642. Trends and cost burden of Legionella urine antigen test

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Session: P-25. Diagnostics: Bacteriology/mycobacteriology

Background: *Legionella* urine antigen (LUAg) testing is used to identify the pathogen *Legionella pneumophila* serotype 1 which accounts for 50 to 70% of Legionella pneumonia and has 80% sensitivity and 95% specificity. The 2019 ATS/IDSA CAP guidelines recommend against routinely testing urine for LUAg except when indicated by epidemiological factors or severe cases of CAP; however, the recommendation is based on a low quality of evidence. In 2014 & 2015 there were 32 and 39 cases, respectively in the state of Mississippi. The purpose of this study was to evaluate the trends of ordering LUAg, positive results and estimate the cost burden at the University of Mississippi Medical Center (UMMC).

Methods: We performed a retrospective study of all patients who received the LUAg test at UMMC from January 3, 2013 to December 31, 2019. Patient Cohort Explorer was used to obtain de-identified patient data from EPIC. We obtained the number of encounters and patients on whom the LUAg test was performed during their inpatient hospitalization. Coding and billing offices provided the cost per LUAg test.

Results: LUAg test was ordered 2,642 times on 2350 patients between 2013 and 2019. 22 LUAg test results were positive in 21 patients. 2,627 tests were done on patients admitted in the hospital. Of the 1,181 tests ordered in female patients, 11 were positive and of the 1461 tests done in male patients, 11 were positive. The minimum age for ordered test was under 1 year while the oldest patient is 89 years old with a median age of 57 years. The youngest patient to be positive is 21 and the oldest patient was 72 years. 1,471 tests were done in African American patients and 1084 tests in Caucasian patients. At the end of study period 1901 were alive and 741 deceased. The median length of stay for the patient receiving the test was 7 days with 1726 patients discharged within 10 days. 174, 255, 301, 433, 467, 395, 613 tests were ordered respectively from 2013 to 2019. At self pay cost of $132.82 in 2019 USD, the total cost of 2642 tests was $350,910.44. About $15,950.47 was spent for each positive LUAg test during the study period.

Conclusion: Incidence of pneumonia from *Legionella* in Mississippi is low. Based on our study, we recommend to follow the current ATS/IDSA guidelines and order the test in select patients as recommended, in efforts to reduce diagnostic costs.

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643. Trends, outcomes and cost analysis of Streptococcus urinary antigen testing.

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Session: P-25. Diagnostics: Bacteriology/mycobacteriology

Background: Streptococcus pneumoniae urinary antigen (SUAg) testing detects the capsular polysaccharide of S. pneumoniae; which has a sensitivity and specificity of about 75% and 95%, respectively. IDSA/ATS guidelines recommend empirically covering those who present with community acquired pneumonia (CAP) for common pathogens including S. pneumoniae. These guidelines also recommend against routinely performing SUAg testing in adults with CAP unless the presentation is severe. However, the guidelines acknowledge that this a conditional recommendation based on a low quality of evidence. This study aims to investigate the utility of testing patients with pneumonia for S. pneumoniae and the economic burden.

Methods: We performed a retrospective study of all patients who received the SUAg test at University of Mississippi Medical Center (UMMC) from January 3, 2013 to December 31, 2019. Patient Cohort Explorer was used to obtain de-identified patient data from EPIC. We obtained the number of encounters and patients on whom the SUAg test was performed. Coding and billing offices provided the self pay cost of $101.37 per SUAg test in 2019 USD.

Results: The SUAg was ordered 2,507 times with 105 (4.18%) total positives results. Age range was 1 to 89 years with a median age of 57 years for ordering the test. 136, 256, 314, 419, 433, 382, 566 SUAg tests were ordered respectively from 2013 to 2019. 59% of the positive results were in female patients while 54% percent of the negative results were in male patients. Current every day smokers were more likely to test positive (29% versus 18% negative). Median length of stay was longer for a negative test (6 days versus 5 days). 16% of the patients with a positive result expired compared to 10.5% with a negative result.

