Asian Journal of Pharmaceutical and Health Sciences
www.ajphs.com

Hospital acquired pneumonia: A multivariate analysis of risk and outcome

Vijayanarayana K[1]*, Rau NR[2], Anantha Naik N[3], Bini John P[1], Rajesh V[1], Sreedharan[1], Thiyagu R[4]

1 Department of Pharmacy Practice, Manipal College of Pharmaceutical Sciences, Manipal University, Manipal, India.
2 Department of Medicine, Kasturba Medical College, Manipal University, Manipal, India.
3 Department of Pharmacy Management, Manipal College of Pharmaceutical Sciences, Manipal University, Manipal, India.
4 Department of Pharmaceutical Health Service Research, School of Pharmacy, University of Maryland, Baltimore, USA.

ARTICLE HISTORY

Received: 10.08.2013

Accepted: 19.09.2013

Available online: 10.11.2013

Keywords:

Hospital acquired pneumonia, Risk factors, mechanical ventilation

***Corresponding author:**

Email : vinpharmacol@hotmail.com

ABSTRACT

Hospital acquired pneumonia (HAP) is one of the most leading hospital-acquired infections with substantial morbidity and mortality. Analysis of the association between different risk factors and outcome in 'HAP' patients will help in understanding the different levels of risks and permit a more rational and effective method of treatment. A prospective observational study, carried out in a tertiary care teaching hospital. HAP patients were identified during daily visits to the emergency wards and were followed from the day of diagnosis to till the day of discharge/death. Patient data like demography, medical history, medication history, co-morbid disease, etiological factors and clinical outcome were recorded in patient case record form. Risk factors were analyzed for their association with outcome by multiple logistic regression. 318 patients were enrolled in the study and among those 277 patients improved and discharged; remaining 41 expired. Patients who were ventilated during their stay in the hospital were 27.6% and those non-ventilated were 72.4%. In the multivariate analysis, the strongest association with mortality was found for ventilation (Odds Ratio: 6.4; 95% Confidence Interval: 2.7-15.2; $p<0.001$), immunosuppression (OR: 3.4; 95% CI: 1.0-11.2; $p<0.05$) and male sex (OR: 2.9; 95% CI: 0.9-8.8; $p<0.05$). Study suggests that mechanical ventilation, immunosuppression and male sex are the independent risk factors with significant effect on mortality.

INTRODUCTION

Pneumonia is an infection of the alveoli, distal airways, and interstitium of the lung which is manifested by increased weight of the lungs, replacement of the normal lung's sponginess by consolidation, and alveoli filled with white blood cells, red blood cells, and fibrin [1]. Pneumonia can result from a variety of causes, including infection with bacteria, viruses, fungi, and chemical or physical injury to the lungs. Pneumonia can be broadly categorized as community acquired or hospital acquired. Hospital acquired pneumonia (HAP) is also called nosocomial pneumonia which occurs during or after hospitalization for another illness or procedure with onset at least 72 hours after admission. Pneumonia is the most common infectious disease in United States with highest mortality, where annual incidence of disease is approximately 4 million cases, a cost of $23 billion burden to the health care system [2]. In India, pneumonia is the fifth leading cause of death and mortality rate is between 10-20% [3].Hospital acquired pneumonia (HAP) remains an important cause of morbidity and mortality, especially in older adults and patients at-risk. In developed countries, almost one half of the total hospitalizations for pneumonia occur in patients over 65 years and pneumonia is a leading cause of death among this age group [4]. So it is important to define relationship between intensive care unit (ICU) acquired infection and outcome from critical illness [5].Epidemiological studies are required to study the incidences of pneumonia caused in patients in the community and hospital settings. The risk factors which are responsible for the outcome of HAP need to be analyzed in each hospital settings for implementation of preventive strategies to reduce patient morbidity, mortality, and hospital costs [6].

The primary objective of this study was to determine the cumulative incidence and the risk factors responsible for the mortality in the patients who are admitted to ICU for more than 72

hours.

METHODOLOGY

A prospective observational study, carried out in a tertiary care teaching hospital. The institutional ethics committee's approval was obtained prior to the study (No.UEC/42/2010). Patients were identified during daily visits to the emergency wards. HAP patients who fulfill the inclusion criteria (e.g., patients admitted to hospital/ICU for more than 72 hours, patients whose diagnosis was confirmed by chest X-ray or by culture as pneumonia and aged above 18 years) were identified during daily visits to the emergency wards & enrolled into the study after taking informed consent. Patients were followed from the day of diagnosis to till the day of discharge/death (clinical outcome). The patient data like demography, social habits, co-morbid disease, interventions (mechanical ventilation), severity assessment and clinical outcome were recorded in the case record forms (CRF). The severity of pneumonia patients was assessed within 24 hours on the day of diagnosis by using APACHE II (Acute Physiological and Chronic Health Evaluation II) score.

