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CARBAPENEMASE-PRODUCING ENTEROBACTERIACEAE IN PATIENTS OF A THIRD LEVEL HOSPITAL IN THE CITY OF GUAYAQUIL-ECUADOR

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Abstract

Introduction: The prevalence of carbapenemases-producing enterobacteria (EPC) is a serious problem in health systems, causing mortality of 18% up to 60%, being essential to adopt measures to control their dissemination.

Objectives: To determine the carbapenemase producing enterobacterium with the highest incidence, to know the age group and the hospital areas most affected by KPC.

Materials and Methods: Analytic, descriptive, retrospective and qualitative-quantitative cross-sectional study, in a period from January to December 2018. The universe was 2710 patients, who underwent rectal swabs and chromogenic cultures (CHROMagarTM KPC supplement). Quantitative variables were detailed in mean (standard deviation) or median (minimum or maximum range). Qualitative variables were detailed in frequency.

Results: A total of 427 positive rectal swabs were obtained for KPC. The microorganism with the highest incidence was *K. pneumoniae* with 96.20%, followed by *E. coli* 1.40%. In the age groups studied, the median was 62 years +- SD, predominantly the group over 60 years with 265 cases corresponding to 62%. The highest incidence of KPC was detected in an intensive care unit with 32%, followed by emergency 19% and observation 16%, with 33% in the other units.

Conclusions: The study determined that the predominant bacterium was **K. pneumoniae*, occurs more frequently in older adults and the most affected areas are those of ICU and emergency correlating to

the level of immunosuppression that characterize the great part of these patients.

Keywords: carbapenemases producing enterobacteria, KPC.

Resumen

Introducción: La prevalencia de enterobacterias productoras de carbapenemasas (EPC) es un grave problema para los sistemas de salud, originando una mortalidad del 18% al 60%, siendo indispensable adoptar medidas para controlar su diseminación. **Objetivos:** Determinar la enterobacteria productora de carbapenemasa con mayor incidencia, conocer el grupo etario y las áreas hospitalarias más afectadas por KPC. **Materiales y Métodos**: Estudio analítico, descriptivo, retrospectivo y cuali-cuantitativo de corte transversal, en un periodo comprendido de enero a diciembre del 2018. El universo lo constituyeron 2710 pacientes a quienes se les realizó hisopados rectales y cultivos en medios cromogénicos (CHROMagarTM KPC supplement). Las variables cuantitativas se detallaron en media (desviación estándar) o mediana (rango mínimo o máximo). Las variables cualitativas fueron detalladas en frecuencia (%). **Resultados:** Se obtuvo 427 hisopados rectales positivos para KPC. El microorganismo con mayor incidencia fue *K. pneumoniae* con un 96.20%, seguido de *E. coli* 1,40%. En los grupos etarios estudiados la mediana fue de 62 años, predominando el grupo de mayores de 60 años con 265 casos que corresponde al 62%. La mayor incidencia de *KPC* fue detectada en unidad de cuidados intensivos con un 32%, seguido de emergencia 19% y observación 16%, teniendo un 33% en el resto de dependencias. **Conclusiones:** El estudio determinó que la bacteria que predominó fue la *K. pneumoniae*, se presenta con mayor frecuencia en adultos mayores y las áreas más afectadas son las de UCI y emergencia correlacionándose al nivel de inmunodepresión que caracterizan a la gran parte de estos pacientes**.**

Palabras clave: enterobacterias productoras de carbapenemasas, KPC

Introduction:

Enterobacteria are part of the usual microbiota of the gastrointestinal tract, the most important are: *Klebsiella pneumoniae, Escherichia coli, Proteus mirabilis, Enterobacter spp., Serratia marcescens, Morganella morganii* and *Citrobacter spp.* Which can be transmitted

by direct contact or through fomites. [(1)]

Enterobacter with more relevance is the Klebsiella pneumoniae, which can colonize the gastrointestinal, respiratory and urinary tracts and produce an

enzyme, carbapenemase, that will confer carbapen ems antibiotic resistance [(2)].

