Cross-sectional, laboratory-based study of measles seroprevalence in Oman

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Abstract

Background: Since the introduction of vaccination in Oman in 1981, measles incidence has decreased, and Oman achieved measles elimination in 2019. Measles cases in the country are currently import-related.

Aim: To understand the measles immunity profile of the Omani population and identify high-risk groups.

Methods: A total of 1990 anonymous blood samples out of 2032 samples collected from all regional referral hospitals and one private laboratory in Oman from November 2015 to January 2016 were tested for measles immunoglobulin G. We grouped the study population into 4 birth cohorts and analysed the data using SPSS version 16.0. We used the χ^2 to test for statistical significance and used Kruskal-Wallis test to calculate the geometric mean for each age group. $P < 0.05$ was considered statistically significant.

Results: The overall measles seropositivity was 84.0%. Seronegativity was significantly higher among the 15–20 years (34.0%) and 20–35 years (24.0%) age groups. There was no significant difference in seropositivity by gender and nationality. Seropositivity was 72.7% in the 1987–1996 cohort and 70.1% in the 1997–2006 cohort. The mean measles antibody level was 2318.5 IU/ml

Conclusion: This study revealed a measles immunity gap among some age groups in Oman, indicating the need for sustained high vaccination coverage, robust surveillance, targeted vaccination campaigns, and timely outbreak response.

Key words: measles, immunization, immunity, immunoglobulin, seroprevalence, seropositivity, seronegativity, Oman

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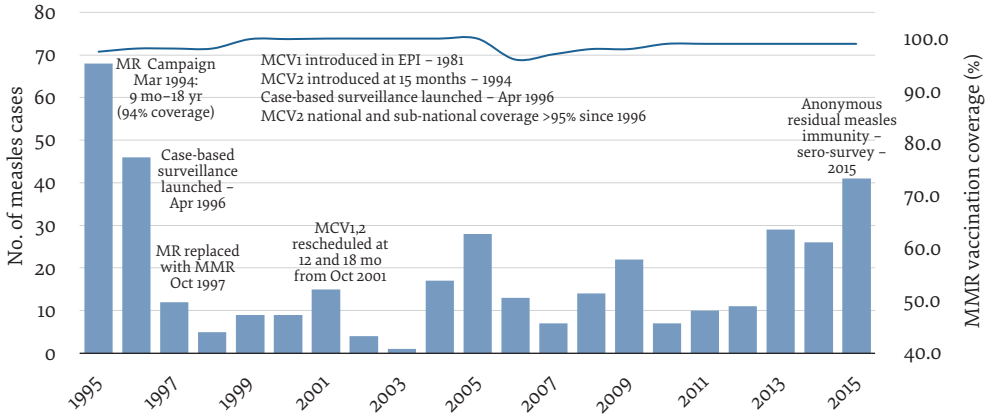
Introduction

Measles is a highly contagious vaccine-preventable disease. It has been assumed that measles may be eliminated for the following reasons: humans are the sole reservoir of the virus; transmission only occurs between humans; the virus is stable; a human carrier state does not exist; and there is a vaccine of proven high efficacy. Despite the availability of an effective and inexpensive vaccine, measles remains a public health problem worldwide, especially in developing countries, with 30–40 million cases occurring annually. Global measles deaths decreased by 79.0% from an estimated 546 800 in 2000 to 114 900 in 2014. Most of the deaths in 2014 were among children aged < 5 years (*1*). However, during 2000–2022, millions of children missed measles vaccinations because of the COVID-19 pandemic, resulting in an 18.0% increase in estimated cases and 43.0% increase in estimated deaths in 2022 compared with 2021. Large or disruptive outbreaks were reported in 37 countries (*2*).

