

Research Article

Seroprevalence of Vaccine Preventable Diseases among Children

Amna Khan¹, Shehzad Saleem², Alishba Rasool³, Mahnoor Khan⁴, Marina Akhtar⁵, Irfan Munir⁶, Saira Afzal⁷

⁽⁶⁾ Internal Medicine, Nephrologist, Fort Wayne, Lutheran Hospital, USA

⁽¹⁻⁵⁾ Mayo Hospital, Lahore / King Edward Medical University Lahore, Pakistan, ⁽⁷⁾ Mayo Hospital, Lahore/ King Edward Medical University Lahore, Pakistan

Abstract:

Millions of children die from vaccine-preventable diseases every year. Seroprevalence of Vaccine Preventable Diseases provides a good estimate of vaccination levels and their coverage. This systematic review has evaluated the findings of 6 seroprevalence surveys worldwide. The articles published between January 2012 and December 2020 were searched from online databases such as Medline, PubMed, and Google Scholar. A total of 6 cross-sectional studies determining seroprevalences in children were included. The aim of the study was to determine seroprevalence of vaccine preventable disease among children. Serosurveys may be crucial in the maintenance of VPDs elimination. Seroepidemiological data for childhood preventable diseases can be used in numerous ways to improve vaccination outcomes and child health indicators. A strong seroepidemiological network in a country must be established. Enhancing the routine Vaccination coverage based on serosurvey results should be essential in preventing vaccine-preventable diseases.

Corresponding Author: Amna Khan

Supervisor: Prof. Dr. Saira Afzal | Department of Community Medicine, KEMU, Lahore.

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INTRODUCTION:

Every year, millions of children die from preventable and treatable causes. Vaccine saves lives. Measles vaccines alone are estimated to have prevented over 21 million deaths between 2000 and 2017¹. The Seroprevalence studies evaluating vaccine preventable diseases estimate the percentage of people in a

population who have proteins called antibodies in their blood that show they have been exposed to a virus or other infectious agent. For example, studying the seroprevalence of antibodies to a specific virus can show how many people have been infected with that virus².

Using cross-sectional studies of antibody prevalence, seroprevalence gives estimates of population-level immunity against diseases that can be prevented by vaccination. Sero-epidemiologic data can be used to highlight the incremental aggregation of susceptible individuals, changes in the age-specific risk of infection, and the potential for outbreaks when paired with computer modeling. This information can assess vaccination programs' effectiveness and assist vaccine policy decisions, such as launching "catch-up" vaccination campaigns to minimize the likelihood of outbreaks³.

In this systematic review, the studies were selected that estimated the seroprevalence of 14 vaccine-preventable diseases which are part of routine vaccination, which are: 1. Polio; 2. Tetanus; 3. Flu (Influenza); 4. Hepatitis B; 5. Hepatitis A; 6. Rubella; 7. Hib; 8. Measles; 9. Whooping Cough (Pertussis); 10. Pneumococcal Disease; 11. Rotavirus; 12. Mumps; 13. Chickenpox and 14. Diphtheria⁴.

MATERIALS AND METHODS:

The systematic review protocol was formulated in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement and Guidelines of 2020, but it did not involve the implementation of a meta-analysis⁵.

The articles that were published between January 2012 and December 2020 were searched from online databases such as Medline, PubMed, and Google Scholar. The keywords used were: Seroprevalence, Vaccine Preventable diseases, and Children.

Observational study types with Seroprevalence estimates, eligible for this systematic review comprised with

the outcome measure of interest as vaccine-preventable diseases.

The studies with data of adult patients were excluded as those were beyond the scope of this systematic review.

Relevant studies were initially assessed based on their titles and abstracts. Complete articles were obtained from databases for those that met the criteria. The final determination of eligibility was made independently, aligning with the Prisma guideline checklist from 2020. After eliminating 2700 duplicate entries, 3425 out of the remaining 3580 articles were deemed irrelevant and excluded. The remaining 155 articles underwent a thorough review for selection, resulting in the inclusion of 6 observational studies for the systematic review. These 6 eligible studies encompassed a combined total of 14,156 participants from various regions around the world. (Table 2).

RESULTS:

According to Hincapié-Palacio¹ et al., an analysis of the surveillance capability for a sample of 5000 specimens revealed that vaccination tactics change over time and that population immunity changes must be checked often every 5 to 10 years⁶.