Over the study period, 2,507 tests cost an estimated $254,134.59 using the 2019 pricing. Therefore, approximately $2420.32 was spent in testing to identify each positive result.

Conclusion: With low positive rate and Streptococci pneumonia that is already covered with empirical antibiotics, we recommend following the current ATS/IDSA guidelines and order the test in select patients as recommended, in efforts to reduce diagnostic burden and health care costs. However a positive result showed a decreased length of stay and higher mortality.

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644. Borrelia miyamotoi and Borrelia burgdorferi Seroprevalence in New England

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Session: P-25. Diagnostics: Bacteriology/mycobacteriology

Background: Diseases vectored by the tick species *Ixodes scapularis* have increased in incidence over the past 50 years and have been expanding into previously non-endemic areas. The emergence of *Borrelia miyamotoi*, a recently described spirochetal pathogen, has been less well documented than that of *Borrelia burgdorferi*, the causative agent of Lyme disease. The objective of this study was to compare the geographic range of human exposure to *B. miyamotoi* and *B. burgdorferi* in New England, the pattern of their spatial expansion, and factors that influence their frequency.

Methods: Serum samples were collected from 11 study sites across New England. Age, gender, race, and residential zip code or county were recorded for each study participant and aggregate data analyzed by study sites, study site zones, and residential county for spatial analysis. Serum samples were tested for *B. miyamotoi* antibody using a multiplex Luminex assay and for *B. burgdorferi* antibody using a recently FDA approved two-tiered ELISA (Zeus ELISA Test Systems). Fischer exact tests and map visualizations in ArcGIS Pro 2.4.2 (Copyright ©2019 Esri Inc.) were used to determine spatial distribution of human *B. miyamotoi* and *B. burgdorferi* infection in New England. A logistic regression model was used to determine any association in seropositivity with tick-borne infection risk factors.

Results: *B. burgdorferi* seroprevalence was greater than that of *B. miyamotoi* at all but one study site. The average *B. burgdorferi* seroprevalence at all study sites was not quite double that of *B. miyamotoi* (mean 2.3% [0.6-6.2%] and mean 4.1% [2.2-7.5%], respectively). No longitudinal or latitudinal gradient was observed for *B. miyamotoi* or *B. burgdorferi* seroprevalence by study site zone or county analysis. Men were twice as likely as women to be seropositive for *B. miyamotoi* and *B. burgdorferi*.

Conclusion: Human exposure to *B. miyamotoi* and *B. burgdorferi* is highly dispersed throughout New England. *B. miyamotoi* seroprevalence is about half that of *B. burgdorferi* in New England. Additional studies are needed to explain the disparity between *B. burgdorferi* and *B. miyamotoi* infection and disease.

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645. Absence of Toxemia in Clostridioides difficile infection: Results from Ultrasensitive Toxin Assay of Serum

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Session: P-25. Diagnostics: Bacteriology/mycobacteriology

Background: *Clostridioides difficile* infection (CDI) is the major cause of hospital-acquired bacterial infectious diarrheacaused by Toxin A (TcdA) and Toxin B (Tcd B), secreted from pathogenic strains of *C.difficile* bacteria. This infection can vary greatly in symptom severity and presentation. In fulminant CDI, these toxins lead to systemic complications such as toxemia, however, identification of toxemia in CDI patients is extremely rare. We hypothesized that this rarity of detection may be due to low concentrations of circulating toxins in the blood, below the limit of detection of commercially available assays.

