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Measles seroprevalence in Chiradzulu district, Malawi: Implications for evaluating vaccine coverage

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ABSTRACT

Introduction: Self-reported measles vaccination coverage is frequently used to inform vaccination strategies in resource-poor settings. However, little is known to what extent this is a reliable indicator of underlying seroprotection, information that could provide guidance ensuring the success of measles control and elimination strategies.

Methods: As part of a study exploring HIV infection and measles susceptibility, we conveniently sampled consenting HIV-uninfected patients presenting at the HIV voluntary counselling and testing centre, and HIV-infected patients presenting for regular care, in Chiradzulu district hospital, Malawi, between January and September 2012.

Results: A total of 2106 participants were recruited between January and September 2012, three quarters of whom were HIV positive. Vaccination cards were available for just 7 participants (0.36%). 91.9% of participants were measles seropositive.

Older age (OR = 1.11 per year increase in age; 95%CI: 1.09–1.14) and being female (OR = 1.90; 95%CI: 1.26–2.87) were both associated with significantly increased odds for seroprotection. Prior vaccination history was associated with lower odds (Odds Ratio (OR) = 0.44; 95% confidence interval (CI): 0.22–0.85) for confirmed seropositivity. Previous measles infection was not significantly associated with seroprotection (OR = 1.31; 95%CI: 0.49–3.51).

Protection by history and serological status were concordant for 64.3% of participants <35 years old. However, analysis by age group reveals important differences in concordance between the ages, with a greater degree of discordance among younger ages.

Vaccination and/or infection history as a predictor of seropositivity was 75.8% sensitive, but just 10.3% specific.

Conclusion: Reported vaccination and previous infection were poor predictors of seropositivity, suggesting these may be unreliable indicators of seroprotection status. Such serosurveys may be indicated in similar settings in which overestimation of the proportion of seroprotected individuals could have important ramifications if used to guide vaccination strategies.

1. Introduction

Measles vaccination was estimated to prevent 15.6 million deaths between 2000 and 2013, although approximately 145,000 deaths still occur each year, mostly in children under 5 years of age [1]; more than 95% of these deaths occur in resource-poor settings in Africa and Asia [2]. In recent years, enormous progress towards measles elimination has been made in some of the most affected countries, leading to a huge reduction in measles-related morbidity and mortality [2]. However a resurgence of measles in some sub-Saharan African countries has been documented [3].

Malawi introduced one dose of measles containing vaccine (MCV) for infants at (or soon after) 9 months of age into the routine immunization programme in 1979 [4]. The routine programme was supplemented with a non-selective catch-up campaign

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targeting all children 9 months to 14 years of age in 1998, regardless of prior vaccination history. Follow-up campaigns targeting children 9–59 months were conducted in 2002, 2005 and 2008. In 2010, a Demographic and Health Survey estimated that 93% of children 12–23 months of age had received MCV [5].

A large and unexpected measles outbreak occurred in Malawi in 2010, during which a total of 134,039 cases and 304 deaths were reported [4]. 42% of the reported cases were under 5 years of age and 30% of cases were reported in children aged 5 to 14 years and 28% in adults (aged 15 years and older). A vaccination coverage survey after the reactive vaccination campaign targeting children 6 months to 14 years of age in Chiradzulu district showed 98.0% coverage (95% CI: 97.4–98.5%) [4] by card confirmation and oral reporting.

As part of a larger study on measles serological protection in HIV infected and uninfected individuals in Chiradzulu district [6], we collected data on measles vaccination and disease history. Our aim was to explore self-reported measles protective status, and comparing this with measles serological result, in order to inform local assessments of vaccine coverage and provide important guidance on how these assessments could be improved to ensure control strategies are successful.

2. Methods

A facility-based study was conducted to assess differences in levels of measles antibodies between HIV-infected and uninfected individuals in Chiradzulu district, Malawi [6]. A secondary objective of this study was to correlate self-reported measles protective status with measles serological result. The sample size was calculated based on the primary objective of the study.

