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An audit of inpatient stool ova and parasite (O&P) testing in a multi-hospital health system

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ABSTRACT

Background & Objectives: Stool ova and parasite (O&P) examinations are routinely ordered initial tests in patients admitted to the hospital with acute diarrhea, despite low test positivity rates. We examined the diagnostic yield of inpatient stool O&P exams and identified risk factors associated with positive tests.

Methods: A retrospective, case-control analysis of inpatients admitted with diarrhea, who underwent O&P examination, was conducted. Clinical and demographic variables of cases were compared with age-and gender-matched controls via uni- and multivariate conditional logistic regression analyses.

Results: The yield of inpatient O&P exams was 2.15% (37/1723). *Blastocystis*spp. represented the most common parasites. All patients with positive tests, excluding *Blastocystis*spp., had at least one of the following risk factors: smoking, prior parasitic disease, HIV-positive status, travel to an endemic area, and institutionalization.

Conclusions: Superfluous inpatient stool O&P exams confer a financial and labor burden to hospital systems. Stool O&P exams should be restricted to individuals admitted to the hospital for <3 days, having diarrhea >7 days and possessing at least one of the following risk factors: smoking, prior parasitic disease, HIV-positive status, travel to an endemic area, and institutionalization. Such selective testing can confer a 51% reduction in testing, costs, and labor.

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1. Introduction

Diarrheal illnesses constitute a major disease burden in the USA (US), with over 179 million cases occurring annually [1,2]. With a growing array of enteric pathogens, matched with increased diagnostic tools available, physicians are faced with the challenge of developing optimal, cost-effective means of diagnosing, managing and preventing diarrheal illnesses.

Currently, over 15 USD billion are expended annually in the US in managing foodborne illnesses, the majority of which present as infectious diarrheas [3]. Although diarrhea may be attributable to bacteria, viruses, or parasites, 90% of the economic burden from these illnesses in the US can be attributed to five pathogens: *Salmonella, Toxoplasma gondii, Listeria monocytogenes, Campylobacter,* and *Norovirus* [3]. Specifically, the prevalence of parasitic disease in hospitalized patients is less than 5%, with the majority of pathogens detected during the first 3 days of hospitalization [4]. Yet, fecal testing for ova and parasites continues to be a popular first-line test in the workup of acute diarrhea in hospitalized patients [5]. Stool ova and parasite studies are expensive, time-consuming, labor-intensive tests requiring a high level of technical expertise. As a result, their excessive employment confers a significant labor and financial burden to both the patient and the institution [6].

The purpose of our study was to examine the diagnostic yield of inpatient stool ova and parasite exams and to identify predictive risk factors associated with positive tests to develop recommendations on appropriate testing.

2. Methods

We analyzed all adult (age ≥18 years) inpatient stool O&P examinations performed between 1 January 2013 and 31 December 2015 at NorthShore University HealthSystem, which is a community-based, four-hospital health network serving over 1.5 million patients in suburban Chicago, Illinois, USA.

Our microbiology laboratory protocols stipulate that multiple stool samples submitted for O&P testing during the same admission are not processed. Furthermore, specimens received from patients hospitalized for over 3 days are not processed. However,

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if the ordering physician contacts the laboratory and makes a request, exceptions can be made to this rule. Of note, our laboratory does not mandate preliminary enzyme immunoassay testing for *Giardia duodenalis, E.histolytica/E.dispar,* or *Cryptosporidium* prior to submitting samples for direct microscopy.

The department of Microbiology's data warehouse system was utilized to extract all inpatient O&P exam data, with corresponding microscopic findings, from the aforementioned period. The data were exported into a secure, limited-access spreadsheet where exams were listed in chronological order.

A positive O&P exam was defined as the identification of potentially pathogenic parasitic organisms via direct microscopy. Tests revealing non-pathogenic commensals were not considered to be positive (Table 1). However, the presence of *Blastocystis*spp., the pathogenicity of which remains controversial, was considered to be a positive outcome in our study if the patient had diarrhea with no other identifiable cause.

In this case-control study, randomly selected age- and gender-matched patients with negative O&Ps served as controls in a 2:1 ratio. We reviewed the electronic medical records of both cases and controls. This included a review of patients' clinical presentation at the time of testing (presence of diarrhea, duration of diarrhea, recent antibiotic use, consumption of suspicious food, animal exposures, etc.), demographic variables (age, gender, and race), past medical history (including history of prior parasitic disease defined as a previous positive O&P test or *Giardia/Cryptosporidium* enzyme immunoassay, chronic liver disease, chronic kidney disease, COPD, congestive heart failure, diabetes, HIV, active malignancy, among others), social history (alcohol consumption, smoking history, sexual history, history of institutionalization, employment in a day care/health facility), medication use (including antibiotics, immunosuppressants, and chemotherapy), travel history (areas endemic for parasitic disease, camping, swimming/drinking unfiltered lake water), blood counts, and exposure risk. This data was logged and stored in a secure spreadsheet.