This enzyme is called carbapenemase type KPC that corresponds to class A in the Ambler classification [(3)].

A colonized patient with KPC can be carrier, and this organism may be transiently in the inanimate environment surrounding the patients whether they are infected or colonized [(4)]; and their spread has become a problem around the world.

Other enterobacteriaceae such as Escherichia coli and Enterobacter spp., Which harbor various types of carbapenemases, such as metallo-beta-lactamases (MBL) and OXA-48, can produce a similar spectrum of disease. Bacterial resistance to carbapenemases by the Enterobacteriaceae family occurs by two mechanisms: 1) modifications in the permeability of the external membrane, associated with extended spectrum beta-lactamases (ESBL) or AmpC hyperproduction. 2) production of beta-lactamases with hydrolytic activity on carbapenemases. [(5)]

The first *KPC* report was made in 1996, in North Carolina [(6)]. In South America, the first *KPC*-

2 report was made in Colombia in 2006 [7]. In Brazil, Uruguay, Ecuador and Argentina, the presence of EPC has also been reported in isolates of *E. coli*, *Pseudomonas spp.*, *K.*

pneumoniae, *Enterobacter spp.*, *S. marcescens* and *K. oxytoca*. [8,9,10]. In Ecuador in 2010, the first case of KPC-type EPC was made in a male patient with a diagnosis of Glioblastoma [11].

It is noteworthy that is considered enterobacteria resistant to carbapenems any enterobacteria (*Klebsiella pneumoniae, Escherichia coli, Proteus mirabilis, Enterobacter spp.,* Etc .), When the values of the Minimum Inhibitory Concentration (MIC) at the least one carbapenem are equal or higher than the cutoff point of resistance established

by the standards of CLSI ; that is, a MIC > 4ug/ml for imipenem, meropenem or doripenem and MIC> 2ug/ml for ertapenem. [12]

It is estimated that 10%-30% of colonized patients will develop infection. [13, 14] Being a serious problem for health systems by giving rates of mortality from 18 up to 60%. [15] The bacteria that predominates worldwide is the *Klebsiella pneumoniae* and its rapid spread is attributed to a combination of social factors such as international travel, patient-patient transmission of micro-organisms producing KPC [16 - 20] and microbiological factors , and that the KPC enzyme is encoded by the bla_{KPC} gene, located in the Tn *4401* transposon [21] that contributes both to the geographic dissemination of KPC and to inter-species transfer.

The KPC gene coding generally resides in transposons, which are transported by conjugative plasmids, increasing their propagation potential [22] and making this enzyme an international clinical and public health concern [23]. Clone ST258 is identified as the main transporter responsible for its worldwide dissemination and the mobile nature of the coding genetic element has contributed to the spread of this enzyme that has now been identified in numerous enterobacteria and other gram-negative bacilli. [24, 25, 26]

In world literature, infections caused by KPC-producing bacteria do not show specificity for an organ or tissue; The patients with the highest risk of contracting this bacterium are : prolonged hospitalization , intensive care unit stay, immunosuppressed patients, invasive devices, previous antimicrobial therapy, reception of solid or hematological organ transplants , mechanical ventilation and use of broad-spectrum antibiotics [27-33] . they are superior in low- and middle-income countries and their clinical and economic impact is magnified in intensive care units; They are long-stay sites that easily generate amplification and spread of pathogens. Although it is important to note that its isolation in non-hospital sites has been documented. Therefore, the compliance of staff hand hygiene in these units and the daily bathing of patients with chlorhexidine are important measures to prevent patient-to-patient transmission [34,35,36].

Knowing the characteristics possessed by the microorganism , it helps to define policies to secure from them, as well to determine the enterobacteria producing KPC most prevalent, that will permit to adopt institutional policies in the use of antibiotics, and to establish the initial scheme and also with it to control the protocols of the invasive procedures , allowing to adopt measures to control its dissemination. Knowing and l microorganism with higher incidence, the group age and the hospital
area most affected are indispensable factors to analyze and monitor in a hospital, hence the validity of the study.

