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The Bacterial Etiology of Early-Onset Ventilator-Associated Pneumonia in Intensive Care Units at Benghazi Medical Center

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Ventilator associated Pneumonia (VAP) poses a significant challenge in Intensive Care Units (ICUs) of several hospitals, contributing to increased mortality rates, prolonged hospital stays and elevated healthcare cost.

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Aim: This study aimed to estimate the incidence rate of VAP in the surgical and medical Intensive Care Units at Benghazi Medical Center (BMC) and identify the causative organisms.
Methods: A retrospective matched cohort study was conducted across surgical and medical Intensive Care Units (ICUs) at Benghazi Medical Center (BMC), Libya. The study included 614 adult patients (≥18 years) admitted between July and December 2019.
Data were extracted from electronic and paper-based medical records, including:
- Demographics: Age, sex, admission date, ICU type.
- Clinical Parameters: Ventilation duration, onset of VAP (defined as radiographic infiltrates + clinical signs [fever, purulent secretions, leukocytosis] + positive respiratory cultures after 48 hours of intubation).
- Microbiological Analysis and Antimicrobial susceptibility testing were performed. Statistical Analysis:
Data were analyzed using SPSS v.22. Categorical variables (e.g., gender, bacterial species) were expressed as frequencies/percentages; continuous variables as mean ± SD or median (IQR). Chi-square/Fisher's exact tests compared proportions; $p<0.05$ was significant.
Results: All early-onset VAP cases were caused by gram- negative bacteria, the most common type is *klebsiella Pneumonia*, then *Acinetobacter Baumannii*, and followed by *Proteus*. The highest infection rates were reported in September and November. Also, high rate of VAP was observed among males and age group between 41-60 year.
Lastly, all isolated bacteria causing VAP infections were resistant to chloramphenicol, Septrin, Cefixime, Tetracycline Meropenem, Ceftriaxone, Ciprofloxacin and Azithromycin.
Conclusion: To reduce VAP incidence in ICUs, medical staff must follow the evidence-based prevention and control guidelines of VAP to protect the patients as well as to decrease the mortality rate and patients stay in hospital.

Keywords: Ventilator-associated pneumonia; mechanical ventilation; antibiotics; multiple-drug resistance; bacterial isolates; prevention; epidemiology; incidence rate.

1. INTRODUCTION

VAP stands for Ventilator -Associated Pneumonia, a type of pneumonia that occurs in patients receiving mechanical ventilation and it develops after 48 hours or more of endotracheal intubation, which ventilator is machine that use to help patient with acute respiratory syndrome by giving oxygen through tube placed in patients' month or nose (CDC, 2020; Gutiérrez et al., 2019). VAP is the second common nosocomial infection after blood stream in hospitals (Gutiérrez et al., 2019; Waters & Muscedere, 2015).

It has negative impacts on patients, elevating the mortality rate for patients with mechanical ventilation compared to patients without VAP (Waters & Muscedere, 2015). Also, it leads to increase the cost and length of stay in hospital (Kollef et al., 2012; Cocanour et al., 2005).

It is caused by several microorganisms, the most causative organisms are *Pseudomonas Aeruginosa, Klebsiella Pneumonia, Staphylococcus Aureus and Acinetobacter Baumannii* (Depuydt et al., 2008; Avery & Nicolau, 2018; Feng et al., 2019; Fathy et al., 2013). Furthermore, Other organism could be causative for VAP are *E. Coli, Candida, Proteus, Methicillin-Resistant Staph. Aureus (MRSA), Streptococci, Polymicrobial, Coagulase Neg. Staphylococci, Vancomycin-Resistant S. Aureus (VRSA), Oxacillin Sensitive Staph. Aureus (OSSA), Oxacillin Resistant S. Aureus (ORSA), Citrobacter, Methicillin Sensitive Staphylococcus Aureus (MSSA), Enterobacter Aeruginosa, Diphtheria* and *Enterococcus Faecalis* (Feng et al., 2019). Besides, Feng et al. suggested that the main causes of nosocomial Pneumonia is gram-negative bacteria. and the reason for that could be related to warmer climate environment (Feng et al., 2019). Also, the most common bacteria that found in early VAP were gram-positive pathogens, however, the gram-negative pathogens were isolated from the late VAP group (More Than 4 Days) (Arumugam et al., 2018).

