D:\Biomedica Vol. 31, Issue 1, Jan. – Mar., 2015\Bio-8.Doc P. 36 – 41 (KC) IV

ORIGINAL ARTICLE

TEMPORAL PATTERN AND CONTROL OF AN OUTBREAK OF EXTENSIVELY DRUG RESISTANT *ACINETOBACTER BAUMANNII* IN AN ICU

TARAR M.R.,[1] NAEEM T.,[1] IQBAL S.,[2] HADJIRUL H.,[3] GHOURI M.,[3] ISHAQ M.[4] AND QURESHI M.[1]
[1]*Department of Pathology, Shalamar Medical and Dental College,* [2]*Shalamar Teaching Hospital*
[3]*Shalamar Nursing College and Director Nursing, Infection Control Nurse*
[4]*Department of Anaesthesia and Intensive Care, Shalamar Medical and Dental College, Lahore*

Abstract

Objective: Acinetobacter baumannii is (XDR – AB) an important human pathogen causing many nosocomial infections. Once introduced into the hospital, it may become difficult to get rid of it. It can cause a range of infections, which are difficult to treat because the organism is usually resistant to many classes of antibiotics. We describe the temporal pattern of a cohort of cases which alerted the infection control committee for action to prevent these infections.

Methods: Spread over a four months period,nine cases of XDR-AB admitted in the ICU, were diagnosed by appropriate cultures. Extensive environmental sampling was done to find a niche for the causative organism. Infection Control Committee compiled and implemented the disinfection protocols and other infection prevention strategies. Close surveillance for any additional cases was instituted.

Results: XDR – AB from all nine cases had similar antibiogram. We identified the index case and determined the temporal pattern of all subsequent cases. The environmental cultures did not yield a growth of XDR – AB. The high level disinfection and observance of standard precautions led to disappearance of new cases for the three months period of follow-up.

Conclusion: An effective infection control program can control the outbreak situation in a hospital, provided all the members of the hospital team (administration, treating physicians & surgeons, microbiology laboratory and infection control committee) work in harmony and follow the standard operating protocols.

Key Words: Acinetobacter, Acinetobacter baumannii, Acinetobacter infections, Infection Control, Pneumonia Ventilator – Associated, Outbreak Control.

Introduction

Acinetobacter baumannii has become increasingly important as a human pathogen over the last 2 decades.[1] A saprophytic bacillus normally present in soil and water and in the hospital environment is now considered an important organism responsible for many nosocomial infections.[2] It may be isolated from colonized or infected patients or from hospital staff, and is predominantly present on the hands.[3] As an opportunistic organism it can cause pneumonia, blood stream infections, urinary tract infection, central nervous system infections and soft tissue (wound) infections.[4] In hospital settings, *Acinetobacter baumannii* has been associated with about one third of ventilator associated pneumonias (VAP).[5] These infections may often be difficult to treat because of multiple or complete resistance to different classes of antibiotics.[3]

In the present study conducted at Shalamar Teaching Hospital, the Infection Control Committee (ICC) was alerted to the increasing incidence of cases of XDR – AB in ICU over a period of 14 weeks. This prompted the ICC to constitute an Outbreak Control team to investigate the issue resulting in this report that describes the temporal pattern of the outbreak and extensive infection control efforts.

MATERIALS AND METHODS

1. Inclusion Criteria

All those patients who were admitted in ICU for more than 48 hours and from whom XDR – AB was isolated from at least one site between September 2013 and January 2014 were included in the study.

