Impact of FilmArray GI Panel on *Shigella* Outbreak Management

N. Kanwar[1], J. Jackson[1], R. Selvarangan[1,2]

[1]Children's Mercy Hospitals and Clinics, and [2]University of Missouri, School of Medicine, Kansas City, MO

ABSTRACT (revised)

Background: Shigellosis is the third most common enteric disease in the United States with highest incidence in children less than five years. Fecal culture for isolation and identification of *Shigella* may take days. The FilmArray Gastrointestinal (GI) Panel is a PCR based assay that detects 22 different enteric pathogens including *Shigella* in an hour. The aim of this study is to evaluate the impact of GI Panel detection of *Shigella* in an emergency department (ED) during an outbreak.

Methods: Children with acute gastroenteritis were prospectively enrolled and stool specimens were tested by GI Panel. Test results were either withheld in pre-intervention (PRE) or reported to clinicians/families in post–intervention (POST) period during the current *Shigella* outbreak in Kansas City area. The impact of the GI Panel testing on patient management and outcomes was measured.

Results: To date, 290 subjects (139 PRE and 151 POST) have been enrolled in the study. There were 61 subjects (29 PRE and 32 POST) who did not submit a stool specimen. Follow up interview could not be performed in 18 subjects (14 PRE and 4 POST). *Shigella* was identified by GI Panel in the PRE (N=30) and POST (N=19) phase. Diarrhea was the most common symptom in subjects (PRE median age of 46 (6-168) and POST 68 (16-180) months). GI panel detected more *Shigella* compared to culture (PRE: culture -8 vs GI panel -10;POST: culture-15 vs GI panel-19)

Azithromycin therapy was prescribed for 6/30 (20%) subjects in the PRE phase and14/19 (74%) subjects in the POST phase (*P*<0.001). Empiric therapy was administered among 5/6 (83%) subjects in the PRE phase and 6/14 (43%) subjects in the POST phase. Eight subjects (57%) received targeted azithromycin therapy following GI panel test result in the POST phase. Time lapsed between clinical encounter and azithromycin therapy following test result availability was shorter in POST phase (n=8); 8.68 hrs (range 6.37-52.37 hrs) versus PRE phase (n=1) ; 72 hrs.

Decision to treat *Shigella* infection with Azithromycin therapy in POST phase seemed to be influenced by severity of infection as measured by number of diarrheal episodes (treated: 5.5(1-27) stools *vs.* not treated: 3 (1-13) stools), bloody diarrhea (treated: 7 vs. not treated: None), and onset of illness (treated: 2 (0-6)days *vs.* not treated: 3(1-4)days).

All *Shigella* positive subjects in PRE (30) and 17 in POST phase completed follow-up. Following initial visit to ED, six subjects in PRE phase visited additional providers compared with none in the POST phase (*P*=0.07). Number of parents that missed work days were found to be comparable in PRE (43.3%) and POST (47.1%) phases (*P*=1.0). Similarly, subjects who missed school/daycare in PRE phase (73%) was comparable with POST phase (71%) (*P*=1.0).

Conclusions: Prompt diagnosis of shigellosis with the FilmArray GI Panel may provide opportunity for prompt antimicrobial therapy and avoid additional visits to providers due to early definitive diagnosis. Laboratory diagnosis of *Shigella* at ED visit has the potential to optimize patient management, and reduce spread of disease.

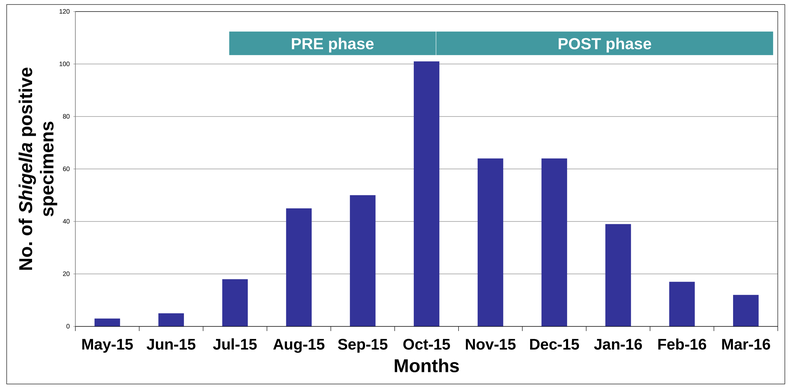
STUDY DESIGN

The GI impact study is a prospective multicenter study evaluating the impact of implementation of FilmArray GI panel on patient management and health outcomes. The sub-study presented here is a part of GI impact study and focuses on evaluating the impact of implementation of FilmArray GI panel during a outbreak situation. Kansas City area experienced a *Shigella* outbreak during 2015-2016. (Figure 1)

- Prospectively enrolled acute gastroenteritis patients <18 years
- Collected stool specimens within 48 hours of enrollment
- Obtained baseline (enrollment day) and day 7-10 questionnaires
- Performed detailed medical chart abstraction
- Compared the patient management and outcome during the two phases of this study. [The study was divided into PRE and POST phases. FilmArray GI panel results were reported to physicians and families only during the POST phase. Physicians ordered standard of care (SOC) culture assay at their discretion.]

