

**Table 1.** Characteristics of pediatric patients with *Shigella* and *Campylobacter* infections

Characteristic	<i>Shigella</i> (%, IQR) <sup>1</sup>	<i>Campylobacter</i> (%, IQR)
Total	59	16
Median age	5 (IQR, 3.5-6)	7 (IQR, 2-14.2)
Gender		
Male	26 (44.1)	11 (68.7)
Female	33 (55.9)	5 (31.3)
Race		
African American/Black	15 (25.4)	0 (0)
Caucasian/White	11 (18.6)	6 (37.5)
Other/Unknown	33 (55.9)	10 (62.5)
Ethnicity		
Hispanic	14 (23.7)	4 (25.0)
Non-Hispanic	31 (52.5)	6 (37.5)
Unknown	14 (23.7)	6 (37.5)
Hospital admission	16 (27.1)	4 (25.0)
Median LOS	1 (IQR, 1-2)	1.5 (IQR, 0.75-2.2)
Outpatient	43 (72.9)	12 (75.0)

<sup>1</sup> Numbers in parentheses indicate percentage (%) except were indicated as interquartile range (IQR)

**Table 2.** Clinical features of pediatric patients with *Shigella* and *Campylobacter* infections

Characteristic <sup>1</sup>	<i>Shigella</i> (n=50)	<i>Campylobacter</i> (n=11)
Symptom		
Fever	40 (80)	5 (45.4)
Diarrhea (bloody)	29 (58)	5 (45.4)
Abdominal pain	33 (66)	8 (72.7)
Seizure	4 (8)	0 (0)
Exposure		
None	30 (60)	7 (63.6)
Daycare	5 (10)	0 (0)
Symptomatic <sup>2</sup> (unconfirmed)	9 (18)	2 (18.2)
Symptomatic (confirmed)	1 (2)	0 (0)
Pet/animal	0 (0)	1 (9.1)
Food	0 (0)	1 (9.1)
Travel	1 (2)	0 (0)
Antibiotic category (definitive)	15 (30)	4 (36.3)
Macrolide	11 (73.3)	3 (75)
Penicillin	1 (6.7)	0 (0)
Cephalosporin	3 (20)	1 (25)
Complications <sup>3</sup>	1 (2)	2 (18.2)

<sup>1</sup> Clinical information not available for *Shigella* (n=9) and *Campylobacter* (n=5) infections.

<sup>2</sup> Unconfirmed indicates exposure to individual with symptoms (e.g. diarrhea) but unknown etiology. Single exposure to individual with known *Shigella* infection (confirmed).

<sup>3</sup> Complications included urinary tract infections (n=1), rectal prolapse (n=1) and splenomegaly (n=1)

**Table 3.** Microbiological features of pediatric *Shigella* and *Campylobacter* infections

Characteristic	<i>Shigella</i> (n=59)	<i>Campylobacter</i> (n=16)
Species	<i>S. sonnei</i> : 57 (96.6) <i>S. flexneri</i> : 2 (3.4)	<i>C. jejuni</i> : 16 (100)
Source		
Stool	55 (93.2)	16 (100)
Urine	4 (6.8)	0 (0)
Resistance <sup>1</sup>		(Not tested)
Ampicillin (n=31)	4 (12.9)	
TMP-SMX (n=55)	40 (72.7)	

<sup>1</sup> Number of *Shigella* isolates tested indicated in parentheses.

**Conclusion.** Infections due to *Shigella* and *Campylobacter* were a significant burden among pediatric patients between 2019 and 2020 in Houston, TX. The observed high frequency of resistance to TMP-SMX and emergence of multi-drug resistant *Shigella* in other countries warrants continued surveillance.

