doi: 10.13241/j.cnki.pmb.2020.10.018

新疆地区三级医院多重耐药菌感染及耐药性分析 *

娃司玛·夏米力 夏木西卡玛尔·阿克木 邵 丽△ 杨学安 尼加提·塔西普拉提
（新疆医科大学第一附属医院手术室 新疆 乌鲁木齐 830054）

摘要 目的：探讨与分析近 3 年新疆地区三级医院多重耐药菌感染及耐药性。**方法**：选择 2016 年 1 月 -2018 年 12 月在新疆地区三级医院进行住院诊治的患者 1100 例作为研究对象，调查与检测多重耐药菌感染及耐药情况，分析导致多重耐药菌感染的危险影响因素。**结果**：在 1100 例患者中，判断为多重耐药菌感染 20 例，感染率为 1.8 %，且呈现显著升高的趋势（P<0.05）。这 20 例患者中检出病原菌 20 株，其中耐甲氧西林金黄色葡萄球菌 10 株、产超广谱 β- 内酰胺酶细菌 6 株、耐万古霉素肠球菌 4 株。甲氧西林金黄色葡萄球菌、产超广谱 β- 内酰胺酶细菌、耐万古霉素肠球菌对呋喃妥因、亚胺培南、哌拉西林有比较高的敏感性，对庆大霉素、氨苄西林、头孢他啶、左氧氟沙星的敏感性比较低。多因素 Logistic 回归分析结果显示除年龄外，外置导管天数、住院时间、糖尿病、使用抗生素种类 >2 种、合并慢性肺部疾病、合并心血管疾病、动静脉置管、使用呼吸机为导致住院患者多重耐药菌感染的危险影响因素（P<0.05）。**结论**：2016 年至 2018 年新疆地区三级医院多重耐药菌感染逐年增加，以甲氧西林金黄色葡萄球菌为主。外置导管天数、住院时间、糖尿病、使用抗生素种类 >2 种、合并慢性肺部疾病、合并心血管疾病、动静脉置管、使用呼吸机为导致住院患者多重耐药菌感染的危险因素，在临床治疗中，应根据患者自身的情况，有效减少接触性感染、控制感染的因素，同时根据药敏试验结果合理选择抗生素的种类和剂量，以阻止院内多重耐药菌的散播。

关键词：新疆地区；三级医院；多重耐药菌；耐药性分析
中图分类号：R197.323.4 **文献标识码**：A **文章编号**：1673-6273（2020）10-1881-04

Analysis of Multi-drug Resistant Infection and Drug Resistance in Tertiary Hospitals in Xinjiang Province*

WA sima·Xiamili, XIA muxikamaer·Akemu, SHAO Li△, YANG Xue-an, NI jiati·Taxipulati
(Operating Room, the First Affiliated Hospital of Xinjiang Medical University, Urumqi, Xinjiang, 830054, China)

ABSTRACT Objective: To explore and analyze the multi-drug resistant infection and drug resistance of tertiary hospitals in Xinjiang in recent three years. **Methods:** 1100 patients who were hospitalized in the tertiary hospitals in Xinjiang from January 2016 to December 2018 were selected as subjects. All the patients were investigated and detected multi-drug resistant infections and drug resistance. Analyzed the dangerous effects of multi-drug resistant influence factors. **Results:** 20 patients were diagnosed among the 1100 patients as multi-drug resistant bacteria, and the infection rate was 1.8%, showing a significant increase trend (P<0.05). 20 strains of pathogens were detected in these 20 patients, including 10 strains of Methicillin-resistant *Staphylococcus aureus*, 6 strains of Extended-spectrum β-lactamase bacteria, and 4 strains of Vancomycin-resistant *enterococci*. Methicillin-resistant *Staphylococcus aureus*, Extended-spectrum β-lactamase-producing bacteria, Vancomycin-resistant *enterococci* have high sensitivity to nitrofurantoin, imipenem, and piperacillin, and have low sensitivity to gentamicin, ampicillin, ceftazidime and levofloxacin. Multivariate logistic regression analysis showed that except age, the number of external catheter days, hospital stay, diabetes, the use of antibiotics >2, combined with chronic lung disease, combined with cardiovascular disease, arteriovenous catheterization and use of ventilator were the influencing risk factors for multidrug-resistant infection in hospitalized patients (P<0.05). **Conclusion:** From 2016 to 2018 years, multi-drug resistant infections in tertiary hospitals in Xinjiang region increased year by year, which are mainly methicillin-resistant Staphylococcus aureus. The number of external catheter days, hospital stay, diabetes, use of antibiotics >2, combined with chronic lung disease, cardiovascular disease, arteriovenous catheterization, use of ventilator are risk factors for multidrug-resistant infection in hospitalized patients. In clinical treatment, the factors of contact infection and infection control should be effectively reduced according to the patient's own condition. At the same time, the type and dose of antibiotics should be reasonably selected according to the results of drug susceptibility test to prevent the spread of multi-drug resistant bacteria in the hospital.