Measles was a common childhood infection in Oman 40 years ago. The disease was endemic with periodic outbreaks. Measles vaccine was introduced at age 9 months in 1981 in the routine Expanded Programme on Immunization schedule. As a result, the cases continued to decrease from ~40 000 during the early 1980s to 41 in 2015 (Figure 1). Since 1999 the number of confirmed cases remained below 30 per year until 2012. During 2013–2015, there was an increase in cases with large outbreaks in 2014 and 2015. In March 1994, a second dose of measles vaccine, as the measles/rubella vaccine, was introduced at age 15 months and a catch-up campaign with this vaccine was conducted in March 1994 for all individuals aged 15 months to 18 years. Vaccination was rescheduled at age 12 and 18 months during 2006. Despite the high vaccination coverage, small outbreaks continued to occur in an interepidemic period with no established endemic transmission. Most cases of measles during this interepidemic period were imported or import related and not because of missed vaccination. Thus, current measles epidemiology in Oman is determined by the characteristics of the imported cases and their susceptible contacts.

Oman adopted the measles elimination by 2015 target of the Eastern Mediterranean Region. The elimination strategies included strong case-based surveillance with laboratory confirmation, zero reporting, high sustained routine immunization and a catch-up campaign. Elimination is not equal to zero cases because when elimination has been achieved, imported cases may

Figure 1 Seropositivity for measles in 4 birth cohorts in Oman, 1995 to 2015



still occur, with limited spread to susceptible people. Eventually, there will be enough susceptible people among the small proportion of vaccine failures to allow an outbreak. Therefore, there is a continued need for surveillance even when no cases are reported (3). From 2000 to 2015, 9 small outbreaks of measles were reported, with a median of 12 cases (range: 2–18).

Immunization coverage and disease surveillance data are primary sources of information for assessing population immunity. These data are routinely collected as part of the effort towards measles and rubella elimination. However, each of these data sources has some limitations. Serological assessments can provide a direct measure of population immunity derived from immunization and natural disease. There was uncertainty about the elimination status of measles in Oman after large outbreaks in 2016–2017 and multiple small outbreaks in previous years. Therefore, a well-designed serological survey that was more accurate than indirect estimates based on extrapolation of coverage and incidence data was conceived. It provided key information to help reduce susceptibility to measles and achieve the elimination goal by conducting targeted vaccination campaigns. This study assessed the measles immunity profile in Oman to determine the risk of outbreaks and identify high-risk population subgroups, to guide immunization policies and strategies and monitor population immunity over time.

Methods

Oman has 4 159 102 inhabitants with a 43.6% expatriate population mostly from Asian countries, according to 2015 estimates. We conducted a cross-sectional laboratory-based study with a representative sample of a national population of all ages by nonprobability sampling. The study was conducted for 6 months and the samples were collected from all regional referral hospitals in the 11 governorates in Oman and 1 private laboratory in Muscat Governorate. The samples were tested at the virology section of the Central Public Health Laboratory in Muscat. An anonymized residue of specimens, originally collected for routine disease investigations, was used for the serosurvey. These leftover samples, submitted for microbiological or biochemical testing to regional referral laboratories across all 11 governorates in Oman, including a designated private laboratory in Muscat Governorate, were sent to the Central Public Health Laboratory for a 3-month period from 1 November 2015 to 31 January 2016, ensuring individuals' identities remained confidential. The method used was sample size for proportion. The minimum sample size was 246 based on the expected prevalence of 80.0%, 5.0% precision, and a population of 4.5 million in OpenEpi using the formula $n=[DEFF \times Np(1-p)]/ [(d2/Z21-\alpha/2 \times (N-1) + p \times (1-p)]$. Considering 20.0% sample rejection the final minimum sample size was calculated to be 295 (4).

During the study period, 2032 samples were collected; of which 42 were not processed because of laboratory issues and incomplete data. A total of 1990 samples were available for analysis. We continued to collect the samples for the entire study period despite reaching the minimum number of samples required. This allowed more precision and stratified analysis according to age and governorate.