In a study by Xaydalasouk et al., 73.4% of people are immune to measles, and age considerably raised the seroprevalence of measles, with 93.0% seroprotected. The anti-rubella IgG seroprevalence was high from an early age. These statistics indicate that Saravan's mandatory childhood immunization program needed to be enhanced, and further research is required to fully understand the apparent low immunogenicity of the measles component of the vaccine for measles and

rubella⁷.

Yixiang Ng et al in a Singapore-based study, which included 1200 youngsters (1-17 years age) showed that the measles and rubella antibodies were present in 98.2% and 94.8% of children. 89.3% of participants were protected against tetanus, while 97.1% of subjects had at least minimal protection against diphtheria. Compared to those who were immune to HBV, the prevalence of chronic HBV carriage was 0.4%, while 45.7% Varicella antibody seroprevalence was 52.9%⁸. In their cross-sectional study in Timor-Leste, Arkell et al. used commercially available chemiluminescent immunoassays or enzyme-linked immunosorbent assays to detect measles immunoglobulin G (IgG), rubella IgG, severe acute respiratory syndrome coronavirus-2 anti-spike protein IgG, hepatitis B surface antibody, and hepatitis B core antigen. The study included 5600 participants. According to the author, Timor-Leste has a sizable VPD immunity gap and a high risk of outbreaks. The reasons were such as the SARS-COV 2 outbreak, and the interruption of the supply⁹.

Lolowa et. al has described data from 227 UAE children of 23 to 71 months of age. The prevalence of positive serological immunity was highest (98%) against measles and rubella and lowest (68%) for varicella¹⁰. In a Vietnam-based study by Choisy et.al the authors compiled data from 6 ecological regions of the country using UNICEF’s Multiple Indicator Clustered Surveys (MICS). The authors have noticed the existence of a difference between the expected levels of vaccination coverage (90%–95%) and population protection (60%–70%); however, the reasons of this discrepancy were found to be unknown¹¹.

Following statistics were extracted from these studies: Study design; the sample size (number of subjects) Seroprevalence percentages and reasons for high of low seroprevalence.

