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ORIGINAL ARTICLE

Family Structure Associated with Measles-Rubella and Varicella Vaccination in Children

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ABSTRACT

BACKGROUND

Delayed vaccination is a well-studied and critical public health issue. However, limited studies have explored whether familial factors influence vaccination delay. This study aimed to determine whether family structure and comorbidities affect the refusal or delayed receipt of measles-rubella and varicella vaccines.

METHODS

We gathered data on all children from birth to 13 months of age between 2006 and 2020 using vaccination records linked with the administrative healthcare claims data from a Japanese city. Multivariable logistic regression analyses were conducted to examine the association of refusal or delay in receiving the first-dose measles-rubella and varicella vaccines with the following factors: the child's sex; presence of parents, siblings, and grandparents; parental and grandparental comorbidities; chronic pediatric comorbidities in the child and siblings; and year of vaccination.

RESULTS

We identified a total of 14,241 eligible children. Refusal or delayed receipt of the first-dose measles-rubella vaccine was associated with an adjusted odds ratio of 2.46 (95% confidence interval, 1.86–3.24) for maternal absence and 1.61 (1.44–1.80) for paternal absence. Similarly, the refusal or delay in receiving the first-dose varicella vaccine was associated with an adjusted odds ratio of 2.04 (95% confidence interval, 1.01–4.16) for maternal absence and 1.37 (1.12–1.69) for paternal absence. The presence of siblings and maternal comorbidities were significantly associated with vaccination delays.

CONCLUSION

The absence of a parent, the presence of siblings, and maternal comorbidities were associated with the refusal or delay in receiving measles-rubella and varicella vaccines. Strategies for vaccine recommendation should therefore consider family structure and maternal comorbidities.

KEY WORDS

Measles-Rubella vaccine, varicella vaccine, vaccine delay, vaccine hesitancy

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INTRODUCTION

Vaccinations have unquestionably been one of the most successful public health approaches, including the eradication of smallpox [1] in the past and the dramatic reduction of bacterial meningitis [2] in more recent years. The World Health Organization (WHO) recommends that measles and varicella vaccines should maintain a vaccination coverage of at least 95% and 80% in the community, respectively [3, 4]. The challenge in achieving this high vaccination rate is vaccine hesitancy. The Strategic Advisory Group of Experts on Immunization Working Group on Vaccine Hesitancy defines vaccine hesitancy as "a delay in acceptance or refusal of vaccination despite the availability of vaccination services" [5]. Studies have shown that the lack of knowledge about vaccines and concerns about safety can lead to refusal of vaccination or delay in vaccination [6–9]. However, most studies used questionnaires and were based on single-center research. Additionally, few studies have examined the impact of family structure or family comorbidities on delayed vaccination. The purpose of this study was to examine whether the family structure and comorbidities affect the refusal of or delay in receiving the first dose of measles-rubella (MR) and varicella vaccinations, using a large dataset from a Japanese municipality.

METHODS

DATABASE

For this study, we used a linked database of resident registers, vaccination records, and administrative claims data from one city in Japan. This city is a commuter town for Tokyo with a population of approximately 600,000 people, approximately 12% of which, account for children under the age of 15 years old. Approximately 6% of participants were non-Japanese.

The resident register contains the dates of birth, gender, personal identification number, and family identification number of all the residents. The administrative claims data contained the dates of clinical visits or hospital admission and discharge, and diagnoses at the time of the clinic visits or hospitalization which were recorded using the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10). The vaccination records contained the type of vaccine and the date of immunization.

Using unique identification numbers, the administrative claims data were linked to the vaccination records in the city office. All personal information was excluded and de-identified data were sent to the researchers for secondary use. The study was approved by the institutional review board of the University of Tokyo (2021187NI-(3)). The requirement for informed consent was waived due to the anonymous nature of the data.

PARTICIPANTS

To determine the annual trends in timely vaccine coverage and vaccine completion for MR and varicella, we first selected children aged 1 year to 1 year and 1 month by year. Data from 2006 to 2021 were used for the MR vaccination because routine MR vaccination in Japan began in 2006 [10]. Whereas data from 2014 to 2021 were used for the varicella vaccination because routine varicella vaccination in Japan began in 2014 [11]. To identify factors influencing timely vaccination, we restricted our analysis to children who resided in the municipality continuously from birth to 13 months. The year 2021 was excluded from this analysis because of the small number of participants. We identified the children's fathers, mothers, siblings, and grandparents using the family identification numbers. We defined a mother as a woman aged between 17 and 50 years, a father as a man aged between 17 and 50 years, siblings as persons aged less than 17 years, and grandparents as persons aged 50 years or older. We used the administrative claims data to determine whether the child had any chronic disease and if the family members had any comorbidities.