2. Patient Sample Collection / Processing

The specimens from these patients included High Vaginal Swab (HVS), Tracheal Aspirate, Sputum, Wound Swab / Aspirate and Blood. All the specimens were collected and processed as per standard policies and procedures.[6] The moderate to heavy growths for specimens with normal flora (HVS and Sputum) and a pure isolate for other specimens was interpreted as significant and processed further. Because we use a manual

Corresponding Author: Dr. Maryam R. Tarar, MBBS, MSc (London), PhD (London), FRCPath
Department of Pathology Shalamar Medical and Dental College, Lahore
Email: maryamtarar@gmail.com Ph: + 92 321 4470070 (Cell)

blood culture system, the subcultures were done after 24 hours incubation. The subcultures were made on Blood Agar, Chocolate Agar and McConkey's Agar.

Acinetobacter baumannii was identified by using Non-Lactose fermenting colonies on McConkey's Agar, Gram Stain morphology and Oxidase reaction. Final identification was done by using API 20E system after 24 – 48 hours incubation at 37°C.[7] Sensitivity test was done by Kirby – Bauer disc diffusion method. The zones of inhibition against selected antibiotics discs were interpreted using CLSI – 2012 criteria.[8]

3. Environmental Sample Collection / Processing

An extensive environmental sampling was done towards the end of January 2014. Altogether 120 samples were collected from the environment of the nine bedded ICU as part of exploratory study. The specimens were obtained from ICU as detailed in table 1. The air samples were collected by settle plates (10 minutes exposure time).

After the environmental sampling, the ICU was closed to new admissions over the weekend to perform the high level disinfection and admissions were resumed after 48 hours.

4. High Level Disinfection

A highlevel disinfection protocol[9-11] was rigorously followed and all ICU surfaces were cleaned with freshly prepared 1% solution of Polyhexamethylenebiguanidehydrochloride (Alpha Guard™) as per manufacturer's instructions, allowing 30 minutes contact time. ICU had 85 items in equipment category which were disinfected.

5. Contact Isolation and Standard Precautions

These were strictly implemented and importance of hand washing before, after and between patients care was stressed to all categories of healthcare staff.

6. Surveillance

Patients admitted after high level disinfection were closely monitored for a period of 12 weeks from 1st February 2014 to 30th April 2014.

RESULTS

Description of the Outbreak

1. **The Index case:** The Index case in this outbreak was a 21 year old female with history of drowsiness, high fever and fits for few hours before her admission to the hospital through Emergency. She had a Caesarean section at a hospital in Gujranwala district a few hours prior to admission in Shalamar Hospital. Her initial CBC revealed a total leukocyte count (TLC) of 16,000 / mm^3. A high vaginal swab obtained for culture and sensitivity on the 1st day of admission, grew XDR – AB that was sensitive to Colistin only. This was the only case from where XDR – AB was grown on Day 1 of admission in the hospital. She stayed in the ICU for 7 days out of which she was mechanically ventilated for last 5 days.

After the Index case, we identified 8 patients who got admitted in the ICU over a period of 14 weeks who fulfilled the inclusion criterion, to be categorized as part of an outbreak. Depending on the time frame overlap, four clusters were identified that constituted this outbreak of XDR-AB.

2. Grouping of cases as Outbreak Clusters

We decided to put patients in clusters or groups based on the fact that each cluster had patients overlapping for their stay in the ICU. If the gap was of more than 48 hours, we considered that as a separate cluster. The eligible patients were placed in four groups, for the purpose of temporal description.

The collective temporal relationship of the index case and remaining 8 cases in the outbreak is summarized in Fig 1. A brief description of these clusters is given below.

Cluster 1

The Index case and two other cases were placed in this Cluster. The second patient was admitted to the ICU a day after the index case expired. She stayed in ICU for 16 days and was not on Ventilator at any time. The third patient had an overlap of 6 days stay in ICU with the second patient. He was on the Ventilator for 6 days during his stay in ICU.

Cluster 2

There was only one case in this cluster and there was a gap of 45 days between this and the last patient in Cluster 1. This patient was in ICU for 10 days and was on the Ventilator all the time during her stay.

Cluster 3

This cluster comprised of two cases. The first in this group was admitted 14 days after the fourth patient. This patient was on Ventilator for 14 days, overlapped by sixth patient for a period of 7 days. The latter case was on Ventilator support for 8 days.

