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Nursing home-acquired pneumonia presenting at the emergency department

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Abstract Nursing home-acquired pneumonia (NHAP) is one of the most common infections arising amongst nursing home residents, and its incidence is expected to increase as population ages. The NHAP recommendation for empiric broad-spectrum antibiotic therapy, arising from the concept of healthcare-associated pneumonia, has been challenged by recent studies reporting low rates of multidrug-resistant (MDR) bacteria. This single center study analyzes the results of NHAP patients admitted through the Emergency Department (ED) at a tertiary center during the year 2010. There were 116 cases, male gender corresponded to 34.5 % of patients and median age was 84 years old (IQR 77–90). Comorbidities were present in 69.8 % of cases and 48.3 % of patients had used healthcare services during the previous 90 days. In-hospital mortality rate was 46.6 % and median length-of-stay was 9 days. Severity assessment at the Emergency Department provided CURB65 index score and respective mortality (%) results: zero: $n = 0$; one: $n = 7$ (0 %); two: $n = 18$ (38.9 %); three: $n = 26$ (38.5 %); four: $n = 30$ (53.3 %); and five; $n = 22$ (68.2 %); and sepsis $n = 50$ (34.0 %), severe sepsis $n = 43$ (48.8 %) and septic shock $n = 22$ (72.7 %). Significant risk factors for in-hospital mortality in multivariate analysis were polypnea ($p = 0.001$), age ≥ 75 years ($p = 0.02$), and severe sepsis or shock ($p = 0.03$) at the ED. Microbiological testing in 78.4 % of cases was positive in 15.4 % ($n = 15$): methicillin-resistant *Staphylococcus aureus* (26.7 %), *Pseudomonas aeruginosa* (20.0 %), *S. pneumoniae* (13.3 %), *Escherichia coli* (13.3 %), others (26.7 %); the rate of MDR bacteria was 53.3 %. This study reveals high rates of mortality and MDR bacteria among NHAP hospital admissions supporting the use of empirical broad-spectrum antibiotic therapy in these patients.

Keywords Pneumonia · Nursing home · Long-term · Emergency department · CURB65 · Sepsis

Introduction

Pneumonia is one of the most common infections arising amongst nursing home residents [1]. Nursing home-acquired pneumonia (NHAP) is a concept emerging from within the definition of Health-case associated Pneumonia (HCAP) and is an entity frequently presenting to the Emergency Department (ED) requiring hospital admission. Patients suffering from this condition are typically of older age, and present a high burden of comorbid conditions. The presence of multi-resistant drug (MRD) pathogens, especially methicillin-resistant Staphylococcus aureus (MRSA) and *Pseudomonas aeruginosa*, is a major concern [2]. For these reasons increased mortality is expected when compared to other types of pneumonia.

The Portuguese population has importantly aged with 19.3 % of the people in the age group $\geq$65 years old, representing a 19.0 % relative increase between 2001 and 2011 [3]. Furthermore the incidence of Community-acquired Pneumonia (CAP) hospital admissions has also been reported to have increased 28.2 % between the first and the second half of the past decade [4]. Therefore, the number of nursing home residents and the frequency of NHAP

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should also be expected to increase, although current data on its incidence are scarce.

The authors aimed to analyze incidence, microbiological results, outcomes and risk factors in NHAP admissions at a tertiary hospital center during the year 2010.

Methods

The was a retrospective cohort study of all adult patients admitted through the Emergency Department (ED) with a primary diagnosis of Pneumonia at Centro Hospitalar Lisboa Central (CHLC), E.P.E., a Portuguese tertiary Hospital Center located in Lisbon's metropolitan area, during the period between 1st January and 31st December of 2010.

Pneumonia diagnostic codes (International Classification of Diseases—9: 480–488) were searched for in the institutional database. "Pneumonia" was defined as hospital admission for acute lower respiratory tract infection associated with de novo radiographic shadowing during the initial 48 h for which there was no other explanation, and was clinically managed as such [5].

Pneumonia episodes were screened for clinical and radiological criteria and selected if these were fulfilled to build a cohort. Patients with nursing home residence were then screened and included in this study. Hospital discharge in the previous 10 days was an exclusion criteria considering re-admission of the same illness or nosocomial pneumonia etiology.