OUTCOME

In Japan, it is recommended that the first dose of MR and varicella vaccines be administered between the first birthday and the first month of the first year [12, 13]. Municipalities mail vaccination tickets to those eligible for vaccines free of charge. In this study, timely vaccination was defined as MR or varicella vaccination between the recommended vaccination period between the first birthday and the first month. Vaccination completion was defined as having received at least one dose of the MR or varicella vaccine during the entire study period.

STATISTICAL ANALYSES

First, we examined the changes in timely vaccination coverage for MR and varicella, and vaccine completion for MR and varicella annually. We conducted multivariable logistic regression analyses to examine the association of refusal or delay in receiving the first dose of vaccination with the following factors: the child's gender, chronic disease, absence of father or mother, presence of

grandparents, number of siblings (none, one, two, or more), comorbidities of the family members, and calendar years. The chronic diseases of the child and his/her siblings were defined as those with one or more chronic diseases in the pediatric complex chronic conditions classification system version 2 (CCC v2) [14]. Comorbidities of the family members were identified with the recorded ICD-10 codes listed in the Charlson Comorbidity Index (CCI), which is widely used for risk adjustment in administrative database studies [15].

All analyses were performed using the Stata version 17 software (StataCorp, College Station, TX, USA). A two-tailed significance level of $p < 0.05$ was employed for all tests.

RESULTS

ANNUAL TRENDS IN TIMELY VACCINE COVERAGE AND VACCINE COMPLETION

We identified 81,767 eligible children who received MR vaccination between 2006 and 2021. **Fig. 1** depicts the changes in timely vaccination coverage and vaccine completion for MR annually. The percentage of timely vaccinations gradually increased, except in 2021, when the percentage reached more than 60% in 2020. The vaccine completion for MR reached over 88% in 2014 but has declined slightly since then.

We identified 40,038 eligible children who received varicella vaccination between 2014 and 2021. **Fig. 2** shows the annual changes in the timely vaccination coverage and vaccine completion for varicella. The percentage of timely vaccinations has gradually increased, except for 2021, when the percentage reached more than 55% by 2020. Vaccine completion for varicella remained close to 90%, except for 2020.

FACTORS INFLUENCING TIMELY VACCINATION

We identified 14,241 children eligible for MR vaccination between 2006 and 2020. **Table 1** shows the results of the multivariable logistic regression analysis for refusal or delay in receiving MR vaccination. Refusal of or delayed MR vaccination was significantly associated with maternal absence (aOR, 2.46; 95% CI, 1.86–3.24) and paternal absence (aOR, 1.61; 95% CI, 1.44–1.80). Other factors significantly associated with the refusal of, or delay in, receiving the MR vaccination included the presence of siblings or grandparents, as well as having a parent (either mother or father) with comorbidities.

We identified 5,529 children eligible for varicella vaccination between 2014 and 2020. **Table 2** shows the results of the multivariable logistic regression analysis for refusal of or delay in receiving varicella vaccination. Delayed varicella vaccination was significantly associated with maternal absence (aOR, 2.04; 95% CI, 1.01–4.16) and paternal absence (aOR, 1.37; 95% CI, 1.12–1.69). Other factors significantly associated with delayed varicella

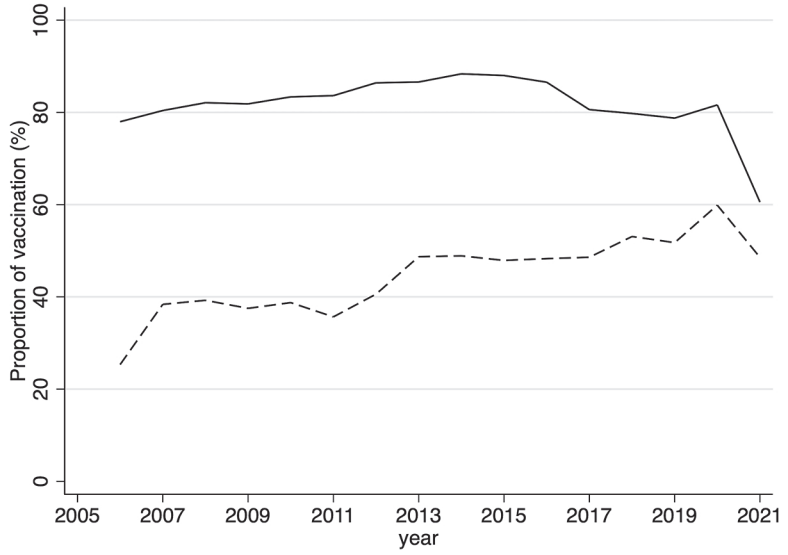

Fig. 1 **Change over time in the proportion of measles-rubella vaccination from 2006 to 2021**

