SMJ Singapore Medical Journal

Measles seroprevalence in Thailand: are adolescents and young adults at risk of measles?

Panit Takkinsatian[1], MD, Kamolmart Wannaphahoon[1], MD, Prasit Upapan[2], MD, Sansnee Senawong[3], MD, Olarn Prommalikit[1], MD

[1]Department of Pediatrics, [2]Department of Medicine, Faculty of Medicine, Srinakharinwirot University, Nakhon Nayok, [3]Department of Immunology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand

Correspondence: Dr Panit Takkinsatian, Department of Pediatrics, Faculty of Medicine, Srinakharinwirot University, Address: 62 Rangsit-Nakhonnayok Road, Ongkharak, Nakhon-Nayok, Thailand 26120. panit_tak@hotmail.com

Singapore Med J 2022, 1–23
https://doi.org/10.11622/smedj.2022058
Published ahead of print:

ABSTRACT

Introduction: During the last decade, measles has become an important re-emerging disease in Thailand. The objective of this study was to measure measles seroprevalence and its influencing factors and to plan for an improved vaccination program.

Methods: A total of 600 participants aged between 9 months and 50 years were divided into seven groups those represent birth cohorts that experienced different measles vaccination policies. Participants' blood samples were obtained to measure measles immunoglobulin G (IgG) levels.

Results: None of the participants in the 9-month age group had measles IgG levels beyond a protective level. Participants in the following age groups: 2 ½, 5–15, 16–29, 30–33, 34–40, and 41–50 years had 82% (95% confidence interval [CI] 73.3–90.7), 50% (95% CI 36.1–63.9), 52% (95% CI 42.3–62.7), 70% (95% CI 61.1–78.9), 88.8% (95% CI 84.1–93.5), and 98.8% (95% CI 96.4–100.0) measles seropositivity, respectively. The study did not find any significant factors affecting measles seropositivity.

Conclusion: Individuals aged 15–34 years are vulnerable to measles infections. Supplementary vaccination in special situations, including post-exposure prophylaxis during an outbreak among young adults or providing for high-risk occupations, such as healthcare personnel, should be encouraged.

Keywords: measles, seroprevalence, Thailand, vaccine

INTRODUCTION

Measles is a highly contagious, airborne-transmitted disease that mostly occurs among children younger than 5 years of age and young adults. It causes high-grade fever, cough, coryza, conjunctivitis, tiny white spots on the inside of the mouth (Koplik's spots), and rash. Measles can also cause various complications, including pneumonia, otitis media, diarrhea, encephalitis, and subacute sclerosing panencephalitis.[1] Measles can be prevented by vaccination; therefore, the World Health Organization (WHO) launched the Measles Strategic Plan in September 2013 to decrease global measles deaths by at least 95% by 2015 compared to the levels in 2000 and to achieve measles elimination in at least five WHO regions by 2020. After implementation, this program objective has proven unlikely to be achieved in some regions, especially in Southeast Asia. Therefore, the high-level consultation between member states in March 2019 concluded that the draft "Strategic Plan for Achieving and Sustaining Measles and Rubella Elimination in the WHO South-East Asia Region: 2020–2024" be adopted and fully implemented by all countries to ensure that the 2023 goal is achieved.[2]

Before the measles vaccine implementation era, all individuals were susceptible to measles. Most people experienced natural infection during childhood. Over 90% of individuals were infected before 10 years of age. Only young infants were protected by passively acquired maternal antibodies after a few months of life. Fortunately, natural infection results in lifelong protection.[3] Currently, the WHO recommend two doses of measles vaccine for all children and proposes the strategy's components, including achieving and maintaining high coverage (>90%) nationally with the routinely scheduled first dose of measles-containing vaccine among children aged 1 year and ensuring that all children receive a second opportunity for measles immunisation.[4] The estimated number of deaths from measles dropped from 750,000 in 2000 to

197,000 in 2007. However, the incidence of measles has been rising again in the past several years, despite vaccine coverage remaining high in many countries. According to the WHO report, measles is still common, particularly in parts of Africa and Asia. In 2018, more than 140,000 people died of measles. The overwhelming majority (>95%) of measles deaths occur in countries with low per capita incomes and weak health infrastructure.

In Thailand, vaccines containing measles have been incorporated into the National Immunisation Program since 1984, and the first dose of monovalent measles vaccine (M) was administered to infants at 9–12 months of age. In 1996, the second dose of measles vaccine was administered to 6-year-old children and was replaced by the trivalent measles–mumps–rubella (MMR) vaccine in 1997. Since 2014, Thai recommendations have adjusted the schedule of the second-dose measles vaccination from 6 years to 2.5 years of age. This latest immunization program of measles is mandatory and implemented homogenously across the country among the populations born and living in Thailand. Therefore, in 2013, measles vaccine coverage in Thailand was relatively high at 98.7% and 93.8% in children aged 9 months and 7 years, respectively.[5] After measles vaccination implementation, the incidence of measles dramatically decreased from 16.49 cases per 100,000 population in 2002 to 4.49 cases in 2008 and subsequently rose again to 8.89 cases per 100,000 population during 2017–2019.[5] There have been many outbreaks in several parts of Thailand, especially in the southern region and some other provinces including Nakhon Nayok. While the vaccine coverage in Nakorn Nayok province was approximately 90% for the last ten years. The WHO aims to reduce the global annual measles incidence to <5 cases per million population. The burden of measles outbreaks does not only affect the general population but also healthcare personnel.[4] Surprisingly, most of the patients were young adults who should have received two doses of the measles-containing

vaccine. Therefore, this study aimed to establish the seroprevalence of measles according to age group in 2018 that represent birth cohorts that experienced different measles vaccination policies and to understand the factors contributing to measles seropositivity.