Goals:

- To determine the highest incidence of carbapenemase enterobacteria, to know the age group and hospital areas most affected by KPC.

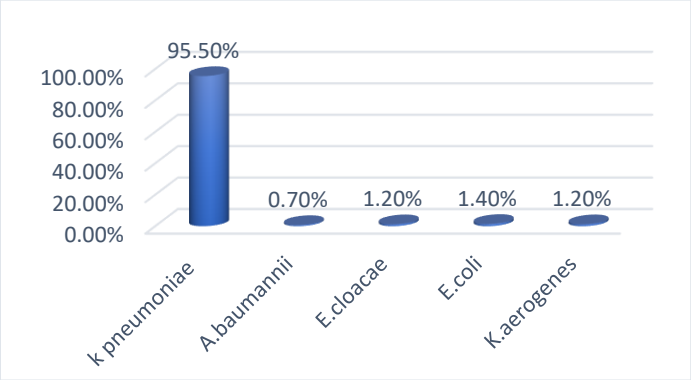
Materials and methods: this is an analytical/descriptive, retrospective and quali-quantitative study; in a tertiary level Hospital, Teodoro Maldonado Carbo Hospital, Guayaquil - Ecuador, in the period study is from January to

December 2018. The universe was composed of 2710 rectal swabs, in which we obtained 427 positives for KPC.

The inclusion criteria included patients who met the rectal swab criteria established by the Ministry of Public Health of Ecuador (MSP) [37]. Then the samples were sent to the microbiology laboratory of the Hospital, the transport was made by the stuart medium, where it was cultive in chromogenic medium (CHROMagar™ KPC supplement) [38], for 18-24 hours at 37°C , thus guarantees the selection of strains of clinical interest; once the growth is detected, bacterial identification and susceptibility was performed in the Vitek2 compact automated system (BioMérieux). Macroscopically we observe that the Chromagar will give a metallic blue coloration if it is a *klebsiella spp., Enterobacter spp. or citrobacter sp p.*, red or dark pink in the case of *e. coli* and cream or translucent if it is *pseudomona spp.* Exclusion criteria in patients with more than one rectal swab in the year of the study. The sampling was not probabilistic of consecutive cases. The variables were gender, age, place of the hospital and microorganism. The confidentiality of personal data was maintained.

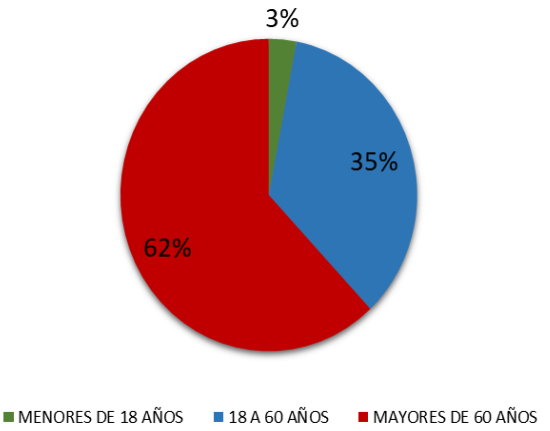
Results:

The most frequently isolated bacteria were *Klebsiella pneumoniae* with 95.5% followed by *Escherichia coli* with 1.40%, thirdly, *E. cloacae and K. aerógenes* were found *with 1.20% and fourthly A. baumannii with 0.70%.* [graphic1]



