Comparative assessment of primary and secondary infection risks in a norovirus outbreak using a household model simulation

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ABSTRACT

Diarrheal diseases can be transmitted via both primary infection due to exposures to contaminated materials from the environment and secondary infection due to person-to-person contacts. Usually, the importance of secondary infection is empirically assessed by fitting mathematical models to the epidemic curves. However, these empirical models may not be applicable to other epidemic cases because they are developed only for the target epidemics and they don't consider the detail routes of infection. In our previous study, we developed a theoretical model taking into account the various routes of infection that commonly occur in households (*e.g.*, shaking hands, food handling, and changing diapers). This model was made flexible and applicable to any epidemics by means of adjusting model parameters. In this study, we proposed a new index "Vulnerability indicator to secondary infection (VISI)", which expressed a ratio of secondary infection to primary infection risks and calculated this index in a simulated *norovirus* (NoV) epidemic that involved 10,000 households. The results demonstrated that households composed of more than three members including infant(s) had much higher levels of VISI (5–45) than two-member-households with VISI (0.1–4). These results concluded that the infants were likely to be a hub of secondary infections in highly dense families and therefore careful handling of diapers was deemed indispensible in such families to effectively control the secondary infections.

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Introduction

Diarrheal disease is one of the largest causes of death and burden of disease in the world. The World Health Organization (WHO) reports 1.8 million people die of diarrheal diseases per year (Water, Sanitation, and World Health Organization, 2004). A large part of diarrheal diseases occur via waterborne infection and cases of such waterborne infectious diarrheas

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still have been reported not only in developing but also in developed countries (Craun et al., 2006). Considering the spread of infectious diarrhea, several studies claim that secondary infections due to person-to-person contacts are more important than primary infections caused by exposures to contaminated materials in the environment (Glass et al., 2009; Solano et al., 2014). To assess the impacts of various infection routes, quantitative microbial risk assessment (QMRA) is highly effective. However, with respect to diarrheal diseases, there have been few risk assessments of secondary infections, whereas risk assessment pertaining to primary infection has been frequently conducted (Ten Veldhuis et al., 2010; Schets et al., 2011).

In our previous study, we developed a theoretical model taking into account the various routes of secondary infections (e.g., shaking hands, food handling, and changing diapers) which often occur in households (Miura et al., 2014). This model was based on the Quantitative Microbial Risk Assessment (QMRA) and could estimate the number of infected persons via each infection route. In the current study, we proposed a new index "vulnerability indicator to secondary infection (VISI)" to reveal the relative risk of secondary infection to primary infection, based on the model application to an epidemic of infectious diarrheal diseases. Furthermore, this study demonstrated the significance of secondary infection compared to primary infection by computing this index in a simulated norovirus (NoV) epidemic.

1. Materials and methods

1.1. Household model

We used a "household model" to evaluate the risks of primary and secondary infections within a household, especially focusing on the transmission of pathogens through hand-to-hand touching. Here "household" was defined as one family where all the people live together in one house and there is at least one parent. Its constituents were classified into four types: "father", "mother", "child" and "baby" defined as an infant who wears a diaper. Other household members (grandparents, relatives, visitors, etc.) were not considered in the model for simplification. The family structure was denoted as "family type" for each household in this study, and was identified using a four digit number format, with each number standing for respective numbers of father, mother, children and babies in the household. For example, family type.1121 refers to a family with one father, one mother, two children, and one baby.

We classified all persons into either "susceptible" or "infected" status in the simulation. Non-infected persons were considered susceptible to pathogens from contaminated environment and infected persons. The persons in "infected" status were further classified into those due to primary and secondary infections. In this study, the secondary infection was limited to the infection caused by "family members" while the infection from outside of household was neglected. Moreover, the route of "primary infection" was limited to contaminated oysters which are suspected as one of the largest factors of NoV epidemics (Nishida et al., 2003; Le et al., 2006).

We considered the following four possible routes of secondary infections in the model: (1) Infected person's feces–Infected person's hands–Foods–Susceptible person's mouth; (2) Infected person's feces–Infected person's hands–Susceptible person's hand–Susceptible person's mouth; (3) Infected person's feces–Susceptible person's hands–Foods–Susceptible person's mouth; (4) Infected person's feces–Susceptible person's hands–Susceptible person's mouth.