Cluster 4

There were 3 cases in this cluster and there was a gap of 5 days from patients in Cluster 3, all overlapped sequentially. The seventh patient was in the ICU for a period of 20 days without Ventilator support. The eighth patient was on Ventilator for 6 days. The last (9th) case was admitted with sepsis and was on Ventilator for 15 days.

3. Environmental Sampling

Altogether 120 samples from the ICU were obtained as

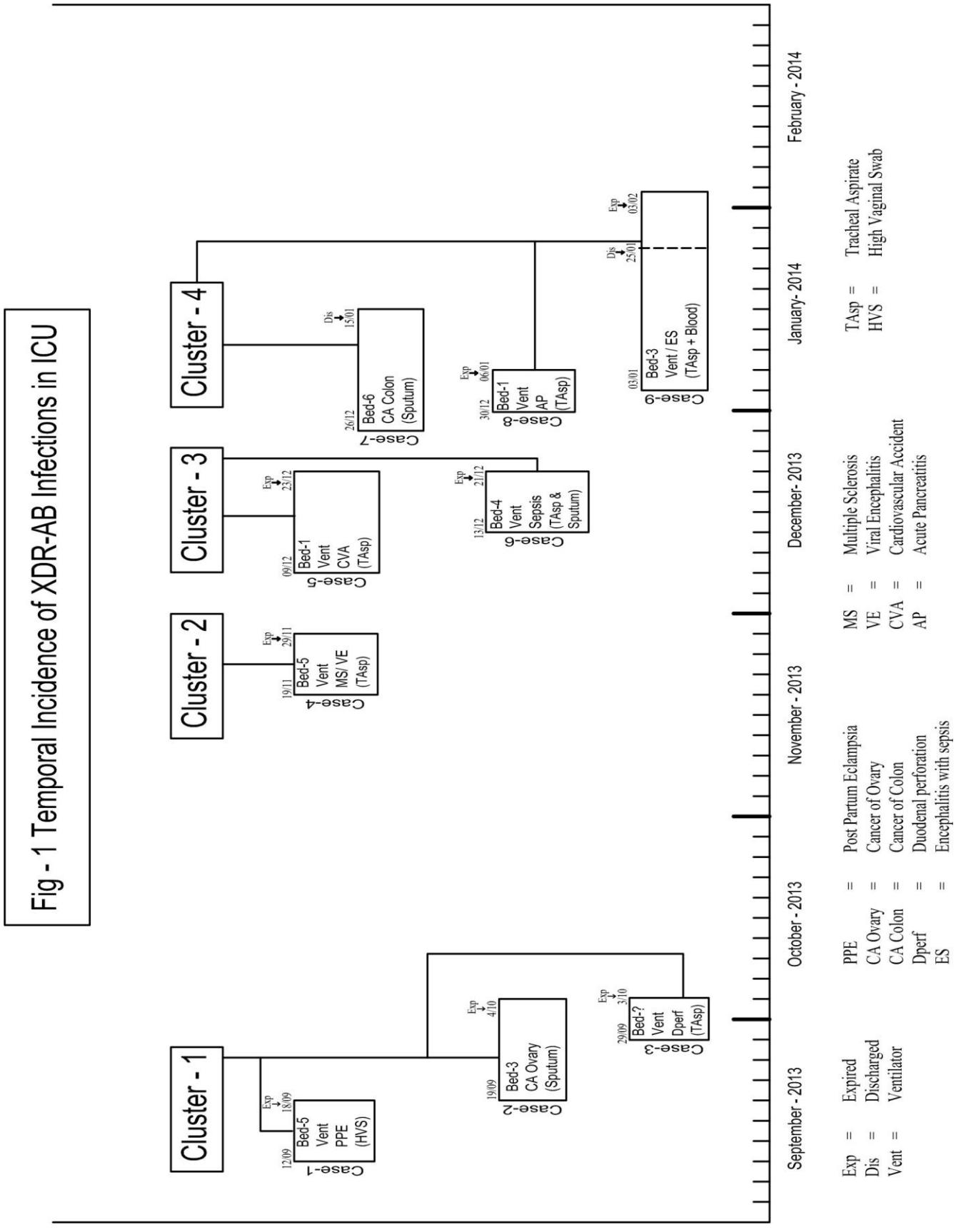
Fig - 1 Temporal Incidence of XDR-AB Infections in ICU
Cluster - 1
Case-1
12/09
Bed-5
Vent
PPE
(HVS)
Exp
18/09
Case-2
19/09
Bed-3
CA Ovary
(Sputum)
Exp
4/10
Case-3
29/09
Bed-?
Vent
Dperf
(TAsp)
Exp
3/10
Cluster - 2
Case-4
19/11
Bed-5
Vent
MS/ VE
(TAsp)
Exp
29/11
Cluster - 3
Case-5
09/12
Bed-1
Vent
CVA
(TAsp)
Exp
25/12
Case-6
13/12
Bed-4
Vent
Sepsis
(TAsp &
Sputum)
Exp
21/12
Cluster - 4
Case-7
26/12
Bed-6
CA Colon
(Sputum)
Dis
15/01
Case-8
30/12
Bed-1
Vent
AP
(TAsp)
Exp
06/01
Case-9
03/01
Bed-3
Vent / ES
(TAsp + Blood)
Dis
25/01
Exp
03/02
September - 2013
October - 2013
November - 2013
December- 2013
January- 2014
February - 2014
Exp = Expired
Dis = Discharged
Vent = Ventilator
PPE = Post Partum Eclampsia
CA Ovary = Cancer of Ovary
CA Colon = Cancer of Colon
Dperf = Duodenal perforation
ES = Encephalitis with sepsis
MS = Multiple Sclerosis
VE = Viral Encephalitis
CVA = Cardiovascular Accident
AP = Acute Pancreatitis
TAsp = Tracheal Aspirate
HVS = High Vaginal Swab

