IDWeek 2013

1382

Changing epidemiology of healthcare-associated *Clostridium difficile* infection from 3 years study in Korea

Jieun Kim[1], Hyunjoo Pai[1], Mi-Ran Seo[1], Jung Oak Kang[2], Tae Yeal Choi[2]

Department of Internal medicine[1] and Laboratory Medicine[2], Hanyang University, Seoul, Korea

Abstract

Background

Clostridium difficile infection (CDI) is one of the most important hospital infections, and during the past decade its incidence has increased markedly worldwide. The objective of this study was to investigate the change in incidence, molecular epidemiology, and severity of healthcare-associated CDI (HA-CDI) in a tertiary hospital in Korea.

Methods

From Feb 2009 through Jan 2012, HA-CDI patients were enrolled in our study at a 900-bed tertiary care facility located in Seoul, Korea. With cultured *C. difficile* organisms, PCR-ribotyping was performed and checked visually. An outbreak was defined when the number of isolates with the same ribotype in a month exceeded double the monthly average.

Results

Median incidence of HA-CDI was 72.0 per 10^5 pt*days, monthly incidence varying from 34.4 to 162.3/10^5 pt*days, but there was no significant difference in incidence among 3 periods. The highest incidence was detected on May 2010 with outbreak of PCR ribotype 018 strains (n=20). The second highest incidence was detected on Feb 2011 with outbreak of PCR ribotype 017 strains (n=8).

Comparing the distribution of PCR ribotypes among 3 periods, period 1 showed 40 identical PCR ribotype with 140 HA-CDI and dominant strain were PCR ribotype 018 (26.4%), 017 (15.7%), and 001 (14.3%). Period 2 had 31 distinct PCR ribotype from 177 HA-CDI isolates. Most common PCR ribotype during period 2 was 017 (33.3%), followed by 018 (32.8%). During period 3, 32 PCR ribotype were identified from isolates of 168 CDI patients. PCR ribotype 018 was dominant strain with 32.1% of all isolates. PCR ribotype 017 was the second most common with 28.0%.

During the study period, PCR ribotype 017 was identified as endemic strain with persistence. PCR ribotype 018 showed clustering pattern with outbreaks. There were 15 cases of HA-CDI caused by binary toxin producing strains. Among them, only 3 strains showed PCR ribotype 027.

Leukocytosis and old age were significantly higher in period 3 than in period 1. Presence of pseudomembrane was not different by period (37.8%, 53.1%, 38.8%, each period, *p* for trend=0.947). Recurrence rate was 21.6%, 19.6%, and 20.2% in each period, respectively and cure rate without recurrence was 59.8%, 63.9%, and 58.5% without significant difference (*p* for trend=0.804, 0.862, respectively). Among all HA-CDI patients, in-hospital mortality rate was 6.7%, 3.8%, and 11.6% and attributable mortality was 0.6%, 1.6%, and 0.6% in each year (*p* for trend=0.076, 0.97).

Conclusion

During 3 years, molecular epidemiology of HA-CDI in Korea has been changed with outbreaks.

Background

Objective of the study is to investigate the change in incidence, disease severity, and molecular epidemiology of healthcare-associated CDI (HA-CDI) in a tertiary hospital in Korea.

Methods

- Study period; from September 2008 through January 2012
- Study patient; who diagnosed with HA-CDI at a 900 bed tertiary care facility located in Seoul, Korea
- Definition of CDI; Patients who showed any positive results listed below
  - Laboratory test; *C. difficile* toxin A&B assay or cultured organisms with *tcdA* or *tcdB* confirmed by PCR
  - Image study; pseudomembrane by endoscopy or histology
- Definition of healthcare-associated CDI
  - developed diarrhoea at least 72 h after hospitalization
  - within 2 months of the last discharge provided that they were not residents in a long-term facility
- Study method
  - Multiplex PCR; with cultured organisms, identify *tcdA*, *tcdB*, *cdtA*, and *cdtB*
  - PCR-ribotyping; compared with reference strains (PCR-ribotype 017, 027, and strains from the ECDC-Brazier collection) visually
- Study definition
  - Diversity Index(DI): the number of distinct ribotypes divided by the total isolates, expressed as a percentage
  - Severity score method 1; sum of four factors
    - 1 point ; Age >60, temperature >38.3℃, hypoalbuminemia (albumin level <2.5 mg/dL), leukocytosis (WBC count >15,000 cells/mm^3)
  - Severity score method 2; leukocytosis (WBC count >15,000 cells/mm^3) + elevated serum creatinine (>1.5 baseline)
  - Treatment response
    - Success; improved diarrhea after the initiation of initial therapy by day 14
    - Recurrence; positive laboratory results with resurgence of symptoms after cessation, at least 10 days after the first episode