"Comorbidity" was considered as any prior history of chronic organic illness, solid or hematologic neoplasm and "anemia": hematocrit <30 %. For risk factor analysis "Confusion" was considered as any acutely altered state of conscience; "polypnea": respiratory rate >20 cycles/min or clinical reference to dyspnea, polypnea, or tachypnea; "hypoxemia": peripheral blood oxygen saturation <90 % or arterial blood oxygen pressure <60 mmHg; "tachycardia": cardiac rate >125 beats/min; "hypotension": systolic blood pressure <90 mmHg or diastolic <60 mmHg; and "nursing home": patient resident at a non-hospital long-term care facility.

Microbiological results considered cultural results from products obtained during the initial 48 h from ED admission, as well as urinary antigens for *Legionella pneumophila* and *Streptococcus pneumoniae* and H1N1 influenza PCR throughout the entire hospital stay.

True bacteriemia was considered as described by Weinstein et al. and cited in the literature [6].

All clinical and laboratory results were obtained from the initial approach at the ED, as well as severity of illness scoring using CURB65 index score [7] and the revised Sepsis classification criteria [8].

To compare NHAP CURB65 discriminative ability for in-hospital death prediction we used data from the group of CAP patients derived from the same original cohort [9].

Statistical tests for data analysis included binomial test for proportion, Fisher's exact Chi-square test for contingency tables, Mann–Whitney test for median values comparison, Kruskal–Wallis test for multiple independent variable and receiver operator curve (ROC) for CURB65 index score analysis. Risk associated variables with p value ≤ 0.15 were included in multivariable analysis. Binary logistic regression using backward method with probability for stepwise removal >0.1 was used for multivariable analysis. Area under the curve (AUC) and significance of the difference between the areas under two independent ROC Curves were analyzed as cited in the literature [10, 11]. Statistical significance was considered when double sided p value was ≤ 0.05. Confidence intervals of 95 % (CI 95 %) were used for odds ratio (OR) and AUC. Statistical software OpenEpi® (Center for Disease Control and Prevention, Atlanta, GA, EUA) and "Statistical Package for the Social Sciences" v17.0. (IBM SPSS®, Ill. EUA) were used for data analyzes.

The study was approved by the Institution's Ethics Committee and Administration.

Results

Patient selection

During the study period there were 29,684 adult hospital admissions from which 1635 had a Pneumonia diagnosis. Eight hundred and eighty two cases were excluded due to: alternative primary admission diagnosis ($n = 272$), lack of digital clinical records ($n = 169$), repetition ($n = 140$), hospital discharge within the 10 previous days ($n = 85$), absence of radiologic shadowing ($n = 65$), radiologic exams unavailable ($n = 25$) and other reasons ($n = 125$) including unknown reason for admission, patient not admitted via ED and age under 15 years old.

There were 753 cases of hospital admission due to pneumonia selected for this cohort and 116 cases of NHAP were included in this study analysis [9].

Epidemiology

Temporal distribution of cases showed bimodal peak incidence in March and July (both 12.1 %) and low in May and December (both 1.7 %).

Male gender corresponded to 34.5 % ($n = 40$) of the study sample ($p < 0.001$). Median age was 84 years old [interquartile range (IQR) 77–90]. Male median age was

80 years old (IQR 75–86) while female median age was 87 (IQR 83–91).

There were comorbidities in 69.8 % ($n = 81$) of cases, including heart failure ($n = 35$), cerebral vascular disease ($n = 33$), anemia ($n = 30$), diabetes mellitus ($n = 22$), lung disease ($n = 17$), renal failure ($n = 13$), history of neoplasm ($n = 9$) and liver disease ($n = 1$).

During the prior 90 days (admissions within the prior 10 days excluded) 48.3 % of these patients had reportedly had healthcare services: 34.5 % had been to ED consultation, 27.6 % had taken antibiotic therapy [penicillin derivates ($n = 19$), cephalosporin ($n = 7$), quinolone ($n = 3$), sulfonamides ($n = 2$) and macrolide ($n = 1$)] and 20.7 % had had hospital admission stay.

Patient characteristics are described in Table 1.

Microbiology

Microbiological testing for etiology was performed in 78.4 % ($n = 91$) of cases yielding a positive result in 15.4 %.