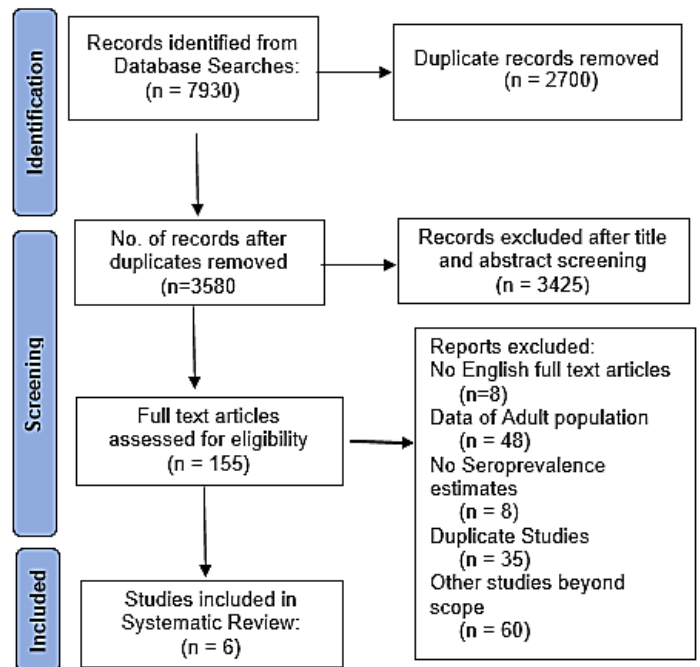


Figure 1: PRISMA Flow Chart

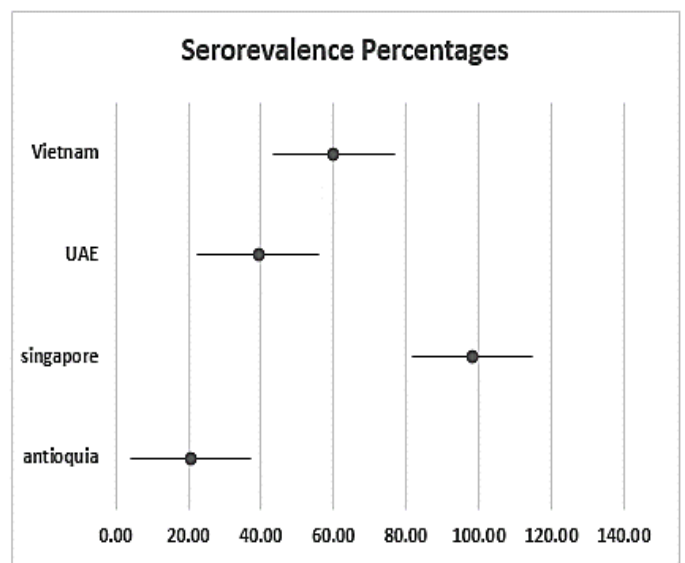


Fig.2: Forest Plot

Table 1: Selected Studies and their Descriptions

Author/s; [Ref.] And (Study Type)	Country	Sample Size	Sero- Prevalence %age	Tests Used	Inference
Hincapié- Palacio1 et al. (6)	Antioquia (Cross- Sectional)	1000	20.5	Pertussis AB From (Umbilical Cord)	Low Vaccination Coverage (Overall)
Xaydalasuk et al. (7)	Southern People's Republic (Cross-Sectional)	Lao 2463	NA	Hb-S Rapid Antigen testing	Low Vaccination Coverage (Overall)
Yixiang et al. (8)	Singapore (Cross- Sectional)	1200	98.2%	Enzyme- linked immunosorbent assays (EIA) or plague reduction neutralization tests (PRNT)	Low Vaccination Coverage (MMR, and DT)
Arkell et al. (9)	Timor- Leste (Cross- Sectional) Cluster Random	5600	NA	IgG AB Measles, Rubella, SIRS, COV2, HB-AB	Low Seroprevalence of Measles, High Seroprevalence of SARS- COV-2
Lolowa et al. (10)	UAE (Cross- Sectional)	231	39.2% (pertussis) 98.3% (rubella) measles (98.2%) (92%) Poliovirus	ELISA was used to Measure IgG Antibody titers in the sera of the participating children.	Immunization tailored to high-risk groups
Choisy et al. (11)	Vietnam (Clustered Ecological Survey)	3662	40% - 80%	ELISA	Reported Coverage is 95% but Seroprevalence is only 70%

DISCUSSION:

The findings of our review suggest that the use of seroprevalence can help health authorities assess how well a vaccination program is reaching the target population. By measuring the prevalence of specific antibodies after vaccination, they can determine the

proportion of vaccinated individuals who have developed protective immunity against the disease. Seroprevalence studies are particularly important for infectious diseases that may have asymptomatic or mild cases, as they can provide a more comprehensive

picture of the true extent of the infection beyond what is reported through clinical surveillance.

Seroprevalence data provides an unbiased overview of the vaccination coverage results and allows us to look past human and data collection errors seen in feedback data. This makes it a more authentic source of monitoring vaccine coverage¹². As shown by Choisy et al. in Vietnam, where Coverage reported was 95%, but Seroprevalence was only 70%.

The low vaccine coverage indicated by the seroprevalence data acquired via Pertussis Antibodies analysis (From Umbilical Cord samples). As shown by Hincapié-Palacio¹ et al. point towards the vaccination tactics that change over time and need reassessment for better coverage. Vaccination tactics, such as the type of vaccine used, vaccination coverage rates, the timing of vaccinations, and the target population, significantly influence the seroprevalence of a particular disease in a population, and hence it can be used as an effective tool to monitor coverage.

Similarly, Xaydalasouk et al. showed that seroprevalence data from Hb-S Rapid Antigen testing identified a gap in the immunogenicity of the Measles and Rubella component of the MMR vaccine. While the mumps and rubella components of the MMR vaccine are also immunogenic and effective in inducing immunity, the measles component tends to generate a more robust and sustained immune response. Some differences exist in their immune response characteristics due to the differences in the viruses themselves, while others are due to the age of the vaccine recipient. Seroprevalence studies can be used to monitor the age-related immunogenic effect of vaccination, including

the immunogenicity of the components in vaccines like the MMR vaccine^{12,13}.