Results

- During 3 years, 552 HA-CDIs were diagnosed with laboratory test or image studies.
- Monthly incidence fluctuated with outbreaks in the range from 34.4 to 162.3/10^5 patient*days (mean 72.0) (Figure 1)
- Comparing the distribution of PCR ribotypes during 3 years, 40 distinct PCR ribotypes were identified from 140 HA-CDI in period 1 (DI 28.6%), 31 PCR ribotypes from 177 HA-CDI isolates in period 2 (DI 17.5%) and 32 PCR ribotypes from 168 CDI patients in period3 (DI 19.0%).
- Incidence of CDI by ribotype 017 and 018 was complementary (Figure 1&2).
  - By Spearman's rank correlation analysis; moderate negative linear relationship (Spearman's rho = -0.527, $p = 0.001$)
- Distribution of PCR-ribotype 017&018 from *C. difficile* isolates over hospital ward (Figure 3)
  - PCR-ribotype 017: dominant PCR-ribotype in M15, M18, and M20
  - PCR-ribotype 018: relatively even distribution over hospital ward
- Distribution of PCR-ribotype 017&018 from *C. difficile* isolates according to admission department (Figure 4)
  - PCR-ribotype 017: more than half of *C. difficile* isolates from pulmonary department
- Clinical characteristics and treatment outcome of HA-CDI are shown in Table 2.
  - Gender and Charlson's score were different by periods
  - Severity score did not differ; however, leukocytosis and old age were different by periods.
  - Treatment outcome of initial HA-CDI episode was not different.

Conclusion

1. The incidence of CDI did not increase over 3 years.
2. The percentage of dominant strains (ribotype 017, 018) increased over 3 years with the decrease of diversity index.
3. Incidence of CDI by ribotype 017 and 018 was complementary.
4. Clinical characteristics and treatment outcome did not change.

Table 1. Distribution of distinct PCR-ribotypes over 3 years

	PCR-ribotypes																								
period	1	2	14	15	17	18	23	27	78	112	122	130	163	267	AB24	other binary	UN17	UN36	UN39	UN48	UN64	UN68	UN81	UN91	other
200902			1			1					1														2
200903					1	3							1												3
200904						3			1																1
200905	2					5																			3
200906	3				3	3	2										1			1					0
200907	2	1	1			3																			4
200908	1	1	2		2	7																			1
200909					2	3		3		1								1	1						0
200910	4		1		1	4									3				1						1
200911	1				4					2		2		1											5
200912	1	1	2		7	4						2					1								2
201001	6	1			2	1				1															2
Diversity Index: 28.6%, PCR ribotype 018 (26.4%), 017 (15.7%), 001 (14.3%)																									
201002	1				6					1								1	1						1
201003					4	3											1								0
201004				1	3	10												2				1			1
201005			1		6	20				1								1							3
201006	1		1		5	5			1												1				0
201007					6	1											1		1				1		2
201008	1		2		3	8												3							0
201009			1		6	6												1							0
201010					7																	2			4
201011	1				6	2															2	3			3
201012	1				5	1														1		1	1		4
201101	2				2	2																			1
Diversity Index: 17.5%, PCR ribotype 017 (33.3%), 018 (32.8%) and unknown ribotype 36 (4.5%)																									
201102	1		1		8	3				1			1		1	1	1							1	0
201103					9	1									1		1					1		1	2
201104					7	2											1						1		2
201105					6	6			1	1							1	1						1	2
201106					9					1															3
201107					2	2				1							1								3
201108					2	3											1			1					1
201109	2				2	3											1			1	1				1
201110	1					7				2						1									0
201111			2		2	6											1							1	4
201112				1	2	9																	1		2
201201				1	1	13														1			1		1
Diversity Index: 19%, PCR ribotype 018 (32.1%), 017 (28.0%) and unknown ribotype 17 (4.8%)																									
Total(N)	31	4	15	3	131	150	2	3	2	13	1	4	2	1	5	3	11	10	4	5	4	8	5	4	64
%	6.4	0.8	3.1	0.6	27	30.9	0.4	0.6	0.4	2.7	0.2	0.8	0.4	0.2	1	0.6	2.3	2.1	0.8	1	0.8	1.6	1	0.8	13.2

Table 2. Clinical characteristics and treatment outcome of HA-CDI according to periods

