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Original Article

Adherence to Community Acquired Pneumonia guideleines and patients outcomes in a peri-urban hospital in Natal, South Africa

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Abstract

Introduction: Community-acquired pneumonia (CAP) is an important cause of mortality and morbidity worldwide. This issue is further exacerbated by the Human Immunodeficiency Virus (HIV) epidemic.

Methodology: The study was a retrospective, clinical record review of hospitalized patients (18 years and older) with a diagnosis of LRTI between the 1st of January 2012 and 31 December 2012, descriptive and comparable analysis was performed.

Results: Number of patients was 274; 142 (51.8%) males. The commonest final diagnosis was Pulmonary Tuberclosis (PTB) in 131 (47.8%) and CAP in 127 (46.4%). The case fatality rate was 25.5% (70/274) and was significantly associated with HIV infection (77.4%) ($p < 0,01$), CD4 cell count ≤ 200 cells (96.3), final diagnosis of TB (65.7%) ($p < 0.01$), female sex (57%) ($p < 0.01$), confusion (50%) ($p < 0.01$), age of 65 years or more (29%) ($p < 0.01$). CURB-65 score (Confusion, Urea more than 7mmol/l, Respiratory rate (RR) ≥30 breaths /min, low blood pressure (less than 90 mmHg systolic and 60mmHg diastolic) and age ≥ 65 years) was only documented in 4 % (11/274) patients. Only 63 patients (23%) met the admission criteria of two or more points when the CURB-65 score was calculated.

Conclusions: Failure to use the CURB-65 score resulted in an increase admission of patients presenting with LRTI. There was an increased case fatality rate in this high HIV prevalence setting.

Key words: Community acquired pneumonia; HIV; Tuberculosis.

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Introduction

Community Acquired Pneumonia (CAP) remains a common serious and potentially fatal disease world-wide particularly in the very young or the old individuals [1-3]. In the United States, pneumonia and influenza continue to be a common cause of death [4]. It is estimated that 1.5 million people per year are affected and approximately 30% die in the first year following pneumonia [5]. The economic burden associated with CAP remains substantial at more than 17 billion dollars annually in the United States [4,6]. In South Africa, influenza and pneumonia is the sixth and seventh highest cause of death in 2015 and 2016 respectively, accounting for 4, 3% of deaths. In KwaZulu Natal, influenza and pneumonia was ranked the eighth common cause of death in 2016 with marked improvement from 2011 where it was the third leading cause of death accounting for 5% of deaths [7]. In addition to acute respiratory symptoms, the South African and international guidelines for the diagnosis and treatment of pneumonia recommend the use of a chest radiograph to assist in the confirmation of CAP diagnosis . Furthermore, the application of CURB-65 score is used to assess the severity of illness score to help decide whether to hospitalize patients and to guide diagnostic work up [8-10]. The CURB-65 severity score is one of the validated scores recommended by most guidelines [11].

Many studies examined the improvement in patient care such as a decrease in time to antibiotic administration, increase in the percentage of patients receiving antibiotics at emergency department (ED), decrease in hospital stay, decrease in mortality, and a reduction in health care resource utilization when the score is used [12,13].

Pulmonary infections is a cause of significant morbidity and mortality in HIV infected individuals [14]. Bacterial pneumonia is considered an important illness in HIV infected individuals [15].

The study was conducted at a peri-urban hospital where the population served has a high HIV seroprevalence. Most patients admitted to this hospital with acute respiratory symptoms are HIV infected or suspected to have HIV infection and although the

