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Prevalence of Ventilator-associated Pneumonia Cases in Intensive Care Units of Two Tertiary-care Hospitals, Mekkah, Saudi Arabia, November 2013 – January 2014

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ABSTRACT

Prevalence of Ventilator-associated Pneumonia Cases in Intensive Care Units of Two Tertiary-care Hospitals, Mekkah, Saudi Arabia, November 2013 – January 2014

By

Abdullah Zaid Alazeri

OBJECTIVE: The primary objective is to determine the prevalence of ventilator-associated pneumonia (VAP) in two tertiary care hospitals in Mekkah, Kingdom of Saudia Arabia (KSA), between November 2013 and January 2014. The secondary objective is to describe the frequency of microorganisms causing VAP in these hospitals.

METHODS: We used secondary data from the intensive-care units (ICUs) of two tertiary-care hospitals in Mekkah. Three months of summarized data were collected on the total number of patients placed on ventilator and the number of patients developing VAP from November 2013 to January 2014. Data were collected on the number of infections in each ward and by floor. Data on different pathogens from each ward in the two hospitals were also collected and analyzed. We calculated the VAP rate using the number of infections/number of device days times 1000. We also calculated the utilization ratio using the number of device days/number of patient days. We estimated the VAP rate and 95% confidence interval (CI) for each hospital in each ICU over the study period. Rates were compared using rate ratios and 95% CIs. Significance was determined at the 5% level using two-sided P-values.

RESULTS: The VAP rates in Herra hospital were 18.87% for November, 10.24% for December, and 24% for January (per 1000 patient days). The VAP rates in Alnoor hospital were 12.20% for November, 8.21% for December, and 17.11% for January (per 1000 patient days). In Herra Hospital's MSICU ward, *Acinetobacter* contributed 67% of all pathogens, and in the NICU, it contributed 76% of all pathogens. In Alnoor Hospital's MED ward, *Acinetobacter* contributed to about 33% of all pathogens, in the ICU to 64%, and in the BURN ward, 67% of all pathogens. Additionally, *Serritia* and *E. Coli* also contributed largely to VAP infections in the CCU ward at Alnoor Hospital.

CONCLUSION: The overall VAP rate for both hospitals during the study period was higher than the expected NHSN rate, and there was no statistically significant difference in VAP rates between hospitals.

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Chapter 1 - Background and Introduction

Ventilator-associated pneumonia (VAP) is an important issue among critically ill patients and patients receiving mechanical ventilation in the Kingdom of Saudi Arabia (KSA). The CDC defines VAP as pneumonia when patient is intubated and ventilated at the time of, or within 48 hours before the onset of the event. It is a lung infection that develops in a person who is placed on a ventilator, among admitted adult patients to intensive care units (ICUs). There is no minimum period of time that the ventilator must be in place for pneumonia to be considered ventilator-associated. VAP diagnosis has to be clinically supported by the evidence of a new fever and cough with purulent sputum, in combination with radiological evidence of a new or progressive pulmonary infiltrate, leukocytosis, a suggestive gram stain, and growth of bacteria in cultures of sputum, tracheal aspirate, pleural fluid, or blood.

VAP increases the in-hospital mortality rate of ventilated patients, which is 46% compared to 32% for ventilated patients who do not develop VAP (Singh, et al., 2010). Additionally, VAP prolongs time spent on the ventilator, length of intensive care unit (ICU) stay, and subsequent cost. In Herra hospital, Mekkah, the overall VAP incidence rate in 2010 was 1.98 per 1000 patients days (Bhuhari et al., 2012).

Subsequently, the Centers for Disease Control (CDC) have recommended the implementation of five simple interventions that can drastically reduce the morbidity and mortality associated with mechanical ventilation. These interventions, called the Bundle, have been implemented in KSA.

We followed up the findings of prior studies to evaluate the current VAP prevalence rates. The goal of any infection control program (ICP) is the prevention of infection as much as possible. It is impossible to have zero infections, but it is always possible to decrease the incidence of disease. In general, the findings of the study show that the rates are higher than the international rate (NHSN rate) which can be to some extent attributed to being coinciding or just after the pilgrimage to the Holly city of Mekkah in which more than 2 million person gather in the same place and the same time which increase the risk of infection that will lead to a high admission rate and a higher chance of acquiring a healthcare-associated infection (HAI). VAP is the most serious HAI, associated with longer stays, more medication, and increased staffing; the case mortality rate is 40 to 50%.

The U.S. CDC recognizes the importance of this infection and has released a specific set of recommendations to reduce the rate of VAP, known as the bundle. Research has shown the application of bundle to be successful in preventing VAP infections. The key components of the bundle are elevation of the head of the bed, daily "sedation vacations" and assessment of readiness to extubate, peptic ulcer disease prophylaxis, deep venous thrombosis prophylaxis, and daily oral care (Marra, 2009).

Objectives:

Define the prevalence of VAP in two tertiary care hospitals in Mekkah, Saudi Arabia, from November 2013 to January 2014

Describe the frequency of microorganisms causing VAP in different populations and identify the most predominant microorganisms causing VAP in both Herra and Alnoor Hospitals.