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### 699. Case-Case Comparison of Exposures among Fluoroquinolone-Resistant and Pan-Susceptible *Campylobacter* Cases, Tennessee, 2016-2018

Samir Hanna, MD, MSPH; Katie Garman, MPH; John R. Dunn, DVM, PhD; Tennessee Department of Health, Nashville, Tennessee

**Session:** P-33. Enteric Infection

**Background.** *Campylobacter* causes an estimated 1.5 million infections each year in the United States. Of those, approximately 448,400 infections are caused by antimicrobial resistant strains, including strains resistant to fluoroquinolones (e.g., nalidixic acid and ciprofloxacin), which are commonly used to treat campylobacteriosis. *Campylobacter* infection is commonly attributed to consuming poultry products. We compared exposure data between fluoroquinolone-resistant and pan-susceptible *Campylobacter* cases reported in 2016-2018 to assess attribution.

**Methods.** Broth microdilution was performed on *Campylobacter* isolates at CDC to determine the minimum inhibitory concentration for nine antimicrobial drugs. Whole genome sequencing (WGS) was performed at the Tennessee (TN) State Public Health Laboratory and the sequence data were analyzed at CDC to determine the genetic resistance determinants. Exposure data was collected through routine case interviews. Exposures among cases with fluoroquinolone-resistant infection and cases with no resistance to antimicrobials were compared.

**Results.** A total of 606 *Campylobacter* isolates from TN were submitted to CDC NARMS. Of those, 123 (20%) isolates were resistant to fluoroquinolones and 304

(50%) isolates were pan-susceptible. The gyr A (86) resistance gene was detected in 46/54 (85%) of resistant isolates. Exposure data were available for 59 (48%) fluoroquinolone-resistant cases and 186 (61%) pan-susceptible cases. Consumption of chicken (OR 2.1, p-value 0.03) and handling raw seafood (OR 3.1, p-value 0.03) were significantly associated with fluoroquinolone-resistance. More fluoroquinolone-resistant cases reported international travel compared to pan-susceptible cases (15% versus 4%) with OR 4.6, and p-value 0.004.

**Conclusion.** Fluoroquinolone-resistant *Campylobacter* infections were acquired domestically and internationally. Exposure to chicken products and handling raw seafood were reported more often among fluoroquinolone-resistant cases. Whole genome sequencing of *Campylobacter* isolates provides predicted resistance data. Coupling predicted resistance data with exposure data facilitates better understanding of source attribution of different strains.

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### 700. Risk Factors and Molecular Epidemiology of Acute and Chronic Norovirus Infection at a Large Tertiary Care Cancer Center

Divya S. Kondapi, MD<sup>1</sup>; Sasirekha Ramani, PhD<sup>1</sup>; Adilene Olvera, MPH MSL (ASCP)<sup>2</sup>; Robert L. Atmar, MD<sup>1</sup>; Mary Estes, PhD<sup>1</sup>; Pablo C. Okhuysen, MD, FACP, FIDSA<sup>2</sup>; <sup>1</sup>Baylor College of Medicine, Coral Gables, FL; <sup>2</sup>The University of Texas MD Anderson Cancer Center, Houston, TX

**Session:** P-33. Enteric Infection

**Background.** Norovirus (NoV) is the leading cause of viral diarrhea in patients with cancer. In this study, we describe risk factors associated with acute and chronic NoV infection in this patient population.

**Methods.** We identified 132 patients with NoV diarrhea (using stool RT PCR) between 2016-2020 at University of Texas MD Anderson Cancer Center (MDACC). Patient data, including demographics, clinical characteristics, NoV treatments, and complications were retrospectively extracted from charts. Stool samples were analyzed for NoV genogroups and genotypes. We compared characteristics and outcomes of patients with acute diarrhea (< 14day; AD) versus chronic diarrhea (>14day or recurrences within 12 weeks; CD) and analyzed the data using Pearson Chi square or Fisher's exact for categorical variables and Wilcoxon rank-sum test for continuous variables.