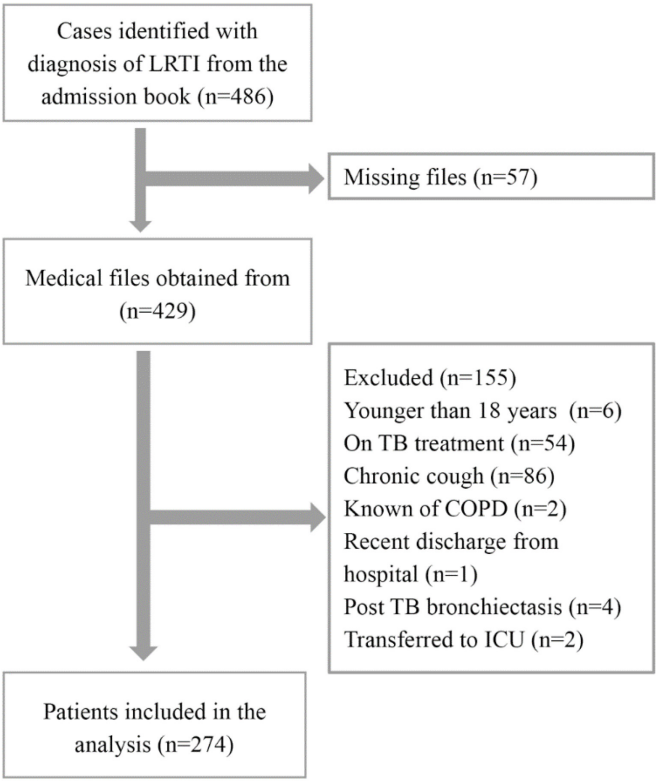
diagnosis of CAP is made in many cases there is always a need to exclude other opportunistic infections such as PTB and pneumocystis Jirovinii pneumonia (PJP). The study sought to determine the adherence to the use of severity of illness scores in the management of patients with respiratory symptoms as per South African management guidelines for CAP, patients outcomes and whether HIV infection which also affect the severity, presentation and outcome of CAP, has an effect in the adherence to the guidelines. Specific objectives of this study were to determine if severity of illness scores (CURB-65) was applied to identify high risk patients at presentation and to determine the final diagnosis and outcome of patients admitted with a diagnosis of LRTI.

Methodology

Study design and patients

The study is a retrospective clinical record review of consecutive adult patients (≥ 18 years) hospitalized with a diagnosis of lower respiratory tract infection from 1 January 2012 and 31 December 2012, at Edendale Hospital, Pietermaritzburg, KwaZulu Natal, South Africa. The hospital has 860 beds (440 regional and 420 district level beds) and runs a large outpatient internal medicine service [16].

Figure 1. Number of patients included and excluded in the study.



Inclusion / exclusion criteria

All patients who were admitted with the diagnosis of LRTI were included in the study. Patients were excluded if a diagnosis of CAP was unlikely (e.g. known PTB patient, and cough for more than two weeks), or if the patient was transferred out of the medical wards for example to the intensive care unit (ICU), or if the patient was discharged recently from hospital where the possibility of hospital acquired pneumonia is high, or if they were involved in a clinical trial or they were for palliative care.

Using the data extraction demographic and clinical data from clinical records of adults 18 years and older admitted with a diagnosis of LRTI was reviewed.

Data collection

All cases with a provisional diagnosis of LRTI were identified from the admission record register. A list with the patient's names and medical file numbers was made and submitted to the medical records department where the patients files were extracted using the patients file number. From the 486 patients identified with such diagnosis, medical records were obtained from 429, using the data extraction form the following information was obtained from the patients' records by researcher, demographic characteristics, the respiratory symptoms and duration (cough, chest pain, shortness of breath), presence of other symptoms (Loss of weight, loss of appetite, etc.), data regarding HIV (status, use of anti-retroviral therapy (ART), CD4 count), the clinical data (blood pressure, heart rate, RR, body temperature, oxygen saturation, assessment of severity using CURB-65 criteria), radiological and laboratory data, initial diagnosis, HIV testing if status unknown, and final diagnosis and clinical outcome upon discharge was also collected.

Statistical analysis: Statistical Package for Social Sciences (SPSS) version 22 statistics software and STATSTICA software was used for data analysis. A descriptive and comparable analysis of variables was performed. Categorical variables were analyzed using the chi-square test. A p value of < 0.05 was considered statistically significant and 95% confidence intervals were calculated. Qualitative variables were expressed as absolute frequencies and percentages, while quantitative variables were summarized as mean and standard deviation.

Results

Baseline patient characteristics

Of the 486 patients identified, medical records were obtained for 429 (88.3%) patients (57 files were

missing). 155 patients were excluded from analysis as they did not meet the inclusion criteria of the study. The total number of patients included in the analysis was 274 (63.9%) (Figure 1).

