Nosocomial pneumonia: risk factors, rates and trends

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الالتهاب الرئوي المستشفَويُّ المنشأ: عوامل الاختطار والمعدلات والاتجاهات

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الخلاصة: استهدفت هذه الدراسة تقدير معدلات وعوامل خطر الالتهاب الرئوي في المرضى الذين أدخلوا المستشفيات في الطائف في المملكة العربية السعودية. وقد أجريت دراسة للحالات والشواهد شملت 211 من المرضى الذين تخرجوا من المستشفيات مع التثبت من إصابتهم بالالتهاب الرئوي و633 من الشواهد غير المصابين بالالتهاب الرئوي، وأجريت مراجعة للسجلات خلال الفترة ما بين 1999 و2003. وقد أظهر التحليل اللوجستي المتعدد للتحوُّف أن كل عامل من العوامل التالية على حدة، مرتبط بازدياد اختطار الالتهاب الرئوي: مدة البقاء في المستشفى، الوحدة التي أدخل إليها، الأمراض الرئوية الانسدادية المزمنة، الغيبوبة، الأنبوب الأنفي المعدي، الأنبوب الرغامي، الأمراض المنهكة، والتنفس الميكانيكي. أما المعدل الوسطي لمحمل العدوى المستشفَويَّة خلال الفترة المذكورة فقد بلغ: 3، في حين بلغ المعدل الوسطي لحدوث الالتهاب الرئوي المستشفَويّ في المرضى المخرَّجين منها: 0.88 لكل 100 مريض مخرَّج.

ABSTRACT This study aimed to estimate the rate of and risk factors for nosocomial pneumonia of patients admitted to hospitals in Taif, Saudi Arabia. A case–control study was conducted of 211 discharged patients with confirmed pneumonia and 633 controls without pneumonia and a review was made of hospital records during 1999–2003. Multiple logistic regression showed that duration of hospital stay, unit of admission, chronic obstructive pulmonary diseases, coma, nasogastric tube, endotracheal tube, debilitating diseases and mechanical ventilation were independently associated with increased risk of pneumonia. The mean incidence of overall nosocomial infection in the period 1999–2003 was 3 per 100 discharged patients, while the mean incidence of nosocomial pneumonia was 0.88.

Pneumonie nosocomiale : facteurs de risque, taux et tendances

RÉSUMÉ Cette étude visait à estimer le taux et les facteurs de risque de pneumonie nosocomiale chez les patients admis dans les hôpitaux de Ta'if (Arabie saoudite). Une étude cas-témoins a été menée sur 211 malades sortants présentant une pneumonie confirmée et sur 633 témoins ne présentant pas de pneumonie, et l'on a examiné les dossiers hospitaliers sur la période comprise entre 1999 et 2003. Une analyse de régression logistique multiple a montré que la durée de l'hospitalisation, le service dans lequel le patient a été admis, les bronchopneumopathies chroniques obstructives, le coma, les sondes gastriques (mises en place par le nez), les sondes endotrachéales, les maladies débilitantes et la ventilation artificielle étaient indépendamment associés à l'augmentation du risque de pneumonie. L'incidence moyenne de l'infection nosocomiale en général pendant la période comprise entre 1999 et 2003 était de 3, alors que l'incidence moyenne de la pneumonie nosocomiale était de 0,88 pour 100 malades sortants.

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Introduction

Nosocomial infection is becoming recognized as a major problem in developing countries. As well as its contribution to the morbidity and mortality of hospitalized patients, nosocomial infection is an economic burden due to the extra days of hospitalization and the more expensive therapy that is required [*1,2*]. Up to 10% of all hospital patients develop nosocomial infections [*3,4*]. Nosocomial pneumonia (NP) is a significant cause of morbidity and mortality among hospitalized patients [*5*]. It is defined as pneumonia that was neither present nor incubating when the patient was admitted to the hospital [*6*]. NP is the 2nd most common nosocomial infection in the United States and worldwide [*6*] and is the most frequent nosocomial infection in intensive care units (ICUs). In recent studies, the incidence was reported to range from 6.8% to 27% [*7–11*]. Patients with NP tend to stay 1 to 2 weeks longer in hospital than those without NP and result in higher costs [*12*]. Prevention and management of such infections require an intimate knowledge of the epidemiology of the infection, including risk factors [*13,14*]. Hospital infection control programmes can prevent 33% of nosocomial infections including pneumonia [*15*].