In the current study we wish to follow up on the findings of prior research and evaluate the current VAP prevalence rates in Mekkah. In addition, we wish to identify the microorganisms associated with VAP.

This study will suggest recommendations for antimicrobial prescription algorithms, helping prevent the development of drug resistance not only in KSA, but globally, as Mekkah is visited by millions of pilgrims throughout the year and drug resistance is a major global issue in combating infections.

Key Terms:

VAP: Ventilator Associated Pneumonia

PICU: Pediatric ICU

MSICU: Medical and Surgical Intensive Care Unit

NICU: Neonatal Intensive Care Unit.

CCU: Coronary Care Unit.

CPB: Cardiopulmonary bypass

TPN: Total Parenteral Nutrition

BURN : Burn unit

Chapter 2 - Literature Review

This literature review will include studies concerning the epidemiology of VAP. After that, we will focus on studies of the clinical characteristics of VAP in terms of rates specific to particular clinical populations and clinical settings.

Definition and Diagnosis

VAP is pneumonia that develops 48 hours or longer after mechanical ventilation is given by means of an endotracheal tube or tracheostomy. VAP results from the invasion of the lower respiratory tract and lung parenchyma by microorganisms. Intubation compromises the integrity of the oropharynx and trachea and allows oral and gastric secretions to enter the lower airways. A large proportion (of nosocomial pneumonias infections are associated with mechanical ventilation. VAP is a complication in as many as 28% of patients who receive mechanical ventilation and the incidence of VAP increases with the duration of mechanical ventilation..

VAP is usually suspected when the individual develops a new or progressive infiltrate on chest radiograph, leukocytosis, and purulent tracheobronchial secretions. Unfortunately, unlike for community-acquired pneumonia, accepted clinical criteria for pneumonia are of limited diagnostic value in definitively establishing the presence of VAP.

When purulent sputum, a positive sputum culture, fever, and leukocytosis are present without a new lung infiltrate, the diagnosis of nosocomial tracheobronchitis should be entertained. In mechanically ventilated patients, nosocomial tracheobronchitis has been associated with a longer ICU stay and time on the ventilator, without increased mortality (Koenig and Truwit, 2006).

In one randomized trial of intubated patients with community- acquired tracheobronchitis, antibiotic therapy resulted in a decreased incidence of subsequent pneumonia and mortality. However, prospective, randomized, controlled trials are required before antibiotic therapy can be recommended for the routine treatment of nosocomial tracheobronchitis. Furthermore, differentiation of tracheobronchitis from pneumonia is dependent upon the radiograph, which in the ICU is portable and often of poor quality. Hence, the clinician should utilize a clinical pulmonary infection score (CPIS) to direct therapy.

Antibiotic administration should be promptly initiated when VAP is suspected and quantitative cultures obtained and should be broad in coverage. Knowledge of local antibiograms should guide the choice of antibiotics, in addition to likelihood of organisms (early- or late-onset VAP). For patients already on antibiotics at the time of suspected VAP, the clinician should choose antibiotics from different classes, as it is likely that resistance to "in-use" antibiotics has developed (Koenig and Truwit, 2006).

Assessment of the likelihood of VAP by day 3 is needed to decide whether antibiotics should be continued. The assessment should include a repeat CPIS, as the change in CPIS can guide clinical decisions, even stoppage of antibiotics. Assessment of quantitative culture results and sensitivities at this juncture is prudent; as it may permit early antibiotic de-escalation by choosing a more narrowly focused agent(s). Monotherapy may be appropriate in many instances of VAP and should reduce the incidence of drug resistance. A change to monotherapy may be possible in a responding patient where organism sensitivity results permit. A short course (6 to 8 days) can be administered to patients with VAP but is

dependent on the patient physiologic response to treatment along with which organisms have been recovered.

Aelami et al. (2014) performed a Medline search for publications prior to 1 May 2014 looking at 3 different criteria in defining VAP cases. They looked at clinical, microbiological and radiological definitions of VAP.

Clinical criteria for healthcare-associated pneumonia include fever, leukocytosis or leucopoenia, purulent secretions, new or worsening cough, dyspnoea, tachypnoea, crackles or bronchial breath sounds, and worsening gas exchange. These criteria are nonspecific and their sensitivity and specificity relative to the underlying pathology is poor.

Clinical findings must be combined with radiologic and microbiologic findings. In a study of 70 children with VAP, the modified CPIS of 6 or higher had a sensitivity of 94%, a specificity of 50%, a positive predictive value of 64%, a negative predictive value of 90%, a positive ratio of 1.9, and a likelihood ratio of 0.1.

Radiologic criteria include the presence of new or progressive pulmonary infiltrates, adhesions or fluid in lobar fissures/pleura, cavitations, air bronchograms, or pneumatoceles on chest x-rays. The presence of air bronchograms has a higher sensitivity (58–83%) than "evolving infiltrates" (50–78%). Sequential chest x-rays (days -3, 0, 2, 7) help to confirm healthcare-associated pneumonia in complex cases, such as children with underlying cardiac or pulmonary disease. Onset and progression of pneumonia in imaging is fast, but improvement takes time, respiratory cultures are obtained by tracheal aspirates, bronchoalveolar lavage (BAL), non-bronchoscopic BAL, or protected brush specimens (PBS)

(Aelami *et* al., 2014).