part of this exploratory study. There was no growth in all specimens except three (table 1). However, we did not grow XDR-AB in any of the samples.

Table 1: *Microbiological Screening of ICU Environment.*

Area / Source of Sample	*No. of Samples (n = 120)*	*Growth of Organism*
Isolation Room		
Floor	01	No Growth
Walls	01	No Growth
Bed Side Rails	03	Pseudomonas *aeruginosa* (in one rail)
Equipment Trolley	01	No Growth
Bed Areas		
Side Railing	08	No Growth
Side Table	08	Staphylococcus *aureus* (on one table)
Food Table	03	No Growth
Ventilators		
Expiratory Valve	05	No Growth
Inspiratory Valve	05	No Growth
Filters	05	No Growth
Other Equipment		
Equipment Trolley	05	No Growth
Monitors	08	No Growth
Suction Jars	08	Fungus (in one jar)
Suction Points	08	No Growth
Oxygen Points	08	Staphylococcus *epidermidis* (in one point)
I/V Stands	08	No Growth
Door Handles	05	No Growth
Air Conditioning Units		
A.C Filters	05	No Growth
Nursing Area		
Counter Desk	02	No Growth
PC / Keyboard	02	No Growth
Telephone Set	01	No Growth

DISCUSSION

*Acinetobacter baumannii*is considered to be a major nosocomial pathogen, associated with significant morbidity and mortality in hospitalized patients and once introduced into the hospital environment; it takes exhaustive infection control efforts to prevent continuing transmission.[12]

An outbreak of XDR – AB that consisted of four sequential clusters in the ICU of a tertiary care hospital is described. It seems plausible to suggest that the Index case introduced this pathogen into the ICU as no such cases were identified prior to September 2013. Four clusters were identified with similar antibiograms. However, the common source origin could not be verified as the isolates were not available for genotypic studies. Bahador et al, from Iran used amplified length polymorphism (AFLP) for genotype profiling of multi drug resistant isolates of *Acinetobacter baumannii* from ICUs in Tehran and they were able to report some novel variants on this basis.[13] It would be of interest to use molecular methods to type our strains in future, for comparison with other centers.

