CLINICAL PROFILE OF CHOLERA IN YOUNG CHILDREN-A HOSPITAL BASED REPORT

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ABSTRACT

Clinical profile of cholera was studied in children attending Diarrhea Training and Treatment Unit from January-December 1993. Out of a total 8714 cases of acute watery diarrhea, 64 children (0.7%) were suspected to have cholera ,s on the basis of acute onset loose watery/rice watery stools, high purge rate with or without excessive vomiting and/or severe dehydration. Stool culture was positive for cholera in 33 cases (51.6%). All the isolates were V. cholerae 01 biotype El Tor serotype Ogawa. Sixty four per cent of stool culture positive cases were below 5 years of age. The results assume importance because out of 28 children <2 years with clinical suspicion of cholera, 11 cases (39.3%) *were culture positive for V. cholerae, youngest child being 3 months old. Comparison of various parameters revealed that presence of vomiting >4 episodes/ day (p <0.005), frequency of stool >12/24 hours (p <0.002), rice watery stools (p <0.001) and presence of severe dehydration (p <0.01) were significant parameters associated with positive stool culture. Bedside examination of stool sample by hanging drop method was an excellent diagnostic tool (p <0.001) with a sensitivity of 51.5%, specificity 100% and positive predictive value of 100%. The isolates of V. cholerae were susceptible to furazolidone, cephelexin, nalidixic acid, norfloxacin and gentamicin.*

Numerous outbreaks of cholera have occurred in different parts of India during the last 25 years(1). Traditionally it occurs as endemics in deltas of tropical and subtropical regions such as Ganges basin where density of population is high. Detection of cases of cholera is higher in endemic areas and during outbreaks of watery diarrhea. However, in non-endemic areas and in the absence of outbreaks the index of suspicion is low and therefore, diagnosis may be missed. This study attempts to identify cholera cases in the absence of an outbreak with a specific objective to assess the magnitude particularly in very young children who are routinely not suspected to have cholera. Clinical predictors of cholera and role of stool examination by a

Our observations indicate that cholera is not uncommon in infants and young children. Like children in the older age group, acute onset diarrhea with watery/rice watery stools and high purge rate with or without excessive vomiting and/or rapid development of severe dehydration should arouse suspicion of cholera in younger children also. They should be investigated for cholera even in non-endemic areas and in the absence of cholera outbreaks.

Key words: *Cholera, V. cholerae, Rice watery stools.*

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simple hanging drop method were also evaluated.

Material and Methods

This prospective study was carried out in the Diarrhea Training and Treatment Unit (DTU) of Kalawati Saran Children's Hospital, New Delhi over **a** period of one year. Cholera is suspected when acute watery diarrhea causes severe dehydration in a child above 2 years of age in an area where cholera is known to be present(2). However, in view of the fact that Delhi was known to have cholera in the past and even children younger than 2 years also had stools culture positive for cholera, our screening critera for "suspected cholera" included all the cases of acute watery diarrhea with sudden onset of loose watery or rice watery stools, and frequency of stools >10/24 hours, with or without >3 episodes of vomiting/24 hours and/or presence of severe dehydration. Detailed clinical profile of these cases was noted which included duration of diarrhea, frequency of stools and episodes of vomiting in last 24 hours, history of fever, and drugs taken before attending the DTU. Other relevant details such as source of drinking water of the family and locality where the family was residing were also recorded. Nutritional status of the cases was assessed as per the recommendation of Nutrition Subcommitee of the Indian Academy of Pediatrics(3). Dehydration was assessed and managed as per standard protocol(2). Stool samples of all suspected cases were subjected to hanging drop test (soon after the first sample was collected in the DTU), stool microscopy for ova or cysts and culture studies. Stool specimens were collected immediately after enrolment in sterile MacCartney bottles using sterile catheters. Each stool sample was examined for *V. cholerae* within 2 hours in the Microbiology Department of the hospital by direct plating on thiosulphate citrate bile salts sucrose agar (TCBS) or by enrichment in alkaline peptone water for 18 hours at 37°C followed by plating on TCBS. The isolates were confirmed and typed by slide agglutination with polyvalent and monovalent antisera. The biotyping of isolates was also carried out(4). Culture studies were also performed for other enteropathogens by inocculating the stool sample on a battery of plating media(5). Only those cases with hanging drop positive were given furazolidone as the first choice of antimicrobial agent. The results of clinical profile were subjected to statistical analysis by making 2x2 tables, finding out odds ratio and applying Chi square test(6). Sensitivity, specificity and predictive values of all the variables which were associated with positive stool culture were determined by standard statistical methods(7).