Key words: Xinjiang area; Tertiary hospital; Multi-drug resistant bacteria; Drug resistance analysis
Chinese Library Classification(CLC): R197.323.4 Document code: A
Article ID: 1673-6273(2020)10-1881-04

* 基金项目：新疆维吾尔自治区自然科学基金项目（2014211C063）
作者简介：娃司玛·夏米力（1988-），女，本科，研究方向：院内感染，电话：13565914326，E-mail：wsmxmlxinjiang@163.com
△ 通讯作者：邵丽（1962-），女，本科，主任医师，研究方向：院内感染，电话：13565914326，E-mail：akejan@126.com
（收稿日期：2019-10-02 接受日期：2019-10-26）

前言

医院感染管理是衡量医院综合管理的重要指标，在三级医院呈现多发态势，在部分地区已成为一个严重的社会问题[1]。当前随着广谱抗生素的广泛应用，细菌耐药性不断增加，并呈现多重耐药等特征[2,3]。多重耐药菌(Multi-drug resistant bacteria，MDR)是指对常见的敏感的 3 种或以上的微生物进行实验室培养，同时呈现出阳性结果，鉴定抗菌药物耐药的菌株[4]。其已经成为医院感染的重要病原菌，不仅增加了患者的住院费用，也增加了患者的死亡率[5,6]。目前医院感染病原菌主要包括对耐甲氧西林金黄色葡萄球菌、耐万古霉素肠球菌、泛耐药鲍曼不动杆菌等[7,8]。特别是当前很多三级医院的住院患者需要进行侵入性手术、留置导管等，这增加了医院感染的机会[9,10]。多重耐药菌感染的早期，无明显的临床特征，诊断一般都进行细菌培养，增加了感染的时间，不利于预后[11,12]。当前初始治疗也是经验性治疗，因此效果不佳[13,14]。本文具体分析了 2016 年至 2018 年新疆地区三级医院多重耐药菌感染及耐药性情况，以了解新疆地区多重耐药菌感染的耐药性状况。

1 资料与方法

1.1 一般资料

选择 2016 年 1 月 -2018 年 12 月在新疆地区三级医院进行住院诊治的患者 1100 例作为研究对象，纳入标准：年龄 20-90 岁；入院前检查无多重耐药菌感染；临床资料与病原菌检测资料完整；住院时间 >48 h；医院伦理委员会批准了此次研究；患者及其家属知情同意此次研究。排除标准：不同意此次治疗或者中途停止治疗的患者；妊娠与哺乳期妇女；精神病史者。其中男 650 例，女 450 例；年龄 29~82 岁，平均年龄 56.22± 11.32 岁；平均住院时间 9.22± 1.49 d；平均体重指数 22.84± 2.41 kg/m^2；收治科室：外科 456 例，骨科 244 例，ICU 科 156 例，肿瘤外科 100 例，其他科室 144 例；合并疾病：糖尿病 122 例，高血压 78 例，慢性肺部疾病 105 例，心血管疾病 95 例，高脂血症 142 例；平均外置导管天数 4.52± 0.32 d。

