2630. Treatment of RSV Lower Respiratory Tract Infection in Two Immunocompromised Children with Polyclonal Immunoglobulin Containing Standardized Levels of Neutralizing Anti-RSV Antibody

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Background: Respiratory syncytial virus (RSV) can cause severe lower respiratory tract infection (LRTI) in immunocompromised children. There is no standard effective treatment, though ribavirin (inhaled or oral), pooled human intravenous immunoglobulin (IVIG), and monoclonal anti-RSV antibody (palivizumab) have been described. RI-002 (ADMA Biologics Inc.) is a pooled human polyclonal IVIG that contains standardized levels of neutralizing anti-RSV antibodies. It was recently FDA-approved for prophylaxis in primary immunodeficiency patients and has been used as compassionate treatment for RSV LRTI in stem cell transplant patients.

Methods: Two children with T-cell lymphoblastic lymphoma, both undergoing delayed intensification chemotherapy, were diagnosed with RSV LRTI. They were both treated with RI-002 under an emergency FDA Investigational New Drug protocol.

Results: Patient 1, a 4-year-old boy, was admitted with fever, neutropenia and nasal congestion, and diagnosed with RSV infection on hospital day (HD) 5. On HD17, he was intubated for respiratory failure. IVIG, palivizumab, and daily oral ribavirin were administered. On HD18, he required high frequency oscillator ventilation, nitric oxide, and paralysis. He was given RI-002 (1.5 g/kg on HD20 and 0.75 g/kg on HD22). He was placed on veno-venous extracorporeal membrane oxygenation (ECMO) on HD23. RSV PCR crossing point (Cp) values trended higher, but remained positive (table). On HD33, RI-002 was re-dosed (0.75 g/kg). Pulmonary compliance and chest CTs improved (figure). On HD52, ECMO support was discontinued. He was discharged on HD88, and currently requires no respiratory support. Patient 2, a 5-year-old boy, was admitted with fever, neutropenia, nasal congestion, cough, and stridor and diagnosed with RSV infection (HD1). He required nasal cannula oxygen. IVIG and daily oral ribavirin were administered. He was given RI-002 (1.5 g/kg on HD3 and 0.75 g/kg on HD5). By HD5, he was afebrile; oxygen was discontinued. He was discharged HD6.

Conclusion: Human polyclonal IVIG containing standardized levels of neutralizing anti-RSV antibodies may be useful in the treatment of RSV LRTI in immunocompromised children. Future studies on the role of RI-002 in treatment of RSV infection in immunocompromised children are warranted.

Figure: Serial Axial Chest CT Images for Patient 1 in Relation to First Dose of RI-002 Treatment

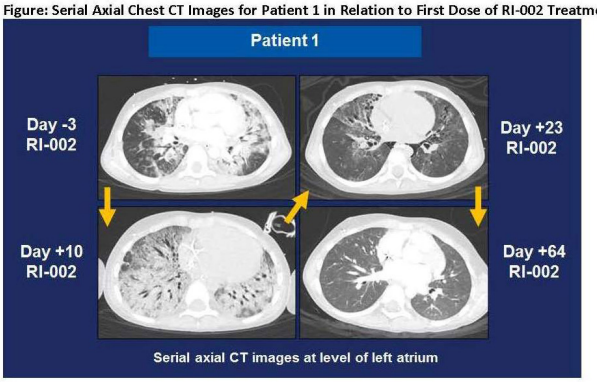

Table: Microbiology data and PCR Crossing Point (Cp) Values from Patient 1

Hospital Day (HD)	RI-002 treatment	Specimen type	RSV PCR Result	RSV PCR Cp*	Viral Culture
HD5		NP swab	Positive	n/a	n/a
HD10		BAL	Positive	21.1	RSV positive
HD17		BAL	Positive	23.2	RSV positive
HD20	1.5g/kg				
HD22	0.75g/kg				
HD24		BAL	Positive	29	No growth
HD29		NP swab	Negative	n/a	n/a
HD29		ETT aspirate	Positive	33.8	No growth
HD33		ETT aspirate	Positive	35.7	No growth
HD34	0.75g/kg				
HD36		ETT aspirate	Negative	n/a	No growth
HD37		NP swab	Negative	n/a	n/a

