BMJ Open

Recent trends in seroprevalence of rubella in Korean women of childbearing age: a cross-sectional study

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To cite: Choi R, Oh Y, Oh Y, *et al*. Recent trends in seroprevalence of rubella in Korean women of childbearing age: a cross-sectional study. *BMJ Open* 2020;**10**:e030873. doi:10.1136/bmjopen-2019-030873

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136bmjopen-2019-030873).

Received 04 April 2019
Revised 01 August 2019
Accepted 29 August 2019

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ABSTRACT

Objectives The aim of this study was to investigate the immunity against rubella using the serological status of rubella-specific IgG antibodies (antirubella IgG) in Korean women of childbearing age (15–49 years).

Design Retrospective cross-sectional study.

Setting Population-based cross-sectional study in South Korea.

Participants Between January 2010 and December 2017, test results from Korean women aged 15–49 years who had visited an obstetric private clinic (nationwide institutions) and had requested rubella-specific IgG antibody tests from Green Cross Laboratories were obtained from the laboratory information system.

Results Between 2010 and 2017, antirubella IgG test results from 328 426 Korean women aged 15–49 years who had visited private obstetric clinics (1438 institutions nationwide) were retrospectively analysed by tested year, age, cohort and geographic regions. Over the 8-year study period, the rate of unimmunised women ranged from 7.8% to 9.7%. Multivariable-adjusted logistic regression models showed that the odds of being immune to rubella (positive and equivocal results of antirubella IgG test) were lower in 2017 compared with 2010, in women in their 40s, in a pre-catch-up cohort and in women living in Incheon, Busan, South Gyeongsang, North and South Jeolla and Jeju provinces ($p<0.0001$).

Conclusions In consideration of the factors associated with prevalence of women unimmunised to rubella, future public health efforts should be focused on catch-up activities. The results of this study could be used to strengthen disease control and prevent rubella, including a nationwide immunisation programme.

Strengths and limitations of this study

- The main strength of the study lies in its sample size, due to the fact that it is a nationwide study with one of the broadest samples to date in South Korea.
- The study provided a recent information of the seroprevalence of antirubella IgG that have not been available at this scale before.
- The huge sample size of this study allowed for precise information of the age-related seroprevalence of antirubella IgG and this study provides valuable information for establishing a catch-up vaccination programme in South Korea.
- One limitation of this study was the lack of detailed clinical information; however, seroprevalence studies are an essential tool to monitor the efficacy of vaccination programmes, to understand population immunity and to identify populations at higher risk of infection.

INTRODUCTION

Rubella disease is caused by rubella virus (belonging to the family Togaviridae and the only member of the genus *Rubivirus*).[1] Although most cases of infection lead to a mild, self-limiting measles-like disease, the real threat arises when rubella virus infects the fetus, particularly during the first trimester when infection can lead to miscarriage or congenital rubella syndrome.[1] Worldwide, over 100 000 babies are born with congenital rubella syndrome every year, and the WHO recommends that all countries that have not yet introduced a rubella vaccine should consider doing so using existing, well-established measles immunisation programmes.[2] The WHO Strategic Advisory Group of Experts on Immunization (SAGE) recommends an increased focus on improving national immunisation systems in general to better control rubella.[2] Under the Global Vaccine Action Plan 2011–2020, rubella is targeted for elimination in five WHO Regions by 2020.[3 4] As has been reported in Europe, suboptimal coverage levels in childhood (<95%) can lead to a prolonged inter-epidemic period and to a paradoxical shift of disease incidence towards older age groups, including women of childbearing age, with a consequent increase of congenital rubella syndrome.[5] Serosurveys may represent an effective instrument to measure infection-induced and vaccine-induced immunity in a specific population, and serosurveys can effectively support strategies aimed at eliminating the disease.[5]

The incidence of rubella infection in South Korea was 107 cases in 2000 that decreased to 7 cases in 2017, corresponding to incidence rates below 0.1 per 100 000 persons according to the Infectious Diseases Surveillance Yearbook, 2017.[6] Although the exact number of cases for congenital rubella syndrome was not available for the surveillance book, 17 cases in 2010 of congenital rubella syndrome were reported, which using the Korean Classification of Disease code P350 for congenital rubella syndrome on the Healthcare Bigdata Hub by the Health Insurance Review and Assessment Service (HIRA).[7] According to the reported measles and rubella cases and incidence rates by WHO member states, 0–3947 confirmed rubella cases corresponding to incidence rates of 0–11.54 per 1 000 000 total population were reported in 2018 in the western pacific region.[8]