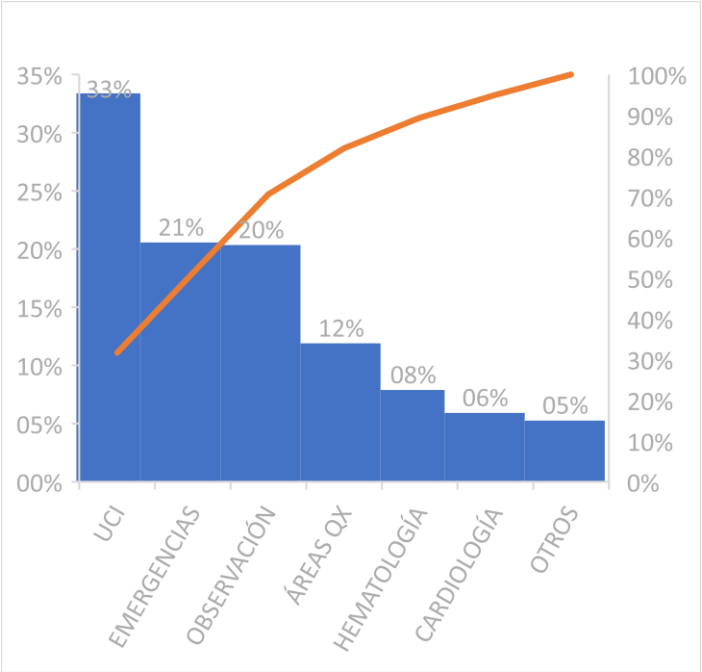
Graph 1.- Type of microorganism found

The 427 positives swab positive for KPC, 274 (64%) correspond to men and 153 (36%) to women. the median age was 62 years, the majority of the cases observed were in the group over 60 years with 265 cases corresponding to 62 % *[*graph 2]



Graph 2.- Age ranges in patients with KPC type EPC.

The highest prevalence of *KPC* was detected in an intensive care unit with 33.4%, followed by emergency 20.6% and observation 20.4%, with 31% in the rest of the dependencies. [Graph 3].



Graph 3.- Dependencies where to find on EPC type KPC.

Discussion:

Comparing with other studies, most EPC infections worldwide are caused by *K. p pneumoniae* as reported by Tzouvelekis LS et al. in Greece [39], as well as in the study conducted by Kohler et. in Canada [40] with 47% *K. p pneumoniae*, 33% *e. coli*; in Spain by Fernández et. to the. at the Central University Hospital of Asturias [41], the most prevalent enterobacterium with 98% was K. pneumoniae, in Turkey by Eser et. to the. in a research hospital third level [42] where *K. pneumoniae* had a 75.5% *E. coli* 15%, *E. cloacae* 4.2% and *K. oxytoca* 1.4%, compared with our study, the most prevalent microorganism was *K. p pneumoniae* in 95.5%, followed by *E. coli* in 1.40%, *E. cloacae* and *K aerógenes* in 1.20% and *A. baumannii* in 0.70%.

It was observed that the average age of the population studied was 62 years, 64% corresponded to the male sex and 36% to the female, compared to the studies carried out by Ocampos Ugarte J. et al. from Paraguay [43] the average age was 51 years and from Argentina by Echavarría et. Al. in the University Hospital of Buenos Aires [44] where its average age was 79 years, in both studies 50% male and the other 50% female, compared with the study by Kohler et. that of Canada [40] where the average age was 70 years, 65% were men and 35% women.

Regarding dependence, it was observed that the highest prevalence of *KPC* was detected in an intensive care unit with 33.4%, followed by emergency 20.6% and observation 20.4%. Studies described by Souli et al. Vera et al. and Correa et al., demonstrated that long-term hospitalization, mechanical ventilation, central venous and urinary catheters, and previous surgery were associated with KPC-producing K. pneumoniae, associated with a serious underlying disease, which means that they are more susceptible to infection [45,46, 50]. Outbreaks of KPC-type carbapenemase producers, mainly of Klebsiella pneumoniae and Enterobacter cloacae, have been reported to have increased in ICU patients. [47-49].

Conclusions:

The study determined that the predominant bacterium was *K. pneumoniae*, which is mainly involved in nosocomial infections and its rapid spread is due to the presence in a wide variety of plasmids that vary in size, nature and structure.

