

COMMUNITY ACQUIRED PNEUMONIA IN TYPE 2 DIABETES MELLITUS: A STUDY OF CLINICAL AND BACTERIOLOGICAL PROFILE

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ABSTRACT

INTRODUCTION

Community-acquired pneumonia (CAP) Is a common and serious illness despite the availability of potent new anti-microbials and effective vaccines. For patients with community-acquired pneumonia, diabetes mellitus is one of the most common underlying diseases.

AIMS AND OBJECTIVES

1) To determine the aetiological agents of CAP in T2DM, 2) To determine what percentage of CAP diagnosed by British Thoracic society guidelines is actually due to M. Tuberculosis in T2DM, 3) To study the clinical profile of CAP in T2DM and 4) To determine the factors predicting mortality.

MATERIALS AND METHODS

1) Cases were selected as mentioned in inclusion criteria. 2) Informed consents were obtained. 3) All patients were evaluated by a detailed history, complete physical examination, CXR, CBC, RBS, RFT, LFT, Sputum and blood cultures and Sputum AFB. 4) Data was analyzed using SPSS v20.0 Tuberculosis cases were excluded when the clinical profile of CAP was studied.

RESULTS

A total of 89 cases were studied. 5 cases were found to have Tuberculosis as an etiology. Microorganisms could be isolated in 19% of the rest of the cases (84). Gram negative organisms were isolated more (56%) than gram positive organisms. Most common bacteria isolated was K. pneumoniae. The mortality was 16%. Out of the factors studied presence of coexisting CKD, COPD; breathlessness, tachycardia, tachypnea, hypotension and altered sensorium at presentation, impaired renal function and thrombocytopenia were significant predictors of mortality.

CONCLUSIONS

Tuberculosis is an important differential to be considered in CAP like presentation. The isolation of organisms by routine sputum and blood cultures is low. Of the organisms isolated Gram Negative organisms predominates in this area. Co-existing COPD, CKD, tachycardia, tachypnea, hypotension and altered sensorium at presentation, impaired renal function and thrombocytopenia are important predictors of mortality in patients of CAP with T2DM.

KEYWORDS

Type 2 Diabetes Mellitus, Community Acquired Pneumonia, Tuberculosis.

HOW TO CITE THIS ARTICLE: Niyas VKM, Kumar KGS. Community acquired pneumonia in type 2 diabetes mellitus: A study of clinical and bacteriological profile. J. Evid. Based Med. Healthc. 2016; 3(17), 656-661. DOI: 10.18410/jebmh/2016/149

INTRODUCTION: Pneumonia is a disease that has been known to mankind for many years and has been studied extensively in the last two centuries.¹ Developments in the field of microbiology and molecular genetics have improved our understanding about this common illness. Tremendous progress in the field of pharmacology has provided newer agents to our armamentarium in combating this illness. Newer antibiotics are helping us to achieve a cure in a large number of patients. Effective vaccines are now available against two of the most common etiological agents of

Pneumonia. Developments in critical care medicine and sepsis management have improved the survival of even severe cases of this disease.

Despite all these developments Pneumonia is still a leading cause of mortality and morbidity across the globe.² It is estimated that 10-12% of patients who are admitted to hospital due to pneumonia die. 20% of the mortality due to infectious diseases in our country are caused by lower respiratory tract infections.³

Diabetes is a disease which has profound deleterious effect on immunity. As a result, it predisposes to a variety of infections. Pneumonia being a common illness deserves special attention. The clinical profile of Community Acquired Pneumonia (CAP) in diabetic patients therefore needs to be better understood. This is especially relevant in India where such studies are lacking. The fact that Tuberculosis can present as community Acquired Pneumonia is also known.

*Submission 27-01-2016, Peer Review 11-02-2016,
Acceptance 19-02-2016, Published 29-02-2016.*

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DOI: 10.18410/jebmh/2016/149

However, this fact also needs to be better understood especially in diabetic patients. Though various studies have assessed the predictors of mortality in Community acquired Pneumonia (CAP), most of them were from the western world.⁴ Studies in this regard are also lacking from our country.