1.2 检验方法

取患者的深部痰液，放置在灭菌容器中，使用 PHOENIX100 全自动微生物分析仪，检测病原菌的种类，采用药敏鉴定病原菌的耐药性。多重耐药菌对抗生素的敏感性试验采用美国 BBL 公司的产品药敏纸片（包括药敏试剂），在同一时间内完成。药敏评价标准参考美国临床实验室标准化研究院 2010 版[15]。

多重耐药菌感染诊断标准：显微镜下检查可见每 30 个视野中半数视野见到细菌，革兰阳性球菌菌落数≥ 10^4 cfu/mL，革兰阴性杆菌菌落数≥ 10^5 cfu/mL。

1.3 统计方法

选择 SPSS20.00，计量数据用($\bar{x}\pm s$)表示，计数数据用%表示，对比用 t 检验与 x^2 检验、多因素分析采用多因素 Logistic 回归分析，其中指标β 表示回归系数，SE 表示标准误 Wald 表示检验的统计量，OR 表示比数比（OR>1 是危险因素；OR<1 保护因素；OR=1 该因素不起作用），检验水准为 α=0.05，P<0.05 有统计学意义。

2 结果

2.1 多重耐药菌感染发生情况

在 1100 例患者中，判断为多重耐药菌感染 20 例，感染率为 1.8%，其中 2016 年、2017 年、2018 年的多重耐药菌感染率分别为 0.7%、1.8%、2.8%，呈现显著升高的趋势(P<0.05)。见表1。

表 1 多重耐药菌感染率对比[例(%)]

Table 1 Comparison of infection rates of multi-drug resistant bacteria [n (%)]

Years	n	Multi-drug resistant infection	Ratio
2016	300	2	0.7
2017	400	7	1.8
2018	400	11	2.8
F			32.157
P			0.000

2.2 病原菌分布

在多重耐药菌感染 20 例患者中，检出病原菌 20 株，其中甲氧西林金黄色葡萄球菌 10 株、产超广谱β- 内酰胺酶细菌 6 株、耐万古霉素肠球菌 4 株。

2.3 耐药性监测

甲氧西林金黄色葡萄球菌、产超广谱β- 内酰胺酶细菌、耐万古霉素肠球菌对呋喃妥因、亚胺培南、哌拉西林有比较高的敏感性，对庆大霉素、氨苄西林、头孢他啶、左氧氟沙星的敏感性比较低。见表 2。

2.4 发生因素分析

以多重耐药菌感染作为因变量，以临床资料作为自变量，多因素 Logistic 回归分析结果显示除年龄外，外置导管天数、住院时间、糖尿病、使用抗生素种类 >2 种、合并慢性肺部疾病、合并心血管疾病、动静脉置管、使用呼吸机为导致住院患者多重耐药菌感染的影响的危险因素(P<0.05)。见表 3。

3 讨论

多重耐药菌感染是当前三级医院面临的重大院内感染，具有难治、高病死率和极易流行暴发等特点，是临床治疗和感染预防控制的一个重点问题[16]。近年来，随着抗生素、免疫抑制剂、激素的滥用，使得多重耐药菌感染发的病原菌种类逐渐增加，严重影响了患者的健康，加重了经济负担[17,18]。

表 2 多重耐药菌对抗生素的敏感性[例(%)]

Table 2 Sensitivity of multi-drug resistant bacteria to antibiotics [n (%)]

Bacterial species	Strain	Ceftazidime	Lev-ofloxacin	Imipenem	Piperacillin	Gentamicin	Ampicillin	Nitrofuran-toin
Methicillin-resistant *Staphylococcus aureus*	10	0(0.0%)	3(30.0%)	8(80.0%)	7(70.0%)	2(20.0%)	1(10.0%)	9(90.0%)
Extended-spectrum β-lactamase producing bacteria	6	3(50.0%)	3(50.0%)	6(100.0%)	3(50.0%)	0(0.0%)	0(0.0%)	6(100.0%)
Vancomycin-resistant enterococci	4	2(50.0%)	0(0.0%)	4(100.0%)	4(100.0%)	2(50.0%)	0(0.0%)	4(100.0%)

表 3 多重耐药菌感染的多因素分析(n=20)

