

## SIMULTANEOUS CLASSICAL AND EL TOR CHOLERA IN BANGLADESH

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### Abstract

Cholera appears annually in Bangladesh, with peak incidence from September through December and April through June. After being absent for a decade the classical biotype of *Vibrio cholerae* reappeared in Comilla and Dhaka on September 1 and 3, 1982, and soon thereafter appeared in many other districts. Cases due to the newly emerged classical biotype of *V. cholerae* rapidly surpassed those due to the El Tor biotype. Before 1970 classical *V. cholerae* had been responsible globally for both endemic and epidemic cholera. In Bangladesh, El Tor first was isolated in 1964. By 1973, it had replaced the classical strain. Subsequently until 1981, only six classical isolates were noted. The new classical strains were almost identical to those isolated a decade earlier, except for their ability to successfully displace El Tor in an epidemic setting. Investigation of the first 10 cholera cases suggests a multiple source outbreak. The age distribution of the classical and El Tor was similar, suggesting a lack of important new antigenic determinants, which could circumvent existing immunity in the population. Both strains followed known seasonal patterns.

*Key words:* *Vibrio cholerae*, New Classical, Existing El Tor, Cholera Epidemiology.

### Introduction

Between 1937 and 1960, apart from occasional outbreaks due to the El Tor biotype of *Vibrio cholerae* in Celebes (Sulawesi, Indonesia), classical cholera was responsible for both endemic and epidemic cholera throughout the world (1). In 1961, El Tor began a major spread across the world from its endemic focus in the Celebes, and was responsible for the seventh cholera pandemic (2).

In 1964, the El Tor biotype first was detected in Bangladesh in Chittagong, but did not cause an outbreak until 1968 (3). El Tor was seen sporadically in Dhaka from 1964 until 1972. In 1973, *Vibrio cholerae* Ogawa biotype El Tor displaced the *Vibrio cholerae* Ogawa biotype classical in Dhaka. Between 1974 and 1981, the El Tor biotype was responsible for both endemic and epidemic cholera. Between 1978 and 1981, in thousands of stool specimens examined annually for *V. cholerae*, only six isolates of the classical biotype were found (4, 5), from different locations. On September 1, 1982 the classical biotype reappeared and rapidly became dominant. A preliminary report of the displacement of classical cholera has been published by Samadi et al (5).

Comparisons of El Tor with classical *V. cholerae* have been made in the past (3, 7, 8), but the concurrent epidemic of the classical and El Tor biotypes provided a unique opportunity for epidemiologic

comparison of the behavior of the two biotypes. Since cholera is a disease of global distribution, any major shift in biotype may herald a new endemic and epidemic strain capable of worldwide spread.

### Materials and methods

The International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) runs three Treatment Centres for diarrhoeal diseases, in Dhaka, Matlab and Teknaf. The main Centre for diarrhoeal diseases in Dhaka serves a wide area, receiving most acute diarrhoeal cases from the wider metropolitan area with a population of about 4 million people. A population of 200,000 is completely served in the Matlab Thana of Comilla District. Moreover, at that location a larger population outside the intensively served population also uses the Matlab facility. The Teknaf Centre serves a population of about 60,000 in the Chittagong District. Also, the ICDDR,B aids the Government Health Ministry and urban and rural Community Treatment Centres in other parts of Bangladesh. Field teams investigate acute diarrhoea outbreaks.

In this study, more than 55,000 rectal swabs/stool specimens, collected from diarrhoea cases in Dhaka, Matlab, Teknaf and other districts, were examined at the ICDDR,B's Microbiology Laboratories, between September 1, 1982 and June 20, 1983.

A detailed investigation of common sources of food and water, contact with other diarrhoeal cases, kinship, geographical distribution, time of occurrence, and age and sex was carried out on the first 10 classical cholera cases which occurred in Dhaka and Matlab.