Results

Out of a total 8714 cases of acute watery diarrhea reporting to the DTU from January-December 1993, 64 children (0.7%) fulfilled our criteria of "suspected cholera". Of these, 33 cases (51.6%) had stool culture positive for cholera. Other enteropathogens isolated /detected in the stool included E. *coli* in 12/64 cases (18.7%), nonpathogenic organisms in 18/64 (28.1%), no growth in 34/64 (53.1%) and cysts/trophozoites of *Giardia lamblia* in 4/64 cases (6.25%). Due to lack of facilities it was not possible to undertake serotyping of E. *coli*

and detection of rotavirus antigen in the stools.

All the isolated strains of cholera were *Vibrio cholerae*-01, biotype ElTor and serotype Ogawa. Majority of the cases were detected during May to August 1993 which had a combination of three environmental factors, *it.,* high relative humidity, high rainfall and high environmental temperature *(Fig. 1).* Nine of the thirty three culture positive cases (27.3%) belonged to Shahdara zone which is an endemic focus for cholera in Delhi state. Rest of the cases came from non-endemic zones of Delhi. However, overall living and hygienic conditions of all the patients were poor. Ten of the thirty three culture positive cases (30.3%) did not have access to municipal tap water, with 6/33 cases (18.2) using a deep hand pump and 4/33 cases (12.1%) used a shallow hand pump water for drinking and cooking purposes. Eighteen of the thirty three cases (54.5%) of the stool culture positive group and 11/31 cases (35.5%) from the culture negative group had duration of diarrhea more than 24 hours and most of them had received some drugs including antibiotics, antidiarrheals and unknown medicines before attending the DTU. None of the cases with diarrheal duration less than 24 hours had received any antibiotics. Duration of diarrhea had no relationship with positivity of stool cultures ($p > 0.05$).

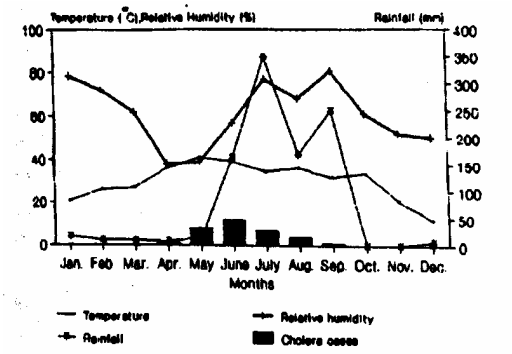

Fig. 1. *Seasonal pattern of V. cholerae isolation.*

Distribution of cases by age showed that nearly one fourth of cases (24.2%) were infants, the youngest child being 3 months old *(Table I).* Evaluation of sensitivity, specificity and predictive values of clinical variables suggested that frequency of stools >12/24 hours, vomiting >4/24 hours, rice watery stool, and presence of severe dehydration were significant predictors of positive stool culture for cholera *(Table II).* Examination of stool by bedside hanging drop method was observed to be a simple and reliable tool for detection of cholera ($p = <0.001$) with a sensitivity and specificity of 51.5% and 100%, respectively. Most of the isolates were susceptible to norfloxacin (100%), gentamicin (100%), furazolidone (95.2%), cephelexin (95.2%), nalidixic acid (95.2%),

TABLE I-*Age Distribution of Cholera Patients*

Age (mo)	Total cases screened (n=64)	Culture positive (n=33)	
		No.	%
0-6	5	3	60.0 (9.1)
7-12	15	5	33.3 (15.1)
13-24	8	3	7.5 (9.1)
25-36	10	5	50.0 (15.1)
37-60	8	5	62.5 (15.1)
>60	18	12	66.7 (36.4)

(Figures in parenthesis depict age wise per-Cent age of total culture positive cases).