Table 3 Multivariate analysis of multi-drug resistant infections (n=20)

Variable	β	SE	Wald	*P*	OR (95%CI)
External catheter days	0.323	0.178	34.119	0.000	1.893(1.541-2.386)
Hospital stay	0.627	0.208	34.396	0.000	2.154(1.82-2.737)
Diabetes	0.451	0.196	28.175	0.000	2.041(1.885-2.786)
Ages	-0.037	0.393	0.914	0.332	-
Use antibiotics > 2 species	0.841	0.434	4.215	0.026	2.828(1.845-10.324)
Combined chronic lung disease	0.547	0.192	6.643	0.014	12.732(3.464-20.125)
Combined with cardiovascular disease	1.032	0.328	11.326	0.000	20.604(3.847-40.712)
Arteriovenous catheter	1.182	0.473	7.921	0.000	3.255(1.832-8.763)
Using a ventilator	0.789	0.448	4.635	0.000	2.972(1.425-5.683)

本研究显示在 1100 例患者中,判断为多重耐药菌感染 20 例,感染率为 1.8 %,且呈现显著升高的趋势。多重耐药菌感染率增加不仅会加重患者的病情,延长患者住院时间,增加患者的经济负担,也会给医疗质量带来严重的负面影响[19,20]。

加强多重耐药菌感染患者的病原菌分析与耐药性监测具有重要的意义[21,22]。本研究的 20 例患者中,检出病原菌 20 株,其中甲氧西林金黄色葡萄球菌 10 株、产超广谱β- 内酰胺酶细菌 6 株、耐万古霉素肠球菌 4 株。说明 3 代头孢菌素具有抗菌谱广、毒性低和耐酶等特点,但是长期大量应用,也会产生耐药株[23,24]。临床治疗首选呋喃妥因,而对于病情较重的感染者,可应用哌拉西林或碳青霉烯类抗生素治疗[25]。同时医院应该规范管理抗生素的使用,治疗时及时进行患者的细菌培养和药物敏感试验,做到早发现早治疗。患者在外置导管期间要严格按照标准进行操作,要做好消毒工作[26,27]。

本研究显示多因素 Logistic 回归分析结果显示外置导管天数、住院时间、糖尿病、使用抗生素种类 >2 种、合并慢性肺部疾病、合并心血管疾病、动静脉置管、使用呼吸机为导致住院患者多重耐药菌感染的独立危险因素。从机制上分析,使用外置导管可破坏机体本身的生理环境,使大量细菌上行至机体导致感染,同时细菌在外置导管表面寄生,形成细菌生物膜,影响机体的免疫能力,引起患者感染[28,29]。住院天数越长,接触的人群越多,也容易发生感染。部分患者伴随有糖尿病、心血管疾病或慢性肺部疾病,机体的各项生理机能下降,免疫力降低,所以极易发生多重耐药菌感染。同时,当进行手术操作或者其他侵入操作时,如呼吸机、动静脉置管、外置导管等,病原菌可以黏附在导管表面,通过插管进入机体内,增加细菌的易感性,引起相关的感染[30-32]。除此之外,使用抗生素种类的增加,也会增加多重耐药菌感染,因此治疗中需要调查患者的个体情况,根据自身情况,给予合适的抗生素种类与剂量。本研究也有一定过的不足,多因素分析纳入资料比较少,且药敏分析的药物比较少,将在后续研究中进行深入分析。

总之,2016 年到 2018 年新疆地区三级医院多重耐药菌感染逐年增加,以甲氧西林金黄色葡萄球菌为主,外置导管天数、住院时间、糖尿病、使用抗生素种类 >2 种、合并慢性肺部疾病、合并心血管疾病、动静脉置管、使用呼吸机为导致住院患者多重耐药菌感染的危险因素,在临床治疗中,应根据患者自身的情况,有效减少接触性感染、控制感染的因素,同时根据药敏试验结果合理选择抗生素的种类和剂量,以阻止院内多重耐药菌的散播。

参 考 文 献(References)