VAP is transmitted from the workers to the medical equipment by their hands, which considered as essential rout of transmission. Moreover, it can be resulted from gastric and oropharyngeal colonization, and bacteria can enter to the lower respiratory tract through aerosols inhalation from nebulization equipment and also, through aspiration of bacteria that

presence on dental plaques, all of these routes were done through direct contact through the hands, and it cannot be considered as airborne infection (Kowalski, 2012).

Risk factors for VAP include Respiratory failure, coma, prolonged ICU stays and types of enteral feeding (Erbay et al., 2004), male gender, pulmonary disease, Acquired Immunity Deficiency Syndrome, trauma in the head, failure in multiple-organ in the body (Weinstein et al., 2004), bronchoscopy, tube thoracostomy, tracheostomy, Acute Physiology and Chronic Health Evaluation (Apostolopoulou et al., 2003).

Furthermore, the incidence rate of VAP has been estimated in several countries, the proportion of VAP cases increased from 14 to 60% (Walaszek et al., 2018). Besides, its incidence rate was estimated about 17.2 % among adult intubated trauma patients in the period from 2010 to 2013 (Arumugam et al., 2018). Moreover, Kollef et al. reported that 2,238 out of 88,689 admitted patients had VAP in united states hospitals, which the rate of incidence was 1.27 cases per 1,000 ventilator days, also, this rate was higher among older and male patients than other groups (Kollef et al., 2012).

1.1 Aim

The study aims to measure the incidence rate of the early-onset VAP and identify the bacterial etiology in surgical and medicine ICUs of BMC from July to December 2019.

2. MATERIALS AND METHODS

2.1 Study Design and Site

Retrospective cohort study was carried out in medicine and surgical Intensive Care Units at Benghazi Medical Center BMC in Benghazi, Libya.

2.2 Method of Data Collection

The data were collected from medical records of intubated patients who admitted to surgical and medicine ICU at BMC from July to December 2019.

2.3 Sample Size

Total patients who admitted into surgical and medicine ICUs were 624 patients over a period of time from July to December 2019, only 20 patients had developed early-onset VAP (after 2 days of ventilation), which the culture was taken after 48 hours of putting patients on ventilator.

2.4 Statistical Analysis

The data were analyzed by using SPSS version 22 software, the percentage, mean, and frequency were calculated.

2.5 Limitation

The authors face problem in obtaining the required samples from the patients directly, so they decided to get information from medical records in the infection control office as well as authors cannot collect data of the whole year (2019) and they just obtain on the data in this result.

3. RESULTS

Table 1 represents the incidence of early onset VAP among intubated patients in surgical and medicine ICUs from July to December 2019, it reported that incidence rate over this period was 3.25%, that means 20 intubated patients were infected with VAP out of 614 in this period of time. Furthermore, the highest incidence rate was reported in September and November, while there was no VAP infected was reported in August.

Table 1. The incidence rate of *VAP* in ICUs at BMC from July to December 2019

Months	Total intubated patients	Number of patients with early onset VAP	Incidence rate
July	86	3	3.48
August	91	0	0
September	92	6	6.52
October	89	2	2.24
November	92	6	6.52
December	90	3	3.33
Total	614	20	3.25

Table 2. Organisms isolated from ventilated patients with *VAP* after 48 hours of intubation

Gram negative bacteria	Gram positive bacteria
Klebsiella pneumonia	-
Acinetobacter baumannii	-
Proteus	-