Data Analysis: Nominal data were described and expressed in percentage. Parametric data were expressed as mean±SD. Univariate analysis (Chi square test) was used to compare the variables affecting the outcome of HAP and calculation of odds ratio (OR). Multivariate analysis (Multiple logistic regression) was used to determine the association of the studied risk factors with clinical outcome. Odds ratios were calculated for the risk factors and variables having statistical significance were entered into the multivariate analysis to develop the prediction model. Statistical analysis was done using SPSS 20.

RESULTS

318 patients were enrolled in the study. Incidence of HAP among ICU patients during the study period was found to be 28.8%. Among 318 HAP patients, 277 were improved and discharged; remaining 41 patients were expired. Demographic characteristics and outcome of 318 HAP patients are summarised in Table 1 and Table 2. The mean age of study patient population was 54.7±16.5 years and 41.8% patients were more than 60 years of age. The majority of patients were males n=229 (65.7%). 96 (27.6%) patients were ventilated during their stay in the hospital. In Univariate analysis twelve variables (age>60 years, sex, mechanical ventilation, APACHE-II score>20, cardiac, pulmonary, renal, immunosuppression, endocrine/metabolic, liver insufficiency, smoking and alcohol intake) were analyzed for possible association with mortality in HAP patients. The results of the Univariate analysis of variables (risk factors) and mortality in HAP are given in Table 3. Variables with statistical significance ($p<0.05$) in Univariate analysis were entered into the multivariate analysis.

The following variables were found to be statistically significant ($p<0.05$), independent predictors of mortality HAP in these patient population: mechanical ventilation (OR: 6.4; CI: 2.7-15.2; $p<0.001$), immunosuppression (OR: 3.4; CI: 1.0-11.2; $p<0.05$) and male sex (OR: 2.9; CI: 0.9-8.8; $p<0.05$). Renal insufficiency, smoking and alcohol intake were showing statistically significant association with mortality in Univariate analysis but did not show statistical significance in multivariate analysis. Results of multiple logistic regression are given in Table 4.

The developed multiple logistic regression prediction model would be-

$$p(\text{mortality}) = \frac{e^{-5.77+1.18\times\text{Male sex}+3.14\times\text{MV}+2.63\times\text{IS}}}{1+e^{-5.77+1.18\times\text{Male sex}+3.14\times\text{MV}+2.63\times\text{IS}}}$$

DISCUSSION

This study was conducted to find out the cumulative incidence of HAP in ICU patients and risk factors associated with mortality in HAP patients. During the study period the cumulative

Table 1: Demographic characteristics of HAP patients

Characteristics	Total number of HAP Patients (n=318)
Patient related Characteristics	
Mean age±SD, years	54.7±16.5
Age> 60 years, n (%)	133 (41.8%)
Male sex, n (%)	229 (72.01%)
Smoking, n (%)	94 (29.6%)
Alcohol, n (%)	68 (21.4%)
Severity assessment	
Mean APACHE Score±SD	146 (42)
APACHE Score >20, n (%)	146 (45.9%)
On mechanical ventilation, n (%)	96 (27.6)

Table 2: Demographic characteristics and outcome of HAP patients

Characteristics	Total number of HAP Patients (n=318)
Co-morbid illness	
Endocrine/Metabolic, n (%)	107 (33.6%)
Cardiac, n (%)	68 (21.4%)
Pulmonary, n (%)	167 (52.5%)
Liver, n (%)	30 (9.4%)
Renal, n (%)	54 (16.9%)
Immunosuppression, n (%)	27 (8.5%)
Duration of hospital stay, days	
Mean±SD	15.1±9.3
Median (IQR)	13 (11)
Out come	
Mortality, n (%)	41 (12.9%)
Recovered, n (%)	277 (87.1%)

Table 3: Results of Univariate analysis of risk factors and outcome (mortality) in HAP patients

Risk Factor	Odds Ratio (OR)	95% Confidence interval (CI)	p value
Age>60 years	2.63	0.97-7.10	0.05
Male sex	3.67	1.16-11.64	0.027
Mechanical ventilation	7.69	3.11-19.02	0.001
APACHE II score>20	12.00	3.69-38.98	0.001
Co-morbid conditions			
Cardiac	1.41	0.49-4.01	0.520
Pulmonary	2.27	0.79-6.46	0.124
Renal	2.53	0.87-7.29	0.086
Immunosuppression	6.30	1.57-25.27	0.009
Endocrine/Metabolic	2.03	0.83-4.99	0.123
Liver insufficiency	5.07	1.33-19.26	0.017
Smoking	1.15	0.39-3.33	0.79
Alcohol intake	1.03	0.34-3.11	0.96

Table 4: Results of multivariate analysis of risk factors and outcome (mortality) in HAP patients