Blood cultures were performed in 83 cases with bacteriemia in 12.0 % and contamination in 2.4 %. Respiratory secretions were collected for culture in 17 cases with agent isolation in 23.5 %, contamination in 23.5 % and inadequate sampling in 23.5 %. Urinary antigens for *L. pneumophila* and *Streptococcus pneumoniae* were searched in 30 and 26 cases, respectively, and H1N1 *Influenza* virus

respiratory swab was taken for PCR analysis in two cases with no positive results.

Identified etiologic agents ($n = 15$) were: MRSA (26.7 %), *Pseudomonas aeruginosa* (20.0 %), *S. pneumoniae* (13.3 %), *Escherichia coli* (13.3 %), *Haemophilus influenzae* (6.7 %), *Enterococcus faecalis* (6.7 %), *Staphylococcus capitis* (6.7 %) and *Streptococcus agalactiae* (6.7 %). *P. aeruginosa* and *H. influenzae* isolations were obtained from respiratory secretions.

Of these isolated agents 53.3 % were MDR pathogens [four MRSA, three *P. aeruginosa* and one extended spectrum beta-lactamase (ESBL) producing *E. coli*].

Hospital results

Overall in-hospital mortality rate was 46.6 % ($n = 54$). Median length-of-stay was 9 days (P25 = 5; P75 = 13).

Male mortality was 40.0 % and female 50.0 %. The median of age for the deceased was 86 years old (IQR 82–91) and 83 (IQR 75–88) for survivors. Mortality in the presence of comorbidities was 45.7 % versus 48.6 % in its absence. Comparison of survivor and non-survivor characteristics is described in Table 2.

Sepsis criteria were confirmed in 115 cases with 43.1 % sepsis, 37.1 % severe sepsis and 19.0 % septic shock and matching mortality rates of 34.0, 48.8 and 72.7 %.

Severity of illness case distribution by CURB65 index score ($n = 103$) and respective 30 day mortality rates, illustrated in Graphic 1, were as follows: zero ($n = 0$); one ($n = 7$), 0 %; two ($n = 18$), 38.9 %; three ($n = 26$), 38.5 %; four ($n = 30$), 53.3 %; and five ($n = 22$); 68.2 % ($p = 0.02$ between groups);with a respective ROC AUC of 0.673 (IC 95 % 0.569–0.776).

When comparing CURB65 AUC ROC discriminative ability for outcome prediction in NHAP to the CAP group (0.789; IC 95 % 0.724–0.854; $n = 314$) from the same cohort the result was not significantly inferior ($p = 0.1$).

Risk factors

Significant risk factors for in-hospital death in univariate analysis were polypnea ($p < 0.001$), hypotension ($p = 0.04$), severe sepsis or shock ($p = 0.01$), age ≥75 years ($p = 0.04$) (Table 2). In multivariable analysis association with mortality was significant for variables polypnea ($p = 0.001$), age ≥ 75 years ($p = 0.02$), and severe sepsis or shock ($p = 0.03$) (Table 3).

The presence of MDR pathogens was associated in univariate analysis with severe sepsis or shock ($p = 0.04$), hypotension ($p = 0.04$) and confusion ($p = 0.04$). In multivariate analysis none of these associations reached significance.

Table 1 Nursing home-acquired pneumonia patient characteristics

$n = 116$	%	n
Female gender	65.5	76
Age (years, median)	84.0	IQR 77–90
Hospital stay (days, median)	9.0	IQR 5–13
Comorbidities	69.8	81
Cardiac	30.2	35
Cerebrovascular	28.4	33
Anemia	25.9	30
Diabetes mellitus	19.0	22
Pulmonary	14.7	17
Renal	11.2	13
Neoplasm	7.8	9
Liver	0.9	1
Previous healthcare contact	48.3	56
ED consult	34.5	40
Antibiotic therapy	27.6	32
Hospitalization	20.7	24
Overall mortality (%)	46.6	54

IQR interquartile range, *ED* emergency department

Table 2 Nursing home-acquired pneumonia survivor vs. non-survivor characteristics comparison