The present study was therefore conducted to study the clinical and bacteriological profile of Community acquired Pneumonia in patients with Type 2 Diabetes Mellitus.

MATERIALS AND METHODS: The study was conducted as a hospital based observational study, in which all patients of Community Acquired Pneumonia (CAP), fulfilling the British Thoracic Society Guidelines among Type 2 Diabetes Mellitus Patients admitted to the wards under Department of General Medicine, Government Medical College, Kozhikode over a period from January 1 2013 to December 31 2013 (One Year) were included.

The BTS Guideline for Diagnosing CAP is as Follows:

- Symptoms of an acute lower respiratory tract illness (cough with or without expectoration, shortness of breath, pleuritic chest pain) for less than 1 week; and
- At least one systemic feature (temperature $>37.7^{\circ}\text{C}$, chills, and rigors, and/or severe malaise); and
- New focal chest signs on examination (bronchial breath sounds and/or crackles) with.
- No other explanation for the illness.

With new radiographic shadowing for which there is no other explanation (not due to pulmonary oedema or infarction). Radiographic shadowing may be seen in the form of a lobar or patchy consolidation, loss of a normal diaphragmatic, cardiac or mediastinal silhouette, interstitial infiltrates, or bilateral perihilar opacities, with no other obvious cause.^{3,4}

Informed consent was obtained from all of these patients. All the patients were evaluated by a detailed history, a complete physical examination, a complete blood count, random blood sugar at admission, a fasting blood sugar on the next day after admission, a renal function test, a liver function test, sputum and blood cultures and sputum AFB staining. The results were analysed by SPSS software.

The Exclusion Criteria was Defined as:

- Hospital Admission within past 28 days.
- Immunosuppression, defined as chemotherapy or neutropenia $<1000/\mu\text{L}$ during the past 28 days; treatment with more than 20mg corticosteroids daily for more 14 days, HIV infection, immunosuppressive therapy after organ or bone marrow transplantation.
- Once a diagnosis of Pulmonary Tuberculosis is made such cases will be excluded from the study of clinical profile.

RESULTS: Out of the total 89 cases studied 5 where sputum positive for Tuberculosis, thus accounting for 6% of the total number of cases.

Excluding the 5 cases of Tuberculosis there were a total of 84 cases. 44 of them (52%) where males and 40 females (48%). Majority of the patients belonged to the age group of 60-69(53.6%) followed by 70-79(20%) and 50-59(19%) groups.

Of the 84 cases studied 12 persons died. The mortality was thus 14.3%. 6 of them were males and six females. The mortality rate was 15% among females and 13.6% among males. The difference was not statistically significant (p value: 0.858). The mortality among cases of age ≥ 65 y years was 17.1% and 12.2% for those below 65. The difference was not statistically significant. (p value 0.527).

29.3% of the patients were smokers, while 14.3% had alcoholism as an addiction. All the smokers and alcoholics were males. Smoking and alcoholism where not significantly associated with mortality.

53.6% of the patients had coexisting Hypertension (HTN). 35.7% had Ischemic Heart Disease (IHD). Co-existing Chronic Kidney Disease (CKD) and Chronic Obstructive Pulmonary Disease (COPD) was present in 17.9% and 14.3% respectively. Coexistent CKD and COPD had significant association with mortality, while no such association could be found for Systemic Hypertension or ischemic heart diseases.

Fever as a presenting symptom was absent in 10.7% of the patients. Cough was present in 96.4%, and 89.3% had history of sputum production. 57% had breathlessness at presentation while 53.6% had history of chest pain. Mortality in those patients who had breathlessness at presentation was 20.8%, while it was 5.6% in those without breathlessness as a symptom. (p value:0.048)

The presence or absence of other symptoms where not significantly associated with mortality.

On physical examination, 31% had tachycardia, 13.1% had hypotension, 20.6% had altered sensorium and cyanosis was present in 14.3%. On examination of the respiratory system, the most common abnormal finding was crepitations (85.7%). Tachypnoea was present in 32.1%, bronchial breath sounds in 30.9% and rhonchi in 7.1%. Among physical signs statistically significant association with mortality was present for tachycardia, hypotension, altered sensorium and tachypnoea.