		2009.2-2010.1	2010.2-2011.1	2011.2-2012.1	*P* value
Total number	N	165	185	172	
Gender-male	N(%)	87(52.7)	85(45.9)	68(39.5)	0.015*
Age	median(1Q,3Q)	64.2(54,75)	65.5(57,76.5)	67.9(61.3,77.8)	0.083**
Hospital days	median(1Q,3Q)	38(11,42)	41(8.5,53)	30(8,41.8)	0.114**
Charlson's score	median(1Q,3Q)	3(1,4)	3.5(3,5)	2.9(1,4)	0.035**
Severity score method 1	median(1Q,3Q)	1.25(1,2)	1.11(1,2)	1.24(1,2)	0.583**
hypoalbuminemia	N(%)	14(8.5)	21(11.4)	17(9.9)	0.676*
leukocytosis	N(%)	27(16.4)	34(18.4)	43(25.0)	0.047*
old age	N(%)	103(62.4)	126(68.1)	131(76.2)	0.006*
fever	N(%)	20(12.1)	27(14.6)	20(11.6)	0.884*
Severity score method 2	median(1Q,3Q)	1(0,1)	1.11(1,2)	1.2(1,2)	0.074**
Pseudomembrane	N(%)	17/45(37.8)	17/32(53.1)	19/49(38.8)	0.947*
Treatment-done	N(%)	116(70.3)	125(67.6)	115(66.9)	0.5*
Initial episode	N	97	97	94	
Success	N(%)	82(84.5)	77(79.4)	75(79.8)	0.398*
Failure	N(%)	9(9.3)	13(13.4)	12(12.8)	0.453*
Loss	N(%)	1(1.0)	7(7.2)	6(6.5)	0.077*
Global cure	N(%)	58(59.8)	62(63.9)	55(58.5)	0.862*
Recur	N(%)	21(21.6)	19(19.6)	19(20.2)	0.804*
Mortality					
in-hospital mortality	N(%)	11(6.7)	7(3.8)	20(11.6)	0.076*
Attributable mortality	N(%)	1(0.6)	3(1.6)	1(0.6)	0.97*

*, *P* for trend

**, Kruskal-Wallis test

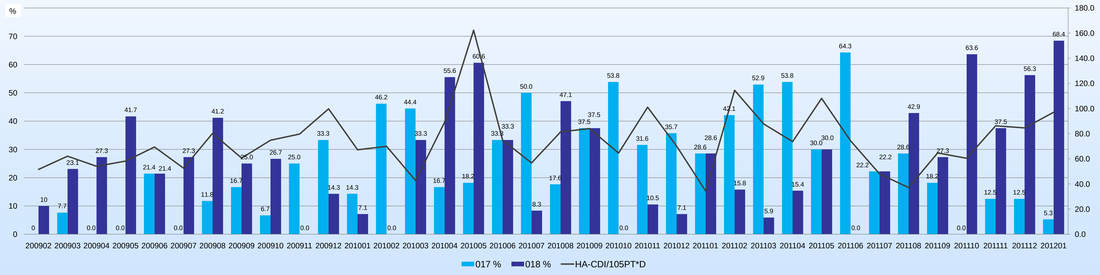

Figure 1. Incidence and dominant molecular epidemiology of healthcare-associated *Clostridium difficile* infection during 3 years

017%, percentage of PCR ribotype 017 among all *C. difficile* isolates; 018%, percentage of PCR ribotype 018 among all *C. difficile* isolates; HA-CDI/10^5PT*D, healthcare-associated *Clostridium difficile* infection/10^5 patient*days

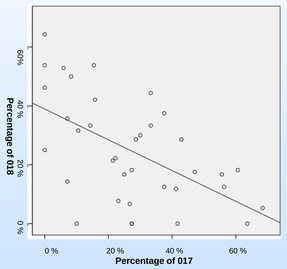

Figure 2. Scatter plots between two variables; percentage of PCR-ribotype 017 and 018

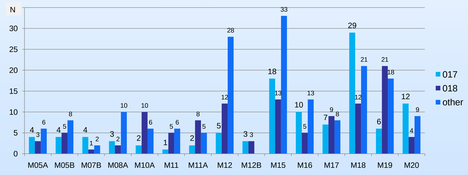

Figure 3. Distribution of ribotypes according to hospital ward

017, PCR-ribotype 017; 018, PCR-ribotype 018; other, PCR-ribotype other than 017&018

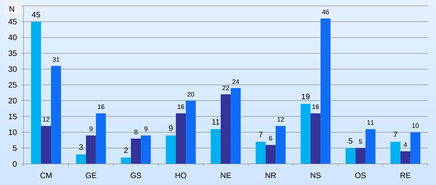

Figure 4. Distribution of ribotypes according to admission department

CM, pulmonary; GE, gastroenterology; GS, general surgery; HO, hemato-oncology; NE, nephrology; NR, neurology; NS, neurosurgery; OS, orthopedics; RE, rehabilitation; 017, PCR-ribotype 017; 018, PCR-ribotype 018; other, PCR-ribotype other than 017&018