TABLE II—*Sensitivity, Specificity, Predictive Values and λ^2 of the Variables*

Variables	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	λ^2	p value
Vomiting >4/24 h	93.9	38.7	62.0	85.7	8.2	<0.005
Frequency of stool >12/24 h	66.7	67.7	68.7	65.6	6.2	<0.02
Duration of diarrhea <24 h	45.5	35.5	42.9	38.0	3.2	>0.05
Fever	15.1	67.7	33.3	42.8	3.6	>0.05
Rice watery stool	72.7	93.5	92.3	76.3	26.4	<0.001
Severe dehydration	54.5	80.6	75	62.5	7.0	<0.01
Positive stool examination by hanging drop method	51.5	100	100	65.9	19.2	<0.001

tetracyline (85.7%) and chloramphenicol , (76.1%). Furazolidone was used as the antimicrobial agent of choice in all our cases in a daily dose of 5 mg/kg in 4 divided doses for 3 days. All the cases favorably responded to this treatment.

Discussion

Cholera has maintained a low profile in Delhi even though it has been endemic in a large geographical tract covering a number of states in eastern, western and southern parts of India. Delhi, which is discontiguous with the main afflicted belt, has reported a low cholera level between 1956 and 1965(7). The incidence of cholera during 1968 and 1969 was as high as 27-30% of all diarrhea cases. With a brief downward trend during 1970-1975, a rising trend was again noticed in 1980(7). Thus, cholera has been prevailing in Delhi at low to moderate level of endemicity for the last 30 years. Biotype ElTor has been isolated in all the epidemiological surveys in Delhi including the outbreak in 1988 which was caused by *V. cholerae* biotype Ogawa and serotype ElTor(l,8). The highest proportion of cholera cases have been detected in two adjacent area of Delhi, one each on either side of the river Yamuna, *i.e.,* Shahdara zone in the east and Civil lines zone in the northwest. Despite the extensive outbreak in 1988, the cases remained confined to these geographic areas which constitute persistent endemic foci of cholera in Delhi(8). The patient population of DTU at Kalawati Saran Children's Hospital is from all over Delhi and adjoining areas. Cases suspected to have cholera and later found to have a positive stool culture

represent a mixed patient population since one third cases were from endemic zone i.e., Shahdara) and two third were isolated cases from non-endemic zones. However, all the positive cultures grew *V. cholerae-01* biotype ElTor and serotype Ogawa, irrespective of the locality from where the patients came, like earlier reported isolates from Delhi in the past. *E. coli* was isolated from the stool in 18.7% cases with almost equal frequency of cholera culture positive as well as culture negative cases. Since it was not possible to perform the serotyping of *E. coli,* it is difficult to comment whether one of the serotypes like ETEC was responsible for cholera like illness in patients with stool culture negative for cholera.

Cholera has a seasonal pattern in endemic areas although the season varies from place to place(9). In Delhi most of the cases are encountered between May-October, this period covers part of summer and the whole of rainy season(l,7). Our observations also indicate that high relative humidity and high rainfalll in the presence of high environmental temperature were associated with emergence of clinical cholera.

