Updates from the World of Pediatric Infectious Diseases

Pediatric Infectious Disease (2022): 10.5005/jp-journals-10081-1347

Source: Lee JJY, Lin E, Widdifield J, Mahood Q, McCrindle BW, Yeung RSM, Feldman BM. The long-term cardiac and noncardiac prognosis of Kawasaki disease: a systematic review. Pediatrics 2022;149(3):e 202,1052567. DOI: 10.1542/peds.2021– 052,567. PMID: 351,18494.

The authors have included 74 studies. A total of 36 studies reported mortality, 55 reported a cardiac outcome, and 12 reported a noncardiac outcome. Survival ranged from 92–99% at 10 years, 85–99% at 20 years, and 88–94% at 30 years. Major adverse cardiovascular events (MACE)— free survival, mostly studied in those with coronary artery aneurysms (CAA), varied from 66–91% at 10 years, 29–74% at 20 years, and 36–96% at 30 years. Seven out of 10 studies reported an increased risk of early atherosclerosis. All six included studies demonstrated an increased risk of allergic diseases.

The notable limitations of this study include that they may have missed associated chronic comorbidities because short-term studies were excluded, the majority of outcomes were evaluated in East-Asian patients, which may limit generalizability, studies frequently excluded patients without CAA and did not compare outcomes to a comparison group.

In plain simple language, the studies demonstrate >90% survival up to 30 years follow-up. MACE is observed in children with CAA but is not well studied in those without CAA.

Source: Nilsson G, Lundström S, Fernell E, Gillberg C. Neurodevelopmental problems in children with febrile seizures followed to young school age: a prospective longitudinal community-based study in Sweden. Acta Paediatr 2022;111(3):586–592. DOI: 10.1111/apa. 16,171. Epub 2021 Nov 23. PMID: 347,17006.

In a community-based cohort of children with previous febrile seizures (FS), researchers from Sweden try to estimate the accumulated prevalence of neurodevelopmental problems from preschool to school age.

The authors found a trend for ADHD symptom scores to be higher in the FS group. They also found non-participants at age 9–10 years had much higher rates of neurodevelopmental problems at 4–5 years, and the total number of such problems at either age 4–5 or 9–10 was 41%.

The authors intend to further follow-up this cohort before definite conclusions can be drawn and shared about whether FS should be considered a marker for more complex neurodevelopmental problems.

Source: Dotan M, Zion E, Bilavsky E, Nahum E, Ben-Zvi H, Zalcman J, Yarden-Bilavsky H, Kadmon G. Adenovirus can be a serious, life-threatening disease, even in previously healthy children. Acta Paediatr 2022;111(3):614–619. DOI: 10.1111/apa. 16,207. Epub 2021 Dec 11. PMID: 348,62832.

Adenovirus infections are exceedingly common in childhood in our settings. However, little is known about the clinical characteristics of children admitted with severe infection to the pediatric intensive care unit (PICU).

During the study period, 69 children with adenovirus infection were admitted to the PICU, representing 5% of all hospitalized children with adenovirus. Thirty-four (49%) were previously healthy children. Five children who had an underlying comorbid condition died. Cidofovir (as an antiadenoviral drug) was used in 21 children, including 11 who were previously healthy. No side effects were attributed to the treatment. During the initial years of the study, viral co-infection rates were 42% in the PICU group and 11% in the control group ($p = 0.002$); however, during the later years of the study, when the viral panel became widespread in their institution, the rates of coinfection were similar in the two groups (32 and 34%, $p = 1.0$).

The bottom line of the study findings suggests that adenovirus may present as a serious, life-threatening disease even in previously healthy children.

Source: Anderson J, Oeum M, Verkolf E, Licciardi PV, Mulholland K, Nguyen C, Chow K, Waller G, Costa AM, Daley A, Crawford NW, Babl FE, Duke T, Do LAH, Wurzel D. Factors associated with severe respiratory syncytial virus disease in hospitalised children: a retrospective analysis. Arch Dis Child 2022;107(4):359–364. DOI: 10.1136/archdischild–2021– 322,435. Epub 2021 Sep 15. PMID: 345,26293.

The authors from Australia have aimed to evaluate factors associated with the severe disease among young children hospitalized with respiratory syncytial virus (RSV) infection.

This is a retrospective cohort study of all children <2 years of age hospitalized for RSV lower respiratory tract infection at a single tertiary pediatric hospital over three RSV seasons (January 2017–December 2019). The children were classified as having "moderate" or "severe" disease based on the level of respiratory intervention.

Among the hospitalized children, 40% were classified as having "severe" and 60% as having "moderate" RSV disease. On analyzing the data, age <2 months, prematurity, and RSV-parainfluenza virus type 3 (PIV3) codetection were independently associated with severe disease. The association between PIV3 and severe RSV disease is a novel finding and warrants further investigation.