To determine risk factors associated with positive tests, we compared these variables via univariate conditional logistic regression analyses and calculated odds ratios with their respective confidence intervals. These analyses were carried out using SAS 9.4 (Cary, NC) software.

Risk factors identified were then applied as filters to the inpatient O&P exam database to recalculate and predict the yield, costs, and labor associated with selective, targeted O&P testing across the study period.

Table 1. Non-pathogenic parasites excluded from positive stool O&P results.

Non-pathogenic intestinal parasites
Chilomastix mesnili
Endolimax nana
Entamoeba coli
Entamoeba hartmanni
Entamoeba polecki
Entamoeba gingivalis
Iodamoeba butschlii
Trichomonas hominis

3. Results

A total of 1723 inpatient stool O&P examinations were conducted between 1 January 2013 and 31 December 2015 at our institution. Of these, 37 examinations were positive for potentially pathogenic organisms, resulting in an overall yield of 2.15%. When *Blastocystis* was excluded as a positive test, the yield was 0.29% (5/1723).

The average cost of performing a single O&P exam in our laboratory was estimated at 10.37 USD This included labor and costs associated with direct wet mount, concentration, and permanent-stain smear preparations. Each microscopic examination was estimated to require an average of 8.5 minutes to complete. As a result, total costs of conducting O&P examinations in the in-patient setting, over the 3-year period, amounted to at least 17,868 USD, with an average of 244 hours of labor time being expended to simply examine specimens via microscopy. Thus, the cost per positive test was 482.91 USD and time expended per positive test was 6 h 36 min, compared to 3573.50 USD and 48 h 49 min per test when *Blastocystis*spp. were excluded as positive tests.

Of the positive cases, 51% of the patients were male (n = 19), 59% were Caucasian (n = 22) and the average age was 64.77 ± 21.94 years. The median duration of symptoms for these patients was 5 days (range: 1–90). Additionally, 86.49% of the analyzed population (n = 111) had stool examinations ordered within 3 days of admission to the hospital. All positive cases were identified via a single stool O&P exam.

The most commonly detected parasites were *Blastocystis*spp. (n = 32, 86.49%) and *Cryptosporidium* species (n = 2, 5.41%). *Blastocystis*spp. abundance was further defined semi-quantitatively as rare (one to two parasites per slide), few (one to two parasites per high-power field), moderate (two to five parasites per high-power field), or many (more than five parasites per high-power field). Of the specimens positive for *Blastocystis*, 12.5% had rare (n = 4), 37.5% had few (n = 12), 37.5% had moderate (n = 12) and 12.5% (n = 4) had many organisms on microscopy. Other parasites detected included *Giardia duodenalis* (n = 1, 2.70%), *Microsporidium* species (n = 1, 2.70%), and *Entamoeba histolytica/Entamoeba Dispar* (n = 1, 2.70%).

Comparisons of the clinical variables assessed between cases and age- and gender-matched controls

are seen in Table 2. Univariate analyses revealed prior parasitic disease (p = 0.0030), HIV-positive status (p < 0.0001), smoking history (p = 0.0013), travel to an endemic area (p = 0.0022), and institutionalization (p = 0.0095) as significant risk factors contributing to positive O&P exams. It is pertinent to note that all patients with positive exams, excluding *Blasto cystis*spp., had at least one of these aforementioned risk factors.

Furthermore, after applying filters for history of smoking, prior parasitic disease and HIV-positive status to our exam database, we found that selective testing would have reduced in-patient stool O&P examinations by 50.9%. This would confer cost savings of 9,104.86 USD and reductions of labor time expended of 124 hours and 23 minutes over a 36-month period.

4. Discussion

Our study represents a multi-hospital health system's experience over a 3-year period with regards to in-patient stool O&P testing. A total of 1723 O&P exams were conducted in the in-patient setting with a very low in-patient yield of at most 2.15%, congruent with those reported by other medical centers in the US and Canada [5,7]. These values reaffirm the scarcity of enteric parasitic disease in North America. Furth ermore, with costs per positive exam approaching 3600 USD and time expended per positive test approaching 49 hours, it is evident that there is superfluous testing of stool for ova and parasites and that current practices pose an excessive financial and labor burden.