**Table 1 – Patient Demographics.**

Characteristic	Acute diarrhea (n=97)	Chronic diarrhea (n=35)	Total (n=132)	p-value
Age at diagnosis in years, median (range)	58 (3-91)	59 (7-91)	59 (3-91)	0.820
Gender				0.350
Male	41 (42)	18 (51)	59 (45)	
Female	56 (58)	17 (49)	73 (55)	
Race				0.281
White	64 (66)	21 (60)	85 (65)	
African American	13 (13)	2 (6)	15 (11)	
Asian	5 (5)	2 (6)	7 (5)	
Other	15 (16)	10 (28)	25 (19)	
Ethnicity				0.780
Non-Hispanic	82 (85)	28 (80)	110 (83)	
Hispanic	12 (12)	6 (17)	18 (14)	
Other	3 (3)	1 (3)	4 (3)	

**Results.** Of 132 patients identified, 124 had an underlying cancer (39 solid tumor, 85 hematological malignancies, Table 1). On univariate analysis, CD patients were more likely to have a hematological malignancy (p=0.002), be a hematopoietic stem cell recipient (p= 0.013), have a history of gastrointestinal graft versus host disease (p=0.011), or have received immunosuppressants or steroids in the 90 days before diarrhea onset (p=0.001, Table 2). CD patients had significantly lower white blood cell counts (p=0.038), absolute neutrophil counts (p=0.049), IgG levels (p= 0.001), and serum albumin levels (p=0.002) at the time of NoV diagnosis (Table 3). Patients with CD more often received symptomatic or NoV targeting treatment, including anti-diarrheal (p=0.005), nitazoxanide (p< 0.001), intravenous immune globulin (p=0.017), and oral IgG (p=0.042). CD patients more often had diarrheal recurrence in the first 4 weeks (p=0.001) or the second month (p< 0.001) after initial diagnosis and needed enteral or parenteral nutrition (p=0.004). We genotyped NoV in 67 patients (Figure 1), resulting in identification of the following genogroups: GI (n=9, 13%), GII.4 (n=23, 34%), and other types of GII (n=35, 52%). Genotype diversity was higher in patients with CD than AD (Figure 1).

**Table 2 – Characteristics of Underlying Malignancy.**

Characteristic	Acute diarrhea (n=97)	Chronic diarrhea (n=35)	Total (n=132)	p-value
<b>Oncologic diagnosis</b>				0.002
No cancer	8 (8)	0 (0)	8 (6)	
Solid	35 (36)	4 (12)	39 (30)	
AML	7 (7)	10 (29)	17 (13)	
CML	2 (2)	1 (3)	3 (2)	
CLL	4 (4)	4 (12)	8 (6)	
ALL	10 (10)	5 (14)	15 (11)	
Lymphoma	14 (15)	4 (12)	18 (14)	
Myeloma	14 (15)	3 (9)	17 (13)	
Other Heme	3 (3)	4 (12)	7 (5)	
Type of cancer				0.002
No cancer	8 (8)	0 (0)	8 (6)	
Solid	35 (36)	4 (12)	39 (30)	
Hematological	54 (56)	31 (88)	85 (64)	
Cancer status				0.188
Not in remission	69 (71)	25 (71)	94 (71)	
In remission	9 (9)	2 (6)	11 (9)	
Remission after HCT or CAR-T	12 (12)	8 (23)	20 (15)	
Not applicable	7 (7)	0 (0)	7 (5)	
Cancer therapy within 90 days	70 (72)	29 (83)	99 (75)	0.210
Conventional chemotherapy within 90 days	34 (35)	14 (40)	48 (36)	0.602
Prior HCT	25 (26) <sup>2</sup>	17 (49)	42 (32)	0.013
HCT type				0.013
Autologous	14 (25)	3 (9)	17 (13)	
Allogeneic	11 (25)	14 (40)	25 (19)	
GVHD (any)	8 (25)	10 (29)	18 (14)	0.085
Gastrointestinal GVHD	4 (25)	9 (25)	13 (10)	0.011
Check point inhibitor within 90 days	4 (6)	3 (9)	7 (5)	>0.300
Any previous checkpoint inhibitor	11 (11)	3 (9)	14 (11)	0.760
CAR-T recipient	6 (6)	3 (9)	9 (7)	0.699
Steroids or other immunosuppressants within 90 days	13 (14)	24 (69)	37 (28)	0.001
Anti-CD20 within 6 months	11 (11)	5 (14)	16 (12)	0.763
Antibiotics within 90 days	70 (72)	24 (69)	94 (71)	0.687