In the cases in our study, it was observed that the time between each cluster shortened considerably towards the later part of the outbreak (Fig. 1). There was a gap of six weeks between thepatients in first and second cluster, which reduced to two weeks between cluster 2 and 3 and barely 3 days between the last two clusters.

Acinetobacter baumannii has been known to become persistent in the hospital environment and, once introduced, is difficult to eradicate.[12] It is possible that after introduction into the unit, it finds a favorable niche to survive and then colonizes and / or infects critically ill or immunocompromized patients.

Ray et al, have reported that patients colonized or infected with XDR – AB contaminate the environment on first or subsequent admission. *Acinetobacter baumannii* was found in 8% of their environmental samples, including patient rooms and a wound care cart.[14] In our study, in spite of exhaustive efforts, we did not find any XDR – AB from more than one hundred environmental samples from within the ICU. However, we did grow Pseudomonas and Staphylococci from some areas. At the time when samples were taken, all the patients in the outbreak had critical illnesses and all were taking more than one class of antibiotics as part of therapy. Except two, all the cases were on Ventilator and had pneumonitis. As VAP is a serious nosocomial infection, exhau-

stive efforts were mounted to investigate the source of XDR – AB for outbreak investigation. We were unable to isolate XDR – AB from any samples obtained from outside surfaces or tubing components of the five Ventilators. The inaccessible parts of the Ventilators were not sampled in our study.

We found a mortality rate of 78% in our patients which is in agreement with other studies that have reported mortality rates between 30 – 75% who had nosocomial VAP caused by *Acinetobacter baumannii*.[15,16] In a recent study, Ozgur et al concluded that VAP caused by *Acinetobacter baumannii* was the cause of high mortality independent of its sensitivity / resistance profile.[16]

The presence of clustered cases has been reported by Tsiatsiou et al in a neonatal intensive care unit, as part of an outbreak that lasted for 2 months in the unit. They reported 8 neonates who developed infections due to Carbapenem resistant *Acinetobacter baumannii*; all isolates harbored blaOXA – 58 and intrinsic chromosomal blaOXA – 51 carbapenemase genes. Active surveillance and infection control efforts contained this outbreak.[17]

Another study has shown that inadequate concentration of sodium hypochlorite used for environmental cleaning resulted in an outbreak that lasted for 5 months in an ICU.[18] Use of infection control measures as described by CDC has also been associated with reduction in infection rates and interruption in transmission of XDR – AB.[19]

Many researchers have published internationally and from Pakistan, highlighting molecular aspects of *Acinetobacter baumannii* isolates from different clinical areas of the hospitals including intensive care units in prevalence studies.[13,17,20,21] However, an outbreak investigation to link the rise of cases in a unit to the admission of a particular case at a particular time has not been reported so far from Pakistan. We have shown in our study that the ICU of a hospital can become a niche for dissemination of XDR – AB to susceptible patients even after a gap of 45 days. In a recent study from Iran by Alfandri et al, who investigated an outbreak of carbapenem resistant *Acinetobacter baumannii* in an ICU, it was shown that although the Index patient was admitted in ICU under strict isolation precautions, it still led to an outbreak 2 months after the patient was discharged. This outbreak persisted despite isolation precautions, patient and staff cohorting, environmental decontamination, terminal disinfection and hydrogen peroxide treatment of the unit. The source of this outbreak was suspected to be the Velcro of blood pressure cuffs. The use of cuffs submersible in a disinfectant stopped this outbreak.[22]

The actions taken to reduce the burden of XDR – AB in our setup included closure of the ICU to new admissions over a weekend and high level disinfection based on published protocols of HICPAC with some customization to cater for local needs.[9-11] Infection Control Team and Outbreak Control Team were instituted under the Infection Control Committee, that took the responsibility of looking into different aspects of the outbreak so that such incidences could be prevented or minimized. Infection Control Nurse was made responsible for an on-going microbiological surveillance of all high risk areas of the hospital. These measures led to complete control of XDR – AB infections in the three months follow up period, highlighting the importance of concerted infection control efforts.