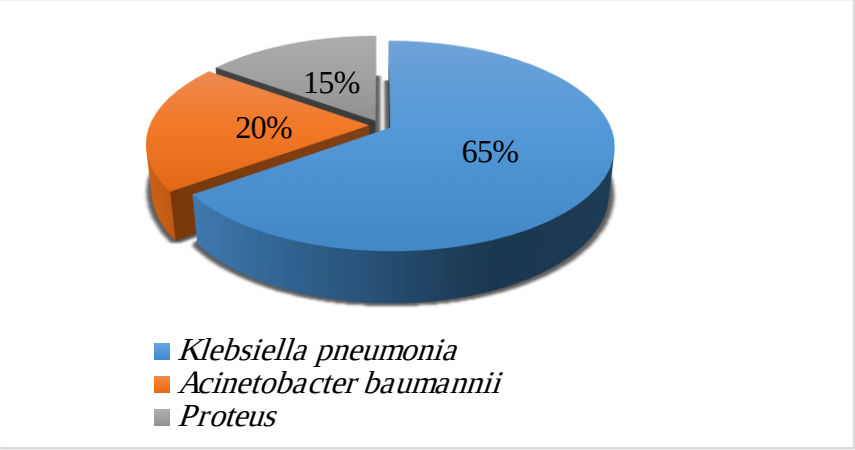

Fig. 1. Proportion of microorganisms detected in early onset *VAP* patients

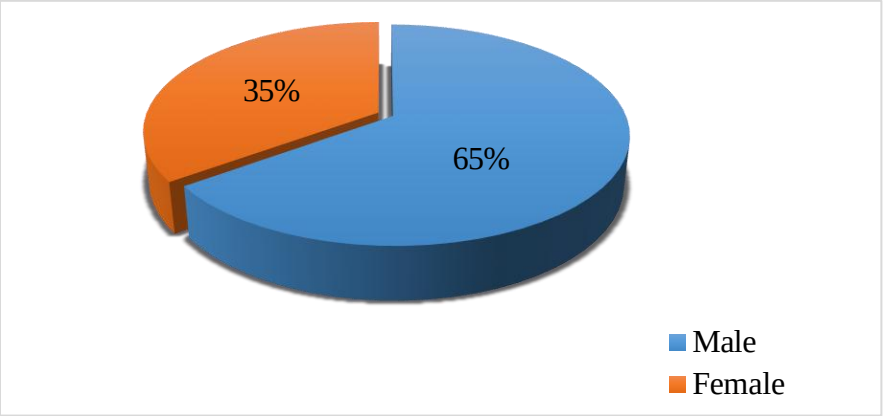

Fig. 2. Gender- distribution of patients who had early onset VAP in *ICU* of *BMC*

Besides, Table 2 shows the causative organisms for early onset VAP in BMC were three organisms; *Klebsiella pneumonia, Acinetobacter baumannii and proteus.*

In more detail, Fig. 1 shows all isolated bacteria are gram negative, and the highest percentage (65%) is *klebsiella pneumonia*, comes next *Acinetobacter baumannii*, while lowest percentage (15%) is *proteus*.

Furthermore, the following diagram (2) shows that the highest percentage of early onset VAP among intubated patients in *ICU* was observed among males with percentage 65%.

In more details, Table 3 shows that highest percentage of male who developed VAP was observed in December and November, while the highest percentage of female was observed in November and December.

Additionally, Table 4 shows the ages categories of infected patient with *VAP*, which the most infected group was in age category of 41 to 60 years old, and there were no cases less than 20 years.

Table 3. Gender- distribution of intubated patients who had developed early onset VAP in *ICUs* of BMC from July to December 2019 (according to gender in each month)

Month	Male	Female
July	2	1
August	0	0
September	5	1
October	1	1
November	4	2
December	1	2
Total	13	7

Table 4. Age distribution of intubated patients who had developed *VAP* in *ICU* of *BMC* from July to December 2019

Age Group	Less than 20	21-40	41-60	More than 60
No. (%)	0	3	11	6

Table 5. Antimicrobial susceptibility pattern of bacteria isolated from infected patients with *VAP* in surgical and medicine *ICUs*

