Measles Vaccination Immunogenicity and Association with Caste in Chandigarh, India

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Abstract. Measles affects those of lower socioeconomic status disproportionately. This study evaluated the impact of measles vaccination on antibody titers 3 months after vaccination across different socioeconomic groups, with a focus on caste. In total, 169 infants in Chandigarh, India, had serum samples collected immediately prior to vaccination at 9 months of age and 3 months later. Overall, 126 infants (76%) were seropositive (antibody titers > 12 mIU/mL), 26 (16%) were borderline (8–12 mIU/mL), and 14 (8%) were seronegative (< 8 mIU/mL). Seropositivity (versus borderline/seronegative infants) was 0.78 times as high among individuals from the historically marginalized scheduled castes/scheduled tribes compared with the others caste grouping (95% CI, 0.62–0.98). Antibody response was not tied to anthropometric measures but was attenuated among scheduled castes/scheduled tribes with higher incomes. This study provides observational evidence that social structures can be associated with individual immune responses.

INTRODUCTION

Children from families of low socioeconomic status (SES) are more likely to be exposed to pathogens and to become ill once exposed.1 In India, the historically most marginalized and “lowest” caste groups are constitutionally referred to as Scheduled Castes and Scheduled Tribes (SC/ST). Along with the SC/ST community, members of Other Backward Castes (OBC) receive some reservations in civil service positions and affirmative action in education throughout India, including in the union territory Chandigarh. More privileged groups are described as Other or Forward Castes. Caste has been linked to literacy, educational attainment, salary, and community infrastructure.2

India provides the measles vaccine free of charge to all children. Although vaccine uptake is lower among the SC/ST communities,3,4 it is unclear whether this is the sole reason for a relatively greater burden of vaccine-preventable disease in low SES populations. The aim of this study was to evaluate whether caste is associated with immune response to measles vaccination.

METHODS

This analysis comes from a larger measles seroprevalence study5 in Chandigarh, India. The purpose of the larger study was to identify the most efficient measles vaccination strategies to prevent future outbreaks. In Chandigarh, we sampled individuals who lived in the catchment areas of Anganwadis (government-run child-care centers). Specifically, we selected 30 communities using a stratified random sampling method with rural, urban, and resettlement colonies selected in proportion to their population. Within each community, we identified pregnant women. Study staff contacted them up to four times before delivery. Phone calls or visits were made at different times on different days of the week. Infants and their mothers were enrolled at birth.

The enrollment inclusion criterion included residence in Chandigarh. The enrollment exclusion criteria included a child’s mother having a health condition that precluded her from participating in normal daily activities; an infant having hemophilia or other blood dyscrasias, characterized by the potential for excessive bleeding; an infant having acute febrile illness.

Infants were monitored at 3, 6, 9, and 12 months of age. For this analysis, we excluded infants without data at both the 9- and 12-month visit, and those who were either seropositive at 9 months (prior to vaccination) or those who had a measles diagnosis. Details about the study population and loss to follow-up are available elsewhere.5

Mothers of infants provided information on caste, income, education, and age. At each visit, study staff used tape measures and scales to take anthropometric measurements, including infant weight, head circumference, and length. Determination of abnormally low head circumference, length-for-age, and weight-for-age were based on WHO child growth standards at 9 months.6

Just prior to vaccination (at 9 months of age), and 3 months later (at 12 months of age), study staff obtained a 1-mL blood sample via venipuncture from the enrolled infants. The serum sample was separated via centrifugation. The serum was then aliquoted, and one aliquot was stored at −20 °C and another at −80 °C (for long-term storage). Antibodies to measles IgG ELISA kits from Immunolab GmbH (Kassel, Germany). Antibody titers > 12 mIU/mL were considered seropositive; 8 to 12 mIU/mL, borderline, and < 8 mIU/mL, seronegative.

We graphically depict the mean and median values of antibody titers across caste with boxplots. To test whether there was a significant difference across caste in an unadjusted analysis, we created a log-transformed outcome of antibody titers at 9 and 12 months. Differences in antibody titer by caste were evaluated through an unadjusted linear regression using survey procedures including clustering by Anganwadis.

A dichotomous outcome (positive versus borderline/negative serostatus) was assessed in two multivariable Poisson regression models, with robust SE estimates and generalized estimating equations with an independent correlation.
matrix across clusters (i.e., the Anganwadis). The model output incidence ratios (IRs). The first model only included caste, along with income, education, and age as covariates. The second model also included an interaction term between caste and income.

All analyses used SAS version 9.4 (SAS Institute, Cary, NC). Significance was assessed at $\alpha = 0.05$.