Hypothesis: Rapid molecular testing and diagnosis of *Shigella* in an outpatient setting is more likely to result in appropriate therapy and reduce repeat health care encounters compared to culture.

Figure 1. *Shigella* Outbreak; Kansas City 2015-16 : Number of *Shigella* positive specimens from routine standard of care testing



RESULTS

Table 1. Overall No. of subjects in the PRE and POST study phase

No. of Subjects	PRE	POST	Total
Enrolled	139	151	290
Submitted stool specimens	110	119	229
Completed follow-up	125	113	238
Shigella positive (Film array GI panel)	30 (27%)	19 (16%)	49
Reflex culture positive of all reflex cultures performed (GI panel positive)	NA	15 /19	15 /19
Shigella culture positive of all SOC cultures ordered	8 /10	5 /5	12 /15*

* FilmArray GI panel detected *Shigella* in all of the 15 samples submitted for culture

Table 2. *Shigella* positive patient demographics and clinical symptoms

	PRE (n=30)	POST (n=19)	P value
Sex	M:14 F: 16	M: 8 F: 11	0.78
Median Age in months (range)	46 (6-168)	68 (16-180)	0.02
Diarrhea (%)	27 (90%)	19 (100%)	0.27
Vomiting (%)	13 (43.3%)	11 (57.9%)	0.39
Fever (%)	25 (83.3%)	9 (47.4%)	0.01
Diarrheal characteristics/ Stool consistency (%)	Median length: 2 (1-7) days Median no: 5.5 (1-20) Bloody: 6 (22.2%) Watery: 21 (77.8%) Mucous: 12 (44.4%)	Median length: 3(1-7) days Median no: 5 (1-27) Bloody: 7 (36.8%) Watery: 15 (78.9%) Mucous: 6 (31.6%)	0. 34 0.57 0.32 0.74 0.76
Vomit Characteristics	Median length: 2 (1-5) days Median no.: 4 (0-9)	Median length: 2(1-5) days Median no.: 3 (0-8)	0.84 0.10

Table 3. IMPACT variables in the PRE and POST study phase

IMPACT variables	PRE (30)	POST (17)*	*P*- value
Contacted additional providers	6 (5 outpatient, 1 ED)	0	0.07
No. of parents that missed work days	13 (43.3%)	8 (47.1%)	1.0
Average no. of days missed by parents	0.8 (1-4)	1.1 (1-5)	0.4
No. of subjects that missed school/day care	22 (73.3%)	12 (70.6%)	1.0
Average no. of days missed by subjects	2.03 (1-8)	1.94 (1-5)	0.9
Disease spread among family members	7 /133 (5.3%)	4 / 91 (4.4%)	1.0

*Follow up interview completed by 17 of the 19 *Shigella* positive subjects

Table 4. Treatment in the PRE and POST study phase

	PRE (n=30)	POST (n=19)	*P*-value
Azithromycin treatment	6 (20%)	14 (73.7%)	<0.001
Empiric treatment	5 (16.7%)	6 (31.6%)	0.3
Targeted treatment (Culture: PRE; Filmarray: POST)	1 (3.3%)	8 (42.1%)	0.001
Time to Rx-ALL (hrs)	2.31 (1.21-72.32)	6.41 (1.14-52.37)	0.82
Time to Targeted Rx (hrs)	72.32	8.68 (6.37-52.37)	.

Table 5. Factors influencing treatment in the PRE and POST study phase

	PRE (n=30)		POST (n=19)	
	Treated Azithromycin (n=6)	Not Treated Azithromycin (n=24)	Treated Azithromycin (n=14)	Not Treated Azithromycin (n=5)
Time _onset of symptom to ED visit Median (range) days	1.5 (0-2)	1 (0-6)	2(0-6)	3 (1-4)
No. of diarrheal episodes Median (range)	7 (5-13)	5.5 (1-20)	5.5 (1-27)	3 (1-13)
Bloody diarrhea	3	3	7	None
Oral rehydration	1	10	7	5
Co-infections	5:*Shigella* 1: Multiple pathogens	10: *Shigella* 14: Multiple pathogens	11: *Shigella* 3: Multiple pathogens	3: *Shigella* 2: Multiple pathogens

CONCLUSIONS

1. Significant increase (*P* value <0.001) in azithromycin treatment was observed in POST phase.
2. FilmArray GI panel test result led to targeted azithromycin treatment in the POST phase in a timely manner compared to the PRE Phase (p=0.001)
3. A decrease in additional provider visits was observed in POST phase compared to PRE phase (*P* value =0.07)
4. Impact variables such as no. of subjects/parents who missed daycare/school/work days and no. of days missed by subjects/parents were found to be comparable in both phases
5. FilmArray GI panel was found to be more sensitive as compared to culture assay (Table 1)
6. Decision to treat patients with azithromycin in POST phase seemed to be influenced by infection severity (Table 4)

ACKNOWLEDGEMENTS

The data presented here are part of the GI IMPACT study which is funded by NIH/NAID grant R01AI104593 to BioFire Diagnostics with additional funding from BioFire Diagnostics.
Thanks to Ashley Formanek for *Shigella* outbreak data