

**Multidrug Resistance in  
*Vibrio cholerae***

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Cholera continues to be endemic in a large geographical tract covering a number of states in the eastern, western and southern parts of India. Even though *V. cholerae* non-01 has been reported from some parts of Delhi(1), *V. cholerae*-01 biotype *Eltor* continues to be the main etiological agent identified from Delhi(2). Rapid replacement of fluid and electrolyte using oral rehydration therapy or intravenous fluids and the subsequent maintenance of hydration remains the mainstay of management in cholera patients. However, the use of specific antimicrobials is known to reduce the duration of diarrhea as well as speed up the clearance of the organisms from the stools(3). The WHO guidelines(4) as well as the National Policy for the Control of Cholera(5) recommend the use of cotrimoxazole in children; the other alternative drugs being tetracycline, furazolidone, chloramphenicol and erythromycin. It has further been suggested that the choice of antibiotic be guided by the local sensitivity patterns prevailing at a particular time.

Multidrug resistant cholera (*Eltor*) was first reported in 1977(6) which was followed by several other reports of multidrug resistant *V. cholerae* causing outbreaks all over the globe. We conducted this study to review the antibiotic sensitivity pattern prevalent amongst the *V. cholerae* isolated from the patients attending the Diarrhea Training and Treatment Unit (DTU) of our hospital.

**Material and Methods**

This prospective study was carried out in the DTU of Kalawati Saran Children's Hospital, New Delhi during the peak diarrhea season from mid-June to September 1995. Based on our previous experience(7) cholera was suspected clinically in cases of acute watery diarrhea with sudden onset of loose watery or rice watery stools, frequency of stools more than 10 per 24 hours, with or without persistent episodes of vomiting and/or presence of severe dehydration. Detailed clinical profile of these patients was recorded with special reference to drugs taken before attending the DTU, area of residence and the source of drinking water.

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*Received for publication: October 30, 1995;  
Accepted: January 11, 1996*

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Dehydration was assessed and managed as per standard protocol(4). The first stool collected was subjected to a hanging drop preparation and the specimen was sent to the Microbiology Department in sterile MacCartney bottles.

The stool specimens were typed by slide agglutination with both polyvalent and monovalent sera. The isolates were also biotyped. The antibiogram of the *V. cholerae* isolates were prepared and studied with standard methodology and laboratory techniques(8).

### Results

Of 3651 cases of acute watery diarrhea attending the DTU a diagnosis of cholera was entertained on clinical grounds in 206 cases (5.6%). Out of these 206 cases, 60 patients (29.1%) had a positive hanging drop while 109 stool samples (52.9%) of the suspected cases grew *Vibrio cholerae*. All the cholera isolates were *V. cholerae*-01 biotype *Eltor* and serotype ogawa.

More than one third of the patients (36.7%) were below 2 years of age (2.7% of the patients were below 6 months of age, 13.8% from 6 months to 1 year, 20.2% between 1-2 years, 36.7% from 2-5 years and 26.6% were aged more than 5 years). Males (67%) outnumbered females (33%). *Table I* shows the antibiotic sensitivity pattern of *V. cholerae*.

### Discussion

Cholera was suspected in 5.6%; of our cases of acute watery diarrhea during the peak summer season of which 109/206 cases (52.9%) grew *V. cholerae*-01 biotype *Eltor* and serotype ogawa from stool culture. This observation is consistent with earlier reports from Delhi(7,9). However, a re-appraisal of sensitivity pattern of *V. cholerae* isolates was deemed necessary in view of several reports from India as well

as other parts of the world during the past decade indicating multidrug resistance of *Vibrio cholerae* (biotype *Eltor*).

Resistance of *V. cholerae* to antimicrobials is usually thought to be chromosomal in origin(10) and rarely plasmid mediated(11). However, some workers in the last few years have also identified plasmid mediated resistance(12). It is not very clear whether this pattern of increasing resistance of *V. cholerae* to many antimicrobials means that the organism is acquiring more of plasmid mediated resistance or is the mass use of antimicrobials responsible for the selection of resistant strains. Multidrug resistance with *Eltor* cholera was reported as early as 1977-78 from Tanzania(6) where sensitivity to tetracycline declined from 100% to 24% within five months of beginning of an epidemic of cholera. Similar reports from India(13,14) have been documented for furazolidone (42%) and tetracycline (63%), while low resistance was reported with gentamicin (1.5%). In a cholera epidemic in Bangladesh during 1992(11) resistance to cotrimoxazole and ampicillin has been reported to the tune of 62%.

Our past experience with cholera cases in 1993(7) indicated some resistance to tetracycline (24%) while there was good *in vitro* sensitivity to furazolidone (95.2%), nalidixic acid (95.2%), gentamicin (100%) and norfloxacin (100%). Considering the cost and effectiveness of the drugs, furazolidone was offered as the drug of choice for cholera to our patient population. However, the present study conducted a year later shows a poor *in vitro* sensitivity to furazolidone (23.8%) whereas there is a good *in vitro* sensitivity to norfloxacin (93.6%). There has been a steady decline in sensitivity to gentamicin from 100% to 64.2%. The resistance pattern with cotrimoxazole (67%) and tetracycline (53.2%) has remained much

the same. Sensitivity to cefotaxime is 78% and like gentamicin this drug is available for parenteral use limiting their utility for routine case management of cholera.

The fast emergence of multidrug resistance *V. cholerae* all over the world especially to drugs recommended by the WHO for control of cholera, is a serious matter. Our aim was to highlight the resistance pattern of local *V. cholerae* isolates so that the health authorities can review the list of recommended antibiotics for Cholera Control Programme. Even though there may be a satisfactory clinical response to antibacterial agents with *in vitro* resistance(6), it is mandatory to maintain a continuous surveillance of sensitivity patterns so that a suitable drug

is used in a particular geographical area. The changing MIC (increasing trend) over the years, even when the organism still has intermediate sensitivity to a particular antibiotic is also alarming. This should alert the health workers about the likelihood of serious drug resistance in the coming years. We have observed intermediate sensitivity to furazolidone (18.3%) and gentamicin (14.7%). Even though these figures appear to be insignificant at present with the increasing MIC levels we may face serious therapeutic problems in the near future. Further studies with detailed MIC testing and clinical response would also be required before the National and WHO recommendations for antimicrobials in management of cholera are restated.

TABLE I—Sensitivity Pattern of Isolates of *V. cholerae*

Drugs	Sensitivity pattern (n=109)					
	Sensitive		Intermediate Sensitive		Resistant	
	No.	%	No.	%	No.	%
Chloramphenicol	59	54.1	4	3.6	46	42.4
Gentamicin	70	64.2	16	14.7	23	21.1
Furazolidone	26	23.8	20	18.3	63	57.8
Oxytetracycline	51	46.8	0	0	58	53.2
Co-trimoxazole	34	31.2	1	0.9	74	67.9
Cefotaxime	86	78.9	2	1.8	21	19.3
Norfloxacin	102	93.6	1	0.9	6	5.5

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