



Original Article

Association of influenza outbreak in each nursery school and community in a ward in Tokyo, Japan[☆]Yoshiyuki Sugishita^{*}, Tamie Sugawara, Yasushi Ohkusa

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ABSTRACT

In nursery schools, influenza outbreaks have occurred every year. However, influenza characteristics of its diffusion among nursery schools, within each nursery school, and among classes of different ages in nursery schools remains unclear. This paper presents an examination of these matters using the Nursery School Absenteeism Surveillance System (NSASSy). All nursery schools in ward A in Tokyo introduced to the NSASSy in 2015. The study period was November 2015 through March 2016. The data of influenza patients were extracted from NSASSy. We examined four definitions of 'starting date of community outbreak' (SDCO) of influenza: 1) the first recorded day of influenza patients (SDCO1), 2) the last day of influenza patients recorded for two consecutive days (SDCO2), 3) three consecutive days (SDCO3), and 4) four consecutive days (SDCO4). We evaluated those four definitions by duration of the initial case at each nursery school from SDCO and evaluated the proportion of nursery schools at which the initial case occurred before SDCO. The average durations of initial cases at respective nursery schools from SDCO1–4 were 40.3, 26.3, 23.1 and 13.3 days. The respective proportions of nursery schools at which the initial case occurred before SDCO1–4 were 3.1%, 6.4%, 9.4% and 40.6%. Results demonstrate that SDCO3 is an appropriate definition of SDCO. Robustness checks for other areas, seasons, and population size constitute the next challenge for research in this area.

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1. Introduction

Influenza outbreaks occur every year. For example, the total number of patients in the 2009/10 season, with its A/H1N1pdm pandemic, was estimated as 9.2 million in Japan [1]. Moreover, some fertility cases caused by encephalopathy [2] or abnormal behaviors [3–5] were reported in children, even though elderly people are expected to be the most affected age class by influenza mortality [6].

In Japan, the children of working parents under six years old can attend nursery school. Because of aging in the Japanese society, both parents with children under six years old tend to work more. Actually, according to the Comprehensive Survey of Living Conditions in Japan, the Employment rate of mothers with children under one year of age increased to 42% in 2017 from 28% in 2005. This

change necessitates greater capacity of nursery schools. Therefore, new nursery schools have been constructed recently in Japan. With quantitative expansion, the quality of nursery schools is anticipated as the next challenge. Infection control is one factor reflecting nursery schools quality.

At nursery schools, influenza outbreaks occur every year. The highest incidence is well known to occur among nursery school-children [7]. It usually diffuses from students in elementary schools or junior high schools; then it comes to affect nursery schoolchildren [8]. However, how it diffuses among nursery schools remains unclear. Many infants of age 0 to 3 and young children of age 4 or 5 years live in nursery schools as a group. Usually, children of the same age belong to a class, but it remains unknown how influenza diffuses among classes of different ages in nursery schools.

Despite the existence of many surveillance programs based on school absenteeism established worldwide [9–14], the Nursery School Absenteeism Surveillance System (NSASSy) uses Japan's own unique nursery school culture: caregivers of children who are absent from nursery schools usually report their symptoms and

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diseases if the child has been diagnosed by a doctor to their nursery school.

Japan has a unique school system. According to the School Health and Safety Act, at all levels of schools except for nursery schools, when students are diagnosed with defined infectious diseases such as influenza, varicella, or mumps, schools must not allow students to attend classes. The absence is designated as “attendance prohibition attributable to infectious disease.” However, such nonattendance does not count as an official absence. Caregivers must notify the school if a child is diagnosed as having a defined infectious disease. Moreover, even if the child has not visited a doctor or has not been diagnosed with any defined diseases, then caregivers usually call the school and report the child’s symptoms, for instance, as fever, vomiting, or diarrhea. In such cases, schools do not apply “the attendance prohibition attributable to infectious disease”.

