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Epidemiology of coronavirus disease 2019 in Yamagata Prefecture, Japan, January–May 2020: The importance of retrospective contact tracing


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Title: Epidemiology of coronavirus disease 2019 in Yamagata Prefecture, Japan, January–May 2020: The importance of retrospective contact tracing

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**Keywords:** close contact, cluster-based approach, infection source, SARS-CoV-2, testing

**Running head:** First wave of COVID-19 in Yamagata, Japan
瀬戸順次 1, 青木洋子 1, 駒林賢一 1, 池田陽子 1, 三瓶美香 1, 小川直美 1, 内海由美子 2, 藤井俊司 2, 千葉真沙美 3, 鈴木恵美子 3, 高橋達也 4, 山田敬子 4, 大谷慈子 5, 蘿野吉弘 5, 荒木京子 6, 加藤丈夫 6, 石川仁 5,7, 池田辰也 1,8, 阿部英明 8, 阿彦忠之 1,8, 水田克巳 1

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SUMMARY

Public health interventions have served an important role in controlling coronavirus disease 2019 (COVID-19), a rapidly spreading infectious disease. To contribute to future COVID-19 countermeasures, we aimed at verifying the results of countermeasures achieved by public health centers (PHCs) against the first wave of COVID-19 in Yamagata Prefecture, Japan. During January–May 2020, 1,253 patients suspected of SARS-CoV-2 infection were invited for testing. Simultaneously, based on retrospective contact tracings, PHCs investigated the infection sources and transmission routes of laboratory-confirmed COVID-19 cases and tested 928 contacts. Consequently, 69 cases were confirmed during March 31 – May 4, 58 (84.1%; 95% confidence interval 75.5–92.7) of whom were found from contacts. The spread of infection was triggered by cases harboring epidemiological links outside of Yamagata. Then, the number of cases increased rapidly. However, PHCs identified epidemiological links in 61 (88.4%; 95% confidence interval 80.8–96.0) of the 69 cases and transmission chains up to the fifth generation. Finally, the spread of infection ended after approximately one month. Our results indicate that the identification of infection sources and active case finding from contacts based on retrospective contact tracing was likely to be an effective strategy to end the first wave of COVID-19 in Yamagata.
INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), spread worldwide after it was first detected in Wuhan, China in December 2019 (1–3). On March 11, 2020, the World Health Organization declared a global pandemic of COVID-19 (4,5). As of September 2020, more than 30 million global cases had been confirmed and approximately 1 million people have died (3). As the infection has spread, public health interventions including contact tracing, isolation, and testing have been crucially important for preventing COVID-19 transmission (6–8).

Typically, COVID-19 causes febrile illness with respiratory symptoms, but some cases are asymptomatic (5,9). Younger persons tend to contract less-severe illness (5). Regarding disease transmission, however, COVID-19 can be transmitted by pre-symptomatic or asymptomatic cases (4,10,11). Accordingly, countermeasures against COVID-19 should be undertaken in consideration of pre-symptomatic and asymptomatic transmission (10,11).

After confirmation of its first case on January 16, 2020, Japan experienced marked peaks of the number of COVID-19 cases in April and August (12). Although 83,179 cases (7 cases per month/100,000 population) had been confirmed in Japan as of
September 2020 (12,13), the notification rate is lower than high-burden countries such as the United States (247 cases per month/100,000 population) (3). One reason for the low case number in Japan is probably the cluster-based approach which has been independently conducted there: the identification of infection sources and transmission routes, and active case finding from close contacts based on retrospective contact tracing conducted by public health centers (PHCs) (14–16). Inclusive studies have examined the cluster-based approach (4,5), but specific local studies including field epidemiological information and testing results are scarce.

