

ORIGINAL ARTICLE

The epidemiology of carbapenem-resistant Enterobacterales in a single center in Oman

Ahmed AL Yarabi¹, Zaina AL Maskari^{2*}, Amal AL Tai², Faryal Khamis³, Eskild Petersen³ and Amina AL Jardani⁴

¹Oman Medical Specialty Board, North Azaiba, Muscat, Oman; ²Royal Hospital Infection Prevention and Control, AL Ghubra South, Muscat, Oman; ³Royal Hospital Department of Medicine, Hospital Infectious Diseases Unit, AL Ghubra South, Muscat, Oman; ⁴Central Public Health Laboratory, Wattiya, Muscat, Oman

Abstract

Background: Carbapenem-resistant Enterobacterales (CRE) are a global public health threat associated with significant morbidity and mortality.

Objectives: The study aims to describe the epidemiology, microbiology and outcome of patients with CRE infection or colonization during an active surveillance program and to determine the risk factors for the acquisition of such organisms in a single center in Oman.

Method: A retrospective case-control study was conducted in a tertiary care hospital in 2015 and 2016. Cases included patients who had a positive screening or clinical sample for CRE and controls included patients who were screened during the same period and never had a positive screening or clinical sample for CRE. Risk factors analyzed were demographics, comorbidities, instrumentation, and antibiotic exposures. Data were analyzed using SPSS for Windows (version 11.5). Variables of interest were analyzed by univariate analysis, and those of significance were analyzed by logistic regression.

Results: Seven hundred and twenty-eight cases were detected from active surveillance screening, and clinical samples and 749 controls were included. Males comprised 417 (57.3%) cases and females 311 (42.7%). The majority of CRE cases were adult patients (88%, $n = 644$) compared to 12% ($n = 84$) paediatric. The total number of CRE screenings was 8,431 samples in 2015 with a positivity rate of 4.2% and 10,231 samples in 2016 with a positivity rate of 3.6%. The annual incidence rate of CRE was 0.8 per 100 admissions in 2015 and 0.76 per 100 admissions in 2016. The annual incidence density was 1.90 and 1.89 per 1000 patient days for both years, respectively. Healthcare-associated acquisition was 99.5%, and only 0.5% was attributed to the community. The most common sites of infections were urine and wound comprising 29% each. *Klebsiella pneumoniae* ($n = 578$, 79%) was the predominant organism followed by *Escherichia coli* ($n = 101$, 14%). CRE acquisition was significantly associated with the presence of a urinary catheter (odds ratio [OR]: 7.3; confidence interval [CI]: 4.6–11.6; $P < 0.0001$ or central line (OR: 3.5; CI: 2.068–6.011; $P < 0.001$), intubation (OR: 0.5; CI: 0.264–0.947; $P < 0.034$), antibiotic exposure (OR: 4.5; CI: 3.101–6.586; $P < 0.0001$), and intensive care unit (ICU) admission (OR: 0.5; CI: 0.297–0.852; $P = 0.011$). In addition, history of a local and an abroad hospital admission significantly increased the risk of CRE acquisition (respectively, local OR: 10.97; CI: 7.878–15.301; $P < 0.000$, abroad OR: 12.4; CI: 6.597–23.617; $P < 0.0001$). Overall mortality was 23.1 and 52.3% among bacteremia cases.

Conclusion: The annual incidence of CRE acquisition is high with a high mortality rate. A multifaceted strategy to control the spread of CRE is fundamental, considering the specific epidemiology of CRE related to our institution and country.

Keywords: carbapenem-resistant Enterobacterales; carbapenemase; epidemiology; surveillance; Oman

Received: 20 June 2021; Accepted: 7 July 2022; Published: 8 June 2023

Carbapenem-resistant Enterobacterales (CRE) are a global public health threat associated with significant morbidity and mortality. In the absence of safe and effective treatment options, infection prevention remains the primary means of mitigating CRE-related morbidity and mortality (1).

In Oman, CRE was reported for the first time in 2011 among *Klebsiella pneumoniae* harbouring NDM-1 and OXA-181 carbapenemases (2, 3). Other reports described the molecular epidemiology of CRE in the country, where the predominant isolates were *Klebsiella pneumoniae*, followed by *Escherichia coli*, *Enterobacter cloacae* and others

that carried bla_NDM, bla_{OXA48}-like and to a lesser extent bla_{VIM} carbapenemases (4, 5). In addition, Balkhair et al. reported in 2013 an overall prevalence rate of 10.8 (95% CI: 9.3–12.4) of multidrug resistant gram-negative bacteria cases per 1,000 admissions (6).