Anonymous samples collected for this study did not require informed consent and ethical committee approval. The study was part of the national programme for measles elimination of the Ministry of Health in Oman, which allowed us to use samples collected for other purposes to estimate measles seroprevalence. Residual serum samples available from all individuals during the study period were included. Patients known to be immunocompromised were excluded.

Serum samples of 1–2 ml were collected from each study subject and transported to the Central Public Health Laboratory at 4–8°C within 24–48 hours. The facility is also a reference laboratory for measles surveillance in the Eastern Mediterranean Region. Enzygnost anti-measles IgG assay (Dade Behring Marburg GmbH, Marburg, Germany) was used to detect antibody to measles virus. Titres ≥ 200 IU/ml were considered positive and < 200 IU/ml negative. IgG avidity testing was performed for 10.0% of the IgG-positive samples from each age group,

Table 1 Seroprevalence status of measles antibodies according to demographic factors

Variable	Seronegative (< 200 IU/ml)		Seropositive (≥ 200 IU/ml)		χ^2 test
	No.	% (95% CI)	No.	% (95% CI)	
Age					
< 12 months	37	43.5 (33.5–54.1)	48	56.5 (45.8–66.5)	2.19, df = 6, $P < 0.05$
12–18 months	2	8.7 (2.4–26.8)	21	91.3 (73.2–97.6)	
18 months–15 years	36	14.0 (10.2–18.7)	222	86.0 (81.3–89.7)	
15–20 years	48	34.0 (26.7–42.1)	93	66.0 (57.8–73.2)	
20–35 years	184	24.0 (21.1–27.1)	583	76.0 (72.8–78.9)	
35–40 years	9	3.8 (2.0–7.1)	225	96.2 (92.8–97.9)	
≥ 40 years	8	1.7 (0.8–3.2)	474	98.3 (96.7–99.1)	
Gender					
Male	172	16.8 (14.6–19.2)	846	83.2 (80.7–85.3)	0.58, df = 1, $P < 0.44$
Female	154	15.8 (13.6–18.2)	818	84.2 (81.8–86.4)	
Nationality					
Omani	307	17.5 (15.7–19.3)	1452	82.5 (80.7–84.2)	16.5, df = 1, $P < 0.05$
Expatriate	17	7.4 (4.6–11.4)	214	92.6 (88.5–95.3)	
Governorate					
Muscat	74	13.3 (10.7–16.3)	482	86.7 (83.6–89.2)	8.3, df = 10, $P = 0.59$
Dakhliyah	32	16.0 (11.6–21.7)	168	84.0 (78.3–88.4)	
Dhofar	36	19.1 (14.2–25.4)	152	80.9 (74.6–85.8)	
Dhahira	13	14.0 (8.3–22.4)	80	86.0 (77.5–91.6)	
Buraimi	17	16.7 (10.7–25.1)	85	83.3 (74.9–89.3)	
North Sharqiyah	19	14.7 (9.6–21.8)	110	85.3 (78.1–90.3)	
South Sharqiyah	22	17.3 (11.7–24.8)	105	82.7 (75.2–88.3)	
North Batinah	50	17.5 (13.5–22.3)	236	82.5 (77.7–86.5)	
South Batinah	42	19.0 (14.4–24.7)	179	81.0 (75.3–85.6)	
Al Wustah	10	20.0 (11.2–33.0)	40	80.0 (66.9–88.7)	
Musandam	9	23.7 (13.0–39.2)	29	76.3 (60.8–87.0)	

CI = confidence interval.