For this study, we aimed at verifying the results of COVID-19 countermeasures including the cluster-based approach conducted by PHCs in Yamagata Prefecture, Japan, during January–May 2020. In the period including the first wave of COVID-19 in Yamagata, we conducted testing of patients suspected of SARS-CoV-2 infection based on the national testing strategy focusing on high-risk groups (5). Simultaneously, we performed testing not only for symptomatic close contacts, which was the strategy of Japanese government at that time (14,15), but also for asymptomatic close contacts along with some non-close contacts. Therefore, this study includes results of active case findings from contacts, irrespective of the presence or absence of symptoms.
MATERIALS AND METHODS

Study setting

Yamagata prefecture has an estimated population of 1.078 million persons (13). Its population density (116 people/km²) is lower than that of Tokyo, the capital of Japan (6,354 people/km²) (13,17). Yamagata is surrounded by four other prefectures including Miyagi, which contains Sendai City, a big city in the northern Japan.

Definition of cases, contacts, and clusters

We defined a suspected case as a patient who met any of the criteria modified from the national strategy (5) as shown in Fig. 1. We defined a laboratory-confirmed case as an individual with a positive test result of real-time reverse transcription PCR for SARS-CoV-2. An asymptomatic case was defined as a laboratory-confirmed case without symptoms at the time of case finding. We defined a contact as a person who contacted laboratory-confirmed cases from two days prior to the onset of symptoms (or from two days before virus detection in asymptomatic cases) until hospitalization (Fig. 1). We defined a close contact and a non-close contact based on the criteria of the official manual (18). We defined a cluster as two or more laboratory-confirmed cases associated with the same location, group, or event around the same time.

Investigation by PHCs
1) Suspected cases

Staff members of PHCs received calls from persons who had possibly been infected with SARS-CoV-2 and conducted interviews to collect information about symptoms, underlying diseases, behavior histories for the past 14 days prior to the onset of symptoms, jobs, etc. The director of PHCs evaluated information comprehensively and selected suspected cases. PHCs invited suspected cases for testing as soon as possible.

2) Contacts

Immediately after confirming laboratory-confirmed cases, PHCs selected contacts based on retrospective contact tracing (14–16) that considered behavior histories of the cases during the 14 days prior to the onset of symptoms. Regarding close contacts, PHCs urged self-quarantine for 14 days, performed health observations by daily telephone for 14 days, and invited testing irrespective of whether they had symptoms or not. Regarding non-close contacts, PHCs strengthened health observations and invited testing when they had symptoms. Furthermore, based on the stipulation of active epidemiological investigation under the Infectious Diseases Control Law, the director of PHCs decided to perform testing for asymptomatic non-close contacts in several facilities such as nursing homes and companies to facilitate early findings of elderly cases and to prevent chains of clusters.
3) Identification of infection sources

In parallel with correspondence with suspected cases and contacts, PHCs investigated the infection sources and transmission chains of laboratory-confirmed cases based on epidemiological information of laboratory-confirmed cases and the test results of contacts. The investigations were performed in cooperation with the responsible PHCs if a cluster formation was suspected among laboratory-confirmed cases living in different areas.

**Testing**

All testing was conducted at the Yamagata Prefectural Institute of Public Health. RNA was extracted from 200 μL of each specimen using a kit (High Pure Viral RNA Kit; Roche Diagnostics GmbH, Mannheim, Germany) according to the manufacturer’s instructions. Two sets of semi-quantitative real-time reverse transcription PCR targeted to the nucleocapsid protein were used for SARS-CoV-2 detection (19).

**Ethics approval**

The study was approved by the ethics committee of the Yamagata Prefectural Institute of Public Health (approval no. YPIPHEC 20-14).

**RESULTS**
**Testing**

During January 31 – May 31, 2020, we tested 2,738 specimens, of which 2,609 (95.3%) were throat or nasopharyngeal swabs and 129 were other specimens, including those missing information. The specimens were collected from a cumulative total number of 2,660 persons (Fig. 2). The 2,660 tests included 220 multiple tests (i.e., 194 persons received testing for 2–6 times until being confirmed as positive or definite negative) and 259 negative confirmation tests for laboratory-confirmed cases. Therefore, 2,181 individuals received testing in Yamagata during the study period. The testing rate was 202 individuals per 100,000 population.