Aelami *et* al. (2014) concluded that VAP is common in mechanically ventilated children with a wide variation of incidence density rates across geographical regions. Surveillance definitions are challenging in pediatric settings because the combination of clinical and radiologic signs leaves too much room for interpretation. This is particularly important in neonates, where CDC and INICC guidelines, and the German KISS program follows mainly the rationale of the definitions for older children.

Gram negative pathogens are the most common microorganisms, particularly *A. baumannii* and *P. aeruginosa* (Aelami *et* al., 2014). Gram-positive organisms are more frequently observed in high-income countries compared to low- and middle-income countries.

VAP Prevention

Similar to the evidence base of adult settings, a number of studies reported effective VAP prevention strategies. Successful programs combined multiple interventions, such as hand hygiene, glove and gown use for endotracheal tube manipulation, backrest elevation, oral care with chlorhexidine, stress ulcer prophylaxis, cuff pressure maintenance where appropriate, use of orogastric tubes, avoidance of gastric overdistension, and elimination of nonessential tracheal suction. When applied as a multimodal strategy by an interdisciplinary team, these interventions are most likely to be successful among neonates, infants, and children, and have proven effectiveness in high, as well as in low- and middle-income countries.

Koenig and Truwit (2006) concluded that simple and effective preventive measures could be instituted easily and at minimal costs. Such measures might include NIV, diligent respiratory care, hand hygiene, elevation of head, oral and not nasal cannulation, minimization of sedation, institution of weaning protocols, judicious use of antibiotics, de-escalation, and leveraging PK/PD characteristics for antibiotics administered. More costly interventions should be reserved for appropriate situations.

Utilizing the preventive, diagnostic, and treatment recommendations outlined in this paper should allow for improved outcomes for a common and serious medical complication seen in ICU mechanically ventilated patients.

The Bundle Approach

In December 2004, the Institute for Healthcare Improvement (IHI) challenged hospitals to save 100,000 lives by June 2006. One of the six evidence-based guidelines to be implemented was the prevention of VAP. The VAP bundle for adults was to (i) avoid/decrease endotracheal intubation and duration of mechanical ventilation whenever possible, (ii) use orotracheal and orogastric tubes to decrease the risk of hospital-acquired sinusitis, (iii) avoid heavy sedation and neuromuscular blockade with depression of cough reflexes, (iv) maintain endotracheal cuff pressures to greater than 20 cm water, (v) prevent condensate in tubing from entering the lower respiratory tract, (vi) maintain head-of-bed elevation at 30° to 45°, (vii) maintain oral care, and (viii) maintain hand hygiene. The CDC developed evidence-based guidelines for the prevention of VAP in North America.

VAP in Various Settings

Suk Lee *et* al*.* (2013) performed a prospective, multi-center, observational cohort study of all VAP cases among patients admitted to 31 community hospitals between July 1, 2007, and June 30, 2011. Trained infection perfectionists identified VAP cases using the National Healthcare Safety Network (NHSN) protocol Suk Lee et *al.* (2013). VAP incidence was reported as number of events per 1,000 ventilator-days Suk Lee et al. (2013). They categorized hospitals into small (<30,000 patient-days/year), medium (30,000–60,000 patient-days/year), and large (>60,000 patient-days/year) groups and compared VAP incidence by hospital size Suk Lee *et* al. (2013). They concluded that VAP incidence was inversely associated with size of hospital. VAP in community hospitals was frequently caused by MRSA and most importantly, predictors of VAP incidence in tertiary care hospitals such as Ventilator Utilization Ratio (VUR) may not be predictive in community hospitals with few ventilated patients Suk Lee *et* al. (2013).

Bonten *et* al.(2011) completed a study on preventing VAP. He concluded that 25 years of clinical trials on VAP prevention in ICUs yielded disappointingly few clear-cut answers. Zero tolerance to VAP is an attractive credo; however, because of the pathogenesis of the disease, it is extremely difficult to imagine that any intervention will completely prevent VAP. Bonten (2011) also concluded that because of the difficulties in reliably diagnosing VAP, we should be very reluctant to embrace measures that have been associated with VAP reductions in small-sized studies but with no benefits on patient outcome documented in sufficiently powered well designed trials. Benson (2011) looked at the prevention of VAP.

The key in the pathogenesis of VAP is colonization of the upper respiratory tract

(oropharynx and trachea) with potentially pathogenic microorganisms, such as Enterobatericeaea, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. Even more important than colonization (actually a condition *sine qua non*) is intubation. The widespread use of noninvasive ventilation in patients with chronic obstructive pulmonary disease and hypercapnia or with acute heart failure in the last decennium has prevented many episodes of intubation and, probably, many episodes of VAP. The same seems to account for strategies reducing the duration of intubation, such as daily interruption of sedation, weaning, or both. However, the efficacy of these measures in preventing VAP is unknown. Considering that the daily risk for developing VAP is not constant but peaks in the first week, reducing the exposure risk at the end of the intubation period may not greatly reduce the occurrence of VAP.