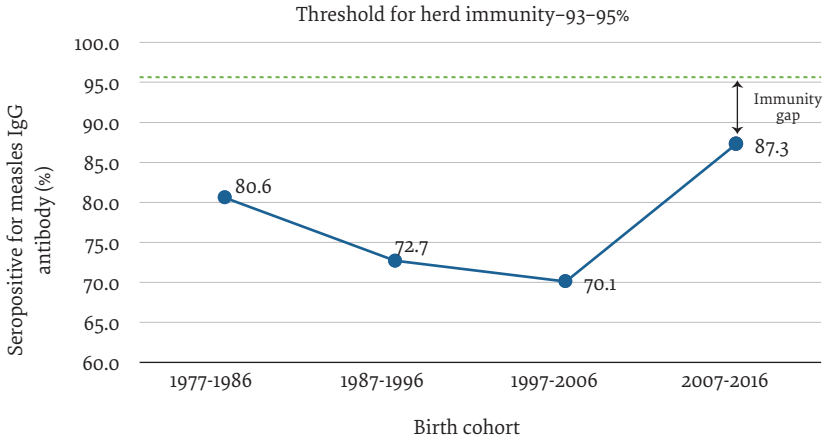
using Euroimmune Measles virus avidity determination purified native antigen strain Edmonston for quality check (5).

The data were compiled in Microsoft Excel and analysed using SPSS version 16.0. The subjects were stratified by sociodemographic factors (age, gender, nationality and governorate). Frequencies and proportions in categorical data were calculated. The study population was grouped into 4 cohorts based on year of birth to capture differences over time in measles antibody response. The geometric mean was calculated for each age group for comparison and categorized according to changes in vaccination policies in Oman. Appropriate 95.0% confidence intervals (CIs) were calculated for prevalence proportional data. The statistical significance was tested using the χ^2 test for categorical data and Kruskal–Wallis test for mean values. $P < 0.05$ was considered statistically significant.

Results

A total of 1990 serum samples were included in the analysis after applying the exclusion criteria. Of the 1990 samples tested, 324 (16.3%) were below the cut-off point of 200 IU/ml (seronegative). Six samples from children aged < 5 years had no detectable antibody level (0.3%). The overall seropositivity was nearly 84.0% (1666/1990). Antibody titres by age, gender, nationality and governorate are presented in Table 1. The age groups were categorized based on the times of measles vaccination. Among the samples from children aged < 1 year, the seropositivity was 56.5% (48/85). Seropositivity was higher among the 12–18 months (91.3%), 35–40 years (96.2%) and ≥ 40 years (98.3%) age groups. Seronegativity was significantly higher among the 15–20 (34.0%) and 20–35 (24.0%) years age groups than the other groups (χ^2 = 2.19, df = 6, $P < 0.05$). There was no significant difference in seropositivity among males and females (χ^2=0.58, df = 1, $P < 0.44$) and different governorates (χ^2 = 8.3, df = 10,

Figure 2 Percentage of measles IgG antibody seropositivity in 4 birth cohorts



P = 0.59). Seronegativity was significantly higher among the Omani population than the non-Omani population (17.5 vs 7.4%, χ^2 = 16.5, df = 1, *P* < 0.05).

Measles IgG antibody seropositivity in the 4 birth cohorts is presented in Figure 2. Seropositivity was below the suggested threshold for herd immunity of 93.0–95.0%, especially in the 1987–1996 (72.7%) and 1997–2006 (70.1%) birth cohorts. The mean measles antibody level was 2318.5 ± 2721.0 IU/ml with a range of 0–16 388 IU/ml. The median was 1213.0 IU/ml with an interquartile range of 3139.0 IU/ml.

Figure 3 presents the mean antibody levels according to age group, based on the vaccination strategy in Oman. The mean levels were significantly lower among individuals aged 6–12 months and 10–35 years than with the other groups (Kruskal–Wallis test, χ^2 = 515.9, df = 6, *P* < 0.005).