**Transmission rate**

The 2,181 individuals divided into 1,253 suspected cases (median age: 43 years; interquartile range [IQR]: 29–65; females: 45.6%) and 928 contacts (median age: 50 years; IQR: 36–65; females: 59.2%) (Fig. 1). The transmission rate (95% confidence interval) of the suspected cases (0.9% [0.4–1.4]; 11 of 1,253 individuals) was lower than that of the contacts (6.3% [4.7–7.9]; 58 of 928 individuals). In terms of groups of contacts, the general transmission rate of households and non-households showed 22.6% and 3.6%, respectively (Table 1). However, the transmission rates of subdivided non-household groups varied. Rates were the highest for groups at bars (15.4%; 4/26 contacts), followed
by groups sharing time and space with friends (10.0%; 4/40), companies (4.2%; 13/309), nursing homes (3.0%; 7/231), medical institutions (0.8%; 1/128), and others (0%; 0/62).

Regarding contact situations, all household contacts were assigned as close-contact based on the criteria of the official manual (18) (Table 1). In contrast, non-household contacts were subdivided into 206 close contacts and 590 non-close contacts; secondary cases were mainly detected from close contacts. It is noteworthy that all the six cases of non-close contacts were symptomatic.

**Laboratory-confirmed cases**

During March 31 – May 4, 2020, 69 laboratory-confirmed cases were ascertained (Fig. 2). The notification rate of COVID-19 in Yamagata during this period was 6.4 cases per 100,000 population. Cases were found mainly in the first half of April. COVID-19 cases in Japan had also surged in the same period (Fig. 2).

The geographical distribution of the 69 cases is presented in Fig. 3. Because large clusters at nursing home A (8 cases; median age: 49 years; IQR: 41–67; females: 100%; Okura Village) and food processing facility B (12 cases; median age: 55 years; IQR: 47–58; females: 92%; Yonezawa City) were formed in Mogami and Okitama areas, respectively, the notification rates were higher than those of other areas (Fig. 3).
Characteristics of the 69 cases are shown in Table 2. Females in their 40s and 50s, mainly staff members of nursing home A and food processing facility B, were predominant. Symptomatic cases were 58 (84.1%; 95% CI 75.5–92.7) of the 69 cases. Fever, fatigue, and sore throat accounted for the top three symptoms concordantly in the three age groups. The finding of pneumonia was observed in four cases at the time of case findings. Finally, one fatal case was reported (case-fatality proportion 1.4%). Additionally, the median number of days from onset of symptoms to positive test in the symptomatic cases was 5 days (IQR 3–7 days).

**Transmission chains**

COVID-19 transmission chains based on the date of onset of symptoms are shown in Fig. 4. An epidemiological link (epi-link) was confirmed in 61 (88.4%; 95% CI 80.8–96.0) of the 69 cases. Case nos. 3, 10, and 34 were laboratory-confirmed cases found from suspected cases. Then, epi-links were identified. In the early epidemic period, a link with Tokyo, Kanagawa, or Miyagi was found for 14 cases. Thereafter, cases had been confirmed continually by active case findings and transmission chains persisted up to the fifth generation (case nos. 57, 58, and 68). The infection spread tended to show links between households and workplaces. Regarding workplace infections, case nos. 5, 10, 16, 24, and 54 had spread COVID-19 in their workplaces (i.e., nursing home A originating
from case no. 5, three companies including food processing facility B originating from case no. 16, and a clinic). In contrast, retrospective contact tracings by two PHCs revealed that case no. 34 had contacted case no. 3 and his family members at a business trip destination.

**Active case findings by PHCs**

We presented two instances related to active case findings to show details of efforts of PHCs in Yamagata.

1) Exhaustive active case findings in a hotel

Case no. 2, a hotel staff member, was suspected of SARS-CoV-2 infection based on a finding of pneumonia. Immediately after confirming his positive result, staff members of the Murayama PHC (PHC-M) performed a health observation and gave a cautionary notification of SARS-CoV-2 infection by telephone to 180 contacts including 48 groups of guests. The PHC-M urged self-quarantine for 14 days to 5 close contacts and 2 symptomatic non-close contacts. Simultaneously, the PHC-M invited the 5 close contacts and 26 non-close contacts (i.e., the 2 symptomatic non-close contacts and 24 hotel staff members) for testing. All 31 contacts accepted testing, yielding no positive case. Thereafter, health observation of the 180 contacts for 14 days was completed, except for one guest who refused contact from the PHC-M. Finally, laboratory-confirmed cases
were not detected among contacts of case no. 2.