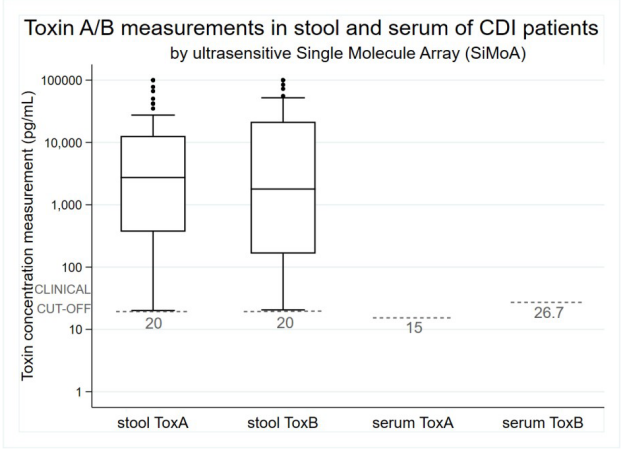
Methods: The previously developed Single Molecule Array (Simoa) assay, capable of detecting TcdA and TcdB in stool, was modified for the detection of toxins in serum and applied to a panel of serum samples from patients with confirmed CDI.

Results: Our cohort included 169 patients with a median age of 68 years (IQR 54-78), most with severe CDI and many with severe clinical outcomes attributed to CDI (Table 1). We found no detectable TcdA or TcdB in the serum of our patient cohort despite a wide range of toxin concentrations in paired stool (Figure 1). The detection of toxin may be limited by the interference of anti-toxin anti-bodies circulating in serum. When serum samples were spiked with TcdA and/or TcdBvarying amounts of IgA, IgG or IgM anti-toxin, high serum anti-toxin antibody concentrations were associated with loss of Simoa signal, suggesting substantial inhibition of toxin measurements.

Table 1. Demographics, Baseline Laboratory Values, and Clinical Outcomes for the cohort

Variable	n = 169	
Demographic Information		
Age Median (IQR)	68 (54 – 78)	
Male Gender	90	53.3%
Race		
White	126	74.6%
African American	21	12.4%
Other	18	10.7%
Unknown	4	2.4%
Ethnicity		
Hispanic	9	5.3%
Not Hispanic	144	85.2%
Unknown	16	9.5%
Laboratory Results		
WBC (10^3 cells/μL) Median (IQR)	11.5 (7.4 – 18.6)	
WBC ≥15 x 10^3 cells/μL	61	36.1%
Creatinine (mg/dl) Median (IQR)	1.1 (0.8 – 1.9)	
Creatinine ≥ 1.5 mg/dl	61	36.1%
Albumin (g/dl) Median (IQR)	3 (2.5 – 3.6) n = 152	
Albumin ≤ 3 g/dl	73 (n = 152)	43.2%
027 / NAP1 / B1 strain	17	10.1%
Severe Clinical Outcomes - Total		
ICU admission	24	14.2%
Colectomy	1	0.6%
Death within 40 days	14	8.3%
Severe Clinical Outcomes – Attributed to CDI		
ICU admission	13	7.7%
Colectomy	1	0.6%
Death within 40 days	2	2.4%
Severity Classifications* n = 153		
IDSA Severe	90	74.4%
ESCMID Severe	93	76.9%
Zar *et al* Severe	73	60.3%
Belmares *et al* Severe	23	19.0%

Figure 1. Comparison of TcdA and TcdB concentrations, as measured by Simoa, in serum and stool. Clinical cutoffs are shown: stool, 20 pg/ml for TcdA and for TcdB; serum 15.0 pg/ml for TcdA and is 26.7 pg/ml for TcdB. Signals below these cut-offs are below backgrounds and so negative.



Conclusion: In contrast to earlier published findings which reported on the presence of detectable toxin in the serum of a small number of patients with CDI, our work did not support this observation. Although Simoa is highly sensitive for detection of picogram quantities of TcdA or TcdB it was unable to detect either toxin in serum during CDI. This result does not support the hypothesis that toxemia develops even in severe *C. difficile* infection.

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646. Adapting the modified Carbapenem Inactivation Method to assess for possible beta-lactamase mediated resistance in Piperacillin-Tazobactam resistant/ Ceftriaxone susceptible Escherichia. coli and Klebsiella pneumoniae

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Session: P-25. Diagnostics: Bacteriology/mycobacteriology

Background: A cluster of piperacillin-tazobactam resistant/ceftriaxone susceptible *Escherichia coli* and *Klebsiella pneumonaie* bacteremias were noted at our institution. A review of the literature suggested this resistance phenotype was mediated by a beta-lactamase. We sought to further corroborate this phenotypically.