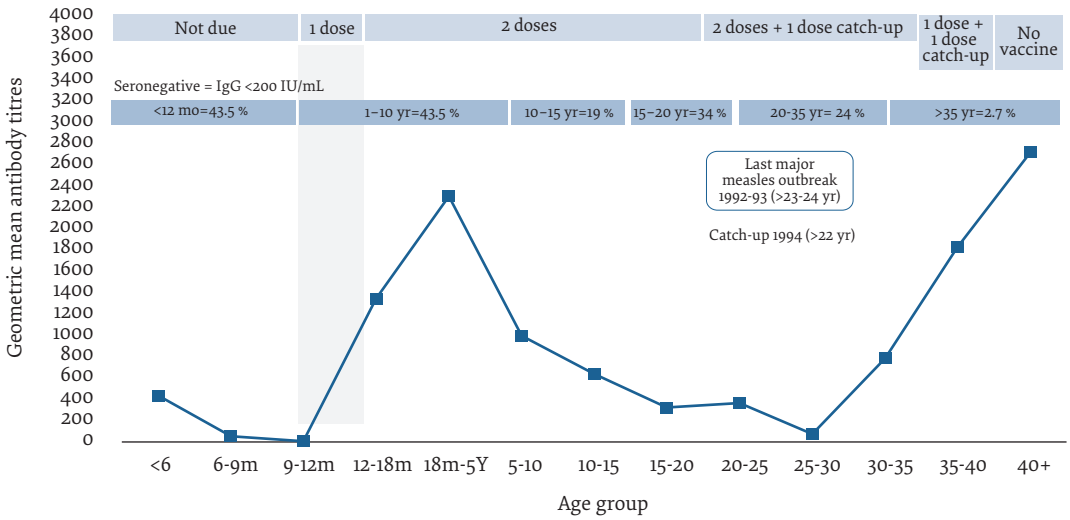
The median measles IgG levels and interquartile range were closer to the cut-off level of < 200 IU/ml in age groups <12 months and 15–35 years, indicating an immunity gap in these age groups.

Discussion

This study revealed an immunity gap caused by accumulation of susceptible individuals over a period of time in Oman. Using the study results, a targeted single dose measles, mumps, rubella vaccination campaign was conducted in Oman for the age group 20–35 years, with 93.0% coverage in 2017. As a result, the number of cases decreased considerably, which interrupted the transmission of measles and closed the immunity gap. In 2019, based on the WHO 5 lines of evidence and 2 criteria, the Regional Verification Commission, Cairo, certified elimination of endemic measles in Oman.

Serological surveys are cross-sectional and measure antibodies from a representative sample to estimate immunity. In our study, the seroprevalence of measles antibodies was 84.0% with > 95.0% national vaccination coverage, which was marginally lower than in Egypt (86.1% with 92.0% coverage) but higher than in the Islamic Republic of Iran (65.8% with 95.0% coverage) and Germany (76.8% with 88.8% coverage) (*6–8*). There was no significant difference in seronegativity among males and

Figure 3 Geometric mean antibody titres by age groups based on measles vaccination history in Oman



females, similar to the studies in Egypt and the Islamic Republic of Iran (*6*, *7*). However, the studies in Germany presented a significant difference by gender (*8*).

Our seroepidemiological results showed a higher rate of seronegativity to measles antibodies among the 10–35 years age group, especially 15–20 years (34.0%), which was similar to studies in Australia, Germany, Finland, Thailand and China. This may have resulted from decreased antibody levels over time (waning immunity) in a highly immunized population with the absence of natural infection (boosting effect) (*8*–*13*).

There is no universal agreement on the threshold level of seroprevalence of measles antibodies in the population required for interruption of endemic transmission. The seropositivity observed in our study was below the suggested threshold of herd immunity of 93.0–95.0%, which is one of the global criteria for measles elimination, especially in the 1987–1996 (72.7%) and 1997–2006 (70.1%) birth cohorts. Therefore, the target for elimination in 2010 was deferred to 2015, similar to several other countries (*14*–*16*).

The serological survey results coincided with the number of doses of measles vaccine. The seronegativity rate was higher than the overall WHO target level of 5.0% in children who had received single-dose vaccination (before the 1994 birth cohort); however, after the introduction of a second dose of vaccine in 1994, the seronegativity decreased. The importance of a 2-dose vaccination schedule is supported by the population-based study in Germany (*8*).