In these routes, we considered virus reductions by three different hand-washing methods (washing with hand soaps, washing with only water and no washing) during daily six routines (after using the toilet, before meals, before snacks, before cooking, after changing diapers, before feeding) as shown in Tables 2 and 4.

We set several assumptions in the model. First, an infected person was able to be infected redundantly, because of the diverse genetic types of NoV that could cause redundant infections by overcoming the immune system (Glass et al., 2009). Second, the difference in human blood types was not considered although it was known to influence the immunity systems against NoV infection (Choi et al., 2008), because the dose–response model can't distinguish different blood-type patients and there is only one dose–response model for NoV. Third, although NoV mainly transmits via both fecal–oral and vomit–oral routes, only the former route was involved in our model prediction; because the simulation of vomiting occurrences with their time-spatial randomness was appeared to be too much complicated.

1.2. Model parameters

Values of model parameters have been estimated on the basis of existing literature, our questionnaire survey and laboratory experiments (Tables 1, 3, and 4). There is a lack of data (e.g., Norovirus emission) for Japan. Thus we referred to values from different countries in this study. In general, QMRA is conducted following the stochastic processes through probability distributions of model parameters in the modeled infection events. In this study, however, we did not consider the probability distributions of parameters due to a small number of data used for the parameter estimation, and the mean values for each parameter were used instead. The mean value of NoV concentration in feces was 107 copy/gas given in previous studies (Ozawa et al., 2007). Virus shedding from patients is dependent on their symptom and elapsed time since the onset of infection but we set a continuous shedding of the constant number of virus for 7 days in the simulation (Ludwig et al., 2008). Besides, the exposures from all infection routes were estimated and integrated, and then the infectious status was judged at the end of the day.

For the parameter estimation, because of their region-dependency, we conducted a questionnaire survey using mailing service to ask family members' habits (e.g., frequencies of touching with others, changing diapers, hand washing, etc.) at randomly selected 500 households with two generations or less. The response rate was found to be 12.6%.

In addition to the above parameters, the doses of NoV due to exposure to contaminated oysters were set to 100 copy/day for mother and father, 50 copy/day for children and 0 copy/day for babies. We supposed that each oyster contains 102 copy/day

Table 1 – Equations for dose calculations from each infection route.

	Equation	Notes
(a) Value of feces transference from a diaper to a hand per day (g/day)	$A_d(i) = V_d \times F_d(i)$	V_d: Deposit by changing a diaper (g) $F_d(i)$: Frequency of changing diapers (num/day)
(b) Value of feces transference from own feces to wiping hand per day (g/day)	$A_e(i) = V_e \times F_e$	V_e: Deposit by wiping own feces (g) F_e: Frequency of diarrhea (num/day)
(c) Transfer rate from person(i)'s hand to person(j)'s hand (–)	$T_{hh}(i) = t_{hh} \times f_{hh}(i\text{–}j)$	t_{hh}: NoV transfer rate from hand to hand (–) $f_{hh}(i\text{–}j)$: Frequency of contact(between person(i) and (j)) (num/day)
(d) Transfer rate from person(i)'s hand to food (–)	$T_{hf}(i) = t_{hf} \times f_{hf}(i)$	t_{hf}: NoV transfer rate from hand to food (–) $f_{hf}(i)$ is classified in following four parameters. $f_c(i)$: Frequency of cooking (person(i)) (num/day) $f_g(i)$: Frequency of eating with hands (meals) (num/day) $f_s(i)$: Frequency of eating with hands (snacks) (num/day) $f_f(i)$: Frequency of feeding (num/day)
(e) Transfer rate from food to person(i)'s mouth (–)	$T_{fm}(i) = t_{fm} \times f_{fm}(i)$	t_{fm}: NoV transfer rate from hand to food (–) $f_{fm}(i)$ is classified in following three parameters. $f_m(i)$: Frequency of eating with hands (meals) (num/day) $f_s(i)$: Frequency of eating with hands (snacks) (num/day) $f_f(i)$: Frequency of feeding (num/day)
(f) Transfer rate from person(i)'s hand to person(i)'s mouth (–)	$T_{hm}(i) = t_{hm} \times f_{hm}(i)$ when $f_{hm}(i) = m_{hm}(i) \times h_{hm}(i)$	t_{hm}: NoV transfer rate from hand to mouth (–) $f_{hm}(f/m/c)$: Frequency of mouthing (Mother, Father and Child) (num/day) $f_{hm}(b)$: Frequency of mouthing (Baby) (num/day) $m_{hm}(f/m/c)$: Frequency of mouthing (Mother, Father and Child) (num/hr) $m_{hm}(b)$: Frequency of mouthing (Baby) (num/hr) $h_{hm}(f/m/c)$: Active time (Mother, Father and Child) (hr/day) $h_{hm}(f/m/c)$: Active time (Baby) (hr/day)
(g) NoV Remaining rate of hand washing (–)	$T_w(i) = (t_{ww} \times p_{xw}(i) + t_{ws} \times p_{xs}(i)$ $+ t_{wn} \times p_{xn}(i)) \times f_w(i)$ ※ p_x: same timings as f	t_w: NoV Remaining rate of each hand-washing (–) ※t_w stands for only water(t_{ww}), soap(t_{ws}) and nothing(t_{wn}) $p_x(i)$: percentages of each method of hand-washing $f_w(i)$ is classified in following six parameters. $F_d(i)$: Frequency of changing diapers (person(i)) (num/day) F_e: Frequency of diarrhea (num/day) $f_m(i)$: Frequency of eating with hands (meals) (num/day) $f_s(i)$: Frequency of eating with hands (snacks) (num/day) $f_c(i)$: Frequency of cooking (num/day) $f_f(i)$: Frequency of feeding (num/day)