It is ***concluded*** that the presence of unusual number of XDR – AB in patients in ICU of a tertiary care hospital, over a four months period, was linked to the admission of a patient from a peripheral hospital. This outbreak was controlled by using high level disinfection and strict hand washing protocol. In the post-outbreak period, no XDR – AB was isolated from any patient highlighting the effectiveness of stringent infection control measures in outbreak situations. Regular microbiological surveillance of high risk areas in a busy hospital setting is the cornerstone of infection control and prevention thus reducing the morbidity and mortality in already seriously sick and immunocompromized patients.

ACKNOWLEDGEMENTS

We wish to thank members of SMDC Research and Grant Review Committee headed by Professor Abdul Wajid, Department of Orthopaedic surgery at Shalamar Teaching Hospital (STH) for prompt approval of the project. We would also to thank Mr. Waqas Saddique of Marketing Department for his contribution in preparation of Fig. 1 and Mr. Mudassar Ahmad for technical support in Microbiology Laboratory of STH.

Work Attribution

The work was carried out in the Intensive Care Unit of Shalamar Teaching Hospital and Infection Control Section of the Department of Pathology Shalamar Medical and Dental College Lahore.

Disclaimers: None.

Source(s) of Support: None.

REFERENCES

1. Gayness R., Edward J. R. National Nosocomial Infections Surveillance System. Overview of nosocomial infections caused by gram-negative bacilli. Clin. Infect. Dis., 2005; 41 (6): 848-54.
2. Villegas M. V., Hartstein A.I. Acinetobacter outbreaks, 1977 – 2000. Inf. Cont. Hosp. Epi. 2003; 24: 284-95.
3. Gales A.C., Jones R. N., Forward K. R., Liñares J., Sader H. S., Verhoef J. Emerging importance of multidrug-resistant *Acinetobacter* species and *Stenotrophomonas-maltophilia*as pathogens in seriously ill patients: geographic patterns, epidemiological features, and trends in