As for the age group, there is a greater percentage in patients with older adults with a median age of 62 years and predominant in areas of ICU and emergency correlating to the level of immunosuppression that characterize most of these patients.

The need to continue with active vigilance to determine KPC in rectal colonization to reduce its spread; To reinforce prevention measures such as those described in CDC and to conduct studies that included the clonality of the strains to be able to identify which is present in our hospital.

Authors' Contribution:

Pamela Cuadrado and Pablo Salgado analyzed the data and wrote the manuscript. Jenniffer Herrera collected clinical data. Tamara Nuñez analyze the microbiology data. Esthela Tinoco designed the study and revised the manuscript.

Conflicts of interest

None.

Approval

This study was approved by the department of investigation at Teodoro Maldonado Carbo Hospital.

Bibliographic References:

[1.] Servizo Galego de Saúde. Abril (2019). Enterobacterias productoras de carbapenemasas. Disponible en: https://www.sergas.es/Saude-publica/Enterobacterias-produtoras-de-carbapenemasas?idioma=es

[2.] Centers for Disease Control and Prevention (CDC). (2009). Guidance for control of infections with carbapenem-resistant or carbapenemase-producing Enterobacteriaceae in acute care facilities. MMWR Morb Mortal Wkly Rep.; 58(10): 256-60.

[3.] Nordmann, P., Cuzon, G., & Naas, T. (2009). The real threat of Klebsiella pneumoniae carbapenemase-producing bacteria. The Lancet Infectious Diseases, 9(4), 228-236. https://doi.org/10.1016/S1473-3099(09)70054-4.

[4.] Oteoa, J., Calbo, E., & Col. (25 de Mayo de 2017). La amenaza de las enterobacterias productoras de carbapenemasas en España: ˜ documento de posicionamiento de los grupos de estudio GEIH y GEMARA de la SEIMC. Recuperado el 13 de octubre de 2017, de Elsevier.

[5.] Nordmann P., Cuzon G. Naas T. (2009). The real threat of Klebsiella pneumoniae carbapenemase – producing bacteria, Lancet Infect Dis.; 9:228-36.

[6.] CDC/NHSN. January 2015. Surveillance Definitions for Specific Types of Infections. Disponible en: http://www.cdc.gov/nhsn/PDFs/pscManual/17pscNosInfDef_current.pdf.

[7.] Centers for Disease Control and Prevention CDC. (2009). Guidance for control of infections with carbapenem-resistant or carbapenemase-producing Enterobacteriaceae in acute care facilities. MMWR Morb Mortal Wkly Rep.; 58:256-60.

[8.] Bush K, Jacoby GA. (2010). Updated functional classification of bet-a-lactamases. Antimicrob Agents Chemother; 54:969-76.

[9.] Oteo J, Calbo E, Rodríguez-Baño J, et al. (2014). La amenaza de las enterobacterias productoras de carbapenemasas en España: documento de posicionamiento de los grupos de estudio GEIH y GEMARA de la SEIMC. Enferm Infecc Microbiol Clin.;32(10):666–70.

[10.] Ministerio de Salud Pública del Ecuador. (2016). Control de enterobacterias productoras de carbapenemasas a nivel hospitalario. 1ª Edición. Quito: Dirección Nacional de Vigilancia Epidemiológica. Disponible en: http://salud.gob.ec

[11.] Iñiguez D., Zurita J., Alcocer I., Ortega D., Gómez A., Maldonado L. (2012) Klebsiella pneumoniae productora de carbapenemasa tipo KPC-2: primer reporte en el Ecuador. Rev Fac Cien Med (Quito); 37: 39-41.

[12.] Martínez Vidal M, Andrés de Cosa R de, Astray Mochales J, López Pérez MA, Ansede Cascudo JC, Ramos Cordero P, coordinadores. (2013). Plan de prevención y control frente a la infección por Enterobacterias Productoras de Carbapenemasas (EPC) en la Comunidad de Madrid. /Internet/citado 2014 nov 19/.