Risk Factor	Coefficient (B)	Odds Ratio (OR)	95% CI	*p* value
Male sex	1.18	2.9	0.9-8.8	0.05*
Mechanical ventilation (MV)	3.14	6.4	2.7-15.2	0.001*
Immunosuppression (IS)	2.63	3.4	1.0-11.2	0.05*
Constant (B_0)	-5.77			

incidence of HAP in ICU admitted patients were 20.8%, which is similar to the results of study conducted by Berba et al., in Philippine General Hospital [7].There were three factors identified in the multivariate analysis as independent predictors of mortality in HAP patients. Among that mechanical ventilation is intervention related and can be modifiable. Mechanical ventilation has been consistently identified as risk factor previous studies conducted elsewhere [7]. Intubation and mechanical ventilation impairs natural host defense mechanism against infection and facilitates the entry and colonization of bacteria into patients lungs.

In contrast the observations of Berba et al., our study showed more mortality in male patients and found to be a predictor of mortality in HAP patients[7]. This may be because of higher incidence of HAP in male patients [8]. Previous studies have shown that male gender is an independent risk factor for the development of ventilator associated pneumonia (VAP) [9].

In our study immunosuppression was also found to be a independent predictor of mortality in HAP patients which is constituent with the findings of Leu H-S et al., [10]. In that study immunosuppressive or leukopenic status found to be predictor of mortality in HAP patients. Risk factors which have been found to be strong predictors of HAP in other studies were not found to be strong predictors of mortality in ICU patients in our study. This is probably due to small number of patients in that particular variable analyzed.In this study no attempt has been made to correlate the clinical outcome (mortality) with microbiological data. Studies on hospital acquired infections are not complete without data microorganism and their susceptibility patterns. Further studies to correlate the clinical outcome with microbiological data are in progress.

CONCLUSION

In summary, the cumulative incidence of HAP in ICU patients during the study period was 20.8%. HAP has contributed significantly to mortality (12.9%). Mechanical ventilation, immunosuppression and male sex were found to be independent predictors of mortality in HAP patients. If these factors are properly addressed mortality may be reduced.

ACKNOWLEDGEMENT

Authors are grateful to Manipal University, Manipal College of Pharmaceutical Sciences, Manipal & Kasturba Hospital, Manipal.

REFERENCES`

1. Marrie TJ, Campbell GD, Walker DH, Low DE. Pneumonia. In: Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, editor. Harrisons Principles of Internal Medicine. 16th ed. New York: McGraw-Hill Medical Publishing Division;2005. p. 1528.
2. Glover ML, Reed MD. In: Dipiro JT, Talbert RL, Yees GR, Matzke GR, Wells BG, Posey LM, editor. Pharmacotherapy: A Pathophysiologic approach. 6th ed. New York: McGraw-Hill Medical Publishing Division: 2005. p.1951.
3. Ramanakumar AV, Aparajita C. Respiratory disease burden in rural India: A review for multiple data sources. The Internet Journal of Epidemiology 2005 [cited 2009, Nov 10]; 2(2). Available from: http://www.ispub.com/journal/the_internet_journal_of_epidemiology/volume_2_number_2_13/article/respiratory_disease_burden_in_rural_india_a_review_from_multiple_data_sources.html
4. Corcoles AV, Gondar OO, Blanco TR, Luria XR, Bertomeu FG. Epidemiology of community-acquired pneumonia in older adults: A population-based study. Respiratory Medicine 2009; 103:310.
5. Fine MJ, Auble TE, Yealy DM, Hanusa BH, Weissfeld LA, Singer DE, Coley CM, Marrie TJ, KapoorW N.A prediction rule to identify low-risk patients with community acquired pneumonia. New England Journal of Medicine1997 Jan 23;336(4):243-50.
6. Craven DE, Barber TW, Steger KA, Montecalvo MA. Nosocomial pneumonia in the 1990s: update of epidemiology and risk factors. Semin Respir Infect. 1990 Sep;5(3):157-72.
7. Berba R, Alejandria M, Rosaros J, Reside I, Ang C, Cordero C, Chavez J, Mendoza M. Incidence, Risk Factors and Outcome of Hospital-Acquired Pneumonia in Critically-Ill Patients at the Philippine General Hospital. Phil J Microbial Infect Dis. 1999; 28(2):29-38.
8. Gannon CJ, Pasquale M, Tracy JK, McCarter RJ, Napolitano LM. Male gender is associated with increased risk for post injury pneumonia. Shock. 2004 May;21(5):410-4.
9. Rello J, Ollendorf DA, Oster G, Vera-Llonch M, Bellm L, Redman R, et al. Epidemiology and Outcomes of

Ventilator-Associated Pneumonia in a Large US Database. CHEST Journal. 2002; 122 (6):2115-21.

10. Leu H-S, Kaiser DL, Mori M, Woolson RF, Wenzel RP. Hospital-acquired pneumonia. American Journal of Epidemiology. 1989; 129(6):1258-67.