METHODS

The participants were healthy children attending well-baby clinics and healthy adults with acute illnesses visiting outpatient clinics and inpatient department at HRH Princess Maha Chakri Sirindhorn Medical Center, Srinakharinwirot University, Thailand. The subjects had to meet the following criteria to include them in the study: be of good general health (apart from acute illness); have no chronic illness; not undergoing immunosuppressive therapy; have no clinical signs of infection with HIV or other immunodeficiency disorders; healthcare providers or those who worked at healthcare facilities were excluded. 600 randomized participants aged between 9 months and 50 years were enrolled in this study from June 2018 to May 2019, and were divided into seven groups by age those represent birth cohorts that experienced different measles vaccination policies, including 9 months (before receiving the first dose of the measles-containing vaccine), 2 ½ years (before receiving the second dose of the measles-containing vaccine), 5–15 years, 16–29 years (who were expected to have already received two doses of the measles-containing vaccine), 30–33 years (who were expected to receive only one dose of the measles-containing vaccine), 34–40, and 41–50 years (who had never received a measles-containing vaccine). General data, such as sex, race, underlying disease, history of measles infection, and vaccination, were recorded in a case record form. Thereafter, 1 mL of blood samples were centrifuged at 3,500–4,000 rpm for 10 min to extract sera specimens and stored at –80 °C in a refrigerator. The presence of specific antibodies against measles from serum samples

was determined using the enzyme-linked immunosorbent assay. We used the EROIMMUN™ semiquantitative measles virus immunoglobulin G (IgG) test (Lübeck, Germany), which allows both qualitative and quantitative interpretation. The concentration of IgG antibodies was calculated from the measured values of optical density and the calibration curve according to the manufacturer's instructions. The results were reported in the international unit (IU/mL). According to instruction of the test kit, the qualitative results were reported as positive (IgG level ≥275 IU/mL), borderline (IgG level of 200–274 IU/mL), and negative (IgG level <200 IU/mL). This study was approved by the Institutional Review Board of Srinakharinwirot University (SWUEC-189/61E).

Statistical Analysis

SPSS Statistics version 22 (IBM SPSS Statistics Inc., Chicago, IL, USA) was used to evaluate the data. Descriptive data, including age, sex, race, residential area, smoking, parental education, and history of measles infection, were calculated, and presented as frequency, percentage, mean and standard deviation. In addition to descriptive statistics, the associations between these factors and measles seroprevalence were tested using multivariate logistic regression, with a p-value <0.05 indicating statistical significance.

RESULTS

A total of 631 people were screened for eligibility but only 600 participants aged 9 months to 50 years were enrolled from June 2018 to May 2019 (fig. 1). The distribution of participants by age group was as follows: 9 months, 8.3%; 2 ½ years, 8.3%; 5–15 years, 8.3%; 6–29 years, 16.7%; 30–33 years, 16.7%; 34–40 years, 28.3%; and 41–50 years, 13.4%. Of these participants, 391 (65.2%) were men, and 99.8% were Thai (Table I).

The overall measles IgG prevalence was 69.7%. (95% confidence interval [CI] 66.3–73.5). The seroprevalence among children aged 9 months who were unvaccinated was 0%. The geometric mean titer (GMC) was 77.7 ± 27.0 IU/mL and increased to 82.0% (95% CI 73.3–90.7), GMC 1,109.8 ± 1,069.8 IU/mL at age 2 ½ years (after receiving a single dose and before receiving the 2nd dose of the vaccine); however, the seropositivity gradually decreased among older children and young adults aged 5–15 and 16–29 years who were expected to have already received two doses of the measles-containing vaccine at 50.0% (95% CI 36.1–63.9) and 52.0% (95% CI 42.3–62.7), respectively, and among those aged 30–33 years who were expected to have received only one dose of the measles-containing vaccine at 70.0% (95% CI 61.1–78.9). Their GMCs were 581.2 ± 871.3, 666.3 ± 926.6, and 1,153.6 ± 1,153.0 IU/mL, respectively. The seroprevalence was highest in participants aged 34–40 and 41–50 years who had not been vaccinated with the measles vaccine at 88.8% (95% CI 84.1–93.5) and 98.8% (95% CI 96.4–100), respectively. Their GMCs were 1,764.2 ± 1,409.9 and 1762.4 ± 1,212.9 IU/mL, respectively. The vaccination history of all participants aged younger than 15 years was retrieved from the medical document but almost all those aged older than 15 years were self-reported (98.1%). The vaccine completion rate was 98% and 82.0% in the 2 ½ and 5-15 years group, respectively. Most participants in 16-29, 30-33, 34-40 and 41-55 years group did not remember their vaccination history (71%, 86%, 83% and 80%, respectively) and reported being fully vaccinated only 3.0%, 1.0%, 0% and 0%, respectively. These data are summarized in Fig. 2 and Table II.