In Korea, a rubella vaccination programme using the measles, mumps in rubella (MMR) vaccine has been included in the national immunisation programme since 1985 for disease control and prevention.[9] A second MMR vaccine dose was introduced in 1997, and a catch-up measles-rubella (MR) vaccine for school-aged children was introduced in 2001.[9] In 2002, a two-dose MMR keep-up programme through the verification of vaccination history was introduced at elementary schools (6–7 years).[9] A new vaccination policy was formed by the 2012 Military Healthcare Service, and since then, MMR vaccines have been routinely administered to all new recruits early in basic training.[10] The national guidelines in Korea regarding ascertainment of rubella immunity are based on laboratory evidence for rubella antibodies and the Korea Centers for Disease Control and Prevention recommends that women of childbearing age whose antirubella specific IgG is negative should receive 1 dose of the MMR vaccine although they did have histories of rubella vaccination (total numbers of vaccination in one individual should be ≤3).[11]

Although there have been several studies on rubella in Korea, most of the studies have only been focused on surveillance of newly identified cases, seroprevalences of rubella IgG in children or had been conducted in the early 1990s.[9 10 12–16] Although a recent meta-analysis assessing global seroprevalence of rubella among pregnant and childbearing age women, no data from Korean populations were included in the study.[5] In a recent 16-year review of seroprevalence studies on rubella, only one Korean study on children and adolescents was included.[3] To our knowledge, no recent data have been collected on rubella immunisation status with rubella-specific IgG antibodies in Korean women of childbearing age in a large study population, which could provide basic knowledge on nationwide immunisation strategies. Green Cross Laboratories is one of the largest referral clinical laboratories throughout South Korea that has its own biologistics and provides clinical specimen analysis services including rubella-specific IgG antibody tests to nationwide clinics and hospitals. According to the provider data on the National Health Insurance Statistical Yearbook 2017 published by HIRA in South Korea, 1319 private obstetric clinics and 1433 hospitals with or without obstetric clinics are providing health services.[17] Among a total of 91 545 healthcare providing institutions (public and private), 4.1% (3746 institutions) were public or national provider institutions.[17] According to the review records of delivery by provider type in the same book, 89.9% (523/582) of delivery institutions nationwide were private obstetric clinics and hospitals.[17] Among the 358 285 deliveries carried out in 2017, 93.5% (335 119) were delivered in private obstetric clinics and hospitals.[17]

Therefore, in this study, we aimed to investigate the immunity against rubella and to share baseline data for future immunisation policies in South Korea. The aim of this study was to investigate the epidemiology of rubella immunisation status using serological assays for rubella-specific IgG antibodies in Korean women of childbearing age. In addition, we assessed rubella immunisation status according to year and age group.

MATERIALS AND METHODS

Participants' involvement and data collection

No patients were involved in the development of the research question or the outcome measures, nor were they involved in developing plans for design or implementation of the study. No patients were asked for advice regarding the interpretation or writing of results. There are no plans to disseminate the study results to the relevant patient community.

Study populations

Between January 2010 and December 2017, test results from Korean women aged 15–49 years who had visited an obstetric private clinics and hospitals (nationwide institutions) and had requested rubella-specific IgG antibody tests from Green Cross Laboratories were obtained from the laboratory information system. Missing data for age, sex and geographic regions were excluded. Test results from women whose tests were duplicated were excluded. All data were anonymised before being transferred to analysis for age-specific, year-specific, birth cohort and geographical region-specific antirubella IgG seroprevalences. This study was conducted according to guidelines in the Declaration of Helsinki.

Data collection

Annual incidence of rubella infection in South Korea was obtained from reported cases in the Infectious Diseases Surveillance Yearbook, 2017 by the Korea Centers for Disease Control and Prevention.[6] Data for the incidence of congenital rubella syndrome was obtained from the Healthcare Bigdata Hub by HIRA using Korean Classification of Disease code P350 in South Korea.[7]

Analytical procedures

All serum samples were tested for antirubella IgG using a chemiluminescent microparticle immunoassay

(Architect i2000SR, Abbott Diagnostics, Abbott Park, Illinois, USA) according to the manufacturer's instructions. For the rubella IgG assay, the presence of ≥10 IU/mL was defined as 'positive'. Antibody levels of 0.0–4.9 IU/mL were defined as 'negative', and antibody levels between 5.0 and 9.9 IU/mL were defined as 'equivocal'. During the 8-year study period, the laboratory protocol was maintained without any changes and all tests requested for antirubella specific IgG were analysed automatically and tested once without retest.