[1] Dalman M, Bhatta S, Nagajothi N, et al. Characterizing the molecular epidemiology of Staphylococcus aureus across and within fitness facility types[J]. BMC Infect Dis, 2019, 19(1): e69

[2] Goyal S, Khot SC, Ramachandran V, et al. Bacterial contamination of medical providers' white coats and surgical scrubs: A systematic review[J]. Am J Infect Control, 2019, 47(8): 994-1001

[3] Li Y, Tang X, Zhao Z, et al. Intranasal immunization with recombinant outer membrane protein A induces protective immune response against Stenotrophomonas maltophilia infection [J]. PLoS One, 2019, 14(4): e0214596

[4] Lorestani RC, Akya A, Elahi A, et al. Gene cassettes of class I integron-associated with antimicrobial resistance in isolates of Citrobacter spp. with multidrug resistance [J]. Iran J Microbiol, 2018, 10(1):

22-29

[5] Fan Y, Mu Y, Lu L, et al. Hydrogen peroxide-inactivated bacteria induces potent humoral and cellular immune responses and releases nucleic acids[J]. Int Immunopharmacol, 2019, 69(4): 389-397

[6] Ganesh R, Shrestha D, Bhattachan B, et al. Epidemiology of urinary tract infection and antimicrobial resistance in a pediatric hospital in Nepal[J]. BMC Infect Dis, 2019, 19(1): 420-426

[7] Gatadi S, Gour J, Shukla M, et al. Synthesis and evaluation of new quinazolin-4 (3H)-one derivatives as potent antibacterial agents against multidrug resistant Staphylococcus aureus and Mycobacterium tuberculosis[J]. Eur J Med Chem, 2019, 175(14): 287-308

[8] Lynch BL, Schaffer K. Can guidelines for the control of multi-drug-resistant Gram-negative organisms be put into practice? A national survey of guideline compliance and comparison of available guidelines [J]. J Hosp Infect, 2019, 102(1): 1-7

[9] Machelart A, Salzano G, Li X, et al. Intrinsic Antibacterial Activity of Nanoparticles Made of beta-Cyclodextrins Potentiates Their Effect as Drug Nanocarriers against Tuberculosis [J]. ACS Nano, 2019, 13(4): 3992-4007

[10] Mesfin EA, Beyene D, Tesfaye A, et al. Drug-resistance patterns of Mycobacterium tuberculosis strains and associated risk factors among multi drug-resistant tuberculosis suspected patients from Ethiopia[J]. PLoS One, 2018, 13(6): e0197737

[11] Milovanovic T, Dumic I, Velickovic J, et al. Epidemiology and risk factors for multi-drug resistant hospital-acquired urinary tract infection in patients with liver cirrhosis: single center experience in Serbia [J]. BMC Infect Dis, 2019, 19(1): 141-153

[12] Munier AL, Biard L, Legrand M, et al. Incidence, risk factors and outcome of multi-drug resistant Acinetobacter baumannii nosocomial infections during an outbreak in a burn unit [J]. Int J Infect Dis, 2019, 79: 179-184

[13] Ijaz M, Siddique AB, Rasool MH, et al. Frequency of multi drug resistant Pseudomonas aeruginosa in different wound types of hospitalized patients[J]. Pak J Pharm Sci, 2019, 32(2): 865-870

[14] Kumarage J, Khonyongwa K, Khan A, et al. Transmission of multidrug resistant Pseudomonas aeruginosa between two flexible ureteroscopes and an outbreak of urinary tract infection: the fragility of endoscope decontamination[J]. J Hosp Infect, 2019, 102(1): 89-94

[15] Hsueh PR, Ko WC, Wu JJ, et al. Consensus statement on the adherence to Clinical and Laboratory Standards Institute (CLSI) Antimicrobial Susceptibility Testing Guidelines (CLSI-2010 and CLSI-2010-update) for Enterobacteriaceae in clinical microbiology laboratories in Taiwan[J]. J Microbiol Immunol Infect, 2010, 43(5): 452-455

[16] Baier C, Pirr S, Ziesing S, et al. Prospective surveillance of bacterial colonization and primary sepsis: findings of a tertiary neonatal intensive and intermediate care unit [J]. J Hosp Infect, 2019, 102 (3): 325-331