The seropositive rate and antibody titers in individuals younger than 33 years (who were expected to have received at least a single dose of the measles vaccine) were significantly lower than in older populations (unvaccinated or expected to have been naturally infected). In

multivariate analysis, various factors, including sex, hometown, place of birth (Government hospital, private hospital or outside hospital), smoking, and level of parental education, did not affect their seropositivity and antibody titers, as shown in Table III.

DISCUSSION

Over the last decade, several measles outbreaks have occurred among infants and young adults in different parts of the world, including Thailand, particularly in the southern region. Although, the overall vaccination coverage in Thailand has been high, approximately 95%.[5] But the vaccine coverage in Nakhon Nayok province (where this study site is located) was relatively low at 90% during the last decade. Normally, a single-dose measles-containing vaccine is 95% effective[6], with more than 99% of children developing immunity after the second dose.[7,8] In this study, the overall measles seropositivity was only 69.7%, which is consistent with the findings of previous studies (71.5–76.8%)[9,10]. The seroprevalence from two previous studies in Thailand in 2009 and 2016 were 78.5% (95% CI 77.6–79.4) and 81% (95% CI 78.8–83.5), respectively[11,12], whereas that from a recent study in Thailand in 2019 and another previous study in the United States demonstrated higher seropositivity at 84.3% (95% CI 82.6–86.0) and 97.8% (95% CI 97.3–98.2), respectively.[13,14] These discrepancies might have originated from the difference in variation of age groups, vaccination program and vaccine coverage in each country; nevertheless, the population aged 5–30 years was the most susceptible in all studies.

Our data demonstrated that the seroprevalence of children aged 9 months who were unvaccinated and expected to have partial immunity against measles from their mother was 0%. Leuridan et al. and Nicoara et al. also showed that the antibodies against measles before 12 months of age were extremely low.[15–17] In addition, previous studies have demonstrated that the

passive antibody is highest in the 1st month of life (2,020 IU/mL) and rapidly declines until almost absent at 8–9 months of age.[10,18–20] We also found low residual maternal measles antibodies (77.7 IU/mL) at 9 months of age. This low preexisting antibody from mothers may interfere with the efficacy of the 1st dose of the measles vaccine but not enough for disease prevention. Primary vaccine failure (a failure to mount an immune response to the 1st dose of measles vaccine) occurred at approximately 18% (measured at 2 ½ years of age before receiving the second dose) in this study, implying that approximately one-fifth of the children aged between 12 months and 2 ½ years are at risk of measles infection. These results are consistent with those of many studies.[7,21] Probably for this reason, 23.8% of reported cases in 2020 involved children of preschool age (particularly in 0-2 years of age).[5,11] However, the Thai National Immunisation Program still recommended that all children be vaccinated with the first dose of MMR at 9 months of age because the incidence in children aged younger than 1 year was as high as 147.5 cases per 100,000 population.[5] But from 2021 onwards, the Advisory Committee on Immunisation Practice of Thailand has consequently modified the recommendation, with the second dose of the MMR vaccine, previously administered to children aged 4–6 years, now being administered at 1.5 years of age instead to minimize this failure gap.[9,22] Conversely, many countries and the United States Centers for Disease Control and Prevention recommend the first dose of measles at 12 months of age or older to avoid this drawback.[22–24]

Moreover, we also found that children aged 5–15, 16–29, and 30–33 years, who were expected to receive at least 1–2 dose(s) of the measles-containing vaccine, had the lowest seroprevalence (50%, 52%, and 70%, respectively), which did not reach the targeted 93–95% for disease prevention on a national scale.[3,25,26] These findings potentially explain the relatively

high measles prevalence among populations aged 15–34 years.[5,27] We hypothesized the unexpectedly low seroprevalence among the population aged 5-34 years might be from the low vaccination rate and waning immunity. Our study demonstrated only 82% of those aged 5-15% has completed vaccination. Only 2% of participants aged 15-34 years confirmed receiving 2 doses of vaccine and most participants did not remember their vaccination history. Moreover, the WHO database demonstrated the national vaccine coverage in Thailand in 1985-1998, 1989-2002 and 2003-2013 was 26%, 80-94% and 91-94%, respectively comparing with 95% in 2015 onward.[28] These results were consistent with those of many previous studies that demonstrated a U-curve pattern of measles seroprevalence. The prevalence and GMC of the antibodies were highest among children aged 3–6 years and extremely low in children and young adults aged 11–30 years.[9,10,13] However, another study from the US reported that measles seroprevalence was highest among those aged 6–11 years and 12–19 years (96.8%, 95% CI 94.5–98.4, and 93.2%, 95% CI 89.8–95.7, respectively).[14] Although the seroprevalence seemed higher than in other studies, the point estimate of these age groups also did not reach 95% in the 20–39-year age group (87.9%, 95% CI 84.8–90.6). In Thailand, one study showed unexpectedly low seropositivity and measles IgG levels in populations aged 1–19 years (76–82% and 21.0–736.2 IU/mL, respectively).[12] Additionally, another study focusing on Thai men revealed moderately low seroprevalence in young adults aged 18–30 years (70.9–92.4%).[11] Furthermore, the latest data in 2014 remained consistent, with older children and young adults also being the most at risk of measles infection.[29]

