Bacterial Pathogens Causing Severe Acute Watery Diarrhea During a Summer Month in a Tertiary Care Setting, Islamabad

Umbreen Akhtar[1], Nabeel Muzaffar Syed[1], Iftikhar Ahmed Malik[1], Mehdi Hassan Naqvi[1], Junaid A. Bhatti[2]

Federal Government Poly Clinic, Post Graduate Medical Institute, Islamabad[1],
Public Health Solutions Pakistan (Pvt.) Limited, Lahore[2].

Introduction

Acute severe watery diarrhea is a major public health problem globally[1]. An estimated 1.5 billion diarrheal episodes lead to about 5% of the disability adjusted life years loss annually worldwide[1,2]. Causes of acute severe watery diarrhoea are divided into bacterial, viral and parasitic and their distribution varies in developed and developing countries[2]. In developing countries bacterial and parasitic agents such as *vibrio cholera* (*V.* cholera), *salmonella, shigella* etc. are frequently observed[2]. These causative agents are mostly water and/or food borne, and frequently lead to epidemic outbreaks[1,2]. Prevention of these agents relies on following hand and food hygiene along with surveillance of causative agents. Unfortunately the reporting mechanisms often work ineffectively in developing Countries[1,3].

Diarrheal diseases are frequent in Pakistan claiming about 118 000 lives each year, most of which are children <5 years[3] living in rural communities[3-5]. It was often observed that adult urban and suburban dwellers also face diarrheal episodes, whose severity could be reciprocated from the admissions in Emergency Department and in the hospitals[6-11]. Systematic examination of care provided with respect to causative agents however, was rarely attempted previously[5]. Such understandings could be useful in prioritizing treatments in a healthcare system with limited resources. Similarly, highlighting factors associated with these cases could be useful in advocating preventive interventions against potential threats. This study aimed to assess causative pathogen as well as factors associated with acute severe watery diarrhea in Pakistan.

Corresponding Author:
Umbreen Akhtar
Federal Government Poly Clinic
Post Graduate Medical Institute
Islamabad.
Email: umbreen.akhtar@yahoo.com

Patients, Methods and Results

The study setting was the Emergency Department, the Department of Medicine and the Medical Intensive Care Unit (ICU) of Federal Government Poly Clinic Hospital, Islamabad from June 15 to July 14, 2011. All patients above 15 years of age who presented with signs and symptoms of acute severe watery diarrhea in emergency department were included in the study. Acute sever watery diarrhoea was defined as any patient with stool frequency more than 5 per day starting within last 48 hours with signs of dehydration or hemodynamic instability (i.e. systolic blood pressure <100mmHg). All patients with coexisting morbidities and pregnant females were included as well. Because of huge load of patients in the study period and due to resource limitations, stool samples of only every third case were examined and sent for culture of *salmonella,shigella* and *vibrio cholera.*

After inclusion, stool samples were collected in sterile plastic bottles and a sterile swab was dipped in each sample. Both the bottle and the swab were labelled and stored in a box at room temperature until they were delivered to the Microbiology Department, National Institute of Health, Islamabad, Pakistan, where routine stool examination for ova and cysts was performed while, the swab was used to culture for *salmonella, shigella* and *V. cholera*. Antibiotic sensitivity was also performed for the positive cultures. Samples collected in morning were sent on the same day and the evening or night samples were sent the next morning. In some cases, samples were collected after the first dose of antibiotic therapy. Cases requiring in-patient care were admitted to the Department of Medicine or the medical ICU as necessary.

The standard treatment for all cases was fluid and electrolyte balance along with usage of parenteral Mertronidazole in severe cases. The symptoms, signs, laboratory results, antibiotics used as well as the disease outcome in terms of complications, hospital stay and discharge were recorded on a proforma.

Umbreen Akhtar, Nabeel Muzaffar Syed, Iftikhar Ahmed Malik, Mehdi Hassan Naqvi, Junaid A. Bhatti

The results of the stool cultures and routine examinations received after 48-72 hours were transcribed as well and antibiotics adjusted accordingly.

The cases with positive and negative stool cultures were compared by computing means with standard deviations and percentages where applicable. The geographical disposition of cases with positive culture was mapped to assess proximity between cases with the same serotype.

A total of 94 acute severe watery diarrhea cases presented to the Emergency Department with slightly more females (55.3%). Mean age of cases was 37.4 years; 31.9% cases required admission for ≥24 hours. Cases were equally distributed between urban and suburban areas.

As every 3rd stool was sent for culture and sensitivity, therefore, out of 29 stool samples cultured; 16 yielded growth of *V. cholerae*; while 13 samples did not yield any growth of *salmonella, shigella* or *vibrio*. Ova and cysts were not seen on microscopy in any case. Of those found positive for *V. cholerae*, 13 were serotype Ogawa and 3 were Inaba.