Baseline patient characteristics are shown in Table 1. There was slightly more males (51.8%) than females (48.2%). The median age was 39 years (range 18-95 years). The majority of the patients (49.4%) were in the 20-40 years range.

CURB-65 score

The CURB-65 score was only documented in 11 of 274 (4%) patients. For those with no documented CURB-65 scores, the calculated scores and different mortality risk groups are presented in Table 2. Only 63 patients (23%) met the admission criteria of two or more points. Of this 12 patients (4.4%) were in the high risk group requiring ICU admission but only two were admitted to ICU.

HIV status and related information

There were 153 (55.8%) patients in whom HIV status was known at admission, of these 134 (48.9%) were HIV infected and 19 (6.9%) were not infected. HIV status was unknown in 121 (43.8%) patients. Of the HIV infected patients 76 (56.7%) were on ART at presentation and 76 patients knew their CD4 count at presentation.

HIV testing was requested in 78 patients during hospital stay. Of these 46 (16.7%) tested positive while 32 (11.7%) were negative for HIV infection .Overall 65.7% of patients were HIV infected and 18.6% HIV uninfected patients. Following discharge, 66 (36.6 %) patients were referred to the local clinic for ART initiation.

Final diagnosis

The commonest final diagnosis was PTB in 131 (48%).Twenty- five patients were diagnosed with both PTB and PJP. Of the TB patients two were confirmed Multi Drug Resistant Tuberculosis (MDR-TB) (1.5%), 46 patients (35.5%) died during the hospital stay and the remaining 83 (63.3%) were referred to the local clinic for continuation of treatment. CAP was the second commonest diagnosis in 127(46.4%), while thirty-two (12%) patients were diagnosed with PJP (25 of them with both PJP and PTB).

Table 1. Base line clinical characteristics of patients (n = 274).

Characteristics	All patients Number (274)
Age (SD) years	Mean = 45 (19)
Gender	
Male (%)	142 (51.8)
HIV status (%)	
Unknown	120 (43.8)
Positive	134 (48.9)
Negative	19 (6.9)
CD4 (cells/mm3)	
CD4 unknown	58 (43.3)
<50	18(6.6)
<100	15 (5.5)
<200	13 (4.7)
<350	12 (4.4)
>350	18 (6.6)
ART use (%)	
On ART	76 (56.7)
Not on ART	58 (48.9)
Symptoms (%)	
Cough	246 (89.8)
Fever	73 (26.6)
Chest pain	77 (28.1)
Shortness of breath	31 (11.3)
Headache	4 (1.5)
Systolic BP	
< 90 mmHg	31 (13.3)
90-139 mmHg	189 (69)
≥ 140 mmHg	22 (8)
Not recorded	32 (11.7)
Diastolic BP	
< 60mmHg	42(15.3)
60 - 80mmHg	168 (61.3)
> 80mmHg	31(11.3)
Not recorded	33 (12)
Outcomes	
In hospital death	70 (25.5)
Discharged home	189 (69)
Transferred to other hospital	9 (2.2)
Unauthorized discharge	6 (2.2)
ICU admission	2 (0.5)

Table 2. CURB-65 variables and risk groups.

CURB-65 variables	Number of patients (%)	CURB-65 score	Number of patients (%)
Confusion	53 (19.3)	0-1 point (Low risk)	211 (77)
Urea>7 mmol	61 (22.3)	2 points (Intermediate risk)	51 (18.6)
Respiratory rate>30/min	56 (20.4)	> 2 points (High risk)	12 (4.4)
Systolic BP<90mmHg	31 (11.3)		
Diastolic BP<60 mmHg	42 (15.3)		
Age > 65years	47 (17.2)		

Table 3. Illustrating a comparison between the Initial and final diagnosis.

Initial differential diagnosis	N (%)	Final diagnosis	N (%)
CAP	53 (19)	CAP	127 (46.4)
PTB	14 (5)	PTB	129 (47)
CAP/PTB	134 (49)	PJP	32 (12)
CAP/PTB/PJP	32 (11.7)	MDR-TB	2 (0.7)
CAP/MDR-TB	8 (3)	CAP with bronchiectasis	3 (1.1)
CAP/CCF	15 (5.5)	CCF	3(1.1)
CAP/HAP	2 (0.7)	Pulmonary embolism	1 (0.4)
ASTHMA	2 (0.7)	TB pericarditis	1 (0.4)
PJP	4 (1.5)	SVC syndrome	1 (0.4)
CAP/PE	1 (0.4)		
CAP/Meningitis	5 (1.8)		
Malignant lesion	2 (0.7)		
CAP/TB pericarditis	1 (0.4)		
CAP/SVC syndrome	1 (0.4)		

Table 4. Factors associated with death.

