Defining incidence of intussusception (IS) in Bangladesh in preparation for a phase III trial of a new Rotavirus vaccine

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Objective:

1. Establish prospective surveillance for IS in a population-based surveillance area in Bangladesh.

2. Collect and review retrospective data from hospitalizations at three ICDDR,B hospitals serving a defined population (i.e. to provide population-based incidence rates) for cases meeting a clinical case definition for IS.

3. Enhance capacity for rapid detection of potential cases of IS, diagnostic confirmation, and non-surgical and surgical management of IS that would be in place during large scale field trials for efficacy of a new rotavirus vaccine.

Rationale

Rotavirus disease is the most common cause of diarrhea and dehydration in young children in both developed and developing country. This global health burden prompted the development of vaccines against rotavirus. Baseline incidence rates of IS would be very useful in preparation for vaccine trials, and also for providing a context during analyses of data from vaccine clinical trials.

Methods

Study period: April 2004 to December 2006

Study site:

The study was conducted in rural Matlab, Bangladesh where the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) has been maintaining a field research project since 1963. Matlab is a low-lying riverine area, which is located 45 km south east of Dhaka, the capital of Bangladesh. The principal occupations of Matlab residents are farming and fishing. Since 1966 a Health and Demographic Surveillance System (HDSS), which consists of regular cross-sectional censuses and longitudinal registration of vital events, has been maintained in the area. A central treatment facility, staffed by physicians and paramedics provides free therapy for 12,000-15,000 diarrhea patients a year. A Maternal, Child Health & Family Planning Program (MCH-FP) has been in operation for half of the population of the HDSS area (current population of HDSS is about 210,000) since 1978 and intensive research has been conducted in this population. The other half serves as a comparison area where regular government health care facilities are available. Each community health research worker (CHRW) in the intervention area covers a population of about 1800. She visits each household monthly and is responsible for recording of respiratory and diarrheal illnesses of children, recording of vital events, immunization to children and referral of severely sick children and mothers etc. The study was conducted in whole HDSS area. ICDDR,B Matlab Hospital and two other ICDDR,B treatment centre

(Nayergaon and Kalirbazar) have serving for the treatment of diarrhea among the people of Matlab HDSS area.

Sample size estimates: The birth cohort in the Matlab HDSS area is 5880 and the number of <2 children is 10,773. If the rate of IS is 50 per 100,000 children <2 years of age, then we will expect to identify about 6 cases per year. Of course, these numbers would be proportionately higher or lower depending upon actual rates.

Recruitment and Training: The medical officer was joined on June 1, 2004 then went to Nuclear Medicine Centre, Sir Salimullah Medical college, Dhaka for training on ultrasonogram. The medical officer received 1 month training on "Role of Ultrasound in Diagnosis of Intussusception". He also received 2 weeks training on Pediatric Ultrasonography from Dhaka Shishu Hospital (Children's hospital). Medical officer provided training to Community Health Research Worker (CHWR) on the symptoms of IS based on Brighton collaboration Criteria (Brighton Collaboration- Intussusception definition and guidelines - www.brightoncollaboration.org). During training medical officer used to show different colored pictures of Intussusception that helps the CHRW to understand about the cases IS. The medical officer provided a referral slip to all the CHRW for referring the patient.

