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Relationship between the number of pediatric patients with rotavirus and telephone triage for associated symptoms

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A B S T R A C T

Background: Earlier syndromic surveillance may be effective in preventing the spread of infectious disease. However, there has been no research on syndromic surveillance for rotavirus. The study aimed to assess the relationship between the incidence of rotavirus infections and the number of telephone triages for associated symptoms in pediatric patients under 4 years old in Osaka prefecture, Japan.
Methods: This was a retrospective observational study for which the study period was the 3 years between January 2015 and December 2017. We analyzed data on children under 4 years old who were triaged by telephone triage nurses using software. The primary endpoint was the number of rotavirus patients under 4 years triaged old per week. Using a linear regression model, we calculated the R square value of the regression model to assess the relationship between the number of patients with rotavirus and the number of telephone triages made for associated symptoms. Covariates in the linear regression model were the week number indicating seasonality and the weekly number of telephone triages related to rotavirus symptoms such as stomachache and vomiting.
Results: During the study period, there were 102,336 patients with rotavirus, and the number of people triaged by telephone was 123,720. The highest correlation coefficient was 0.921 in the regression model with the number of telephone triages for “stomachache + nausea/vomiting” and “stomachache + diarrhea + nausea/vomiting”.
Conclusion: The number of telephone triage symptoms was positively related to the incidence of pediatric patients with rotavirus in a large metropolitan area of Japan.
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1. Introduction

Rotavirus infection is the most common gastrointestinal infectious disease among children aged 4 years or less, causing 215,000 deaths around the world every year [1]. Recently, surveillance for this disease has been conducted in African countries based on World Health Organization recommendations [2-5]. However, it takes much time from occurrence to publication of the results of traditional surveillance conducted by public health departments [6]. Therefore, earlier syndromic surveillance using existing data may be effective in preventing the spread of infectious disease. There are many studies on syndromic surveillance for gastrointestinal disease and waterborne disease such as Cryptosporidium using absenteeism records [7] and pharmacy drug sales [8-10]. However, there is no research on syndromic surveillance for rotavirus. Vaccination against rotavirus has spread in many developed countries in recent years. If syndromic surveillance for rotavirus can be conducted, it may be possible to prevent the spread of rotavirus infection in children through such surveillance.

In Osaka prefecture, Japan, telephone triage service has been provided to the local population since 2012. The triage nurse uses software to determine the urgency of the client for each symptom and provides necessary services such as ambulance dispatch and guidance from medical institutions based on the result. Therefore, the number of telephone triages by symptom can be calculated in real time with this software. If

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there is a relationship between the number of telephone triage symptoms such as stomachache, nausea/vomiting and diarrhea that are related to rotavirus infection and the number of patients with rotavirus infection, it may be possible to predict the spread of rotavirus infections earlier. The purpose of this study was to assess the relationship between the incidence of rotavirus infections and the number of telephone triages for associated symptoms in pediatric patients under 4 years old in Osaka prefecture, Japan.

2. Materials and methods

2.1.1. Study design, population and study setting

This was a retrospective observational study for which the study period was the 3 years between January 2015 and December 2017. Osaka prefecture is the largest urban area in western Japan, with an area of 1905.14 km^2 and a population of 342,645 children who are 4 years old or younger among 8.8 million people [11]. In this study, we analyzed the data on children under 4 years old who were triaged by telephone triage nurses using software in Osaka prefecture. This study was approved by the Ethics Committee of Osaka University Graduate School of Medicine (approval no. 16070). As the telephone triage data was anonymized, the necessity of obtaining informed consent from the subjects was waved.

2.1.2. Outpatient surveillance in Japan

The infectious disease surveillance program of Japan was initiated in 1981 and was revised and updated to its present form following the revision of the Infectious Disease Control Law in 1999 [6,12-14]. The system is currently called National Epidemiological Surveillance for Infectious Diseases (NESID), which includes a mandatory reporting system for nationally notifiable diseases and sentinel surveillance systems for various kinds of infectious diseases [15].

Rotavirus falls under the sentinel surveillance arm of the program. Weekly numbers of patients with rotavirus are reported from 3000 medical institutions nationwide to local health centers. Sentinel sites were designated among the hospitals that met certain criteria according to their geographic distribution and population densities. These sentinels use the following criteria for reporting patients with rotavirus: 1) diarrhea of 3 times or more, 2) vomiting of one time or more and 3) any one of the following test results a) separation and identification by fecal culture, b) detection of pathogen antigens by immunochromatography and c) detection of pathogen genes by PCR. Sentinel sites report the age and sex of the patients on a weekly basis, but the report does not include personal information such as names or addresses. This information is transferred from local health centers to the prefectural government where it is aggregated into a prefectural report. The report is then forwarded to the National Institute of Infectious Diseases in Tokyo, which is affiliated with the Ministry of Health, Labour and Welfare. Within Osaka prefecture, 197 pediatric medical institutions report influenza patients to 10 local health centers.