Definition

Positive rubella-specific IgG results are indicative of past exposure to rubella virus or being vaccinated.[18] Women who had 'negative' results were defined as 'unimmunised'. Women were classified as 'immune' if their antirubella IgG was positive or showed equivocal results.[18] Birth cohorts were defined based on the vaccination programme: pre-catch-up, 1976–1984; catch-up, 1985–1993 and keep-up, ≥1994.[9] The pre-catch-up (1976–1984) cohort was women who had presumptively limited MMR vaccination coverage with only one dose provided by the public programme. The catch-up (1985–1993) cohort was woman who had limited MMR vaccination coverage but were given the MR vaccine during the 2001 catch-up campaign.[9] The keep-up (≥1994) cohort was women who were candidates for the keep-up programme.[9]

Statistical analysis

Categorical variables are presented as frequencies and percentages. The χ^2 test was used to compare categorical variables. The Cochran-Armitage test for trend was performed to evaluate the seroprevalence of antirubella IgG by year and cohort. Multivariable-adjusted logistic regression models were used to estimate the OR of being immune to rubella based on the results of the antirubella IgG seroprevalence test for the tested years, age, birth cohort and geographic region in South Korea. Variables with univariate p values less than 0.05 were included as adjusted variables for the multivariable analysis. Statistical analysis was executed using MedCalc Statistical Software V.18.5 (MedCalc Software bvba, Ostend, Belgium). P values were considered significant at the 0.05 level.

RESULTS

General characteristics of the study population

Between January 2010 and December 2017, antirubella IgG test results from 328 426 Korean women age 15–49 years who had visited obstetric private clinics (from 1438 institutions nationwide) and had requested rubella-specific IgG antibody tests from Green Cross Laboratories were obtained from the laboratory information system and included in the study. The numbers for antirubella IgG results for the study subjects by each year and age group are summarised in table 1.

Rubella immunity in Korean women of childbearing age

The overall proportion of IgG-negative women who were defined as 'unimmunised' was 8.6%, and the overall proportion of IgG-equivocal women was 15.0% and IgG-positive women was 76.4%. Rubella-specific IgG antibody test results with an annual incidence of rubella infection and congenital rubella syndrome from surveillance data by year are summarised in figure 1. There were significant differences in the rate of unimmunised women during the 8-year study period ($p<0.05$), although there was no significant trend ($p>0.05$). There was a decrease in the rate of women who had positive rubella-specific IgG antibody results (from 81.0% in 2010 to 73.0% in 2017, $p<0.05$) and an increase in the rate of women who had 'equivocal' results from 2010 to 2017 (11.0% in 2010 to 17.6% in 2017, $p<0.05$, figure 1). There were significant differences in the rate of unimmunised women among different age groups, cohorts and geographic regions ($p<0.05$). For example, less than 1000 women had been tested for antirubella IgG in the Gangwon province and Ulsan.

Multivariable–adjusted logistic regression models showed that the odds of being immune to rubella (positive and equivocal results of antirubella IgG tests) were decreased in 2017 compared with 2010 (OR 0.63, 95% CI 0.60 to 0.67, $p<0.0001$) and women in their 40s (OR 0.85, 95% CI 0.79 to 0.90, $p<0.0001$, table 2). Among different cohorts, catch-up (being born in 1985–1993) and keep-up (born ≥1994) cohorts had higher ORs for being immune to rubella compared with pre-catch-up cohorts (born in 1976–1984, $p<0.0001$). Among different geographic regions, women living in Incheon, Busan, South Gyeongsang, North and South Jeolla and Jeju provinces had lower ORs and women living in Sejong city and Daejeon had higher ORs for being immune to rubella in comparison with women living in Seoul ($p<0.0001$).

DISCUSSION

In this study, we investigated the seroprevalence of rubella in Korean women of childbearing age within the past 8 years. The strength of this study was the large study population over a long study period (8 years) and the novelty of the study population (Korean women of childbearing age were assessed for the first time in Korea). Because previous studies focused on the different measurement methods and immunisation status, this suggested that equivocal results might be due to being immune to rubella infection;[18 19] thus, the authors focused on and analysed factors associated with those whose antirubella IgG results were negative.