Bacterial species	C	S	CFM	CFD	GN	TE	MEM	AK	CFX	IPM	CIP	AT	CT
Klebsiella pneumonia	R	R	R	R	R	R	R	S	R	R	R	R	S
Klebsiella pneumonia	R	R	R	R	R	R	R	R	R	R	R	R	S
Klebsiella pneumonia	R	R	R	S	R	R	R	R	R	R	R	R	S
Klebsiella pneumonia	R	R	R	S	R	R	R	R	R	R	R	R	S
Klebsiella pneumonia	R	R	R	R	R	R	R	R	R	R	R	R	S
Klebsiella pneumonia	R	R	R	R	R	R	R	S	R	R	R	R	S
Klebsiella pneumonia	R	R	R	R	R	R	R	R	R	R	R	R	S
Klebsiella pneumonia	R	R	R	R	S	R	R	S	R	S	R	R	S
Klebsiella pneumonia	R	R	R	R	S	R	R	S	R	R	R	R	S
Klebsiella pneumonia	R	R	R	R	S	R	R	R	R	R	R	R	S
Klebsiella pneumonia	R	R	R	R	S	R	R	S	R	R	R	R	S
Klebsiella pneumonia	R	R	R	R	R	R	R	R	R	R	R	R	R
Klebsiella pneumonia	R	R	R	R	R	R	R	R	R	R	R	R	R
Acinetobacter baumannii	R	R	R	R	R	R	R	R	R	R	R	R	R
Acinetobacter baumannii	R	R	R	R	R	R	R	R	R	R	R	R	S
Acinetobacter baumannii	R	R	R	R	R	R	R	R	R	R	R	R	S
Acinetobacter baumannii	R	R	R	R	R	R	R	R	R	R	R	R	S
Proteus	R	R	R	S	R	R	R	S	R	R	R	R	S
Proteus	R	R	R	S	R	R	R	S	R	R	R	R	S
Proteus	R	R	R	R	R	R	R	R	R	R	R	R	R

** chloramphenicol (C), Septrin (S), Cefixime (CFM), Ceftazidime (CFD), Gentamicine (GN), Tetracycline (TE) Meropenem (MEM), Amikacin (AK), Ceftriaxone (CFX). Imipenem (IPM), Ciprofloxacin (CIP), Azithromycin (AT), Colistine (CT)*

Regarding the resistance profile, VAP were the resistance 100% to chloramphenicol, Septrin, Cefixime, Ciprofloxacin and Azithromycin, and its resistance to Imipeneme was 95% and 80% for Ceftazidime and Gentamicin separately. Also, its resistance to Amikacin was 65%, on the other hand, its sensitivity was 80% to Colistin, 5% to Imipeneme, 35% for Amikacin, 20% for Gentamicin and ceftazidime separately (See Table 5).

4. DISCUSSION

4.1 VAP Incidence Rate among Admitted Patients in Surgical and Medicine ICUs at BMC

The present study found that 20 out of 614 had early onset VAP (incidence rate is 3.25%) in medicine and surgical care units at the Benghazi medical center (BMC) over six months from July to December in 2019, also, it reported that VAP incidence rate was higher in September and November, the reasons for low rate could be small sample size and short time of the study. Although the knowledge level of nurses in ICUs of BMC was poor, the incidence of early onset VAP is low (Gawili et al., 2023).

Moreover, the incidence rate was estimated in several hospitals around the world, and the incidence of this study is considered very low compared to Belay et al. and Elliott et al. studies, which Belay et al. observed that 87 out of 312 ventilated patients developed VAP ICU of in Bahir Dar Specialized Hospitals in 2021 (Belay et al., 2022), while Elliott et al. reports that 29 out of 169 patients had VAP in 10 intensive care units of public hospitals in Australia and New Zealand (Elliott et al., 2015). Alongside this, another study assessed the incidence rate of VAP in both medical and surgical ICUs in tertiary China hospital for 18 months, which it found that incidence rate of VAP was 26.85%. in period from April 2015 to March 2016 (Song et al., 2014). Furthermore, Resende et al. found incidence of VAP was 26.2% in admitted patients in ICU of a public hospital in Macapá, northern Brazil, and mortality rate among infected patients with VAP was 78.8% (Resende et al., 2013).

