

Research Article

A study on measles immunity among pregnant women in Sri Lanka, conducted concurrently with the country's efforts to eliminate the disease

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Abstract

Introduction: Indigenous transmission of measles was eliminated in Sri Lanka in 2019, but a resurgence has been observed recently. High population immunity is considered to be the key element in sustaining the elimination status. Measles seroprevalence data in Sri Lanka are sparse. As pregnant women and neonates are two groups who would experience the most detrimental complications of measles, data on it is important to ascertain maternal immunity. The objective of this study was therefore to determine measles IgG seroprevalence among a selected group of pregnant mothers and to determine factors associated with seropositivity.

Methodology: A descriptive cross-sectional study was conducted at antenatal clinics of a leading tertiary care maternity hospital in Colombo, Sri Lanka. Testing for measles IgG was carried out at the Department of Microbiology, Faculty of Medicine, University of Colombo Sri Lanka. Sociodemographic data was collected. Measles-specific IgG was determined using a validated commercial assay (AccuDiag™ measles IgG quantitative ELISA).

Results: Of 391 participants, measles IgG was positive in 91.3% (95% CI 89.5-95.0%). Eleven (2.8%) had equivocal results. The geometric mean titre was 0.48 IU/ml (SD 0.28). Seropositivity fell from 100% in the oldest age group (41-45 years) to 71.4% in the youngest age group (15-19 years). No difference in the mean antibody titre was observed among age groups. Having ≥ 4 household members during childhood was the only other factor significantly associated with seropositivity apart from age.

Conclusions: Immunity against measles was high among the study population. However, the younger age groups had a higher susceptibility.

Keywords: Measles, pregnancy, Sri Lanka, immunity, seroprevalence

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Introduction

Measles is a highly infectious viral infection with up to 90% of susceptible exposed contacts developing the disease. It causes significant mortality and morbidity both in children and adults. The measles virus is a single-stranded ribonucleic acid (RNA) virus belonging to the genus *Morbillivirus* in the family of *Paramyxoviridae*.¹ Measles used to be a common childhood illness in the pre-vaccination era and caused significant morbidity and mortality. It can cause complications including pneumonia and encephalitis, which are commoner at extremities of life.¹ Neonates and children less than two years are particularly at a higher risk of a rare but life-threatening complication, subacute sclerosing panencephalitis (SSPE). This is a degenerative neurological disorder that has a gradual progressive course leading to death in 1-3 years.² SSPE occurs at a rate of 4-11 in 100,000 cases of measles, and the risk is 16 times greater when the infection is acquired during infancy compared to children who acquire the infection at five years or above.^{2,3}

Measles in pregnancy can cause harmful effects to both the mother and the developing foetus. Numerous studies have demonstrated increased measles-related morbidity and mortality among pregnant women,⁴ Pneumonia is the most commonly detected complication among mothers, while adverse pregnancy outcomes, including miscarriage, preterm delivery, and intrauterine growth retardation are known to occur when the foetus is infected any time during the pregnancy.^{2,5} However, measles in pregnancy is not associated with any congenital abnormalities.⁴

Measles is spread through aerosols and respiratory secretions and is highly infectious. Thus, infection control is a real challenge. Pooled human normal immunoglobulin when given within 14 days of exposure is recommended as a method of post-exposure prophylaxis against measles in pregnancy.³ The most effective preventive method against measles is vaccination using the live attenuated measles vaccine, which is usually combined with mumps and rubella vaccines (MMR). Before the age of nine months, an infant's protection against measles largely depends on transferred maternal antibodies.

In Sri Lanka, a measles-containing vaccine was first introduced in 1984 following a large outbreak of measles in 1983.⁶ Initially, this was offered as a single dose at nine months of age.⁶ The second dose of measles vaccine was introduced in 2001 for children aged three years, and the age of the first dose was delayed to one year. This was due to the presumption that preexisting maternal antibodies would neutralise the vaccine virus. However, the age for the first dose of the vaccine was again advanced to nine months from 2015. This was after the measles outbreak occurred in 2013-2014, which involved a significant number of infants, showing that a significant proportion of cases were children under the age of one year.⁷⁻⁹ The efficacy of a single dose of the vaccine against measles is 75%-93%, depending on the age of administration, and increases to 88%-97% with two doses.^{1,7}

The strengthening of measles immunisation strategies, with the goal of eliminating measles by the year 2020⁸ in line with the World Health Organization (WHO) measles elimination targets¹⁰ was top priority for the country for many years. There have been no cases of indigenous measles since 2016, and the country was declared to have eliminated measles in July 2019.¹¹ However, there

were resurgences of measles cases from mid-March to May 2019¹² and in May 2023,¹³ which continued up to December 2023.¹⁴ This highlights the importance of strengthening population immunity further.