The solid line shows the proportion of completed vaccinations, and the dashed line shows the proportion of timely vaccinations.

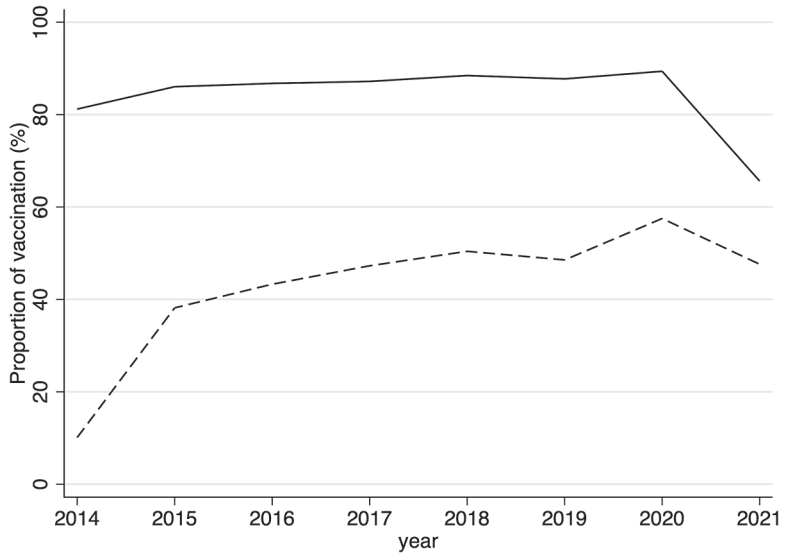

Fig. 2 **Change over time in the percentage of varicella vaccination from 2014 to 2021**

The solid line shows the proportion of completed vaccinations, and the dashed line shows the proportion of timely vaccinations.

vaccination included having siblings and the presence of a mother or family members other than parents with comorbidities.

The timely vaccination with MR and varicella vaccines improved over the years.

DISCUSSION

The proportions of timely vaccination and completed vaccination for MR and varicella vaccines increased after the introduction of routine vaccination. In 2021, a decrease in the proportion of timely vaccinations was observed for both vaccines. The reason for this decrease in 2021 remains unclear. In the Japanese metropolitan area, the novel coronavirus epidemic began around April 2020, and it was not until January 2021 that the number of daily cases reached 1,000 or more. It is conceivable that the coronavirus epidemic may have caused people to withhold vaccination visits for fear of contracting the coronavirus. Previous studies have also reported that coronavirus outbreaks have reduced the number of people receiving routine measles vaccinations [16].

The results of this study revealed that the refusal of or delayed MR vaccination was associated with the absence of either the mother or father, having siblings or grandparents, and having a parent with comorbidities. Similarly, the absence of a parent, the presence of siblings, or having a mother with comorbidities was associated with delayed varicella vaccination.

Many studies have been conducted on vaccination delays and hesitancy. An online survey in the United States reported that the proportion of vaccine hesitancy for routine vaccines was 6.1% and that for influenza vaccines was more than 25% [17]. A systematic literature review found that a low level of education, lack of awareness of diseases and their vaccines, and religious and cultural beliefs are commonly cited as major factors in vaccine hesitancy [7]. However, few studies have examined the impact of family structure and family comorbidities on vaccination. A previous study in the United States used 2003 National Immunization Survey data and reported that having single mothers and siblings was associated with a delay of six months or more with four or more vaccines.

In the present study, we evaluated the association of family structure and comorbidities with timely vaccination using a large dataset from a municipality. The presence of siblings is found to be associated with delayed vaccination. This association may be partly explained by the possible presence of infectious diseases in siblings and the transmission of the infectious disease between them. However, the presence of siblings may increase caregivers' knowledge about vaccines, possibly resulting in timely vaccination.