On the other hand, Rello et al. indicated that 842 (9.3%) out of 9,080 admitted patients to ICU in US had VAP, also, it found that its incidence was higher among patients with trauma admission, also, it was higher among male was higher than females and that comes in agreement with present study (Rello et al., 2002).

In addition, another study conducted in United State hospital in 2012, it found that incidence rate was 1.27 %, also, it found that rate was higher among older and Male patients than other groups (Kollef et al., 2012), while in other study conducted in seven ICUs in southern Poland from 2013 to 2015, it found that incidence rate was 8.0% (Walaszek et al., 2018).

The variations in the incidence rates among previous studies could result from differences in patient`s sociodemographic, sample size, location of healthcare facilities and criteria that used to diagnosis of VAP.

4.2 Causative Organisms Isolated from Ventilated Patients in Surgical and Medicine ICUs at BMC from July to December 2019

The present study reported that the VAP is caused by only gram-negative bacteria and the findings of the present study are consistent with the findings of studies reported by Feng et al. which reported the main causes of nosocomial Pneumonia is gram-negative bacteria. and they suggested the reason for is a warmer climate environment (Feng et al., 2019), along similar lines, the current study observed that VAP infection is caused by three types of organisms in medicine and surgical care units at Benghazi medical center, which are *klebsiella pneumonia, Acinetobacter Baumanii and Proteus,* and the most common type is klebsiella pneumonia, which caused 63% of infection, this comes in agreement to a previous study conducted at Trauma center of Hamad General Hospital, it found that the commonest identified microorganism is *klebsiella pneumoniae* (36.1%), then comes *Hemophilus influenza* (29.8%), followed by *Staphylococcus aureus* (28.1%), *Streptococcus pneumoniae* (15.8%), *Enterobacter cloacae* (12.3%) and *Pseudomonas aeruginosa* (12.3%) (Arumugam et al., 2018). In contrast, Another study was performed in ICUs of Tanta University Hospital in Egypt, it found that the most common causative microorganisms of VAP gram positive bacteria, which is *Pseudomonas Aeruginosa* (37.5%), then comes *Klebsiella Pneumonia* (25%) (Elkolaly et al., 2019). On the other hand, another study conducted in cardiac surgical intensive care unit at Escorts Heart Institute and Research Centre in New Delhi, India in2003, it found that most

common microorganisms cause VAP was *Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, Staphylococcus species and Acinetobacter* (Pawar et al., 2003).

Besides, *Pseudomonas Aeruginosa* (34.4%), *Acinetobacter spp*. (34.4%) and the *Enterobacteriaceae family (Klebsiella, Enterobacter, and E. coli* 25 %) is the most common organisms that causes VAP infection in an intensive care unit at general public hospital in northern Brazil in 2013 (Resende et al., 2013).

4.3 VAP Incidence Rate among Admitted Patients in Surgical and Medicine ICUs at BMC and Its Relation to Gender

The present study indicated that large proportion of infected patients with VAP were males in the ICUs of BMC, which are 13 males out of 20. This comes in agreement with study conducted in Egypt, it reported that 66.7% of infected patients were males in ICUs at Tanta University Hospitals from April 2015 to March 2016, while the incidence rate for females was 33.3% (Elkolaly et al., 2019). Besides, another study conducted by review board of the Health Sciences Center at the University of Tennessee, it found that VAP infection rate was higher in males (79%) than in females, which was 21% as well as the mortality rate among males was higher than females in ICU of Presley Regional in 2014 (Sharpe et al., 2014). Also, another study reported that 69.8% of male had VAP and 30.1% of female had VAP in Department of Microbiology and Medical Intensive Care Unit at a tertiary care hospital in 2010 (Goel et al., 2012). Additionally, the incidence rate of VAP was higher among males in multidisciplinary ICUs at Hamad General Hospital in Qatar between January 2010 and December 2012. However, the death rate was more common for cases female of the age group of 60 years than males (Ali et al., 2016).