All new classical and existing El Tor *Vibrio cholerae* isolated at the Microbiology Laboratories in Matlab and Dhaka were analyzed for the monthly distribution of *V. cholerae* by biotype.

The data for alternate years from 1964 to 1974, as well as for 1975, 1977, 1980 and 1982, the peak years, were analyzed to determine serotype changes.

The microbiological techniques used have been described earlier (5). All serologically confirmed cases of *V. cholerae* were checked for biotypes. A strain was designated as "classical" if it did not agglutinate chicken erythrocytes, was sensitive to classical group IV phage, was resistant to El Tor group V phage, and was sensitive to polymyxin B.

Statistical analysis was performed, using the Z test for comparison of proportions.

## Results

Reviewing hospital records from 1964 to 1982, we found that shifts in serotypes between Ogawa and Inaba occurred in both biotypes (Table 1). Inaba classical predominated up to 1970 and Ogawa classical in 1972, while Inaba and Ogawa El Tor predominated from 1973 to 1982.

In 1982, the first case of classical cholera was identified at Matlab Hospital, and came from

Hajiganj, about 15 miles away. The 2nd case seen at Matlab occurred at a place more than 12 miles from the first case. The 3rd, 4th, 5th and 6th cases occurred in an adjacent neighborhood, but no epidemiological association between cases could be made. At the Dhaka hospital, *V. cholerae* due to the classical biotype was first isolated from a patient from Narayanganj, about 30 miles north of Hajiganj, the location of the first case. There is poor communication between the two areas. The second case seen in Dhaka occurred about 10 miles further upstream, in Keraniganj. Investigation of the first 10 cases in Dhaka did not indicate a point source spread of the infection (Fig. 1).

Following its reappearance in early September, classical cholera rapidly became dominant. By January and February 1983, the El Tor biotype had almost disappeared. However, the number of El Tor cases increased again from March, 1983. We found the peak incidence for the classical biotype during this outbreak to be in November and December, while the El Tor biotype retained its traditional peak in October-November (Fig. 2).

The appearance of classical cholera by time sequence (month) and geographical locations are shown in Fig. 3. There were almost simultaneous outbreaks in different districts. The geographical locations were scattered, suggesting multiple points of outbreak.

There were a total of 7,250 microbiologically confirmed cases of *V. cholerae* treated at the Dhaka and Matlab hospitals between September 1, 1982 and June 30, 1983. Of these, 2,274 cases (31.4%) were El Tor and 4,976 (68.6%) were classical.

The classical strains isolated in the present

TABLE I — CHANGES OF SEROTYPES AND BIOTYPES OF *V. CHOLERA*E IN DHAKA

Year	No. of cholera	Inaba classical %	Inaba El Tor %	Ogawa classical %	Ogawa El Tor %
1964	579	75.1	0	24.4	0.5
1966	1504	94.9	0	5.1	0
1968	892	93.3	0	0.3	6.4
1970	2968	94.1	0	1.3	4.6
1972	702	5.7	0.1	85.2	9.0
1974	5050	0	10.9	0	89.0
1975	3357	0	54.4	0	45.6
1977	1864	0	99.8	0	0.2
1980	2834	0	37.9	.03	62.0
1982	6024	40.9	29.0	.05	30.0
All	25,774	31.0	27.4	3.3	38.2