In contrast, our participants aged older than 30 years, especially adults aged over 40 years, who had never received any measles-containing vaccine and were expected to have had past natural infection, had higher seroprevalence and mean antibody titer. This finding

corroborates the results of most previous studies.[10,13,14] Despite the high prevalence, most of our participants aged 34–50 years (88.8%) could not recall any history of measles vaccination or measles infection, which contrasts with their seroprevalence and antibody titer. According to the National immunization program implementation, although, these age groups represented the population who were expected to never be received or received only one dose of the measles vaccine, and additionally, the national vaccine coverage during 1978–1985 was extremely low. Conversely, WHO reported the incidence of measles in Thailand was very high before 1990. The peaked number of measles cases was approximately 47,000 and 38,500 cases per year during 1980–1985 and 1986–1990.[30] Because of these measles outbreaks, we proposed that the higher seroprevalence of the participants aged 30–39 years and older might be from the natural infection which could produce higher antibody level than vaccine-induced antibody. Some previous study hypothesized that the vaccine-induced antibody against measles may decrease over time because of the lack of a natural booster.[11] The measles IgG level in those aged younger than 33 years who represented vaccinated birth cohort was approximately two-times lower than that in those aged over 40 years who represented unvaccinated birth cohort (844.2 vs. 1763.6 IU/mL). Many studies have reported similar results, in which immunity against measles from natural infection remains longer and more potent than vaccine-induced immunity.[18,29,32] However, many guidelines still recommend two doses of the measles-containing vaccine as evidence of immunity.[1,23] Currently, there has been a breakout of measles infections globally.[33] Despite the measles-vaccine failure, cases of illness remain milder in the vaccinated population than those occurring in unvaccinated patients,[34] and these cases still require considerable public health efforts to prevent an outbreak.

Possible factors, including age group, parental education, residence region (rural vs. urban area), place of birth (e.g. in or outside the hospital), and smoking (direct and passive smoker) did not affect measles seropositivity on multivariate analysis. Most previous studies did not indicate any influencing factors. Nevertheless, one study in the northern and southern America regions indicated that the seroprevalence of measles antibodies in non-Hispanic Blacks was significantly higher than that in non-Hispanic Whites, and the seroprevalence among Mexican Americans was lower than that in non-Hispanic Whites.[35] Moreover, another study in Thailand during 2007–2008 discovered that higher education level was also related to higher seropositivity.[12] Measles seroprevalence was lowest in the northern region and highest in the southern region;[11] however, most measles outbreaks have occurred in the southern region in the past five years. Unfortunately, our study was unable to assess whether certain influencing factors, especially nationality and regions, affected seroprevalence because this was a single-site study and approximately all participants were Thai.

There were some limitations to our study. First, our data were collected from a single site, thus not representing the overall seroprevalence in the whole country. The ELISA assay was used in this study while plaque reduction neutralisation test (PRNT) is the gold standard for evaluating humoral immunity to measles because of higher sensitivity. But PRNT is a complicated assay, tends to be operator-dependent and very limited in Thailand especially in the rural area. The seroprevalences were probably higher especially in borderline/negative cases if PRNT was used. Additionally, most participants, particularly adults and elderly persons, could not remember their history of measles vaccination and measles infection accurately. However, the seroprevalence of our participants who reported a history of measles infection was high

(97.6%, 95% CI 93.0–100). These data indicated that we could partially rely on reported history of measles infection as evidence of immunity.

This serosurveillance study could provide the opportunity to clarify the local measles immune status. The measles vaccination should be vigorously promoted to maintain highest coverage. At given time point, the individuals aged 15–34 years are relatively vulnerable to measles infections. Supplementary vaccination in special situations, including post-exposure prophylaxis during an outbreak among young adults or providing for high-risk occupations, such as healthcare personnel, should be encouraged.

CONFLICT OF INTEREST AND SOURCE OF FUNDING

The authors declare that they have no conflicts of interest. This study was funded by Srinakharinwirot University, Thailand (No. 429/2562).

REFERENCES

1. American Academy of Pediatrics. Measles. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Redbook: 2018 Report of the Committee on Infectious Diseases, Itasca, IL: American Academy of Pediatrics, 2018: 537–50.
2. World Health Organization. Revising the goal for measles elimination and rubella/congenital rubella syndrome control. Available at: http://origin.searo.who.int/mediacentre/events/governance/rc/72/en/. Accessed July 13, 2020.
3. Measles vaccines: WHO position paper. Wkly Epidemiol Rec 2009; 84:349–60.
4. Measles vaccines: WHO position paper – April 2017. Wkly Epidemiol Rec 2017; 92:205–

27.