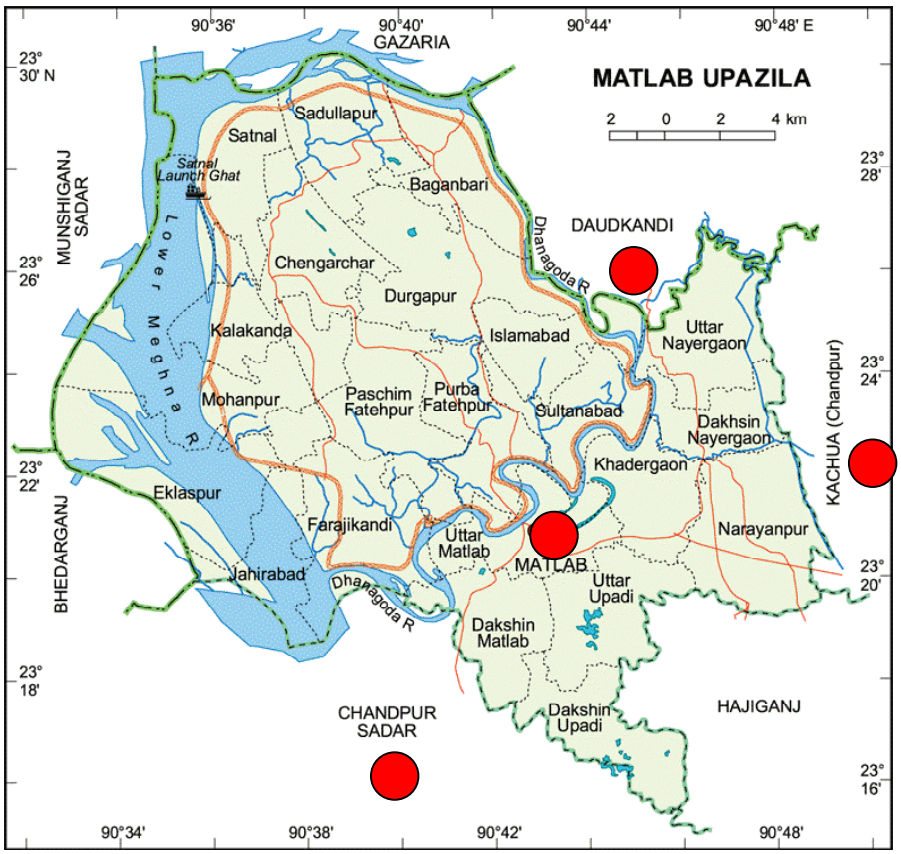
Retrospective surveillance

All medical records of hospitalized patients of Matlab and community treatment centres at Nayergaon and Kalirbazar were reviewed for the period Jan 2001-August 2004 to identify patients who meet a clinical case definition of IS, put forward by the "Brighton Collaboration" (Brighton Collaboration-intussusception definition and guidelines).

Prospective surveillance

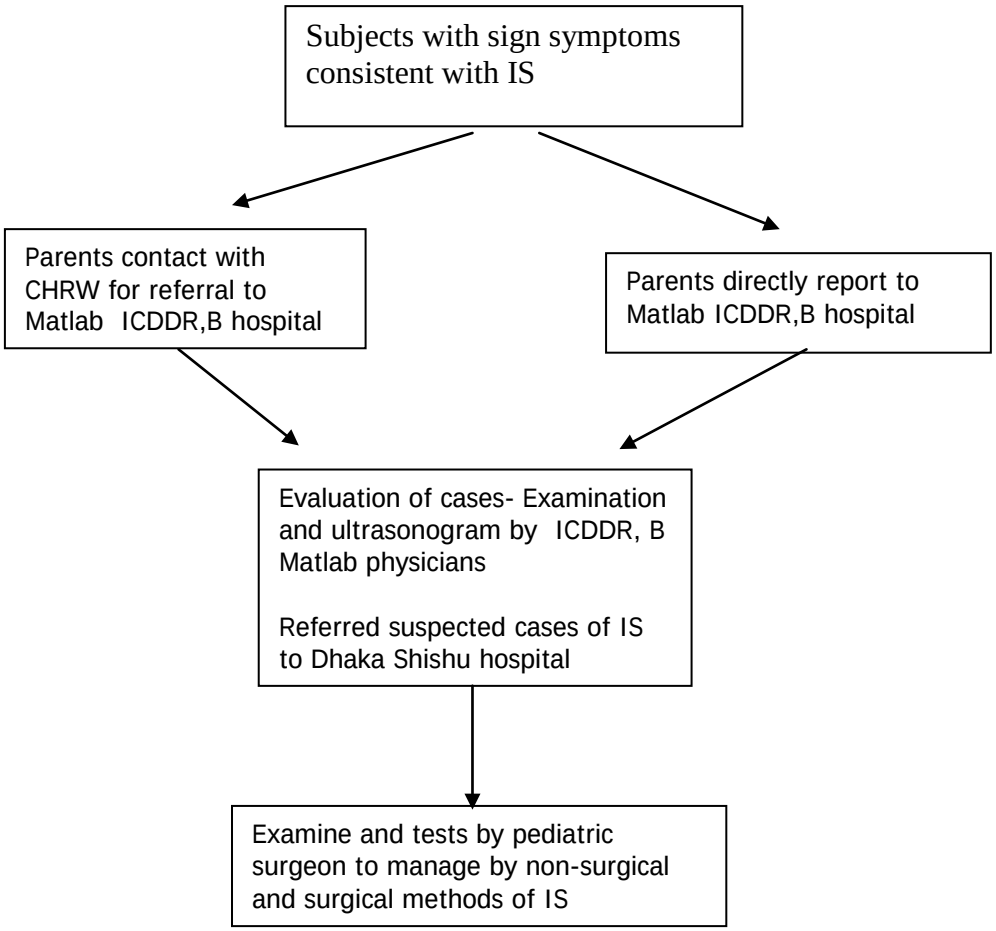
A prospective surveillance was established for IS among children living within Matlab HDSS area. This was established at the three ICDDR,B treatment centres serving Matlab, 4 District and sub-districts (upazilas) government hospitals (Chandpur Sadar Hospital, Matlab Upazila Health Complex, Kachua Upazila Health Complex, Daudkandhi Upazila Health Complex) and 3 district-based private clinics (Chandpur Central Hospital, Chandpur Royal Hospital and General Hospital), serving people living in the Matlab area. The medical officer visited these hospital and clinic every 2 weeks. As part of their routine monthly visit CHRW visited homes and asked whether children <2 years of age had experienced symptoms consistent with IS (based on Brighton criteria). They asked about abdominal pain and distention, abdominal mass, bile stained vomiting and passage of red current jelly or blood. The figure 1 showing the locations of different Upazila visited by the study medical officer.