of NoV, a detection limit by a PCR method (European Food Safety Authority, 2012). The duration of eating raw oysters was set at 120 days based on the period of oyster harvesting in Japan (from November to February).

1.3. Simulation and risk assessment

In the developed model, daily behaviors and customs of each individual were simulated for one year starting from November 1st, then each person's doses due to primary and secondary exposures were evaluated. The dose due to primary exposure was calculated using the following Eq. (1):

$$D_1 = C_1 \times V_1 \times F_1 \qquad (1)$$

where, D_1 (NoV copy/day is the daily dose of NoV due to primary exposure, C_1 (NoV copies/g) is the NoV concentration in oysters, V_1 (g/num) is the weight of oyster and F_1 (num/day) is the daily consumption of oysters. The dose due to secondary exposure was calculated using the following Eq. (2):

$$D_2 = C_2 \times A \times T \qquad (2)$$

where, D_2 (NoV copies/day) is the dose of NoV due to secondary exposure, C_2 (NoV copies/g) is the NoV concentration in feces, A (g/day) is the weight of feces transferred to hand per day, and T is the transfer rate of virus (–) which is calculated by multiplying its components as $Thh \times Thf$ in one infection route (Table 2).

We calculated the respective risks of primary and secondary infections for each person per day using a dose–response model based on estimated doses (Teunis et al., 2008). Then, we judged the infection status of each simulated person by means of the Monte Carlo method. This one-day simulation had been continued for 365 days and repeated for 10,000 times per family type in order to obtain the statistically stable outputs of infection risk. The initial number of patients was set as zero.

For the comparative assessment of primary and secondary infection risks, we separately calculated probabilities that one person had been infected via the primary and secondary routes at least once during the simulation period, respectively. Similarly, in case of risk assessment for the whole family level, we calculated the primary (Ph1) and secondary infection risks (Ph2) of a household. The risks at family-level were defined as probabilities that any members in a given family

Table 2 – Value of parameters based on references.