Data regarding the incidence of CRE in Oman and risk factors for CRE infection or colonization are lacking. This study aims to describe the epidemiology, microbiology, and outcome of patients who acquired CRE infection or colonization during an active surveillance program and determine the risk factors for the acquisition of such organisms in a single center in Oman.

Methods

The Royal Hospital is a tertiary care hospital with 769-bed capacity delivering care to the Omani population through the divisions of Child Health, Medicine, Surgery, Obstetrics and Gynecology, Oncology and Cardiothoracic Surgery. The hospital has 25 adult intensive care unit (ICU) beds (16 beds covering medical and surgical service and nine adult post-cardiac surgery beds). The paediatric ICU has 25 beds (nine medical and surgical beds, 10 neonatal and six paediatric post-cardiac surgery). In addition, the hospital has a step-down unit for critical adult patients that is located within the Adult ICU, which sometimes admits ventilated patients and accommodates chronically ventilated patients. The critical patients move between these two units frequently, and staff are shared between them. Therefore, the infection prevention and control department (IPCD) consider the two units as one when looking at the epidemiological link to acquisition and infection control interventions.

The hospital has well-established CRE surveillance that commenced in 2012 and is conducted by the IPCD. The surveillance criteria have changed over the years except during 2015 and 2016 when there was no change in screening indications and no outbreaks encountered. Surveillance involves screening patients at risk of CRE at admission and patients who have had contact with a CRE-positive case not under contact precautions. Weekly CRE screening is applied during outbreak situations.

This is a retrospective case-control study. We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations (Appendix I: The completed STROBE checklist) (7). The study was approved by the hospital's Ethics and Research Committee (SRC#114/2017). The cases included all patients who had a positive CRE screening or grew CRE from any clinical samples at admission or after admission during the study period. Only one sample is included for each case with repeated positive cultures if they remained positive from screening samples. Only a clinical sample is included for patients who had a positive culture from screening and then were positive from another clinical sample. The

controls were selected randomly from patients admitted during the same study period who had negative CRE screening and never grew CRE from any clinical samples during their hospital stay and throughout the study period. The case-to-control ratio was 1:1 because of the large number of cases identified.

Demographic data and clinical characteristics were extracted from the hospital information system (AL Shifa #3+, The Omani Health Information System). We studied the various risk factors that patients were exposed to in the 3 months prior to the detection of a CRE sample. We included presence of a nasogastric tube, central line, tracheostomy, urinary catheter, surgery, endoscopy, ICU admission or previous ICU admission (abroad and local), and antibiotic use. Case records were reviewed by an experienced microbiologist to categorise cases as infection versus colonization.

Definitions

Colonization: positive culture from a clinical non-sterile site sample or screening sample without the presence of signs and symptoms of infection and the patient received no antibiotic treatment for the duration of admission.

Infection: positive culture from clinical sterile and/or non-sterile samples with the presence of symptoms and signs of infection. If the patient was treated with antibiotics by the caring clinician, the event was considered an infection.

Community acquired: acquisition of CRE with no identified epidemiological link to healthcare institutions and the positive culture was collected within the first 48 h of admission.

Hospital-acquired: acquisition of CRE with the presence of an epidemiological link to healthcare institutions such as admission, dialysis, or daycare or the positive culture for CRE was obtained 48 h after admission.

Microbiology

Patients with risk factors were screened on admission with rectal swabs in addition to endotracheal tube secretions for ventilated patients, catheter urine for patients with urinary catheter, and wound swab for patients with chronic wounds. Samples were collected by staff nurses as per infection prevention and control screening criteria described in Appendix II. CRE swabs were directly inoculated in CRE chromogenic agar plates (CHROMagar™ mSuperCARBA™ Medisinal, Chromagar, Paris, France). The plates were incubated at aerobic conditions at 35–37°C for 18–24 h. Typical colonies as per colony forming units (CFUs) were identified and susceptibility tested using the BD Phoenix™ automated identification and susceptibility testing system (Becton, Dickinson and Company, Franklin Lakes, NJ, USA). Carbapenemase production is suspected based on Clinical and Laboratory

Standards Institute (CLSI) breakpoints of 2–4 mg/L for imipenem and meropenem and 2 mg/L for ertapenem with no routine confirmatory tests done (8).

