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Review

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Trend in Measles Seroprevalence in the Western Pacific Region: A Systematic Review

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No potential conflict of interest relevant to this article was reported.

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ABSTRACT

Despite improvements in vaccine coverage, a resurgence of measles has been reported, especially in the infant and adult populations in recent years. We conducted a systematic review of seroprevalence studies conducted in the Western Pacific Region (WPR) to provide insights into seropositivity trends in different countries. This systematic review aimed to collect data from all available measles seroprevalence studies to characterize the differences in population immunity against measles in different countries. We searched the online databases PubMed and Embase to identify: 1) observational studies that investigated seroprevalence in all age groups, and 2) results reported as antibody levels. The following variables were extracted from different study arms: paper identification (title, first author, publication year), inclusion and exclusion criteria, study site, age of subjects, number of subjects, country/area, population, methods, and seropositivity (%). The search yielded a total of 69 studies included in the review. Among the 1–6-year-old group, seropositivity remained relatively high, at 81–100% in China, 86–94% in Korea, and 77–91% in Australia. In adolescents aged 7–18-years old, seropositivity was relatively constant in China and Australia over time; however, a decreasing trend was noted in Korea in 2011 (66%), 2014 (69%), and 2014 (50%) in this age group. A similar downward trend was observed among Korean adults aged 19–39 years in 2011 (74%), 2019 (71%), and 2019 (64%). Children are likely to be protected by universal vaccination programs in WPR countries and regions. However, susceptible individuals with waned immunity may be present among the adult population.

Keywords: Measles; Seroprevalence; Vaccination; Vaccine

INTRODUCTION

Measles is a highly contagious viral disease caused by the measles virus that places a significant burden on children.[1] The virus is transmitted via respiratory droplets from infected individuals and presents with typical symptoms, such as fever, rash, cough, and rhinorrhea. Measles is preventable through vaccination and widespread vaccination has led to a significant reduction in cases in many parts of the world.[2]

The Western Pacific Region (WPR) comprises 37 countries and regions, encompassing almost 1.9 billion people. Over the past decades, the incidence of measles has decreased

in many parts of the world, especially in the WPR, since the introduction of the 2nd dose of measles-containing vaccines in the 1990s.[3]

Despite these improvements, a resurgence of measles has been reported in recent years, especially in infant and adult populations.[4] Factors associated with resurgent cases can be attributed to decreased vaccination coverage, resulting in the loss of herd protection, and an increase in the volume of international travel, facilitating the spread of the disease.[5,6] Following childhood vaccination, adults may lack sufficient immunity due to secondary vaccine failure.[7] However, the evidence of trend changes in age-specific immunity requires further investigation.

Hence, we conducted a systematic review of seroprevalence studies conducted in the WPR to provide insights into seropositivity trends in different countries. This systematic review aimed to collect data from all available measles seroprevalence studies to characterize the differences in population immunity against measles in different countries.

MATERIALS AND METHODS

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We searched the online databases of PubMed and Embase to identify studies using a combination of the following search terms in “all fields”: "measles” [MeSH Terms] AND (“seroepidemiologic” [All Fields] OR “seroprevalence” [All Fields]) AND (Western Pacific OR Australia OR Brunei OR Cambodia OR China OR Cook Island OR Fiji OR Japan OR Kiribati OR Lao Malaysia OR Marshall Island OR Micronesia OR Mongolia OR Nauru OR New Zealand OR Niue OR Palau OR Papua New Guinea OR Philippines OR Korea OR Samoa OR Singapore OR Solomon Island OR Tonga OR Tuvalu OR Vanuatu OR Viet Nam OR Vietnam). The databases were searched for observational studies published through to December 2019.

Two investigators (J Park, YJ Choe) independently selected studies in accordance to the defined inclusion criteria, and extracted the data using a uniform method. From eligible studies, following information was collated: author, year, country, study design, study population, method of collection, sample size, test method, age range, seropositivity (%). Eligible studies met the following inclusion criteria: 1) observational studies that investigated seroprevalence in all age groups and 2) results reported as antibody levels. We excluded post-vaccination immunogenicity studies conducted during clinical trials, non-original articles, and studies on preterm infants. Descriptive analyses were performed separately for countries and areas in all groups. We examined seropositivity among the results of different studies.

RESULTS

The initial literature search yielded 206 studies (**Fig. 1**). After the removal of duplicates, the 136 remaining studies were screened according to their title and abstract; 96 of these studies were selected for full-text review. A final total of 69 studies were included in the review.