2.1.3. Telephone triage service in Osaka

The telephone triage service in Osaka prefecture is a public service similar to that in Tokyo [16] and can be used freely by anyone. In this service, a triage nurse uses software with a protocol developed for telephone triage in Japan and determines the urgency of the client. There are 97 different protocols of telephone triage for chief complaints in Japan, and the urgency of the client is determined for each chief complaint by selecting the symptom and sign related to that complaint. As with telephone triage service in the departments of veterans' affairs in the United States [17], Canada and United Kingdom [18-20], telephone service in Osaka prefecture provides the client with necessary services such as ambulance dispatch and guidance from medical institutions based on the result of the urgency [21]. The software records the sex and age group of the client, the times when the telephone triage was started and ended, the chief complaint and selected symptoms and signs, the urgency of the client and the presence or absence of ambulance dispatch.

2.1.4. Endpoint

The primary endpoint was the number of patients with rotavirus per week in Osaka prefecture. The number of patients with rotavirus per week was obtained from the data published on the web site of the Osaka Institute of Public Health [22].

2.2. Statistical analysis

Using a linear regression model, we calculated the R square value of the regression model to assess the relationship between the number of telephone triages and the number of patients with rotavirus in Osaka prefecture. The covariates in the linear regression model were the week number indicating seasonality and the weekly number of telephone triages related to rotavirus symptoms such as stomachache and vomiting. We defined the week number as a binary variable, with the week including January 1st as "week number = 1". In this study, we selected three chief complains related to rotavirus: stomachache, diarrhea and nausea/vomiting among the telephone triage categories. The seven input patterns of these three variables into the linear regression model are "stomachache", "diarrhea", "nausea/vomiting", "stomachache + diarrhea", "stomachache + nausea/vomiting", "diarrhea + nausea/vomiting" and "stomachache + diarrhea + nausea/vomiting". We calculated the correlation coefficient and R square and adjusted R square values of each linear regression model. Next, according to the season (January–March, April–June, July–September, October–December), we calculated the Spearman's correlation coefficient, R square value between the predicted weekly number of rotavirus patients from the best linear regression model and the weekly number of rotavirus patients for each season. Statistical significance was defined as $P < 0.05$, and statistical analysis was performed with SPSS version 23.0J (IBM Corp., Armonk, NY).

3. Results

During the study period, there were 102,336 patients with rotavirus, and 123,720 in Osaka prefecture were triaged by telephone. Table 1 shows the characteristics of the children aged 4 years or less in Osaka prefecture between January 2015 and December 2017. The age group requesting the highest amount of telephone triage was the 0-year-old group (39,139; 31.6%). There were 67,606 (54.6%) males and 56,003 (45.3%) females. The most frequent telephone caller was the family of the patient (122,538; 99.0%). The number of telephone triages conducted during the daytime was 53,918 (43.6%) and that during the nighttime was 69,802 (56.4%). The number of telephone triages conducted in 2015 was 41,488 and that conducted in 2017 was 41,273. The number of telephone triages conducted during the study period did not change significantly. The most common chief complaint among the incidents of telephone triage was vital sign abnormalities such as no response or breathing (119,355; 45.7%). Telephone triages were conducted for 2216 (0.8%) complaints of stomachache, 3271 (1.3%) complaints of diarrhea and 11,549 (4.4%) complaints of nausea/vomiting.

Table 2 shows the correlation coefficient and R square and adjusted R square values for each regression model. The highest correlation coefficient was 0.921 in the regression model with the number of telephone triages for "stomachache + nausea/vomiting" and "stomachache + diarrhea + nausea/vomiting". Although the highest R square was 0.848 in the regression model with the number of telephone triages for "stomachache + diarrhea + nausea/vomiting", the highest adjusted R square was 0.768 in the regression model with the number of telephone triages for "stomachache + nausea/vomiting". Fig. 1 shows the weekly predicted number of rotavirus patients for the linear regression model

Table 1
Demographic and clinical characteristics of children <5 years old judged by telephone triage between 2015 and 2017 in Osaka.