The present study also indicated that the presence of a mother with comorbidities was associated with delayed vaccination. A plausible reason for this may be that mothers with comorbidities may have difficulty taking

Table 1 Factors associated with refusal of or delay in receiving measles-rubella vaccination

Variables	Overall (N = 14,241)	Not received MR vaccine (N = 5,273)	Unadjusted		Adjusted		
			Odds ratio	95% confidence interval	Odds ratio	95% confidence interval	p value
Personal information							
Male	7,272 (51.1%)	3,217 (51.3%)	1.02	0.95–1.09	1.01	0.95–1.09	0.668
Chronic diseases	60 (0.4%)	27 (0.4%)	1.04	0.62–1.73	0.96	0.57–1.63	0.886
Family structure							
Mother not present	290 (2.0%)	199 (3.2%)	2.84	2.21–3.64	2.46	1.86–3.24	<0.001
Father not present	1,398 (9.8%)	813 (13.0%)	1.88	1.68–2.10	1.61	1.44–1.80	<0.001
Grandparents present	632 (4.4%)	326 (5.2%)	1.37	1.17–1.61	1.21	1.03–1.42	0.023
Number of siblings							
No siblings	9,224 (64.8%)	3,675 (58.6%)	Reference				
One sibling	4,070 (28.6%)	2,025 (32.3%)	1.50	1.39–1.61	1.52	1.41–1.64	<0.001
Two or more siblings	947 (6.6%)	573 (9.1%)	2.31	2.02–2.65	2.27	1.97–2.61	<0.001
Family history of comorbidities							
Mother	93 (0.7%)	51 (0.8%)	1.55	1.03–2.33	1.60	1.05–2.43	0.030
Father	90 (0.6%)	45 (0.7%)	1.27	0.84–1.93	1.63	1.05–2.53	0.029
Family members other than parents	133 (0.9%)	77 (1.2%)	1.76	1.24–2.48	0.78	0.53–1.15	0.204
Fiscal year							
2006	869 (6.1%)	467 (7.4%)	Reference				
2007	1,184 (8.3%)	531 (8.5%)	0.70	0.59–0.83	0.72	0.60–0.86	<0.001
2008	1,160 (8.1%)	533 (8.5%)	0.73	0.61–0.87	0.75	0.62–0.89	0.001
2009	1,193 (8.4%)	569 (9.1%)	0.78	0.66–0.94	0.80	0.67–0.96	0.016
2010	1,138 (8.0%)	549 (8.8%)	0.80	0.67–0.96	0.85	0.71–1.02	0.072
2011	1,135 (8.0%)	617 (9.8%)	1.03	0.86–1.22	1.09	0.91–1.30	0.348
2012	1,025 (7.2%)	488 (7.8%)	0.78	0.65–0.94	0.83	0.69–1.00	0.050
2013	1,008 (7.1%)	377 (6.0%)	0.51	0.43–0.62	0.55	0.46–0.66	<0.001
2014	1,028 (7.2%)	400 (6.4%)	0.55	0.46–0.66	0.59	0.49–0.71	<0.001
2015	970 (6.8%)	416 (6.6%)	0.65	0.54–0.78	0.68	0.57–0.82	<0.001
2016	945 (6.6%)	361 (5.8%)	0.53	0.44–0.64	0.56	0.46–0.68	<0.001
2017	844 (5.9%)	333 (5.3%)	0.56	0.46–0.68	0.59	0.48–0.71	<0.001
2018	733 (5.1%)	279 (4.4%)	0.53	0.43–0.65	0.54	0.44–0.67	<0.001
2019	593 (4.2%)	215 (3.4%)	0.49	0.40–0.61	0.51	0.41–0.64	<0.001
2020	416 (2.9%)	138 (2.2%)	0.43	0.33–0.55	0.45	0.36–0.58	<0.001

Table 2 Factors associated with refusal of or delay in receiving varicella vaccination