The window of vulnerability to measles infection in Oman, as assessed by serological survey, begins at 6–12 months of age. In the current schedule of childhood vaccination, the first dose of measles-containing vaccine is administered at 12 months. As infants lose maternally derived antibodies, they become increasingly vulnerable to measles. In 2015, 57.1% of the measles cases reported in Oman were in children aged < 12 months. Similarly, the universal coverage of > 95.0% with measles-containing vaccine second dose has resulted in a large number of young mothers with vaccine-induced measles antibodies that are at a lower level than those induced by natural infection. Therefore, infants born to these mothers would receive fewer passively transferred antibodies. The immunity gap observed in the these age groups is also supported by the age distribution (< 12 months and 20–35 years) of the measles clusters reported from 2014 to 2016. An immunity gap among young adults was also observed in Thailand and other countries (*17*, *18*).

In our study, seroprevalence of measles antibodies in the population was 83.7%. If the status quo is maintained, then small clusters of measles cases will continue to occur in different locations in the country as a result of imported infection from endemic countries of Asia.

Possible reasons for the immunity gap in our study were: low herd immunity; susceptibility of children too young to be vaccinated; waning vaccine-induced immunity in adolescents and young adults; absence of booster effect due to natural infection; a large proportion of the resident population being from endemic countries; and reduced transfer of passive antibodies to infants from vaccinated mothers.

It is recommended to conduct serological surveys periodically because they help provide data on population immunity to predict the at-risk populations. Also, they are a direct measure that can be useful to vaccination programmes where there is an immunity gap, and can encourage political commitment to an appropriate intervention (*19*). Seropositivity is not necessarily the same as protection against a pathogen, as specific IgG does not correlate well with the level of functional protective antibodies (*20*). Therefore, we recommend inclusion of disease status and date of vaccination in future studies.

Our study had some limitations. First, there was a possibility of bias due to the cross-sectional study design. Second, vaccination status and disease history were not verified, which may have affected interpretation of seropositivity. The anonymous survey methodology limits the assessment of disease impact on immune status and often omits key patient details such as age, gender and laboratory information. Future studies that include vaccination status and history of measles and other underlying diseases may yield better results.

Conclusion

Seroprevalence surveys have important implications for the management of vaccination programmes and contribute to the prevention of disease transmission. In this study seropositivity among infants and the 20–35 years age group was significantly less than among adolescents and older adults. Age group is an important contributor to the overall risk of disease, along with population immunity. Our results revealed an immunity gap in Oman in some age groups. It is important to address the immunity gaps through sustained high vaccination coverage, robust surveillance, targeted vaccination campaigns and instant outbreak response.

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Competing interests: None declared.

Étude transversale, en laboratoire, de la séroprévalence de la rougeole à Oman

Résumé

Contexte : Depuis l'introduction de la vaccination à Oman en 1981, l'incidence de la rougeole a diminué et le pays a obtenu le statut d'élimination de cette maladie en 2019. Les cas de rougeole dans le pays sont actuellement dus à une importation de la maladie.

Objectifs : Comprendre le profil d'immunité de la population omanaise contre la rougeole et identifier les groupes à haut risque.

Méthodes : Un total de 1990 échantillons de sang anonymes sur 2032 prélevés dans tous les hôpitaux régionaux de référence et un laboratoire privé à Oman entre novembre 2015 et janvier 2016 ont été testés pour l'immunoglobuline G. Nous avons regroupé la population d'étude en quatre cohortes de naissance et analysé les données à l'aide du logiciel SPSS version 16.0. Nous avons utilisé le test du χ^2 pour évaluer la signification statistique et utilisé le test de Kruskal-Wallis pour calculer la moyenne géométrique pour chaque groupe d'âge. Une valeur *p* inférieure à 0,05 était considérée comme statistiquement significative.