The Infectious Diseases Society of America (IDSA) recommends O&P examination of stool specimens in patients with diarrhea lasting greater than 7 days, especially if they are immunocompromised [1]. In the in-patient setting, these tests should be conducted within the first 3 days of admission [1]. The majority of in-patient testing at our institution was conducted in a timely fashion, congruent with these recommendations. A cut-off of 7 days for symptom duration did not achieve statistical significance in our study as a predictor of positive O&P exams. The limitations in determining the precise duration of symptoms prior to admission via retrospective chart review may explain this finding.

All positive O&P specimens in our study were identified via a single examination, reaffirming that multiple in-patient exams may not be necessary for the successful identification of parasitic causes of diarrhea [8]. O&P exams at our institution include

Table 2. Comparison of demographic and clinical variables between cases and age- and gender-matched controls.

	CASES (n = 37)		CONTROLS (n = 74)		
	Mean±sd	Median(range)	Mean±sd	Median(range)	p value
Age (years)	64.77 ± 21.94	67.41(17.55–98.27)	64.24 ± 21.49	65(19–98)	0.8389
Duration of Symptoms (days)	10.74 ± 16.59	5(1–90)	6.54 ± 9.9	3(0–60)	**0.0406**
Duration between Admission and Testing (days)	1.97 ± 2.52	1(0–11)	1.64 ± 2.38)	1(0–14	0.5396
	n(%)		**n(%)**		
Prior Parasitic Disease	5(13.89)		0(0)		**0.0031**
Chronic Liver Disease	3(8.11)		2(2.7)		0.3310
Congestive Heart Failure	4(10.81)		18(24.32)		0.0923
Chronic Kidney Disease	9(24.32)		14(18.92)		0.5077
COPD	2(5.41)		10(13.51)		0.3309
Diabetes	7(18.92)		10(13.51)		0.4560
Inflammatory Bowel Disease	5(13.51)		12(16.22)		0.7094
Chronic Hepatitis	0(0)		0(0)		n/a
HIV-Positive Status	5(38.46)		1(1.75)		**<0.001**
Congenital Immunodeficiency Syndrome	0(0)		0(0)		n/a
History of Malignancy	10(27.03)		14(18.92)		0.3280
Active Treatment for Malignancy	5(13.51)		7(9.46)		0.5298
Immunosuppressant Use	8(21.62)		6(8.11)		0.0663
Steroid Use	3(8.11)		15(20.27)		0.1013
Recent Antibiotics (within 2 weeks of symptoms)	14(37.84)		25(33.78)		0.6732
Proton Pump Inhibitor Use	8(21.62)		29(39.19)		0.0642
Use of Biological Agents	0(0)		5(6.76)		0.1672
History of Smoking	21(56.76)		19(25.68)		**0.0013**
Excessive Alcohol Consumption	10(27.03)		23(31.08)		0.6596
Recent Travel to an Endemic Area	8(21.62)		2(2.7)		**0.0022**
Immigrant Status	6(18.18)		6(8.11)		0.1826
Consumption of Exotic or Spoiled food	5(13.51)		4(5.41)		0.1570
Day-Care Exposure	0(0)		0(0)		n/a
Institutionalized	12(16.22)		0(0)		**0.0095**
Cattery or Kennel Exposure	0(0)		0(0)		n/a
Male Gender	19(51.35)		38(51.35)		1.0000
Symptoms > 7 days (days)	13(37.14)		17(22.97)		0.1220
Elevated Eosinophil Counts (>5%)	3(8.33)		7(10.14)		1.0000

n = number of subjects; *sd* = standard deviation.

evaluation for helminthic species. Notably, no helminths were identified during the studied period, confirming that intestinal parasitic infections in the US are largely attributable to protozoan species [9].

As seen in our study, *Blastocystis*spp. represents the most frequently isolated parasites on O&P exams in the US. However, the commonest parasitic causes of infectious diarrhea in the US are *Giardia duodenalis, Entamoeba histolytica/Entamoeba dispar,* and *Cryptosporidium* species [7,9–11]. There is currently a debate regarding whether *Blastocystis*spp. are intestinal commensals, true pathogens, or markers of dysbiosis. There are few observational studies and animal models suggesting a direct relationship between *Blastocystis* infection and disease [12–14]. On the contrary, several studies have shown no correlation between *Blastocystis*spp. and symptoms [15,16]. Interestingly, *Blastocystis*spp. has been found in stool samples in association with other potential pathogens, leading some reports to infer that in patients with *Blastocystis*spp. in their stools, another pathogen may be identified on further examination. In our study, across the entire 3-year duration, only one stool sample revealed a second identifiable organism in addition to *Blastocystis*spp. and that too of *Endolimax nana*, a non-pathogenic intestinal commensal. Given conflicting studies with regards to its pathogenicity, there are currently no consensus guidelines on the treatment of *Blastocystis* infection. Some authors assert that treatment can be considered if symptoms are present and if more than 5 cysts per high-power field are seen on stool microscopy [17]. It should be noted however that the association between parasite concentration and symptoms is also under contention [18–20].