Variables	Overall (N = 5,529)	Not received varicella vaccine (N = 2,927)	Unadjusted		Adjusted		
			Odds ratio	95% confidence interval	Odds ratio	95% confidence interval	p value
Personal information							
Male	2,805 (50.7%)	1,499 (51.2%)	1.04	0.94–1.16	1.06	0.95–1.19	0.286
Chronic diseases	60 (1.1%)	36 (1.2%)	1.34	0.80–2.25	1.18	0.67–2.06	0.565
Family structure							
Mother not present	43 (0.8%)	29 (1.0%)	1.85	0.98–3.51	2.04	1.01–4.16	0.048
Father not present	428 (7.7%)	266 (9.1%)	1.51	1.23–1.84	1.37	1.12–1.69	0.003
Grandparents present	190 (3.4%)	101 (3.5%)	1.01	0.76–1.35	1.04	0.76–1.43	0.787
Number of siblings							
No siblings	3,582 (64.8%)	1,784 (60.9%)	Reference		Reference		
One sibling	1,583 (28.6%)	902 (30.8%)	1.33	1.19–1.50	1.50	1.32–1.70	<0.001
Two or more siblings	364 (6.6%)	241 (8.2%)	1.97	1.57–2.48	2.21	1.74–2.81	<0.001
Family history of comorbidities							
Mother	93 (1.7%)	62 (2.1%)	1.79	1.16–2.77	1.77	1.13–2.79	0.013
Father	90 (1.6%)	50 (1.7%)	1.11	0.73–1.69	1.35	0.86–2.14	0.196
Family members other than parents	70 (1.3%)	37 (1.3%)	1.00	0.62–1.60	0.55	0.32–0.95	0.032
Fiscal year							
2014	1,028 (18.6%)	901 (30.8%)	Reference		Reference		
2015	970 (17.5%)	547 (18.7%)	0.18	0.15–0.23	0.17	0.14–0.22	<0.001
2016	945 (17.1%)	424 (14.5%)	0.11	0.09–0.14	0.11	0.09–0.14	<0.001
2017	844 (15.3%)	362 (12.4%)	0.11	0.08–0.13	0.10	0.08–0.13	<0.001
2018	733 (13.3%)	308 (10.5%)	0.10	0.08–0.13	0.09	0.07–0.12	<0.001
2019	593 (10.7%)	234 (8.0%)	0.09	0.07–0.12	0.09	0.07–0.11	<0.001
2020	416 (7.5%)	151 (5.2%)	0.08	0.06–0.11	0.08	0.06–0.10	<0.001

their children out of the home.

This study showed a significant improvement over the years in the timely vaccination of both MR and varicella vaccines. This improvement may reflect an increase in parental awareness following the incorporation of these vaccines into the routine immunization schedule.

Our results may be useful in considering strategies for vaccine recommendations. A high-risk approach to families where one parent is absent or where the mother has comorbidities may reduce delayed vaccinations. Specifically, for families dealing with the absence of one parent, the presence of siblings, and maternal comorbidities, potential solutions could include the proactive use of free telephone consultation services introduced at the time of postpartum discharge, and the utilization of home visits after discharge.

STRENGTHS AND LIMITATIONS

The strength of this study is that we analyzed a relatively large sample size using administrative data, accurate residency information, and vaccination records.

This study had several limitations. First, parents' education level, household income, race/ethnicity, and religion were unknown in this study. These factors have

been found to influence vaccination in previous studies [7–9]. In Japan, MR and varicella vaccines are available free of charge, to ensure vaccinations in low-income households. Additionally, the percentage of foreigners in the city was approximately 6%, and race/ethnicity may have little impact on the results. Second, there is a possibility of misclassification of parents, grandparents, and siblings because they were defined only by age. There is a possibility of underestimation due to misclassification, as chronic diseases are also being determined based on diagnosis names. Third, from the database, it is not known whether non-timely vaccination was simply due to delay or intentional refusal. For this reason, we analyzed them as a category together without distinguishing between them. Finally, regarding family structure, we do not have detailed information on whether they live together or on the division of family roles.

CONCLUSIONS

In this study, we found that the absence of one parent, the presence of siblings, and maternal comorbidities may be associated with the refusal of or delay in the administration of the first doses of MR and varicella vaccines, respectively. Family structure and comorbidities should be considered to reduce the refusal of or delays in receiving vaccinations.

CONFLICT OF INTEREST

Nobuaki Michihata, Yamana Hayato, and Taisuke Jo were members of the Department of Health Services Research, a cooperative program between the University of Tokyo and Tsumura. Sachiko Ono is a member of the Department of Eat-loss Medicine, a cooperative program between the University of Tokyo and ITO EN Ltd and received grants from the Ministry of Health, Labour, and Welfare, Japan, and the Ministry of Education, Culture, Sports, Science and Technology, Japan, outside the submitted work. Hideo Yasunaga received grants from the Ministry of Health, Labour, and Welfare, Japan, and the Ministry of Education, Culture, Sports, Science and Technology, Japan, outside the submitted work. The other authors report no potential conflicts of interest.

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