[13.] Paño J., Serrano S., Ramos J., Pintadob V. (2014). Infections caused by carbapenemase-producing Enterobacteriaceae: Risk factors, clinical features and prognosis. Enfermedades Infecciosas y Microbiología Clínica,32, 41-48.

[14.] Akova M, Daikos GL, Tzouvelekis L, Carmeli Y. (2012). Interventional strategies and current clinical experience with carbapenemase-producing Gram-negative bacteria. Clin Microbiol Infect; 18:439-48.

[15.] Tumbarello M, Trecarichi EM, De Rosa FG, Giannella M, Giacobbe DR, Bassetti M, et al. (2015). Infections caused by KPCproducing Klebsiella pneumoniae: differences in therapy and mortality in a multicentre study. J Antimicrob Chemother.; 70(7): 2133-43.

[16.] Queenan A M, Bush K.(2007). Carbapenemases: the versatile beta-lactamases. Clin Microbiol Rev.; 20: 440-58

[17.] Goodman K E, Simner P J, Tamma P D, Milstone A M. (2016). Infection control implications of heterogeneous resistance mechanism in carbapenem-resistant Enterobacteriaceae (CRE). Expert Rev Anti Infect Ther.; 14: 1-14.

[18.] Nordmann P, Poirel L. (2014). The difficult-to-control spread of carbapenemase producers among Enterobacteriaceae worldwide. Clin Microbiol Infect.; 20: 821-30.

[19.] Bush K, Fisher J F. (2011). Epidemiological expansion, structural studies, and clinical challenges of new β-lactamases from gram-negative bacteria. Annu Rev Microbiol; 65: 455-78.

[20.] Sidjabat H E, Silveira F P, Potoski B A, AbuElmagd K M, Adams-Haduch J M, Paterson D L, et al. (2009). Interspecies spread of Klebsiella pneumoniae carbapenemase gene in a single patient. Clin Infect Dis.; 49: 1736-8

[21.] Escandón-Vargas K, Reyes S, Gutiérrez S, Villegas M V. (2017). The epidemiology of carbapenemases in Latin America and the Caribbean. Expert Rev Anti Infect Ther; 15: 277-97.

[22.] Gupta, N., Limbago, B. M., Patel, J. B. & Kallen, A. J. (2011). Carbapenem- resistant Enterobacteriaceae: epidemiology and prevention. Clin Infect Dis 53, 60–67.

[23.] Leung, V., Loo, V. G., Frenette, C., Domingo, M. C., Bourgault, A. M. Robson, H. G. (2012). First Canadian outbreak of Enterobacteriaceaeexpressing. Klebsiella pneumoniae carbapenemase type 3. Can J Infect dis Med Microbiol 23, 117–120.

[24.] Bou Arévalo G, Chávez Sánchez F, Oliver Palomo A, Oteo Iglesias J. (2015). Métodos microbiológicos para la vigilancia del estado de portador de bacterias multirresistentes. Oteo Iglesias J (coordinador). Procedimientos en Microbiología Clínica. Cercenado Mansilla E, Cantón Moreno R (editores). Madrid: Sociedad Española de Enfermedades infecciosas y Microbiología Clínica (SEIMC).

[25.] Paciel D, Seija V, Prieto J, Vignoli R, Medina J, Savio E. (2011). Enterobacterias productoras de KPC (Klebsiella pneumoniae carbapenemasa). Tendencias en Medicina; 39: 47-52.

[26.] Córdova E, Lespada MI, Gómez N, Pasterán F, Oviedo V, Rodríguez-Ismael C. (2012). Descripción clínica y epidemiológica de un brote nosocomial por Klebsiella pneumoniae productora de KPC en Buenos Aires, Argentina. Enferm Infecc Microbiol Clin.; 30: 376-9.