<sup>2</sup>The numbers contributing to the results are the overall number unless otherwise noted (e.g., with a denominator)

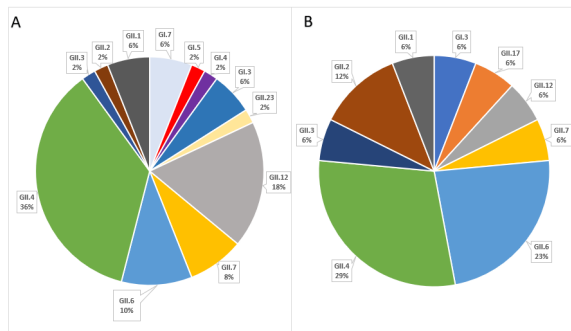
Abbreviations – AML, acute myelogenous leukemia; CML, chronic myelogenous leukemia; CLL, chronic lymphocytic leukemia; ALL, acute lymphocytic leukemia; HCT, hematopoietic cell transplantation; CAR-T, chimeric antigen receptor T cell; MUD, matched unrelated donor; AGRD, matched related donor; GVHD, graft-versus-host disease.

Table 3 - Laboratory Profile of Patients with Acute and Chronic Diarrhea.

Lab Parameter	Acute diarrhea (n=97)	Chronic diarrhea (n=35)	Total (n=132)	p-value
WBC K/uL, median (range)	6 (0-39.6)	4 (0.3-35.5)	5 (0-39.6)	0.038
ANC K/uL, median (range)	3.2 (0-22.8)	2.3 (0-9.6)	2.9 (0-22.8)	0.049
ANC < 500/mm <sup>3</sup>	16 (16)	8 (23)	24 (18)	0.403
ALC K/uL, median (range)	0.8 (0-40.6)	0.7 (0-24)	0.8 (0-40.6)	0.418
ALC < 1000/mm <sup>3</sup>	55 (57)	23 (66)	78 (59)	0.353
IgG < 400 mg/dL	9/41 (22)	14/21 (67)	23/62 (37)	0.001
Prior IVIG	17 (18)	9 (26)	26 (20)	0.296
IgA < 85 mg/dL	19/32 (59)	10/12 (83)	29/44 (66)	0.171
Serum albumin mg/dL, median (range)	3.7 (1.7-5.2)	3.2 (0.2-4.5)	3.6 (0.2-5.2)	0.002
Serum creatinine mg/dL, median (range)	0.8 (0.1-1.8)	0.8 (0.3-4.2)	0.8 (0.1-1.8)	0.853

Abbreviations – WBC, white blood cell count; ANC, absolute neutrophil count; ALC, absolute lymphocyte count; IgG, immunoglobulin G; IVIG, intravenous immunoglobulin; IgA, immunoglobulin A.

Figure 1 - Genotypic diversity in patients with acute (panel A) and chronic diarrhea (panel B)



Patients with chronic diarrhea (n=17) had a higher genotypic diversity compared to those with acute diarrhea (n=50) (Simpsons reciprocal diversity index: 3.65 vs 3.18). About 50% of samples in both groups could not be genotyped.

**Conclusion.** In patients with cancer, CD from NoV is associated with severe immunosuppression, is refractory to therapy and can be caused by a variety of NoV genotypes/genogroups.

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### 701. An Open-label Phase 2a Study of Ibezapolstat, a Unique Gram-positive Selective Spectrum (GPSS) Antibiotic, for Patients with *Clostridioides difficile* Infection