Figure-1 showed that cholera cases were equally distributed between urban and suburban areas with evident proximity. All three patients with serotype Inaba were suburban dwellers (Bhara Kahu area). Positive stool culture was higher in those aged >45 years (56.2% vs. 15.4%) and female gender (43.8% vs. 7.7%). Cases with positive cultures had more severe diarrhoea of almost 30 stools a day as compared to 18 stools a day in those where culture was negative. Culture positive cases had similar symptoms in other family members (62.5% vs. 30.8%), low urine output and drowsiness but none of them developed fever or bloody diarrhea (Table-1). No differences in the blood complete picture, liver function tests or electrolyte levels were found between positive and negative culture cases.

Four patients were discharged after treatment from the Emergency Department whereas 20 were admitted in the Department of Medicine and 5 in the Medical Intensive Care Unit. Four of of the 5 admitted in medical ICU also had *V. cholerae*. Overall, eleven cases developed serious medical complications which included acute renal failure (8 cases) while cardiovascular shock, hypokalemic paralysis and Guillain-Barré syndrome (GBS) were also seen. A 75 year old female with pre-existing ischemic heart disease died while undergoing treatment. Seven cases with medical complications as well as the one reported death had positive stool cultures. The median length of hospital stay for cases with positive cultures was longer than those of negative cultures (5 vs. 2 days). The longest hospital stay (21 days) was for the case with hypokalemic paralysis.

Table 1: Comparison of culture negative and culture positive patients, Federal Government Polyclinic, Islamabad (Jun-Jul 2011).

	Culture negative N=13 % or mean	Culture positive* N=16 % or mean
Age (in years)		
- 15-25	61.5	31.2
- 26-45	23.1	12.5
- >45	15.4	56.2
Gender		
- Male	92.3	56.2
- Female	7.7	43.8
Signs & symptoms		
- Stool frequency per day (SD)†	18.1 (15.4)	30.9 (11.4)
- Decreased urine output	15.4	43.8
- Drowsiness	30.8	62.5
- Fever	23.1	0.0
- Bloody stools	30.8	0.0
Symptoms in other family members	30.8	62.5
Stool examination		
- Pus cells	46.2	43.8
- Ova/cysts	0	0
- Red Blood Cells	30.8	6.2
Complications		
- Acute renal failure	23.1	31.2
- Other‡	7.7	12.4
Outcome		
- Discharged from ED after >24hrs	7.7	18.8
- Admitted to medical ward	84.6	56.2
- Admitted to intensive care unit	7.7	25.0
- Deaths	0	6.3(n=1)
Hospital stay in days (Median)	2	5

* All were positive for *Vibrio cholerae*
† Standard Deviation is given in brackets
‡ One case each developed cardiovascular shock, hypokalemic paralysis and Guillain-Barré syndrome (GBS)

Table 2: Antibiotic Sensitivity of *Vibrio 9holera* serotypes Ogawa and Inaba.

	Ogawa serotype (N=13)	Inaba serotype (N=3)
Ampicillin	Sensitive	Sensitive
Chloramphenicol	Sensitive	Sensitive
Ciprofloxacin	Sensitive	Sensitive
Doxycycline	Sensitive	Sensitive
Erythromycin	Sensitive	Sensitive
Nalidixic Acid	Resistant	Resistant
Metronidazole	Resistant	Resistant
Co-trimaxazol	Resistant	Resistant
Tetracycline	Resistant	Intermediate

Both serotypes (Ogawa and Inaba) were resistant to Cotrimoxazole, Tetracycline, Nalidixic acid and Metronidazole (Table-2), although 87.5% of these patients received metronidazole empirically.

Comments

This study showed that one third of the acute severe watery diarrhea cases admitted in the Emergency Department had cholera infection.

The endemicity and re-emergence of Cholera in Pakistan and India had been reported in recent studies[7-11]. A previous study showed that *V. cholerae* was reported in one of ten cases aged in their early 20s[8]. This study indicated that adult cases despite being well-informed about hygiene practices were also vulnerable to Cholera[9]. Interestingly, distribution of Cholera did not differ between urban and suburban areas of Islamabad, the capital territory which has relatively better healthcare and sanitation resources. Therefore, the potential risk of epidemic outbreaks could not be neglected in Pakistan and other regional countries[7,9]. Our findings showed that three of five acute severe watery diarrhea cases reported to be in contact with a family member with similar symptoms which again reiterated the epidemic potential of cholera in the selected setting[9-11]. Although, vaccinations are available for both of the identified serotypes[9]. Currently, such vaccination programs are not being considered but findings were suggestive that emergency vaccination plans should be in place if Cholera posed threat at a larger level in the future along with strengthening of ongoing health awareness campaigns and overall sanitation[3,9].