Figure 1. Location of Matlab and other Upazilas Visited by the study medical officer



Children with any of these symptoms were referred to ICDDR,B Matlab hospital for further assessment by physician (figure 2). Ultrasonogram was done for all these cases. CHRWs also reminded and encouraged parents to bring their children to ICDDR,B Matlab hospital should their child develop relevant symptoms. A child with suspected intussusception was referred to Dhaka Shishu hospital (Children's hospital) rapidly. Epidemiologic information and diagnostic specimens (to determine etiology when possible) were obtained from all suspected cases of IS. A detailed history of feeding practices, immunization history, illness history was obtained from the subjects.

Figure 2. Flow chart showing of a child who presents with symptoms of IS



Result:

Retrospective:

Retrospective charts for the period January 2001 to August 2004 of all admitted patients at ICDDR,B Matlab Hospital and other ICDDR,B treatment centers (Nayergaon and Kalirbazar) serving the people of Matlab HDSS area were reviewed according to Brighton Collaboration Criteria (a working group of experts which defined the symptoms of IS). The findings were as follows:

Place-Year	No. of patients	Probable case	Possible case
Matlab Hospital - 2001	638	1	7
Matlab Hospital - 2002	788	2	4
Matlab Hospital - 2003	667	0	1
Matlab Hospital - 2004	452	1	6
Nayergaon – 2001-2004	253	0	0
Kalirbazar – 2001-2004	58	0	1
Total	2856	4	19

Characteristic of possible and probable case of Intussusception

Variables	Possible case n= 19 (%)	Probable case n= 4 (%)
Age in months		
0-5	9 (47.4)	2 (50.0)
6-11	8 (42.1)	0 (0)
12-23	2 (10.5)	2 (50.0)
Sex		
Male	19 (100)	3 (75.0)
Female	0	1 (25.0)
Minor criteria		
Age <1 yr and male	17 (89.5)	1 (25.0)
Abdominal pain	1 (5.2)	3 (75.0)
Vomiting	19 (100)	3 (75.0)
Lethargy	18 (94.7)	-
Pallor	11 (57.9)	-
Hypovolumic shock	11 (57.9)	-
X-ray abdomen showing abnormal but non specific gas pattern	1 (5.2)	1 (25.0)
Major criteria		
Bleeding per rectum	-	3 (75.0)
Stool containing 'Red current jelly' material	-	2 (50.0)
Intestinal prolapse	-	3 (75.0)
Blood detected on rectal examination	-	1 (25.0)

Prospective:

Prospectively during the study period (August 2004-December 2006), study medical officers routinely visited all ICDDR,B treatment centers, 4 government hospitals and 3 district based clinics to detect cases of IS. They also examined all <2 years children admitted at ICDDR,B Matlab Hospital and community treatment centers with complaints of diarrhoea. As a part of their routine visit Community Health Research Workers (CHRW) enquired about all children <2 years of age in Matlab Surveillance area if they have any symptoms consistent with IS (based on Brighton Collaboration Criteria). They asked about abdominal pain and distention, abdominal mass, bile stained vomiting and passage of red current jelly or blood. CHRW's referred 41 children <2 years with suspected case of IS to Matlab hospital for further evaluation, clinical examination and ultra-sonogram by medical officer. Of these only 2 cases met the definition of 'probable case' of IS set by the Brighton Collaboration Criteria.