Table 1 shows the number of studies included from each country and area. There was a total of 19 studies from China,[8-26] followed by 14 from Korea,[27-40] 13 from Japan,[41-53] 11 from

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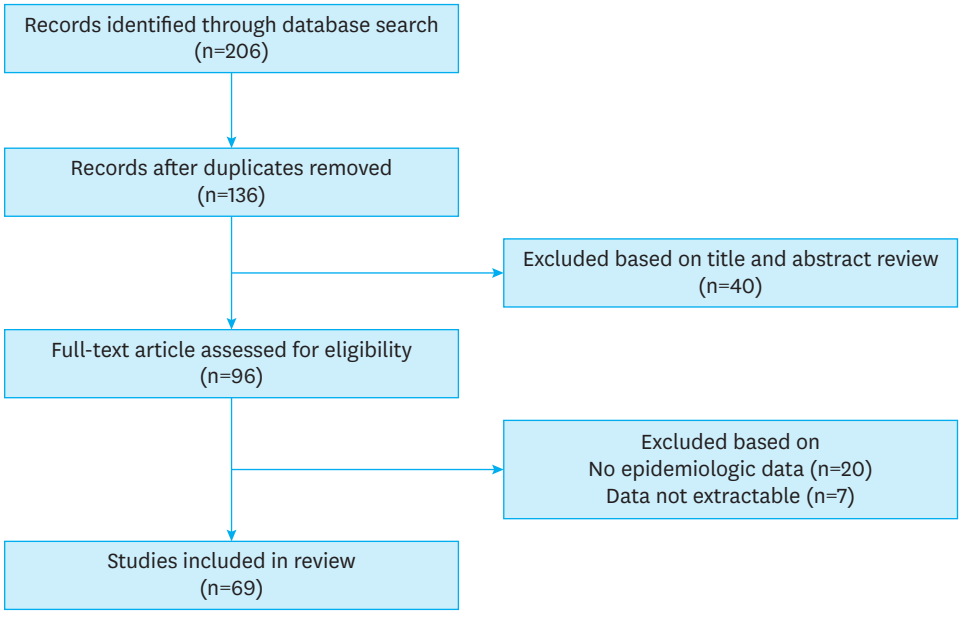

Fig. 1. Flow diagram of the search strategy and the number of articles included and excluded at each stage.

Table 1. Number of studies included in the review per countries and areas

Countries and areas	No. of studies
China	19
Republic of Korea	14
Japan	13
Australia	11
Singapore	4
Lao PDR	2
New Zealand	2
American Samoa	1
Cambodia	1
Hong Kong SAR	1
Northern Mariana Islands	1
Total	69

Australia,[54-64] four from Singapore,[65-68] two each from Lao PDR[69,70] and New Zealand,[71,72] and one each from American Samoa,[73] Cambodia,[74] Hong Kong SAR,[75] and the Northern Mariana Islands.[76]

Table 2 describes the seroprevalence of measles in detail. Studies conducted in China between 2004 and 2009 showed a seropositivity range of 70.6–89%,[10,12,14,16,23,25] whereas those conducted between 2011 and 2018 showed a seropositivity range of 79.8–93.4%.[15,17,20-22,24,26] In Korea, seropositivity ranged from 87.8%[34] in 2000 to 91% in 2017.[27] Seropositivity was high in Japan, between 92.6% in 2000[42] and 94.8% in 2013.[52] In Australia, the seropositivity increased from 80% in 1995[56] to 89.7% between 2012–2013.[57]

Fig. 2 shows the annual seropositivity trends by age group in China, Korea, and Australia. Among the 1–6-year-old group, seropositivity remained relatively high in all three countries: 81–100% in China,[10,12-17,21-24] 86–94% in Korea,[27,28,30-33,39,40] and 77–91% in Australia.[54-60] In adolescents aged 7–18 years old, seropositivity was also relatively constant in China and Australia over time; however, a decreasing trend was noted in Korea in 2011 (66%), 2014

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Table 2. Description of measles seroprevalence studies included in the systematic review