Studies on NP have mainly been reported from the United States and European countries, and studies from around the world are scarce. This study aimed to estimate the rates of overall nosocomial and pneumonia and their linear trends over the last 5 years (1999–2003) and to determine the potential risk factors for NP of patients admitted to hospitals in Taif, Saudi Arabia, in order to establish a plan for reducing the incidence of NP in these hospitals.

Methods

To fulfil the objectives of this study, 2 strategies were adopted: a case–control study to determine the risk factors for NP and a record review to calculate NP rates.

Case–control study

The case–control study was carried out between April 2003 and March 2005 at Al-Hada (351 beds), Al-Rehab (100 beds) and Prince Sultan (50 beds) military hospitals, Taif, Saudi Arabia. These 3 hospitals are under the same administrative programme and serve military people and their families. All patients hospitalized at these hospitals for at least 72 hours throughout the study period were considered eligible for the study. Among these, patients proven to have pneumonia were considered cases. Nosocomial pneumonia was considered when new and persistent (more than 48 hours) pulmonary infiltrates not otherwise explained appeared on chest radiographs. Moreover, at least 2 of the following criteria were also required: (1) fever > 38 ºC; (2) peripheral leukocyte count > 10 000/mm^3; (3) purulent endotracheal secretions with a Gram stain showing 1 or more types of bacteria [*6*]. Ventilator-associated pneumonia was considered when the onset of pneumonia was after 48 hours of mechanical ventilation [*16*].

After exclusion of patients who did not fulfil the eligibility criteria, 3 controls for each case were enrolled by simple random selection from a list of patients hospitalized for more than 72 hours who did not develop any type of nosocomial infections. Nosocomial infections were diagnosed based on the Centers for Disease Control and Prevention criteria for diagnosis of nosocomial infections [*17*]. For all participants (cases and controls), the following information was col-

lected: age, sex, unit of admission, smoking history, nasogastric tube, endotracheal tube, mechanical ventilation, history of surgery (head, neck, or thoracoabdominal), chronic obstructive pulmonary diseases (COPD), coma, diabetes mellitus, history of immunosuppressive drug intake, inappropriate use of antibiotics, history of debilitating diseases (cancer, liver failure, uraemia) as well as duration of hospital stay.

Appropriate antibiotic therapy included the administration of at least 1 empirical antibiotic with *in vitro* activity against the bacterial pathogens isolated from the patient's respiratory secretions, as well as from blood and pleural fluid when applicable [*18*].

The data from the patients' records were collected during the hospital stay of the patients by a trained nosocomial infection surveillance team from the Department of Preventive Medicine.

Record review

Hospital records, providing the number of hospitalized patients and the numbers of nosocomial infections (crude and site-specific) per month were reviewed. The overall annual nosocomial infection rate and NP rates were calculated during the period 1999–2003 by dividing the total number of nosocomial infections (crude and pneumonia) pooled throughout all months by the total number of hospital patients discharged including hospital deaths (× 100). Critically ill patients (those admitted to the medical, surgical, neonatal or burns ICUs), were treated as a separate group. Overall nosocomial infection and NP rates were calculated for this particular group.

Statistical analysis

Statistical analysis was carried out with *SPSS*, version 11.0. A linear trend was applied to search for evidence of change in the incidence rate of overall nosocomial and pneumonia over time. Age, sex, duration of stay in hospitals, unit of admission, smoking, nasogastric tube, endotracheal tube, mechanical ventilation, surgery, COPD, coma, diabetes mellitus, underlying debilitating diseases and history of immunosuppressive drugs were treated as categorical variables. The crude measure of association between single putative risk factors and NP was expressed as the odds ratio (OR) with 95% confidence interval (95% CI). Multiple associations were evaluated in multiple logistic regression models based on the backward stepwise selection. This process allowed the estimation of the strength of the association between each independent variable and the dependent variable, taking into account the potential confounding effects of the other independent variables. The covariates were removed from the model if the likelihood estimates had a probability > 0.10. Each category of the predictor variables was contrasted with the initial category (reference category). An adjusted odds ratio with 95% CI that did not include 1.0 was considered significant. The significance level of the *P* value was set at 0.05.

Results

A total of 211 discharged patients with NP and 633 controls without NP were recruited. Their baseline characteristics (age and sex) are reported in Table 1. The age of cases ranged from 2 days to 91 years [mean 42.8 (standard deviation 29.3) years; median 47.0 years], while for controls it ranged from 2 days to 87 years [mean 40.7 (SD 29.4) years; median 46.0 years]. The difference between the 2 groups was not statistically significant ($P = 0.27$). Females represented 49.3% and 45.2% of cases and controls, with no significant difference ($P > 0.05$).