Understanding the spread of infectious diseases and designing optimal control strategies is a major goal of public health.[20 21] In the present study, the seronegativity prevalence was 8.6% in Korean women of childbearing age. A recent 16-year review of seroprevalence studies on rubella assessing 97 articles between January 1998 and June 2014 had reported that seroprevalence ranged from 53.0% to 99.3% for rubella studies.[3] A recent meta-analysis of rubella among pregnant and childbearing age women had reported that approximately 88% of the

Table 1 Test results for antirubella IgG by each tested-year and age for 328 465 Korean women tested for rubella IgG antibodies

Test year	15–20 years				21–30 years				31–40 years				41–49 years			
	N	E	P	Total	N	E	P	Total	N	E	P	Total	N	E	P	Total
2010	8	48	312	368	1332	2499	13628	17459	1640	1601	16691	19932	87	102	623	812
	2.2%	13.0%	84.8%	9.4%	7.6%	14.3%	78.1%	14.1%	8.2%	8.0%	83.7%	10.4%	10.7%	12.6%	76.7%	8.6%
2011	25	64	451	540	1717	3024	13376	18117	2167	2600	17668	22436	120	103	687	910
	4.6%	11.9%	83.5%	13.8%	9.5%	16.7%	73.8%	14.6%	9.7%	11.6%	78.8%	11.8%	13.2%	11.3%	75.5%	9.6%
2012	30	105	439	574	1381	2899	13388	17668	2321	3438	19407	25166	225	137	1125	1487
	5.2%	18.3%	76.5%	14.7%	7.8%	16.4%	75.8%	14.2%	9.2%	13.7%	77.1%	13.2%	15.1%	9.2%	75.7%	15.8%
2013	23	113	379	515	1195	2491	11989	15675	2477	3867	18106	24450	135	106	875	1116
	4.5%	21.9%	73.6%	13.2%	7.6%	15.9%	76.5%	12.6%	10.1%	15.8%	74.1%	12.8%	12.1%	9.5%	78.4%	11.8%
2014	35	100	405	540	778	2032	11793	14603	2142	3662	17906	23710	111	108	919	1138
	6.5%	18.5%	75.0%	13.8%	5.3%	13.9%	80.8%	11.8%	9.0%	15.4%	75.5%	12.4%	9.8%	9.5%	80.8%	12.1%
2015	29	84	398	511	674	2032	11596	14302	2407	4361	18467	25235	137	91	997	1225
	5.7%	16.4%	77.9%	13.1%	4.7%	14.2%	81.1%	11.5%	9.5%	17.3%	73.2%	13.2%	11.2%	7.4%	81.4%	13.0%
2016	39	79	389	507	651	1887	11152	13690	2573	4532	18304	25409	142	105	1029	1276
	7.7%	15.6%	76.7%	13.0%	4.8%	13.8%	81.5%	11.0%	10.1%	17.8%	72.0%	13.3%	11.1%	8.2%	80.6%	13.5%
2017	39	78	228	345	779	1985	9922	12686	2689	4709	17151	24549	162	118	1196	1476
	11.3%	22.6%	66.1%	8.8%	6.1%	15.6%	78.2%	10.2%	11.0%	19.2%	69.9%	12.9%	11.0%	8.0%	81.0%	15.6%
Total	228	671	3001	3900	8507	18849	96844	124200	18416	28770	143700	190886	1119	870	7451	9440
	5.8%	17.2%	76.9%		6.8%	15.2%	78.0%		9.6%	15.1%	75.3%		11.9%	9.2%	78.9%	

E, equivocal; N, negative; P, positive.