	Symbol	Value	Reference	Note
NoV concentration in feces (NoVcopies/g)	C_2	10^7	Ozawa et al. (2007)	–
NoV emission period (day)	–	7	Ludwig et al. (2008)	–
Immunity (–)	–	Excluded	–	–
Latent status and latent period (–)	–	Excluded	–	–
Dose–response model	–	$P_{inf}(d) = 1-(1+\frac{d}{\beta})^{-\alpha}$ $\alpha = 0.631, \beta = 6.50 \times 10^5$	Teunis et al. (2008)	Premise: all family member's blood types are Se+
Deposit by changing a diaper (g)	V_d	0.1	Gibson et al. (2002)	–
Deposit by wiping own feces (g)	V_e	0.01	–	Lab-data (in preparation)
NoV transfer rate from hand to mouth (–)	t_{hm}	0.35	Nicas and Best (2008)	*Influenza A virus*
NoV transfer rate from hand to hand (–)	t_{hh}	0.16	Chen et al. (2001)	*Enterobacter*
NoV transfer rate from hand to food (–)	t_{hf}	0.16	Chen et al. (2001)	*Enterobacter*
NoV transfer rate from food to mouth (–)	t_{fm}	1	–	–
NoV Remaining rate of washing by triclosan-antibacterial soap [–]	t_{ws}	0.13	Gibson et al. (2002)	*E. coli*
NoV Remaining rate of washing without a soap (–)	t_{ww}	0.32	Bloomfield (2001)	*E. coli*
NoV Remaining rate of non-washing (–)	t_{wn}	1	–	–
Frequency of diarrhea (num/day)	F_e	6.5	Cheng et al. (2010)	*Norovirus*
Frequency of mouthing (Mother, Father and Child) (num/hr)	m_{hm}	8	Nicas and Best (2008)	–
Frequency of mouthing (Baby) (num/hr)	m_{hm}	19	Xue et al. (2007)	This value is the mean value from 6-month children to 6-years-old children
Activity time (Mother, Father and Child) (hr/day)	h_{hm}	16	National Heart, Lung, and Blood Institute (2005)	–
Activity time (Baby) (hr/day)	h_{hm}	8	National Heart, Lung, and Blood Institute (2005)	–
Frequency of cooking (Father) (num/day)	t_{hf}	0.16	–	Results of questionnaires
Frequency of cooking (Mother) (num/day)	t_{hf}	3	–	Results of questionnaires
Frequency of cooking (Child) (num/day)	t_{hf}	0.31	–	Results of questionnaires
Frequency of cooking (Baby) (num/day)	t_{hf}	0	–	Premise
Frequency of eating (All) (num/day)	f_m	3	–	Premise

type had been infected by either of the primary or secondary exposure at least once during the simulation period.

We proposed a new index of Vulnerability Indicator to Secondary Infection (VISI) as follow Eq. (3):

$$\text{VISI} = \frac{Ph2}{Ph1} \qquad (3)$$

This index expressed the ratio of secondary infection to primary infection risks at the family-level. There must be an association between primary and secondary infections and therefore the impact of secondary infection needs to be evaluated comparing with the primary infection. Actually, this equation was similar to a "secondary attack rate (SAR)", which was the ratio of secondary to primary cases and used in epidemiological surveys (Glass et al., 2009). However, SAR was calculated only by using the number of cases surveyed in actual epidemics and sometimes included uncertainties owing to difficult identification of secondary cases separately from primary cases. Moreover, asymptomatic cases had been excluded in the calculation of SAR, although they might shed viruses as well as symptomatic cases. Another disadvantage of SAR was that this index based on a specific epidemic could hardly be generalized for other places. On the other hand, VISI could be applied to any places if the parameters had been changed according to the target place.

Table 3 – Frequencies of person-to-person contact via touching, eating with hands, changing diapers and feeding within a household, estimated by the questionnaire survey (N = 58).

Route		Classification	Symbol	Value
Frequency of touching (day^{-1})	Father–Mother	–	$f_{hh}(f,m)$	1.2
	Father–Child	–	$f_{hh}(f,c)$	2.6
	Father–Baby	–	$f_{hh}(f,b)$	5.2
	Mother–Child	–	$f_{hh}(m,c)$	5.9
	Mother–Baby	–	$f_{hh}(m,b)$	8.4
	Child–Baby	–	$f_{hh}(c,b)$	6.5
	Child(1)–Child(2)	–	$f_{hh}(c,c')$	3.5
Frequency of eating with hands (day^{-1})	Father	Meals	$f_g(f)$	0.9
		Snacks	$f_s(f)$	1.4
	Mother	Meals	$f_g(m)$	1.0
		Snacks	$f_s(m)$	1.7
	Child	Meals	$f_g(c)$	1.6
		Snacks	$f_s(c)$	2.1
	Baby	Meals	$f_g(b)$	0.0
		Snacks	$f_s(b)$	0.0
Frequency of changing diapers (day^{-1})	Father	–	$F_d(f)$	0.8
	Mother	–	$F_d(m)$	5.8
	Child	–	$F_d(c)$	0.0
	Baby	–	$F_d(b)$	0.0
Frequency of feeding (day^{-1})	Father	–	$f_f(f)$	1.0
	Mother	–	$f_f(m)$	3.0
	Child	–	$f_f(c)$	0.0
	Baby	–	$f_f(b)$	0.0