In endemic areas, cholera may be associated with development of some immunity in the population leading to higher rates of asymptomatic infection in adults and a shift in the age distribution towards young children, many of whom are experiencing their initial infection(10). Epidemiological studies in endemic areas like Bangladesh show that case fatality rate of cholera in children 1-5 years old is ten times higher than in adults(11). However, mechanism for the increased susceptibility of children to enterotoxin induced diarrhea is unknown. It may be due to increased exposure to infectious agents, impaired host immunity and/or increased sensitivity to elaborated toxin. Cholera in children is an alarming clinical situation which can rapidly lead to death. Even though the common age group affected is believed to be 2-15 years(10), one-third of our cases were less than 2 years of age and one-fourth less than 1 year. This may be due to the fact that majority of our cases came from non-endemic areas and the first infection can be acquired at a younger age particularly because of poor hygiene in our study population. However, younger infants seem to run a higher risk of infection irrespective of the endemicity since 2/9 cases (22.2%) even from the endemic zones were infants. Our observations suggest that cholera should be suspected even in younger infants who have a high purge rate, rice watery sools and severe dehydration and subjected to stool examination by hanging drop method for screening since a positive hanging drop examination had a specificity and positive predictive value of 100%.

Clinical manifestations of infection with *V. cholerae* vary from asymptomatic infection to severe diarrhea(11). In most cases, cholera is characterized by the onset of vomiting, voluminous watery stools and rapidly progressing dehydration, the severity of which depends entirely on total losses. Children with cholera may also lose as much as 2.9-3.6 ml/kg of water per hour from the skin(12,13) which is critical in the presence of dehydration. Symptoms such as fever, lethargy, seizures, altered

consciousness and hypoglycemia are seen more commonly in children than in adults; the last two are important risk factors for death(ll). This would emphasize the need for early diagnosis of cholera particularly in young children(ll).

Rapid replacement of fluid and electrolytes with oral rehydration therapy or intravenous fluids and maintenance of hydration remains the mainstay of treatment of cholera. However, antimicrobial agents are indicated in cholera(3) even though they are not as "life saving" as they are for many other severe infections(14) since the aim of antimicrobials is to kill *V. cholerae* in the gut so that there is no subsequent production of toxin, resulting in decrease in volume and duration of purging in cholera(15). However, antimicrobials have no effect on already produced toxins already fixed to the epithelium. Therefore, they should be used judiciously in children to effectively reduce the purge rate, to increase the success rate with oral rehydration therapy and to minimize the nutritional onslaught which is so common with prolonged diarrhea. Inview of the reports of resistance of *V. cholerae* to tetracyclines and other antibiotics from East Africa(16) and Bangladesh(17), it may be important to periodically determine the sensitivity of the antimicrobial agents. During the outbreak of 1988 in Delhi, most of the isolates were sensitive to commonly used antimicrobial agents but resistance to furazolidone was substantially higher than previous years(8). Our results showed excellent *in vitro* sensitivity with gentamicin and norfloxacin and a higher resistance pattern with tetracycline and chloramphenical. However, furazolidone continued to have a good *in vitro* sensitivity and was preferred to other drugs in view of its oral administration, cost of therapy and safety in children.

Antimicrobial agents are also recommended in 'clinically suspected cases of cholera' when acute watery diarrhea causes severe dehydration in a child above 2 years of age and in adults in an area where cholera is known to be present(2) since it is not practically possible to perform the stool culture studies in every patient. However, these recommendations have to be taken with great caution because a number of bacterial and viral enteropathogens other than *V. cholerae* can have a similar clinical presentation. Therefore, antimicrobials should be used only when cholera is confirmed or very strongly suspected.

Some of the clinical parameters suggesting infection with *V. cholerae* have been evaluated in this study in order to identify "suspected cases of cholera" out of a large number of patients of acute watery diarrhea, for further evaluation and management besides appropriate fluid replacement. Presence of vomiting >4/24 hours, frequency of stool >12/24 hours, rice watery stools and severe dehydration were statistically significant parameters associated with stool culture positive for *V. cholera.* It was also an important observation that only 18/33 culture positive cases (54.5%) had "no" or "some dehydration". Thus a significant proportion of stool culture positive cases may have a milder illness and therefore, may not even require any antimicrobial therapy. However, the ones who present with

severe dehydration associated with a clinical picture strongly suggestive of cholera and with a positive hanging drop examination of stool may be benefitted by treatment with appropriate antimicrobial agents.

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