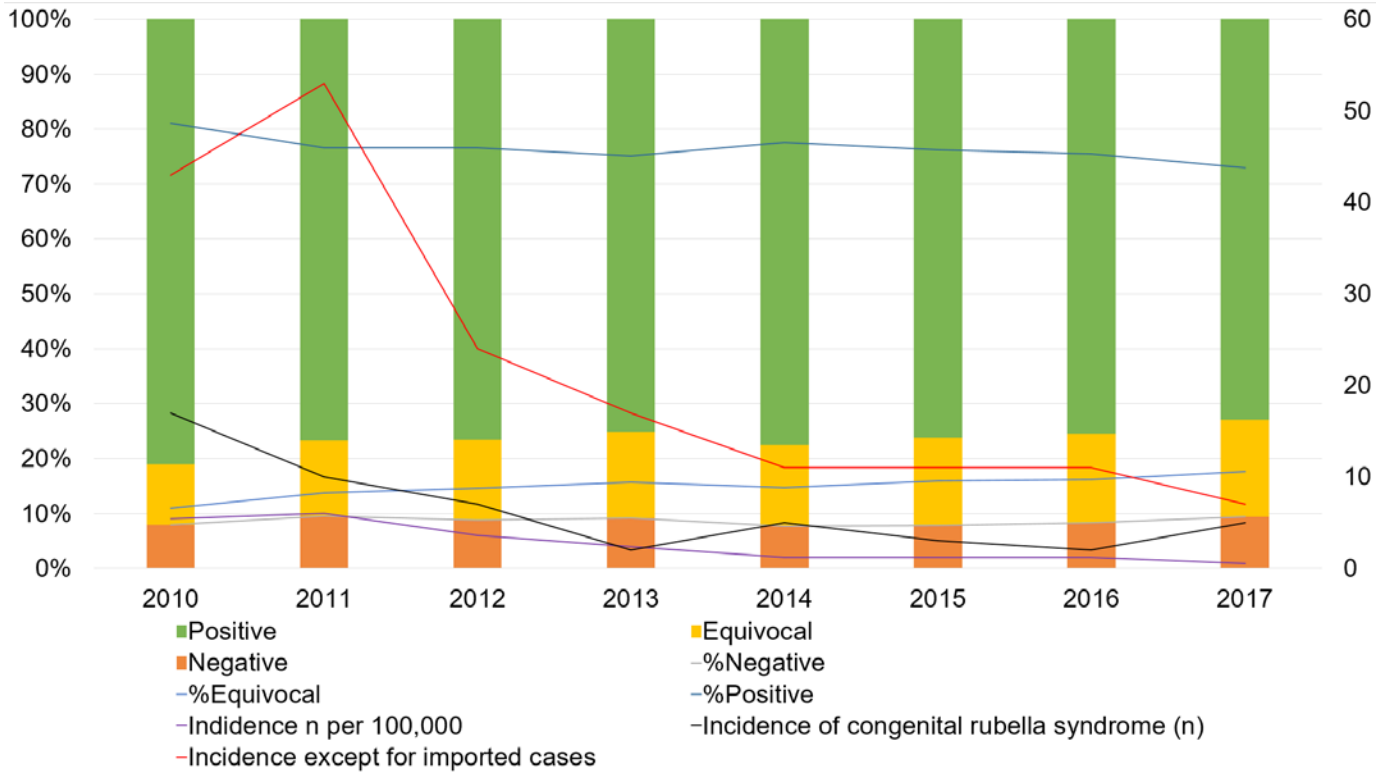

Figure 1 Rubella-specific IgG antibody test results with annual incidence of rubella infection and congenital rubella syndrome from surveillance data by year (2010–2017). Percentage of rubella specific IgG results in this study (left axis) and numbers of cases for incidence of rubella from surveillance data (right axis) are plotted against years tested.

studies conducted on pregnant women had reported a seronegativity rate >5%, and the pooled rubella seronegativity prevalence was 9.3%.[5] The study had reported that global seronegativity prevalence was of concern, considering that WHO set the rubella susceptibility threshold at 5% for women of childbearing age. Previous studies that had been included in the meta-analysis had used more than 1000 subjects and had been published within the past 10 years are summarised in table 3.

The seroprevalence of rubella in Korean populations was assessed previously in infants, children and adolescents.[12–16] One study on 5393 students from eight elementary schools in the Gyeonggi province, Korea in 1993, 1996 and 1996 had reported that the age-adjusted rubella susceptibility rate was 22.9%.[14] Another study performed during the same study period had reported that rubella antibody loss rates were 14.3%–15.8% in Korean children.[12] In a 2005 population-based survey in Nonsan, Korea, age-appropriate immunisation among urban-rural children aged 24–35 months had reported that the age-appropriate MMR immunisation rate was 61.1%–97.4%.[16] A recent study conducted between September 2009 and December 2010 assessing seroprevalence of rubella in 295 infants and 80 of their mothers had reported that seropositive rates were 22.4% in infants and 98.8% in mothers (79/80).[13] In that study, because none of the infants had a history of MMR vaccination, natural infection or contact with an infected person, it was assumed that specific antibodies were passed from their mothers to their infants.[13] Moreover, among the 80 mothers, 55 (68.8%) had experienced either immunisation or past rubella infection.[13]

The historical immunisation coverage in preschool children right before admission to elementary school, which was evaluated based on a telephone survey, reported 99.5% in 2001 and 97.3% of school-aged children (catch-up cohort) were vaccinated with the MR vaccine.[22] According to the Infectious Disease Surveillance Yearbook 2017, published by the Korean Ministry of Health and Welfare and the Korean Centers for Disease Control and Prevention, the incidence rate of rubella from 2001 to 2017 decreased (from 0.17 per 100 000 population in 2001 to 0.01 per 100 000 population in 2017).[6] In this study, ORs for being immune to rubella infection were higher in the catch-up (born 1985–1993) and keep-up (born ≥1994) cohorts than in pre-catch-up cohorts (born 1976–1984) which suggests that catch-up and keep-up immunisation was effective.[22] The vaccine coverage rate was maintained at >95% from 2010 to 2017 in South Korea (ranges 97.0% in 2012 to 99.8% in 2010).[22] No rubella outbreak had been reported in South Korea over 8 years (2010–2017) according to the Infectious Disease Surveillance Yearbook. Among the different age groups, older women were more likely to have negative IgG results and no protection from rubella infection. Women in their 30s had the lowest rate of IgG+ results in this study. According to recent data from Korean Statistical Information (KOSIS), the average maternal age at delivery for Korean women was 32.4 years in 2016.