5. Epidemiology of Disease Control, Minister of Health, Thailand. Measles. Available at: http://www.boe.moph.go.th/boedb/surdata/disease.php?ds=21. Accessed July 14, 2020.
6. Demicheli V, Rivetti A, Debalini MG, et al. Vaccines for measles, mumps and rubella in children. Cochrane Database Syst Rev 2012; 2:CD004407.
7. Moss WJ, Griffin DE. Measles. Lancet 2012; 379:153–64.
8. Meissner HC, Strebel PM, Orenstein WA. Measles vaccines and the potential for worldwide eradication of measles. Pediatrics 2004; 114:1065–9.
9. Poethko-Müller C, Mankertz A. Seroprevalence of measles-, mumps- and rubella-specific IgG antibodies in German children and adolescents and predictors for seronegativity. PLoS One 2012; 7:e42867.
10. Kang HJ, Han YW, Kim SJ, et al. An increasing, potentially measles-susceptible population over time after vaccination in Korea. Vaccine 2017; 35:4126–32.
11. Gonwong S, Chuenchitra T, Khantapura P, Islam D, Mason CJ. Measles susceptibility in young Thai men suggests need for young adult measles vaccination: a cross sectional study. BMC Public Health 2016; 16:309.
12. Tharmaphornpilas P, Yoocharean P, Rasdjarmrearnsook AO,Theamboonlers A, Poovorawan Y. Seroprevalence of antibodies to measles, mumps, and rubella among Thai population: evaluation of measles/MMR immunization programme. J Health Popul Nutr 2009; 27:80–6.
13. García-Comas L, Sanz Moreno JC, Ordobás Gavín M, et al. Seroprevalence of measles and rubella virus antibodies in the population of the Community of Madrid, 2008-2009. J Infect Public Health 2015; 8:432–40.
14. Lebo EJ, Kruszon-Moran DM, Marin M, et al. Seroprevalence of measles, mumps, rubella

and varicella antibodies in the United States population, 2009-2010. Open Forum Infect Dis 2015; 2:ofv006.

15. Leuridan E, Hens N, Hutse V, Ieven M, Aerts M, Van Damme P. Early waning of maternal measles antibodies in era of measles elimination: longitudinal study. BMJ 2010; 340:c1626.
16. Leuridan E, Van Damme P. Passive transmission and persistence of naturally acquired or vaccine-induced maternal antibodies against measles in newborns. Vaccine 2007; 25:6296–304.
17. Nicoara C, Zäch K, Trachsel D, Germann D, Matter L. Decay of passively acquired maternal antibodies against measles, mumps, and rubella viruses. Clin Diagn Lab Immunol 1999; 6:868–71.
18. Smetana J, Chlibek R, Hanovcova I, et al. Decreasing Seroprevalence of Measles Antibodies after Vaccination - Possible Gap in Measles Protection in Adults in the Czech Republic. PLoS One. 2017; 12:e0170257.
19. Techasena W, Sriprasert P, Pattamadilok S, Wongwacharapipoon P. Measles antibody in mothers and infants 0-2 years and response to measles vaccine at the age of 9 and 18 months. J Med Assoc Thai 2007; 90:106–12.
20. Boulton ML, Wang X, Wagner AL, et al. Measles Antibodies in Mother-Infant Dyads in Tianjin, China. J Infect Dis 2017; 216:1122–9.
21. Moss WJ, Strebel P. Biological feasibility of measles eradication. J Infect Dis 2011; 204 Suppl 1:S47-53.
22. Macartney K, Gidding HF, Trinh L, et al. Evaluation of Combination Measles-Mumps-Rubella-Varicella Vaccine Introduction in Australia. JAMA Pediatr 2017; 171:992–8.
23. McLean HQ, Fiebelkorn AP, Temte JL, Wallace GS. Prevention of measles, rubella,

congenital rubella syndrome, and mumps, 2013: summary recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Reports Morb Mortal Wkly Report Recomm Reports 2013; 62:1–34.

24. Atchison CJ, Hassounah S. The UK immunisation schedule: changes to vaccine policy and practice in 2013/14. JRSM Open 2015; 6:2054270415577762.
25. Anderson RM, May RM. Directly transmitted infections diseases: control by vaccination. Science 1982; 215:1053–60.
26. Gay NJ. The theory of measles elimination: implications for the design of elimination strategies. J Infect Dis 2004; 189 Suppl 1:S27-35.
27. Zhang MX, Ai JW, Li Y, Zhang BY, Zhang WH. Measles Outbreak among Adults, Northeastern China, 2014. Emerg Infect Dis 2016; 22:144–6.
28. World Health Organization.Thailand: WHO and UNICEF estimates of immunization coverage:2019 revision. Available at: https://www.who.int/immunization/monitoring_surveillance/data/tha.pdf/. Accessed August 30, 2021.
29. Wanlapakorn N, Wasitthankasem R, Vichaiwattana P, et al. Antibodies against measles and rubella virus among different age groups in Thailand: A population-based serological survey. PLoS One 2019; 14:e0225606.
30. World Health Organization. Factsheet 2020 Thailand Expanded programme on immunization (EPI). Available at:https://apps.who.int/iris/rest/bitstreams/1316663/retrieve/. Accessed August 30, 2021.
31. Christenson B, Böttiger M. Measles antibody: comparison of long-term vaccination titres, early vaccination titres and naturally acquired immunity to and booster effects on the measles virus. Vaccine 1994; 12:129–33.

