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Age-related seroprevalence trajectories of seasonal coronaviruses in children including neonates in Guangzhou, China

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Objectives: Four seasonal coronaviruses, including human coronavirus (HCoV)-229E and HCoV-OC43, HCoV-NL63, and HCoV-HKU1 cause approximately 15-30% of common colds in adults. However, the full landscape of the immune trajectory to these viruses that covers the whole childhood period is still not well understood.

Methods: We evaluated the serological responses against the four seasonal coronaviruses in 1886 children aged under 18 years by using enzyme-linked immunosorbent assay. The optical density values against each HCoV were determined from each sample. Generalized additive models were constructed to determine the relationship between age and seroprevalence throughout the whole childhood period. The specific antibody levels against each seasonal coronaviruses were also tested from the plasma samples of 485 pairs of postpartum women and their newborn babies.

Results: The immunoglobulin (Ig) G levels of the four seasonal coronaviruses in the mother and the newborn babies were highly correlated (229E: r = 0.63; OC43: r = 0.65; NL63: r = 0.69; HKU1: r = 0.63). The seroprevalences in children showed a similar trajectory in that the levels of IgG in the neonates dropped significantly and reached the lowest level after the age of around 1 year (229E: 1.18 years; OC43: 0.97 years; NL63: 1.01 years; HKU1: 1.02 years) and then resurgence in the children who aged older than 1 year. Using the lowest level from the generalized additive models as our cutoff, the seroprevalences for HCoV-229E, HCoV-OC43, HCoV-NL63, and HCoV-HKU1 were 98.11%, 96.23%, 96.23% and 94.34% at the age of 16-18 years.

Conclusion: Mothers share the HCoV-specific IgGs with their newborn babies and the level of maternal IgGs waned around 1 year after birth. The resurgence of the HCoV-specific IgGs was found thereafter with the increase in age suggesting repeated infection occurred in children.

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Introduction

SARS-CoV-2 has become highly transmissible since it was discovered in 2019 and is now persistent in the human population. It is reasonable to expect that most people will be exposed to
the virus for the first time during their childhood. Understanding the development of acquired immunity against the seasonal coronaviruses (human coronavirus [HCoV]-NL63 and HCoV-229E, HCoV-OC43 and HCoV-HKU1) in the young age group will thus give us a clue on the impact of SARS-CoV-2 on humans in the post–COVID-19 era. The HCoVs have been circulating in the human population for many years and are accounted for approximately 15–30% of upper respiratory tract infections [1]. Infection of these viruses mainly causes self-limiting flu-like illnesses, but severe pediatric respiratory infections are not rare [2–4]. Children are not entirely immunologically naive when they are born [5]. Immunoglobulin (Ig) G antibodies in neonates are transferred from their mothers so as to provide a transient immune barrier against the potential infection [6,7]. This transferred immunity plays a protective role before the infants establish their own specific adaptive immunity to the same pathogen. So far, there is a paucity of data to describe the transition period from transferred immunity to acquired immunity for the seasonal coronavirus in children. Moreover, the accumulation of immune response to seasonal coronaviruses in children is also not yet well understood. A longitudinal study showed that adults are repeatedly infected by the seasonal HCoV every 12 months [8]. Although it was found that the induction of antibodies after each infection is short-lasting, frequent reinfections lead to persistent levels of antibodies to the four seasonal coronaviruses in most adults [9]. These pre-existing antibodies against seasonal coronaviruses were recently found to be associated with the neutralizing antibody response against SARS-CoV-2 that may mitigate disease manifestations from SARS-CoV-2 infection [10]. In this study, we determined the serological response against four seasonal coronaviruses in the plasma samples of children and modeled the seroprevalence trajectories of the four viral subtypes during childhood.

Methods

Sample collection

1886 pediatric patients aged under 18 years and without signs of influenza-like illness in non-respiratory diseases wards were recruited from January and March 2020 in our study. All plasma samples were obtained from the ethylendiaminetetraacetic acid anti-coagulated peripheral blood samples in the Guangdong Women and Children Hospital, Guangzhou, China. Peripheral blood samples were centrifuged at 3000 x g for 10 minutes at room temperature for plasma collection. All plasma samples were kept at −80°C until used. Moreover, 485 plasma samples from healthy postpartum women were collected between January and March 2020 in the same hospital, with paired plasma samples collected from their healthy newborn babies. Of note, the blood samples, which were from the pediatric patients recruited from different departments or the paired maternal and infant, were collected for routine examination in the Department of Clinical Laboratory. Neonate was defined as those who were 4 weeks old or younger and the definition of children covers neonates and male/female under 18-year-old. All study procedures were performed after informed consent. The study was approved by the Human Research Ethics Committee at the Guangdong Women and Children Hospital (Approval number: 202101231).

