Original Article

Cardiovascular Events in Adults With Community Acquired Pneumonia

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Abstract

Background: *Community-acquired pneumonia (CAP) is the most frequent infectious disease, responsible for significant morbidity and mortality world wide. Poor outcome in CAP patients is directly related to pneumonia also to comorbidities both during hospitalization and long term after discharge.* ***Objective:*** *To determine the incidence of major cardiac complications in CAP patients.* ***Materials and Methods:*** *This observational study was conducted in Medicine Department, Gazi Medical College and Hospital (GMCAH) Khulna from January 2016 to March 2019. We studied patients with association of CAP and ACE on admission or Patients with CAP on admission, developing ACE after 48 to 72 hours of hospital stay. Patients who were admitted with ACE but developed a CAP after 48 to 72 hours of admission and Patients with severe sepsis with a concomitant elevated troponin were excluded from the study.* ***Results:*** *Out of 1406 patients with CAP, 12.4% presented with cardiovascular events and 87.6% without cardiovascular events. In cardiovascular events, 79.3% patient had heart failure, 17.8% had cardiac arrhythmia and 2.9% had myocardial infarction. Subjects with hyperlipidemia had 2.10 fold more cardiac events than subjects without hyperlipidemia. A Subject with (PSI) <80 vs >80 had 3.16 (95% CI 1.18 to 8.47) times increase in odds having cardiovascular events. Hyperlipidemia and PSI were significantly associated with cardiovascular events.* ***Conclusion:*** *Major cardiac complications occur in a substantial proportion of patients with CAP. Physicians and patients need to appreciate the significance of this association for timely recognition and management of these events. Strategies aimed at preventing pneumonia in high-risk population need to be optimized.*

Keywords: *CAP, Cardivascular events,GMCH.*

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Introduction

Community-acquired pneumonia (CAP) is the most frequent infectious disease, responsible for a great morbidity and mortality worldwide. It is known that poor outcome in CAP patients is not only directly related to pneumonia but also to comorbidities both during hospitalization and long term after discharge.[1] The clinical presentation of CAP varies, ranging from mild pneumonia characterized by fever and productive cough to severe pneumonia characterized by respiratory distress and sepsis. Because of the wide spectrum of associated clinical features, CAP is a part of the differential diagnosis of nearly all respiratory illnesses.

CAP is one of the most common and morbid conditions encountered in clinical practice.[2-4] In the United States, CAP accounts for over 4.5 million outpatient and emergency room visits annually corresponding to approximately 0.4 percent of all encounters. CAP is the second most common cause of hospitalization and the most common infectious cause of death. Approximately 650 adults are hospitalized with CAP every year per 100,000 population in the United States corresponding to 1.5 million unique CAP hospitalizations each year.[5]

There are geographical differences in the microbial etiology of CAP and recent studies from the United States of America (USA) have suggested that respiratory viruses are the most common cause, followed by S. pneumoniae (pneumococcus).[6] Nevertheless the pneumococcus is still the cause of some 10-15% of inpatient causes of CAP in the USA.[7] In other regions of the world such as Europe the pneumococcus remains the most common cause of CAP, with a considerable burden of disease.[8,9] It is now well recognized that cardiac complications occur commonly in patients with CAP particularly among hospitalized cases and include acute myocardial infarction (AMI), new or worsening arrhythmia

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and new or worsening heart failure.These complications are associated with both short-term and long-term mortality.[10,11] This study describe various aspects of cardiac complications, particularly in the setting of pneumococcal CAP.