This study was approved by the University of Michigan Health Sciences and Behavioral Sciences Institutional Review Board (HUM00104905); the Institutional Ethics Committee of the Postgraduate Institute of Medical Education and Research, Chandigarh; and the Health Ministry Screening Committee of the Government of India. Enrolled mothers provided written informed consent to participate. Either parent provided written informed consent for enrollment of their infants.

RESULTS

Of 194 infants who presented for measles vaccination at 9 months, 180 also returned at 12 months. Of these, 14 were excluded because they declined blood sampling ($n = 4$), had a clinical diagnosis of measles before the visit ($n = 7$), or were seropositive at 9 months prior to measles vaccine receipt ($n = 3$). In total, data for 166 infants were analyzed.

Figure 1 shows the distribution of antibody titers across different caste groupings. The median and interquartile range (IQR) antibody titer at 9 months was 1.3 mIU/mL (IQR, 1.0–1.8) for the Other group, 1.3 mIU/mL (IQR, 1.1–1.6) for the OBC group, and 1.4 mIU/mL (IQR, 1.1–1.7) for the SC/ST group. At 12 months, these titers increased to 26.4 (IQR, 16.7–48.6), 29.6 (IQR, 19.5–53.4), and 21.6 mIU/mL (IQR, 9.4–34.4), respectively. In an unadjusted linear regression model with caste as the predictor and the log-transformed outcome of antibody titers, there was no difference between the SC/ST and Other groups at 9 months ($P = 0.2316$), but there was at 12 months ($P = 0.0322$).

At the 12-month visit after vaccination, 126 infants (76%) were seropositive, 26 (16%) were borderline, and 14 (8%) were seronegative (Table 1). Seropositivity was similar by income, ranging from 73% for those with a household income of 10,000 to 25,000 rupees each month to 81% for those with a household income of ≥ 25,000 rupees. In terms of mother’s age, 81% of infants born to mothers 18 to 24 years old were seropositive compared with 73% born to mothers 30 years and older.

Only 64% of individuals in the SC/ST group were seropositive at 12 months, compared with 78% of individuals in the OBC group and 80% in the Other group. In a multivariable model, the odds of seropositivity were 0.78 (95% CI, 0.62–0.98) among the SC/ST group compared with the Other group, with no significant difference was noted between the Other and OBC groups. In the model with a caste × income interaction, there was a significant term for SC/ST and the highest income group (IR, 1.81; 95% CI, 1.26–2.59), indicating attenuation of the relationship between caste and seropositivity in higher income groups.

Overall, eight infants (5%) in the study had abnormally small head circumference, 10 (6%) had a low length-for-age, and five (3%) had a low weight-for-age. No anthropomorphic measure varied substantially by caste status (results not shown), nor were any anthropomorphic measures related significantly to measles seropositivity. For children with abnormally small head circumference versus not, the IR was 1.14 (95% CI, 0.74–1.22); for children with a low length-for-age versus not, the IR was 1.12 (95% CI, 0.67–1.05); and for children with a low weight-for-age versus not, the IR was 1.11 (95% CI, 0.91–1.36). We conclude there was no evidence of mediation between caste and seropositivity by the observed anthropometric measures.

DISCUSSION

This study from Chandigarh, India, explored the potential role of caste in the immunological response to measles vaccination and has potential implications in the context of measles control efforts in India, especially in infants born into castes occupying lower SES strata (i.e., SC/ST).

One possible mechanism for the observed differential efficiency of measles vaccination by caste would be differences in allostatic load. Deeply embedded historical constructs that reinforce social hierarchies can lead to high exposures to stress and hyperactivation of the hypothalamic–pituitary–adrenal axis, which in turn can affect inflammatory parameters. Although the allostatic load associated with caste in India has not been well studied, there is likely a greater cumulative burden of stress among individuals of historically disadvantaged castes. How this would affect immunogenicity in infants is unclear.

Other potential mechanisms include micronutrient deficiencies. Arlappa et al. found vitamin A deficiency to be 88% among children in the ST group compared with 52% in other caste groupings. Vitamin A supplementation at the time of measles vaccination has been linked to a stronger
Caste could affect measles immune response negatively among infants belonging to historically disadvantaged castes. That caste affects seropositivity significantly highlights that we need to be cognizant of SES when administering preventive programs. Future studies can study the physiological mechanism underlying lower rates of seropositivity among the SC/ST group.  

CONCLUSION

Caste could affect measles immune response negatively among infants belonging to historically disadvantaged castes. That caste affects seropositivity significantly highlights that we need to be cognizant of SES when administering preventive programs. Future studies can study the physiological mechanism underlying lower rates of seropositivity among the SC/ST group.

REFERENCES