Enzyme-linked immunosorbent assay

The S1 subunits of spike protein (His tag) of HCoV-229E (Seattle/USA/SC1073/2016), HCoV-HKU1 (Hong Kong/isolate NS/5/2006), HCoV-NL63 (Florida/UF-2/2015) and the hemagglutinin-esterase (HE) protein (His Tag) of HCoV-OC43 (Seattle/USA/SC9741/2016) were purchased from Sino Biological (China). A 96-well enzyme-linked immunosorbent assay (ELISA) plate (Nunc MaxiSorp, Thermo Fisher Scientific) was first coated overnight with 100 ng per well of purified recombinant protein in phosphate-buffered saline (PBS) buffer. On the next day, plates were washed three times with PBS containing 0.1% Tween 20. The plates were then blocked with 100 μl of Chondrex block/sample dilution ELISA buffer (Chondrex Inc, Redmon, US) and incubated at room temperature for 1 hour. Each human plasma sample was diluted to 1:100 in Chondrex blocking/sample dilution ELISA buffer and then added into the ELISA plates for a 2-hour incubation at 37°C. After three times of washing with PBS containing 0.1% Tween 20, each well in the plate was further incubated with the anti-human IgG secondary antibody (1:5000, Thermo Fisher Scientific) for 1 hour at 37°C. The ELISA plates were then washed five times with PBS containing 0.1% Tween 20. Subsequently, 100 μl of Goat anti-Human secondary IgG (horseradish peroxidase) substrate (Ncm TMB One; New Cell and Molecular Biotech Co. Ltd, Suzhou, China) was added into each well. After 10 minutes of incubation, the reaction was stopped by adding 50 μl of 2 M H2SO4 solution and analyzed on a Sunrise (Tecan, Männedorf, Switzerland) absorbance microplate reader at 450 nm wavelength.

Modeling

Generalized additive model (GAM) was fitted to investigate the association between age and the ELISA results. The restricted cubic splines (smooth curve) with five knots were used to construct the model [11]. Of note, percentile places knots at five spaced percentiles of the explanatory variable, which are the 5th, 25th, 50th, 75th, and 95th percentile. R version 4.0.4 was used for the analysis.

Statistical analysis

Significance between the two groups was determined by the Mann-Whitney test, with a P-value >0.05 being considered statistically significant. Correlation between plasma samples were evaluated using Pearson’s correlation coefficients.

Results

We tested the seroprevalence to the four seasonal coronaviruses by the ELISA using the plasma samples collected from 1886 children (Female: 43.9%) with age ranging from 0 (Neonates) to 18 years old in Guangzhou, China between January and March 2020. Among our cohort, 259 participants were >6 months old, 161 were between >6 months to <12 months, 278 were >1 to <3 years old, 603 were >3 to <7 years old, 466 were >7 to <12 years old, 66 were >12 to <16 years old, 53 were >16 to 18 years old (Table 1). The S1 domains of the spike protein were used for measuring the serological response to 229E, NL63, and HKU1. Although the homology of the S1 protein between HKU1 and OC43 is low, they both bind to receptors that carry 9-O-acetylated sialic acid. HE but not S1 of OC43 was thus used for the ELISA assay to further reduce the cross-reactive signal. HE acts as a receptor-destroying enzyme that facilitates the release of viral progeny from infected cells [12–14]. It is expressed on the surface of the OC43 and is also highly immunogenic. The IgG levels to the four seasonal coronaviruses were determined from each plasma sample (Supplementary Figures S1 and S2). The association between the IgG level and the age in each seasonal coronavirus was constructed by GAM (Figure 1) [11]. The restricted cubic splines (smooth curve) with five knots were used to visualize the association. We found that the seroprevalences of the four seasonal coronaviruses showed a similar trajectory

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Table 1
Prevalence of the seasonal coronaviruses in children.