Methods: We adapted the "carbapenem inactivation method" utilizing piperacillin-tazobactam and ceftriaxone discs on all *E. coli* and *K. pneumoniae* isolated from blood and demonstrating piperacillin-tazobactam resistance but with ceftriaxone susceptibility. We utilized pan-susceptible and carbapenem resistance *Enterobacteriaceae* reference strains as well as third generation cephalosporin resistant, piperacillin-tazobactam susceptible isolates as controls.

Results: 96% of the piperacillin-tazobactam resistant, ceftriaxone susceptible strains demonstrated the capacity to degrade the piperacillin-tazobactam discs while 100% spared the ceftriaxone discs. 75% of the piperacillin-tazobactam susceptible, ceftriaxone resistant control strains spared the piperacillin-tazobactam discs while degrading the ceftriaxone discs.

Conclusion: The resistance phenotype observed is due to beta-lactamase production and the modified carbapenem inactivation method can be adapted to probe for other beta-lactamases. Further study is required to definitively identify which beta-lactamase is responsible.

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647. Adoption of the updated fluoroquinolones breakpoints for Gram negative bacteria in clinical microbiology laboratories

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Session: P-25. Diagnostics: Bacteriology/mycobacteriology

Background: Despite the multiple safety warnings related to fluoroquinolones (FQs) treatment, their use remains unavoidable in several occasions due to their broad spectrum of coverage including activity against multi-drug resistant glucose non-fermenting Gram-negative bacteria such as *Pseudomonas* spp., and high oral bioavailability. The Clinical and Laboratory Standards Institute (CLSI) has lowered the FQs minimal inhibitory concentrations (MICs) breakpoints for *Salmonella* spp. in 2012 and 2013, and for the *Enterobacterales* and *P. aeruginosa* in 2019. We aim to explore the number of hospitals that adopted the revised breakpoints.

Methods: We conducted a cross-sectional phone-based survey querying the 43 microbiology laboratories that serve 100% of the acute care and long-term hospitals in Connecticut to determine use of revised FQs MIC breakpoints for Gram-negative bacteria.

Results: Six laboratories refer antimicrobial susceptibility testing to another local hospital microbiology laboratory or to a national reference laboratory. Thus, we obtained information about the study question from a total of 37 microbiology laboratories. Eight laboratories (21.6%) were affiliated to university hospitals and 29 (78.4%) were community-based. Microscan Beckman coulter MicroScan was the most common antimicrobial susceptibility test method used in 15 (40.6%) microbiology laboratories followed by BioMérieux Vitek 2 in 13 (35.1%) laboratories. Four laboratories (10.8%) only adopted the revised CLSI FQs breakpoints for *Enterobacterales, P. aeruginosa*, and *Salmonella* spp, 5 (13.5%) implemented the revised breakpoints for *Enterobacterales* and *P. aeruginosa* but not for *Salmonella* spp., and 8 (21.6%) laboratories adopted the revised CLSI breakpoints for *Salmonella* spp. but not for *Enterobacterales* and *P. aeruginosa*.

Conclusion: The use of outdated CLSI breakpoints for FQs against Gram-negative bacteria remains common in the microbiology laboratories. There is an urgent need to mitigate the impact of using the outdated FQs breakpoints and reporting false susceptibility to FQs.

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648. BioFire® FilmArray® Pneumonia plus Panel Performance Evaluation: A Multicenter, International Collaborative Study

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Session: P-25. Diagnostics: Bacteriology/mycobacteriology

Background: Classical methods to identify causes of community acquired, healthcare and ventilator associated pneumonia can be insensitive and slow, leading to unnecessary or inappropriate antimicrobial therapy. The BioFire® FilmArray®