Source: Liu W, Rodgers GP. Olfactomedin 4 is a biomarker for the severity of infectious diseases. Open Forum Infect Dis 2022;9(4):ofac061. DOI: 10.1093/ofid/ofac061. PMID: 352,91445; PMCID: PMC 891,8383.

Biomarkers of infectious diseases are essential tools for patient monitoring, diagnostics, and prognostics. The authors review recent advances in our understanding of olfactomedin 4 (OLFM4) in neutrophil biology and of OLFM4 as a new biomarker for certain infectious diseases.

OLFM4 is a neutrophil-specific granule protein that is expressed in a subset of human and mouse neutrophils. OLFM4 expression is upregulated in many viral and bacterial infections, as well as in malaria. OLFM4 appears to play an important role in regulating host innate immunity against bacterial infection. Further, higher expression of OLFM4 is associated with the severity of disease for dengue virus, respiratory syncytial virus, and malaria infections. In addition, higher expression of OLFM4 or a higher percentage of OLFM4 + neutrophils is associated with poorer outcomes in septic patients.

Considering these properties, as discussed in an exhaustive review, OLFM4 appears to be a promising biomarker and potential therapeutic target in certain infectious diseases.

Source: Ahmad M, Verma H, Deshpande J, Kunwar A, Bavdekar A, Mahantashetti NS, Krishnamurthy B, Jain M, Mathew MA, Pawar SD, Sharma DK, Sethi R, Visalakshi J, Mohanty L, Bahl S, Haldar P, Sutter RW. Immunogenicity of fractional dose inactivated poliovirus vaccine in India. J Pediatric Infect Dis Soc 2022;11(2):60–68. DOI: 10.1093/jpids/piab091. PMID: 347,91350; PMCID: PMC 886,5014.

Following the withdrawal of Sabin type 2 from trivalent oral poliovirus vaccine (tOPV) in 2016, the introduction of ≥1 dose of inactivated poliovirus vaccine (IPV) in routine immunization was recommended, either as one full-dose (0.5 mL, intramuscular) or two fractional doses of IPV (fIPV-0.1mL, intradermal). India opted for fIPV. The authors conducted a four-arm, open-label, multicenter, randomized controlled trial for comparative assessment of IPV and fIPV. A total of 799 infants were enrolled in the study. The seroconversion against type 2 poliovirus with two fIPV doses was 85.8% when administered at age 6 and 14 weeks, 77.0% when given at age 10 and 14 weeks, compared to 67.9% following one full-dose IPV at age 14 weeks.

This study demonstrates the superiority of two fIPV doses over one full-dose IPV in India and also concludes that the doses of fIPV given at 6 and 14 weeks were more immunogenic than those given at 10 and 14 weeks in the trial.

Source: Reddy A, Sathenahalli V, Shivanna N, Benakappa N, Bandiya P. Ten vs 14 days of antibiotic therapy in culture-proven neonatal sepsis: a randomized, controlled trial. Indian J Pediatr 2022;89(4):339–342. DOI: 10.1007/s 12,098-021- 03,794-6. Epub 2021 Jun 7. PMID: 340,97231.

The researchers from India compare the efficacy of 10 days vs 14 days of antibiotic therapy in neonates with culture-positive sepsis.

In this study, a total of 70 neonates were randomized to receive either 10 days (n = 35) or 14 d (n = 35) of antibiotic therapy. Gram-negative infections were encountered in the majority of the neonates. Treatment failure (which was defined as readmission to the NICU within 4 weeks of discharge with blood culture growing the same organism with a similar antibiogram or any readmission with signs of sepsis with negative blood culture) occurred in 1 neonate in 10-day group and none in the 14-day group. The duration of hospital stay was significantly less in the 10-day group as compared to the 14-day group (16 days vs 23 days, $p < 0.01$).

The researchers found that 10 days of antibiotics in neonates with culture-positive sepsis, who have achieved clinical and microbiologic remission at day 7, was noninferior to 14 days of therapy. However, a larger adequately powered trial may address this issue with certainty.

The duration of treatment for uncomplicated neonatal sepsis may vary from a minimum duration of 7 days to a maximum of 14 days, depending on the causative organism and the severity of illness. The choice of empirical antibiotic therapy should be based on the prevalence of organisms and their sensitivity pattern in the hospital. Antibiotics can be escalated or de-escalated based on the blood culture report. It will be safer to stop antibiotics if the infant becomes asymptomatic with negative screening tests and blood culture. However, neonates with deeper infections like meningitis and bone infection will require a longer duration (3–4 weeks) of therapy. The treating physician should carefully review each case at regular intervals in order to individualize and fine-tune the duration of therapy. Antibiotic stewardship should also be in place in all hospitals caring for infants and children.

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