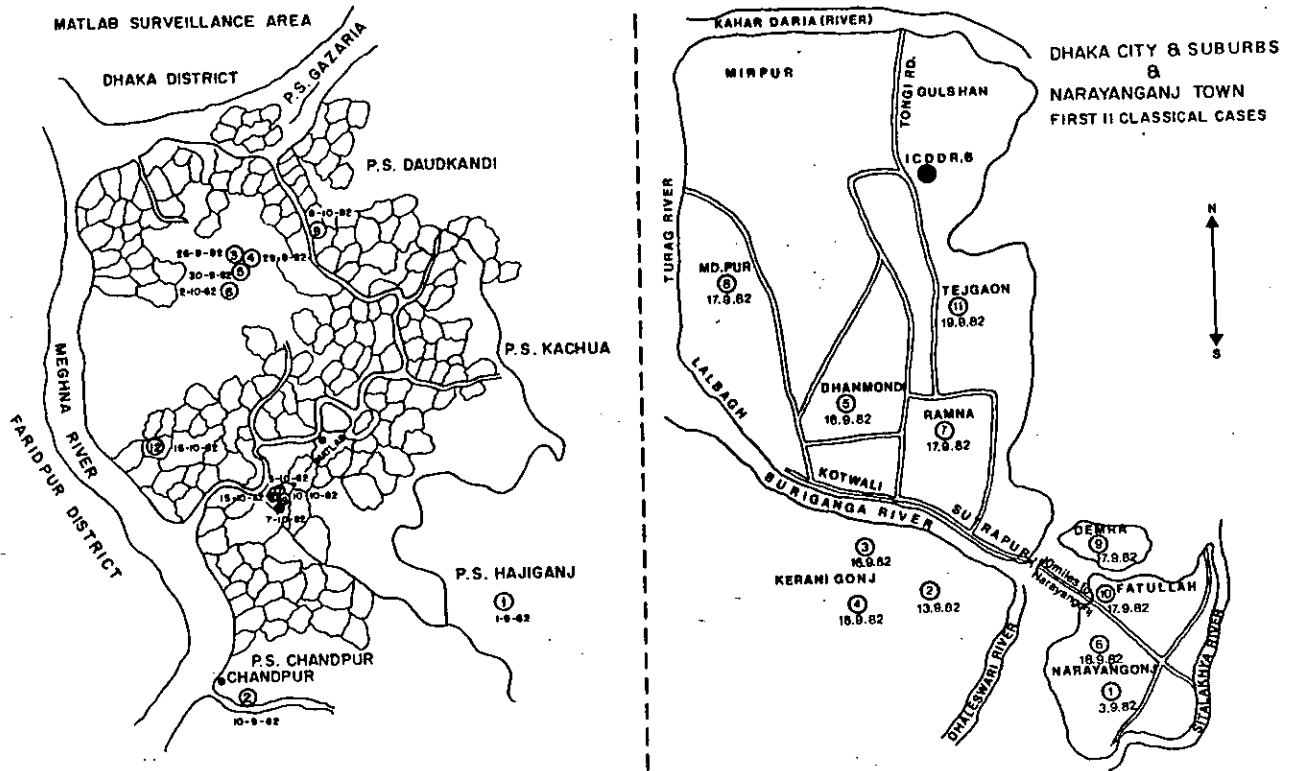


Fig 1—Showing the location of first 12 classical cholera cases.

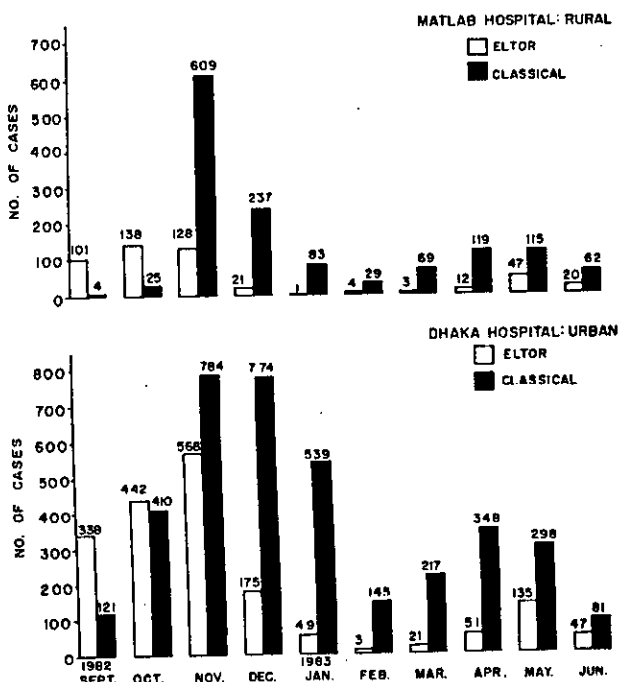


Fig 2—El Tor and classical cholera cases of Dhaka and Matlab Hospitals by months.