Bonten *et* al. (2011) also said if incubation cannot be avoided and will last for several days, the likelihood of colonization of the upper respiratory tract with potentially pathogenic microorganisms is high, as is the likelihood of aspiration of these pathogens into the lower respiratory tract, where they can cause pulmonary inflammation. In addition to reducing the time at risk, efforts to prevent VAP have been based on preventing aspiration of potentially pathogenic microorganisms and preventing colonization with potentially pathogenic microorganisms of the upper respiratory tract (Bonten *et* al., 2011). Until recently, both concepts seemed to be mutually exclusive; interventions either aimed to prevent aspiration, but accepted colonization with potentially pathogenic microorganisms, or aimed to modulate colonization, with no attempts to prevent aspiration (Bonten *et* al., 2011).

Walkey, Reardon, Sulis, Nace, Joyce-Brady (2009) performed a retrospective study of

prospectively identified cases of VAP to characterize the epidemiology and microbiology of VAP in a long-term acute care hospital (LTACH). They used data on the occurrence of VAP collected prospectively as part of routine infection surveillance at Radius Specialty Hospital. After March 2006, Radius Specialty Hospital implemented a bundle of interventions for the prevention of VAP (hereafter referred to as the VAP-bundle approach). They defined a case of VAP as a patient who required mechanical ventilation at Radius Specialty Hospital for at least 48 hours before any symptoms of pneumonia appeared and who met the CDC criteria for VAP.

Sputum samples were collected from a tracheal aspirate if there was clinical suspicion of VAP, and these samples were semi- quantitatively cultured (Walkey *et* al., 2009). They concluded that the VAP rate in the LTACH was lower than the VAP rate reported in acute care hospitals. Cases of VAP in the LTACH were frequently polymicrobial and were associated with multidrug resistant pathogens and increased length of stay. The guidelines from the CDC that are aimed at reducing cases of VAP are effective even in the LTACH setting (Walkey, Reardon, Sulis, Nace, Joyce-Brady, 2009).

Foglia, *et* al. (2007) studied the VAP in Neonatal and Pediatric Intensive Care Unit Patients. They found out that VAP is associated with increased morbidity in PICU patients, specifically, a longer duration of mechanical ventilation.

VAP Among Children

Fischer *et* al. (2000) performed a prospective cohort study to determine the delay of extubation attributable to VAP among neonates and children undergoing repair of congenital

heart disease in a tertiary care university hospital that serves Eastern and Southern Switzerland. Twenty-six of the 272 patients enrolled over a 22-month period-developed VAP (9.6%). VAP diagnosis was made when the following criteria were met: fever exceeding 38.5°C, tachypnea and/or otherwise unexplained increased oxygen requirement, elevated white blood cell count (>15 × 109 cells/liter), a cultured pathogen from tracheal aspirate together with a positive gram stain, and increased leukocyte contents, plus an infiltrate on chest radiographs persisting for 48hrs or more Fischer et al. (2000).

Using a Cox proportional hazards model to control for complexity of surgery, other respiratory complications, and secondary surgeries, those investigators found that the median delay of extubation attributable to VAP was 3.7 days (average of 5.2 versus 1.5 for patients with and without VAP, respectively). VAP rates increased dramatically for patients intubated for long periods of time Fischer et al. (2000). Among patients extubated within the first 3 days of surgery, only 4% developed VAP, compared to 40% of postoperative cardiothoracic surgery patients intubated longer than 30 days. Of the 26 VAP cases, 19 occurred within the first 3 to 6 days after surgery (Foglia, Meier, and Elward, 2007).

Foglia, Meier, and Elward (2007) found out that presumed VAP is also associated with additional resource utilization with respect to antibiotic administration. VAP is the most common reason for the initiation of empirical antibiotics among PICU patients. A prospective cohort study at an academic tertiary care center performed in a PICU (n = 456) found that over half (56.6%) of all patients (n = 258) received antibiotics Foglia, Meier, and Elward (2007). Treatment for suspected VAP comprised 616 of 1,303 (47%) of the antibiotic treatment days. Those authors reviewed medical records to determine whether patients had

evidence of an alternative explanation for the symptoms attributed to VAP, such as a viral infection. For 40% of the antibiotic days (552/1,303 treatment days), patients were classified as having no infection (i.e., did not meet clinical criteria as defined by the CDC) or as having a viral infection. Those authors concluded that an intervention targeted at decreasing antibiotic use for VAP would have the greatest impact on antibiotic use, Foglia, Meier, and Elward (2007).

Foglia, Meier, and Elward (2007) concluded that VAP is the second most common hospital-acquired infection among PICU patients. Empirical therapy for VAP accounts for approximately 50% of antibiotic use in PICUs. VAP is associated with an excess of 3 days of mechanical ventilation among pediatric cardiothoracic surgery patients. The attributable mortality and excess length of ICU stay of VAP have not been defined in matched case control studies. VAP is associated with an estimated $30,000 in attributable cost. Surveillance for VAP is complex and usually performed using clinical definitions established by the CDC. Invasive testing via BAL increases the sensitivity and specificity of the diagnosis, Foglia, Meier, and Elward (2007).