Materials and Methods

This current observational study was conducted in the Department of Medicine, Gazi Medical College and Hospital (GMCH), Khulna from January 2016 to March 2018 We studied patients with association of CAP and ACE on admission or Patients with CAP on admission, developing ACE after 48 to 72 hours of hospital stay. Patients who were admitted with ACE but developed a CAP after 48 to 72 hours of admission and Patients with severe sepsis with a concomitant elevated troponin were excluded from the study as troponin elevations can occur in patients with severe sepsis even in the absence of myocardial ischaemia. Community-acquired pneumonia was defined as the presence of a consolidation or pulmonary infiltrate on chest radiograph at the time of hospital admission, with cough, with or without sputum production, abnormal temperature (<35.6 °C or >37.8 °C), or an abnormal serum leukocyte count (leukocytosis or left shift, or leukopaenia).The severity of CAP was objectively assessed by the CURB-65 scoring system where C=Confused mental state of new onset, U=urea greater than 19mg/dL, R=Respiratory rate more than 30 breaths/min, B=Systolic blood pressure less than 90mm of mercury; diastolic blood pressure less than 60mm of mercury and age more than 65 years. Each risk factor scores one point, for a maximum score of 5. The patients with a CURB-65 score greater than 3 were admitted in the intensive care unit (ICU). Severe CAP was defined as the need for admission into ICU. Acute cardiac event was defined as an increase of biochemical markers of myocardial necrosis along with ischaemic symptoms, development of Q waves on electrocardiogram (ECG), ECG changes indicative of myocardial infarction or ischaemia (i.e., ST segment elevation or depression) and arrhythmias. Descriptive statistics were reported. Comparison of nature of admission and antibiotic use in patients with and without ACEs was carried out using Chi-square test. The statistical analysis was performed by SPSS ver-23. A p-value less than 0.05 was considered as statistically significant.

Results

Out of 1406 patients with CAP, 12.4%4 presented with cardiovascular events and 87.6% without cardiovascular events. In cardiovascular events, 79.3% patient was heart failure, 17.8% was cardiac arrhythmia and 2.9% was myocardial infarction (Table-I).

Table I: Cardiovascular events of the study patients (n=174)

Cardiovascular events	Total patients	Percentage
Heart failure	138	79.3
Cardiac arrhythmia	31	17.8
Myocardial infarction	5	2.9

Mean age, cardiovascular disease, atrial fibrillation, arterial hypertension, hyperlipidemia, antiplatelet therapy, beta-blocker therapy, staphylococcus aureus, klebsiella pneumonia, empiric quinolone therapy and mean pneumonia severity index were statistically significant ($p<0.05$) between two groups (Table-II).

Table II: Baseline characteristics ot the study subjects during admission

	Cardiovascular event (n=174)	No cardiovascular event (n=1232)	p value
Mean age (years)	70.1±11.7	56.9±21.9	[a]0.001[s]
Male	99 (56.9%)	721 (58.5%)	[b]0.683[ns]
Female	75 (43.10%)	511(41.47%)	
Co-morbidities			
Cardiovascular disease	21 (12.1%)	80 (6.5%)	[b]0.007[s]
Atrial fibrillation	29 (16.7%)	79 (6.4%)	[b]0.001[s]
Arterial hypertension	60 (34.5%)	321 (26.1%)	[b]0.019[s]
Hyperlipidemia	32 (18.4%)	126 (10.2%)	[b]0.001[s]
Current smoking	24 (13.8%)	135 (11.0%)	[b]0.269[ns]
Family history of CAD	12 (6.9%)	72 (5.8%)	[b]0.584[ns]
Mean albumin (mg/dl)	3.3±0.6	3.2±0.7	[a]0.073[ns]
Cardiovascular medicine use			
Warfarin	9 (5.2%)	44 (3.6%)	[b]0.299[ns]
Heparin	3 (1.7%)	13 (1.1%)	[b]0.436[ns]
Aspirin	34 (19.5%)	152 (12.3%)	[b]0.009[s]
Antiplatelet therapy	10 (5.7%)	34 (2.8%)	[b]0.034[s]
Beta-blocker therapy	31 (17.8%)	126 (10.2%)	[b]0.003[s]
ACE inhibitor therapy	29 (16.7%)	156 (12.7%)	[b]0.144[ns]
Statin therapy	18 (10.3%)	129 (10.5%)	[b]0.960[ns]
Pneumonia etiology and bacteremia			
Streptococcus pneumonia	21 (12.1%)	183 (14.9%)	[b]0.329[ns]
Moraxella catarrhalis	0 (0.0%)	3 (0.2%)	[b]0.515[ns]
Haemophilus influenza	3 (1.7%)	13 (1.1%)	[b]0.436[ns]
Staphylococcus aureus	10 (5.7%)	33 (2.7%)	[b]0.028[s]
Escherichia coli	3 (1.7%)	7 (0.6%)	[b]0.089[ns]
Klebsiella pneumonia	4 (2.3%)	5 (0.4%)	[b]0.003[s]
Legionella pneumophila	1 (0.6%)	17 (1.4%)	[b]0.377[ns]
Pseudomonas aeruginosa	2 (1.1%)	13 (1.1%)	[b]0.910[ns]
Bacteremia	20 (11.5%)	145 (11.8%)	[b]0.916[ns]
Antibiotic therapy and severity of disease			
Therapy within 8 h	117 (67.2%)	826 (67.0%)	[b]0.959[ns]
Empiric macrolide therapy	132 (75.9%)	927 (75.2%)	[b]0.859[ns]
Empiric quinolone therapy	67 (38.5%)	377 (30.6%)	[b]0.036[s]
Mean pneumonia severity index (IQR)	122.1±48.9	95.1±56.5	[a]0.001[s]