Statistical analysis

Data were analyzed using SPSS Statistics for Windows version 11.5 (SPSS Inc., Chicago, IL, USA).

Statistical analysis included frequency and percent distributions. Significant variables in the univariate analysis were included in the logistic regression model for the multivariate analysis. P-values were interpreted together with 95% confidence interval (CI) for the logistic regression model. Statistical significance was set at a *P*-value of ≤ 0.05 .

Results

Demographic characteristics of CRE cases and controls

The total number of CRE-positive cases identified during the study period was 728. Males comprised 417 (57.3%) cases and females 311 (42.7%). The majority of CRE cases were adult patients 644 (88.5%) compared to 84 (11.5%) in the pediatric age group. The mean age of CRE carriage was 51 ± 21 . The total number of controls was 749 patients. The majority of the control group were adults 611 (81.6%) compared to 138 (18.4%) pediatric patients. The percentages of underlying diseases were much higher in the cases compared to the controls as shown in Table 1.

Incidence of CRE

The number of patients screened during the study period was 8,431 in 2015 and 10,231 in 2016, with a positivity rate of 4.2% in 2015 and 3.5% in 2016 (Table 2). The total numbers of admissions, CRE cases identified through

Table 1. Demographic characteristics of carbapenem-resistant Enterobacterales cases and controls

Demographic	Cases		Controls	
	N = 728	%	N = 749	%
Age (years)				
Adult	644	88.5	611	81.6
Pediatric	84	11.5	138	18.4
Gender				
Male	417	57.3	338	45.1
Female	311	42.7	411	54.9
Underlying condition				
Hypertension	332	45.6	247	33.0
Diabetes mellitus	296	40.7	233	31.1
Chronic kidney disease	283	38.9	102	13.6
Malignancy	152	20.9	53	7.1
Hemodialysis	126	17.3	72	9.6

Table 2. Admissions and annual incidence and incidence density of carbapenem-resistant Enterobacterales

Year	2015	2016
Total number of admissions (n)	43,516	49,287
Total adult patient admission (n)	32,696	37,742
Total pediatric patient admission (n)	10,820	11,545
Total number of screening samples (n, %)	8,431 (19.4%)	10,231 (20.8%)
Total adult patient screened (n, %)	6,829 (81%)	7,941 (77.6%)
Total pediatric patient screened (n, %)	1,602 (19%)	2,290 (22.4%)
Total number of positive (n, %)	356 (4.2%)	372 (3.6%)
Inpatient days	188,752	205,218
Total admissions	44,279	49,252
Incidence/100 admission	0.80	0.76
Incidence density/1,000 patient days	1.90	1.89

active surveillance, the incidence rates, and the incidence density of CRE, in 2015 and 2016 are shown in Table 2.

The vast majority of CRE cases were healthcare-acquired 724 (99.5%), and only four (0.5%) were attributed to community acquisition. Approximately 53.6% were acquired at Royal Hospital, 31.3% acquired from other local hospitals and 14.6% acquired from hospitals abroad.

Although the highest percentage of CRE cases acquired at Royal Hospital was in the adult medical service for both years (35.8% in 2015, 43.5% in 2016), the highest incidence density of acquisition was in adult critical care service (3.05 per 1,000 patient days in 2015, 3.82 per 1,000 patient days in 2016) (Table 3). Table 3 shows the services where cases acquired CRE at Royal Hospital. The incidence density of bacteremia was 0.12 per 1,000 patient days in 2015 and 0.11 per 1000 patient days in 2016, as shown in Table 4.

Microbiologic and clinical characteristics of CRE Species

The majority of CRE samples 480 (66%) represent colonization mainly from active surveillance screening cultures (97%), and only 3% of patients were colonized in urine, sputum, and wounds. Infection was identified in 248 (34%) of the cases. The most common sites of infections were urine and wound comprising 29% each, followed by respiratory (21%) and blood (17%). *Klebsiella pneumoniae* ($n = 578$, 79%) was the predominant organism in both colonized and infected patients accounting for 82% and 74%, respectively. *Escherichia coli* ($n = 101$, 14%) was the second most commonly isolated organism in 2.1% of colonization and 13% of infections. The microbiological characteristics are summarised in Table 5.