Country and area	Authors	Year of data	Region	Population	Method of collection	Sample size	Test method	Age range	Seropositive (%)
China	Yu et al.[23]	2004	Xinjiang	All ages	Direct sampling	2,014	EIA	0–35 yr	89
	Fu et al.[10]	2008	Guangzhou	All ages	Direct sampling	4,036	EIA	0–60 yr	70.6
	Liu et al.[13]	2008	Jiangsu	All ages	Direct sampling	4,627	EIA	-	88.7
	Ma et al.[16]	2006	Heilongjiang	All ages	Direct sampling	1,050	HI + EIA	-	93.9
	Zhang et al.[25]	2009	Qinghai	Infants	Direct sampling	434	EIA	0–8 mon	79.2
	He et al.[12]	2009	Zhejiang	Children	Direct sampling	1,961	EIA	8 mon–19 yr	88
	Xiong et al.[22]	2011	Dongguan	All ages	Direct sampling	1,960	EIA	0–60 yr	93.4
	Wang et al.[21]	2011	Zhejiang	All ages	Direct sampling	1,015	EIA	0–81 yr	93.6
	Ma et al.[15]	2013	Hunan	All ages	Residual sera	632	EIA	0–34 yr	74.5
	Zhang et al.[24]	2014	Zhejiang	All ages	Residual sera	307	EIA	>2 mon	90.9
	Wang et al.[20]	2014	Shaanxi	Children	Direct sampling	755	EIA	2–4 yr	91.13
	Pei et al.[17]	2016	Shaanxi	All ages	Direct sampling	3,574	EIA	2 mon–49 yr	85.9
	Zhang et al.[26]	2018	Beijing	All ages	Direct sampling	2,144	EIA	0–76 yr	79.8
	Han et al.[11]	2005–2014	Dongguan	Infants	Direct sampling	708	EIA	0–11 mon	55.9
	Liu et al.[13]	2008–2010	Jiangsu	All ages	Direct sampling	4,610	EIA	-	88.7–93.6
	Tang et al.[19]	2009–2015	Jiangsu	All ages	Direct sampling	1,070	EIA	9 mon–49 yr	82.7–93.2
	Chong et al.[9]	2010–2011	Hubei	All ages	Direct sampling	2,578	EIA	-	88
	Boulton et al.[8]	2011–2015	Tianjin	All ages	Direct sampling	2,818	EIA	1–49 yr	72.7
	Su et al.[18]	2011–2015	Tianjin	All ages	Direct sampling	3,318	EIA	0–49 yr	75.8
Korea	Bae et al.[34]	2000	Nationwide	Children	Direct sampling	939	EIA	7–9 yr	87.8
	Kim et al.[40]	2002	Nationwide	All ages	Residual sera	5,826	EIA	0–34 yr	93.1–97.1
	KCDC[29]	2004	Nationwide	Children	Residual sera	7,131	EIA	7–16 yr	92.3
	KCDC[30]	2006	Nationwide	Children	Direct sampling	2,983	EIA	4–6 yr	97.3
	Kim et al.[39]	2010	Nationwide	Children	Residual sera	1,400	EIA	2–18 yr	86
	Pang and Choi[32]	2011	Goyang	Children visiting hospital	Direct sampling	408	EIA	7–20 yr	67.4
	Kang et al.[38]	2014	Nationwide	All ages	Residual sera	3,050	EIA	0–50 yr	80.1
	Kim et al.[33]	2014	Nationwide	Children	Direct sampling	1,000	EIA	0–9 yr	49.5
	Shin[27]	2017	Seoul	Healthcare workers	Direct sampling	2,956	-	-	91
	Chang et al.[35]	2019	Daegu	Healthcare workers	Direct sampling	9,132	EIA	≥20 yr	75.9
	KCDC[28]	2000–2001	Nationwide	Children	Direct sampling	18,139	EIA	7–18 yr	89.4
	KCDC[31]	2007–2008	Nationwide	All ages	Residual sera	5,150	EIA	0–48 mon, 15–44 yr	72.8–97.6
	Cho et al.[36]	2009–2010	Seoul	Infants	Direct sampling	295	EIA	0–11 mon	33.3
	Jung et al.[37]	2014–2018	Seoul	Healthcare workers	Direct sampling	7,411	EIA	≥20 yr	73
Japan	Asari et al.[42]	2000	Osaka	Healthcare workers	Direct sampling	271	EIA	21–50 yr	92.6
	Hatakeyama et al.[43]	2002	Tokyo	Healthcare workers	Direct sampling	860	HI + EIA	20–65 yr	98.5
	Shibata et al.[50]	2005	Izumo	Healthcare workers	Direct sampling	898	EIA	-	94
	Watanabe et al.[41]	2012	Gifu	Healthcare workers	Direct sampling	1,385	EIA	-	87.6
	Takemoto et al.[52]	2013	Aichi	Umbilical cord blood	Direct sampling	561	EIA	0	94.8
	Tsuji et al.[53]	1994–1995	Urawa City	All ages	Residual sera	1,591	HI + NT	0–90 yr	68.7–95
	Kanda et al.[45]	2004–2010	Tokyo	Pregnant women	Direct sampling	10,349	NT	-	88.6
	Kumakura et al.[48]	2005–2009	Izumo	Healthcare workers	Direct sampling	1,811	EIA	19–64 yr	95.3
	Kimura et al.[47]	2007–2012	Gunma	Healthcare students	Direct sampling	1,746	EIA	-	52.7–96.6
	Nishiura et al.[49]	2009–2010	Tokyo	White collar workers	Direct sampling	509	EIA	19–30 yr	93.3
	Katsuyama et al.[46]	2012–2015	Ibraki	Female college students	Direct sampling	168	EIA	20–21 yr	100
	Kanamori et al.[44]	2012–2013	Miyagi	Healthcare workers	Direct sampling	2,664	EIA		95.5
	Shoho et al.[51]	2015–2018	Gunma	Female college students	Direct sampling	841	EIA	18.5 yr (mean)	86.9