Table 2 Association between seroprevalence of antirubella IgG (being immune to rubella)* and population characteristics

	Total	Immune		Univariable logistic regression			Multivariable logistic regression		
	n	n	%	OR	95% CI	P value	OR	95% CI	P value
Tested year									
2010	38571	35504	92.0						
2011	42002	37973	90.4	0.81	0.78 to 0.86	<0.0001	0.79	0.75 to 0.83	<0.0001
2012	44895	40938	91.2	0.89	0.85 to 0.94	<0.0001	0.85	0.81 to 0.89	<0.0001
2013	41756	37926	90.8	0.86	0.81 to 0.90	<0.0001	0.78	0.74 to 0.82	<0.0001
2014	39991	36925	92.3	1.04	0.99 to 1.10	0.1368	0.91	0.86 to 0.96	0.0003
2015	41273	38026	92.1	1.01	0.96 to 1.07	0.6586	0.84	0.80 to 0.89	<0.0001
2016	40882	37477	91.7	0.95	0.90 to 1.00	0.0520	0.75	0.72 to 0.79	<0.0001
2017	39056	35387	90.6	0.83	0.79 to 0.88	<0.0001	0.63	0.60 to 0.67	<0.0001
Age of women									
15–20 years	3900	3672	94.2						
21–30 years	124200	115693	93.2	0.84	0.74 to 0.97	<0.0001			
31–40 years	190886	172470	90.4	0.58	0.51 to 0.67	<0.0001			
41–49 years	9440	8321	88.1	0.46	0.40 to 0.54	<0.0001	0.85	0.79 to 0.90	<0.0001
Cohort									
Pre-catch-up (1976–1984)	228176	205536	90.1						
Catch-up (1985–1993)	94056	88887	94.5	1.89	1.84 to 1.95	<0.0001	1.99	1.92 to 2.05	<0.0001
Keep-up (≥1994)	6194	5733	92.6	1.37	1.24 to 1.51	<0.0001	1.50	1.36 to 1.65	<0.0001
Geographic locations									
Seoul	65380	59821	91.5						
Gyeonggi Province	131157	120183	91.6	1.02	0.98 to 1.05	0.3078			
Incheon	9611	8747	91.0	0.94	0.87 to 1.01	0.1111	0.93	0.86 to 1.00	0.0382
Gangwon Province	703	654	93.0	1.24	0.93 to 1.66	0.1478			
Sejong City	3859	3623	93.9	1.43	1.25 to 1.63	<0.0001	1.20	1.05 to 1.37	0.0076
Daejeon	12496	11553	92.5	1.14	1.06 to 1.22	0.0004	1.07	1.00 to 1.15	0.0484
North Chungcheong Province	11186	10306	92.1	1.09	1.01 to 1.17	0.0252			
South Chungcheong Province	8390	7710	91.9	1.05	0.97 to 1.14	0.2178			
Daegu	14781	13473	91.2	0.96	0.90 to 1.02	0.1739			
Ulsan	660	625	94.7	1.66	1.18 to 2.34	0.0037			
North Gyeongsang Province	2075	1891	91.1	0.96	0.82 to 1.11	0.5577			
South Gyeongsang Province	4426	3994	90.2	0.86	0.78 to 0.95	0.0039	0.85	0.77 to 0.95	0.0023
Busan	12574	11376	90.5	0.88	0.83 to 0.94	0.0002	0.86	0.81 to 0.91	<0.0001
Gwangju	2035	1845	90.7	0.90	0.78 to 1.05	0.1848			
North Jeolla Province	11911	10890	91.4	0.99	0.92 to 1.06	0.8031	0.93	0.87 to 0.99	0.0213
South Jeolla Province	13621	12233	89.8	0.82	0.77 to 0.87	<0.0001	0.79	0.75 to 0.84	<0.0001
Jeju Province	23561	21232	90.1	0.85	0.81 to 0.89	<0.0001	0.83	0.79 to 0.87	<0.0001

*Positive and equivocal results of antirubella specific IgG test results were defined as 'immune' in this study.[18]

Because of this, public health efforts should be focused on catch-up activities. The results of this study could be used as basic knowledge to support strengthening disease control and prevention of rubella, including a nationwide immunisation programme.