2) Early detection of cases and clusters through cooperation of two PHCs

Case no. 10 was suspected of SARS-CoV-2 infection from his symptoms and a contact history with a friend from Tokyo. Retrospective contact tracings by the PHC-M revealed that the friend had also contacted others in the Okitama area. That information was conveyed immediately to the Okitama PHC (PHC-O). The PHC-O conducted testing of the close contacts and confirmed four cases in the early timing (case nos. 12, 14, 15, and 16). Furthermore, the PHC-O urged self-quarantine for contacts of the four cases and conducted testing of close contacts. Consequently, a cluster originating from case no. 15 and a cluster at food processing facility B originating from case no. 16 were confirmed. Thereafter, the PHC-O continually and widely administered testing of close contacts and some non-close contacts at food processing facility B. Finally, 11 cases were confirmed. Particularly, it is noteworthy that 10 cases were female staff members sharing a small, nearly airtight changing room.

Including those two instances, staff members of the five PHCs in Yamagata thoroughly and politely conducted 1) investigation of the infection sources and contacts of laboratory-confirmed cases based on retrospective contact tracing, 2) request of self-quarantine to close contacts, 3) health observation of close and non-close contacts for 14
days, 4) testing of close contacts irrespective of the presence or absence of symptoms, 5) testing of symptomatic non-close contacts, and 6) testing of asymptomatic non-close contacts in several facilities (e.g., nursing home A and food processing facility B) considering the possibility of severity of elderly contacts and chains of clusters. Almost all cases and contacts were cooperative with PHC investigations in Yamagata.

**DISCUSSION**

This report described the results of COVID-19 countermeasures applied in Yamagata during January–May 2020. In consequence of testing of suspected cases and contacts, 69 laboratory-confirmed cases were ascertained during March 31 – May 4, 58 (84.1%) of whom were found from contacts. Furthermore, an epi-link was identified in 61 (88.4%) of the 69 cases by thorough investigations of infection sources and transmission routes, suggesting that the chains of transmission were suppressed. Our results indicate that the identification of infection sources and active case finding from contacts based on retrospective contact tracing was likely to be an effective strategy to end the first wave of COVID-19 in Yamagata.

Active case finding from contacts was effective for COVID-19 control in Yamagata. To elucidate the circumstances of infection spread and to end each cluster in
the early timing, we performed testing of close contacts including asymptomatic persons and some non-close contacts. Consequently, most cases were identified from contacts. Furthermore, the proportion of epi-link findings obtained from this study (88.4%) was higher than that in local cases of Japan during January–March 2020 (63%) (5). Therefore, local PHCs that administrates areas of low population density (13,17) may have a significant advantage to conduct active case findings.

In contrast, testing of asymptomatic non-close contacts was regarded as controversial. Because the transmissibility of SARS-CoV-2 and prevention measures of COVID-19 were uncertain in our study period, PHCs performed testing of non-close contacts regardless of the presence of symptoms at several facilities. Consequently, we confirmed 6 cases from 590 non-close contacts, but all of them were symptomatic (Table 1). Therefore, testing of non-close contacts might be fundamentally restricted to symptomatic persons for detecting SARS-CoV-2 infected persons efficiently.

Suppression of human mobility may have generated a positive impact on preventing COVID-19 transmissions in local settings. The first wave of COVID-19 in Yamagata was triggered by persons who had an epi-link with the Tokyo metropolitan area or Miyagi (Fig. 4). However, inflow of SARS-CoV-2 from outside of Yamagata was not confirmed after the declaration of the state of emergency on April 7, 2020 (20).
Interruption of human mobility between epidemic and non-epidemic areas is likely to be a key factor in preventing the infection spread of COVID-19.