(continued to the next page)

Table 2. (Continued) Description of measles seroprevalence studies included in the systematic review

Country and area	Authors	Year of data	Region	Population	Method of collection	Sample size	Test method	Age range	Seropositive (%)
Australia	Ferson et al.[56]	1995	New South Wales	Children	Direct sampling	430	EIA	12–59 mon	80
	Gilbert et al.[59]	1999	Nationwide	Children	Residual sera	5,854	EIA	1–18 yr	85–90
	Riddell et al.[64]	1999	Victoria	Children	Direct sampling	1,155	EIA	5–19 yr	93–94
	Kelly et al.[61]	1999	Victoria	Children	Residual sera	376	EIA	6–16 yr	93–94
	Hogg et al.[60]	1995	Nationwide	Children	Residual sera	923	EIA	12–60 mon	86
	Gidding et al.[57]	2002	Nationwide	All ages	Residual sera	3,761	EIA	1–34 yr	64.9–92.1
	Andrews et al.[54]	2002	-	All ages	Residual sera	3,774	EIA	1–34 yr	89.2–92.1
	Causer et al.[55]	1992–1995	Sydney	Children	Direct sampling	580	EIA	18 mon–4 yr	88
	Kelly et al.[62]	1999–2002	Victoria	Adults	Direct sampling	282	EIA	17–31 yr	83.9–85.5
	Paxton et al.[63]	2000–2002	Melbourne	Immigrant children	Direct sampling	115	EIA	8.7 yr (mean)	90
	Gidding et al.[58]	2012–2013	Nationwide	All ages	Residual sera	2,729	EIA	1–49 yr	89.7
Singapore	Tan et al.[68]	2014	-	Healthcare workers	Direct sampling	147	EIA	-	93.8
	Ong et al.[67]	1989–1998	-	All ages	Direct sampling	2,026	EIA	6 mon–45 yr	77.9–91.5
	Ho et al.[66]	1989–2010	-	All ages	Direct sampling + residual sera	7,379	EIA	–	83.1–91.4
	Ang et al.[65]	2008–2010	-	Children	Residual sera	1,200	EIA	1–17 yr	83.1
Lao PDR	Hachiya et al.[69]	2014	Nationwide	All ages	Direct sampling	2,135	EIA	1–81 yr	83.9
	Phengxay et al.[70]	2007–2008	Vientiane	Children	Direct sampling	411	EIA	6–12 yr	97.6
New Zealand	Weir et al.[71]	2009	Nationwide	All ages	Direct sampling	2,859	EIA	6–44 yr	91.1–97.0
	Williamson et al.[72]	2009	Aukland	Healthcare workers	Direct sampling	424	EIA	-	91
American Samoa	Mahamud et al.[73]	2011	-	Children	Direct sampling	509	EIA	5–9 yr	92
Cambodia	Mao et al.[74]	2012	Nationwide	Women of child-bearing age	Direct sampling	2,154	EIA	15–39 yr	95.9
Hong Kong SAR	Chuang et al.[75]	1990–1996	-	Children	Residual sera	-	EIA	1–19 yr	85.5–92
Northern Mariana Islands	Stambos et al.[76]	2006	-	Female guest workers	Direct sampling	153	EIA	17–51 yr	74.5–100

Abbreviations: EIA, enzyme-linked immunosorbent assay; HI, hemagglutination inhibition; NT, neutralization test.