Characteristic	Total	
	(n = 123,720)	
Age, years, n (%)		
0	39,139	(31.6)
1	36,178	(29.2)
2	20,350	(16.4)
3	15,801	(12.8)
4	12,252	(9.9)
Sex, n (%)		
Male	67,606	(54.6)
Female	56,003	(45.3)
Unknown	111	(0.1)
Person who initiated telephone consultation, n (%)		
Patient principal	703	(0.6)
Patient's family	122,538	(99.0)
Other person	469	(0.4)
Unknown	10	(0.0)
Time of telephone consultation and triage, n (%)		
Daytime (09:00 to 17:59)	53,918	(43.6)
Nighttime (18:00 to 8:59)	69,802	(56.4)
Year, n (%)		
2015	41,488	(33.5)
2016	40,959	(33.1)
2017	41,273	(33.4)
Season, n (%)		
January to March	28,361	(22.9)
April to June	33,114	(26.8)
July to September	31,536	(25.5)
October to December	30,709	(24.8)
Contents of telephone consultation and triage for chief complaint		
Abnormal vital signs	119,355	(45.7)
Fever	30,856	(11.8)
Head injury	18,008	(6.9)
Nausea/vomiting	11,549	(4.4)
Rash/hives	8308	(3.2)
Accidental ingestion of foreign substance	7570	(2.9)
Cough	5320	(2.0)
Toothache, tooth damage	4133	(1.6)
Diarrhea	3271	(1.3)
Injury to the face and extremities	3003	(1.2)
Stomachache	2216	(0.8)
Other	47,341	(18.1)

(Model 5) with the number of telephone triages for "stomachache + nausea/vomiting" and the actual weekly numbers of rotavirus patients.

Fig. 2 shows scatter plots of the weekly numbers of rotavirus patients and the predicted numbers of rotavirus patients from the linear regression model for "nausea/vomiting" by season. The vertical axis shows the predicted number of rotavirus patients calculated from the regression model, and the horizontal axis shows the actual number of rotavirus patients per week. The season with the highest Spearman's correlation coefficient ($R = 0.923$) was in October–December ($P < 0.001$), followed in order by April–June ($R = 0.793$, $P < 0.001$), January–March ($R = 0.712$, $P < 0.001$) and July–September ($R = 0.659$, $P < 0.001$).

4. Discussion

This study revealed a positive relationship between the telephone triage data and the number of pediatric patients with rotavirus under 4 years old in a large metropolitan community of Japan. We compared the R square value for each linear regression model, and the R square values were high in all seven models. Furthermore, a difference was found in the correlation coefficient of the linear regression model depending on season. In this study, the contribution rate of the linear regression model using the telephone triage data was high, and the forecast of rotavirus epidemics using these data may allow earlier announcement than the warning based on the traditional surveillance and thus be useful in preventing the spread of rotavirus.

Several syndromic surveillance models for gastrointestinal infectious disease have been reported previously. Pivette et al. reported that a syndromic surveillance model using non-prescription drug sales data could detect epidemics on average 2.25 weeks earlier than surveillance of traditional sentinel data [8]. Bjelkmar et al. also reported that the number of telephone consultations was effective in the detection of early outbreaks in the study of Cryptosporidium in Skelleftea, Sweden in 2011 [23]. However, in a systematic review of syndromic surveillance, it was reported that syndromic surveillance using drug sales data and nurse advice line calls was timely but non-specific, whereas traditional surveillance using hospitalization data and laboratory test results was not timely but more specific [24]. Our study showed a high correlation between the traditional surveillance data and the number predicted from the linear regression model, indicating that it would be possible to predict an epidemic of rotavirus earlier than with traditional surveillance. If a system such as nurse advice line or telephone triage can be constructed in an area where traditional surveillance is used, that data may be useful in the surveillance of rotavirus.

Next, among the linear regression models, the R square values were higher in the models including the number of triages for "diarrhea" than in those not including this number. The number of telephone triages for "diarrhea" was the largest, and there were fewer telephone triage cases for "stomachache" and "nausea/vomiting" than for "diarrhea". Because we included children who were 4 years old or younger in this study, they might be unable to appropriately tell their parents about chief complaints such as stomachache and nausea. Thus, the number of telephone triages related to objective symptoms such as diarrhea may have been higher than that for subjective symptoms such as stomachache and nausea. Indeed, in syndromic surveillance, a high correlation was reported when the number of explanatory variables was large, but no correlations were found when the number of explanatory variables was small [17]. In the present study, the high correlation coefficient of the linear regression model including the number of telephone triages for "diarrhea" may be related to the high number of telephone triages for this symptom. As all of the linear regression models including the number of telephone triages for "diarrhea" had high correlation coefficients, we consider that any of these models could be used in the prediction of rotavirus epidemics.