32. Hutchins SS, Redd SC, Schrag S, et al. National serologic survey of measles immunity among persons 6 years of age or older, 1988-1994. MedGenMed 2001:E5.

33. Cherry JD, Zahn M. Clinical Characteristics of Measles in Previously Vaccinated and Unvaccinated Patients in California. Clin Infect Dis an Off Publ Infect Dis Soc Am 2018; 67:1315–9.

34. Cherry JD, Zahn M. Clinical Characteristics of Measles in Previously Vaccinated and Unvaccinated Patients in California. Clin Infect Dis 2018; 67:1315-9

35. McQuillan GM, Kruszon-Moran D, Hyde TB, Forghani B, Bellini W, Dayan GH. Seroprevalence of measles antibody in the US population, 1999-2004. J Infect Dis 2007; 196:1459–64.

FIGURES

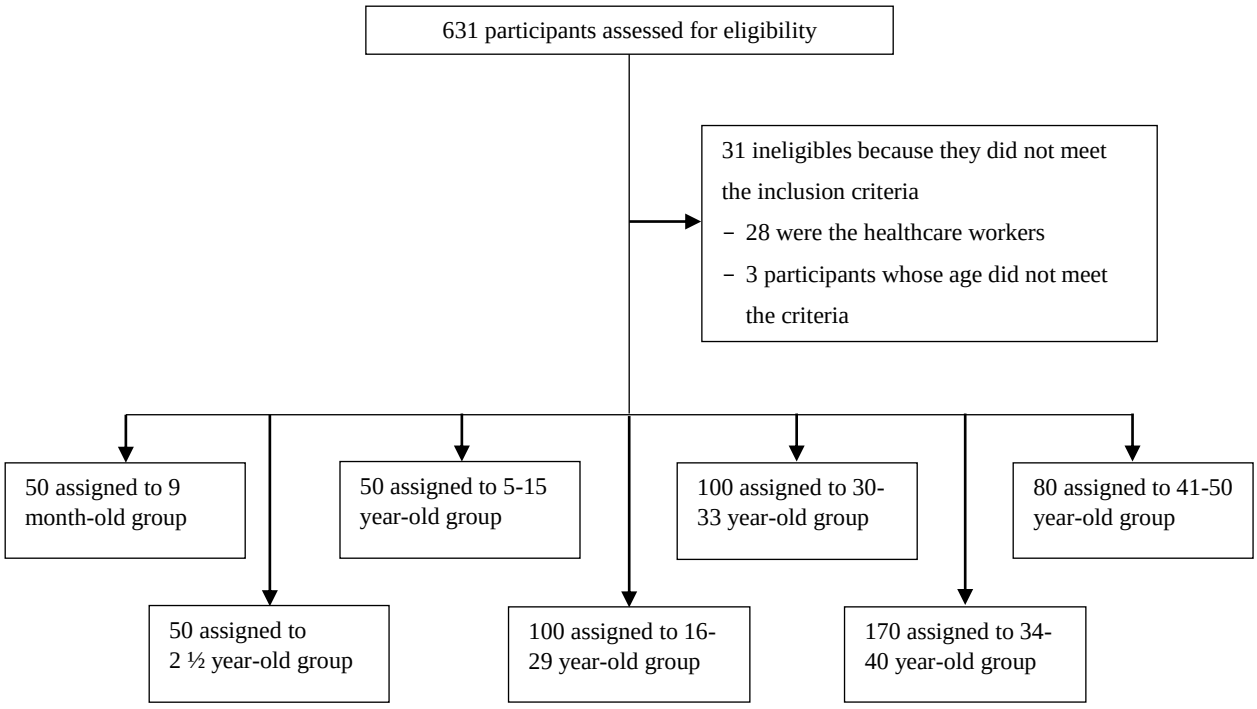

Fig. 1 600 individuals aged between 9 months and 50 years were enrolled and divided into 7 groups by age those represent birth cohorts that experienced different measles vaccination policies to evaluate measles IgG prevalence in each age group.