Nursery schools, however, are not classified as education institutions but as welfare facilities. Therefore, the School Health and Safety Act does not apply to nursery schoolchildren; so they do not fall under “the attendance prohibition attributable to infectious diseases” even if they were diagnosed with a defined infectious disease. Even if such a disease is not diagnosed or if the child did not visit a doctor, then nursery school child’s caregivers usually report the child’s health condition to the nursery school. Of course, the law does not obligate them to do so, but almost all nursery schools require caregivers to report based on the guideline from the Ministry of Health, Labour, and Welfare. Additionally, the culture, custom, or rule among schoolchildren’s caregivers might affect caregivers’ behavior because nursery school children might be little brothers or sisters of schoolchildren within a family.

Therefore, surveillance can be accomplished based on symptoms and diagnoses of diseases using information from caregivers. However, school surveillance in the remainder of the world [9–14] cannot similarly perform because they have no culture of notification by caregivers about the reason for absence. Therefore, at best, their school surveillance counts only the total number of absences, irrespective of the reason, or absences caused by illness or influenza-like illness.

For influenza in Japan, if children have influenza-like symptoms, then almost all of them visit a doctor, who will at least diagnose them using a rapid test. Subsequently, they report the results to nursery schools based on rapid tests, which are regarded as more reliable than clinical diagnosis without a rapid test or self-report of influenza-like illness. Sensitivities of the rapid test were estimated to be 54.4–91.6%. Specificities were estimated to be higher than 98% [15]. Nurses or other staff of nursery schools provided information to NSASSy via the internet. They register nursery school children’s diagnosed diseases into NSASSy at once for one episode, which is defined to be from onset to recovering or coming back to the nursery schools, in a school year. Therefore, duplication of registration of the same disease for the same children never occurs in the same school year. The NSASSy information is used by nursery schools themselves to recognize the situation in surrounding areas and to inform staff, children, and caregivers, thereby promoting precautionary measures if some outbreaks are reported in surrounding areas, but not at their own nursery school. The NSASSy information is also shared among schools, nursery school doctors, local government offices for nursery schools, public health centers, and local medical associations. That shared information encourages earlier awareness of infectious diseases, which engenders earlier responses to the initial stage of outbreaks in nursery schools. Moreover, having such a large trove of data related to children’s health facilitates large epidemiological studies [16–20]. It has been developed by the research group headed by Dr. Ohkusa, one author of this report, funded by the Ministry of Health, Labour and Welfare

since 2007 and has been keeping its copyright. Today in 2018, the system is operated by the Japanese Society of School Health and almost 10,000 nursery schools nationwide, accounting for approximately 40% of all nursery schools in Japan.

This paper presents an examination of how influenza diffuses among nursery schools, within each nursery school, and among classes of different ages in nursery schools using NSASSy. Then we consider the timing of community outbreak start and kick off of precaution intensively. This paper is the first of a study using daily data by age for all nursery schools in an area.

2. Materials and methods

This study was conducted in ward A, which is a special administrative area composed of 23 wards in metropolitan Tokyo with 141 thousand populations of all ages and 8.8 thousand in 0–5-year-old children in the 2015 Population Census. Ward A is located in an urban area in central Tokyo. All 32 nursery schools that satisfied establishment criteria regulated by the central government and which were approved by local government in ward A had introduced NSASSy in 2015. We used data compiled by NSASSy for 32 nursery schools.

The study period included data of November 2015–March 2016. The influenza patient refers to a person who was absent from the nursery school due to influenza. We defined an ‘outbreak’ of influenza at each nursery school as patients occurring continually without intervals longer than eight days. In other words, if no patient is reported for eight days, then we consider the outbreak as ceased. If a patient was diagnosed on one day, but no patients is reported thereafter during a period longer than eight days, then this case satisfies this definition of “outbreak”.

We examined four definitions of the ‘starting date of community outbreak’ (SDCO) of influenza for all nursery schools in ward A: 1) the first recorded day of influenza patients (SDCO1), 2) the last day of influenza patients recorded for two consecutive days (SDCO2), 3) three consecutive days (SDCO3), and 4) four consecutive days (SDCO4). To measure consecutive days, we excluded dates on which all nursery schools were closed, such as Sunday, national holidays, and 1–3 January. For example, if we have some patient on Saturday and the following Monday, then it was at least, but in truth more than, two consecutive days.