Table 2
Spearman correlation coefficient and R square and adjusted R square values for each linear regression model.

Model no.	Variables	Spearman correlation coefficient	R^2	Adjusted R^2[a]
1	Number of telephone triages for stomachache	0.864	0.747	0.619
2	Number of telephone triages for diarrhea	0.844	0.712	0.567
3	Number of telephone triages for nausea/vomiting	0.917	0.840	0.759
4	Number of telephone triages for stomachache and diarrhea	0.867	0.751	0.622
5	Number of telephone triages for stomachache and nausea/vomiting	0.921	0.847	0.768
6	Number of telephone triages for diarrhea and nausea/vomiting	0.917	0.840	0.757
7	Number of telephone triages for stomachache, diarrhea and nausea/vomiting	0.921	0.848	0.766

[a] Adjusted R^2 was adjusted by the number of variables in the linear regression model.

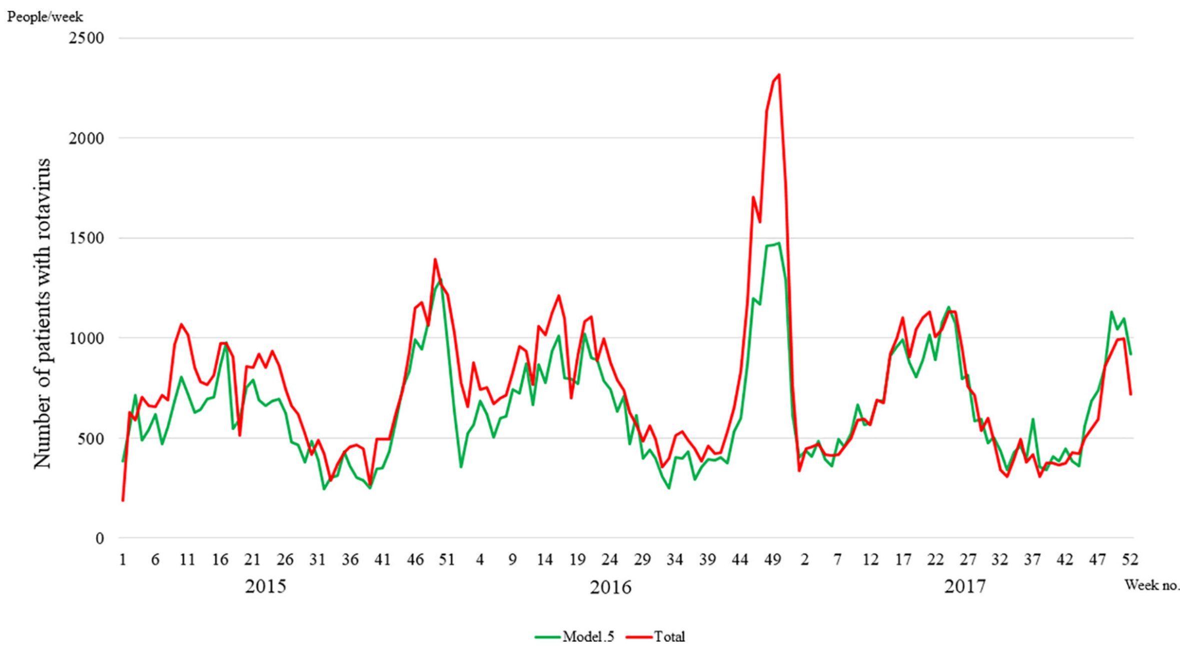

Fig. 1. The total number of pediatric patients with rotavirus and the predicted number of these patients from linear regression model 5 during the study period.

Finally, in the subgroup analysis divided into the four seasons, the linear regression model in October–December showed the highest correlation. However, the mechanism for this finding was not sufficiently revealed in this study. Rotavirus infection is a gastrointestinal infection that infects infants and children year round. The fact that other infectious gastrointestinal diseases such as those caused by *Salmonella* and *Vibrio parahaemolyticus* are prevalent in warmer seasons may have influenced the results in this study. In any case, syndromic surveillance with the present linear regression model for rotavirus showed a high correlation coefficient throughout the year, which could help to prevent epidemics of rotavirus infection.