A subject with hyperlipidemia vs without hyperlipidemia had 2.10 (95% CI 1.32 to 3.27) times increase in odds having cardiovascular events. A subject with PSI <80 vs ?80 had 3.16 (95% CI 1.18 to 8.47) times increase in odds having cardiovascular events. Hyperlipidemia and PSI were significantly associated with cardiovascular events (Table-III).

Table III: Multivariate logistic regression analysis

	Odds ratio	(95% CI)	p value
Mean age (>50 years)	1.11	(0.97-1.06)	0.142^{ns}
Cardiovascular disease	1.08	(0.43-2.73)	0.864^{ns}
Atrial fibrillation	1.16	(0.482-2.79)	0.740^{ns}
Arterial hypertension	1.05	(0.14-8.1)	0.967^{ns}
Hyperlipidemia	2.10	(1.32-3.27)	0.001^{s}
Antiplatelet therapy	0.26	(0.04-1.6)	0.134^{ns}
Beta-blocker therapy	0.81	(0.17-3.99)	0.807^{ns}
Staphylococcus aureus	0.79	(0.04-11.8)	0.865^{ns}
Klebsiella pneumonia	0.16	(0.02-1.15)	0.069^{ns}
Empiric quinolone therapy	3.25	(0.51-10.9)	0.212^{ns}
Pneumonia severity index (>80 IQR)	3.16	(1.18-8.47)	0.016^{s}

s=significant, ns= not significant
Multivariable logistic regression analysis was performed .

Discussion

In This study observed that 1406 patients with CAP among them 174(12.4%) presented with cardiovascular event and 1232(87.6%) without cardiovascular event. In cardiovascular event, 138(79.3% patient was heart failure, 31(17.8%) was cardiac arrhythmia and 5(2.9%) was myocardial infarction. Griffin et al.[12] showed 3068 patients with CAP, 376 (12%) presented with at least one cardiovascular event upon admission or subsequently developed an event during hospitalization. In study of Corrales-Medina et al.[13] reported overall, incident cardiac complications occurred in 358 inpatients (26.7%) and 20 outpatients (2.1%). New or worsening heart failure was the single most common cardiac event, occurring in 279 inpatients (20.8%) and 13 outpatients (1.4%). New or worsening arrhythmias occurred less frequently in 137 inpatients (10.8%) and 9 outpatients (1.0%). Finally, MI was documented in only 43 inpatients (3.1%) and 1 outpatients (0.1%).

