Despite Protective Antibody Levels Children remain more Vulnerable to Influenza

Researchers investigated the interplay between pre-season immunity, exposure intensity, viral shedding kinetics, and age in shaping the transmission dynamics of household influenza.

The study's analysis drew on the Prospective Household cohort study of Influenza, Respiratory Syncytial virus, and other respiratory pathogens community burden and Transmission dynamics in South Africa (PHIRST) cohort and comprised data from 1,518 participants across 327 households in rural and urban communities.

The study's findings revealed that pre-season serum hemagglutination inhibition (HAI) titers of at least 1:40 were associated with a reduced risk of infection for three of the four viruses studied. Furthermore, children exhibited age-dependent susceptibility and prolonged viral RNA shedding even after the models accounted for pre-season HAI antibody levels.

Study

The present study aimed to address these empirical uncertainties and inform future influenza prevention research by examining how measured immunity, age, viral shedding, and exposure were associated with the pathogen's real-world transmission dynamics.

The study dataset was obtained from PHIRST and included 1,518 participants across 327 households. PHIRST combined pre-season serum collection with twice-weekly virological testing of participants regardless of symptoms across three consecutive influenza seasons, 2016–2018.

Viral shedding trajectories were subsequently modeled for 623 distinct infection episodes covering two influenza A subtypes and two influenza B lineages: A(H1N1)pdm09 (n = 133), A(H3N2) (n = 195), B/Victoria (n = 220), and B/Yamagata (n = 75).

Multiplex real-time reverse transcription polymerase chain reaction (rRT-PCR) cycle threshold (Ct) values were used in Bayesian hierarchical piecewise-linear models, thereby enabling estimation of the rise-to-peak viral shedding and the subsequent clearance phase for each infection episode.

These shedding parameters were subsequently integrated into daily multivariable transmission survival models to simultaneously quantify: 1. Household force of infection (FOI; the sum of

infected household members' estimated daily shedding intensities), 2. Community FOI (daily, site-specific cohort infection prevalence), 3. Pre-season HAI titers (≥1:40 versus <1:40), and 4. Individual demographic factors (age, sex, household size, and HIV status).

Results

The study's multivariable transmission survival models showed that exposure intensity was strongly associated with infection acquisition. Specifically, each 10-unit increase in the modeled household shedding-intensity measure was associated with a 65% to 95% higher infection hazard across subtypes and lineages, for example, A(H1N1)pdm09 hazard ratio (HR) 1.96, 95% confidence interval (CI): 1.58–2.44; B/Victoria HR 1.77, 95% CI: 1.42–2.20.

Similarly, a one-percentage-point increase in site-specific cohort influenza prevalence, used as a proxy for community exposure, was associated with a 70% to 100% increase in infection risk across all four subtypes and lineages. In addition, participants with a pre-season HAI titer ≥1:40 had a significantly lower infection risk for three out of the four investigated circulating viruses.

This elevated HAI titer was associated with a 70% reduction in acquisition risk for A(H1N1)pdm09 (HR 0.30), 35% for A(H3N2) (HR 0.65), and 52% for B/Victoria (HR 0.48). However, the categorical threshold of 1:40 was not significantly associated with a lower risk for B/Yamagata, although higher titers were associated with lower risk when analyzed as a continuous variable.

Age remained strongly associated with infection risk even after adjustment for exposure levels and baseline titers. Notably, children younger than 5 years had an estimated 170% to 460% higher risk of infection with A(H1N1)pdm09, B/Victoria, and B/Yamagata compared with adults older than 40 years.

Children younger than 5 years were also estimated to shed viral RNA for 3 to 5 days longer than older adults for A(H1N1)pdm09, A(H3N2), and B/Victoria after adjustment for pre-season HAI titer status.

Conclusion

The present study showed that pre-season serum HAI titers were associated with reduced influenza acquisition for three of the four viruses studied, while age remained associated with infection risk after adjustment for measured household and community exposures and HAI titers, and with shedding duration after adjustment for HAI titers and other individual factors.

The study's authors noted that the dataset was limited by the absence of detailed intra-household contact network tracking. The study also had 2- to 3-day sampling gaps and used Ct values as indirect proxies for viral load, which may have led to very short infections being missed and introduced uncertainty into viral-load estimates.

Additional limitations included assuming that HAI titers remained constant throughout each season, excluding coinfections, using infections detected within the cohort as a proxy for community exposure, and having fewer B/Yamagata infections. The statistical analyses were not adjusted for multiple comparisons. The absence of current-season vaccination among participants and the use of pre-COVID-19 data may also limit the applicability of the findings to other populations and periods.

The authors therefore suggested that further research should examine age-appropriate correlates of protection and immune mechanisms beyond serum HAI antibodies, including antibodies targeting neuraminidase and the HA stalk, as well as influenza-specific B- and T-cell memory.

Source:

https://www.news-medical.net/news/20260803/Children-remain-more-vulnerable-to-influenza-despite-protective-antibody-levels.aspx