*PCR Cp values are a semi-quantitative determination of strength of positivity
NP, nasopharyngeal; BAL, bronchoalveolar lavage; ETT, endotracheal; n/a, not available; Cp, crossing point

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2631. Influenza-Associated Intensive Care Unit Hospitalizations and Deaths in Children, During 2010–2019 in Greece

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Background: The clinico-epidemiological characteristics of children with severe influenza-related intensive care unit (ICU) admissions in Greece during 2010–2019 are described.

Methods: All laboratory-confirmed influenza cases (real-time PCR), in children 0–16 years old, admitted to Pediatric ICUs throughout the country, are reported using a mandatory notification system to the National Public Health Organization of Greece. Case fatality rates (CFR) were analyzed according to age and presence of comorbidities.

Results: From October 2010 to April 2019, 131 influenza cases [7.2/100,000 children, 65 (49.6%) girls] with PICUs admissions were recorded. The majority of cases (n = 78; 60%) occurred in the age group 0–4 years-old [31 (24%) children were < 12 months-old]. Sixty-five (49.6%) children had underlying comorbidities (22 neurological disease, 12 congenital syndromes, 7 cancer, 5 chronic respiratory, 19 other). The most common diagnosis was febrile ARDS and 67 (51.14%) had severe pneumonia (40% viral, 7% bacterial). Seventy-five (57.2%) children required invasive ventilation. Influenza A accounted for 102 (77.86%) of cases; out of 86 (84.31%) subtyped, 68 (79%) were AH1N1pdm09, and 18 (21%) were AH3N2. Influenza B accounted for 29 (22.13%) of cases. All children received oseltamivir. Median length of stay was 10 days (range 1–90). A total of 32 deaths was recorded (CFR 24.4%, total rate: 1.76/100,000 children); 13 (40.1%) deaths occurred in children with no known co-morbidity. Mortality rates were higher in children aged > 4 years (18/53, 33.9% vs. 14/78, 17.9%, P = 0.04) while there was a trend for children with comorbidities (19/65, 29.2% vs. 13/66, 19.69%, P = 0.1). Only 4% of children were previously immunized against influenza.

Conclusion: AH1N1pdm09 accounted for the vast majority of severe cases and influenza associated deaths in children in Greece over the last 10 years. Severe disease occurred also in children with no comorbitidies. Longitudinal clinico-epidemiological data should be considered in shaping the national immunization program.

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2632. Cord Blood Vitamin D and Maternal Vaccination Status Associated with Decreased Laboratory Confirmed Influenza Infections in Infants

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Background: Maternal influenza vaccination has been demonstrated to reduce influenza infections in infants. Influenza infections generally peak during the winter season, and several studies support the association between low levels of vitamin D during winter months and an increase in respiratory infections, including influenza. We examined the effects of vitamin D and maternal influenza vaccination status on laboratory confirmed influenza infections in infants less than 6 months of age.

Methods: Pregnant Bangladeshi mothers were randomized to receive influenza vaccine or pneumococcal vaccine as part of the Mother's Gift study. Mothers reported breastfeeding frequency, along with episodes of infant respiratory illness with fever, every week for the first 6 months of life. If a respiratory illness with fever was reported, nasal swabs were obtained from the infant and tested with a commercial rapid influenza test. Infants with confirmed influenza disease were matched with four controls by birth month and sex, for a total of 84 controls. We measured 25-hydroxyvitamin D levels from cord blood in all cases and controls. A conditional logistic regression was performed to test the effect of vitamin D on the odds of laboratory confirmed influenza while controlling for birth weight, gestational age, crowding, number of siblings, and socioeconomic status score.

