



WEEKLY EPIDEMIOLOGICAL REPORT

A publication of the Epidemiology Unit
Ministry of Health

231, de Saram Place, Colombo 01000, Sri Lanka
Tele: + 94 11 2695112, Fax: +94 11 2696583, E mail: epidunit@slt.net.lk
Epidemiologist: +94 11 2681548, E mail: chepid@slt.net.lk
Web: http://www.epid.gov.lk

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Carbapenem Resistant Enterobacteriaceae Infection

Introduction

Antimicrobial resistance has become one of the most serious public health concerns worldwide. It is a global rather than a local issue, as antimicrobial resistance can spread between countries or continents. Massive increases in trade and long-distance travel have enabled the rapid spread of resistant pathogens. Although circumstances may vary by region or country, it is clear that some Asian countries are epicenters of resistance, having seen rapid increases in the prevalence of antimicrobial resistance of major bacterial pathogens. In these locations, however, the public health infrastructure to combat this problem is very poor.

What is CRE?

Carbapenem-resistant *Enterobacteriaceae* (CRE) is a group of *Enterobacteriaceae*, such as *Escherichia coli* and *Klebsiella pneumoniae* that are resistant to both carbapenems (Imipenem, Meropenem) and broad-spectrum β -lactams. Types of CRE are sometimes known as KPC (*Klebsiella pneumoniae* carbapenemase) and NDM (New Delhi Metallo-beta-lactamase). KPC and NDM are enzymes that break down carbapenems and make them ineffective. Both of these enzymes, as well as the enzyme VIM (Verona Integron-Mediated Metallo- β -lactamase) have also been reported in *Pseudomonas*.

CREs cause respiratory tract infections such as pneumonia, urinary tract infections, surgical site infections, catheter-related bacteremia, sepsis and meningitis. While more common among

immune compromised patients, postoperative patients or patients treated with antimicrobials for an extended period of time, CREs may also cause infection in otherwise healthy patients. CREs are often the cause of nosocomial infections.

Table 1-Laboratory criteria required for full-filling definition of Carbapenem resistance

- A) MIC for Meropenem $\leq 2\mu\text{g/ml}$ or zone diameter of Meropenem disk (KB) $\leq 22\text{mm}$
- B) Fulfilment of both i) & ii)
 - i) MIC for imipenem $\geq 2\mu\text{g/ml}$ or zone diameter of Imipenem disk(KB) $\leq 22\text{mm}$
 - ii) MIC for Cefmetazole $\geq 64\mu\text{g/ml}$ or zone diameter of Cefmetazole disk(KB) $\leq 12\text{mm}$

MIC: minimum inhibitory concentration

Carbapenem resistance mechanisms-

Mechanism of carbapenem resistance includes production of various carbapenemases, production of AmpC type or extended-spectrum β -lactamases combined with mutation(s) resulting in the decreased permeability of the cellular membrane. Carbapenemase-producing bacteria are clinically important as they are often resistant not only to broad-spectrum β -lactams but also to other classes of antimicrobials.

Epidemiological Surveillance

CRE infection is a category V infectious disease under the Infectious Diseases Control Law. Phy-

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sicians who make the diagnosis of CRE infection must notify all cases. Only infections determined to be caused by CRE are notifiable; asymptomatic CRE carriers are not. For determining carbapenem resistance, resistance to meropenem or resistance to both imipenem and cefmetazole are methods currently used. Among them, use of meropenem is most recommended on account of its sensitivity and specificity. Imipenem resistance was included in the reporting criteria because imipenem has been widely used as an indicator in the clinical setting. However, in order to exclude those that are resistant to imipenem but susceptible to other cephem antimicrobials and do not produce carbapenemase (e.g. Genus *Proteus*), reporting is limited to those resistant to both imipenem and cefmetazole. According to research, The prevalence of KPC-type carbapenem resistance in *Enterobacteriaceae* isolated in the NHSL is 7.9% and A statistically significant relationship (P<0.001) between the more than five days duration of hospital stay and the KPC-type carbapenemase production was observed.

Horizontal gene transfer and nosocomial infection

In most cases, the carbapenemase gene is found on plasmids. It is transmitted to other bacteria belonging to *Enterobacteriaceae* by conjugation or other horizontal gene transfer mechanisms. Some *Enterobacteriaceae* bacteria possessing carbapenemase gene may be phenotypically susceptible to carbapenems. Such bacteria may become carbapenem-resistant through elevated expression of the drug resistance gene(s) or through cellular membrane change and capable of transmitting the resistance gene(s) to other bacteria of other species. As such events may go unnoticed, such possibilities should be kept in mind for surveillance. In fact, dissemination of the carbapenem resistance gene to multiple bacteria species in the clinical setting has already been reported.