In South Korea, national guidelines in force to control and prevention measles and rubella include national immunisation programme and active disease surveillance system.[2 4 22] MMR vaccination has been covered by national health insurance that provides free of charge immunisation to all children aged ≤12 years, and clinical laboratory screening for rubella immunisation status using antirubella-specific IgG tests in pregnant women has been covered by the national health insurance free of charge for women visiting obstetrics clinics.[17] Susceptible woman of childbearing age is indeed a priority, and public health efforts should be focused on catch-up activities in order to reduce the rate of susceptible young adults, especially for all women of childbearing age.[23] Gynaecologists and general practitioners should be

Table 3 Previous studies on rubella seronegativity in women that included more than 1000 subjects and were published within the past 10 years, grouped by WHO region

WHO region	Publication year	N	Country	Seronegativity (%)	Population	Reference	Measurement method
AFR	2009	7430	South Africa	6.2	WCBA	Schoub *et al*[26]	Bio-Rad Platelia Rubella IgG ELISA
AMR	2009	8939	Brazil	28.4	Pregnant	Inagaki *et al*[27]	Q-Preven IgG-DBS kit
AMR	2011	9610	Brazil	11.6	Pregnant	Artimos de Oliveira *et al*[28]	Beckman Coulter Access RUBELLA IgG ChLIA or bioMérieux VIDAS RUB IgG II ELFA
AMR	2016	54 717	Brazil	4.5	Pregnant	Avila Moura *et al*[29]	Q-Preven IgG-DBS kit
AMR	2009	5783	Canada	7.0	Pregnant	McElroy *et al*[30]	Hemagglutination inhibition test
AMR	2013	459 963	Canada	4.4	WCBA	Lim *et al*[31]	Abbott AxSYM Rubella IgG MEIA
AMR	2015	157 763	Canada	15.9	Pregnant	Lai *et al*[32]	Abbott ARCHITECT Rubella IgG CMIA
EMR	2014	4062	Kuwait	6.8	Pregnant	Madi *et al*[33]	Abbott ARCHITECT Rubella IgG CMIA
EMR	2013	2284	Morocco	9.8	Pregnant	Belefquih *et al*[34]	Siemens Enzygnost Anti-Rubella-Virus IgG EIA
EMR	2014	10 276	Saudi Arabia	8.7	Pregnant	Alsibiani *et al*[35]	Dade Behring ELISA BP III
EUR	2012	424 876	England	2.6	Pregnant	Byrne *et al*[36]	Microgen Mercia Rubella G EIA
EUR	2013	1090	Germany	1.6	Pregnant	Enders *et al*[37]	Hemagglutination inhibition test
EUR	2013	74 810	Ireland	6.2	Pregnant	O'Dwyer *et al*[38]	Method not described
EUR	2012	2385	Italy	8.0	Pregnant	De Paschale *et al*[39]	DiaSorin ETI-RUBEK-G PLUS EIA
EUR	2015	22 681	Spain	5.9	Pregnant	Vilajeliu *et al*[40]	Siemens ADVIA Centaur Rubella G ChLIA
EUR	2010	41 637	Sweden	4.2	Pregnant	Kakoulidou *et al*[41]	Abbott AxSYM Rubella IgG MEIA
EUR	2009	1972	Turkey	3.9	Pregnant	Tamer *et al*[42]	Abbott AxSYM Rubella IgG MEIA
EUR	2012	5959	Turkey	1.9	Pregnant	Uysal *et al*[43]	bioMérieux VIDAS RUB IgG II ELFA
EUR	2011	11 987	UK	4.4	Pregnant	Matthews *et al*[44]	DiaSorin ETI-RUBEK-G EIA
EUR	2016	19 046	UK	6.3	Pregnant	Ogundele *et al*[45]	Roche E602 MODULAR analyzer
SEAR	2011	2224	Nepal	9.2	WCBA	Upreti *et al*[46]	Enzygnost Anti-Rubella-Virus IgG EIA
SEAR	2014	1988	Vietnam	28.9	Pregnant	Miyakawa *et al*[47]	bioMérieux Mini VIDAS EIA
WPR	2008	1020	Australia	2.7	WCBA	Nardone *et al*[48]	Siemens Enzygnost Anti-Rubella-Virus IgG EIA
WPR	2008	2741	Japan	6.7	Pregnant	Okuda *et al*[49]	Hemagglutination inhibition test
WPR	2013	13 924	Japan	2.7	Pregnant	Hanaoka *et al*[50]	Hemagglutination inhibition test
WPR	2014	20 363	Japan	4.7	Pregnant	Yamada *et al*[51]	Hemagglutination inhibition test
WPR	2017	782 293	China	33.8	WCBA	Liu *et al*[52]	Method not described
WPR	2011	43 640	Taiwan	10.9	Pregnant	Lin *et al*[53]	Abbott AxSYM Rubella IgG MEIA and Beckman Coulter Access RUBELLA IgG ChLIA
WPR	2012	14 090	Taiwan	6.5	Pregnant	Lin *et al*[54]	Abbott AxSYM Rubella IgG MEIA
WPR	2019	327 637	Republic of Korea	8.7	WCBA	This study	Abbott ARCHITECT Rubella IgG CMIA