| Age (years) | Participants | Number | 229E-S1 | NL63-S1 | OC43-HE | HKU1-S1 |
|-------------|--------------|--------|---------|---------|---------|---------|
| Male        | <0.5         | 155    | 124 (80.00) | 98 (63.22) | 108 (69.68) | 107 (69.03) |
|             | >0.5 to < 1  | 99     | 22 (22.22) | 31 (31.31) | 25 (25.25) | 18 (18.18) |
|             | >1 to < 3    | 151    | 47 (31.13) | 57 (37.75) | 62 (41.06) | 48 (31.79) |
|             | >3 to < 7    | 332    | 185 (55.72) | 256 (77.11) | 281 (84.64) | 245 (73.80) |
|             | >7 to < 12   | 266    | 191 (71.80) | 235 (88.35) | 261 (98.12) | 231 (86.84) |
|             | >12 to > 16  | 32     | 31 (96.88) | 28 (87.50) | 31 (96.88) | 28 (87.50) |
|             | >16 to > 18  | 23     | 23 (100.00) | 23 (100.00) | 23 (100.00) | 23 (100.00) |
| Female      | <0.5         | 104    | 92 (88.46) | 53 (50.96) | 74 (71.15) | 86 (82.69) |
|             | >0.5 to < 1  | 62     | 32 (51.61) | 19 (30.65) | 11 (17.74) | 25 (40.32) |
|             | >1 to < 3    | 127    | 42 (33.07) | 43 (33.86) | 52 (40.94) | 55 (43.31) |
|             | >3 to < 7    | 271    | 163 (60.15) | 194 (71.59) | 215 (79.33) | 232 (85.61) |
|             | >7 to < 12   | 200    | 157 (78.50) | 159 (79.50) | 193 (96.50) | 189 (94.50) |
|             | >12 to > 16  | 34     | 32 (94.12) | 28 (82.35) | 31 (91.18) | 34 (100.00) |
|             | >16 to > 18  | 30     | 29 (96.67) | 27 (90.00) | 29 (96.67) | 28 (93.33) |
| Overall     | <0.5         | 259    | 228 (88.03) | 155 (59.85) | 182 (70.27) | 193 (74.52) |
|             | >0.5 to < 1  | 161    | 62 (38.51) | 51 (31.68) | 37 (22.98) | 38 (23.60) |
|             | >1 to < 3    | 278    | 100 (35.97) | 97 (34.89) | 114 (41.01) | 98 (35.25) |
|             | >3 to < 7    | 603    | 364 (60.36) | 448 (74.30) | 505 (83.75) | 472 (78.28) |
|             | >7 to < 12   | 466    | 365 (78.33) | 401 (86.05) | 456 (97.85) | 423 (90.77) |
|             | >12 to > 16  | 66     | 63 (95.45) | 57 (86.36) | 61 (92.42) | 62 (93.94) |
|             | >16 to > 18  | 53     | 52 (98.11) | 51 (96.23) | 51 (96.23) | 50 (94.34) |

Figure 1. Seroprevalence trajectory of the four seasonal coronaviruses in children. The plasma samples were collected from 1886 children who aged from 0 (neonates) to 18 years old. Each sample was tested by enzyme-linked immunosorbent assay against either S1 (HCoV-229E, HCoV-NL63 or HCoV-HKU1) or hemagglutinin-esterase (HCoV-OC43) protein. GAMs was used to model the association between the serological data and the age. The black lines showed the fitted values and gray areas showed the 95% confidence intervals. Each sample was tested in duplicate, and the results were represented by the mean of the two values. The solid line represents the cutoff of the negative control (PBS). The dashed lines represent the cutoff of the lowest point in GAMs and the solid lines represent the background (PBS) of the assay.