There were several limitations in this study. First, weekly numbers of patients with rotavirus are reported from sentinel medical institutions to local health centers based on the Infectious Disease Control Law, and not all rotavirus patients may have been reported. Second, we simultaneously assessed the correlation between the number of children triaged by telephone and the number of pediatric patients with rotavirus; this study was not an observational study that followed up the children for whom telephone triage was conducted or that calculated the prevalence of rotavirus. Third, the generalizability of our findings is limited due to areas where people can use systematic telephone triage system. Fourth, as this study was an observational study, unknown confounding factors may be present.

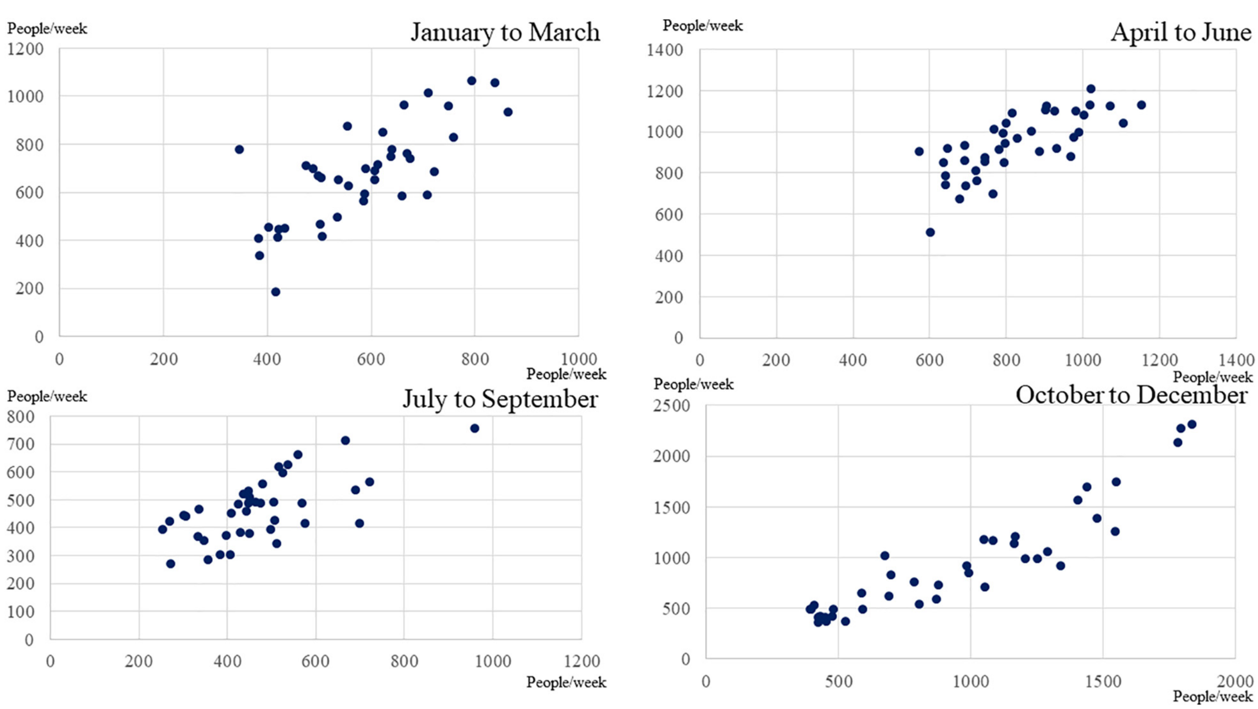

Fig. 2. The actual weekly number of rotavirus patients and the predicted number of rotavirus patients from linear regression model 3 by each season.

5. Conclusion

The number of telephone triage symptoms was positively related to the incidence of rotavirus infections in pediatric patients in a large metropolitan area of Japan. Early prediction of rotavirus epidemics using telephone triage data may help to prevent the spread of this common infection.

CRediT authorship contribution statement

Yusuke Katayama: Conceptualization, Methodology, Software, Formal analysis, Investigation, Resources, Writing - original draft, Visualization, Project administration, Funding acquisition.**Kosuke Kiyohara:** Software, Formal analysis.**Sho Komukai:**Software, Formal analysis. **Tetsuhisa Kitamura:**Methodology, Investigation, Resources, Writing - review & editing, Visualization.**Kenichiro Ishida:**Methodology.**Tomoya Hirose:**Writing - review & editing.**Tasuku Matsuyama:**Methodology. **Takeyuki Kiguchi:**Writing - review & editing.**Takeshi Shimazu:**Supervision, Project administration.

Declaration of competing interest

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Data sharing statement

No additional data.

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