Table 1 **Baseline characteristics of participants in the case–control study of risk factors for nosocomial pneumonia**

Baseline characteristics	Cases (*n* = 211)		Controls (*n* = 633)		Total (*n* = 844)	
	No.	%	No.	%	No.	%
Age (years)[a]						
≤ 15	38	18.0	156	24.6	194	23.0
> 16–45	53	25.1	162	25.6	215	25.5
> 46–65	40	19.0	133	21.0	173	20.5
> 65	80	37.9	182	28.8	262	31.0
Mean (SD)	42.8 (29.3)		40.7 (29.4)		41.8 (29.1)	
Median	47.0		46.0		46.0	
Range	2 days–91 years		2 days–87 years		2 days–91 years	
Sex[a]						
Male	107	50.7	347	54.8	454	53.8
Female	104	49.3	286	45.2	390	46.2

[a]P ***> 0.05.***
SD = standard deviation.

The results of univariate analysis of risk factors for NP are summarized in Table 2. Patients aged > 65 years were more liable to develop NP compared with those aged ≤ 15 years (OR = 1.80; 95% CI: 1.13–2.88). Nosocomial pneumonia was significantly associated with stay in hospital > 3 weeks as opposed to < 1 week (OR = 5.44; 95% CI: 3.14–9.42). Patients admitted to surgical, ICU or burns units were more liable to develop NP than those admitted to medical units (OR = 2.15; 95% CI: 1.39–3.32; OR = 3.96; 95% CI: 2.38–6.59; and OR = 3.09; 95% CI: 1.77–5.36 respectively). Presence of nasogastric tube and insertion of endotracheal tube were also associated with NP. Patients with a history of presence of nasogastric tube had an increased risk of NP as compared with patients with no history of nasogastric tube (OR = 2.35; 95% CI: 1.45–3.80). Patients with a history of insertion of endotracheal tube had a 3-fold risk as opposed to those with no history of endotracheal tube (OR = 3.14; 95% CI: 1.71–5.77). Mechanical ventilation history was strongly and positively related to NP (OR = 6.69; 95% CI: 4.40–10.19). The presence of underlying debilitating disease and COPD were also significantly associated with an increased NP risk (OR = 3.08; 95% CI: 1.91–4.97 and OR = 3.52; 95% CI: 1.15–10.93 respectively). Comatose patients had a 4-fold increased risk of NP (OR = 4.60; 95% CI: 1.14–19.59). History of inappropriate use of antibiotics was associated with a higher risk of NP (OR = 1.75; 95% CI: 1.02–2.99). Patient's sex, history of smoking, history of immunosuppressive drugs, presence of diabetes mellitus, as well as history of surgery were not independently associated with NP.

The results of multivariate logistic regression analysis of the studied risk factors for NP are summarized in Table 3. Nosocomial pneumonia was significantly associated with stay in hospital for > 3 weeks as opposed to < 1 week (OR = 2.18; 95% CI: 1.24–3.29). Regarding unit of admission, patients admitted to the ICU or burns unit were more liable to develop NP than those

Table 2 **Risk factors for nosocomial pneumonia from the univariate analysis (211 cases and 633 controls)**

Risk factors	No. of cases/ controls	Crude OR	95% CI
Age (years)			
≤ 15[a]	38/156	1.0	
16–45	53/162	1.34	0.82–2.21
46–65	40/133	1.23	0.73–2.10
> 65	80/182	1.80	1.13–2.88*
Sex			
Male[a]	107/347	1.0	
Female	104/286	1.18	0.85–1.63
Duration of stay in hospitals (weeks)			
< 1[a]	125/453	1.0	
1–3	44/152	1.05	0.70–1.58
> 3	42/28	5.44	3.14–9.42*
Unit of admission			
Medical[a]	78/369	1.0	
Surgical	50/110	2.15	1.39–3.32*
Intensive care unit	41/49	3.96	2.38–6.59*
Burns	30/46	3.09	1.77–5.36*
Other	12/59	0.96	0.47–1.95
Smoking			
No[a]	166/515	1.0	
Yes	45/118	1.18	0.79–1.77
Inappropriate use of antibiotics			
No[a]	185/586	1.0	
yes	26/47	1.75	1.02–2.99*
Nasogastric tube			
No[a]	175/582	1.0	
Yes	36/51	2.35	1.45–3.80*
Endotracheal tube			
No[a]	186/607	1.0	
Yes	25/26	3.14	1.71–5.77*
Mechanical ventilation			
No[a]	133/582	1.0	
Yes	78/51	6.69	4.40–10.19*
Surgery[b]			
No[a]	204/617	1.0	
Yes	7/16	1.32	0.49–3.48
Coma			
No[a]	205/629	1.0	
Yes	6/4	4.60	1.14–19.59*