Results: A total of 21 infants had laboratory confirmed influenza disease. There were no significant differences in birth weight, crowding, family size, gestational age, socioeconomic status score, infant gender, and smokers in the home between cases and controls (Table 1). Frequency of maternal influenza vaccine was lower in cases when compared with controls (23.81% vs. 58.33%). Serum vitamin D was lower in cases than in controls (8.73 ± 3.34 vs. 10.67 ± 4.08, Table 2).

Conclusion: Both vitamin D levels and maternal vaccination status have medically relevant, and statistically significant, independent effects on the odds of infants contracting influenza. Although the vitamin D levels in the infants at birth were low, there was a significant association of lower levels at birth with an increased risk of influenza virus infection. Further study with a larger sample-size is needed to explore these effects.

Table 1: Characteristics of participants

Variable	Sub-Category	Case (n = 21)	Control (n = 84)	P-TT	P-LR
Birth weight (in kilograms)		3.07 ± 0.58 (20)	3.06 ± 0.49 (83)	0.9081	.
Family size (number of people)		4.29 ± 2.22 (21)	4.73 ± 2.52 (84)	0.466	.
Crowding (Family size/rooms in home)		1.43 ± 1.15 (21)	1.57 ± 0.99 (84)	0.5893	.
Weeks gestation		39.83 ± 1.79 (21)	39.80 ± 1.77 (84)	0.9405	.
Socioeconomic status score		36.92 ± 3.62 (21)	37.61 ± 3.25 (84)	0.3966	.
Maternal Vaccine	Influenza	5 (23.81%)	49 (58.33%)	.	**0.0039**
	Pneumococcal	16 (76.19%)	35 (41.67%)	.	***
Infant Gender	Female	13 (61.90%)	45 (53.57%)	.	0.49
	Male	8 (38.10%)	39 (46.43%)	.	***
Smoker In Home	No	13 (61.90%)	53 (63.10%)	.	0.9197
	Yes	8 (38.10%)	31 (36.90%)	.	***

P-TT: *p* value for t-test
P-LR: *p* value for Chi-square test

Table 2: Vitamin D levels in cord blood in cases versus controls

Variable	Case (n = 21)	Control (n = 84)	P (t-test)
25(OH)D (ng/ml)	8.73 ± 3.34 (21)	10.67 ± 4.08 (81)	**0.048**

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2633. Influenza and Tdap Vaccination Coverage among Pregnant Women in the PREVAIL Cohort

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Background: The ACIP recommends influenza and Tdap vaccination during pregnancy to reduce the risk of influenza and pertussis in the mother and her infant. We assessed influenza and Tdap vaccination coverage and associated factors among pregnant women enrolled in PREVAIL, a prospective birth cohort study in Cincinnati, OH. We assessed sensitivity and specificity of self report for both vaccines against state registry, maternal healthcare provider, and work-place records.

Methods: We enrolled and interviewed 265 pregnant women regarding self-reported receipt of influenza and Tdap vaccines, and obtained vaccine records from registry, electronic medical record, provider, employer, or pharmacy. We grouped subjects by documented vaccination status and analyzed demographic variables and vaccine attitudes regarding efficacy, safety, and hesitancy using unadjusted Fisher exact tests. We analyzed sensitivity and specificity of maternal recall.

Results: We identified documentation of influenza and Tdap vaccine receipt during pregnancy in 172/265 (64.9%) and 238/265 (89.8%) of women, respectively (Figure 1); by self report, 177/265 (66.8%) reported receiving influenza and 221/265 (83.4%) Tdap vaccine. The two most common primary reasons cited for receiving influenza vaccine were "to protect my baby" (36.7%) and "to protect myself" (26%; Figure 2). Pregnant women were more likely to get Tdap vaccine if a healthcare worker recommended it (OR 5.4). Subjects were more likely to get influenza vaccine if they believed it was effective in preventing influenza in themselves (OR 9.0) or their babies (OR 8.1). While positive recall had a high concordance (95.2% and 93.4% for influenza and Tdap, respectively), 12.5% and 32.1% of mothers incorrectly recalled not receiving an influenza or Tdap vaccine, respectively, that was documented as received in the records (Figure 3).