However these cases were not confirmed by ultra-sonogram. Findings from prospective part of the study as follows:

	August 2004 ~ December 2006
CHRW referred case	41
Hospitalized patient seen	1471
Ultrasonogram done	123
Probable case	2
Possible case	0

Details of 2 probable cases (Prospective studies)

Case 1: Male child aged 10 months referred to Matlab hospital with complaints of passage of liquid stool mixed with blood for 4 days, abdominal pain for 4 days and vomiting for 4 days. He had history of pneumonia about 8 months back and acute watery diarrhea 2 months back. He had a history of cough, running nose and tonsillitis 10 days ago. Child was exclusive breastfed up to 6 months then added cows milk with rice powder. Length of the child was 75 cm and weight was 7.6 kg. The child received all EPI vaccines except measles. On general examination the appearance was irritable, no dehydration, pulse was 125/min, respiration was 40/min, temperature was 37.5^0 C, abdomen was soft, bowel sounds were present and blood detected on rectal examination.. He had the following major and minor criteria according to Brighton collaboration case definition:

Major Criteria	Minor Criteria
1. Passage of blood per rectum	1. Predisposing factors: age <1 yr & male
2. Passage of a stool containing "red currant jelly"	2. Abdominal pain
3. Blood detected on rectal examination	3. Vomiting
	4. X-ray abdomen showed abnormal but non-specific gas pattern

USG of abdomen: No mass

Prognosis- The child recovered with conservative management

Case 2: Female child aged 14 months referred to Matlab hospital with the complaints of passage of liquid bloody stool for 5 days, vomiting for 4 days and abdominal pain. The child had history of common cold and pneumonia. She was exclusive breastfed for 2 months and then started cow's milk. The length of the child was 73 cm and weight was 6 kg. She received all EPI vaccines. The child was lethargic, dehydration was some, pulse was 125/min, respiration was 36/min,temperature was 37.5^0 C, abdomen was soft, bowel sounds were present and blood detected on rectal examination. She had the following major and minor criteria according to Brighton collaboration case definition:

Major Criteria	Minor Criteria
▪ Passage of blood per rectum	▪ Abdominal pain
▪ Blood detected on rectal examination	▪ Vomiting
	▪ Pallor
	▪ X-ray abdomen showed abnormal but non-specific gas pattern

USG findings: No features of Intussusception.

Prognosis- The child recovered with conservative management

BRIGHTON COLLABORATION CRITERIA:

(Brighton Collaboration- Intussusception definition and guidelines- www.brightoncollaboration.org)

Major Criteria

1. Evidence of intestinal obstruction

History of bile-stained vomiting
Acute abdominal distension and abnormal or absent bowel sound
X-ray abdomen showing fluid levels & dilated bowel loops

2. Features of intestinal invagination

Abdominal mass
Rectal mass
Intestinal prolapse
X-ray abdomen showing visible soft tissue mass

3. Evidence of intestinal vascular compromise or venous congestion

Passage of blood per rectum
Passage of a stool containing “red currant jelly” material
Blood detected on rectal examination

Minor criteria

1. Predisposing factors: age <1 year and male sex
2. Abdominal pain
3. Vomiting

4. Lethargy
5. Pallor
6. Hypovolumic shock
7. X-ray abdomen showing abnormal but non-specific gas pattern

Scoring For Diagnosis

Probable Case:

- Two or more major criteria
- One major (Excluding blood per rectum) and three or more minor criteria

Possible Case:

- Four or more minor criteria

Diagnostic Certainty

Level 1:

- Surgical criteria
- Radiological criteria
- Autopsy criteria

Level 2:

- Two major criteria or one major and three minor criteria

Level 3:

- Four or more minor criteria

Summary

There were few probable and possible cases of IS detected. The IS surveillance system has been fully established at Matlab surveillance area to diagnose, treat and referral of potential cases. This would be useful to provide data on background rates of IS and to initiate necessary management of patients during the rotavirus vaccine trials. Collaboration with Government (GoB) hospitals and private clinics have been established and continuing.