outbreak were indistinguishable by standard tests from either those isolated a decade earlier or from the few isolates of 1979, 1980 and 1981. However, when grown competitively with El Tor, the present classical isolates appeared to have a growth advantage compared to those formerly isolated (11).

The age distribution curves for both the new classical strains and existing El Tor were similar. Most patients were children aged 1-9 years. Children aged less than one year constituted 2.9% of all cases. Among both the Matlab and Dhaka patients, more male children (<15 years) than females were affected by both biotypes. In adults (15-44 years), more females contracted cholera in comparison to males (Fig. 4,  $p < .01$ ).

In the past, classical has been found to be more severe than El Tor (7). Case fatality rates and frequency of deaths are shown in Table II. The case fatality rates and the frequency of deaths in 2 days were not significantly different for the El Tor and classical biotypes.

### Discussion

The first 10 cases of classical cholera in 1982

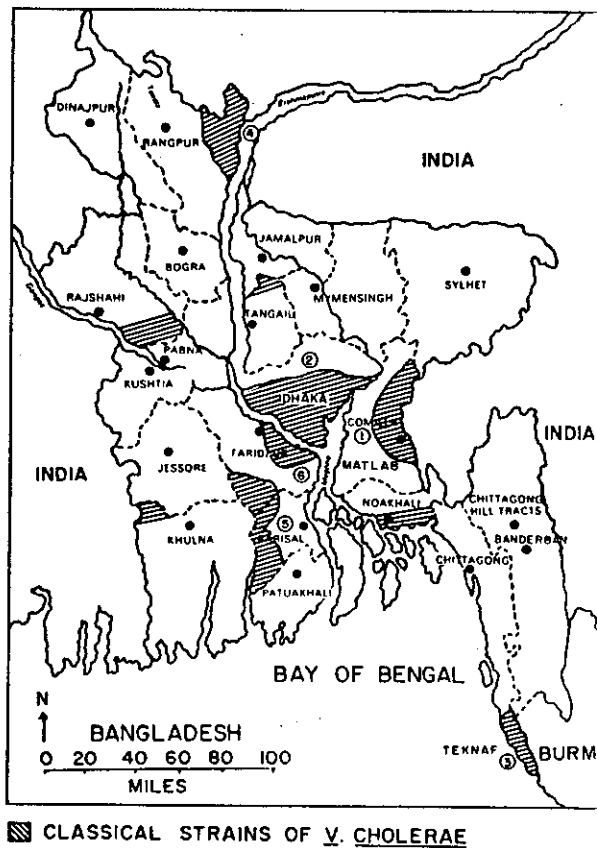
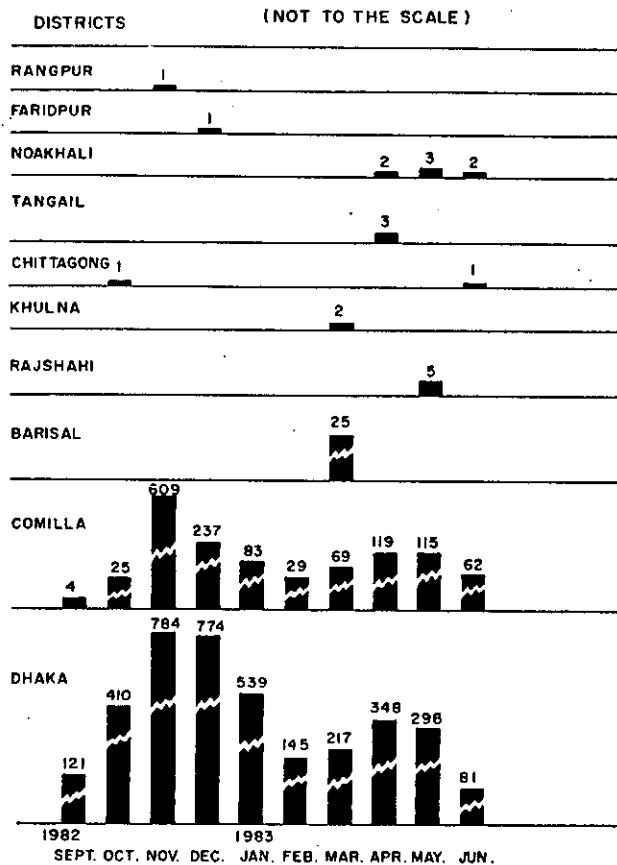