Eligible participants were those aged 18 months and older who were able to understand the patient information sheet and who gave informed consent to participate. All individuals meeting the inclusion criteria attending voluntary counselling and testing services or presenting for follow-up care at Chiradzulu District Hospital were invited to participate. A convenient sample of all consecutive individuals consenting to participate who presented during the study period was enrolled until the desired sample size was reached.

2.1. Sample collection and processing

Venous blood samples were collected from each participant by a qualified phlebotomist. Serum samples were extracted and stored at −20 °C until tested for measles IgG antibodies at the National Institute for Communicable Diseases (NICD) in Johannesburg, South Africa.

Quantitative measurement of measles IgG was performed using an enzyme linked immunosorbent assay (ELISA; Enzygnost Anti-Measles IgG, Dade Behring, Germany). The assay was calibrated against the international reference preparation. Kit dependent parameters were used to express results as an antibody concentration (mIU/ml) derived from the optical density (OD) according to the manufacturer's instructions. Samples were categorized as seropositive (IgG titre > 330 mIU/ml), seronegative (IgG < 120 mIU/ml) and equivocal (IgG titre 120–330 mIU/ml). Equivocal samples were retested and classified accordingly. Those still equivocal after retest were considered negative as equivocal results are below the 330 mIU/ml protection threshold.

2.2. Interview

Information on demographic characteristics, previous measles vaccination and previous measles infection were collected from each participant using a structured questionnaire administered by trained interviewers in Chichewa, the local language. When available, vaccination cards were used to complement recall of previous vaccination.

Following the verbal histories, participants were categorized as "protected" (reported previous vaccination and/or infection), "susceptible" (reported no previous vaccination and no previous infection), and 'unknown' (missing information for previous vaccination and previous disease).

"Protected" participants were categorized as protected by vaccination if protection was established from vaccination only; or as protected by disease if they declared a past measles infection independently of reported vaccination.

2.3. Data collection

Anonymized data were double-entered into an EpiData database mask (EpiData Association 2010). Data were cleaned and exported to Stata 13.0 (College Station, TX, USA) for analysis.

2.4. Statistical analysis

MCV seroprevalence and descriptive analysis of measles antibodies included all study participants with known titres (analysis A). In a second analysis (analysis B), logistic regression models were used to calculate the odds of seroprotection according to measles vaccination and infection history, age, sex and HIV status in univariable and multivariable models. In these analyses only participants aged <35 years of age for whom a measles history questionnaire was completed were included. Participants aged ≥35 years old were excluded from this analysis because they had not been targeted by MCV vaccination activities.

Serological results were log-transformed to obtain a more normal distribution. Differences on geometric mean titres (GMTs) amongst groups were analysed using linear regression.

Additionally, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of reported vaccination status/previous infection were calculated using measles seropositivity as the 'gold-standard' reference measure.

2.5. Ethical considerations

This study adhered to the principles that govern biomedical research involving human subjects. The study protocol was approved by the National Health Sciences Research Committee of Malawi. The Declaration of Helsinki was followed, aiming to provide assurance that the rights, integrity, and confidentiality of trial subjects were protected.

Informed consent was sought from the study participants or from their parent/guardian if they were under the age of 18 years. Participation in the study was voluntary, entailing no obvious benefits or risks.

3. Results

In total 2106 participants were recruited from the District Hospital in Chiradzulu district, Malawi, between January and September 2012. A measles serological result and complete questionnaire are available for 1929 individuals. The mean age of enrolled participants was 36.9 years (median = 37) with a sex ratio of male/female of 0.6. There were only 9 participants in the 18 months to 4 years age group. On interview, only 7 participants (0.36%) showed a vaccination card to the interviewer. Three quarters of the participants were HIV positive (Table 1).

Overall, 61.8% of participants (1192) reported having received a measles vaccine. Reported measles vaccination was high, even amongst participants aged ≥35 years old with no opportunities

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