Risk factors for CRE acquisition

In the multivariate analysis, CRE acquisition (infection or colonization) was significantly associated with the presence of a urinary catheter (OR: 7; CI: 4.6–11.6; $P < 0.0001$) or central line (OR: 3.5; CI: 2.068–6.011; $P < 0.001$), intubation

Table 3. The Royal Hospital (RH) acquisition by service and bacteremia data

Hospital service	2015		2016	
	Number (%)	Incidence per 1,000 patient days	Number (%)	Incidence per 1,000 patient days
Total number of RH-acquired CRE cases	190		200	
Adult Critical Care	32 (16.8)	3.05	45 (22.5)	3.82
Adult Medical Service	70 (36.8)	1.49	87 (43.5)	1.86
Adult Surgical Service	38 (20.0)	1.51	32 (16.0)	1.28
Adult Hemato-oncology Service	12 (6.3)	1.08	9 (4.5)	0.93
Adult Cardiac Service	7 (3.7)	0.51	3 (1.5)	0.16
Obstetrics/Gynecology Service	5 (2.6)	0.17	3 (1.5)	0.09
Pediatric Critical Care	8 (4.2)	0.60	8 (4.0)	0.53
Pediatric Medical Service	8 (4.2)	0.29	4 (2.0)	0.14
Pediatric Surgical Care	0 (0)	0	3 (0.5)	0.14
Pediatric Hemato-oncology Service	8 (4.2)	1.21	5 (2.5)	0.76
Pediatric Cardiac Service	2 (1.1)	1.03	1 (0.5)	0.22

Table 4. Bacteraemia data

Type of bacteraemia	2015		2016		Total number %
	Number	Incidence per 1,000 patient days	Number	Incidence per 1,000 patient days	
Number of bacteremia	22	0.12	22	0.11	44
RH Acquired bacteremia	17		16		33 (75)
Other Hospital Acquired	5		6		11 (25)
Primary bacteremia	2		7		9 (20.5)
Secondary bacteremia	20		15		35 (79.5)
Mortality	9		14		23 (52.3)

Table 5. Carbapenem-resistant Enterobacterales species identified at Royal Hospital

Bacterial strains	Colonization		Infection	%	Total N	%
	N = 480	%				
<i>Klebsiella pneumoniae</i>	395	82	183	74	578	79
<i>Escherichia coli</i>	68	14.2	33	13	101	14
<i>Enterobacter species</i>	13	2.7	27	11	40	5
Other Enterobacterales	10	2.1	10	5	15	2
Culture source						
Screening ¹	465	100	0	0		
Urine	7	1.5	72	29		
Wound/tissue	11	2	71	29		
Sputum/endotracheal tube secretions	1	0.2	52	21		
Blood	0	0	44	17		
Fluid ²	0	0	8	3		
Colonization vs. Infection						
Colonization	480	66				
Infection	248	34				

¹Rectal swab only; ²Fluids include peritoneal and pleural.

Table 6. Multivariate analysis of risk factors among carbapenem-resistant Enterobacterales cases and controls

Variable	Cases	Control	P	OR (95% CI)
	N (%)	N (%)		
Abroad admission	540 (74)	148 (20)	0.0001*	12.48 (6.60, 23.62)
Local admission	138 (19)	18 (2)	0.0001*	10.98 (7.88, 15.30)
Urinary catheter	453 (39)	75 (10)	0.0001*	7.37 (4.66, 11.65)
Antibiotic exposure	642 (88)	333 (45)	0.0001*	4.52 (3.10, 6.59)
Tracheostomy	61 (8)	2 (0.3)	0.077	3.92 (0.86, 17.80)
Central line	384 (53)	124 (17)	0.0001*	3.53(2.17, 6.01)
Royal Hospital admission	653 (89)	619 (82)	0.237	1.29 (0.84, 1.98)
Nasogastric tube	281 (53)	113 (15)	0.316	0.75 (0.42, 1.32)
Surgery	202 (28)	101 (14)	0.068	0.64 (0.40, 1.03)
Intubation	324 (45)	126 (17)	0.034*	0.50 (0.26, 0.95)
Intensive care admission	210 (29)	124 (17)	0.011*	0.50 (0.30, 0.85)

(OR: 0.5; CI: 0.264–0.947; $P < 0.034$), and antibiotic exposure (OR: 4.5; CI: 3.101–6.586; $P < 0.0001$). In addition, history of local and abroad hospital admission significantly increased the risk of CRE acquisition (local: OR: 10.97; CI: 7.878–15.301; $P < 0.0001$, and abroad: OR: 12.48; CI: 6.597–23.617; $P < 0.0001$). ICU admission in our hospital was a significant risk factor for acquisition of CRE (OR: 0.5; CI: 0.297–0.852; $P 0.011$); however, admission to our hospital did not reach a statistical significance (OR: 1.294; CI: 0.844–1.982; $P 0.237$). Multivariate analysis of risk factors among CRE cases and controls is summarized in Table 6.