AFR, Africa region; AMR, American region; EMR, Eastern Mediterranean Region; EUR, European region; SEAR, South-East Asian region; WCBA, women of childbearing age; WPR, Western Pacific region.

encouraged to propose rubella screening for women of childbearing age before they become pregnant to identify those women who lack rubella antibodies, whether acquired as the result of vaccination or a natural infection.[23] Finally, active surveillance from laboratories that perform rubella immunity testing should be planned; laboratories should notify the Public Health Authority about every woman of childbearing age with a negative test, and the Public Health Authority should engage these women to promote immunisation against rubella.[23] Serological surveillance is an important tool for the evaluation of vaccination programmes and avoids the limitations of passive disease reporting systems; this is one of the entry points for congenital rubella syndrome surveillance, where gaps limit the ability to monitor progress towards its elimination.[23]

In this study, women living in Sejong city were the most protected from rubella infection. In early 2007, the South Korean government had created a special administrative district from parts of the South Chungcheong and North Chungcheong provinces, near Daejeon, to relocate nine ministries and four national agencies from Seoul. Various government programmes for encouraging more births, such as incentives, in different regions may have affected the results.[4] In this study, less than 1000 women had been tested for antirubella IgG in the Gangwon province and Ulsan. This may affect the per cent seropositivity of antirubella IgG in the present study. Future studies are needed to define the effect of regional differences of government strategies on rubella seroprevalences.

One limitation of this study was the lack of clinical information, such as vaccination history or contact history with rubella-infected individuals. The results of this study were prone to ascertainment bias because the study population was based on mostly private obstetric clinics; thus, results might be different from those obtained from individuals using national or public healthcare providing institutions, although the use of a population-based study minimised selection bias.[24] Because the exact proportions of pregnant women in Korea who used public health facilities to test for antirubella IgG, and their sociodemographics as well as rubella vaccine coverage among the population seeking healthcare from private and public sectors and the proportion of pregnant women as well as the general population seeking care from the private sector across provinces were not available, future studies to evaluate those factors associated with rubella control and prevention are needed. However, we do not yet understand what surrogate markers, other than antibodies, show longer-term cell-mediated immunity and protection from disease.[1] Seroprevalence studies are an essential tool to monitor the efficacy of vaccination programmes, to understand population immunity and to identify populations at higher risk of infection.[25] This study is a cross-sectional study and merely descriptive analyses were adopted in this study. The results of this study were prone to ascertainment bias. The present study did not include men, women with older ages or foreigners living in South Korea. Therefore, the findings are not generalisable to these groups. A systems-level approach to understanding the development and maintenance of acute and long-term immunity to rubella and a rubella-containing vaccine is needed.[1]

CONCLUSION

In conclusion, this study investigated immunisation status of rubella among Korean women of childbearing age. Considering the immunisation status by age group and the increased prevalence of women with equivocal results, future public health efforts should be focused on catch-up activities. The results of this study could be used as foundational knowledge for strengthening disease control and prevention of rubella, including a nationwide immunisation programme.

Contributors All authors contributed to manuscript preparation. RC and SGL: conception, design, statistical analyses and interpretation of the data. RC, YoO, SHK and SGL: data acquisition. RC: article drafting. RC, SGL and EHL: critical article revision for important intellectual content. SGL and EHL: obtaining funding. RC, YoO, YeO and SHK: administrative and technical support. RC, YoO and SHK: collection and assembly of data. All authors read and approved the final manuscript.

Funding This work was supported by Abbott Diagnostics Korea.

Disclaimer The sponsor had no involvement in the study design, data interpretation, or writing of the manuscript.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval All procedures involving human subjects were approved by the Institutional Review Board of Green Cross Laboratories (GCL 2017-1010-02).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request.

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