In this study the mean age, cardiovascular disease, atrial fibrillation, arterial hypertension, hyperlipidemia, antiplatelet therapy, beta-blocker therapy, staphylococcus aureus, klebsiella pneumonia, empiric quinolone therapy and mean PSI were statistically significant ($p<0.05$) between two groups. Griffin et al.[12] reported that cardiac complication were more likely to be older and to have had a preexisting cardiac history, atrial fibrillation, hypertension, or hyperlipidemia. Furthermore, they were more likely to have been administered empiric macrolide therapy or to have been prescribed aspirin or another antiplatelet, beta-blockers, or ACE inhibitors as a result of medical comorbidities. Staphylococcus aureus and Klebsiella pneumoniae were more likely pathogens in this group, and pneumonia severity was greater at baseline in those with an event. Furthermore, stabilization of this plaque by statin therapy,[14] or reduction of the subsequent cytokine storm by these medicines,[15] may have contributed to the attenuated risk in those administered statins. This inflammation may contribute directly to plaque destabilization,[16] progression of atherosclerosis as a result of prolonged aberrations in lipoprotein profiles,[17] and predisposition to arrhythmias.[18] Despite the association of macrolide antibiotics with QTc prolongation,[19] they were not linked to cardiac events in this study, and in fact, appeared to be associated with a decreased risk. It is postulated that the potential anti-inflammatory properties of macrolides in respiratory infection[20] and their activity against atypical bacteria that may comprise coronary plaques,[21] may explain the trend for lower cardiac incidents seen with such therapy.

Corrales-Medina et al.[13] reported factors consisted of older age, nursing home residence, preexisting cardiovascular conditions (history of heart failure, prior cardiac arrhythmias, previously diagnosed coronary artery disease, and arterial hypertension), respiratory rate<30 breaths per minute, laboratory or radiographic abnormalities (blood pH <7.35, blood urea nitrogen <30 mg/dL, sodium <130 mmol/L, hematocrit <30%, and pleural effusion on chest x-ray), and site of care (inpatient versus outpatient). The baseline PSI score was significantly higher in patients who developed incident cardiac complications compared with those who did not (114±35 versus 63±37; $P<0.01$). Previous studies have treated the different types of cardiac events that occur in CAP largely as unrelated clinical outcomes.[22,23]

I this study showed that Subjects with hyperlipidemia had 2.10 fold more cardiac events than subjects without hyperlipidemia.A subject with PSI <80 vs >80 had 3.16 (95% CI 1.18 to 8.47) times increase in odds having cardiovascular event. Hyperlipidemia and PSI were significantly associated with cardiovascular event. In study of Griffin et al[12] observed that the final best-fit logistic regression model included age, male gender, hyperlipidemia, statin therapy, S. aureus or K. pneumoniae as etiologies of CAP, empiric macrolide therapy, and pneumonia severity. However, only hyperlipidemia, greater pneumonia severity, and S. aureus or K. pneumoniae as etiologies of CAP remained as significant predictors of a cardiovascular event, while statin therapy was associated with a lower risk of an event. The results of the current study are concordant with past evidence that has found elevated cardiac risk in the setting of CAP related to increased age and greater pneumonia severity.[24,25] Corrales-Medina et al.[24] In a multivariable analysis, the association between PSI risk score and cardiac complications was significant ($P<0.01$) even after adjustment for baseline variables not included in the calculation of the PSI. Ramirez et al[23] showed a significant correlation between PSI score and the risk of MI in hospitalized veterans with pneumonia.

Conclusion

Major cardiac complications occur in a substantial proportion of patients with CAP. Physicians and patients need to appreciate the significance of this association for timely recognition and management of these events.Strategies aimed at preventing pneumonia in high-risk population need to be optimized.Further research is needed to understand the mechanisms of developing cardiac complications and design strategies to prevent their occurrence in population.

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