	OR	95% CI	P
Female sex	0.846	1.591-5.091	< 0.01
Age ≥ 65	1.482	0.759-2.891	< 0.01
HIV infection	1.481	1.330-1.650	< 0.01
Confusion	1.215	1.125-1.310	< 0.01
O2 saturation ≤ 90 %	1.102	0.804-1.582	< 0.05
Sys BP ≤ 90	0.557	0.452-0.687	< 0.01
Dias BP ≤ 60	0.4	0.300-0.533	< 0.01
Urea ≥ 7mmol	1.826	0.705-2.334	0.06
CD4 ≤ 200 (cell/ml)	0.111	2.126-4.552	< 0.01
Final diagnosis	2.782	1.576-4.909	< 0.01

Table 5. Comparison between patients who died and those who were discharged home.

	Died (%) N = 70	Discharged home (%) N = 189	P value
Female	40 (57.1)	92 (48.7)	< 0.01
Age ≥ 65 years	20 (29)	27 (14.2)	0.01
HIV infected	54 (77.2)	118 (62.4)	< 0.01
CD4 count (cells/mm)			
≤ 200	52(96.3)	18 (8.8)	< 0.01
>200	2 (3.7)	38 (18.6)	
Oxygen saturation <90%	20 (28.6)	28 (15)	0.05
Systolic BP < 90mmHg	11 (16)	20 (10)	< 0.01
Diastolic BP < 60 mmHg	11 (16)	31 (16.4)	< 0.01
Confusion	35 (50)	18 (9)	0.001
CURB-65 (documented)	2 (2.8)	9 (4.7)	0.56
Final diagnosis			
CAP	24 (33.3)	103 (54.4)	
PTB	46 (65.7)	83 (43.9)	< 0.01
Others	0	3 (1.6)	

Table 3 shows a comparison of the initial and final diagnosis. Patients who were diagnosed with CAP were more likely to be male (58.2% vs. 44%), have consolidation on the chest radiograph (44% vs. 29%) and less prominent chest infiltrates (30% vs. 52%) compared to those who had a diagnosis of PTB .The proportion of those with HIV infection was slightly lower in patients with CAP (39% vs. 47%), but there was no significant difference in outcome. Comparison between the two groups is presented in Table 6.

Outcomes and factors associated with death

Death occurred in 70 (25.5%) patients whilst 189 (69%) were discharged home. Nine cases (3.3%) were transferred to another hospital (pulmonology unit, cardiothoracic unit or MDR-TB hospital) and six patients (2.2%) left the hospital (unauthorized discharges). Death was significantly associated with HIV status ($p < 0.01$), CD4 cell count ($p < 0.01$), female sex ($p < 0.01$), age ≥65 ($p < 0.01$), level of consciousness ($p = 0.01$), O2 saturation ($p = 0.05$), low systolic and diastolic blood pressure ($p < 0.01$), blood urea (P=0.06) and the final diagnosis of TB ($p < 0.01$).

HIV infection was more common in patients who died compared to those who survived (66% vs. 43%) (p<0.01). There was a higher mortality in females (57.1% vs. 48.1%), people 65 years and older (29% vs. 14%) and those with low CD4 count and low systolic blood pressure. Those who died were more likely to be diagnosed with PTB (65.7 vs. 33.3).A comparison between the two groups is presented in Table 5.

Discussion

The CURB-65 score is a validated score that predicts CAP severity and both in-hospital mortality and risk of 30-day mortality [17]. It also enables an assessment of the need for mechanical ventilation, and the rate of hospital re-admission [18]. This study shows that CURB-65 score was not used to risk stratify patients prior to hospital admission, despite the individual variables that make up the score being documented and available in patient files. As a result; an increased number of patients were admitted resulting in an increased utilization of health care resources and increased cost of treatment. However, it is most likely that the score was not utilised because most of the patients were HIV infected with low CD4 cell counts and not on antiretroviral treatment at the time of presentation. The poor use of the score also resulted in few high risk patients who required ICU management to be identified (2/12).