GAMs, Generalized additive models; HCoV, human coronavirus; OD, optical density; PBS, phosphate-buffered saline.
from the GAMS. Compared with the entire childhood period, the levels of IgG in the neonates dropped significantly and reached the lowest level of the GAM after the age of 1 year (1.18 years: HCoV-229E: 0.97 years: HCoV-OC43; 1.01 years: HCoV-NL63; 1.02 years: HCoV-HKU1) (P < 0.001). The levels of IgG then increased and accumulated when the children became older. The IgG levels against HCoV-OC43, HCoV-NL63, and HCoV-HKU1 increased to the comparable levels in children at the age of 8, 9, and 6 years respectively. However, it was intriguing to find that the IgG to the HCoV-229E increased slowly compared with other seasonal coronaviruses and it reached the comparable level in children at the age of 16 years. The serological results of each coronavirus were further stratified into two sex groups (male/female) and were further compared (Figure 2). Importantly, we found that the IgG waning of all four seasonal coronaviruses in male children were much faster than that in female. The time required for dropping the IgG of each coronavirus to their lowest level of the GAMS in male children were 1.95 (HCoV-229E: 0.75[M] vs 1.46[F]), 1.84 (HCoV-OC43: 0.63[M] vs 1.16[F]), 1.69 (HCoV-NL63: 0.68[M] vs 1.15[F]), 1.71 (HCoV-HKU1: 0.67[M] vs 1.15[F]) folds faster than that of the female children (P < 0.001).

The relatively high levels of IgG antibody against four seasonal coronaviruses in the children under 1-year-old suggested a vertical transfer of the maternal immune response. It has been recently shown that the passive immunity against SARS-CoV-2 of children was contributed by their mothers [7]. We collected plasma samples from 485 pairs of postpartum women and their newborn babies for testing the levels of their IgG to the four seasonal coronaviruses using similar serological assays. We found that the maternal IgG level was linearly associated with their neonatal IgG levels in each seasonal coronavirus: HCoV-229E (r = 0.63, 95% CI: 0.57-0.68, P < 0.0001), HCoV-OC43 (r = 0.65, 95% CI: 0.60-0.70, P < 0.0001), HCoV-NL63 (r = 0.69, 95% CI: 0.64-0.74, P < 0.0001), HCoV-HKU1 (r = 0.63, 95% CI: 0.58-0.69, P < 0.0001) (Figure 3).

Interestingly, when we compared the antibody levels between the mothers and their newborn babies using Wilcoxon pairwise test, the newborn babies showed a lower level of 229E antibody compared with their corresponding mothers (Supplementary Figure S3). However, no significant differences were found in HCoV-OC43, HCoV-NL63, or HCoV-HKU1. While comparing with the previous report that maternally derived antibodies against SARS-CoV-2 could persist up to 6 months of age in their infant [15], our results indicated that the passive transferred immunity against the seasonal coronaviruses in children can maintain longer time (1.25 years: HCoV-229E; 1 years: HCoV-OC43; 1.08 years: HCoV-NL63; 1.08 years: HCoV-HKU1) (Figure 1).

Prevalence of the seasonal coronaviruses in children is determined either by detecting the specific nucleic acids from the respiratory specimen or through serology test. However, it is difficult to define and collect true negative reference samples because the seasonal coronaviruses are highly circulating in children. Previous studies adopted an approach in which the cutoffs were de-
and mined

The seasonal

antibody levels against (a) HCoV-229E-S1, (b) HCoV-NL63-S1, (c) HCoV-OC43-HE, and (d) HCoV-HKU1-S1 were determined and the correlations between the paired samples in the four seasonal coronavirus groups were shown. The black lines showed the fitted values and gray areas showed the 95% confidence intervals. The r represented the correlation coefficient.

HCoV, human coronavirus; Ig, immunoglobulin.

terminated from a small subset of reference samples who the children were between 1-2 years old, and the tested samples were defined as positive if the results were above the mean of the references [16,17]. Here, we estimated the prevalence of the seasonal coronaviruses by using the lowest level in the GAMs as our negative reference (Table 1). As shown in the figure, the lowest point in GAMs for four seasonal coronaviruses are optical density 0.13 (HCoV-229E), 0.18 (HCoV-OC43), 0.27 (HCoV-NL63) and 0.17 (HCoV-HKU1) respectively. We assumed that children with IgG level above this point indicate infection of the corresponding seasonal coronaviruses and thus defined it as seropositive. 91.12%, 82.24%, 79.92%, and 84.17% of seropositivity to HCoV-229E, HCoV-OC43, HCoV-NL63 and HCoV-HKU1 respectively were found in those under 6 months of age. In infants with the age between 6 months and 12 months, the seropositive rates dropped to 44.72% (HCoV-229E), 43.48% (HCoV-OC43), 45.96% (HCoV-NL63), and 45.96% (HCoV-HKU1) (P <0.001). The seropositivity of each seasonal coronavirus increased with age and was over 64.51% of prevalence in the children at their preschool age (3-6 years). The seroprevalences for HCoV-229E, HCoV-OC43, HCoV-NL63, and HCoV-HKU1 kept increasing and were 98.11%, 96.23%, 96.23%, and 94.34%, respectively, at the age of 16-18 years.

