, food handlers; D, clinical and social care staff.

<sup>†</sup>Food handlers, healthcare workers, and social staff caring for vulnerable persons.

demics. Because the main route of transmission is the fecal to oral route, prolonged fecal shedding of infectious organisms has a significant impact on public health. It is difficult to compare the durations of fecal shedding in the various NNID because our study was retrospective and most of the patients received antibiotic therapy. However, there was a tendency for a longer duration of fecal shedding in cases of shigellosis and EHEC infections than in cases of cholera, typhoid and paratyphoid fever (Table 1). The duration of fecal shedding is known to differ according to the type of dis-

ease and patient status. Bacteria are excreted for 3 days or less in cases of cholera receiving adequate antibiotic treatment.<sup>9</sup> In typhoid fever and paratyphoid fever, there is concern about long term fecal excretion and carriers of *Salmonella*,<sup>6</sup> but secondary transmission through contact with patients is not likely to occur frequently.<sup>10-12</sup> On the other hand, the period of fecal shedding is longer in shigellosis and EHEC infections, and secondary attack rates are relatively high, especially in children.<sup>13-16</sup> Therefore, measures to prevent the spreading of gastrointestinal communicable

diseases in the community should differ depending on the etiologic agent. The main targets of infection control should be shigellosis and EHEC infections.

Compliance with the Korean guidelines was found to be generally very low in this study (2.6-50.0% depending on the disease). Compared with international guidelines, the Korean national guidelines were very rigid and intended to be universally applied in all clinical settings, regardless of the type of NNID (Table 2). Adherence to these guidelines was frequently unrealistic, mainly because the guidelines recommended that all the patients should be hospitalized under contact precautions until microbiological clearance was confirmed. The duration of hospitalization to meet the minimal criteria for relief from quarantine usually exceeded one week, and in cases of typhoid fever and paratyphoid fever, patients were required to be hospitalized for at least two weeks for antibiotic therapy and microbiological follow-up. This was resource-intensive and could substantially limit individual freedom and rights in the name of public benefit. Thomas, et al.<sup>12</sup> have also reported considerable difficulties in following strictly national guidelines for typhoid and paratyphoid fever in the United Kingdom. Therefore, it seemed desirable to reevaluate the scientific background of the 2011 Korean national guidelines to make them more realistic. In a survey regarding measures used for isolation of patients with group 1 NNIDs in 2011, the majority of infectious diseases specialists in Korea believed that the current national guidelines should be changed.<sup>17</sup>

Based on the results of this study, we suggest following rational measures to prevent spreading of group 1 NNIDs in the community. First, the decision whether the patient is hospitalized should not be based on law but depend on the clinical judgment of the physician. Also, the duration of quarantine should be individualized according to the type of disease, severity of acute illness, and patient characteristics, not based on the results of follow-up stool cultures after treatment. Strict isolation should be limited to cases of shigellosis and EHEC infection, which have longer periods of fecal shedding of etiologic agents and higher rates of secondary attack.<sup>13-16</sup> International guidelines also recommend hospitalization and isolation of patients in selected cases (Table 2). Second, follow-up for fecal shedding after antibiotic treatment should be targeted only to the risk groups. While follow-up tests were performed at least once in 75.4-87.5% of the cases in this study, substantial numbers of cases were not screened according to the guidelines which recommended two or three tests at least 48 hours after the end of anti-

biotic treatment (Fig. 1). We think that it is not necessary for all patients and carriers to be followed up for fecal shedding after adequate antibiotic treatment, provided that they can maintain good personal hygiene and present no risk of becoming a source of outbreak; for example, food handlers do. In 2012, the Korean Government changed its recommendations for control and isolation of patients with group 1 NNIDs to more targeted measures, based on the type of disease and patient.<sup>18</sup> This change was made partly because hepatitis A, the incidence of which increased rapidly in the young-adult population in the 2000s,<sup>19</sup> had been classified as a group 1 NNID in 2010, and it was not realistic to apply the same quarantine policy to all patients with hepatitis A. Further studies and changes of strategy based on scientific grounds are warranted to improve patient convenience and healthcare workers' compliance.

This study has some limitations. First, it was retrospective, and we did not collect data from small community-based hospitals. These factors can be sources of selection bias. Small community-based hospitals have limited resources for microbiological diagnosis of group 1 NNIDs and also more difficulty in adhering to infection control measures. Therefore, the real level of compliance with the Korean national guidelines is probably much lower than indicated by the results of this study. Second, the study was performed in a country where the prevalence of infectious diarrhea and food-borne illness is relatively low. Therefore, our suggestions may not be validly extrapolated to other countries, especially where the prevalence of gastrointestinal communicable diseases is high and resources for infection control are limited. Third, the results should be interpreted with cautions because low compliance with the national guidelines might have resulted not only from the rigidity of the national guidelines, but also a lack of knowledge about quarantine or isolation among Korean healthcare workers. Fourth, we did not evaluate the changes of compliance with the new national guidelines which were implemented in 2012. Further studies are needed to evaluate the knowledge level of healthcare workers about the national guidelines and whether compliance was improved after implementation of the new guidelines.

In conclusion, compliance with the previous national guidelines for preventing transmission of group 1 NNIDs was very low in Korea. Future guidelines should be selectively applied to highly communicable diseases such as shigellosis and EHEC infections and to patient groups with a high risk of transmission.

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