Since measles vaccination is contraindicated during pregnancy, non-immune women should receive the vaccination before conception or during the postpartum period. Although human normal immunoglobulin is recommended for post-exposure prophylaxis in pregnancy,⁴ it is often not available due to the significant cost.¹⁵

Published data concerning measles susceptibility and its associated risk factors among pregnant women is sparse in Sri Lanka. This data will be useful in understanding and mitigating the risk posed to non-immune pregnant women, particularly at times of measles resurgence. Lack of immunity in the mother will also leave the newborn infants susceptible due to the lack of transplacentally transferred maternal antibodies.

We carried out this study to determine the seroprevalence of anti-measles IgG in pregnant women to assess susceptibility in this vulnerable group and describe factors associated with immunity. Data obtained through this study will complement the currently available estimates of population immunity and will be useful to understand the risk of re-introduction of measles as an endemic disease.

Methods

Study design and setup

A hospital-based descriptive cross-sectional study was conducted among pregnant mothers attending selected antenatal clinics (ANCs) at De Soyza Maternity Hospital (DMH), Colombo, over six consecutive months. All mothers attending ANCs were considered eligible. The minimum required sample size was estimated at 385 participants, assuming a prevalence of 50% in order to maximize the sample size, with a 95% confidence level and a 5% margin of error. The calculation was performed using Winpepi statistical software (version 11.39).

All mothers who provided informed written consent were consecutively included from each clinic until the required sample size was achieved. Data were collected using a pre-tested interviewer-administered questionnaire. The questionnaire included information including age, race, period of amenorrhoea, educational level, occupation, number of household members the participant lived with during their childhood (up to 12 years), number of children the participant has currently, and past history of fever and rash suggestive of measles.

Specimen processing

The presence and titre of anti-measles IgG were determined using AccuDiag™ measles IgG quantitative ELISA (Enzyme-Linked Immunosorbent Assay) by Diagnostic Automation/Cortez Diagnostics, Inc., following the manufacturer's instructions.¹⁶ Sensitivity and specificity of the assay were 99.3% and 91.0% respectively.¹⁵ IgG antibodies to measles were categorised based on Index Standard Ratio (ISR) values as follows: ISR of ≤ 0.90 (seronegative); ISR of 0.91–1.09 (equivocal); and ISR of ≥ 1.10 (seropositive). Samples that initially tested equivocal were re-tested in duplicate, and the results of two of the three tests were considered. Positive ISR values were

converted to international units using the α -method as specified by the manufacturer. For quality assurance, 10% of the randomly selected samples were re-tested and their results compared with the original findings.

Data analysis

Seroprevalence was calculated as follows:

$$\text{Measles seroprevalence} = \frac{\text{Number of measles IgG positive samples}}{\text{Number of examined samples}}$$

Subjects with repeatedly equivocal results were excluded from further analysis. The terms ‘susceptibility’ and ‘immunity’ were used to indicate the absence or presence of measles-specific IgG respectively. According to their current permanent address, the study group was divided into urban, rural, and estate sectors as per definitions provided by the Department of Census and Statistics, Sri Lanka. A past history of measles was defined as having an acute illness with fever and a generalised non-blistering rash.

Statistical analysis was done using SPSS statistical software version 21.0. (SPSS, Illinois USA). Level of significance (p) was set at 0.05. Chi’s square test and one-way ANOVA were used where appropriate.

Results

Population characteristics

A total of 391 mothers were enrolled. The mean age of the study sample was 28.5 years with a Standard Deviation (SD) of 5.6 years.; Age range was 17 to 42 years. Table 1 describes the general characteristics of the study sample.

Table 1 : Characteristics of the study population

Characteristic	Value	
	n	%
Mean age (years)	28.5 (± 5.5)	
Educational level		
Below GCE O/L*	89 (%)	22.8
GCE O/L and above	302 (%)	77.2
Residence		
Rural	182 (%)	46.5
Urban	209 (%)	53.5
Race		
Sinhalese	231 (%)	59.0
Tamil	74 (%)	18.9
Burger	8 (%)	2.0
Muslim	78 (%)	19.9
Mean POA (weeks)	25.8 (± 8.6)	

*GCE O/L: General Certificate of Education-Ordinary Level
POA : Period of amenorrhoea

Of all participants, 129 (33.0%) had <4 household members during their childhood, while 262 (67.0%) had four or more members. Regarding the current number of children, the majority (181, 46.3%) had no other children except for the current pregnancy, 139 (35.5%) had one child, and 71 (18.2%) had two or more children.