Individual measures at households might be important to prevent the transmission chains of COVID-19. This study showed the highest secondary attack rate in contacts of households. Furthermore, transmission chains from households to workplaces were observed multiply (Fig. 4). Previous studies have demonstrated that pre-symptomatic or asymptomatic persons can transmit COVID-19 (4,10,11). Moreover, initial symptoms are difficult to distinguish from those of the common cold (4,9) (Table 2). Individual measures in households such as quarantine of possibly infected person(s), wearing mask, and ventilation are desired when family member(s) might be infected with SARS-CoV-2 (7,21-23).

The methodology of a cluster-based approach for COVID-19 conducted in Japan (14–16) is quite similar to that used for tuberculosis (TB) control. In Japan, PHCs were established in 1937 with the primary mission of TB prevention (24). Even in modern times, TB control is an important mission of PHCs. Public health nurses of PHCs constantly perform testing of close contacts and investigation of infection sources of TB patients based on exhaustive retrospective contact tracings (25). Therefore, experiences of TB control in PHCs were likely to give positive effects to COVID-19 countermeasures
in Yamagata and perhaps in Japan (16).

Our study has some limitations. First, PHCs selected suspected cases from consulted persons who reported symptoms. Furthermore, a few contacts declined testing. Accordingly, this study might include undiagnosed SARS-CoV-2 infected persons.

Second, we were unable to analyze symptom data of suspected cases and contacts. Even though PHCs have been working in extraordinary circumstances during the pandemic, the symptom database should have been accumulated daily. The final limitation is that we investigated symptoms of laboratory-confirmed cases up to case findings (Table 2) because that is the period during which infection can occur. Although earlier reports have described that symptoms of a proportion of cases worsened after admission (9,26), this information is unclear from results of this study.

In conclusion, our results show that investigations of infection sources and active case findings from contacts can engender the early detection of SARS-CoV-2 infected persons, the elucidation of transmission chains, and the prevention of further spread of infection. Those countermeasures based on retrospective contact tracings might be one option to control COVID-19 during the early epidemic period.

Acknowledgments
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Conflict of interest

None to declare.
References


Figure legends

**Fig. 1** Flow chart of COVID-19 testing strategy.

**Fig. 2** Number of testing and laboratory-confirmed COVID-19 cases in Yamagata. COVID-19 cases in Japan (12) and periods of the declaration of the state of emergency (20,27) are also shown.

**Fig. 3** Geographical distribution of 69 laboratory-confirmed COVID-19 cases in Yamagata during March–May 2020. Prefectures in the map of Japan, which corresponded to Fig. 4, show locations of confirmed epidemiological links with laboratory-confirmed case(s).

**Fig. 4** Transmission chains of 69 laboratory-confirmed COVID-19 cases. Cases are shown by nodes with case numbers. The nodes are shown on the date of onset of symptoms, but those of 11 asymptomatic cases (*) along with case no. 66, whose date of onset was unclear, were shown on the date of confirmation minus 5 days (the median number of days from onset to positive test in symptomatic cases). Lines between cases represent epidemiological links. In clusters of three or more cases, a case showing symptoms on the earliest day and others are connected. Therefore, lines do not necessarily represent direct contact. ‘Tokyo’ denotes a person who came from Tokyo and contacted cases of the ends of the dashed line. ‘Kanagawa’ and ‘Miyagi’ denote that the cases
themselves came from or visited those prefectures. Locations of the three prefectures are presented in Fig. 3.
Table 1 Demographic composition of 928 contacts stratified by contact type

<table>
<thead>
<tr>
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<th>Secondary cases</th>
<th>Secondary attack rate</th>
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<td>Household</td>
<td>Non-household</td>
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<td>General transmission rate</td>
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<td>29/796</td>
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<td>20-39 years</td>
<td>6/32</td>
<td>10/213</td>
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<td>40-59 years</td>
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<td>60-79 years</td>
<td>3/18</td>
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<tr>
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<td>9/317</td>
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<td>23/206</td>
</tr>
<tr>
<td>Non-close contact</td>
<td>…</td>
<td>6/590</td>
</tr>
</tbody>
</table>

Data are laboratory-confirmed COVID-19 cases/total contacts or secondary attack rate (95% confidence interval).

