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Muhammad Mehmood Riaz
Aga Khan University

Muhammad Junaid Patel
Aga Khan University

Muhammad Shoaib Khan
Aga Khan University

Muhammad Ali Anwar
Aga Khan University

Muhammad Tariq
Aga Khan University

See next page for additional authors

Authors
Muhammad Mehmood Riaz, Muhammad Junaid Patel, Muhammad Shoaib Khan, Muhammad Ali Anwar, Muhammad Tariq, Harith Hilal, Safia Awan, and Shahzad Razi

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Muhammad Mehmood Riaz,[1] Muhammad Junaid Patel,[2] Muhammad Shoaib Khan,[3] Muhammad Ali Anwar,[4] Muhammad Tariq,[5] Harith Hilal,[6] Safia Awan,[7] Shahzad Razi[8]

Department of Medicine,[1,2,5] Research Assistant,[3,4,6-8] Aga Khan University, Karachi, Pakistan.

Abstract

Objective: To identify the presenting features and spectrum of pathogens in adult patients with acute diarrhoea and to determine the predictors of stool culture positivity.

Methods: A descriptive study was conducted in a tertiary care hospital from April 1, 2005 to March 31, 2006. Medical records of all consecutive adult patients with history of acute diarrhoea were reviewed between June 2006 to December 2006 for clinical characteristics and laboratory investigations.

Results: A total of 454 patients were admitted from April 1, 2005 to March 31, 2006. Stool cultures were performed in 233 (50%) patients, 96 (42%) had positive results. Patients with positive stool culture compared to a negative culture were found to have a younger mean age (43 vs. 53), greater number of unformed stools (16 vs. 11) and low serum bicarbonate level (16 vs. 20). Vibrio cholerae (86%) was found to be the most prevalent organism followed by Salmonella spp (6%), Campylobacter spp (5.2%), Shigella spp (2%). Ciprofloxacin was given to 97% patients along with fluid administration, and 78% were found to be resistant to quinolones. Most patients recovered before the finalized stool culture results.

Conclusion: Careful selection of the patients based on their clinical presentation and initial laboratory work up can help to decide ordering of stool culture in adults with diarrhoea. Fluid resuscitation remains the main stay of treatment.

Keywords: Gastroenteritis, Diarrhoea, Bicarbonate, Predictors of stool culture (JPMA 62: 20; 2012).

Introduction

Acute diarrhoea in adults is one of the most common diagnoses in general practice,[1] and is responsible for considerable morbidity and mortality around the world.[2] In industrialized countries, the incidence of acute diarrhoea is estimated to average 0.5-2 episodes per person per year, and the corresponding figure could be much higher in developing and underdeveloped countries. The data from Pakistan is lacking particularly for adult population. Despite reduction in mortality worldwide, diarrhoea still accounts for more than 2 million deaths[3] annually and is associated with impaired physical and cognitive development in resource-limited countries.[4]

Thorough clinical evaluation of a patient who presents with acute diarrhoea is essential in order to guide a cost effective and evidence based approach to initial diagnostic testing and therapy. The initial clinical evaluation of the patient with acute diarrhoea should focus on assessment of the severity of illness, need for rehydration, and the identification of likely causative factors from clinical history and examination. Most practitioners believe that the impact of stool culture investigations on the treatment of individual patients is most often minimal. However, to our knowledge, this has not been formally studied and quantified in indexed literature. In six countries, studies conducted between 1980 and 1997, the diagnostic yield of stool cultures ranged from 1.5 to 5.6 percent.[5] The estimated cost of Rs 600-800 for each stool culture investigation can be reduced through improved selection of the patients and guidelines for the appropriate use of this lab investigation for local setting need to be developed.

Therefore, the objective of this study were to investigate the etiology and characteristics of community acquired acute gastroenteritis requiring hospitalization in adults in a tertiary hospital and to determine the predictors of stool culture positivity.

Materials and Methods

A review of charts of patients admitted with acute diarrhoea from April 1, 2005 to March 31, 2006, at the Medicine department of the Aga Khan University Hospital Karachi, Pakistan was undertaken. The time frame of the data documentation was from June 2006 to December 2006. Cases were identified through the ICD-9-CM coding system using the key words "acute gastroenteritis" and clinical records traced. The inclusion criteria for the study were patients' age ≥16 years, presentation with symptoms of acute diarrhoea, treated as inpatients in the medical ward and having stool culture and sensitivity done. A comprehensive tool was developed and it was ensured that all data was correctly filled. Demographic features (for example, age, sex, date of presentation, and history of recent travel); presenting symptoms (body temperature, passage of bloody stools, number of stools per day, and the duration of illness, abdominal pain, and vomiting); laboratory record of the specific pathogens identified and essential lab parameters were entered into a database. Data describing the presenting clinical features of each patient were recorded according to the definitions listed below:

Operational definition of clinical parameters obtained from record review

Highest body temperature

The highest oral temperature recorded during the stay in hospital.