We evaluated the validity of those four definitions of SDCO by the duration of the initial case at each nursery school from the SDCO. Moreover, we tested it through the proportion of nursery schools at which the initial case occurred before SDCO. If the lead time of SDCO to the initial case in each nursery school was longer than one month, it might be too early to prevent infection. Conversely, if the lead time is shorter than one week, it might be difficult to prepare to prevent infection. Therefore, we prefer that it would be longer than two weeks and shorter than one month. However, to prepare precautions, we prefer a definition of SDCO that brings a lower proportion of nursery schools at which the initial case occurred before SDCO for many nursery schools.

We also examined diffusion from the initial case to a secondary case or other age/classes, especially infant classes in each nursery school and the length of outbreak at each nursery school. The length of outbreak at each nursery school was defined as the period from the initial case to the last case, during which there were no cases for eight days prior, twice the maximum incubation period, after the last case onset. For calculation of the outbreak length, we excluded some outbreaks during which total number of patients was only one. If some cases were observed at a nursery school after 23 March, 2016, we excluded those outbreaks to calculate the outbreak length because the last case of the outbreak cannot be confirmed with an eight-day interval. For diffusion from initial case

to other age/classes, we also excluded some outbreaks for which there was no case in an age/class other than the initial case. For diffusion from the initial case to infant age/classes, we also excluded some outbreaks for which there was no case in infant age/classes and for which the initial case occurred in the infant class.

Additionally, we calculated the length from the initial case to the last case until 31 March 2016 at each nursery school. Nursery schools with only one patient during the study period were excluded from calculation for length of outbreak. It might straddle multiple outbreaks at each nursery school. If some cases were observed in a nursery school after 23 March, 2016, we excluded those outbreaks from this calculation.

Infants were defined as age 0, 1, and 2 children. Classes in nursery schools were defined by age on 2 April for each school year. The school year in Japan was defined as extending from April through March of the following year. A class to which same-age children on second April belongs was denoted as the age/class.

The influenza cumulative incidence rate was defined as the number of children in some age/class as the denominator and the number of influenza patients in those classes as the numerator. Because NSASSy records absence days, we defined the initial date of absence caused by influenza as onset. We examined the age distribution of the initial case of influenza at each nursery school.

Data were obtained from NSASSy by the Public Health Center of ward A in Tokyo.

2.1. Ethical considerations

NSASSy includes only anonymous data that have been de-linked from individual patient information with no private information such as a name, address or phone number. Moreover, we used only the counted number of children. The “Ethical Guidelines for Medical and Health Research Involving Human Subjects” (Ministry of Education, Culture, Sports, Science and Technology and Ministry of Health, Labour and Welfare (22 December, 2014, revised in 28 February 2017)) were not applicable because this study satisfied its Chapter 1, 3) Coverage, 1) Applied study, c) Of samples or information, research using only

the following, 3) The anonymity processing information or non-identifying processing information that it has been already created before study. For that reason, no written informed consents or formal ethical review was required.

3. Results

The number of children in 32 nursery schools in ward A was 91.1 on average, 149 at maximum, and 44 at minimum. The numbers of infants were the following: children under three years old were 43.1 on average, 59 at maximum, and 21 at minimum. All 32 nursery schools had experienced more than one influenza outbreak during the study period. Moreover, 24 nursery schools had experienced multiple outbreaks: twice in 10 nursery schools, three times in 9, four times in 3, and five times in 2. In total, 77 outbreaks occurred at 32 nursery schools. Of those, 26 outbreaks had only one patient during the outbreak.

Fig. 1 depicts the influenza epidemic curve for all 32 nursery schools from November 2015 through March 2016 and the SDCO by four definitions. Results show that SDCO was 15 December for SDCO1, 31 December for SDCO2, 4 January for SDCO3, and 21 January for SDCO4.

Table 1 presents the duration of the initial case at each nursery school from the SDCO and the proportion of nursery schools at which the initial case occurred before SDCO according to four definitions of SDCO. The former data do not include the nursery schools that satisfied the definition of SDCO, but the latter data include those nursery schools. The average duration of the initial case at each nursery school from SDCO1 was 40.3 days. By definition, at least one nursery school, which had the first influenza patient in ward A, the day that the initial case occurred should be SDCO1. The proportion of nursery schools at which the initial case occurred before SDCO1 was 3.1%.

