OS0315 - CARBAPENEM RESISTANT *ENTEROBACTERIACEAE* PREVALENCE IN PATIENTS ADMITTED AT THE EMERGENCY DEPARTMENT: NEW RISK FACTORS AND CARBAPENEM RESISTANCE FOUND IN COMMUNITY PATIENTS

Matias Chiarastelli Salomão

Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, SP, Brazil

Session OS063 - Changing face of Gram-negative resistance epidemiology

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Disclosures:

- Nothing to disclose

- Carbapenemases became a great concern in the latest 15 years since the first description of *Klebsiella pneumoniae* carbapenemase (KPC)

Yigit H, et al. 2001. Antimicrob Agents Chemother 45:1151– 1161.

- Carbapenemases:
  - KPC, NDM, VIM and IMP → harbored in plasmids
    - Spread among other bacteria
    - Intestinal carriage:
      - Reservoir for multi-drug resistant organisms
      - Exchange resistance mechanisms between intestinal bacteria
      - Nosocomial dissemination of CRE and possible outbreaks

Geffen Y, et al. 2010. J Hosp Infect. 76(4):355-6.

- Screening for CRE carriage:
  - Strategy to control cross transmission
  - Early identification and isolation of colonized patients
  - Intensive care units (ICU)

Kochar S, et al. 2009. Infect Control Hosp Epidemiol 30:447– 452.
Enfield KB, et al. 2014. Infect Control Hosp Epidemiol 35:810 – 817.
Calfee D, et al. 2008. Infect Control Hosp Epidemiol 29:966 –968.

- In Brazil:
  - Colonization with CRE:
    - 30.4% of patients of an ICU
    - Our hospital - CRE carriage on admission in the ICU: 20%

Perez LR, et al. 2015. Braz J Infect Dis;19:436–438.

- The Emergency Department (ED):
  - 30% of our patients are admitted *via* the ED
    - Referral unit in our public health system
  - Overcrowded wards result in delayed transfers from ED to other units
    - Long periods of care in the ED
    - Probably facilitates cross transmission → Unknown

Objectives:

- To investigate the prevalence of patients harboring CRE on admission to the emergency ward
- To investigate risk factors associated with CRE colonization on admission to the emergency ward
- To investigate the CRE acquisition rate within the emergency ward

Materials and Methods:

- Cohort study
- Hospital das Clínicas:
  - 1000 bed teaching hospital
  - Affiliated to the University of São Paulo, Brazil
- Emergency Department:
  - Responsible for 20 hospital admissions per day
  - Capacity for 50 beds - not uncommon to have more than 90 patients hospitalized in this area

- During the period of May 31st to July 7th, 2016, 1088 patients were admitted to the ED and 676 consecutive patients were prospectively included in this study
- All patients were screened for CRE colonization in the first 24hours after admission
- Two rectal swabs
  - Classical culture
  - Real-time polymerase chain-reaction (RT-PCR)
    - Two patients were only screened for CRE colonization with the rectal culture

- Previous exposure to healthcare was considered if the patient had undergone:
  - Hospitalization in the last year
  - Surgery in the last year
  - Day-hospital treatment in the last year
  - Hemodialysis in the last month
  - Cancer treatment in the last month

- Comorbidities:
  - Hepatopathy
  - Diabetes
  - Acute and chronic kidney disease
  - Stem cell transplantation
  - Solid organ transplantation
  - Solid organ malignancies
  - Hematological malignancies
  - HIV infection
  - Neutropenia
  - Use of immunosuppressive drugs
  - Use of antibiotics in the last month

- Re-screening for CRE colonization at the ED with rectal culture and RT-PCR:
  - Seventh day after admission and then weekly
  - Stop screening if:
    - CRE was identified
    - Patient was discharged, died or transferred to another ward in the hospital
  - If the patient was transferred to an Intensive Care Unit (ICU), screening for CRE colonization with rectal swab culture was done on admission to the new unit

- **Microbiology**
- CRE cultures:
  - Specimens were collected with swabs and enriched in liquid media for 24 hours
  - Cultured in an Agar plate with carbapenem disks according to the CDC methodology. (CDC, 2006)
  - Isolates were identified with MALDI-TOF and automatized antimicrobial susceptibility testing was performed with Vitek2® (BioMerieux®, MarcyL'Étoile, France)

- **Microbiology**
- Minimal inhibitory concentration of carbapenems and colistin were determined by disk-diffusion and E-test (BioMérieux®, MarcyL'Étoile, France)

Clinical and Laboratory Standards Institute - CLSI 2014

- **Molecular biology**
- Resistance genes detection was performed directly from the samples by RT-PCR:
  - KPC
  - NDM
  - VIM
  - IMP-1
  - OXA-48
  - OXA-181
  - OXA-232

    Cepheid® Xpert® Carba-R

- **Data analysis**
- All the data obtained regarding the clinical data, demographic information and potential risk factors for CRE colonization were evaluated
- CRE colonized patients on admission were compared with non-colonized patients
- Covariates associated with CRE colonization on bivariate analysis were submitted to a logistic regression model
- We compared results obtained using PCR and culture (gold standard)
- p-value of <0.05 was considered significant
- Statistical analysis were performed using EPI Info v3.5.1

- **Results:**
- 676 patients were consecutively included
- 52% (353 patients) were male
- Mean age 57 years (range 2-94 years, median 60 years)

- **Results:**
- 45 (6.7%) patients were colonized by CRE based on at least one laboratory method
  - Culture was positive for 37 (5.5%) patients, all *Klebsiella pneumoniae*
  - RT-PCR was positive for 35 (5.2%), all KPC
- PCR Accuracy: 97.32%

- Prevalence on admission for Carbapenem resistant Enterobacteriacea, as positivity by test, RT-PCR and rectal swab culture.