Figure 3. Correlation between the maternal and neonatal IgG levels of the four seasonal coronaviruses. 485 paired of maternal and neonatal plasma samples were collected and tested by enzyme-linked immunosorbent assay. Antibody levels against (a) HCoV-229E-S1, (b) HCoV-NL63-S1, (c) HCoV-OC43-HE, and (d) HCoV-HKU1-S1 were determined and the correlations between the paired samples in the four seasonal coronavirus groups were shown. The black lines showed the fitted values and gray areas showed the 95% confidence intervals. The r represented the correlation coefficient.

Discussion

Our study described the transition from passive to acquired immunity against seasonal coronaviruses in children. The established approach here provides a view to identify the waning period of immunity against coronavirus after birth, which will be useful to apply on SARS-CoV-2. The best timing to receive COVID-19 vaccine is still being debated. Though US CDC suggested that COVID-19 vaccination is recommended for children aged 6 months or older, it is mainly based on the safety concerns rather than aiming for better protection. Defining the waning period in SARS-CoV-2 using our approach will provide scientific evidence to determine the vaccination window for children in post-COVID era.

Full spike protein was used in the previous study to detect the antibody against the four seasonal coronaviruses in 218 children [18]. It is known that there is 63-98% of sequence similarity at the S2 among the seven HCoVs. Binding from the cross-reactive antibodies at the S2 domain may lead to an overestimation of the seroprevalence. The homology of the S1 amino acid sequences among the four HCoVs is between 40-68% only. We expected that using S1 as the antigens for detection should represent the specific serological response. However, as HKU1 and OC43 both bind to receptors
carrying 9-O-acetylated sialic acid, we used HE to replace the S1 in the assay for measuring the antibody to OC43. The homology of S1 and HE between the two viruses is 68% and 66% respectively. Interestingly, despite using S1 or HE domain to evaluate the specific antibody response for the seasonal coronaviruses, the trajectory of the seroprevalence of the four subtypes were still very similar.

Although seasonal coronaviruses are responsible for only 4%-6% of acute respiratory tract infections in children [19–21], our serology study showed that the infections are indeed very common in this age group. The low detection rate may be because most of the infections were either asymptomatic or very mild. We observed that the levels of IgG to the seasonal coronaviruses increased with the age of children. Among the four subtypes, the level of IgG to HCoV-229E rises comparatively slower than the HCoV-OC43, HCoV-NL63, and HCoV-HKU1. It was reported that HCoV-229E was less frequently detected in humans including children [22]. The recent study also showed that HCoV-229E evolves slower than the HCoV-OC43 over time [23] and the previous human-challenge study showed that individuals infected with HCoV-229E were resistant to reinfection with the same strain but partially susceptible to an antigenicity different strain [24].

Previous studies showed that maternal antibody levels are associated with the protection for neonates against bacteria and viruses [5, 25]. In this study, we first reported that high levels of IgG to the four seasonal coronaviruses in neonates are linearly correlated with their corresponding maternal IgG levels and this suggested that the vertical transmission of coronavirus-specific antibodies from mothers to neonates. It drops within the first year after the babies are born and male children showed a faster decline in the antibody production compared with female children. However, further investigation is needed to determine whether male children may have a higher risk for serious infection if they catch seasonal coronavirus during their early life. On the other hand, the previous results showed that though maternal antibody provide protection for infant, maternal antibody may also suppress the B cell response by epitope masking or inhibition of infant B cell activation by Fcy-receptor mediated signaling [26, 27]. Therefore, future studies should explore the positive and negative effect of the maternal antibodies, which will provide important insights into the antibody response with pre-existing maternal antibodies.

There were some limitations in our study. Firstly, the trajectories were illustrated using cross-sectional samples from population age groups, not in the longitudinal cohort. Secondly, the seroprevalences from our cohort were determined by ELISA only. The neutralizing effect to the seasonal coronaviruses was not evaluated. Thirdly, although the children were recruited from the nonrespiratory ward or routine body check center, we did not collect their clinical background for analysis in this study.