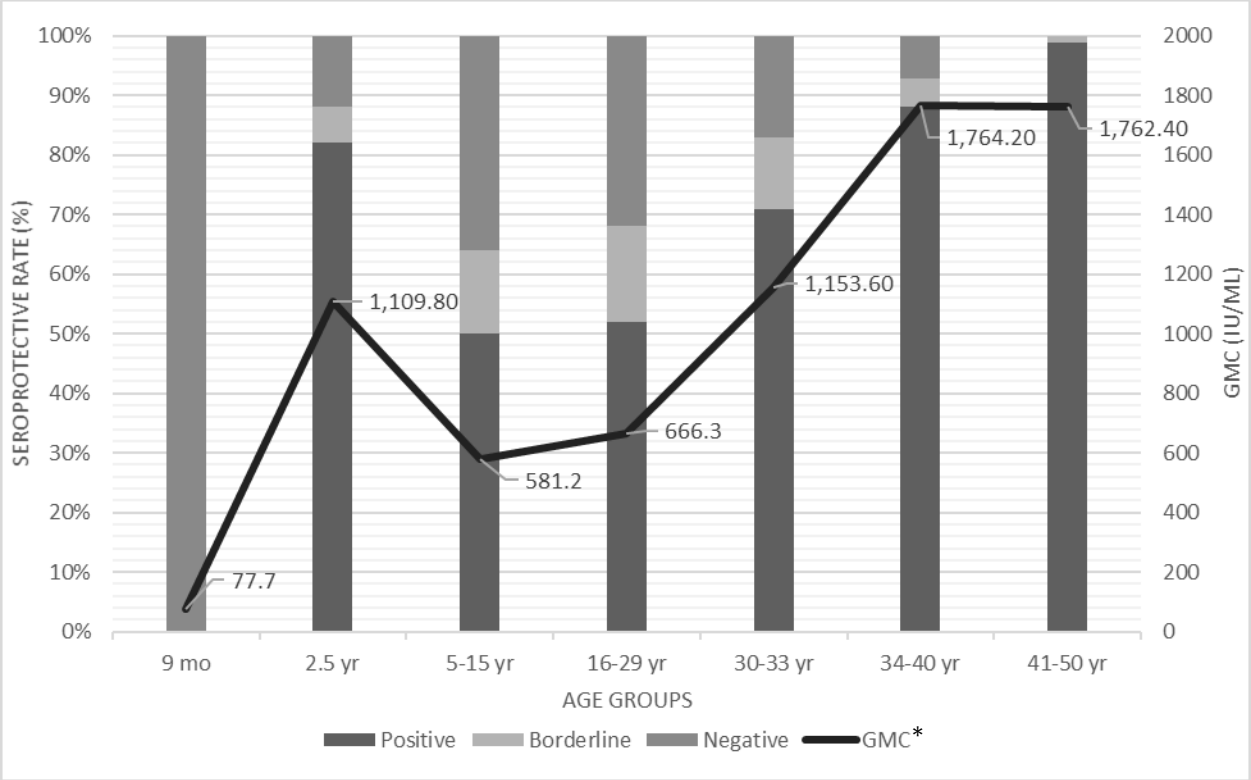

Fig. 2 Measles seropositive rate and IgG level across all age groups. Each age group represents an expected vaccination history. The scale on the left represents the percentage seropositive rate according to the cutoff point of the measles IgG level: positive, ≥275 IU/mL; borderline, 200–274 IU/mL; and negative, <200 IU/mL. The scale on the right represents the mean measles IgG level. *GMC, geometric mean titer

Table I Demographic characteristics of study participants

Characteristics	Number (%)	Measles seroprevalence		
		Positive, % (95% CI□)	Borderline, % (95% CI□)	Negative, % (95% CI□)
Overall	600 (100)	69.7 (66.1-73.3)	7.8 (6.8-7.8)	22.5 (19.2-25.7)
Age				
9 months	50 (8.3)	0	0	100
2 ½ years	50 (8.3)	82 (73.3-90.7)	6 (0-12.5)	12 (3.0-21.0)
5-15 years	50 (8.3)	50 (36.1-63.9)	14 (4.4-23.6)	36 (22.7-49.3)
16-29 years	100 (16.7)	52 (42.3-62.7)	16 (8.9-23.1)	32 (22.9-31.1)
30-33 years	100 (16.7)	70 (61.1-78.9)	12 (5.7-18.3)	18 (10.5-25.5)
34-40 years	170 (28.3)	88.8 (84.1-93.5)	4.7 (1.6-7.8)	6.5 (2.8-10.2)
41-50 years	80 (13.4)	98.8 (96.4-100)	1.3 (0-3.7)	0
Sex				
Male	209 (34.8)	66 (59.6-72.4)	9.1 (5.3-12.9)	24.9 (19.1-30.7)
Female	391 (65.2)	71.6 (67.2-76)	7.2 (4.7-9.7)	21.2 (17.2-25.2)
Hometown				
Central	500 (75)	68.4 (64.4-72.4)	8.2 (5.8-10.6)	23.4 (19.7-27.1)
North	11 (1.8)	81.8 (70.2-93.4)	0	18.2 (0-41.0)
South	6 (1.0)	100	0	0
East	66 (11.0)	71.2 (60.3-82.1)	9.1 (2.2-16.0)	19.7 (10.2-29.2)
West	4 (0.7)	75 (33.0-100)	25 (0-67.4)	0
Northeast	63 (10.5)	71.4 (60.3-82.5)	4.8 (0-10.0)	23.8 (13.3-34.3)