The average duration of the initial case at each nursery school from SDCO4 was 13.3 days. Moreover, the proportion of nursery schools at which the initial case occurred before SDCO4 was 40.6%.

The average duration of the initial case at each nursery school from SDCO2 was 26.3 days. Similarly, the average duration of the

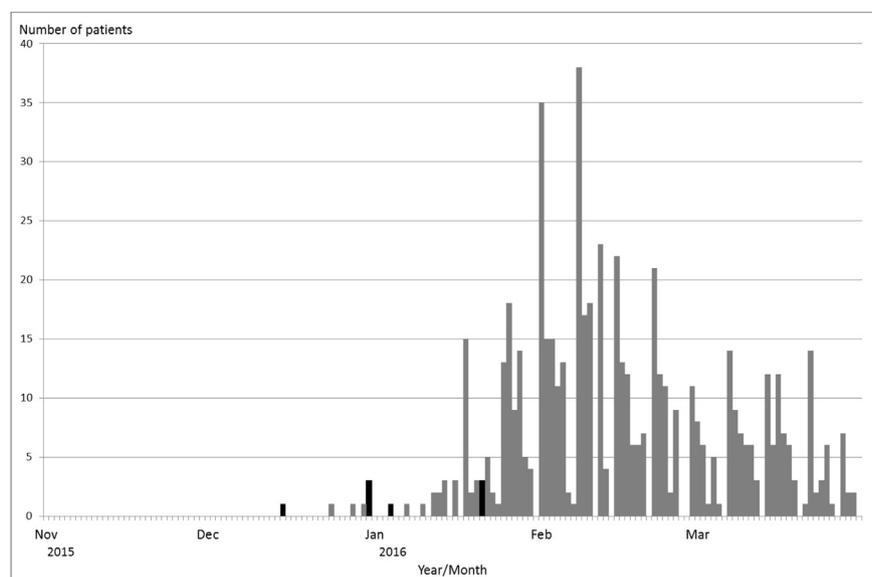


Fig. 1. Influenza epidemic curve for all nursery schools and starting dates of community outbreak in ward A in Tokyo, November 2015–March 2016. Note: The bars of the influenza patients were shown at the first day of absence caused by influenza after diagnosis for all nursery schools in ward A: the black bar denoted the first recorded day on 15 December, the last day of influenza patients recorded for two consecutive days on 31 December, three consecutive days on 4 January, and four consecutive days on 21 January. The x axis of this figure included Sundays, national holidays, and the New Year vacation of January 1–3. However, the definition of ‘consecutive days’ excluded those nursery schools’ closed days.

Table 1
Duration of the initial influenza case in each nursery school from the 'starting date of community outbreak' (SDCO) of influenza and the proportion of nursery schools at which the initial case occurred before SDCO by four definitions of SDCO.

Definition of SDCO	Duration of the initial case at each nursery school from the SDCO			Number and proportion of nursery school at which initial case occurred before SDCO	
	Number of days			N	%
	Average	Maximum	Minimum		
First recorded day	40.3	84	9	1	3.1
Two consecutive days	26.3	68	4	2	6.4
Three consecutive days	23.1	64	3	3	9.4
Four consecutive days	13.3	48	2	13	40.6

Note: The four definitions of 'starting date of community outbreak' are as follows: 1) the first recorded day of influenza patients in the second row, 2) the last day of influenza patients recorded for two consecutive days in the third row, 3) three consecutive days in the fourth row, and 4) four consecutive days in the last row. "Duration of the initial case at each nursery school from the SDCO" does not include the nursery schools which satisfied the definition of SDCO, but "Number and proportion of nursery school at which initial case occurred before SDCO" includes those nursery schools.

initial case at each nursery school from SDCO3 was 23.1 days. In addition, the proportion of nursery schools at which the initial case occurred before SDCO was 6.4% in the former and 9.4% in the latter. Therefore, we regard SDCO2 and 3 as apparently not different, but better than SDCO1 or SDCO4.

Table 2 presents the diffusion of influenza outbreaks at each nursery school. There were 44 outbreaks, excluding some outbreaks in which the total number of patients was only one and in which the last case of the outbreak cannot be confirmed with an eight-day interval. The average duration from the initial case to the secondary cases in the same nursery school was 3.0 days. The average duration from the initial case to the other age class was 3.9 days. The average duration from the initial case to the infant class was 6.6 days. The average length of outbreak was 14.4 days. The average duration from the initial case to the last case was 42.0 days.