Kevin W. Garey, Pharm.D., M.S., FASHP<sup>1</sup>; Khurshida Begum, PhD<sup>1</sup>; Chenlin Hu, PhD<sup>2</sup>; Weiqun Wang, Ph.D.<sup>3</sup>; Chris Lancaster, MS<sup>2</sup>; Anne J. Gonzales-Luna, PharmD<sup>1</sup>; Caroline Loveall, BS<sup>2</sup>; M. Jahangir Alam, PhD<sup>1</sup>; Michael Silverman, MD<sup>4</sup>; <sup>1</sup>University of Houston College of Pharmacy, Houston, Texas; <sup>2</sup>University of Houston, Houston, Texas; <sup>3</sup>University of Houston, College of Pharmacy, Houston, TX; <sup>4</sup>Acurx Pharmaceuticals, LLC, White Plains, NY

for the Ibezapolstat Study Group

Session: P-33. Enteric Infection

**Background.** Ibezapolstat, a DNA polymerase III inhibitor, currently in Phase 2 clinical development for treatment of *C. difficile* infection (CDI). Its unique mechanism of action targets low G+C content Gram-positive bacteria primarily Firmicutes including *C. difficile*. Phase I healthy volunteer results demonstrated a favorable microbiome profile suggestive of an anti-recurrence effect. The purpose of this study was to report clinical outcomes, pharmacokinetics, and microbiome changes from this Phase 2a clinical study and to continue to test for anti-recurrence microbiome properties.

**Methods.** Ibezapolstat 450 mg was given twice daily for 10 days to patients with mild-moderate CDI defined as diarrhea plus a positive *C. difficile* toxin test. Test of cure was evaluated at day 12 and sustained clinical cure at day 38. Stool samples were evaluated for *C. difficile* cultures and microbiome changes.

**Results.** Ten subjects (female: 50%) aged 50 ± 15 years were enrolled. All ten subjects experienced a clinical cure by the test of cure visit at day 12 and all 10 subjects experienced a sustained clinical cure at the day 38 visit. Ibezapolstat was well tolerated with 1 adverse event (nausea) probably related to drug. Ibezapolstat systemic exposure was minimal with no plasma level reaching 1 ug/mL any time during therapy. Ibezapolstat colonic concentrations averaged 400 ug/g stool at day 3 and greater than 1,000 ug/g by day 10 of dosing. Six of the seven available baseline stool samples grew toxigenic *C. difficile* of various ribotypes including RT078-226 and RT014-020 (Ibezapolstat MIC range: 0.25-1 ug/mL). Follow-up cultures were no growth starting from day 3 stool cultures. Microbiome changes included overgrowth of Actinobacteria and/or Firmicute phylum species while on therapy.

**Conclusion.** Favorable clinical efficacy and safety results were observed in ibezapolstat patients with CDI including 100% clinical cure and sustained clinical cure. These results begin to validate our approach to ibezapolstat development in that the favorable microbiome effects seen in healthy Phase 1 volunteers may be predictive of

beneficial patient outcomes, including low rates of recurrence. These results support the continued clinical development of ibezapolstat.

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### 702. Risk Factors for Acute Gastroenteritis Among Patients Hospitalized in 5 Veterans Affairs Medical Centers, 2016–19

Neha Balachandran, MBBS MPH<sup>1</sup>; Jordan Cates, PhD<sup>2</sup>; Anita Kambhampati, MPH<sup>3</sup>; Vincent Marconi, MD<sup>4</sup>; Sheldon T. Brown, MD<sup>5</sup>; Maria C. Rodriguez-Barradas, MD<sup>6</sup>; David Beenhouwer, MD<sup>7</sup>; Mark Holodniy, MD, CIC<sup>8</sup>; Cynthia A. Lucero-Obusan, MD, CIC<sup>8</sup>; Cristina Cardemil, MD<sup>2</sup>; Umesh D. Parashar, MD<sup>9</sup>; Sara Mirza, PhD<sup>2</sup>; <sup>1</sup>Oak Ridge Institute for Science and Education, Oak Ridge, TN, Atlanta, GA; <sup>2</sup>Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; <sup>3</sup>IHR, Inc. contracting agency to the Division of Viral Diseases, Centers for Disease Control and Prevention, Atlanta, GA; <sup>4</sup>Atlanta VA, Atlanta, GA; <sup>5</sup>James J Peters VAMC, Bronx, NY; <sup>6</sup>Michael E. DeBakey VAMC, Houston, TX; <sup>7</sup>VA Greater Los Angeles, Los Angeles, CA; <sup>8</sup>Department of Veterans Affairs, Palo Alto, CA; <sup>9</sup>Division of Viral Diseases, Centers for Disease Control and Prevention, Atlanta, GA

Session: P-33. Enteric Infection

**Background.** In the United States, an estimated 179 million acute gastroenteritis (AGE) episodes occur each year. Identifying factors contributing to AGE susceptibility and severity is important to address the high disease burden of AGE among adults. The primary objective of this analysis was to identify risk factors for all-cause AGE, norovirus-associated AGE and severe AGE among hospitalized adults.