Birthplace				
Government hospital	527 (87.8)	67.4 (63.4-71.4)	8.2 (5.9-10.5)	24.5 (20.9-28.1)
Private hospital	16 (2.7)	75 (53.8-96.2)	6.3 (0-18.2)	18.8 (0-37.9)
Others/unknown	57 (9.5)	89.4 (81.5-97.3)	5.3 (0-11.1)	5.3 (0-11.1)
Smoking				
Direct smoker	45 (7.5)	80 (68.4-91.6)	15.6 (5.0-26.2)	4.4 (0-23.3)
Passive smoker	93 (15.5)	59.1 (49.2-69.0)	8.6 (3.0-14.2)	32.3 (22.8-41.8)
Non-smoker	462 (77.0)	70.8 (66.7-74.9)	6.9 (4.6-9.2)	22.3 (18.6-26.0)
Parental education				
Kindergarten	2 (0.3)	100	0	0
Primary school	310 (51.7)	79.4 (74.9-83.9)	6.8 (4.0-9.6)	13.9 (10.1-17.7)
Junior high school	58 (9.7)	63.8 (57.9-69.7)	17.2 (7.5-26.9)	19.0 (0.9-29.0)
High school	126 (21.0)	61.1 (52.6-69.6)	7.1 (2.7-11.5)	31.7 (28.0-35.4)
Bachelor's degree	89 (14.8)	52.8 (42.5-63.1)	4.5 (3.7-5.3)	42.7 (37.7-47.7)
Master's degree or higher	11 (1.8)	63.6 (49.7-76.9)	9.1 (0-26.6)	27.3 (1.0-53.6)
Unknown	4 (0.7)	50 (1.0-99.0)	50 (1.0-99.0)	0
History of measles infection				
Yes	41 (6.8)	97.6 (93.0-100)	0	2.4 (0-7.0)
No	559 (93.2)	67.6 (63.8-71.4)	8.4 (6.2-10.6)	24 (20.5-27.5)

*****CI, confidence interval

Table II Measles seroprevalence, IgG level, rate of vaccination and national vaccine coverage according to age group and expected vaccination history

Expected vaccination history	Age as of 2018	Birth year	National vaccine coverage[28]	Rate of vaccination (%)			Seropositive rate % (95% CI*)	GMC (IU/mL) ± SD
				Yes	No/ incomplete	Unknown/ cannot remember		
Maternal immunity or pre 1st dose of vaccination (n=50)	9 months	2017	95% (MCV2)	0	50 (100)	0	0	77.7 ± 27.0
Pre 2nd dose of vaccination (n=50)	2 ½	2015-2016	95% (MCV2)	49 (98.0)	1 (2.0)	0	82 (73.3-90.7)	1,109.8 ± 1,069.8
Post 2 doses of vaccination (n=50)	5-15 years	2003-2013	91-94% (MCV2)	41 (82.0)	3 (6.0)	6 (12.0)	50 (36.1-63.9)	581.2 ± 871.3
Post 2 doses of vaccination (n=100)	16-29 years	1989-2002	80-94 (MCV2)	3 (3.0)	26 (26.0)	71 (71.0)	52 (42.3-62.7)	666.3 ± 926.6
Post single dose of	30-33	1985-	26%	1 (1.0)	13 (13.0)	86 (86.0)	70 (61.1-78.9)	1,153.6 ±

vaccination (n=100)	years	1988	(MCV1)					1,153.0
Natural infection (n=170)	34-40 years	1978-1984	-	0	29 (17.0)	141 (83.0)	88.8 (84.1-93.5)	1,764.2 ± 1,409.9
Natural infection (n=80)	41-50 years	1968-1977	-	0	16 (20.0)	64 (80.0)	98.8 (96.4-100)	1,762.4 ± 1,212.9

*****CI, confidence interval; GMC, geometric mean titer; SD, standard deviation; MCV1, one dose of measles vaccine coverage; MCV2, two doses of measles vaccine coverage

Table III Multivariate odds ratios between measles seropositivity and possible influencing factors.

Factors	Crude analysis			Adjusted analysis		
	Crude OR*	95%CI†	p-value	adjusted OR	95%CI	p-value
Sex						
Male	1.23	0.83-1.83	0.308	1.42	0.87-2.31	0.158
Female	Ref	-	-	Ref	-	-
Hometown						
Central	1.22	0.77-1.93	0.391	1.38	0.81-2.35	0.237
Other	Ref	-	-	Ref	-	-
Smoking						
Smoker/passive smoker	1.06	0.67-1.67	0.802	1.28	0.75-2.19	0.366
Non-smoker	Ref	-	-	Ref	-	-
Parental education						
Junior high school or lower	0.31	0.21-0.46	0.001	1.07	0.63-1.82	0.798
High school or higher	Ref	-	-	Ref	-	-
Birthplace						
Government hospital	5.51	1.69-17.95	0.005	1.70	0.50-5.83	0.40
Private hospital	3.92	0.70-21.74	0.118	0.66	0.10-4.14	0.655
Outside hospital	Ref	-	-	Ref	-	-

*OR, odd ratio; †CI, confidence interval