Bloody diarrhoea

Either suspected by history from patient, or confirmed by inspection of stool, and not attributable to local anorectal bleeding.

Duration of diarrhoea (days)

The duration of diarrhoea from onset of illness to discharge from ward.

Number of unformed stools per day

Can be assessed by history (maximum number per day) on presentation, or recorded in the unit charts during the stay in ward, whichever is higher in number.

Duration of abdominal pain (in days)

The duration of abdominal pain from onset of diarrhoea to recovery.

Duration of vomiting (in days)

The duration of vomiting from onset of diarrhoea to the completion of stay in hospital.

Stool Cultures:

Stool samples were investigated for the presence of Salmonella spp, Shigella spp, Campylobacter spp, and Vibrio cholerae according to standard laboratory procedures, followed by antibiotic susceptibility testing. Standard solid media, i.e. MacConkey, xylose lysine deoxycholate, bismuth sulfite and Salmonella-Shigella agars, as well as selenite and tetrathionate (Preuss) were used to detect Salmonella, Shigella and Vibrio species. In addition, Skirrow agar supplemented with 10% sheep blood was inoculated for the detection of Campylobacter species. The turnaround time for stool culture results was four days. Any change in management based on culture report was recorded from the case notes and reconfirmed from pharmacy records. At the time of the study, no policy was in place in our department as to which patients

should have stool culture investigation done.

Statistical Analysis:

All analyses were conducted by using the Statistical package for social science SPSS (Release 16.0, standard version, copyright © SPSS; 1989-02). Categorical variables were presented as percentages and continuous variables were presented as mean followed by standard deviation. In univariate analysis, differences in proportions were assessed by using the Chi-square test. For contrasts of continuous variables, independent t-test was used to assess the difference among stool culture positive and negative groups. To assess univariate associations between the positive stool culture and clinical features, Odds Ratio (OR) and their 95% confidence intervals (CIs) were computed by logistic regression analysis. All significant factors on univariate analysis were considered for inclusion in the multivariable logistic model. All p-values were two sided and considered as statistically significant if ≥ 0.05.

Results

During the defined study period, 454 adult patients were admitted to the medical ward with acute gastroenteritis. Two hundred and thirty three patients met inclusion criteria. Out of those, 117 (50%) were male and 116 (49%) were female. Stool culture was found positive for an organism in 99 (42%) cases. V. cholerae was found to be the most frequently detected pathogen. Demographics, clinical features and laboratory values for various pathogens identified, are shown in Table-1. The mean age of patients with positive culture was 43 ± 17.3 years while that of negative culture patients was 53 ± 17 years. On univariate logistic regression, it was identified that younger patients were more likely to have positive stool cultures. Likewise, it was also noticed that positive stool culture cases were more likely to present with vomiting, greater number of unformed stools per day, shorter mean duration of diarrhoea, higher creatinine level, lower bicarbonate level and presence of faecal leukocytes. However, they were less likely to have frank blood or Red Blood Cells (RBCs) present in their stool samples. Sixteen patients had acute renal failure due to severe dehydration, out of which nine were culture positive. No marked difference was noted in the serum electrolytes of both groups. Gender was found to have no association with the outcome of stool culture results. Average duration of hospitalization (2.8 vs 2.4 ± 1.4 days) was almost similar for both positive and negative stool culture groups. Almost half of the patients (45%) having positive stool cultures had no abdominal pain on initial presentation. Therapeutic management changed only in three (3%) patients after the stool culture results were available. It remained unchanged in rest of the 94 cases (97%). For detailed comparison of demographic and clinical features of culture positive and culture negative patients, refer to Table-2. When all clinical and laboratory parameters that were significantly associated with positive stool cultures were considered for inclusion in the multivariate logistic model; only younger age [adjusted Odds Ratio (aOR): 0.96, 95% CI: 0.94-0.98], number of unformed stools per day [adjusted Odds Ratio (aOR): 1.05, 95% CI: 1.004-1.09] and low bicarbonate level [adjusted Odds Ratio (aOR): 0.87, 95% CI: 0.80-0.95] remained significantly associated with positive stool culture, after adjusting for WBC and RBC.