**Methods.** We analyzed data from 1029 inpatient AGE cases and 624 non-AGE controls enrolled prospectively from December 1, 2016 – November 30, 2019 from 5 Veterans Affairs Medical Centers (Atlanta, Bronx, Houston, Los Angeles, Palo Alto). Standardized patient interviews and medical chart abstractions were conducted to collect demographics, exposure history, and underlying medical conditions. Stool samples from participants were tested for 22 pathogens using the BioFire Gastrointestinal Panel. Severity of AGE was determined using a 20-point modified Vesikari score (MVS) and severe AGE was defined as a MVS score of ≥ 11. Multivariate logistic regression was performed to assess associations between potential risk factors and outcomes.

**Results.** Of the total AGE cases, 551 (54%) had severe AGE; 44 (4%) were norovirus positive. Risk factors for all-cause AGE vs. non-AGE controls included household contact with a person with AGE in the past 7 days (aOR=2.9, 95% CI:1.3-6.7), severe renal disease (aOR=3.1, 95% CI:1.8-5.2), human immunodeficiency virus (HIV) (aOR=3.9, 95% CI:1.8-8.5), and immunosuppressive therapy (aOR=5.6, 95% CI:2.7-11.7). Factors associated with norovirus positivity by univariate analysis were contact with a person with AGE outside (OR=4.4, 95% CI:1.6-12.0) and within (OR=5.0, 95% CI:2.2-11.5) the household in the past 7 days. Detection of any viral pathogen (aOR=4.0, 95% CI:1.7-9.5) was a risk factor for severe AGE.

**Conclusion.** Our findings suggest that inpatients with HIV or severe renal disease, on immunosuppressive therapy, or in contact with a person with AGE within household are at higher risk for all-cause AGE. Patients with these medical conditions should be monitored for AGE related hospitalizations and may benefit from targeted AGE prevention messaging.

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### 703. Peritoneal Coccidioidomycosis in a Pediatric Patient: An Extremely Rare Presentation and Literature Review

Barbara Ximenes Braz, MD<sup>1</sup>; Chantal Soobhanath, MD<sup>1</sup>; Amelia B. Thompson, MD, MPH<sup>2</sup>; <sup>1</sup>AdventHealth Orlando, Orlando, Florida; <sup>2</sup>AdventHealth for Children, Orlando, Florida

Session: P-33. Enteric Infection

**Background.** Chronic peritonitis is an unusual manifestation of coccidioidomycosis (CM) that is challenging to diagnose and manage due to its propensity for relapse. It is even more unusual to diagnose peritoneal CM in the pediatric population, with only two other cases reported in the literature.

**Methods.** We present the case of a previously healthy 5-year-old Filipino female in Florida who was diagnosed with peritoneal CM. After months of unintentional weight loss and worsening abdominal distention, she presented to medical care. Imaging revealed significant abdominal ascites and nodularities throughout the peritoneum. The peritoneal fluid demonstrated a lymphocytic pleocytosis and infectious workup was benign. CA125 levels were elevated, but peritoneal adenosine deaminase was within normal limits. A biopsy of the affected tissue revealed diffuse granulomas surrounding spherules that were positive on GMS and PAS staining, concerning for CM. Exposure history revealed that she was raised in California and moved to Florida one year prior to presentation. Complement fixation titers were significantly elevated at ≥ 1:512 and immunodiffusion titers were positive. A Coccidioides PCR was sent from the tissue to the Mayo clinic and was positive, and fungal cultures from the tissue grew *C. immitis/posadasii*. Immunologic workup was reassuring. She was started on oral Fluconazole with rapid resolution of her symptoms.