[27.] Nordmann P, Cuzon G, Naas T. (209). The real threat of Klebsiella pneumoniae carbapenemase producing bacteria. Lancet Infect Dis.; 9: 228-36

[28.] Marchaim D, Navon-Venzia S, Schwaber M J, Carmeli Y. (2008). Isolation of imipenem-resistant Enterobacter species; emergence of KPCcarbapenemase, molecular characterization, epidemiology and outcomes. Antimicrob Agents Chemother ; 52: 1413-8.

[29.] Bratu S, Landman D, Haag R, Recco R, Eramo A, Alam M, et al. (2005). Rapid spread of carbapenem-resistant Klebsiella pneumoniae in New York City. Arch Intern Med ; 165: 1430-5.

[30.] Correa L, Valle M, Siqueira I, Pasternak J, Gales A, Silva C, et al. (2013). A hospital based matched case control study to identify clinical outcome and risk factors associated with carbapenem resistant Klebsiella pneumoniae infection. BMC Infect Dis.;13(80).

[31.] López J, Echeverri L. (2010). Klebsiella pneumoniae: ¿la nueva superbacteria? Patogenicidad, epidemiología y mecanismos de resistencia. Revista medica Universidad de Antioquia.,23(2)

[32.] Hoenigl M, Valentin T, Zarfel G, Wuerstl B, Leitner E, Slazer H, et al. (2012). Nosocomial outbreak of Klebsiella pneumoniae carbapenemase producing Klebsiella oxytoca in Austria. Antimicrob Agents Chemother.;56(4):2158---61.

[33.] Woodford N, Tierno P, Young K, Tysall L, Palepou M, Ward E, et al. (2004). Outbreak of Klebsiella pneumoniae producing a new carbapenem hydrolyzing class A ˘-lactamase, KPC-3, in a New York medical center. Antimicrob Agents Chemother.;48:4793---9.

[34.] Ajao AO, Johnson JK, Harris AD, Zhan M, McGregor JC, Thom KA, et al. (2013). Risk of acquiring extended-spectrum beta-lactamase-pro¬ducing Klebsiella species and Escherichia coli from prior room oc¬cupants in the intensive care unit. Infect Control Hosp Epidemiol;34(5):453-8. DOI: 10.1086/670216.

[35.] Harris AD, Perencevich EN, Johnson JK, Paterson DL, Morris JG, Strauss SM, et al.

(2007). Patient-to-patient transmission is important in extended-spectrum beta-lactamase-producing Klebsiella pneu¬moniae acquisition. Clin Infect Dis.;45(10):1347-50. PMID: 17968833. DOI: 10.1086/522657.

[36.] Nseir S, Blazejewski C, Lubret R, Wallet F, Courcol R, Durocher A. (2011). Risk of acquiring multidrug-resistant Gram-negative bacilli from prior room occupants in the intensive care unit. Clin Microbiol Infect.;17(8):1201-8. PMID: 21054665. DOI: 10.1111/j.1469- 0691.2010.03420.x.

[37.] Ministerio de Salud Pública del Ecuador (2016). Manual Control de enterobacterias productoras de carbapenemasas a nivel hospitalario de Salud.

[38.] Bravo Ríos, Karina Grissel,Olmos Villegas, Víctor Miguel . (2013). "Comparación de métodos para la detección de klebsiella pneumoniae productora de carbapenemasa (KPC) en muestras de hisopados rectales procesadas en el c.h.dr.a.a.m, agosto a noviembre 2013". Universidad de Panamá, Facultad de Medicina, 42.

[39.] Tzouvelekis LS, Markogiannakis A, Psichogiou M, Tassios PT, Daikos GL. (2012). Carbapenemasas en Klebsiella pneumoniae y otras enterobacterias: una crisis evolutiva de dimensiones globales. Clin Microbiol Rev.; 25: 682-707.