Fig. 3—Classical cholera by time (month) and district, 1982-83.

TABLE II — ONSET-DEATH INTERVAL AND DEATH RATES IN CLASSICAL AND EL TOR CHOLERA CASES (SEPTEMBER 1982-JUNE 1983)

Location	El Tor			Classical			P
	Cases	Deaths	Rate %	Cases	Deaths	Rate %	
Dhaka	1790	23	1.3	3618	32	0.9	> 0.5
	Death in	1-2 Days	82.6	Death in	1-2 Days	87.5	> 0.5
Matlab	492	9	1.8	1375	15	1.1	> 0.5
	Death in	1-2 Days	88.9	Death in	1-2 Days	80.0	> 0.5

occurred in close succession in different locations. There was no common food or water source, and epidemiological investigations did not reveal any point source of spread. The progression to rapid dominance by the classical biotype in many parts of Bangladesh suggests a multi-focal pattern of emergence, with a cryptic but definite biological

advantage of the newly-emerged biotype over the existing El Tor. Microbiological findings suggest that the new classical biotype has a growth advantage over earlier classical isolates, when it is grown competitively with El Tor (11). Because of the high velocity of appearance of classical, we expected all El Tor biotypes to disappear. How

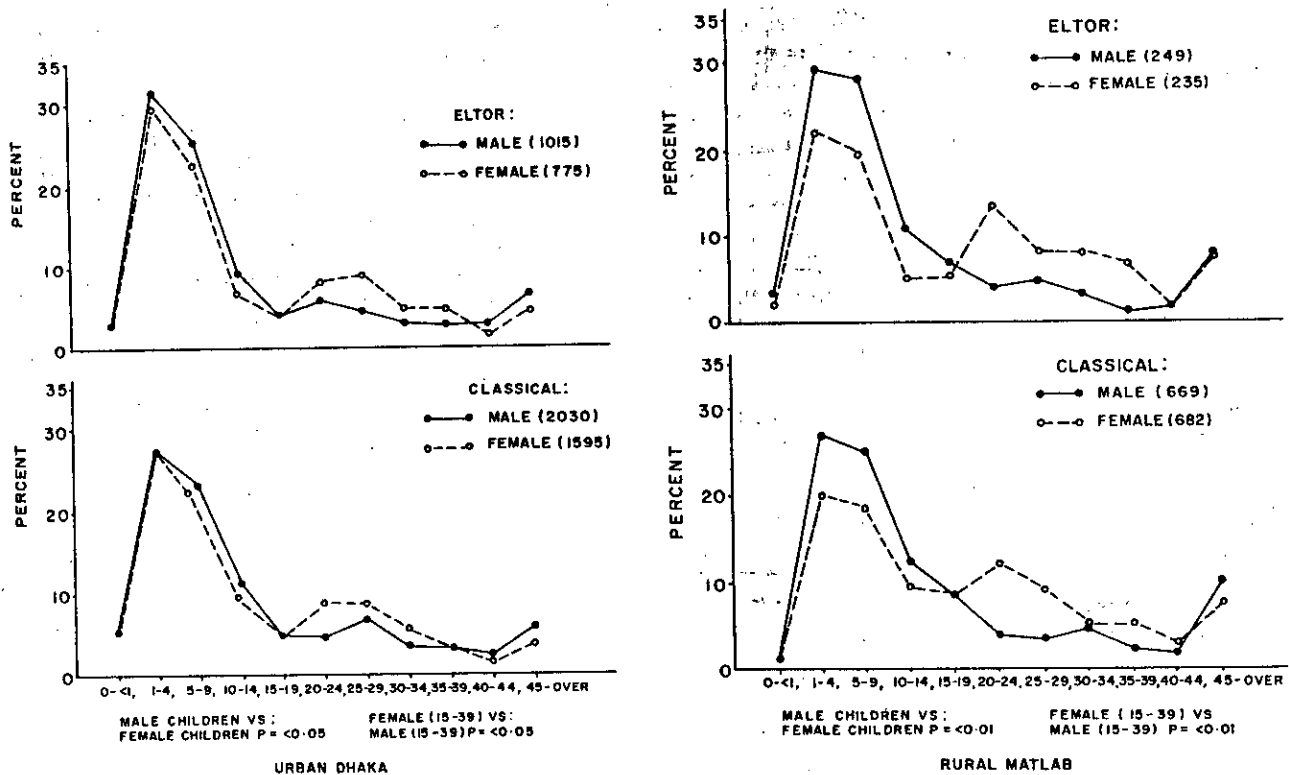


Fig. 4—Distribution of El Tor and classical cases of urban Dhaka and rural Matlab by age and sex.

ever, El Tor has persisted alongside the new classical strain.

Traditional seasonal patterns also persisted, with the peak incidence of classical cholera in November and December, following that of the El Tor in September and October (9). Firm conclusions on this point must await further observation of the emergent classical biotype, since the competitive dynamics could have obscured a late seasonal El Tor peak. Variations in seasonal peak between these biotypes have been documented previously (12).

The age distribution was identical for both biotypes, with no differences in attack rates between age groups for either biotype. This phenomenon suggests a lack of important new antigenic determinants, which could circumvent existing immunity in a population.