The pathogenesis is poorly understood in children, but several prospective cohort studies suggest that aspiration and immunodeficiency are risk factors. In children, educational interventions and efforts to improve adherence to hand hygiene have been associated with decreased VAP rates. More consistent and precise approaches to the diagnosis of pediatric VAP are needed to better define the attributable morbidity and mortality, pathophysiology, and appropriate interventions to prevent this disease, Foglia, Meier, and Elward (2007).

Shaath *et* al*.* (2004) performed a prospective surveillance study on children admitted to the PCICU for cardiac surgery from March 2010 until the end of September 2010 at King Abdulaziz Cardiac Center in King Abdulaziz Medical City, Riyadh, Saudi Arabia. The institution is a tertiary-care unit receiving patients with congenital heart disease (CHD) from the entire Arabian Gulf region. The PCICU has 9 beds dedicated for critical medical and surgical pediatric cardiac patients. During 2010, they admitted 462 patients, 346 of whom underwent cardiac surgery wherein 84 % of cases were subjected to CPB. The incidence of VAP in children after cardiac surgery and its impact on morbidity and mortality.

They divided into two groups: the VAP group and the non-VAP group, Demographic data and perioperative risk variables were collected for all patients. One hundred thirty-seven patients were recruited, 65 (48%) female and 72 (52%) male. VAP occurred in 9 patients (6.6%). Average body weights in the VAP and non-VAP groups were 5.9 ± 1.24 and 7.3 ± 0.52 kg, respectively. In our PCICU, the mechanical ventilation (MV) use ratio was 26% with a VAP-density rate of 29/1000 ventilator days. Univariate analyses showed that the risk variables to develop VAP are as follows: prolonged cardiopulmonary bypass (CPB) time, use of total parenteral nutrition (TPN), and prolonged ICU stay ($p < 0.002$ for all).

Thirty-three percent of VAP patients had Gram-negative bacilli (GNB). VAP Patients require more MV hours, longer stay, and more inhaled nitric oxide. Mortality in the VAP group was 11% and in the non-VAP group was 0.7 % ($p = 0.28$). VAP incidence is high in children after cardiac surgery mainly by GNB. VAP increases with longer CPB time, administration of TPN, and longer PCICU stay. VAP increases morbidity in postoperative cardiac patients Shaath *et* al. (2004).

Almuneef *et* al. (2004) performed a prospective surveillance study of VAP among all patients receiving mechanical ventilation for 48 hours or more admitted to a pediatric intensive care unit (PICU) in KSA from May 2000 to November 2002 used National Nosocomial Infections Surveillance (NNIS) System definitions. Their results showed three hundred sixty-one eligible patients were enrolled. Most were Saudi with a mean age of 28.6 months. Thirty-seven developed VAP. The mean VAP rate was 8.87 per 1,000 ventilation-days with a ventilation utilization rate of 47%. The mean duration of mechanical ventilation was 21 days for VAP patients and 10 days for non-VAP patients. The mean PICU stay was 34 days for VAP patients and 15 days for non-VAP patients. Among VAP patients,

Pseudomonas aeruginosa was the most common organism, followed by *Staphylococcus aureus*. Other gram-negative organisms were also encountered. On multiple logistic regression analysis, only prior antibiotic therapy, continuous enteral feeding, and bronchoscopy were independent predictors of VAP. They concluded that, the mean VAP rate in this hospital was higher than that reported by NNIS System surveillance of PICUs Almuneef *et* al.(2004)

Risk Factor Meta Analysis

Liu *et* al. (2013) conducted a meta-analysis with a systematic literature search of the Cochrane Library, PubMed [1966-2013], OVID [1993-2013] and Web of Science [1950-2013] to identify relevant articles using search terms that included risk factors AND (VAP OR ventilator associated pneumonia OR VAP) AND (PICU OR PICUs OR PICU OR intensive care unit for children OR intensive care unit for infant). Their results showed that out of the 205 initially retrieved articles, 9 articles remained in the meta-analysis while the remainder

were excluded for various reasons. All 4,564 patients were enrolled, including 213 patients with VAP and 4,351 patients without VAP. Among fourteen risk factors, six factors had statistical significances Liu *et* al. (2013). Risk factors of VAP and its value of OR were as follows: genetic syndrome (OR =2.04; 95% CI: 1.08-3.86), steroids (OR =1.87; 95% CI: 1.07-3.27), reintubation or self-extubation (OR =3.16; 95% CI: 2.10-4.74), bloodstream infection (OR =4.42; 95% CI: 2.12-9.22), prior antibiotic therapy (OR =2.89; 95% CI: 1.41-5.94), bronchoscopy (OR =4.48; 95% CI: 2.31-8.71) Liu *et* al. (2013). They concluded that special methods of prevention should be taken in the light of risk factors of VAP in PICU so as to decrease the rate.