Résultats : La séropositivité globale à la rougeole était de 84,0 %. Elle était significativement plus élevée parmi les tranches d'âge de 15 à 20 ans (34,0 %) et de 20 à 35 ans (24,0 %). Aucune différence significative n'a été observée entre les taux de séropositivité selon le sexe et la nationalité. La séropositivité était de 72,7 % dans la cohorte pour la période 1987-1996 et de 70,1 % dans la cohorte pour la période 1997-2006. Le taux moyen d'anticorps antirougeoleux était de 2318,5 UI/ml.

Conclusion : La présente étude a révélé un écart d'immunité contre la rougeole parmi certains groupes d'âge à Oman, ce qui indique le besoin d'une couverture vaccinale élevée soutenue, d'une surveillance robuste, de campagnes de vaccination ciblées et d'une riposte rapide aux flambées épidémiques.

دراسة مختبرية مقطعية بشأن الانتشار المصليِّ للحصبة في عُمان

بدر الرواحي، براكاش باتل، نورة الفارسي، حنان الكندي، أمينة الجرداني، انتصار الشكري، سميرة المحروقي، عايشة البوسعيدي، أنيتا هانجارج، سيف العبري

الخلاصة

الخلفية: منذ بدء التطعيم في عُمان في عام 1981، انخفض معدل الإصابة بالحصبة، وتخلصت عُمان من هذا المرض في عام 2019. أمَّا حالات الحصبة الموجودة حاليًّا في عُمان، فترتبط بوفود الفيروس إليها من الخارج.

الأهداف: هدفت هذه الدراسة الى فَهْم خصائص المناعة ضد الحصبة عند السكان العُمانيين، وتحديد الفئات الشديدة التعرض للخطر.

طرق البحث: أجرينا اختبارًا لما مجموعه 1990 عينة دم مجهولة المصدر من أصل 2032 عينة جُمعت من جميع مستشفيات الإحالة الإقليمية ومختبر خاص واحد في عُمان، في الفترة من نوفمبر/ تشرين الثاني 2015 إلى يناير/ كانون الثاني 2016 لفحص الجلوبولين المناعي G للحصبة. وقد جمعنا عينات الدراسة في 4 مجموعات بحسب تاريخ ميلاد أصحابها، وحلَّلنا البيانات بالإصدار 16.0 من برمجية SPSS. واستخدمنا χ^2 لتحليل الدلالة الإحصائية، واستخدمنا اختبار كروسكال واليس لحساب المتوسط الهندسي لكل فئة عمرية. وقد عُدت قيمة الاحتمال < 0.05 ذات دلالة إحصائية.

النتائج: بلغ إجمالي نسبة الإيجابية المصلية للحصبة 84.0٪. وكانت السلبية المصلية أعلى كثيرًا عند الفئتين العمريتين 15–20 سنة (34.0٪) و20–35 سنة (24.0٪). ولم يكن هناك فرق ملحوظ في الإيجابية المصلية بحسب الجنس والجنسية. وكانت نسبة الإيجابية المصلية 72.7٪ في الفئة 1987–1996، و70.1٪ في الفئة 1997–2006. وبلغ متوسط مستوى الأجسام المضادة للحصبة 2318.5 وحدة دولية/ مل. وقد كان العمر عاملًا مهمًّا في تقدير عيار الأجسام المضادة للحصبة على النحو المشار إليه في منحنى خصائص فعل المُستقبِلات (0.68، احتمال < 0.05).

الاستنتاجات: كشفت هذه الدراسة عن وجود فجوة في التحصين ضد الحصبة بين بعض الفئات العمرية في عُمان، وهو ما يوضِّح الحاجة إلى تغطية عالية ومستدامة بالتطعيم، وترصُّد قوي، وحملات تطعيم موجَّهة، ومواجهة الفاشيات في الوقت المناسب.

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