Table 4 – Percentages of persons' washing hands estimated by the questionnaire survey (*n* = 58).					
	Timing	Symbol	Nothing(–)	Only water (–)	Soap (–)
Father	After using the toilet	$p_{en,ew,es}(f)$	0.10	0.74	0.17
	Before meals	$p_{mn,mw,ms}(f)$	0.29	0.38	0.33
	Before snacks	$p_{sn,sw,ss}(f)$	0.64	0.33	0.02
	Before cooking	$p_{cn,cw,cs}(f)$	0.04	0.57	0.39
	After changing diapers	$p_{dn,dw,ds}(f)$	0.50	0.00	0.50
	Before feeding	$p_{fn,fw,fs}(f)$	0.00	1.00	0.00
Mother	After using the toilet	$p_{en,ew,es}(m)$	0.00	0.60	0.40
	Before meals	$p_{mn,mw,ms}(m)$	0.13	0.51	0.36
	Before snacks	$p_{sn,sw,ss}(m)$	0.38	0.45	0.17
	Before cooking	$p_{cn,cw,cs}(m)$	0.02	0.38	0.60
	After changing diapers	$p_{dn,dw,ds}(m)$	0.00	0.40	0.60
	Before feeding	$p_{fn,fw,fs}(m)$	0.00	1.00	0.00
Child	After using the toilet	$p_{en,ew,es}(c)$	0.00	0.71	0.29
	Before meals	$p_{mn,mw,ms}(c)$	0.13	0.38	0.50
	Before snacks	$p_{sn,sw,ss}(c)$	0.50	0.29	0.21
	Before cooking	$p_{cn,cw,cs}(c)$	0.00	0.33	0.67
	After changing diapers	–	–	–	–
	Before feeding	–	–	–	–

2. Results and discussion

2.1. Results of questionnaire survey and determination of parameters

These tables demonstrated the results of questionnaire survey on activities inside the household and hand-washings, respectively. The mother was found to have high frequencies in baby-associated activities such as touching (8.4), diapering (5.8), feeding (3.0) compared to other family members (Table 3). Among family members, the mother mainly cooks, changes diapers and feeds baby(s). Therefore, the mother could be a hub of secondary infections within a household. The estimated model parameters have been summarized in Tables 2–4.

Fathers and children generally washed their hands less than mothers (Table 4). Besides, almost all members didn't wash their hands or washed only by water before eating snacks. These results indicated that father and children had been more easily exposed to viruses via their hands and the food handlings could be a high risk activity at the household as reported in previous studies (Moe, 2009).

2.2. Temporal changes of primary and secondary infection risks during an outbreak event

We conducted the simulation using the parameters listed in Tables 2–4. Fig. 1 shows the temporal changes of primary and secondary infection risks for the family type. 1111 during the simulated time starting from November 1st. Overall, the proportion of secondary infection was found to be greater than primary infection throughout the whole period. The primary infection risk was constant over the time until the last day (120th day) of exposure to contaminated oysters, and suddenly disappeared afterwards. On the other hand, the secondary infection risk exhibited a dynamic profile - increased
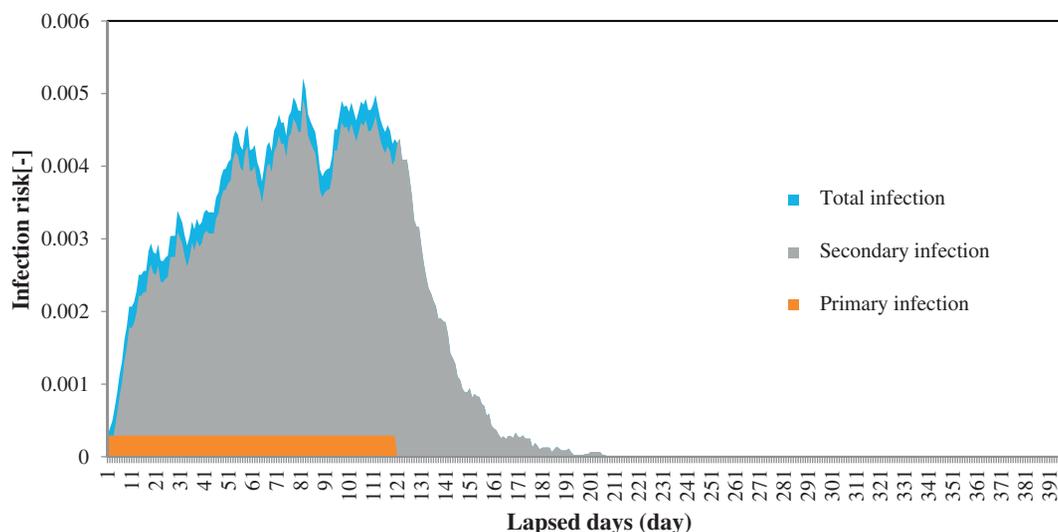