In conclusion, we described that IgG antibody against four seasonal coronaviruses could be transferred from mother to their infant by conducting a large-scale cohort. Importantly, we reported that this transferred immunity waned for one year after birth and children could acquire immunity against four seasonal coronaviruses with the increase in age. Overall, these results provide a comprehensive analysis of the antibody dynamic in the early life of the children.

Declaration of competing interest
The authors have no competing interests to declare.

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Author contributions
H.L., N.C.W. and C.K.P.M. conceived the research idea and designed the study. Y.L., Y.S. CL., YD., B.L. and X.M coordinated and carried out cohort recruitment. H.L., S.Z., K.K., C.K.P.M. and H.M.T., analyzed the data. Y.L., H.L., C.C., W.L., Q.W.T., R.Y.S., Y.L. ZD., J.Z., D.Z. and J.F. performed the experiments. H.L., R.B., H.M.T., and C.K.P.M. wrote the manuscript.

Supplementary materials
Supplementary material associated with this article can be found, in the online version, at doi: 10.1016/j.jidi.2022.11.044.

References
[1] Desforges M, Le Coupance A, Dubeau P, Bourgoiuin A, Lajoie L, Dubé M, et al. Human coronaviruses and other respiratory viruses: underestimated opportunistic pathogens of the central nervous system? Viruses 2019;12:14. doi: 10.3390/v12010034.
[2] Huang AT, Garcia-Carreras B, Hitchings MDT, Yang B, Katzelnick LC, Ratti- gan SM, et al. A systematic review of antibody mediated immunity to coronaviruses: kinetics, correlates of protection, and association with severity. Nat Commun 2020;11:4704. doi: 10.1038/s41467-020-18450-4.
[3] Paloniemi M, Lappalainen S, Vesikari T. Commonly circulating human coronaviruses do not have a significant role in the etiology of gastrointestinal infections in hospitalized children. J Clin Virol 2015;62:114–17. doi: 10.1016/j.jcv.2014.10.017.
[4] Talbot HK, Crowe JE, Jr Edwards KM, Griffin MR, Zhu Y, Weinberg GA, et al. Coronavirus infection and hospitalizations for acute respiratory illness in young children. J Med Virol 2009;81:853–6. doi: 10.1002/jmv.21443.
[5] Langel SN, Blasi M, Pernmar SR. Maternal immune protection against infectious diseases. Cell Host Microbe 2022;30:660–74. doi: 10.1016/j.chom.2022.04.007.
[6] Albrecht M, Arch PC. Vertically transferred immunity in neonates: mothers, mechanisms and mediators. Front Immunol 2020;11:555. doi: 10.3389/fimmu.2020.00555.
[7] Shook LL, Attee CG, Yonker LM, Fasano A, Gray JK, Alter G, et al. Durability of anti-Spike antibodies in infants after maternal COVID-19 vaccination or natural infection. JAMA 2022;327:1087–9. doi: 10.1001/jama.2022.1206.
[8] Edridge AW, Kaczorowska J, Hoste ACR, Bakker M, Klein M, Loens K, et al. Seasonal coronavirus protective immunity is short-lasting. Nat Med 2020;26:1691–3. doi: 10.1038/s41591-020-1083-1.
[9] Gorse GJ, Patel CB, Vitale JN, O’Connor TZ. Prevalence of antibodies to four human coronaviruses is lower in nasal secretions than in serum. Clin Vaccine Immunol 2010;17:1875–80. doi: 10.1128/CVI.00278-10.
[10] Sagar M, Reiffer K, Rossi M, Müller NS, Sinha P, White LF, et al. Recent endemic coronavirus infection is associated with less-severe COVID-19. J Clin Inser 2021;131:e143380. doi: 10.1111/jepi.143380.
[11] Nieboer D, Vergouw G, Roobol MJ, Ankerst DP, Kattan MW, Vickers AJ, et al. Nonlinear modeling was applied thoughtfully for risk prediction: the prostate biopsy collaborative group. J Clin Epidemiol 2015;68:426–34. doi: 10.1016/j.icep.2014.11.022.
[12] Hulswitra RJG, Lang Y, Bakkers MJG, Li W, Li Z, Schouten A, et al. Human coronaviruses OC43 and HKU1 bind to S-0-acetylated sialic acids via a conserved receptor-binding site in spike protein domain A. Proc Natl Acad Sci U S A 2019;116:2681–90. doi: 10.1073/pnas.1809677116.
[13] Tortorici MA, Walls AC, Lang Y, Wang C, Li Z, Koechlin D, et al. Structural basis for human coronavirus attachment to sialic acid receptors. Nat Struct Mol Biol 2019;26:681–9. doi: 10.1038/s41594-019-0233-y.
[14] Vlasak R, Luypjes W, Spaan W, Palese P, Human and bovine coronaviruses recognize sialic acid-containing receptors similar to those of influenza C viruses. Proc Natl Acad Sci U S A 1988;85:4526–8. doi: 10.1073/pnas.85.12.4526.
[15] Song D, Prah M, Gah SL, Narasimhan SR, Rai DS, Huang A, et al. Passive and active immunity in infants born to mothers with SARS-CoV-2 infection during pregnancy: prospective cohort study. BMJ (Open). 2021;11:e053036. doi: 10.1136/bmjopen-2021-053036.
[16] Galipeau Y, Siragam V, Lecoq J, Godin G, Marion E, Greig M, McIntyre M, et al. Relative ratios of human seasonal coronavirus antibodies predict the efficiency of cross-neutralization of SARS-CoV-2 spike binding to ACE2. Elife Medicine 2021;74:103700. doi: 10.1016/j.ebiom.2021.103700.
[17] Lu H, Tsang OT, So RTY, Wang Y, Yuan M, Liu H, et al. Homologous and heterologous serological response to the N-terminal domain of SARS-CoV-2 in humans and mice. Eur J Immunol 2021;51:2296–305. doi:10.1002/eji.202149234.