Roeleveld *et* al. (2011) performed a retrospective cohort study in an academic tertiary care center to characterize VAP in pediatric patients after cardiac surgery in The Netherlands. They included all patients following cardiac surgery and mechanically ventilated for ≥24 h. The primary outcome was development of VAP while secondary outcomes included duration of mechanical ventilation and length of ICU stay. Their results show a total of 125 patients were enrolled. Their mean age was 16.5 months. The VAP rate was 17.1/1,000 mechanical ventilation days. Frequently found organisms were *Haemophilus influenzae, Moraxella catarrhalis, Staphylococcus aureus* and *Pseudomonas aeruginosa*. Patients with VAP had longer duration of ventilation and longer ICU stay Roeleveld *et* al. (2011). Risk factors associated with the development of VAP were a PRISM III score of ≥10 and transfusion of fresh frozen plasma. Roeleveld *et* al. (2011) concluded the mean VAP rate in this population is higher than that reported in general pediatric ICU populations. Children with VAP had a prolonged need for mechanical ventilation and a longer ICU stay.

Chapter 3 - Methods

Setting and Data Collection

We conducted a secondary analysis on data collected from the ICUs of the two tertiary care hospitals in Mekkah, KSA. Alnoor Specialist Hospital and Herra Hospital have been collecting data on ventilator usage since 2010. We used data from November 2013 to January 2014 obtained from the Ministry of Health (MoH) in KSA.

Alnoor Hospital, with 640 beds, and Herra Hospital, with 420 beds, are the two largest hospitals providing tertiary services in Mekkah. According to the MoH and personal email communication (Dr. Hala Roshidi on March 2, 2014) data from these hospitals are rigorously crosschecked and independently validated. These hospitals cater to the population living in Mekkah and pilgrims visiting Mekkah for the holy pilgrimage of Hajj.

Ethical Considerations

This analysis was conducted on secondary, de-identified data made available by the Saudi MoH; the data did not contain any PHI identifiers and was determined to be exempt from Emory IRB review.

Data Analyses

We collected 3 months of summarized data on the total number of people placed on the ventilator and the number of people who developed VAP from November 2013 to January 2014.

We calculated the VAP rate using the formula:

$$\frac{Number\ of\ infections}{Number\ of\ Device\ Days}\ x\ 1000$$

We calculated the utilization ratio using the formula:

$$\frac{Number\ of\ Device\ Days}{Number\ of\ Patient\ Days}$$

We estimated the VAP rate and 95% confidence interval for each hospital, in each ICU, per month over the 3-month time period. Significance was determined at the 5% level using two-sided P values. Rates were compared using rate ratios and 95% confidence intervals (CIs).

Data was collected on the number of infections in each department by floor. The departments analyzed were the MSICU, PICU and NICU for Herra Hospital, and the BURN, CCU, ICU and MED for Alnoor Hospital. Data on the different pathogens found in each department were also collected and analyzed. Tables were constructed showing the frequency of microorganisms detected in VAP patients over the study period.

Chapter 4 – Results

The overall VAP rate and utilization ratio were calculated for each hospital from November 2013 to January 2014 for Alnoor (Tables 1-3) and Herra Hospitals (Tables 4-6). The VAP rates for each ICU, by month, and overall ICU VAP rates were calculated by type of ICU plus the NHSN rate and utilization ratio.

In terms of VAP rate by month, in November Alnoor's ICU had a VAP rate of 11.4, which is high compared to the NHSN rate of 1.0. In December, the VAP rate was 6 in the ICU and 9 in the CCU. For the month of January, there were infections in the BURN, CCU and ICU units. The VAP rates were 6.9 in the BURN unit, 1.2 in the CCU, and 8.5 in the ICU. The VAP rates were all higher than the NHSN rates over the study period. The overall VAP rate demonstrated minor fluctuations (Table 7).

In Herra, VAP rates were determined for three different ICUs: the MSICU, PICU and NICU. The VAP rate for all ICUs fluctuated over the study period: the rate was 56 in November, 10 in December, and 12 in January.

We compared the rate ratios each month between hospitals and found no statistically significant difference in VAP rates between them. Chi-Square test for proportions indicated no significant differences between the ICUs in the two hospitals in a particular month. P-Values showed no differences between the two hospitals.

Table 8 shows the percentages of the contribution of each pathogen to the infection of VAP in Herra Hospital. The most common VAP-causing organism was the *Acinetobacter* pathogen. In Herra's MSICU ward, *Acinetobacter* contributed to 67% of cases and in the NICU

it contributed to 76% of cases.

Table 9 shows that *Acinetobacter* caused the highest number of VAP infections in Alnoor hospital as well. It also shows the percentages of the contribution of each pathogen to VAP infections in Alnoor Hospital. In the MED ward, *Acinetobacter* accounted for 33% of VAP cases, in ICU it accounted for 64% of cases, and in the BURNS ward, it accounted for 67% of VAP cases. *Serratia* and *E. coli* were also major contributors to VAP infections in the CCU.

Table 1. VAP Rate and Utilization Ratio in Alnoor Hospital, Mekkah, Kingdom of Saudi Arabia, November 2013 (Moharrm 2013).

Type of ICU	# of VAP	Device Days	Patient Days	VAP Rate	NHSN Rate	Utilization Ratio
MED	1	-	1568	-	.5	-
BURN	0	7	196	-	.27	.04
CCU	0	33	697	-	1	.05
ICU	6	534	713	11.24	1	.75
Total	**7**	**574**	**3174**	**12.6**		**.18**

- VAP Rate could not be calculated.