In Campylobacter spp positive patients, mean duration of diarrhoea was almost 5 days indicating a relatively severe illness. They had fewer numbers of loose stools per day. None of the cases had blood or RBCs present in their stool samples. Salmonella spp were noted to have a predilection for older population. Shigella spp positive cases presented with bloody diarrhoea and had greater number of stools per day, i.e., mean 22 stools per day. The organism was sensitive to quinolones and ceftriaxone. Mean duration of diarrhoea was more than 4 days. V. cholerae positive patients had mean duration of diarrhoea of more than 3 days. Most of the cases were

Table-1: Demographics, clinical features & laboratory parameters of patients with positive stool culture according to pathogens isolated.

Characteristics	Positive Stool Mean ± SD	Salmonella Mean ± SD	Shigella Mean ± SD	Campylobacter Mean ± SD	Vibrio Cholera Mean ± SD
Total Number (%)	96 ± 42	6 ± 6.2	2 ± 2.1	5 ± 5.2	83 ± 85.6
Clinical Features					
Mean highest body temperature	37.7°C ± 0.77	38.5°C ±0.78	38.1°C ±0.4	37.3°C± 0.46	37.7°C ±0.7
Mean duration of diarrhoea in days	3.65 ± 1.78	4.3 ± 1.5	4.5 ± 3.5	4.8 ± 4.6	3.5 ± 1.48
Mean number of unformed stools per day	15.77 ± 10	11.3 ± 6.5	22 ± 25.4	9.7 ± 4.5	16.5 ± 9.8
Mean duration of abdominal pain in days	1.27 ± 1.6	1.3 ± 1.7	0.5 ± 0.7	0.2 ± 0.4	1.3 ± 1.7
Mean duration of vomiting in days	2.12 ± 1.4	3.6 ± 1.2	0.5 ± 0.7	2.6 ± 3.1	2 ± 1.2
Laboratory Parameters					
Mean Potassium level mmol/l	3.7 ± 0.6	3.86 ± 0.8	3.6 ± 0.1	3.3 ± 0.6	3.7 ± 0.6
Mean Sodium level mmol/l	135.7 ± 3.7	131.6 ± 2.0	135.5 ± 2.1	134.8 ± 1.7	136.1 ± 3.6
Mean Creatinine level mg/dl	2.1 ± 2.3	2.2 ± 1.0	1.05 ± 0.3	1.5 ± 0.7	2.1 ± 2.5
Mean BUN level mg/dl	20.2 ± 10.2	33.8 ± 10.6	18.0 ± 15.5	13.4 ± 9.1	19.4 ± 9.3
Mean Bicarbonate level mmol/l	15.9 ± 4.4	17.6 ± 4.5	13.8 ± (--)	17.6 ± 4.2	15.8 ± 4.3

SD = Standard deviation.

Table-2: Features associated with positive and negative stool cultures.

Demographics, Clinical features & Lab parameters	Positive stool Mean ± SD	Negative stool Mean ± SD	Odds Ratio (95% CI)	p-value
Demographics				
Age (years)	42.5 ± 17.57	52.9 ± 17.4	0.96 (0.95-0.98)	<0.001
Clinical Features				
Mean duration of hospitalization (days)	3.0 ± 1.63	3.1 ± 3.4	0.96 (0.88- 1.05)	0.429
Mean highest body temperature (°C)	37.7 ± 0.77	37.8 ± 0.8	0.80 (0.57-1.12)	0.19
Mean duration of diarrhoea (days)	3.6 ± 1.79	5.3 ± 7.1	0.91 (0.83-0.99)	0.03
Mean number of unformed stools (day)	15.7 ± 10	10.5 ± 7.0	1.07 (1.03-1.12)	<0.001
Mean duration of abdominal pain (days)	1.27 ± 1.66	1.9 ± 3.3	1.10 (0.98-1.24)	0.88
Mean duration of vomiting (days)	2.1 ± 1.4	2.3 ± 3.3	0.97 (0.88-1.07)	0.59
Laboratory Parameters				
Mean Potassium level mmol/l	3.7 ± 0.6	3.7 ± 0.7	0.91 (0.62-1.34)	0.663
Mean Sodium level mmol/l	135.7 ± 3.7	135.3 ± 5.9	1.01 (0.96-1.06)	0.58
Mean Creatinine level mg/dl	2.1 ± 2.3	1.4 ± 1.19	1.45 (1.12-1.88)	0.004
Mean BUN level mg/dl	20.2 ±10.2	19.1 ±13.1	1.008 (0.98-1.03)	0.507
Mean Bicarbonate level mmol/l	15.9 ±4.4	20.1 ±5.0	0.83 (0.78-0.89)	<0.001

sensitive to ampicilin and tetracycline (87%) while resistant to quinolones and cephalosporins. Overall susceptibility of organisms to quinolone therapy was quite low (22%).