[18] Zhou W, Wang W, Wang H, Lu R, Tan W. First infection by all four non-severe acute respiratory syndrome human coronaviruses takes place during childhood. BMC Infect Dis 2013;13:433. doi:10.1186/1471-2334-13-433.

[19] Chiu SS, Chan KH, Chu KW, Kwan SW, Guan Y, Poon LL, et al. Human coronavirus NL63 infection and other coronavirus infections in children hospitalized with acute respiratory disease in Hong Kong, China. Clin Infect Dis 2005;40:1721–9. doi:10.1086/430301.

[20] Gaunt ER, Hardie A, Claas EC, Simmonds P, Templeton KE. Epidemiology and clinical presentations of the four human coronaviruses 229E, HKU1, NL63, and OC43 detected over 3 years using a novel multiplex real-time PCR method. J Clin Microbiol 2010;48:2940–7. doi:10.1128/JCM.00636-10.

[21] Ruyssers J, Martin ET, Heugel J, Wright N, Morrow R, Englund JA. Clinical disease in children associated with newly described coronavirus subtypes. Pediatrics 2007;119:e70–6. doi:10.1542/peds.2006-1406.

[22] Monto AS, DeJonge PM, Callear AP, Bazzi LA, Capriola SB, Malosh RE, et al. Coronavirus occurrence and transmission over 8 years in the HIV cohort of households in Michigan. J Infect Dis 2020;222:9–16. doi:10.1093/infdis/jiaa161.

[23] Kistler KE, Bedford T. Evidence for adaptive evolution in the receptor-binding domain of seasonal coronaviruses OC43 and 229E. eLife 2021;10:e64500. doi:10.7554/eLife.64509.

[24] Reed SE. The behaviour of recent isolates of human respiratory coronavirus in vitro and in volunteers: evidence of heterogeneity among 229E-related strains. J Med Virol 1984;13:179–92. doi:10.1002/jmv.1890130208.

[25] Fouda GG, Martinez DR, Swamy GK, Permar SR. The impact of IgG transplacental transfer on early life immunity. Immunohorizons 2018;2:14–25. doi:10.1093/imimm/hmy0057.

[26] Edwards KM. Maternal antibodies and infant immune responses to vaccines. Vaccine 2015;33:6469–72. doi:10.1016/j.vaccine.2015.07.085.

[27] Kim D, Huey D, Oglesbee M, Niewierski S. Insights into the regulatory mechanism controlling the inhibition of vaccine-induced seroconversion by maternal antibodies. Blood 2011;117:6143–51. doi:10.1182/blood-2010-11-320317.