Asymptomatic CRE carriers are not rare. Although they are not notifiable, if they are hospitalized and a nosocomial outbreak is suspected, such carriers should be reported to health centers and necessary measures taken promptly with the assistance of an existing local network of medical institution. Though this notice will be updated soon, the requirements for notification will remain unchanged. If genotyping or further analysis of resistance gene(s) is deemed necessary for infection control purposes, research institutes, including the Medical research Institute should be consulted.

Sources

CREI available at <http://www.who.int/drugresistance/documents/surveillancereport/en/>

IASR available at <http://www.nih.go.jp/niid/en/iasr-e/865-iasr/5274-tpc418.html>

Compiled by Dr. C U D Gunasekara of the Epidemiology unit.

**Table 1 : Water Quality Surveillance
Number of microbiological water samples December/ 2014**

District	MOH areas	No: Expected *	No: Received
Colombo	12	72	26
Gampaha	15	90	NR
Kalutara	12	72	65
Kalutara NIHS	2	12	10
Kandy	23	138	NR
Matale	12	72	65
Nuwara Eliya	13	78	NR
Galle	19	114	82
Matara	17	102	0
Hambantota	12	72	NR
Jaffna	11	66	8
Kilinochchi	4	24	NR
Manner	5	30	19
Vavuniya	4	24	2
Mullatvu	4	24	96
Batticaloa	14	84	5
Ampara	7	42	NR
Trincomalee	11	66	0
Kurunegala	23	138	36
Puttalam	9	54	31
Anuradhapura	19	114	6
Polonnaruwa	7	42	0
Badulla	15	90	54
Moneragala	11	66	53
Rathnapura	18	108	45
Kegalle	11	66	16
Kalmunai	13	78	NR

* No of samples expected (6 / MOH area / Month)
NR = Return not received

Table 1: Selected notifiable diseases reported by Medical Officers of Health 10th - 16th Jan 2015 (03rd Week)

RDHS Division	Dengue Fever		Dysentery		Encephalitis		Enteric Fever		Food Poisoning		Leptospirosis		Typhus Fever		Viral Hepatitis		Human Rabies		Chickenpox		Meningitis		Leishmaniasis		WRCD	
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	T*	C**
Colombo	302	870	2	13	0	0	0	1	0	0	6	15	0	0	2	4	0	0	2	17	2	3	0	0	81	19
Gampaha	45	285	0	2	0	0	1	1	0	0	3	16	0	1	1	4	0	0	0	2	0	1	0	0	33	67
Kalutara	47	177	3	4	0	1	2	5	2	3	8	30	0	0	2	2	0	0	2	7	2	4	0	0	100	0
4Kandy	43	141	5	18	0	0	1	2	0	0	4	4	3	11	7	23	0	0	4	16	0	2	0	1	96	4
M31atale	47	93	1	2	0	0	0	1	0	0	4	6	1	1	0	1	0	0	0	1	0	0	0	0	69	31
NuwaraEliya	4	14	2	13	0	0	1	1	0	0	2	2	0	1	0	18	0	0	1	1	0	3	0	0	62	38
Galle	33	74	3	8	0	0	0	0	1	4	2	16	2	5	0	0	0	0	6	14	3	7	0	0	80	20
Hambantota	11	25	3	4	0	0	0	3	0	0	3	12	0	2	0	1	0	0	0	4	0	0	3	16	92	8
Matara	8	40	2	4	0	0	0	1	0	18	3	14	0	3	0	0	0	0	3	14	1	4	0	4	94	6
Jaffna	119	447	15	47	2	3	8	29	0	0	1	4	51	161	1	3	0	0	6	11	1	1	0	0	100	0
Kilinochchi	0	6	3	9	0	0	1	1	0	2	0	0	0	1	0	0	0	0	0	0	0	0	0	0	50	50
Mannar	5	37	0	1	0	0	0	0	1	1	0	0	0	2	0	0	0	0	0	0	0	0	0	0	80	20
Vavuniya	3	9	1	4	1	1	4	0	0	1	4	1	3	0	0	0	0	0	1	1	0	0	0	0	100	0
Mullativu	5	19	0	5	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	60	40
Batticaloa	52	150	2	12	1	1	0	0	0	0	1	1	0	0	0	0	0	0	1	1	0	2	0	0	93	70
Ampara	2	6	1	10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	15	1	3	0	0	71	29
Trincomalee	17	46	0	1	0	0	1	2	0	22	0	4	0	0	0	0	0	0	0	3	0	0	0	0	83	17
Kurunegala	40	159	1	12	0	1	1	1	0	0	3	19	0	4	0	1	0	0	4	13	0	2	1	1	89	11
Puttalam	27	122	0	4	0	0	0	0	0	0	4	4	0	0	0	0	0	0	0	0	0	1	0	0	62	38
Anuradhapura	19	56	0	3	0	0	0	0	1	1	17	32	1	3	0	0	0	0	1	7	0	3	1	8	84	16
Polonnaruwa	7	21	1	4	0	0	0	0	0	0	6	18	0	0	0	1	0	0	3	10	1	2	1	2	86	14
Badulla	38	109	1	11	0	0	0	1	0	0	0	0	2	3	2	7	0	0	3	6	0	3	0	0	71	29
Monaragala	10	26	6	14	0	0	0	2	0	1	13	33	0	2	0	1	0	0	0	1	0	0	0	2	100	0
Ratnapura	20	66	3	12	1	1	0	2	0	0	3	10	0	4	4	13	0	0	2	2	2	3	3	3	83	17
Kegalle	17	58	2	4	0	0	1	10	0	0	5	12	0	2	3	11	0	0	2	5	2	4	0	0	82	18
Kalmune	55	143	3	13	0	0	0	0	1	4	1	1	0	0	0	0	0	0	3	9	0	0	0	0	77	23
SRI LANKA	976	3199	60	234	5	8	17	67	7	57	81	257	61	209	22	90	0	0	41	160	15	49	9	37	81	19