Test	RT-PCR +	RT-PCR -	Total
Rectal Culture +	27	10	37
Rectal Culture -	8	629	637
Total	35	639	674

- **Results:**
- Mean length of stay in the ED: 11.59 days (range 0-105 days)

- **Results:**
- 275 patients were not colonized for CRE on admission and were hospitalized for more than one week in the ED
  - 54 of these were re-screened for CRE
  - 10 (18.5%) became colonized by CRE during their stay in the ED

- In-hospital mortality:
  - All patients: 13% (85/671)
  - Colonized on admission: 25% (11/44)
  - Non-colonized: 12% (74/627)
    - (*p* 0.12)

- Origin of patients:
  - Community 319/537 (59.4%)
  - Previous exposure to healthcare 218/537 (40.6%)
    - Long-term care facilities (LTCF): 3
    - Healthcare during imprisonment: 3

- Six patients who came from community were colonized on admission:

Patient	Case	Previous use of antibiotics
65 yo male	- Complicated urinary tract infection (UTI) - Prostate hyperplasia	Levofloxacin
85 yo male	- UTI - Alzheimer disease and diabetes	Levofloxacin
42 yo male	- Systemic lupus erythematosus - Febrile neutropenia	No previous use of antibiotics in the last month
26 yo female	- Chronic portal vein thrombosis - Cholangitis	No previous use of antibiotics in the last month
69 yo female	- Acute aortic aneurism dissection - Parkinson's Disease	Antibiotic for UTI
56 yo male	- Polytrauma - No comorbidities	No previous use of antibiotics in the last month

	Bivariate Analysis					Multivariate Analysis		
Risk factors	**Patients exposed to risk factor**	**Patiens colonized by CRE (%)**	**Relative risk**	**95% CI**	**p**	**OR**	**95% CI**	**p**
Previous exposure to healthcare	218	31 (14%)	1.14	1.08 - 17.81	<0.0001	**6.72**	**2.59-17.42**	**0.0001**
Comorbidities	368	32 (9%)	1.05	1.01 – 10.10	0.0193	1.29	0.37-4.48	0.679
Hepatopathy	68	11 (16%)	1.13	1.01 – 1.26	0.0009	**3.62**	**1.42-9.24**	**0.007**
Diabetes	153	13 (8%)	1.03	0.97 – 1.08	0.3054			
Acute Kidney Injury	73	10 (14%)	1.09	0.99 – 1.20	0.0107	2.49	0.94-6.62	0.0655
Chronic Kidney Disease	107	12 (11%)	1.06	0.99 – 1.14	0.0390	1.19	0.46-3.06	0.7137
Solid Organ Transplantation	39	7 (18%)	1.15	0.99 – 1.33	0.0037	2.39	0.82-6.93	0.1064
Solid Organ Malignancies	60	2 (3%)	0.96	0.11 - 1.01	0.3985			
Hematological Malignancies	17	0 (0%)	0.93	0.91- 0.96	0.5253			
HIV infection	16	2 (13%)	1.07	0.89 – 1.29	0.6997			
Neutropenia	12	2 (17%)	1.12	0.87 – 1.45	0.4210			
Use of imunossupressive drugs	47	2 (4%)	0.97	0.91 – 1.04	0.6838			
Hemodialysis	42	2 (5%)	0.98	0.91 – 1.05	0.8310			
Surgery in the last year	81	4 (5%)	0.98	0.92 – 1.03	0.6527			
Day Hospital patient	91	9 (10%)	1.04	0.97 – 3.89	0.1896			
Use of antibiotics in the last month	165	24 (15%)	1.13	1.06 – 1.21	<0.0001	**4.72**	**2.08-10.67**	**0.0002**

- **Multivariate analysis:**
- Independent risk factors for colonization by CRE at admittance in the ED:
  - Previous exposure to healthcare
  - Hepatopathy
  - Use of antibiotics in the last month

- **Discussion:**
- Rectal swabs PCR:
  - Very sensitive and specific method to detect CRE carriage
  - Expensive

Viau R, et al. 2016. Clin Microbiol Rev 29:1-27.

- The emergency department:
  - Thought to be a low prevalence area
- Our study:
  - Prevalence on admission: 6.7%
  - Acquisition rate: 18.5%
  - Demonstrates that this population is at a relatively high risk for colonization

Nüesch-Inderbinen M, et al. 2013. Antimicrob Resist Infect Control. 4;2:23.

- Risk factors for CRE colonization:
  - Our study:
    - Hepatopathy as a new risk factor
    - Known risk factors: previous exposure to healthcare and previous use of antibiotics

Viau R, et al. 2016. Clin Microbiol Rev 29:1-27.

- Next steps:
  - Potential strategy for CRE control in the ED:
    - Identify high risk patients
    - Screening (PCR)
    - Cohort/Isolation of carriers

Our Team

- Anna S Levin
- Silvia Costa
- Icaro Boszczowski
- Thais Guimarães
- Infection Control Committee
- Alberto Duarte
- Flávia Rossi
- Leila Suemi
- Medical Residents
- ED Staff

Matias C. Salomão
matias.salomao@hc.fm.usp.br