Fig. 2 depicts cumulative incidence rate by age. The highest rate was observed in the age 4 class, followed by the age 5 class. In total, the cumulative incidence rate in all ages at all nursery schools was 18.2%. Fig. 3 portrays the age distribution of the initial case at each nursery school by age/class. The highest was the age 2 class, followed by ages 3 and 5. Results show that the initial case at each nursery school occurred frequently in the age 2 class.

4. Discussion

Results show that SDCO2 and 3 are apparently not different, but better than either SDCO1 or SDCO4 and demonstrate that more

than three weeks passed from SDCO2 or SDCO3 to the initial case at each nursery school, on average. Results also demonstrate that the cumulative incidence rate was higher at ages 4 and 5 and that the average duration from the initial case to secondary cases in the same or other class was approximately three to four days.

Three weeks passed from SDCO2 or SDCO3 to the initial case at each nursery school, which might be sufficient lead time to prepare precautions for influenza, including hand washing and respiratory etiquette. However, the guidelines for influenza vaccination for children under 13 years old recommend vaccination twice at four-week interval [21]. Consequently, if children receive the first dose before SDCO, then the receipt of the second dose warrants a reminder and appropriate enforcement. If not, then a child probably will not receive second dose at the four-week interval before timing that the initial case will occur at their nursery school.

The lead time in SDCO1 was longer than one month, which is apparently too early. Conversely, the proportion of nursery schools at which the initial case occurred before SDCO4 was greater than 40%. It is apparently too late.

Although NSASSy started in November 2015 in ward A, Tokyo, some nursery schools had already joined the system before that date. Actually, some influenza patient data were recorded in October. From our analyses, data of those cases were excluded. However, if those cases were included into the analyses explained above, then SDCO1 or SDCO2 would be identified in October. In these cases, the duration from SDCO to the initial case at each nursery school cannot help becoming very long. Therefore, the

Table 2
Diffusion of influenza outbreaks at each nursery school.

Number of days	Duration of diffusion in the same nursery school			Length of an outbreak at each nursery school*4	Length of initial case to final case *5
	From initial case to the second case*1	From initial case to other age/classes*2	From initial case to infant class*3		
Average	3.0	3.9	6.6	14.4	42.0
Maximum	8	10	33	44	75
Minimum	0	1	1	1	2

Note: Duration of an outbreak at each nursery school was defined as from the initial case to the last case for which there was no case for eight days, twice of maximum incubation period, and after the last case onset.

*1–*4 Some outbreaks for which the total number of cases was only one were excluded from calculation. If some cases were observed in a nursery school after 23 March, 2016, we excluded those outbreaks from calculation because the last case of the outbreak cannot be confirmed with an eight-day interval.

*1 There were 44 outbreaks to calculate.

*2 There were 35 outbreaks to calculate in which there were diffused cases in other age/classes from the age/classes where the initial case had occurred in the same nursery school.

*3 Infants were defined as age 0, 1, and 2 children. Some outbreaks in which infants were not infected at all or the initial cases occurred in infant class were excluded to calculate these statistics. There were 20 outbreaks to calculate.

*4 There were 44 outbreaks to calculate.

*5 It shows the length of the initial case to final case until the end of March 2016. Nursery schools with only one patient were excluded from calculation. If some cases were observed in a nursery school after 23 March, 2016, we exclude those outbreaks from calculation. There were 28 nursery schools to calculate. The period might straddling multiple outbreaks at each nursery school, and 20 nursery schools had experienced multiple outbreaks.