Discussion

Stool culture is a frequently ordered laboratory investigation in diarrhoeal illness but its significance has been questioned; mainly because of its low yield. In various studies the reported yield of stool culture ranged from 2% to 6.4%.[6,7] Most of the cases require no change of treatment after the test results are obtained.[8] In our study, we observed that stool cultures were requested in almost half of the cases of acute diarrhoea and stool culture positivity was around 42%. This is a relatively good yield, but notably, 98% of patients recovered by the time culture results were available. These findings necessitate looking for better clinical predictors of positive stool culture for more selected ordering of this investigation. Literature review revealed that there is no single agreed upon criteria of predicting positive stool culture. The American College of Gastroenterology (ACG) recommends that stool cultures be obtained in the presence of severe diarrhoea (>6 times in a 24 hour period), a temperature of >38.5°C (orally), passage of bloody stools, or persistent diarrhoea (>3 days).[9] How precisely these parameters help in identifying culture positive cases needs to be analyzed for local settings. Moreover, ACG does not advocate these guidelines to be the only acceptable approach and emphasizes upon its flexibility according to regional experiences.[9]

The identification of clinical predictors of positive stool culture will help the physician in determining the necessity for stool requests. Our results indicated, severity of diarrhoea (measured by total number of stools per day) is an important physical indicator of stool culture positivity. This finding is consistent with that of previous studies.[10-12] However; contrasting evidence exists regarding duration of diarrhoea. Koplan et al[8] and our results associate it with positive stool culture while Chan SS et al[10] report longer duration of diarrhoea in patients with negative stool culture. Many researchers have found higher body temperature in patients with positive stool cultures,[8,10,13] however; our findings did not support this. Previous studies have also shown that blood in stool, whether it is occult or gross, increases the likelihood of obtaining positive stool culture.[8] That was not the case in our study. With regard to the predictive value of faecal leukocytes, besides Koplan et al[8] most of the studies found it to be the best screening tool and strongly associated with culture positivity both in adult[14,15] and paediatric[9,10] patients. Based on the above discussion, it seems that there is no single agreed upon physical or laboratory parameter of stool culture positivity and predictors tend to vary across regions.

Commonly encountered etiologies of Acute Gastroenteritis (AGE) tend to vary geographically; as Campylobacter spp found to be the most frequently cited etiology of AGE in the literature from the industrialized nations;[15-17] whereas, Cholera continues to pose a threat in the underdeveloped Asian[18,19] and African[20] countries and is recognized as one of the most commonly detected bacterial species causing AGE in Pakistan.[18,19] Both environmental and patient related factors may contribute to enhanced cholera vulnerability. Studies have found decreased gastric acid secretion to be an important explanation of enhanced cholera predisposition[21] yet numerous environmental factors cannot be underestimated. In this study almost 86% cholera cases exhibited WBCs in their stools; however, this finding seems quite unusual for a toxin induced diarrhoeal illness like cholera. Review of literature revealed that O1 strain of V. cholerae has been associated with WBCs in the stool of those infected with this specific organism. Several studies have shown Vibrio Cholerae O1 to be the causative agent of

diarrhoea in this region of the world.[22-24]

High proportion of cholera among culture positive cases warrants the use of antibiotics that have been found exceedingly sensitive against a specific organism according to the local or regional laboratory pathogen susceptibility report. Ampicilin and tetracycline seem promising instead of quinolone from our study results. Although fluid replacement is the main stay of treatment in acute diarrhoea, thoughtful selection of antibiotics may play a part in the rapid recovery, shorter hospital stay and hence the cost of treatment of adult patients with diarrhoea. Our study has identified several variables (younger age, vomiting, greater number of unformed stools per day, shorter mean duration of diarrhoea, higher creatinine level, lower bicarbonate level and presence of faecal leukocytes) that may be predictive of positive stool culture in adult patients. Contrary to the belief, we found that neither high grade temperature nor blood in stool was associated with positive stool culture. Recently, a rapid laboratory system (real time PCR) has been developed and evaluated that can simultaneously identify major diarrhoeagenic bacteria including Salmonella enterica, Vibrio parahaemolyticus, Campylobacter jejuni and Shiga toxin-producing E. coli, in stool specimens.[25] Because of its insensitivity for many organisms and poor selection of cases for testing, routine stool culture has been one of the costly and ineffective microbiological tests. Future investigations should include more robust methods of direct identification of bacteria in stool specimens like the real time PCR so that they can be evaluated for and the cost-effective utilization of this emerging technique in our setting.

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