Source: Weekly Returns of Communicable Diseases (WRCD).

*T=Timeliness refers to returns received on or before 16th January, 2015 Total number of reporting units 337 Number of reporting units data provided for the current week: 277 C**=Completeness

Table 2: Vaccine-Preventable Diseases & AFP

10th - 16th Jan 2015 (03rd Week)

Disease	No. of Cases by Province									Number of cases during current week in 2015	Number of cases during same week in 2014	Total number of cases to date in 2015	Total number of cases to date in 2014	Difference between the number of cases to date in 2014 & 2015
	W	C	S	N	E	NW	NC	U	Sab					
AFP*	00	00	00	01	00	01	00	00	00	02	03	06	03	+50%
Diphtheria	00	00	00	00	00	00	00	00	00	00	00	00	00	0%
Mumps	02	00	03	00	00	00	01	00	00	06	06	15	66	-77.3%
Measles	05	01	13	00	02	05	02	00	00	28	99	68	280	-75.7%
Rubella	00	00	00	00	00	00	00	00	00	00	00	02	00	0%
CRS**	00	00	00	00	00	00	00	00	00	00	00	00	00	0%
Tetanus	00	00	00	00	00	00	00	00	00	00	00	00	00	0%
Neonatal Tetanus	00	00	00	00	00	00	00	00	00	00	00	00	00	0%
Japanese Encephalitis	01	00	00	00	00	00	00	00	00	01	02	02	05	-60%
Whooping Cough	00	01	00	00	00	00	00	00	00	01	00	05	01	+400%
Tuberculosis	35	18	00	15	12	03	02	02	14	101	166	366	685	-46.6%

Key to Table 1 & 2

Provinces: W: Western, C: Central, S: Southern, N: North, E: East, NC: North Central, NW: North Western, U: Uva, Sab: Sabaragamuwa.
 RDHS Divisions: CB: Colombo, GM: Gampaha, KL: Kalutara, KD: Kandy, ML: Matale, NE: Nuwara Eliya, GL: Galle, HB: Hambantota, MT: Matara, JF: Jaffna, KN: Killinochchi, MN: Mannar, VA: Vavuniya, MU: Mullaitivu, BT: Batticaloa, AM: Ampara, TR: Trincomalee, KM: Kalmunai, KR: Kurunegala, PU: Puttalam, AP: Anuradhapura, PO: Polonnaruwa, BD: Badulla, MO: Moneragala, RP: Ratnapura, KG: Kegalle.

Data Sources:

Weekly Return of Communicable Diseases: Diphtheria, Measles, Tetanus, Neonatal Tetanus, Whooping Cough, Chickenpox, Meningitis, Mumps., Rubella, CRS,

Special Surveillance: AFP* (Acute Flaccid Paralysis), Japanese Encephalitis

CRS** =Congenital Rubella Syndrome

AFP and all clinically confirmed Vaccine Preventable Diseases except Tuberculosis and Mumps should be investigated by the MOH

Influenza Surveillance in Sentinel Hospitals - ILI & SARI								
Month	Human					Animal		
	No Received	ILI	SARI	Infl A	Infl B	Pooled samples	Serum Samples	Positives
December	3777	388	62	67	17	1667	877	0

Source: Medical Research Institute & Veterinary Research Institute

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ON STATE SERVICE

Dr. P. PALIHAWADANA
 CHIEF EPIDEMIOLOGIST
 EPIDEMIOLOGY UNIT
 231, DE SARAM PLACE
 COLOMBO 10