Table 2 **Risk factors for nosocomial pneumonia from the univariate analysis (211 cases and 633 controls)** ***(concluded)***

Risk factors	No. of cases/ controls	Crude OR	95% CI
Chronic obstructive pulmonary disease			
No[a]	203/626	1.0	
Yes	8/7	3.52	1.15–10.93*
Diabetes mellitus			
No[a]	147/470	1.0	
Yes	64/163	1.26	0.88–1.79
Underlying debilitating disease[c]			
No[a]	170/587	1.0	
Yes	41/46	3.08	1.91–4.97*
Immunosuppressive drugs			
No[a]	198/612	1.0	
Yes	13/21	1.91	0.89–4.09

[a]Reference category.
[b]Head, neck, thoracoabdominal.
[c]Cancer, liver failure, uraemia.
****P < 0.05.***
OR = odds ratio; CI = confidence interval.

admitted to medical units (OR = 2.73; 95% CI: 1.68–4.01 and OR = 3.05; 95% CI: 1.74–4.13 respectively). Presence of nasogastric tube and insertion of endotracheal tube were associated with NP. Patients with history of presence of NG tube had an increased risk of NP as compared to patients with no history of NG tube (OR = 2.18; 95% CI: 1.22–5.14). Patients with history of insertion of endotracheal tube had a 3-fold risk as opposed to those with no history of insertion of endotracheal tube (OR = 3.01; 95% CI: 1.87–6.21). Mechanical ventilation history was strongly and positively related to NP (OR = 6.27; 95% CI: 2.22–9.52). The presence of underlying debilitating disease and COPD were also significantly associated with an increased NP risk (OR = 3.11; 95% CI: 1.29–8.18 and OR = 2.96; 95% CI: 1.98–14.13 respectively). Comatose patients had a 3-fold increased risk of NP (OR = 3.99; 95% CI: 2.87–17.03). Age, sex, history of smoking, history of immunosuppressive drugs and inappropriate use of antibiotics, diabetes mellitus, as well as history of surgery were not independently associated with NP.

The incidence of overall nosocomial infection during the study period (1999–2003) ranged from 2.1 to 3.5 per 100 discharged patients with a mean of 3.0, while the incidence of NP ranged from 0.6 to 1.1 per 100 discharged patients with a mean of 0.88 with no significant trend ($P > 0.05$) (Table 4). NP represented approximately 30.9% of overall nosocomial infection during the study period.

Regarding critically ill patients as a separate group, the mean overall nosocomial infection and NP rates were 15.42 and 8.0 per 100 patients respectively throughout the study period (Table 4). There was an

Table 3 **Risk factors for nosocomial pneumonia from the multivariate analysis**

Risk factor	Adjusted OR	95% CI
Duration of stay in hospitals (weeks)		
< 1[a]	1.0	
1–3	1.06	0.68–2.14
> 3	2.18	1.24–3.29*
Unit of admission		
Medical[a]	1.0	
Surgical	1.91	0.96–4.01
Intensive care unit	2.73	1.68–4.01*
Burns	3.05	1.74–4.13*
Others	1.16	0.71–1.52
Nasogastric tube		
No[a]	1.0	
Yes	2.18	1.22–5.14*
Endotracheal tube		
No[a]	1.0	
Yes	3.01	1.87–6.21*
Mechanical ventilation		
No[a]	1.0	
Yes	6.27	2.22–9.52*
Underlying debilitating disease[b]		
No[a]	1.0	
Yes	3.11	1.29–8.18*
Coma		
No[a]	1.0	
Yes	3.99	2.87–17.03*
Chronic obstructive pulmonary disease		
No[a]	1.0	
Yes	2.96	1.98–14.13*

P < 0.05.
[a]Reference category.
[b]Cancer, liver failure, uraemia.
OR = odds ratio; CI = confidence interval.
Age and history of prolonged inappropriate use of antibiotics were removed from the final model.

increasing trend in the incidence of NP and in the ratio of NP to total nosocomial infections during the entire study period ($P <$ 0.05). NP represented around half of overall nosocomial infections (51.7%).