[40.] Kohler, P. P., Melano, R. G., Patel, S. N., Shafinaz, S., Faheem, A., Coleman, B. L....McGeer, A. (2018). Emergence of Carbapenemase-Producing Enterobacteriaceae, South-Central Ontario, Canada. Emerging Infectious Diseases, 24(9), 1674-1682. https://dx.doi.org/10.3201/eid2409.180164.

[41.] Fernández-Verdugo, A., Fernández, J., Escudero, D., Cofiño, L., Forcelledo, L., Telenti, M., ... Vazquez. F. (2017). Vigilancia epidemiológica para microorganismos multirresistentes en una UCI polivalente. Revista Española Quimioter, 30(3), 201-206. Recuperado de http://www.seq.es/seq/0214-3429/30/3/fernandez05apr2017.pdf.

[42.] Eser F., Yılmaz GR, Güner R, Hasanoğlu İ, Ürkmez Korkmaz FY, Açıkgöz ZC, Taşyaran MA. (2019). Risk factors for rectal colonization of carbapenem-resistant Enterobacteriaceae in a tertiary care hospital: a case-control study from Turkey. Turkish Journal of Medical Sciences. 49(1):341-346. doi: 10.3906/sag-1810-65.

[43.] Ocampos Ugarte J., Takahasi Alvarez V. (2015). Enterobacterias productoras de carbapenemasas en pacientes del servicio de Clínica Médica del Hospital Nacional de Itauguá. Revista virtual de Sociedad Paraguaya de Medicina Interna, 2, 33-42.

[44.] Echavarría G., Guevara D., Bertona E., De paulis A., Predari S., Benchetrit G. (2017). Colonización por klebsiella pneumoniae productora de carbapenemasa tipo KPC en un hospital universitario medicina (Buenos Aires) 2017; 77: 105-110.

[45.] Souli, M., Galani, I., Antoniadou, A., Papadomichelakis, E., Poulakou, G., Panagea, T., Vourli, S., Zerva, L., Armaganidis, A. & Kanellakopoulou, K. (2012). An outbreak of infection due to b-lactamase Klebsiella pneumoniacarbapenemase 2-producing K. pneumoniae in a Greek university hospital: molecular characterization, epidemiology, and outcomes. Clin Infect Dis 50, 364–373.

[46.] Correa, L., Martino, M. D., Siqueira, I., Pasternak, J., Gales, A. C., Silva, C. V., Camargo, T. Z., Scherer, P. F. & Marra, A. R. (2013). A hospital- based matched case-control study to identify clinical outcome and risk factors associated with carbapenem-resistant Klebsiella pneumoniae infection. BMC Infect Dis 13, 80.

[47.] Tofteland, S., Naseer, U., Lislevand, J. H., Sundsfjord, A. Samuelsen, O. (2013). A long-term low-frequency hospital outbreak of kpc-producing Klebsiella pneumoniae involving intergenus plasmid diffusion and a persisting environmental reservoir. PLoS One 8, e59015–59018.

[48.] Yang, J., Ye, L., Guo, L., Zhao, Q., Chen, R., Luo, Y., Chen, Y., Tian, S., Zhao, J. & other authors (2013). A nosocomial outbreak of kpc-2-producing Klebsiella pneumoniae in a Chinese hospital: dissemination of ST11 and emergence of ST37, ST392 and ST395. Clin Microbiol Infect 19, E509–E515.

[49.] Azim A, Dwivedi M, Rao PB, Baronia AK, Singh RK, Prasad KN, et al. (2010). Epidemiology of bacterial colonization at intensive care unit admission with emphasis on extended-spectrum beta-lactamase-and metallo-beta-lactamase-producing Gram-negative bacteria- -an Indian experience. J Med Microbiol.;59(Pt 8):955-60. PMID: 20413621. DOI: 10.1099/jmm.0.018085-0.

[50.] Vera A, Barría C, Carrasco S, Lima D, et al. (2017). KPC: Klebsiella pneumoniae carbapenemase, main carbapenemase in Enterobacteriaceae. Rev. chil. infectol. vol.34 no.5 Santiago oct. 2017