Seroprevalence of measles immunity

Measles seropositivity rate was 91.3% (95% CI 89.5-95.0%). Eleven (2.8%) had equivocal results. Mean measles IgG geometric titre was 0.48 IU/ml (SD 0.28). Subjects having equivocal results were excluded from further analysis.

Participants were placed in six age categories, and the seroprevalence for each category was calculated (Table 2).

Measles immunity was significantly lower among younger age groups when compared to older age groups (Table 2 and Figure 1). The Geometric Mean Titre (GMT) remained close to the population mean (0.48 IU/ml) in most age groups except the youngest (0.51 IU/ml) and the oldest (0.38 IU/ml) age groups. However, these differences were not statistically significant.

Table 2 : Measles seroprevalence and antibody titres according to age category

Age category (years)	Sero-status		Total	Adjusted residual values for sero-positivity	GMT (IU/ml) ($\pm$ SD)
	Negative	Positive			
15-19	6 (28.6%)	15 (71.4%)	21	-4.5	0.51 ($\pm$ 0.29)
20-25	10 (10.3%)	87 (89.7%)	97	-2.0	0.47 ($\pm$ 0.28)
26-30	4 (3.4%)	115 (96.6%)	119	1.5	0.47 ($\pm$ 0.28)
31-35	3 (2.9%)	99 (97.1%)	102	1.5	0.48 ($\pm$ 0.29)
36-40	0 (0%)	35 (100%)	35	1.6	0.49 ($\pm$ 0.31)
41-45	0 (0%)	6 (100%)	6	0.6	0.38 ($\pm$ 0.08)
Total	23	357	380		

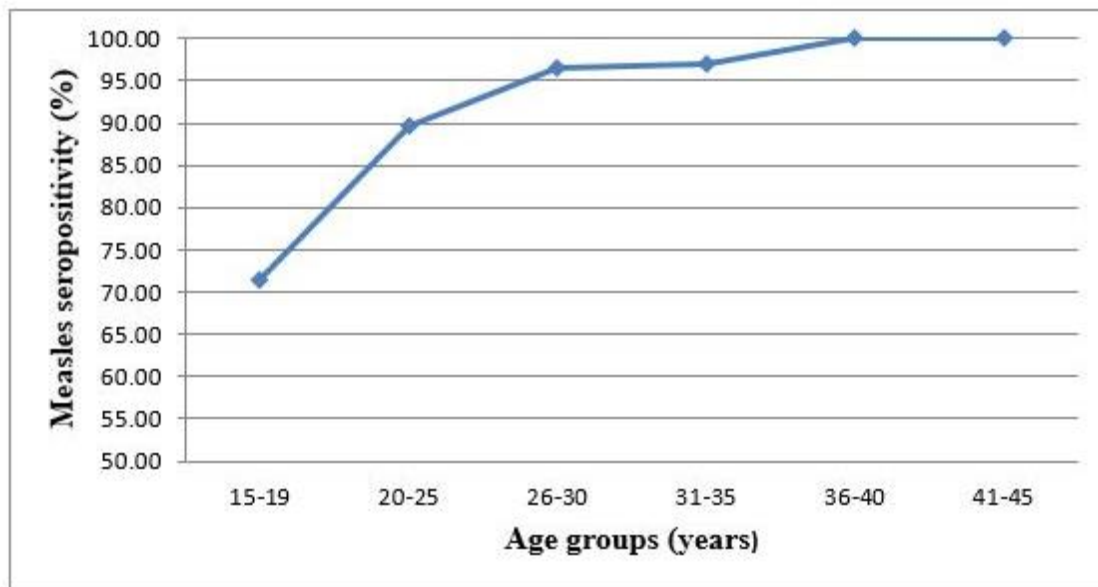


Figure 1 Distribution of measles immunity across age groups

Factors associated with immunity

Table 3 Frequency distribution of history of measles and measles sero-status

Past history of measles	Measles IgG		Total
	Negative	Positive	
Cannot recall	2	12	14
Present	2	72	74
Absent	19	273	292
	23	357	380

A total of 74 participants reported a history of an illness with rash suggestive of natural measles, and 97.3% of these were seropositive. Among those who reported a negative past history or could not recall, 93.1% were seropositive (Table 3). Seropositivity was not associated significantly ($p=0.26$) with a past history of measles in this study group.

Table 4 Factors associated with measles sero-status

	Positive	Negative	<i>P</i> value
Residence			
Urban	192	12	$P=0.881^{**}$
Rural	165	11	
Educational level			
Below GCE O/L	81	5	$P=0.916^{**}$
Up to /above GCE O/L	276	18	
Number of household members			
≤4 members	245	11	$P=0.039^{**}$
>4 members	112	12	
Number of children			
None	159	14	$P=0.296^{**}$
1	183	8	
≥2	15	1	

*Independent sample t test; **Chi square test

GCE O/L- General certificate of education Ordinary Level

The association between several other factors and measles serostatus was also determined (Table 4). Having four or more household members during childhood was the only significant factor associated with seropositivity. ($P=0.039$).