(69%), and 2014 (50%) in this age group.[32,33,38] A similar downtrend was noted for Korean adults aged 19–39 years old in 2011 (74%), 2019 (71%), and 2019 (64%).[32,35,37]

DISCUSSION

In this study, we found a downward trend in seropositivity among adolescent and adult populations in Korea, despite a mass vaccination campaign and a vaccine available for the childhood population. Our findings highlight the need to assess the long-term protective effects of measles-containing vaccines. A previous study in the United States evaluated the persistence of measles antibodies among children who received two doses of vaccination and showed positive antibody titers 10 years after the second vaccination for measles.[77] This finding suggests that the slowly declining trend of antibody titers would lead to an increase in the potentially susceptible population by 33% at 20 years after the second dose of vaccination, whereas the proportion of the seronegative population was not projected to reach 1% until 30 years after the second dose. Another study carried out in Italy to evaluate the long-term immunogenicity of the measles vaccine in medical students and residents showed a protective immunoglobulin G titer in 84.8% of participants with a mean age of 21

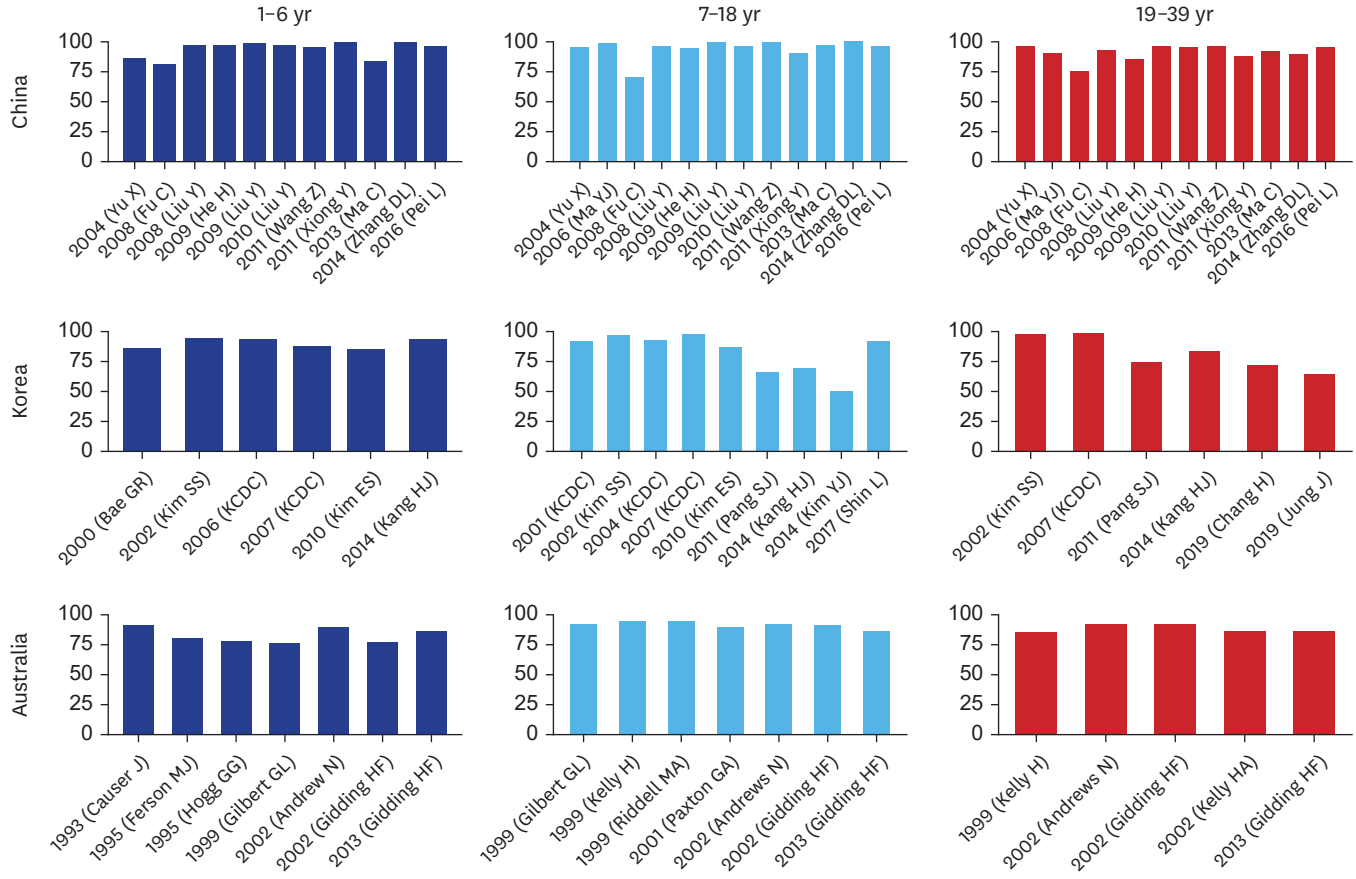

Fig. 2. Trend in age-specific seropositivity by countries.