Mortality

The overall 30-day mortality in CRE infection or colonization was 23.1% ($n = 168$). In addition, the mortality among CRE bacteremia cases was 52.3% ($n = 23$). Nine (20.5%) cases had primary bacteremia with no focus identified, and 35 (79.5%) cases had secondary bacteremia.

Discussion

Our hospital initiated the continuous active CRE screening surveillance program as part of a multifaceted approach to control the spread of CRE since 2012. The annual incidence of CRE acquisition per 100 admissions and the incidence density per 1,000 patient days remained stable during the study period with minor trending downward. The majority of the CRE identified in this study were healthcare acquired, and only a minority were community acquired. The finding of community-acquired CRE is of concern although highlighted previously by Tang et al. (9) who reported 29.5% of CRE were community acquired and Kelly et al. (10) who reported the percentage of community-associated or community-onset CRE ranged from 0 to 29.5%, with the percentage of community-based CRE highest in parts of Asia.

The highest incidence density of CRE acquisition, found amongst adult ICU patients followed by adult

medical service, should lead the IPCD to prioritise infection control interventions in these two services. Adesanya et al. (11) found the highest proportion of carbapenem-resistant infections from patients in surgical wards as well as in the ICU although they did not report the incidence density in their study.

In our study, the significant risk factors for acquisition of CRE infection and/or colonization were presence of invasive devices (urinary catheter, central line, intubation), antibiotic exposure, previous abroad hospital admission, other local hospital admission, and previous or current ICU admission. Our findings for risk factors are similar to those reported by Teo et al. (12). Our study did not address other risk factors such as duration of hospital stay prior to acquisition or comorbidities *per se* as reported in the literature although we noticed the number of comorbidities were higher among cases than controls (13–15).

The most common CRE in our study was *Klebsiella pneumoniae* followed by *Escherichia coli* and *Enterobacter* species. which is more or less the same finding reported by Kalisvar et al. (1), Sonnevend et al. (5) Garbati et al. (14) and but slightly different to Tang et al. (10) who reported *Enterobacter* species as the second most common followed by *Escherichia coli* as the third. The most common clinical samples from which CRE was isolated because of infection were wound/tissue and urine followed by blood and sputum, which is similar to other studies (1, 5).

In this study, the overall mortality among patients who acquired CRE was high as reported by other investigators (14, 16). Not surprisingly, the mortality among bacteremia patients was high. Tamma et al. (17) found that the odds of dying within 14 days were more than three times greater in Carbapenemase-producing CRE compared with non-Carbapenemase-producing CRE bacteremic patients (OR: 3.20; 95% CI: 1.06–9.61) and Li et al. (18) reported 65% mortality among CRE bloodstream

infections. The cases in this study had more comorbidities than the controls, and we assessed all-cause mortality, which might explain the higher mortality.

The strength of our study is that it included large numbers of patients in both paediatric and adult groups and a case-control design that enabled the identification of risk factors specific to our population. However, several limitations are observed. Firstly, the study is retrospective in nature. Secondly, we could not identify the risk factors for infection *per se* as we included one sample for each case and we took the infection sample if the case had previous colonization with same organism. Thirdly, the molecular typing of the strains that caused infections were not performed. Fourthly, this is a single centre study that may not represent the national epidemiology of the CRE. A multi-centre prospective design that includes molecular epidemiology could enrich the epidemiology of these organisms in our setting.

Conclusion

The annual incidence of CRE acquisition in our facility is high with a high mortality rate among bacteremic patients. The risk factors identified significantly for acquisition of CRE were invasive devices (urinary catheter, central line, ventilation), antibiotic exposure, and previous healthcare admission (other hospital and abroad). A multifaceted strategy to control the spread of CRE is fundamental, considering the specific epidemiology of this organism related to our institution and country.

Ethical approval

The study was approved by the Royal Hospital Ethics and Research Committee (SRC#114/2017). The participants have not consented as there were no interventions done in the study. Only their data were extracted from the electronic medical records.