Fig. 1 – Temporal changes of primary, secondary and total infection risks of family type.1111. The simulation started from November 1st. VISI (vulnerability indicator to secondary infection) for family type.1111 was 11.5.

rapidly (ca. 80 days), then saturated at a high constant level until the end of primary exposure (ca.120 days), followed by an exponential attenuation. The similar result was obtained for all of the 21 simulated family types (data is not shown).

The total infection risk had been started decreasing from the day 121 to the final day of the simulation, and the same pattern was observed in the secondary infection risk. Until the day 120, all family members had both risks of primary and secondary infections except for baby eating no oyster; hence, the total risk was found to be increased as infected persons in the household increased. From the day 121, since no primary infection happened anymore, the total risk equals to the secondary infection risk and the total risk became decreased with the recovery of infected persons in the household. This meant that primary infection was necessary to prolong epidemics, although secondary infection greatly contributed to disease transmission in the households as above discussed.

2.3. Effect of family type on infection risk

The total infection risks for each member in the 21 simulated family types have been summarized in Table 5. The average risk of each member during one simulation period (365 days) was generally in the order of 10–2. Babies were found to have the highest total risk (sometimes nearly 1.0) probably due to the high frequency of mouth touching and hand-touching with others.

Besides, babies could not wash their hands by themselves and it caused their low reduction rates of NoV. This result agreed with the results of previous studies (Perry et al., 2005). Interestingly, in most of the family types, mother indicated higher risks than father in spite of the mother's good behaviors of hand washing in family members (Table 4). Possible explanations for this could be mother's high frequency of touching with other family members and mother's frequent exposure to fecal sources through their diapering activities. Changing diapers must increase contacts with the fecal sources which had the highest NoV concentration among all the contaminant sources modeled in this study.

Using VISI, we compared the 21 family types in terms of the relative importance of the secondary infections risk over the primary infection risk for family-level (Fig. 2). In most of the family types, the secondary infection risk was found to be higher than the primary infection risk (i.e., VISI >1). Especially, households composed of more than three members or including baby(s) showed much higher VISI (5–45) than two-member households (VISI = 0.1–4.0). This was possibly due to the increased contact probability in highly dense families. In addition, the presence of baby(s) could also increase the frequency of touching feces for other members, especially mother, in their diapering behaviors.

Family types that include both mother and baby were prone to show higher VISIs. If either of them was lacking from a family, VISIs decreased drastically. This implied that coexistence of baby was the most susceptible to infections and the mother who had the highest touching frequency among family members served as a hub of the infection network in a household, leading to the highly effective spread of infections.

Table 5 – Total infection risk (the probability to get either primary or secondary infection at least once) for each member in each family type. Unit is 10^{-2}.