1) All secondary cases are symptomatic.
| Table 2 Characteristics of laboratory-confirmed COVID-19 cases stratified by age groups |
|----------------------------------------|-----------------|-----------------|-----------------|-----------------|
|                                       | Age groups      |               |               | Total (n = 69)  |
| Median age                            | 21 (20–27)      | 52 (48–55)    | 75 (64–83)    | 49 (26–59)     |
| Sex                                    |                 |                |                |                 |
| Female                                 | 12 (50.0)       | 20 (71.4)      | 10 (58.8)      | 42 (60.9)      |
| Male                                   | 12 (50.0)       | 8 (28.6)       | 7 (41.2)       | 27 (39.1)      |
| Symptoms 1)                           |                 |                |                |                 |
| Fever                                  | 13 (54.2)       | 15 (53.6)      | 8 (47.1)       | 36 (52.2)      |
| Fatigue                                | 7 (29.2)        | 9 (32.1)       | 4 (23.5)       | 20 (29.0)      |
| Sore throat                            | 6 (25.0)        | 9 (32.1)       | 4 (23.5)       | 19 (27.5)      |
| Rhinitis                               | 6 (25.0)        | 6 (21.4)       | 2 (11.8)       | 14 (20.3)      |
| Cough                                  | 3 (12.5)        | 8 (28.6)       | 2 (11.8)       | 13 (18.8)      |
| Headache                               | 5 (20.8)        | 4 (14.3)       | 2 (11.8)       | 11 (15.9)      |
| Hypogeusia/hyposmia                    | 5 (20.8)        | 3 (10.7)       | 2 (11.8)       | 8 (11.6)       |
| Arthralgia                             | 2 (8.3)         | 4 (14.3)       | 6 (8.7)        | 6 (8.7)        |
| Sputum                                 | 3 (12.5)        | 3 (10.7)       | 6 (8.7)        | 6 (8.7)        |
| Anorexia                               | 2 (11.8)        |                | 2 (11.8)       | 2 (2.9)        |
| Diarrhea                               | 1 (3.6)         |                | 1 (1.4)        | 1 (1.4)        |
| Asymptomatic                           | 5 (20.8)        | 4 (14.3)       | 2 (11.8)       | 11 (15.9)      |

Data are years (interquartile range) or n (%).

1) At the time of case-findings.
Fig. 1

Suspected cases \((n = 1,253)\)
1. Patients showing fatigue and/or upper respiratory tract symptoms for approximately 1 week and pneumonia-like symptoms (i.e., fever \([37.5 \degree C \text{ or higher}]\) and/or lower respiratory tract symptoms) for approximately 2–4 days
2. Patients having a factor of infection exposure (e.g., travel history to epidemic regions) and any of the following symptoms: common cold symptoms for 4 or more days, a fever \([37.5 \degree C \text{ or higher}]\) for 4 or more days, severe fatigue, and difficulty breathing
3. Patients belonging to a high risk population (e.g., hospital staff members)

Consultation with public health centers
Reverse transcription PCR
Laboratory-confirmed cases \((n = 11)\)

Residents of Yamagata Prefecture

Close contacts*
Non-close contacts*

Retrospective contact tracings
Persons who contacted laboratory-confirmed cases from two days prior to the onset of symptoms until hospitalization.

Tested contacts \((n = 928)\)
Reverse transcription PCR

Retrospective contact tracings
Persons who contacted laboratory-confirmed cases from two days prior to the onset of symptoms (or from two days before virus detection in asymptomatic cases) until hospitalization.

Laboratory-confirmed cases \((n = 58)\)

*Classified based on the official protocol (ref. 18)
Fig. 3

( ) = cases/100,000 population of the region

Miyagi Pref.

Mogami

Shonai

Murayama

Okitama

Yamagata City

Tokyo

Kanagawa

Miyagi

Japan

Yamagata

Murayama

Shonai

Okitama

Yamagata City

( ) = cases/100,000 population of the region