The sex distribution by age for patients treated in hospitals was similar, concurring with previous observations (8). Both male and female children (<15 years) are more prone to the disease, due to lower immunity and closer contact with patients and a greater use of contaminated environments. A higher hospital admission rate for male children

has been noted before (12). The higher incidence of cholera in female adults (15-44 years), for both the classical and El Tor strains, agrees with previous observations (3,8), suggesting that females, who are in closer contact with patients and contaminated materials, contract disease more often than do males. There was no difference with respect to sex in older adults (>45 years) for both biotypes. A prospective family study showed no differences in the infection rate, case rate, and infection/case ratio among contacts of families affected by the El Tor and classical biotypes (13). However, a higher hospitalization rate was noted for contacts of classical cholera cases.

In summary, we have documented that classical cholera has resumed dominance over El Tor in Bangladesh. The only epidemiological differences between the current classical and El Tor biotypes were: an earlier seasonal peak incidence of El Tor, and a higher isolation of the classical *Vibrio cholerae* from a mixture of both, compared to the old classical *Vibrio cholerae*. Several hypotheses could be suggested to explain this phenomenon. It is possible that changes in serotypes and biotypes of *Vibrio cholerae* occur cyclically in the environment

in endemic areas. The fact that the biotypes have similar antigenic determinants suggests that modifications are occurring in the vibrio population in Bangladesh, rather than being introduced from outside. The mechanisms of this shift remain to be elucidated. Environmental and host factors may modulate this shift. Although no data is presently available, it is possible that the classical biotype may reappear in other areas. Rare classical cholera cases were reported concurrently with El Tor in India (14), but in no instance has classical dominance occurred. Further investigation of this significant event is important, as the results may provide leads resulting in the eventual prevention and control of cholera.

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