Table 2. VAP Rate and Utilization Ratio in Alnoor Hospital , Mekkah, Kingdom of Saudi Arabia, December 2013 (Safar 2013).

Type of ICU	# of VAP	Device Days	Patient Days	VAP Rate	NHSN Rate	Utilization Ratio
MED	1		1849	-	.5	-
BURN	0	5	241	-	.27	.02
CCU	1	110	712	9.1	1	.15
ICU	3	494	673	6.07	1	.73
Total	**5**	**609**	**3475**	**8.21**		**.18**

Table 3. VAP Rate and Utilization Ratio in Alnoor Hospital , Mekkah, Kingdom of Saudi Arabia, January 2014 (Rabi Awal 2014).

Type of ICU	# of VAP	Device Days	Patient Days	VAP Rate	NHSN Rate	Utilization Ratio
MED	3		1542	1.95	.5	-
BURN	2	15	288	6.94	.27	.05
CCU	1	129	772	1.3	1	.16
ICU	6	557	698	8.6	1	.80
Total	**12**	**701**	**3300**	**17.11**		**.21**

Table 4. VAP Rate and Utilization Ratio in Herra Hospital , Mekkah, Kingdom of Saudi Arabia, November 2013 (Moharrm 2013).

Type of ICU	# of VAP	Device Days	Patient Days	VAP Rate	NHSN Rate	Utilization Ratio
MSICU	6	357	535	16.81	.9	.67
PICU	0	129	178	-	.8	.72
NICU	6	150	1202	40	.2	.12
Total	**12**	**636**	**1915**	**18.87**		**.33**

Table 5. VAP Rate and Utilization Ratio in Herra Hospital , Mekkah, Kingdom of Saudi Arabia, December 2013 (Safar 2013).

Type of ICU	# of VAP	Device Days	Patient Days	VAP Rate	NHSN Rate	Utilization Ratio
MSICU	3	299	543	5.52	.9	.55
PICU	0	83	170	-	.8	.48
NICU	6	225	1273	4.71	.2	.18
Total	**9**	**607**	**1986**	**10.24**		**0.31**

Table 6. VAP Rate and Utilization Ratio in Herra Hospital , Mekkah, Kingdom of Saudi Arabia, January 2014 (Rabi Awal 2014).

Type of ICU	# of VAP	Device Days	Patient Days	VAP Rate	NHSN Rate	Utilization Ratio
MSICU	3	285	505	5.94	.9	.56
PICU	0	47	146	-	.8	.32
NICU	9	168	1375	6.55	.2	.12
Total	**12**	**500**	**2026**	**24**		**.25**

Table 7. VAP Rates in Alnoor and Herra Hospitals, Mekkah, Kingdom of Saudi Arabia, November 2013 to January 2014 (Maharrm 2013-Rab Awal 2014).

Month	Hospital	VAP Rate	p-value
November	Alnoor	12.20	.29
	Herra	18.87	
December	Alnoor	8.21	.16
	Herra	10.24	
January	Alnoor	17.11	.15
	Herra	24	

Table 8. VAP Infection by Pathogen and Ward, Herra Hospital, Mekkah, Saudi Arabia, November 2013 – January 2014 (Maharrm 2013-Rabi Awal 2014).

Pathogen	MSICU		NICU		PICU	Total
Acinetobacter spp	8	67%	16	76.19%	0	24
Klebsiella Pneumonia	1	8%	1	4.76%	0	2
MRSA	1	8%	0	0.00%	0	1
Enterococcus spp	1	8%	0	0.00%	0	1
E. Coli	1	8%	1	4.76%	0	2
Citrobacterspp	0	0%	1	4.76%	0	1
S. Aureus	0	0%	1	4.76%	0	1
Pseudomonas aeruginosa	0	0%	1	4.76%	0	1
Total	**12**	**100%**	**21**	**100%**	**0**	**33**

Table 9. VAP Infection by Pathogen and Ward, Alnoor Hospital, Mekkah, Saudi Arabia, November 2013 – January 2014 (Maharrm 2013-Rabi Awal 2014).

Pathogen	MED		ICU		BURN		CCU		Total
Klebsiella Pneumonia	1	17%	1	7%	0	0%	0	0%	2
Serrita	1	17%	0	0%	0	0%	1	50%	2
Acinetobacter spp	2	33%	9	64%	2	67%	0	0%	13
Candida	1	17%	2	14%	0	0%	0	0%	3
VRE	1	17%	0	0%	0	0%	0	0%	1
MRSA	0	0%	1	7%	1	33%	0	0%	2
E. Coli	0	0%	1	7%	0	0%	1	50%	2
Total	**6**	**100%**	**14**	**100%**	**3**	**100%**	**2**	**100%**	**25**

Chapter 5 - Discussion

The VAP rate by month at each hospital was analyzed. In November, Alnoor's ICU had a high VAP rate of 11.2 compared to the NHSN rate of 1.0. In December, the VAP rate was 6 in the ICU and 9 in the CCU. In January, there were infections in the BURN, CCU and ICU units. The VAP rate was 6.9 in the BURN, 1.2 in the CCU, and 8.5 in the ICU.