The effectiveness of seroprevalence studies in detecting subclinical and mild cases was demonstrated by the ELISA testing done by Yixiang Ng et al. in a Singapore-based study. The data identified the low coverage for Mumps and Diphtheria, which can guide the appropriate vaccination efforts towards these programs. This approach can be effectively utilized in detecting early infections in subclinical populations. A similar result has also been previously studied in asymptomatic children infected with *H. Pylori*^{15,17}. Seroprevalence studies have also proven groundbreaking in shaping the response to outbreaks and pandemics¹². Arkell et al. showed high SARS-COVID-2 anti-spike protein IgG levels via chemiluminescent immunoassays or enzyme-linked immunosorbent assays. This data identified a gap in immunity and outbreak potential in the community. This proves that the seroprevalence predictor model can also be effectively utilized against numerous childhood diseases to control their spread.

The study done by Lolowa et al. suggests using seroprevalence data to detect high-risk populations and tailor immunization according to them. Immunization tailored for high-risk groups is a crucial and effective public health strategy to protect vulnerable populations from infectious diseases. High-risk groups are individuals who may be more susceptible to severe complications or have a higher likelihood of exposure to certain diseases due to various factors such as age, underlying health conditions, occupation, or other specific circumstances¹⁶.

The advantages of seroprevalence studies are numerous and should be explored in further research. Experimental data on developing more efficient techniques for these studies is important and a strong avenue for future research. A strong seroepidemiological network in a country must be established. Enhancing the routine Vaccination coverage bound with serosurvey results should be essential in preventing vaccine-preventable diseases. Addressing this topic will prove crucial in ensuring elimination of VPDs (22).

Our systematic review has some limitations. Concerning methodology, the systematic review did not explore other databases and libraries like SCOPUS, MedLine, Cochrane, etc; the search only included studies in English, and literature in other languages was excluded. There is also a likelihood of publication bias since our systematic review does not explore the literature on the challenges of using seroprevalence studies. Potential challenges, including the testing accuracy, varying vaccine types schedules, logistical and finances are, however, considerable in this regard¹⁴. The lack of Expanded Program of Immunization, proper vaccine records and sufficient studies in this region are some other limitations²³.

This study will provide a foundation for further investigations. Future research could focus on comparative studies, longitudinal studies, intervention studies, qualitative research, multidisciplinary approaches, comparative international studies, and evaluations of policy implementation²⁰. By building upon the initial research, these subsequent studies would enhance our understanding and contribute to a better understanding

of seroprevalence of vaccine preventable diseases²¹. The public's acceptance of vaccination is critical to the success of any immunization program¹⁹.

CONCLUSION:

There is a strong link between vaccination status and seropositivity to measles, rubella, diphtheria, and tetanus. The level of immunity, especially against childhood vaccines, is assessed in different studies in this review, and the results show a similar pattern - with high seroprevalence against measles and relatively low levels in the case of pertussis, rubella, and mumps. Seroprevalence against diphtheria was found to be low in Singapore compared to UAE. Although they are still rarely used, ecological surveys for measles and rubella may be able to detect susceptibility directly.

Seroepidemiological data for childhood preventable diseases can be used in numerous ways to improve vaccination outcomes and child health indicators. Vaccine coverage monitoring, measurement of immunogenicity, and detection of early subclinical infections are some potential benefits of seroprevalence studies in children.

Building a seroepidemiology network in a country can be difficult because of the issues with funding, ethics, epidemiology, and laboratory frameworks required. However, the patterns of immunity anticipated from disease monitoring and vaccine coverage data may reveal crucial complexities related to the vaccination process¹⁸. The National Immunization Strategy should focus on developing an infrastructure for tracking diseases preventable by vaccines.

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REFERENCES:

1. Child health and survival [Internet]. [cited 2023 Aug 10]. Available from: <https://www.unicef.org/child-health-and-survival>
2. NCI dictionaries [Internet]. [cited 2023 Aug 10]. Available from: <https://www.cancer.gov/publications/dictionaries>
3. Wilson SE, Deeks SL, Hatchette TF, Crowcroft NS. The role of seroepidemiology in the comprehensive surveillance of vaccine-preventable diseases. *CMAJ*. 2012;184(1):70-6.
4. Diseases and the vaccines that prevent them [Internet]. Centers for Disease Control and Prevention; 2019 [cited 2023 Aug 23]. Available from: <https://www.cdc.gov/vaccines/parents/diseases/index.html>
5. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP ,et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Annals of internal medicine*. 2009 ;151(4):65.
6. Hincapié D, Acevedo M, Hoyos MC, Ochoa J, González C, Pérez PA, et al. Serosurveillance for vaccine-preventable diseases: A look inside the pertussis experience. *Biomedica*. 2019 ;39(2):130-143.
7. Xaydalasouk K, Sayasinh K, Hübschen JM, Khounvisith V, Keomany S, Muller CP, et al. Age-stratified seroprevalence of vaccine-preventable infectious disease in Saravan, Southern Lao People's Democratic Republic. *Int J Infect Dis*. 2021;107(1):25-30.
8. Ng Y, Chua LAV, Cui L, Ang LW, Tee NWS, L in RTP, et al. Seroprevalence of vaccine-preventable diseases among children and adolescents in Singapore: Results from the National Paediatric Seroprevalence Survey 2018. *Int J Infect Dis*. 2020 ;929(1):234-240.
9. Arkell P, Sheridan SL, Martins N, Tanesi MY, Gomes N, Amaral S, et al. Vaccine Preventable Disease Seroprevalence in a Nationwide Assessment of Timor-Leste (VASINA-TL): study protocol for a population-representative cross-sectional serosurvey. *BMJ open*. 2023 ;13(5):1-10
10. Al-Mekaini LA, Kamal SM, Al-Jabri O, Soliman M, Alshamsi H, Narchi H, et al. Seroprevalence of vaccine-preventable diseases among young children in the United Arab Emirates. *Int J Infect Dis*. 2016 ;50(1):67-71.
11. Choisy M, Trinh ST, Nguyen TND, Nguyen TH, Mai QL, Pham QT, et al . Sero-Prevalence Surveillance to Predict Vaccine-Preventable Disease Outbreaks; A Lesson from the 2014 Measles Epidemic in Northern Vietnam. *Open Forum Infect Dis*. 2019 ;6(3):1-7.
12. Wilson SE, Deeks SL, Hatchette TF, Crowcroft NS. The role of seroepidemiology in the comprehensive surveillance of vaccine-preventable diseases. *CMAJ* 2012;184(1):70–6.

13. Gupta D, Faridi MMA, Aggarwal A, Kaur I. Seroprevalence of anti Vi antibodies and immunogenicity of Typhim Vi vaccine in children. *Hum Vaccin* 2008;4(1):305–8.
14. MacNeil A, Lee C-W, Dietz V. Issues and considerations in the use of serologic biomarkers for classifying vaccination history in household surveys. *Vaccine* 2014;32(1):4893–900.
15. Babatola AO, Akinbami FO, Adeodu OO, Ojo TO, Efere MO, Olatunya OS. Seroprevalence and determinants of *Helicobacter pylori* infection among asymptomatic under-five children at a Tertiary Hospital in the South-Western region of Nigeria. *Afr Health Sci* 2019;19(1):2082–90.
16. Stephens MM, Kavanaugh E. Improving Immunization Coverage in Special Populations. *Prim Care* 2020;47(1):453–65.
17. HernandezSuarez G, Saha D, Lodroño K, Boonmahittisut P, Taniwijaya S, Saha A, et al. Seroprevalence and incidence of hepatitis A in Southeast Asia: A systematic review. *Plos one*. 2021;16(12):1-19.
18. Elduma AH, LaBeaud AD, A Plante J, Plante KS, Ahmed A. High Seroprevalence of Dengue Virus Infection in Sudan: Systematic Review and Meta-Analysis. *Trop Med Infect Dis* 2020;5(1):120.
19. Afzal S. Misinformation and Misconceptions About COVID-19 Vaccination in Pakistan: The Need to Control Infodemic. *Annals of King Edward Medical University*. 2021;27(4):471-3.
20. Knowledge and Perception of Gynecologist Against Sexual Assault-Multi Center Trial. *Annals of King Edward Medical University*. 2023;28(4):441-8.
21. Ashraf S, Haider G, Ashraf M. Violence against Women with Disabilities: A Qualitative Investigation. *Annals of King Edward Medical University*.2018;23(4):540-5
22. Yusuf A, Ghauri SS. The Healthcare Reforms Process. *Annals of King Edward Medical University*. 2019;25(S):16-23.
23. Afzal S, Bint-e-Afzal B. Risk factors associated with the outbreak of measles in Lahore, Pakistan. *Annals of King Edward Medical University*. 2014;20(4):302–4.