	Survivors (n = 62)		Non-survivors (n = 54)		p value
	n	%	n	%	
Male gender	24	38.7	16	25.8	0.33
Age (years; median)	83	IQR 75–88	86	IQR 82–91	0.01
Hospital stay (days; median)	10	IQR 8–15	5	IQR 2–10	<0.001
Comorbidities (overall)	44	71.0	37	68.5	0.84
Cardiac	17	28.3	18	34.6	0.54
Cerebrovascular	21	34.4	12	23.5	0.22
Anemia	13	21.0	17	32.7	0.20
Diabetes mellitus	15	24.2	7	13.0	0.16
Pulmonary	9	15.0	8	16.0	1.00
Renal	5	8.3	8	15.1	0.38
Neoplasm	3	4.9	6	11.3	0.30
Liver	0		1	2.0	
Previous healthcare contact	30	48.4	26	48.1	1.0
ED consultation	20	32.3	20	37.7	0.56
Antibiotic therapy	19	31.1	13	26.0	0.67
Hospitalization	11	17.7	13	24.1	0.49
Confusion	37	59.7	38	73.1	0.17
Urea >40 mg/dL	44	72.1	43	81.1	0.18
Polypnea	24	43.6	41	78.8	<0.001
Hypotension	20	32.3	28	51.9	0.04
Age >75 years	48	77.4	50	92.6	0.04
Tachycardia	37	59.7	39	72.2	0.17
Creatinine >1.20 mg/dL	18	29.0	23	44.2	0.12
Severe sepsis/shock	28	45.2	37	68.5	0.01

IQR interquartile range, *ED* Emergency Department

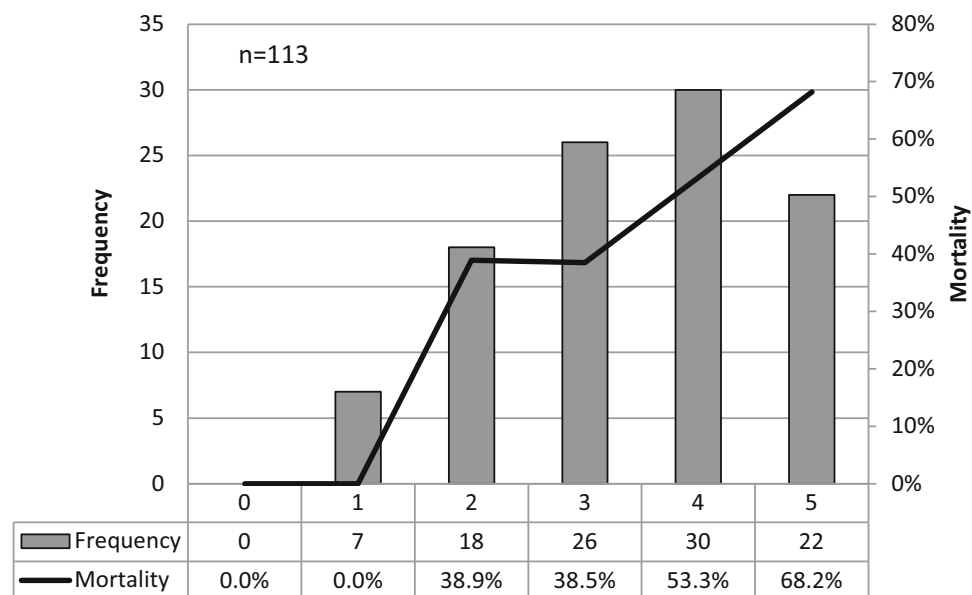**Graphic 1** CURB65 index score and 30 day in-hospital mortality distribution of nursing home-acquired pneumonia patients

	0	1	2	3	4	5
Frequency	0	7	18	26	30	22
Mortality	0.0%	0.0%	38.9%	38.5%	53.3%	68.2%

Table 3 Multivariable backward stepwise logistic regression for in-hospital mortality associated risk factors

	p value	Odds ratio	95 % CI	
Polypnea	0.001	5.1	2.0	12.7
Age ≥75 years	0.02	4.5	1.2	16.6
Severe sepsis or shock	0.03	2.7	1.1	6.6
Creatinine >1.20 mg/dL	0.08	2.3	0.9	5.9

Two step analysis. Variable hypotension removed from model due to *p* value 0.93 in the first step

Limitations

There are limitations to this study, namely the absence of (1) a standard clinical procedure protocol, including (2) serological or PCR research for atypical etiologic agents; (3) antibiotic therapy prescription analysis, (4) time interval analysis between ED admission and antibiotic administration (these last two with an impact on survival), (5) potential admission bias and (6) single center data precluding the generalizability of results.