Cost-effective, best practice advisory guidelines establishing criteria for conducting stool O&P exams can be developed based on the identification of predictive risk factors. In the literature, these risk factors include: Diarrhea lasting more than 7 days, previous history of parasitic disease, immunocompromised status, day-care attendees/employees, institutionalization, consumption of untreated lake or river water, travel to an endemic area, men who have sex with men and exposure to young animals in kennels or catteries [7].

While our findings allow us to validate recent travel to an endemic area, prior parasitic disease, HIV-positive status and institutionalization as significant risk factors for positive stool O&P exams, we also raise a novel consideration. We found smoking to be a strong, predictive risk factor for positive O&P exams. Interestingly, in vitro studies have postulated that tobacco and cigarette smoke exposure may confer anti-helminthic properties [21,22]. On the other hand, cigarette smoking has been associated with increased IL-4 and IgE levels, which promote Th2 cell differentiation, while blunting Th1 activity – a key process in the pathogenicity conferred by helminths [23]. Further studies are thus necessary to clearly elucidate the effects of cigarette smoking and nicotine exposure on risk for parasitic infection.

Given that at least one of the aforementioned significant risk factors was present in all the positive O&P tests in our study, we postulated that revision of laboratory criteria to mandate the presence of history of smoking, prior parasitic disease, HIV-positive status, travel to an endemic area, or institutionalization could mitigate unnecessary testing and thereby improve cost-effective laboratory use. We were able to validate this inference using our laboratory database, which predicted a decrease in inpatient stool O&P examinations by 50.9%.

The labor-intensive nature of the traditional O&P exam, requiring a skilled technician, has led to the development of alternative methods of detecting fecal parasites. Direct fluorescent antibody tests, enzyme immunoassays, and immunochromatographic lateral flow assays, while more sensitive and specific than O&P exams, are available for only a limited number of organisms and are generally more expensive than direct microscopic examination [24]. As testing methods advance, laboratories will need to re-evaluate the availability of equipment, skill level of technicians, testing volume, test performance characteristics, specimen collection requirements and kit costs when deciding on the most ideal method to detect ova and parasites [24].

Our study has several limitations, the first of which pertains to the retrospective, single-institution design. Although we observed a sizable, consecutive sample in a large hospital network, our study took place in a limited geographic area and there were a small number of positive specimens. Furthermore, given that identification of risk factors was largely dependent on patient reporting and physician documentation, it is possible that patients under-reported high-risk behaviors known to raise the risk of parasitic gastroenteritis or physicians may not have inputted information regarding potential contributory risk factors into the patients' charts. Nevertheless, a thorough chart review of all patients' encounters was conducted in order to offset this inherent limitation. Lastly, while attempting to calculate reductions in stool O&P testing with the application of selective testing criteria, we were unable to include travel to an endemic area and institutionalization as filters as they could not be automatically extracted from the database.

We conclude that the prevalence of gastrointestinal parasitic disease in hospitalized patients is very low and that current patterns of superfluous stool O&P testing burden both patients and the institution. In addition, we agree that the highest yield of inpatient O&P exams is within the first 3 days of admission and posit that a single examination may be sufficient for diagnosis. The IDSA's recommendations to test individuals with diarrhea for more than

7 days, especially if immunocompromised, in addition to the '3-day rule' proposed by multiple groups, are not inclusive of all the risk factors for parasitic disease. To this end, our study adds to the literature by identifying the history of smoking, prior parasitic disease, HIV-positive status, travel to an endemic area, and institutionalization as significant risk factors of a positive O&P exam. Furthermore, we found that restricting in-patient stool O&P testing to patients with these significant risk factors can reduce the number of tests conducted and by extension, costs, and expended labor time, by up to 51%, while successfully identifying all positive specimens. Thus, we propose that laboratory criteria for ova and parasite testing be amended to necessitate the presence of at least one of the aforementioned risk factors, in addition to symptom duration greater than 7 days and specimen collection within 3 days of admission.

We plan on validating these inferences via a prospective study that will audit stool O&P testing after establishment of a best practice alert in our electronic medical record system. These pop-up alerts will limit the ordering of in-patient O&P exams to those patients with (1) diarrhea for over 7 days; (2) specimens collected within the first 3 days of admission; and (3) at least one of the following risk factors: history of smoking, prior parasitic disease, HIV-positive status, travel to an endemic area, and institutionalization. If specimens are rejected based on these criteria, physicians will have the opportunity to contact the laboratory directly to justify testing.

Disclosure statement

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Prior presentations

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