|	1100	1001	1010	0101	0110	1101	1110	1002	1020	0102	0120	1102	1111	1120	1103	1112	1121	1130	1131	1122	1113	Mean
Father	1.30	1.52	1.48	–	–	2.93	1.80	2.05	2.10	–	–	21.32	6.21	2.84	62.12	50.18	15.08	5.85	34.22	73.28	78.32	21.33
Mother	1.28	–	–	2.88	1.69	5.33	2.01	–	–	15.08	3.33	42.27	11.84	3.55	88.47	78.37	27.37	7.86	54.46	93.54	96.12	31.50
Child	–	–	1.43	–	1.77	–	2.11	–	2.62	–	3.86	–	7.20	4.35	–	53.68	20.01	10.14	46.64	80.43	80.22	24.19
Baby	–	1.29	–	3.35	–	9.14	–	2.73	–	36.61	–	80.47	23.77	–	99.72	98.82	53.86	–	86.49	99.95	99.98	53.55
ALL	2.56	2.79	2.89	6.14	3.44	16.51	5.80	7.32	7.16	65.87	10.65	98.27	41.51	14.27	100.00	100.00	81.79	37.05	99.38	100.00	100.00	43.02
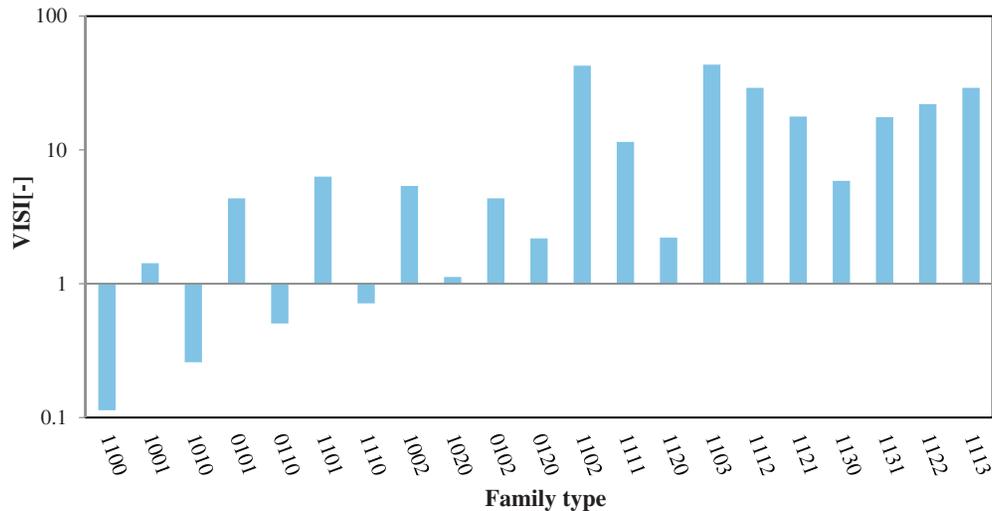
Fig. 2 – The relative secondary infection risk to primary infection risk for each family type expressed using the VISI indicator. VISI: vulnerability indicator to secondary infection.

As already mentioned, secondary infections contributed to disease transmission in the households, while primary infection triggered and prolonged the epidemic. Great efforts to reduce primary infection had been made, for example, by a strict quality control of foods like oysters, but it is still impossible to achieve almost zero risk. Reduction of secondary infection by more hygienic behaviors in the households after primary cases happened was a key to prevent a large scale of epidemics and keeping VISI less than 1 might be used as a target for secondary risk control. Further case studies using our developed model and assessment of VISI would certainly deepen the understanding on what hygienic behaviors at the households were required for the achievement.

In future studies, it is necessary to increase the accuracy and reality of the developed risk assessment tool by incorporating stochastic processes in the model (*e.g.*, giving probability distribution to model parameters). Moreover, other potential infection routes via daily commodities, droplets and vomiting-oral routes should be considered. In addition, the modeling for secondary infection outside the households would also be an important consideration to assess the city-level epidemics. These future improvements of the model would enable us to predict the city-level epidemics more precisely and hence the assessment could be applicable to wider cases and places even with limited available epidemic data.

3. Conclusions

In this study, we proposed a new index, VISI, to quantify the relative impact of secondary infection to primarily infection in epidemic of infectious diarrheal diseases based on an application of household model simulation. The results demonstrated a higher significance of secondary infection than primary infection in a simulated norovirus (NoV) epidemic. Households composed of more than three members including infant(s) showed much higher VISI (5 to 45) than two-member-households with VISI of 0.1 to 4. This was possibly due to increased frequencies of contact among household members and high-risk behaviors such as changing diapers. The above results from model prediction suggested that households of more than three members were likely to become hubs of infection during an epidemic and that careful handling of diapers might be an effective countermeasure for the reduction of secondary infection within the households. Besides, these results are regional, especially in Japan, because these simulation settings and values were applicable only for the target region. However, the risk of infection in other regions can be assessed using our previous household model and the VISI if the values are changed according to the simulated region.

Acknowledgments

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