years who received two doses of the measles vaccination.[78] As shown in previous studies, catch-up vaccination in adulthood may be needed by healthcare providers caring for young infants who are not immune to measles.

We also found a relatively high seropositivity among childhood populations across the WPR. The region has facilitated the annual establishment of national verification committees and one subregional verification committee to provide comprehensive reports documenting their steady progress towards elimination.[79] Substantial progress has been made in the region to control measles transmission. However, the measles virus continues to circulate, causing outbreaks. As noted in a previous review, Korea has experienced a series of measles resurgences due to imports and healthcare-associated transmission in infants.[80] However, the overall incidence and surveillance indicators met the World Health Organization (WHO) criteria for measles elimination.

Our study had some limitations. First, we were unable to perform a meta-analysis and excluded sampling or selection bias from the overall compilation of the results. Second, the data included in this review were derived from various age groups and serological assays with different cut-off thresholds. This heterogeneity may have affected the comparison between seroprevalence studies and the interpretation of longitudinal changes. A low seroprevalence of 49.5% was noted in Korean children aged 0–9 years; however, the study does not present the percentage of infants who are not eligible for measles-containing vaccine.[33] Third, the

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data was from eleven WPR countries and regions, which account for less than one thirds of all territories within the WPR oversight. Therefore, our result must be interpreted cautiously.

Despite these limitations, the compiled data highlighted consistent changes in measles susceptibility and may aid in identifying vulnerable populations in the WPR. Measles vaccination has clearly reduced susceptibility among childhood populations, and our study confirms the significant impact of the universal childhood vaccination program in reducing susceptibility in children. This finding may be useful for informing countries that plan to implement measles vaccination in their public health programs.

Data from previously published measles seroprevalence studies suggest that children are likely to be protected by the universal vaccination program introduced in the 1980s. Currently, measles is clearly not prevalent in children; susceptible individuals are more common among the adult population in Korea, who may have waning immunity. Despite the low seroprevalence among adult population, sustained measles elimination status may be explained by other factors. Heightened protection through cellular immune response may be one of the reasons for sustained measles elimination status in many countries.[81] As in other vaccine-preventable diseases such as varicella, mumps, and rubella, the immune correlate of protection should be further investigated in regard to cellular immunity for measles as well.

In conclusion, our finding suggest that children are likely to be protected by universal vaccination program in WPR countries; however, susceptible individuals with waned immunity may be present among the adult population.

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요약

홍역의 예방을 위한 백신이 도입되었음에도 불구하고, 최근 십수년 간 영유아 및 성인 인구에서 홍역 발생이 지속되고 있다. 본 종설에서는 서태평양지역(Western Pacific Region, WPR)에서 수행되었던 홍역 항체양성도 연구들을 체계적으로 검토하여 홍역에 대한 집단면역도의 추이를 평가하고자 하였다. 서태평양지역에서 수행된 항체양성도 연구에서 도출된 전 연령대의 항체 유병율을 조사한 관찰 연구를 탐색하기 위해 온라인 데이터베이스 PubMed과 Embase를 검색하였다. 다음 변수들이 서로 다른 연구군에서 추출되다: 논문 식별자(제목, 제1 저자, 발행 연도), 포함 및 제외 기준, 연구 장소, 대상 연령, 대상 수, 국가/지역, 인구, 방법 및 혈청양성도(%). 검색 결과, 총 69건의 연구가 포함되었다. 1-6세 연령 그룹 중에서의 항체양성도는 중국이 81-100%로, 한국 86-94%로, 호주 77-91%로 상대적으로 높게 나타났다. 7-18세 청소년에서는 중국과 호주에서의 양성도는 시간이 지나도 상대적으로 일정하게 유지되었지만, 한국에서는 2011년(66%), 2014년(69%), 2014년(50%) 등으로 감소하는 추세가 있었다. 비슷한 하향 추세가 한국 성인 인구 중 19–39세에서 2011년(74%), 2019년(71%), 2019년(64%)에서도 관찰되었다.