

High mortality rate in one year cohort study among patients with *Clostridium difficile* infection (CDI) in a large tertiary hospital

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Background (1)



- Toxin mediated disease
- Wide spectrum of disease: asymptomatic carriage to self-limited mild and watery diarrhea, to colitis, to life-threatening, fulminant colitis, pseudomembranous colitis, and death
- One of the most important causes of hospital infectious diarrhea
- Major risk factors: ATB, advanced age and hospitalization

Background (2)



- Increasing incidence and severity
- New strain (027) identified as cause of outbreaks in North America and Europe
- Population that previously had been thought to be at low risk

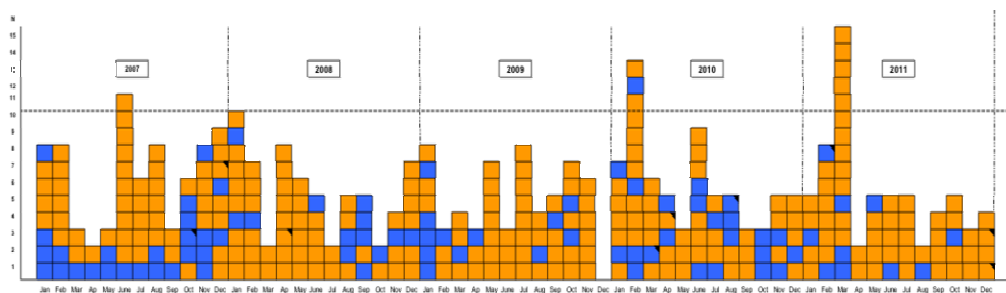
Background-French situation



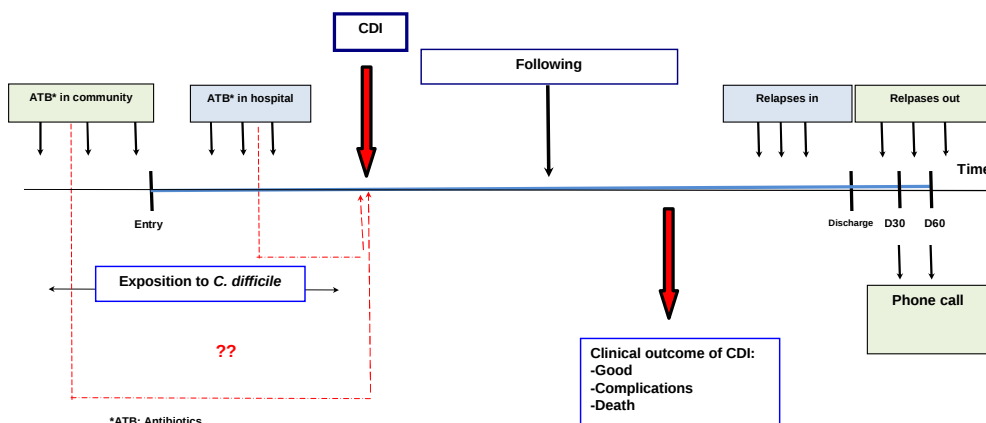
- **Incidence not well known**
 - Mortality and hospital data: 0.5-3 /10 000 patient-days
 - National study, ICD RAISIN (March to August 2009): 2.28/10 000 patient-days (acute care) and 1.14/10 000 patient-days (long term care)
 - European hospital based study (2008): 2.1/10 000 patient-days
- **2006** first outbreak
- **Mandatory notification** of severe cases or outbreaks

Background-Local situation at Eduard Herriot hospital

- Large University hospital, 860 beds
- Active surveillance (since Nov 2006)
 - 3.29 /10 000 pd (2009) and 3.61 /10 000 patient-days (2010)



Prospective Cohort study



Objectives



Main objective

Description of the prognosis of CDI (relapses, cure or death)

Secondary objectives

- Description of population, onset of the disease, history of previous CDI
- Analysis in various populations (surgery, ICU, internal medicine, geriatrics...)
- Latency between antibiotic treatment (s) and onset of CDI
- Description of antibiotics use (factors associated with relapse)
- Assess the rate of CDI recurrences at 30 & 60 days of follow-up
- Estimate the proportion of antibiotic-associated diarrhea in the population that are confirmed CDI

Microbiological diagnosis



- **Until November 7, 2011:** EIA Toxins A & B + culture
- **Since November 8, 2011:** EIA GDH + EIA Toxins A & B + culture
- **Molecular biology** collaboration with the *National Reference Center* (CNR) of Clostridium, Paris-France

Definitions (1)



- **Bacteriologic case of CDI** patient with a positive result of EIA assay and/or with a positive toxigenic culture result
- **Origin**
 - HA-CDI: ≥ 48 h after admission, or within 4 weeks of discharge from a healthcare facility
 - CA-CDI: within 48h of admission and over 12 weeks following discharge from a healthcare facility