The present study also has implications on clinical management of these cases. Stool culture and sensitivity is not routinely performed even in tertiary care settings and antibiotics are prescribed almost immediately without following standard protocols for antibiotic use[6,7]. A previous study from Pakistan showed that Inaba serotype outnumbered Ogawa serotype[8] which is contrary to our findings. Furthermore, a similar study[8] suggested that both strains were sensitive to Tetracycline[8] but our study showed that both serotypes were intermediately sensitive or resistant to Tetracycline, which was one of the commonly prescribed medicines in acute severe watery diarrhea cases. We also observed that nine of ten *V. cholerae* cases received Metronidazole. Stool culture in all cases requiring antibiotic use could potentially reduce such misuse of antibiotics[8]. Hence, making available and promoting comprehensive stool culture tests could directly impact the acute severe watery diarrhea outcomes by identifying causative agents, avoiding antibiotics misuse, reducing hospital stay, complications and patients' inconveniences[6,7,9].

The present study showed that acute severe watery diarrhea has resulted as an important disease burden on our hospital in terms of admissions and related treatment costs[9,12]. Re-emergence of Cholera in Pakistan as indicated in recent report by the World Health Organization[6] is a potential threat of epidemic outbreak in the coming future unless timely preventive measures are taken. Detection of *V. cholerae* as a causative agent of acute severe watery diarrhea in a relatively resource poorl setting is clearly suggestive of initiating effective health awareness campaigns, improving sanitation as well as putting in place emergency vaccination plans to deal with such potential threats.

This study had several limitations. Firstly, it was conducted in only one tertiary care hospital for a limited duration of time; therefore, the findings cannot be generalized to disease frequency. Secondly, the stool examinations were not performed on all patients because of resource limitations. Thirdly, stool samples of some of the patients were collected after starting antibiotics. Moreover, there was a delay in transporting the stool samples to the Microbiology laboratory in National Institute of Health which might have decreased the number of viable bacteria. These could result in false negative culture reports.

References

1. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med 2006;3:e442.
2. World Gastroenterology Organisation. *World Gastroenterology Organisation practice guideline: Acute diarrhea.* Milwaukee, WI: World Gastroenterology Organisation; 2008. [Available from URL: http://www.worldgastroenterology.org/assets/downloads/en/pdf/guidelines/01_acute_diarrhea.pdf] [Accessed 2012 Jan 20]
3. Eastern Mediterranean Regional Office of World Health Organization. *Health System Profile: Pakistan.* Cairo: Regional Health System Observatory: 2007.
   [Pakistan: the role of contractual arrangementsin improving health sector performance: country profile Draft.[Cairo]: WHO Regional Office for the Eastern Mediterranean.] Available from URL:http://gis.emro.who.int/HealthSystemObservatory/PDF/Contracting/Pakistan.pdf
4. Shaikh BT, Haran D. Treating common illnesses among children under five years: a portrayal of health-seeking behaviours and practices in the northern areas of Pakistan. World Health Popul 2011;12:24-34.
5. Qazi R, Sultana S, Sundar S, Warraich H, un-Nisa T, Rais A, et al. Population-based surveillance for severe rotavirus gastroenteritis in children in Karachi, Pakistan. *Vaccine* 2009;27 (Suppl-5):F25-30.

6. Outbreak news. Cholera, Haiti, cholera, Pakistan, Crimean-Congo haemorrhagic fever (CCHF) and dengue fever, Pakistan. Wkly Epidemiol Rec. 2010;85:437-9.

7. Jabeen K, Hasan R. Re-emergence of Vibrio cholerae O139 in Pakistan: report from a tertiary care hospital. J Pak Med Assoc. 2003;53:335-8.

8. Jabeen K, Zafar A, Hasan R. Increased isolation of Vibrio cholerae O1 serotype Inaba over serotype Ogawa in Pakistan. East Mediterr Health J. 2008 May-Jun;14(3):564-70.

9. Zuckerman JN, Rombo L, Fisch A. The true burden and risk of cholera: implications for prevention and control. Lancet Infect Dis 2007;7:521-30.

10. Sobani ZA, Shakoor S, Malik FN, Malik EZ, Beg M. Gastrointestinal helminthiasis presenting with acute diarrhoea and constipation: Report of two cases with a second pathology. Trop Biomed 2010; 27: 348–50.

11. Sarkar BL, Kanungo S, Nair GB. How endemic is cholera in India. Indian J Med Res 2012;135:246-8.

12. Ahmad A, Alam I, Hussain I. Patients cost per hospital bed in a tertiary health care facility. Pak J Med Res 2004;43:22-8.