Acknowledgements

The authors would like to thank Noor AL Aufi and Asad AL Mammary for their help in data collection.

Conflicts of interest and funding

All authors declare no potential conflicts of interest.

References

- Marimuthu K, Venkatachalam I, Khong WX, Koh TH, Cherng BPZ, Van La M, et al. Clinical and molecular epidemiology of carbapenem-resistant enterobacteriaceae among adult inpatients in Singapore. *Clin Infect Dis*. 2017; 64(suppl_2): S68–75. doi: 10.1093/cid/cix113
- Poirel L, Al Maskari Z, Al Rashdi F, Bernabeu S, Nordmann P. NDM-1-producing *Klebsiella pneumoniae* isolated in the Sultanate of Oman. *J Antimicrob Chemother*. 2011; 66(2): 304–6. doi: 10.1093/jac/dkq428
- Potron A, Nordmann P, Lafeuille E, Al Maskari Z, Al Rashdi F, Poirel L. Characterization of OXA-181, a carbapenem-hydrolyzing class D beta-lactamase from *Klebsiella pneumoniae*. *Antimicrob Agents Chemother*. 2011; 55(10): 4896–9. doi: 10.1128/AAC.00481-11
- Dortet L, Poirel L, Al Yaqoubi F, Nordmann P. NDM-1, OXA-48 and OXA-181 carbapenemase-producing Enterobacteriaceae in Sultanate of Oman. *Clin Microbiol Infect*. 2012; 18(5): E144–8. doi: 10.1111/j.1469-0691.2012.03796.x
- Sonnevend A, Ghazawi AA, Hashmey R, Jamal W, Rotimi VO, Shibl AM, et al. Characterisation of CRE in the Arabian Peninsula. *PLoS One*. 2015; 10(6): e0131372. doi: 10.1371/journal.pone.0131372
- Balkhair A, Al-Farsi YM, Al-Muharrmi Z, Al-Rashdi R, Al-Jabri M, Neilson F, et al. Epidemiology of multi-drug resistant organisms in a teaching hospital in oman: a one-year hospital-based study. *ScientificWorldJournal*. 2014; 2014: 157102. 6 pages. doi: 10.1155/2014/157102
- STROBE. Strengthening the reporting of observational studies in epidemiology. Available from: <https://www.strobe-statement.org/checklists/> [cited March 2019].
- Performance Standards for Antimicrobial Susceptibility Testing. 26th Edition. CLSI M100-S26, Clinical Laboratory Standard Institute, CLSI; 2016, Available from: <https://clsi.org/microbiology/documents/m100> [cited January 2018]
- Kelly AM, Mathema B, Larson EL. Carbapenem-resistant Enterobacteriaceae in the community: a scoping review. *Int J Antimicrob Agents*. 2017; 50(2): 127–34. doi: 10.1016/j.ijantimicag.2017.03.012
- Tang HJ, Hsieh CF, Chang PC, Chen JJ, Lin YH, Lai CC, et al. Clinical significance of community- and healthcare-acquired carbapenem-resistant Enterobacteriaceae isolates. *PLoS One*. 2016; 11(3): e0151897. doi: 10.1371/journal.pone.0151897
- Adesanya OA, Igwe HA. Carbapenem-resistant Enterobacteriaceae (CRE) and gram-negative bacterial infections in south-west Nigeria: a retrospective epidemiological surveillance study. *AIMS Public Health*. 2020; 7(4): 804–15. doi: 10.3934/publichealth.2020062
- Teo J, Cai Y, Tang S, Lee W, Tan TY, Tan TT, et al. Risk factors, molecular epidemiology and outcomes of ertapenem-resistant, carbapenem-susceptible enterobacteriaceae: a case-case-control study. *PLoS One*. 2012; 7(3): e34254. doi: 10.1371/journal.pone.0034254
- van Loon K, Voor In 't Holt AF, Vos MC. A systematic review and meta-analyses of the clinical epidemiology of Carbapenem-resistant Enterobacteriaceae. *Antimicrob Agents Chemother*. 2017; 62(1): e01730-17. doi: 10.1128/AAC.01730-17
- Garbati MA, Sakkijha H, Abushaheen A. Infections due to Carbapenem resistant enterobacteriaceae among Saudi Arabian hospitalized patients: a matched case-control study. *Biomed Res Int*. 2016; 2016: 3961684. doi: 10.1155/2016/3961684
- Zarakolu P, Eser OK, Aladag E, Al-Zahrani IA, Day KM, Atmaca O, et al. Epidemiology of carbapenem-resistant *Klebsiella pneumoniae* colonization: a surveillance study at a Turkish university hospital from 2009 to 2013. *Diagn Microbiol Infect Dis*. 2016; 85: 466–70. doi: 10.1016/j.diagmicrobio.2016.05.012
- Falagas ME, Tansarli GS, Karageorgopoulos DE, Vardakas KZ. Deaths attributable to carbapenem-resistant