[17] Bidaud AL, Chowdhary A, Dannaoui E. Candida auris: An emerging drug resistant yeast - A mini-review [J]. J Mycol Med, 2018, 28(3): 568-573

[18] Cadot L, Bruguiere H, Jumas-Bilak E, et al. Extended spectrum beta-lactamase-producing Klebsiella pneumoniae outbreak reveals incubators as pathogen reservoir in neonatal care center [J]. Eur J Pediatr, 2019, 178(4): 505-513

[19] Cara A KS, Zaidi S TR, Suleman F. Cost-effectiveness analysis of low versus high dose colistin in the treatment of multi-drug resistant pneumonia in Saudi Arabia [J]. Int J Clin Pharm, 2018, 40 (5): 1051-1058

[20] Peters C, Dulon M, Nienhaus A, et al. Occupational Infection Risk with Multidrug-Resistant Organisms in Health Personnel-A Systematic Review[J]. Int J Environ Res Public Health, 2019, 16(11)

[21] Phodha T, Riewpaiboon A, Malathum K, et al. Excess annual economic burdens from nosocomial infections caused by multi-drug resistant bacteria in Thailand [J]. Expert Rev Pharmacoecon Outcomes Res, 2019, 19(3): 305-312

[22] Rello J, Kalwaje Eshwara V, Conway-Morris A, et al. Perceived differences between intensivists and infectious diseases consultants facing antimicrobial resistance: a global cross-sectional survey [J]. Eur J Clin Microbiol Infect Dis, 2019, 38(7): 1235-1240

[23] Widmer F C, Frei R, Romanyuk A, et al. Overall bioburden by total colony count does not predict the presence of pathogens with high clinical relevance in hospital and community environments[J]. J Hosp Infect, 2019, 101(2): 240-244

[24] Williams P CM, Waichungo J, Gordon NC, et al. The potential of fosfomycin for multi-drug resistant sepsis: an analysis of in vitro activity against invasive paediatric Gram-negative bacteria [J]. J Med Microbiol, 2019, 68(5): 711-719

[25] Wyres KL, Wick RR, Judd LM, et al. Distinct evolutionary dynamics of horizontal gene transfer in drug resistant and virulent clones of Klebsiella pneumoniae[J]. PLoS Genet, 2019, 15(4): e1008114

[26] Yadav K, Yavvari PS, Pal S, et al. Oral Delivery of Cholic Acid-Derived Amphiphile Helps in Combating Salmonella-Mediated Gut Infection and Inflammation[J]. Bioconjug Chem, 2019, 30(3): 721-732

[27] Rohde C, Wittmann J, Kutter E. Bacteriophages: A Therapy Concept against Multi-Drug-Resistant Bacteria [J]. Surg Infect (Larchmt), 2018, 19(8): 737-744

[28] Vijayashree Priyadharsini J, Smiline Girija AS, Paramasivam A. An insight into the emergence of Acinetobacter baumannii as an oro-dental pathogen and its drug resistance gene profile - An in silico approach[J]. Heliyon, 2018, 4(12): e01051

[29] Wang M, Wei H, Zhao Y, et al. Analysis of multidrug-resistant bacteria in 3223 patients with hospital-acquired infections (HAI) from a tertiary general hospital in China [J]. Bosn J Basic Med Sci, 2019, 19 (1): 86-93

[30] Cheung YM, Van K, Lan L, et al. Hypothyroidism associated with therapy for multi-drug-resistant tuberculosis in Australia [J]. Intern Med J, 2019, 49(3): 364-372

[31] Ciofi Degli Atti M L, D'amore C, Gagliotti C, et al. Strategies to control antibiotic resistance: results from a survey in Italian children's hospitals[J]. Ann Ig, 2019, 31(1): 3-12

[32] Crepin S, Ottosen EN, Peters K, et al. The lytic transglycosylase MltB connects membrane homeostasis and in vivo fitness of Acinetobacter baumannii[J]. Mol Microbiol, 2018, 109(6): 745-762