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Antibody persistence after Pandemic H1N1 2009 influenza vaccination among healthcare workers in Pune, India

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The healthcare workers having seroprotection at 3 weeks (n = 127) following Pandemic H1N1 2009 influenza vaccination were followed up for antibody persistence. Seroprotection at 12 mo (60.2%) was significantly lower as compared with 3 weeks (74.7%), 3 mo (77.8%) and 6 mo (75.4%). The vaccine provided seroprotection up to one year.

India experienced severe Pandemic H1N1 2009 influenza.[1] It caused widespread community transmission, mostly among school-aged children, with the most infections being asymptomatic or mild.[2] The Government of India approved a split-virion inactivated unadjuvanted monovalent Pandemic H1N1 2009 influenza vaccine (Panenza) for intramuscular administration of 0.5 ml single dose containing 15 μg of haemagglutinin (HA) units for vaccination of healthcare workers in India in April 2010. The vaccine was reported to be highly immunogenic and safe among 170 vaccinees during the field use in India.[3] We studied only 127 vaccinees detected with seroprotection at 3 weeks for antibody persistence at 3, 6 and 12 mo. Participants were allowed to drop out and then be included again at a later time point as indicated in the flowchart (**Fig. 1**).

Healthcare workers included doctors, nurses, counselors, hospital staff and attendants. The ethical approval was obtained from the Institutional Human Ethical Committee. We obtained the written informed consent for participation. Demographic details and co-morbid conditions were recorded at baseline and past or current illness at follow up visits. The vaccinees deposited 5 ml blood samples at 3 weeks and at 3, 6 and 12 mo.

Sera were subjected to haemagglutination inhibition (HI) assay using 0.5% turkey red blood cells and as per WHO recommended protocols.[4] Pandemic H1N1 2009 influenza virus A/Jalna/NIV9436/2009(H1N1) (GenBank accession numbers-HM204573; HM241701–07) isolated at the National Institute of Virology was used in the study. It was similar to the A/California/7/2009 vaccine strain of pandemic H1N1 2009 influenza virus. The HI antibody titer of ≥ 1:40 was defined as seroprotection.[5] The primary outcome was the percentage of healthcare workers having seroprotection at 3, 6 and 12 mo.

Seroprotection was calculated by considering only the vaccinees that could be followed up at the specified time points. A sample size of 138 subjects was estimated assuming 90% immunogenicity with 5% precision and 95% desired confidence level. Geometric mean titers (GMTs) were also calculated. Seroprotection percentages and GMTs were reported with the 95% confidence intervals (95% CIs). We used Chi-square tests for comparing seroprotection percentages and t-tests for comparing GMTs of antibody levels at 3, 6 and 12 mo follow up with reference to 3 weeks following vaccination.

Among a total of 127 vaccinees considered for the follow up study (**Table 1**), majority were males (59.8%) and young adults (64.6% aged 18–39 y). We used the age of 40 y as the cut-off for younger vs. older adults as reported in influenza vaccine trials.[5] Underlying co-morbid conditions were reported by 34 vaccinees including obesity (body mass index ≥ 30 Kg/m^2) among 18 vaccinees. Baseline seroprotection before vaccination was minimal. None of the vaccinee received the seasonal influenza vaccination in the past. Pandemic H1N1 2009 influenza illness confirmed by RT-PCR was reported by 5 vaccinees before vaccination. Only 2 of these 5 vaccinees had baseline seroprotection.

The follow up could be achieved in 99, 69 and 98 vaccinees at 3, 6 and 12 mo respectively (**Fig. 1**). These included 65 vaccinees sampled at all three time points. The percentage seroprotection and GMTs with 95% CIs at 3 weeks and at 3, 6 and 12 mo are presented in **Table 2**. The seroprotection at 3 mo and 6 mo was not significantly different than at 3 weeks. Whereas, only 60.2% (95% CI 50.5–69.8) vaccinees had seroprotection at 12 mo as compared with 74.7% - 95% CI (68.2–81.2) vaccinees at 3 weeks ($p < 0.05$). However, GMTs of HI antibody titers at 3 mo, 6 mo and 12 mo were not significantly different than at 3 weeks.

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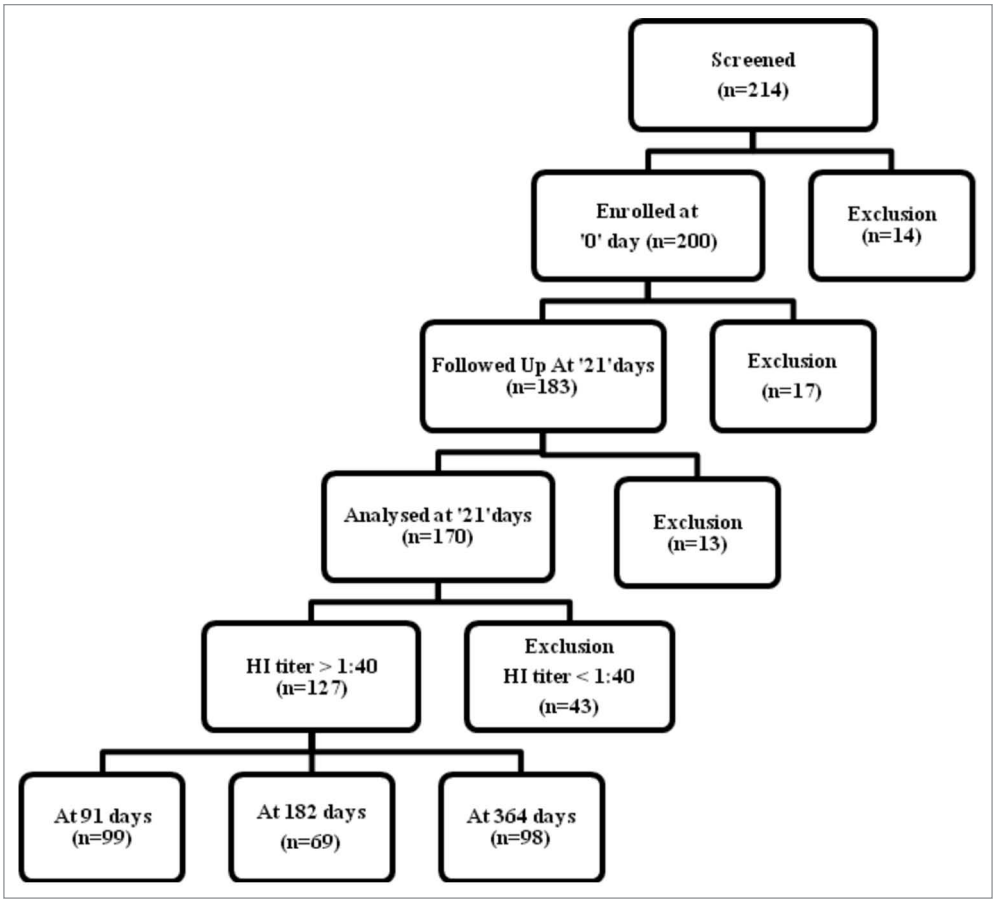