- Enterobacteriaceae infections. *Emerg Infect Dis.* 2014; 20(7): 1170–5. doi: 10.3201/eid2007.121004
17. Tamma PD, Goodman KE, Harris AD, Tekle T, Roberts A, Taiwo A, et al. Comparing the outcomes of patients with carbapenemase-producing and non-carbapenemase-producing carbapenem-resistant Enterobacteriaceae Bacteremia. *Clin Infect Dis.* 2017; 64(3): 257–64. doi: 10.1093/cid/ciw741
18. Li X, Ye H. Clinical and mortality risk factors in bloodstream infections with Carbapenem-Resistant enterobacteriaceae. *Can*

J Infect Dis Med Microbiol. 2017; 2017: 6212910. doi: 10.1155/2017/6212910

***Zaina AL Maskari**

P. O. Box: 1331,
Postal Code: 111,
Muscat, Sultanate of Oman
Email: zainamaskri2000@gmail.com

Appendix I. STROBE Statement – Checklist of items that should be included in reports of case-control studies

Section headings	Item no	Recommendation	Relevant text from manuscript
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Mentioned in the abstract
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Done
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Done in the introduction
Objectives	3	State specific objectives, including any prespecified hypotheses	Stated in the abstract and method
Methods			
Study design	4	Present key elements of study design early in the paper	Mentioned in methos section
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Done
Participants	6	(a) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	Done
		(b) For matched studies, give matching criteria and the number of controls per case	Un-matched case control study
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Outcomes are defined in the methods section
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Done
Bias	9	Describe any efforts to address potential sources of bias	Not applicable
Study size	10	Explain how the study size was arrived at	Included all cases detected during active surveillance
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Mentioned in the analysis section
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	
		(b) Describe any methods used to examine subgroups and interactions	Not applicable
		(c) Explain how missing data were addressed	Retrospective design, however data were taken from day by day infection preventionist list and from electronic data and ensured all cases were included
		(d) If applicable, explain how matching of cases and controls was addressed	Not applicable
		(e) Describe any sensitivity analyses	Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study – e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	All participants were followed for the whole study period
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	Not applicable
Descriptive data	14*	(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders	Done in results section
		(b) Indicate number of participants with missing data for each variable of interest	Not applicable

Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure	Done in results section
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g. 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Not applicable
		(b) Report category boundaries when continuous variables were categorized	Done
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done – e.g. analyses of subgroups and interactions, and sensitivity analyses	Reported in colonization/infection group
Discussion			
Key results	18	Summarise key results with reference to study objectives	Done
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Done
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Done
Generalisability	21	Discuss the generalisability (external validity) of the study results	It is a single centre study which may represent the epidemiology in Oman however multi-centre is better and phrased in the discussion
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Not applicable

*Give information separately for cases and controls.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plos-medicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

Appendix II. Royal Hospital carbapenem-resistant Enterobacterales screening indications

Indications for screening	Site of sampling
1. All cases were previously admitted to the Royal Hospital or another local hospital within the past 3 months.	-Rectal swab for screening
2. All cases coming from abroad hospitals for direct admission or have a history of admission to an abroad hospital within the past 6 months.	-Tracheostomy site swab for tracheostomized patients
3. Known previously to have a positive CRE screening or clinical sample (for the purpose of de-isolation).	-Urine from catheterized patients
3. Roommates of positive patients not on isolation precautions (exposure for 24 h).	-Endotracheal tube secretion from ventilated patients.
4. Admitted to the ICU (patient transferred from other hospital and patient transferred from another ward within our hospital).	-Wound (if present)
5. If advised by infection control practitioner.	
All criteria apply to pediatric and adult patients	
Patient must be kept under contact precautions until the screening results are ready	
For patients frequently admitted to RH, send screening once every month	