Conclusion: We found high concordance between maternal recall and verification for both influenza and Tdap vaccines. In this single-site cohort of 265 women, self report was a reliable measure of vaccination status among pregnant women. Provider communication to pregnant women regarding effectiveness of influenza and Tdap vaccinations for themselves and their infants may lead to higher maternal vaccination rates.

Figure 1. Demographic characteristics of the population stratified by verified vaccine receipt status.

Group	Category	All Enrolled		Influenza vaccine verified as received			Tdap vaccine verified as received		
		n=265	% of total	n=172	% Yes	*p* value	n=238	% Yes	*p* value
Age group (at baseline)	18-24	57	21.5%	34	59.6%	0.6	53	93.0%	0.5
	25-34	166	62.6%	109	65.6%		149	89.8%	
	35-49	42	15.9%	29	69.0%		36	85.7%	
Race/ethnicity	White/non-Hispanic	132	49.8%	95	72.0%	0.06	115	87.1%	0.08
	Black/non-Hispanic	117	44.2%	66	56.4%		110	94.0%	
	Hispanic	6	2.3%	5	83.3%		5	83.3%	
	Other	9	3.4%	5	55.6%		7	77.8%	
Education	≤ High School	126	47.6%	73	57.9%	0.001	119	94.4%	0.07
	Some college	40	15.1%	21	52.5%		34	85.0%	
	Bachelor's	54	20.4%	40	74.1%		45	83.3%	
	Graduate degree	45	17.0%	38	84.4%		40	88.9%	
Marital Status	Married/lives with partner	174	65.7%	125	71.8%	0.001	156	89.7%	0.3
	Single	91	34.3%	47	51.6%		82	90.1%	
Insurance	Private	111	41.9%	84	75.6%	0.001	97	87.4%	0.3
	Public	152	57.4%	86	56.6%		139	91.4%	

Vaccine compliance by maternal demographics. P values represent significance level of difference in proportion between vaccine verified received group and vaccine not received/unverified group (Fisher's exact test).

Figure 2. Maternal primary reasons for receiving influenza vaccine.

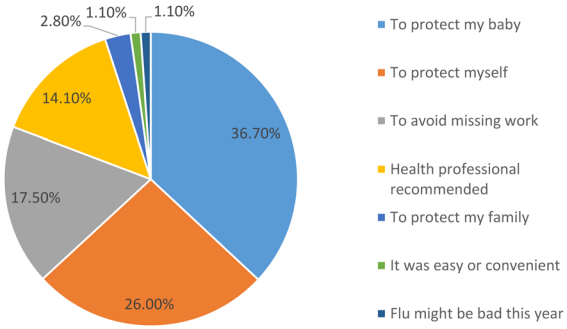

Figure 3. Maternal recall versus verification of influenza and Tdap vaccine receipt.

Influenza Vaccine Recall Concordance

Vaccine Recall		Documented vaccination		
		Yes	No	
	Yes	158	5	Sensitivity: 95.2% Specificity: 87.5% PPV: 96.9% NPV: 81.4% % Agreement: 93.7%
	No	8	35	

Concordance between maternal recall of influenza vaccine receipt at baseline interview and verification of vaccine receipt from state registry, maternal healthcare provider, and work-place records. Only subjects whose vaccine status was verified as yes or declined were included (*n*=206). Six subjects who recalled not receiving a vaccine, but received a vaccine after the baseline visit as well as well as 59 subjects whose vaccine status was not verified were excluded.

Tdap Vaccine Recall Concordance

Vaccine Recall		Documented vaccination		
		Yes	No	
	Yes	212	9	Sensitivity: 93.4% Specificity: 67.9% PPV: 95.9% NPV: 55.9% % Agreement: 90.6%
	No	15	19	

Concordance between maternal recall of Tdap vaccine receipt at baseline interview and verification of vaccine receipt from state registry, maternal healthcare provider, and work-place records. Only subjects who responded to the recall question were included in analysis (*n*=255).

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