the SENTRY Antimicrobial Surveillance Program (1997-1999). Clin. Infect. Dis., 2001; 32 (Suppl. 2): S104–S113.
4. Allen D.M., Hartman B.J. Acinetobacter species chapter *In* Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases Seventh Edition. Churchill Livingston Elsevier Philadelphia PA 19103 USA; 2010.
5. Behnia M., Logan S. C., Fallen L. and Catalano P. Nosocomial and ventilator – associated pneumonia in a community hospital intensive care unit: a retrospective review and analysis. BMC Research Notes, 2014; 7: 232-240.
6. York M. K. Aerobic Bacteriology Section in Clinical Microbiology Procedure Handbook Vol. I, Second Edition. American Society for Microbiology Washington DC 20036 USA 2004.
7. Forbes B. A., Sahm D. F., Weissfeld A. S. (Eds). *In* Bailey and Scott's Diagnostic Microbiology Eleventh Edition. Mosby Inc, St Louis, MI 63146 USA 2002.
8. Clinical Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing M 100 – S 22. Clinical Laboratory Standards Institute, Wayne, PA 2012.
9. Rutala W. A., Weber D. J. Healthcare Infection Control Practices Advisory Committee (HICPAC) Guideline for Disinfection and Sterilization in Healthcare facilities. Centre for Disease Control and prevention (CDC) 2008.
10. Seigel J. D., Rhineheart E., Jackson M., Chaiarello L. Healthcare Infection Control Practices Advisory Committee (HICPAC) 2007 Guideline for Isolation Precautions: Preventing transmission of infectious agents in healthcare settings. Am J Infect Control, 2007; 35 (10) Suppl. 2: S65-164.
11. Brown-Hadjirul H. C. The Manual of Infection Control. Shalamar Institute of Health Sciences, Lahore, 2013.
12. Zavascki A. P., Carvalhaes C. G., Picão R. C., Gales A. C. Multidrug – resistant Pseudomonas aeruginosa and Acinetobacter baumannii: resistance mechanisms and implications for therapy. Expert Rev Anti Ther. 2010; 8 (1): 71-93.
13. Bahador A., Raoofian R., Taheri M., Pourakbari B., Hashemizadeh Z., Hashemi F. B. Multidrug resistance among Acinetobacter baumannii isolates from Iran: Changes in antimicrobial susceptibility patterns and genotypic profile. Microb Drug Resist, 2014; 20 (6): 632-40.
14. Ray A., Perez F., Beltramini A. M., Jakubowycz M., Dim ick P., Jacobs M. R., et al. Use of vaporized hydrogen peroxide decontamination during an outbreak of multidrug – resistant Acinetobacter baumannii infection at a long-term acute care hospital. Infect Control Hosp Epidemiol, 2010; 31 (12): 1236-41.
15. Sunenshine R. H., Wright M. O., Maragakis L. L., Harris A. D., Song X., Hebden J., et al. Multidrug-resistant Acinetobacter infection mortality rate and length of hospitalization. Emerg Infect Dis, 2007; 13 (1): 97-103.
16. Özgür E. S., Horasan E. S., Karaca K., Ersöz G., Naycı-Atış S., Kaya A. Ventilator – associated pneumonia due to extensive drug – resistant Acinetobacter baumannii: risk factors, clinical features, and outcomes. Am J Infect Co-ntrol, 2014; 42 (2): 206-8.
17. Tsiatsiou O., Iosifidis E., Katragkou A., Dimou V., Sarafidis K., Karampatakis T., et al. Successful management of an outbreak due to carbapenem – resistant Acinetobacter baumannii in a neonatal intensive care unit. Eur J Pediatr, 2015; 174 (1): 65-74.
18. Liu W.L., Liang H.W., Lee M.F., Lin H.L., Lin Y.H., Chen C.C., et al. The impact of inadequate terminal disinfection on an outbreak of imipenem resistant Acinetobacter baumannii in an intensive care unit. PLos One. 2014; 25 (9): 9.
19. Enfield K.B., Huq N.N., Gosseling M.F., Low D.J., Hazen K.C., Toney D.M., et al. Control of simultaneous outbreaks of carbapenemase – producing enterobacteriaceae and extensively drug resistant Acinetobacter baumannii in an intensive care unit using interventions promoted in the Center for Disease Control and Prevention 2012 carbapenemase resistant Enterobacteriaceae Toolkit. Infect Control Hosp Epidemiol. 2014; 35 (7): 810-7.
20. Begum S., Hasan F., Hussain S., Ali Shah A. Prevalence of multi drug resistant Acinetobacter baumannii in clinical samples from Tertiary care hospital in Islamabad, Pakistan. Pak J Med Sci. 2013; 29 (5): 1253-8.
21. Hasan B., Perveen K., Olsen B., Zahra R.J. Emergence of carbapenem – resistant Acinetobacter baumannii in hospitals in Pakistan. Med Microbiol. 2014 Jan; 63 (1): 50-5.
22. Alfandari S., Gois J., Delannoy P.Y., Georges H., Boussekey N., Chiche A.M., et al. Management and control of a carbapenem-resistant Acinetobacter baumannii outbreak in an intensive care unit. Med Mal Infect. 2014; 44 (5): 229-31.