4.4 VAP Incidence Rate among Admitted Patients in Surgical and Medicine ICUs at BMC and Its Relation to Age

This study found that the most patients who infected with VAP was at age groups between 41-60 years, while there were no cases of VAP recorded in age less than 20 years old in the ICUs of BMC. This comes in agreement with Kollef et al., they found that VAP rate was higher among patients who their ages between 45 to 64 years than other age groups (Kollef et al., 2012). In contrast, Ali et al. reported that the most intubated patients who infected with VAP were at age more than 60 years old in ICUs at Hamad General Hospital in Qatar between January 2010 and December 2012 (Ali et al., 2016). similarly, Elkolaly et al. reported that the most infected patients with VAP in the intensive care unit at Combined Military Hospital were at age group 61-90 years, which were 45% in period from March 2011 to April 2013 (Elkolaly et al., 2019). On the other hand, another study was conducted in ICUs at Tanta University Hospitals in Egypt over one-year from April 2015 to March 2016, it found that mean age of infected patients with VAP was 38.87 years (Ahmed et al., 2014).

4.5 Antimicrobial Susceptibility Pattern of Bacteria Isolated from Infected Patients with VAP

According to the antimicrobial susceptibility profile of bacteria isolated from patients in ICUs of BMC, this study reported that all isolated bacteria were resistance to chloramphenicol (C), Septrin (S), Cefixime (CFM), Tetracycline (TE) Meropenem (MEM), Ceftriaxone (CFX), Ciprofloxacin (CIP) and Azithromycin(AT).

On the other hand, the antimicrobial pattern of bacteria isolated from patients in ICU of a tertiary care hospital in India showed that the main pathogens was pseudomonas, it was more resistant to the antibiotics cefoperazone, piperacillin-tazobactip, amikemacin and Imipenem (Chaudhury et al., 2016). Also, another study conducted in central care of ICU in general public hospital in northern Brazil, it found that Gram-negative bacteria had antibiotic resistance between 50 to 80% to piperacillin, cefepime, aztreonam, ceftazidime and ciprofloxacin, while it was less resistant to amikacin, tobramycin, piperacillin / tazobactam as well as it concluded that *P. aeruginosa* and *acinetobacter* had a high level of resistance to carbapenems, cephalosporins, and fluoroquinolones. In addition, it indicated that *S. aureus* had resistance to penicillin, erythromycin, clindamycin, and tetracycline and it was sensitive to some antagonist's vancomycin, quinupristin / dalfopristin, and linezolid (Resende et al., 2013).

5. CONCLUSION

The incidence rate of early onset VAP in surgical and medicine ICU at BMC was low, which were and the majority early onset VAP cases was developed in September and November. Also, it

found that most infected patients were males and were at age category of 41- to 60-years old and there were no case less than 20 years. Additionally, the *Klebsiella Pneumonia* is the common causative organisms of early onset VAP in ICUs of BMC, next comes *Acinetobacter baumannii* and *Proteus*. Lastly, the isolated bacteria were resistant to antibiotics and that pose main issue in ICUs that need to an appropriate strategy and intervention to reduce VAP during the development of an infection. Additionally, nurses require training and supervision on control protocols and the correct use of antibiotics. Also, follow the evidence - based guidelines of VAP prevention and control such as Using closed endotracheal suction system, changing the ventilator circuit for every new patient, use Heat and Moisture Exchangers for patients without contraindications, and avoid using hot water circuits, Changing humidifier every week, Using Endotracheal tubes with extra lumen for drainage of subglottic secretions to decrease the risk for VAP, apply Semi-recumbent position for ventilated patients, and Using kinetic beds to improve the patient's condition in intensive care unit.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Approval has obtained from the manager of Benghazi Medical Centre to allowing enter ICUs and collect the required information.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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