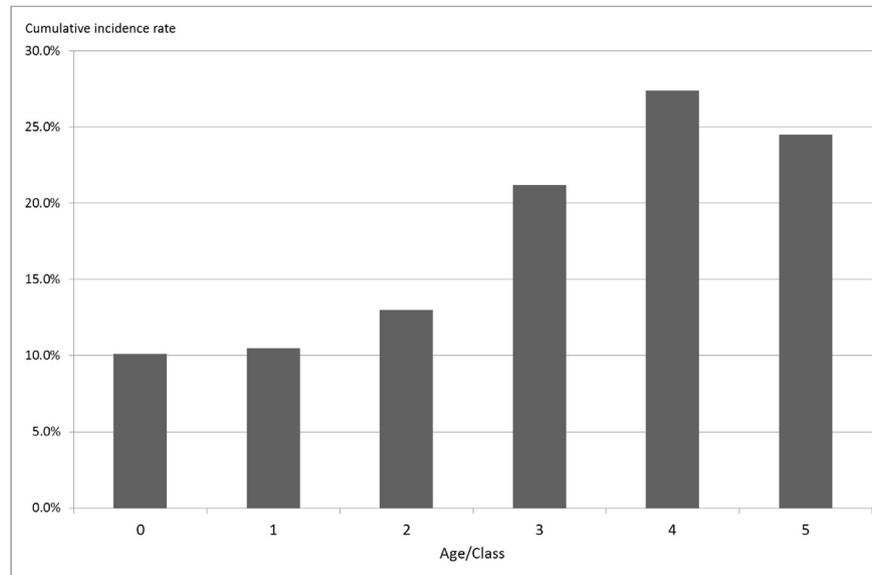


Fig. 2. Cumulative incidence rate of influenza by age at all nursery schools in ward A in Tokyo, November 2015–March 2016. Note: A class to which same-age children on second April belongs was denoted as the age/class. The cumulative incidence rate was defined as the number of all children in a nursery school with the denominator and the number of influenza patients in the nursery school as the numerators. In total, the cumulative incidence rate in all age at all nursery schools was 18.2%.

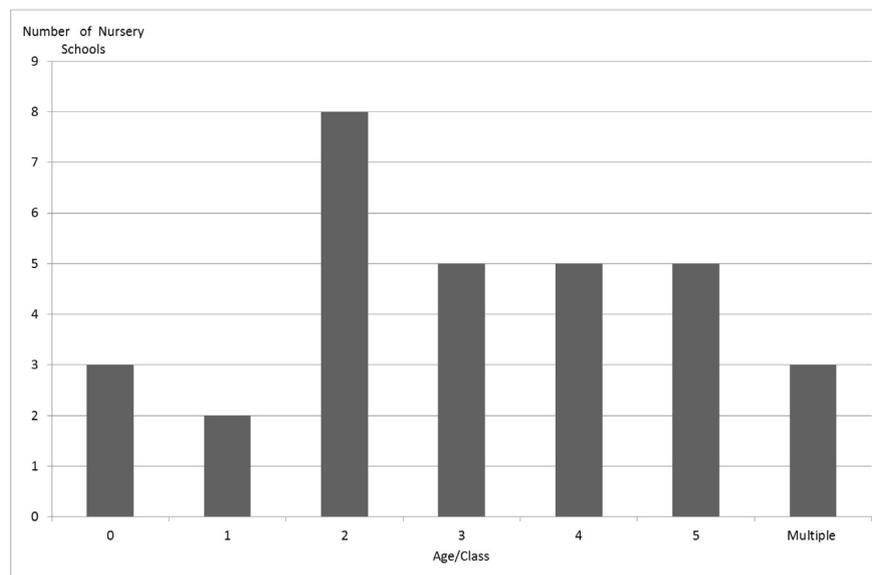


Fig. 3. Age distribution of the initial case of influenza in each nursery school in ward A in Tokyo, November 2015–March 2016. Note: A class to which same-age children on second April belongs was denoted as the age/class. 'Multiple' means that the initial case occurred in multiple age/classes in a nursery school on the same day. It included classes of ages 1 and 3, 2 and 5, 3 and 5, and 4 and 5.

validity of those definitions of SDCO should be discounted heavily. Conversely, SDCO3 and SDCO4 would be unaffected even if data in October were included. In this sense, SDCO3 is the most appropriate definition of SDCO.

As revealed by earlier research [8], influenza diffuses from junior high school students to elementary school students and eventually to nursery school children. We can infer that children at those ages are closely related to students in kindergarten or elementary schools in family as siblings or playmates. For that reason, they might be affected strongly by an outbreak at kindergarten or elementary school. However, we also found that children in age two classes were infected much earlier at each nursery school. We cannot confirm the reason for that result, but it

might be explained by age-related tendencies of physical contact and hygiene. We must confirm the validity of this phenomenon in other area than A ward.