Discussion

During the study period Hospital Center Lisboa Central (CHLC) included hospitals São José, Santo António dos Capuchos and Santa Marta caring for a population of approximately 191.000 adults with a high proportion (24.2 %) of people aged ≥65 years old [3].

In our study the typical NHAP patient profile was rendered by a clear predominance of the female gender, advanced age and preexisting comorbidities, with more than one-third of the study population having had healthcare services during the prior 3 months indicating a somewhat expected decaying health status and high use of healthcare resources.

Hospital results showed high mortality rates particularly among the most advanced ages and most severely ill patients, which could be interpreted in the light of the vulnerability of this population due to comorbidities and extremes of age conveying limited organic functional reserve and end-of life pneumonia. In selected cases admission to Intensive Care and mechanical ventilation may have been limited although this was not assessed in our study.

Clinical severity of illness assessment tools, Sepsis criteria and CURB-65, were useful at the ED discriminating risk groups for outcome. Several studies have demonstrated the usefulness of CURB65 in NHAP and HCAP [12–14] although it may show reduced discriminating ability as compared to its original use in CAP populations. This is demonstrated in our study by a non-significant inferior CURB65 ROC AUC comparison result between NHAP and CAP groups derived from the same original cohort [9].

Multivariate analysis for significant in-hospital mortality risk factors revealed association with polypnea, age ≥75 years old and severe sepsis or shock at the ED all of which is to be expected. Regarding risk factors for isolation of MDR pathogens no significant associations were unveiled possibly due to the small number of patients.

The most frequently isolated agents in this study were MRSA and *P. aeruginosa* and over half of all isolated bacteria were MDR. This observation is of the utmost importance due to implications on initial patient approach and initial empirical therapy.

Previous fundamental works have addressed NHAP within the HCAP definition considering high risk of MDR pathogens, namely MRSA and *P. aeruginosa*, and recommend empirical treatment with broad-spectrum antibiotic therapy, as opposed to CAP [18, 19]. A major concern regarding this approach is the overuse of empirical broad-spectrum antibiotics and the development of further bacterial resistance to these therapeutical agents.

Recent studies report *S. pneumoniae* as one of the principal etiological NHAP agent, as well as indicate a low prevalence of MDR pathogens and question the recommendation to treat these patients with empirical broad-spectrum antibiotics [15–18].

Research data from both HCAP and NHAP populations have provided with heterogeneous microbiological results and thus failed so far to produce changes in current treatment recommendations. The issue here concerned may be the importance of understanding local realities and adapting to them. It is possible that part of the heterogeneity of microbiological results in NHAP studies reflect differences in study methodologies and regional contrasts regarding socio-economic and healthcare factors affecting nursing home resident populations (*What is the nursing home user profile? How is the quality of nursing and medical assistance and antibiotic prescription?*). Our study aimed to analyze NHAP from an in-patient perspective and does not focus on the questions regarding the out-patient and the quality of nursing home care.

We believe that current NHAP recommendations for aggressive empirical broad-spectrum antibiotic therapy should apply to our study population as suggested by the high rates of mortality and MDR bacteria observed. The importance of clinical pro-active etiological investigation to guide individual treatment options and provide epidemiologic data must be stressed at this point. NHAP should be regarded as a separate entity from HCAP and investigation (including both in-patients and out-patients to avoid admission bias) should be encouraged for the development of tailored therapeutic strategies.

Conclusion

In this NHAP study in-hospital mortality was very high and associated with extremes of age, polypnea and severe sepsis or shock at the ED. The most frequent pathogens were MRSA and *P. aeruginosa* and the majority of isolated bacteria were MDR supporting the recommendations for empirical broad-spectrum antibiotic therapy. Understanding NHAP as a separate entity is crucial and further research should lead to the development of tailored therapeutic strategies.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Statement of human and animal rights The study was approved by the Institution's Ethics Committee and Administration. All human ethical standards were respected in the study.

Informed consent Informed consent was waved due to complete patient anonymity.

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