Discussion

Hospital-acquired pneumonia represents a significant impairment in the quality of health care. The reported incidence of NP in ICUs varies across different studies, which may be explained by the presence of different populations with variable ages, underlying diseases and other associated risk factors. Incidence ranges from 6.8% to 27% [*7–11,19*]. In this study it was 8%. Independent risk factors associated with NP included prolonged hospital stay, endotracheal tube, nasogastric tube, mechanical ventilation, underlying debilitating diseases, coma and COPD. Those risk factors could prove useful in identifying patients at high risk for NP, as well as in developing preventive measures such as avoiding unnecessary nasogastric feeding or endotracheal intubations.

Mechanical ventilation increases the risk of NP 3- to 10-fold [*7,20–22*]. Generally, the duration of mechanical ventilation increases the risk: Cook et al. reported that the rate of ventilator-associated pneumonia increased 3% per day in the 1st week of ventilation, 2% per day in the 2nd week, and 1% per day in the 3rd week [*23*]. In our study, patients on mechanical ventilation had a 6-fold higher risk for developing NP than the non-ventilated patients. Consequently, the use of noninvasive mechanical ventilation should be preferred whenever possible since it has lower rates of nosocomial infections [*24*].

Coma was described as another important risk factor for NP. In these patients, local defence mechanisms of the respiratory airway are altered, allowing microorganisms to better attach to and colonize the

Table 4 **Distribution of total discharged patients and critically ill patients according to the presence of nosocomial infection and pneumonia, Al-Hada, Saudi Arabia (1999–2003)**

Year	All patients						Critically ill patients[a]					
	Total discharged	Nosocomial infection		Nosocomial pneumonia		Nosocomial pneumonia/ total nosocomial infection rate	Total discharged	Nosocomial infection		Nosocomial pneumonia		Nosocomial pneumonia/ total nosocomial infection rate
	No.	No.	%	No.	%	%	No.	No.	%	No.	%	%
1999	14 391	298	2.1	86	0.6	28.9	901	136	15.1	64	7.1	47.1
2000	10 672	373	3.5	116	1.1	31.1	686	101	14.7	49	7.1	48.5
2001	9 114	274	3.0	93	1.0	33.9	572	89	15.6	44	7.7	49.4
2002	9 782	224	2.9	81	0.8	36.2	620	98	15.8	55	8.9	56.1
2003	12 685	441	3.5	108	0.9	24.5	885	141	15.9	81	9.2	57.4

[a] *Critically ill patients were those admitted to the medical, surgical, neonatal or burns intensive care units.*

mucosal surface. Furthermore, depression of the level of consciousness significantly increases the chance of aspiration and can result in development of NP [*19*]. In the current study, comatose patients had a 4-fold increased risk of NP.

As Gram-negative bacteria are documented to be the most common causative agents of NP [*25*], prior antibiotic therapy and COPD (leading to colonization with Gram-negative aerobic pathogens) were reported to be risk factors for the development of NP [*26,27*]. In our patient population, univariate analysis suggested that previous prolonged antibiotic treatment and COPD increased the risk of pneumonia, but only COPD was an independent risk factor in the multivariate analysis. Furthermore, the presence of a nasogastric tube was found to be a risk factor in our study population. NG tubes impair the function of the gastroesophageal sphincter and increase the risk of maxillary sinusitis, oropharyngeal colonization and reflux, all of which may lead to migration of bacteria [*28*]. However, to reduce the risk of NP, it is important to avoid unnecessary enteral nutrition [*29*]. The highest rates of NP were observed in ICUs, which are also the units in which the most severely ill patients are treated and in which the highest mortality rates are observed. Similar findings were found in another study [*30*]. In the literature, the insertion of an endotracheal tube is described as a significant risk factor for NP. Bronchial colonization during the procedure and prolonged continuation of sedation after the procedure will further increase the occurrence of NP [*27*], which is what was seen in the current study. Patients with endotracheal tube had a 3-fold increased risk of NP. In accordance with our findings, numerous studies have demonstrated that severe underlying illness predisposes

patients in the ICU to the development of pneumonia [*22,31*].

In conclusion, pneumonia comprises approximately one-third of nosocomial infections in our hospitals in Saudi Arabia. To reduce the incidence of NP, it is important to take into consideration the risk factors for NP that can be managed, and all those involved in hospital management need to set practical and effective guidelines for prevention of nosocomial infection.

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