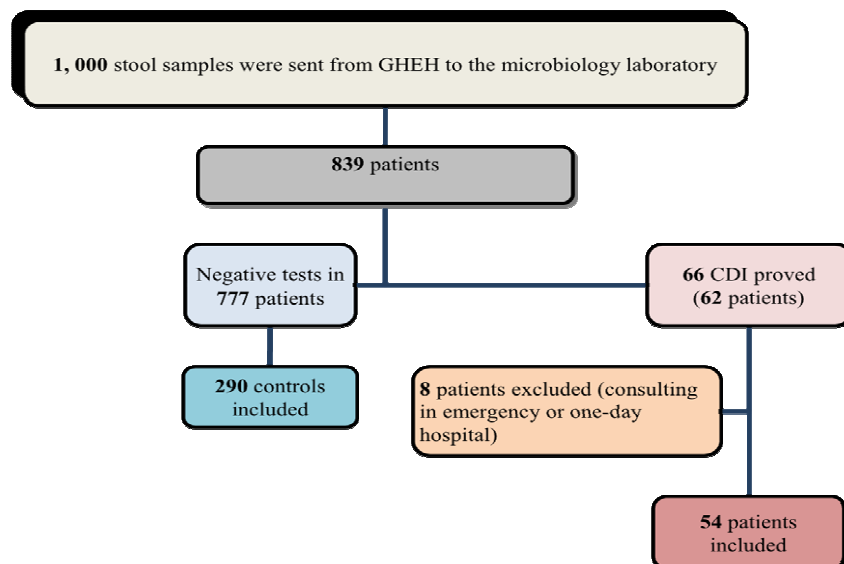
Definitions (2)



- **Reccurent case** a patient with resurgence of symptoms at least 10 days, but no more than 2 months, after the onset of the last episode, with a positive test result for *C. difficile*
- **Severe case**
 - Presence of fever (temperature $\geq 38^{\circ}\text{C}$), abdominal pain and leukocyte count $\geq 10,000$ cells/mm³; **OR**
 - Endoscopically or histologically proven pseudomembranous colitis; **OR**
 - Complications, such as death within 30 days with CDI as the primary or a contributing cause, toxic megacolon, perforation, colectomy, or septic shock requiring admission to the intensive care unit

Results (1)

Between February, 2011 and January, 2012



Results (2)

- **Gender** 24 women (44.4%) and 30 men (55.6%)
- Mean of **age** 66.8 years (min-max: 21-93)
- **Provenance** Home (54.5%); another hospital (21.8%), same hospital (16.4%) and other (7.3%)

Ward of diagnosis	N (%)
Medicine (hematology, internal and nephrology)	17 (30.9)
ICU	11 (20)
Emergency	11 (20)
Geriatrics	8 (14.5)
Surgery (general, GI and urology)	8 (14.5)

Results (3)



Past medical history	n (%)
Cardiovascular	30 (55.6)
Nervous system	4 (7.4)
Endocrinology	17 (31.5)
Oncology	22 (40.7)
Mental disorder	13 (24.1)
Nephrology	20 (37)
Gastro-intestinal	18 (33.3)
Other	42 (77.8)

Results (4)



- **Previous exposure to antibiotics** 42 (76.4%)
 - 3rd Cephalosporin 45.5%
 - Quinolones 36.4%
- **Recent hospitalization** 38 (69.1%)
- **Previous exposure to antiacids** (IPP and/or anti H2) 36 (65.5%)
- **Stay in nursing home** 5 (9.3%)
- **Previous CDI** 9 (16.4%)

Results (5)



Clinical presentation	n (%)
Duration of diarrhea	
Mean (min-max)	15.4 (2-62)
Median (IQR)	12 (8-17)
Temperature (fever >38°)	23 (41.8)
Abdominal pain	16 (29.1)
Vomiting	12 (21.8)
Dehydration	11 (20)
Nausea	6 (10.9)
WBC (Leucocytes/mL)	
Mean (min-max)	14,049 (2,170-76,000)
Median (IQR)	10,590 (7,690-17,375)

Results (6)



Laboratory tests

Toxins A&B, n (%)				
Culture, n (%)	+		-	
	+	25 (45.5)	13 (23.6)	38 (69.1)
	-	17 (30.9)	0 (0)	17 (30.9)
		42 (76.4)	13 (23.6)	55 (100)

- Mean time between the onset of diarrhea and the microbiological diagnosis: 7.63 days
- Mean time to have the complete result: 8 days
- 24 episodes: result of culture after discharge or patient death

Results (7)



■ Origin of CDI

- Hospital-acquired: 81.8% (n=45)
- Community-acquired: 9.1% (n=5), 75% were female
- Unknown: 9.1% (n=5)

Variables	CA- CDI n= 5	HA- CDI n=44 (45 episodes)	P value
Previous exposure to antibiotics	1 (20)	36 (80)	0.004
Temperature (fever >38°C)	5 (100)	15 (33.3)	0.004
Abdominal pain	3 (60)	9 (20)	0.047

Results (8)



Outcome of CDI episode	N (%)
Good outcome	33 (60)
Death	11 (20)
Complications	8 (14.5)
Unknown	2 (3.6)

- Severe case: 16 (29.1%)

Results (9)



Complications related to CDI episode	Evolution
Renal failure and septic choc	Good
Pancolitis (n=3)	Good (2 patients) and late death (D78)
Diffuse colitis and ileus (transfer to ICU)	Good
Renal failure and peritonitis	Death (D10 after the onset of symptoms)
Renal failure and septic choc	Death (D27 after the onset of symptoms)
Peritonitis and perforation	Death (D40 after the onset of symptoms)



Hôpitaux de Lyon



Lyon 1

Results (10)



- At **D30**: death rate 22% (11 over 50 patients), 50% of cases death occurred the first 6 days; relapse in one patient (1.8%) and one case of colitis (1.8%)
- CDI: primary cause of death for one patient and a contributing cause in 3 deceased patients from complications
- At **D60**: 2 cases of relapse (4.7%)

Advantages and limits



■ Limits

- One center
- University hospital: more severe cases?

■ Advantages

- Prospective design
- Standardized form for data collection and definition
- All tests were performed in the same microbiological laboratory

Conclusion



- High **mortality** rate
- **Severe and Complicated** cases
- **CA are different** from HA
- CDI should be considered as a cause of diarrhea in patients **without classical risk** factors
- **Food** may serve as a source of human infection (with or without exposure to ATB): limited epidemiologic evidence

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