The VAP rates over the study period were all higher than the NHSN rates. The overall VAP rates at Alnoor were 11.2 in November, 15.1 in December, and 18.7 in January. The VAP rate was especially high in January because that is when many make pilgrimage to Mekkah. These results are consistent with those of Almuneef, *et* al., who examined the VAP rates in the PICU and showed that the mean VAP rate was higher than the NHSN rate. Their results are also consistent with others in the scientific literature.

The results were not much different at Herra Hospital, where data was analyzed from three different ICUs. We looked at the MSICU, the PICU, and the NICU. The VAP rate for all three ICUs was 56.0 in November 10 in December, and 12 in January.

To see how the hospitals compared, the number of cases in each hospital and the numbers of device days for each month was used to calculate the p-value, using the Epi Info program. There was no statistical significant different evidence between these hospitals in terms of VAP rates compared to the National Health Care Safety Network (NHSN) rates over the 3-month study period at 5% significance level. The NHSN is the most widely used healthcare associated infection tracking system nationwide.

This study also looked at the contribution of pathogens as sources of VAP infections.

The results were consistent with other studies, showing that *Acinetobacter* is the most common pathogen causing VAP in both hospitals (Almuneef, 2004). *Acinetobacter* accounts for 65% of all pathogens in the two hospitals. The p-values show no statistical difference between the VAP rates of the two hospitals. This could be attributed to the fact that they are both tertiary hospitals serving serve almost the same population.

These results are significant because most studies of pathogens in ICUs have found *Acinetobactor* to be the most resistant VAP-causing pathogen. These results are consistent with past research by Aelami, *et* al. and Almuneef, *et* al., who both looked at microorganisms causing VAP. In their studies, *Acinetobactor* was the most common pathogen. We found that *Pseudomonas aeruginosa* also contributed to many VAP infections in the NICU, which is consistent with the findings of Aelami, *et* al. and Vardakas, *et* al. These researchers concluded that *Acinetobactor* is the most studied bacteria due to its high frequency as the source of patient infections. At Alnoor Hospital, *E. coli* and *Serratia* each accounted for about 50% of the infections in the CCU.

There were a few limitations to the study. First, individual level data was not available for analysis, and therefore more specific analyses were not possible. Secondly, since we used summarized data, there were inexplicable discrepancies within the data reporting and summation.

Successfully treating these infections is critical due the fact that the mortality rate is 50% among those infected with VAP. Our results reiterate those of previous studies and remind us that eliminating VAP is extremely difficult.

Chapter 6 - Conclusion and Recommendations

VAP continues to be a serious infection in ICUs around the world. It increases respiratory morbidity and overall mortality, prolongs hospital stays and increase medical costs. As a general rule, patients should be extubated as soon as possible, which is the main strategy for preventing VAP.

We found that the overall VAP rates for the two tertiary hospitals were higher than the NHSN rates. A previous study showed the VAP rate to be very high in acute care hospitals. Our p-values showed no significant difference between the VAP rates at Alnoor and Herra hospitals and may indicate similar care practices that contribute to high VAP rates. This finding is important, as no previous study has compared VAP rates between hospitals in the same geographic location.

Once an increase in the VAP rate has been identified, an infection control team should pay vigilant attention to the monthly surveillance data. A multi-disciplinary team consisting of infection control committee members and ICU healthcare workers should initiate an investigation by looking into the possible causes for the high rate and the possibility of an outbreak.

We recommend the use of a closed suction system in the ICU environment and the monitoring of the sterilization or disinfection of ventilators. Hand hygiene should be made a priority.

Monthly surveillance data should be tracked to see if there is a reduction in the VAP rate as recommendations are implemented. With regard to microorganism infection, an

antibiotic policy should be developed and implemented. This will lead to a reduction in the overuse of antibiotics and an eventual reduction of the VAP rate, some of which is attributable to multi-drug resistant organisms. Other evidence-based preventive measures include avoiding intubation and early extubation when possible.

One of the protocols that have been used to help reduce the rate of VAP is education and training of healthcare workers who fail to implement the bundle approach. These healthcare workers should be required to pass a training program in VAP prevention, and the infection control team should follow up with this staff to ensure compliance. If improvements in critical care do not occur, hospital authorities should get involved, and the healthcare worker should be written up if he or she fails multiple times. By the same token, people who are compliant with the bundle approach should be rewarded with a bonus or time off as an incentive.

Future research should focus on more hospitals in the Mekkah area. In addition, more individual data should be collected, with an eye to its accuracy, and stored for easy access for more rigorous research. As Bonten (2011) suggests, we should not focus on small-sized studies, which do not benefit the patient in the end.

In terms of policy, more resources should be put towards training hospital staff on how to maintain cleanliness and hygiene in the ICUs. Additional resources should also be provided for hospitals to collect more detailed data, which can be used to determine the types of patients admitted to these hospitals and placed on the ventilator, as this will inform the care of these patients before they are put on a ventilator.

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