Three to four days durations from the initial case to secondary cases in the same or other classes is apparently almost equal to the average length of the incubation period. Our findings suggest that insufficient time exists to cease playing with playmates of different ages or to rearrange of working schedules of caregivers when the initial case at each nursery school is detected. At that time, secondary cases have already been infected, but they are at incubation period. For those secondary cases, it is possible that no measure will be effective against infection after the initial case is detected at each nursery school. Therefore, nursery schools

should take measures, such as abandoning play with children of different ages or rearrangement of working schedule of caregivers, after SDCO but before the initial case in each nursery school is detected.

Infants and young children are quite different in the respect of independent use of a lavatory or hand-washing as well as physical capacity or immunization status. Consequently, measures for contact infection are difficult with infants. Moreover, mask wearing is apparently difficult for them unlike younger children. Therefore, countermeasures against droplet infection are also difficult for infants. Our findings revealed that the duration from the initial case to diffusion in infant classes is approximately seven days. Any measure for infection after the initial case in each nursery school is detected might be ineffective to protect infants. Therefore, nursery schools should take measures to protect infants after SDCO but before the initial case in each nursery school is detected. Particularly, it might be more important because of risks of encephalitis and encephalopathy posed to infants by influenza.

The average length of the initial case to the last case at each nursery school was found to be six weeks. However, this length was defined until the end of March. If an outbreak continues even after April or May, this length might become longer than six weeks. Information on the incidence period of influenza helps to understand when careful observation of the child's health condition is needed. By knowing the standard of the incidence period of influenza, the caregivers can prepare to change the working schedules.

Because we cannot trace outbreaks at nursery schools across school years at the end of March, we excluded some outbreaks that showed cases after 23 March, 2016. If we regard the final case after 23 March, 2016 as the last case of the outbreak, even though there was no longer than an eight-day interval, then seven outbreaks might be added to Table 2. If so, the numbers in averages of Table 2 would change from 3.0 to 3.2, 3.9 to 4.1, 6.6 to 6.3, 14.4 to 15.3, and 42.0 to 52.3. Except for the last column, averages in Table 2 remain almost unchanged. Our findings and evaluation were therefore no meaningfully affected by the seven restored outbreaks. However, the length of the initial case to the final case alone was affected. It was extended more than ten days. Even so, our main findings and conclusions are apparently unaffected.

As described above, an 'outbreak' of influenza at each nursery school was defined as patients occurring continually without longer intervals than eight days. That interval length of eight days, was decided as twice the maximum incubation period following WHO criterion [22]. This definition allows an outbreak with only one patient. It might be an overly small number for influenza. However, because the purpose of this study was earlier detection of outbreaks and appropriate kicking off of intensive precaution, we pretend to classify only one case as an outbreak.

This study has some limitations. First, because we analyzed one ward in Tokyo, we cannot apply the obtained results to all of Tokyo or other prefectures, even in Japan. We must check the robustness of the obtained result for other seasons, other areas, and other population sizes.

Another limitation is that we did not use some information for outbreaks at schools. As an earlier study showed [8], influenza diffuses from higher ages to younger ages among children. Therefore, information related to outbreaks in schools is expected to be useful for nursery school children. Finally, because information related to vaccine coverage in nursery school children was unavailable, we cannot control the situation of immunization in nursery schools. If it was available, then we could estimate vaccination effects of influenza vaccine in a nursery school situation; it also might improve to precision of SDCO. Elucidating those points remains as a challenge for future research.

5. Conclusion

We concluded that since the last day of influenza patients recorded for three consecutive days among nursery school children, community outbreak among nursery schools had started. Nursery schools and families should start precautionary measures intensively at that day. We also showed the duration from the initial case to the secondary cases in the same or other classes, or to other classes were almost equal to the average or maximum length of the incubation period. Robustness confirmation for other areas, seasons, and population sizes remain as challenge for future research.

Conflicts of interest

No author has any conflict of interest, financial or otherwise, to declare in relation to this study.

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