Figure 1. Flowchart of vaccinees followed up at different time points.

Table 1. Demographic data and co-morbidity status of 127 followed up vaccinees

Characteristics	No. (%) of vaccinees
Gender	
Males	76 (59.8)
Females	51 (40.2)
Age (years)	
18–39	82 (64.6)
40–59	45 (35.6)
Co-morbidity	34 (26.8)
Obesity	18 (14.2)
Baseline seroprotection	11 (8.7)
PCR-confirmed Pandemic H1N1 2009 illness	5 (3.9)

PCR, polymerase chain reaction.

In a subset of 65 vaccinees sampled at all three follow up time points, seroprotection was 61.5% (95% CI 49.3–72.7) at 12 mo as against 75.4% (95% CI 63.9–84.7) at 3 mo and 76.9% (95% CI 65.6–86.0) at 6 mo. We did not find significant difference in seroprotection between males and females; and between young adults (18–39 y) and older adults (40–59 y) at all the time points. Influenza like illness was not reported by any vaccinee during the follow up.

The present study provides information about the antibody persistence following a single dose of Pandemic H1N1 2009 influenza vaccine among healthcare workers during the year 2010 in Pune, India. There was a slightly higher seroprotection at 3 mo (77.8%) as compared with 3 weeks (74.7%). This could be due to boosting of immunity by natural subclinical or asymptomatic infections during the ongoing influenza season. The seroprotection at 6 mo was 75.4%. Similar findings were also noted in a subset of 65 vaccinees sampled at all three follow up time points in our study. In a clinical trial using a similar vaccine, 76.8% adults had seroprotection at 6 mo.[6] Similarly, 87% seroprotection was reported at 6 mo in a clinical trial involving 53 adults.[7] However, only 35.1% vaccinees had seroprotection at 9 mo in a field evaluation in China.[8] Similarly, only 34% of 86 vaccinees had seroprotection at 6 mo in China.[9] The antibody persistence in 75.4% vaccinees at 6 mo in our study is acceptable during field use.

At 12 mo, 60.2% vaccinees had seroprotection in our study. The lung transplant patients maintained seroprotection for approximately 11 mo between seasons.[10] Seroprotection rate in all age groups declined markedly over the 12-mo period in a study of seasonal trivalent vaccine in Korea.[11] Such evidence is needed in guiding the vaccination policies for optimal timing of vaccination campaigns in relation to influenza seasonality. Influenza

Table 2. Seroprotection levels and geometric mean titers at different follow up time points

Time points	No. with seroprotection/ No. investigated*	Seroprotection % (95% confidence interval)	P value	Geometric mean titers (95% confidence interval)	P value
3 weeks	127/170	74.7 (68.2–81.2)	Reference	84.7 (67.3–106.5)	Reference
3 mo	77/99	77.8 (69.6–86.0)	> 0.05	76.2 (60.3–96.3)	> 0.05
6 mo	52/69	75.4 (65.2–85.5)	> 0.05	64.1 (48.0–85.7)	> 0.05
12 mo	59/98	60.2 (50.5–69.8)	< 0.05	42.9 (33.9–54.3)	> 0.05

*Indicates the vaccinees available for follow up at different time points after vaccination.

like illness was not reported by the vaccinees during the follow up in our study. However, under-reporting of influenza like illnesses could not be ruled out in the absence of active surveillance. In addition, this study has a weakness in terms of a very small data set available at follow up. We did not find any gender and age-group wise difference in seroprotection as reported in earlier studies.[8,9] We could not compare obese and non-obese groups due to inadequate sample size.

In conclusion, a single dose of the monovalent Pandemic H1N1 2009 influenza vaccine provided seroprotection up to one year among adults indicating the expected performance of the vaccine in Indian population during field use.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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Contributors

B.V.T. planned and executed the study, managed and analyzed data, wrote the manuscript and approved the final submission as corresponding author. S.D.P. managed specimen-testing protocols, analyzed and interpreted data, revised and approved the manuscript. Y.K.G. contributed in planning, execution and data management and reviewed and approved the final version of the manuscript. S.S.P. managed the assay protocols and performed assays. A.C.M. provided administrative support, provided inputs for study design, reviewed and approved the manuscript for submission.

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