Our study shows a high case fatality rate of 25% despite only 23% of patients meeting the admission criteria for CAP according to calculated CURB-65 score.

This discrepancy could be related to the high prevalence of HIV infection [19]. Many studies investigated the association between pneumonia and HIV infection and found that the incidence of pneumonia in HIV infected patients is five to tenfold higher than in HIV un-infected patients [20-22] and pneumonia is more severe and fatal in the presence of HIV infection [23].

The lack of validation of the CURB-65 score in areas with high HIV burden setting limits the utility in this setting. It is recommended that these scores be used only in HIV infected patients with a CD4 cells count more than 200 cell/ml while all patients with CD4 cell count less than 200 cell/ml be admitted to hospital [24]. In our study we found more than 96% of patients who died had CD4 cell count less than 200 cell/ml (Table 3). The South African CAP guidelines suggest that severity

Table 6. Comparison between the patients who had a final diagnosis of CAP and those who were diagnosed with PTB.

	CAP N = 127 (%)	**PTB N = 131(%)**
Male	74 (58.2)	56 (42.8)
Females	53 (42)	75(57.2)
HIV infected	75 (59)	99 (75.6)
Pre TB	24 (19)	25 (24)
Confusion	16 (13)	11 (11)
Urea		
<7 mmol	65 (51.2)	47 (45.2)
≥7mmol	28 (22)	14 (14)
Outcome		
Death	24 (19)	46 (35.1)
Discharged home	103 (81)	83 (63.4)
HIV status		
Unknown	66(52)	50 (38.2)
Positive	50 (39.3)	73 (55.7)
Negative	11 (8.7)	8 (7.7)

score should not be used as a sole determinant of site of care.

Gender is thought to play an important role in the incidence and outcomes of many diseases [25] and many studies investigated the association between female sex and outcomes in patients with sepsis, some showed that mortality was unaffected by gender [26]; whilst others found that for lung related sepsis, female sex is associated with severe disease and more mortality and have suggested adding female sex as risk factor for poor outcomes [27]. In this study we found that women constituted 57% of mortality.

We found around 17% of our study population were 65 years and older. In this age group, 20/47 (42.5%) died during their hospital stay. This accounted for one third of the mortality (Table 4). Several studies have found that age of 65 or more is a strong predictor of death in patients with LRTI, and this is independent of other components of CURB-65 score [28,29].

The findings of higher mortality of those with HIV infection and TB at increased risk of mortality is in keeping with other studies from Africa.TB is the commonest presenting illness in those with HIV infection and is the major contributor to HIV associated mortality[30]. South Africa is one of the countries with the highest TB burden and has the highest TB/HIV co-infection in the world according to World Health Organisation (WHO) reports between 2016 to 2018 [31,32].

The results reported herein should be viewed in the light of some limitations. Firstly, the retrospective study design resulted in missing data and hence may limit the generalisability of the findings. Secondly, some of the factors and co-morbidities strongly associated with mortality and morbidity in CAP such as tobacco smoking history, alcohol use, diabetes and chronic obstructive pulmonary disease (COPD) were not collected and included in the analysis. Another limitation is that the study did not report on the outcome of high risk patients who required admission to ICU but were treated in the general medical wards, Lastly although in the majority of patients PTB was confirmed smear positive TB, the diagnosis of CAP and PTB was a clinical diagnosis which might affect the accuracy of results and contribute to bias.

Conclusions

Poor use of CURB-65 score resulted in an increase in admission of patients presenting with lower respiratory tract infection as recommended by The South African CAP guidelines but this finding must be considered in light of the poor predictability of severity in the setting of advanced HIV infection.

There is a high case fatality rate in patients presenting with LRTI in a high HIV prevalence setting, depite low CURB-65 score which might indicate that severity scores is not be a senstive indicator for disease severtiy in the presence of HIV infection. Future research may consider adjusment and validation of severity scores for HIV infected individuals with low CD4 cell count. CAP and PTB remained a major cause of mortality and morbidity in HIV infected individuals especially in patients not on ART and with low CD4 cell count.

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