Discussion

We detected an overall seroprevalence of 91.3% for the given population of women, with 8.7% being susceptible. This rate is above the overall world measles immunity level (88%) but less than that for WHO South-East Asia region (93.2%) to which Sri Lanka belongs.¹⁷ This rate is comparable to the overall seroprevalence found in a large study conducted in 2009-2010 in the United States of America,¹ as well as a study conducted in Haiti, which detected a seropositivity rate of 94.1%.¹⁸ Our susceptibility rate is slightly lower than the 10.41% rate reported in a large study conducted among pregnant women in France.¹⁹ Japan reported a susceptibility rate of over 28% in a study conducted among more than 10,000 antenatal mothers using a neutralisation assay.²⁰ The required level of herd immunity ranges from 90 to 95% when considering basic reproductive value (R_0) for measles from 10 to 20 respectively. While our study sample as a whole

has reached this level the required level of herd immunity was not seen in the age groups ≤ 25 years within the study group.

In line with the WHO 2012 measles elimination goals,¹⁰ Sri Lanka has also set its target to eliminate measles from the country, a goal achieved in 2019.¹¹ Achieving an overall vaccination coverage for both doses of vaccine in $\geq 95\%$ ¹⁰ of the population was one of the key strategies to attain this goal, and Sri Lanka has reported an excellent coverage of 98% in 2019.¹⁷

However, it was observed that seropositivity rates were significantly lower among younger age groups compared to older age groups, with the rate for the youngest group (≤ 19 years) being 71.4%. This finding aligns with studies from other countries.²¹ One reason for this could be that women in younger age groups may rely solely on vaccine immunity, which might wane more rapidly by adulthood compared to natural immunity.^{21,22} This is further supported by the fact that Sri Lanka is in an elimination setting, where natural boosting by the wild virus is minimal. Moreover, as only a single dose of the vaccine was offered from 1984 to 2001, seroconversion rates may have been lower compared to those with two doses which may be the case for those aged 20-25 years. Identifying clusters with low immunity is crucial, especially for countries in an elimination setting, as these vulnerable populations could serve as foci for reintroducing the virus into the country.

Measles IgG levels detected by ELISA in our study had a mean GMT of 0.48 IU/ml. Although the Plaque Reduction Neutralisation Test (PRNT) is considered the gold standard, ELISA is an accepted method to assess immunity.^{23,24} A study conducted in Korea²⁵ demonstrated that IgG titres from the ELISA and PRNT showed good agreement, with Pearson's and Spearman's correlation coefficients of 0.9271 and 0.954 respectively ($p < 0.0001$ for both).

A past history of measles was not significantly associated with measles immunity, probably because this population may have been exposed to vaccination programmes and several outbreaks.⁶ However, the participant's childhood family size was associated with immunity, implying that overcrowding predisposes individuals to infection. Although factors such as educational status and the number of current children were associated with immunity in some studies,¹⁹ this was not observed in the present study.

The strength of the study include the large sample size and the heterogeneity of the sample, which comprised a mixture of all ethnic groups and rural/urban residents. Although Colombo is a highly urbanised district, being a tertiary care hospital, DMH caters to an unusually high proportion of rural residents, as reflected in this study sample. This heterogeneity is a factor that makes the results more generalisable. A main limitation of the study was the unavailability of personal vaccination records and participants not being able to reliably recall their vaccination history.

In conclusion, the prevalence of measles immunity among this sample of Sri Lankan pregnant women is high. However, the lower seropositivity rates among younger age groups should be taken into consideration, especially in elimination settings. Wider studies should be carried out to accurately assess the susceptibility to measles among younger pregnant mothers.

Declarations

Conflict of interest: Authors declare that they have no conflicts of interest

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Ethics Statement: The study was approved by the Ethics Review committees of Medical Research Institute, Colombo (No.50/2016) and National Hospital of Sri Lanka (AAJ/ETH/COM/2017-07). Procedures followed were in accordance with the ethical with the Helsinki Declaration of 1975, as revised in 2000.

Author contributions:

IP : Conceptualized and designed the study, analysed and interpreted data, drafted the manuscript

CM: Carried out laboratory investigations, entered data and contributed to the drafting of the manuscript.

RJ: Contributed to the designing of the study, contributed in specimen collection, carried out laboratory investigations and entered data

PA : Contributed to the designing of the study, contributed in specimen collection, entered and analysed data and contributed on drafting the manuscript

All authors reviewed the final version of the manuscript and are accountable for all aspects of the work

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