Among blood investigations thrombocytopenia, increased Blood Urea Nitrogen and elevated serum creatinine had significant association with mortality. Hyponatremia, hypokalaemia, hypoalbuminemia and elevated transaminase levels did not have statistically significant association with mortality.

65.5% of the patients had a Random Blood Sugar (RBS) level $\geq 200\text{mg/dl}$ at presentation. Fasting Blood Sugar (FBS) on the next day after admission was $\geq 140\text{mg/dl}$ in 76.2%. Mortality for those with an RBS $\geq 200\text{mg/dl}$ was 18.2%, while it was 6.9% for those with an RBS $<200\text{mg/dl}$ at presentation. This difference however was not statistically significant. (p value 0.917)

Patchy consolidation (36%) was the most common finding in X-ray followed by interstitial infiltrates (32%).

Lobar consolidation was present in 19% and loss of a normal diaphragmatic, cardiac or mediastinal silhouette in 13%.

Etiological agents could be isolated in 16 cases (19%). Gram negative organisms predominated among the etiological agents isolated. All the isolates were from sputum culture and no organisms could be isolated by blood culture. *Klebsiella pneumoniae* was isolated from 6 cases, *Streptococcus pneumoniae* from 4 cases and *Staphylococcus aureus* from 3 cases. *E. coli*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* from one case each. Individual etiological agents did not have any significant association with mortality.

DISCUSSION: The study included 89 cases of Diabetic patients with Community Acquired Pneumonia (CAP) diagnosed as per the British Thoracic Society Guidelines.

Tuberculosis Presenting as CAP: Of the 89 patients 5 persons where sputum positive for Tuberculosis. Thus Tuberculosis accounted for 6% of CAP like presentation in the study. Previous studies on CAP differs on the contribution of *Mycobacterium tuberculosis* for CAP like presentation. In a Malaysian study *M. tuberculosis* was isolated in 4.9% cases of CAP.⁵ In a study by Shah et al in Srinagar no cases of *M. Tuberculosis* were reported among CAP cases.⁶ However Tuberculosis accounted for 6% of all CAP cases in a study by Acharya et al conducted in Karnataka.⁷ Thus Tuberculosis is an important differential diagnosis to be considered in CAP like presentation especially in parts of the world where prevalence of Tuberculosis is very high.

Demographics: Excluding Tuberculosis there were 84 cases of CAP studied. Among them 44(52%) where males and 40 females. 53.6% of the patients belonged to an age group of 60-69years, followed by those in the age group of 70-79 years (20%) and 50-59 years (19%).

The study did not find any significant association between age ≥ 65 years and mortality. Previous larger studies however have established that age ≥ 65 is definitely associated with a higher mortality.⁸ This finding therefore needs further verification.

Mortality: Of the 84 patients of CAP studied, 12 died. The mortality thus was 14%. As per earlier studies the mortality of CAP is between 10 and 12%.^{9,10} In an Indian study by Shah et al the mortality was 14%.⁶ Our study thus shows a comparable mortality in CAP with respect to earlier studies in this regard.

Addictions: Addictions were found in a good percentage of the patients. 32% of the patients were smokers and 14.3% where alcoholics. All these patients were males. Tobacco has been identified as an important risk factor for CAP. In a Spanish study by Almirall et al the proportion of CAP cases attributable to ever having consumed any type of tobacco was 32.4%. The odds ratio for development of Pneumonia

was 2 in smokers compared to nonsmokers.¹¹ Even passive smoking increases the risk of CAP in adults.¹²

Alcoholism is also proven to increase the risk of Pneumonia. One study has established a monotonic dose-response relationship between alcohol and pneumonia.¹³

Neither Smoking nor Alcoholism were found to have any statistically significant association with mortality in the present study. However, there are previous studies to indicate that smoking increases the risk of mortality among CAP patients.¹⁴

Comorbid Illnesses: Chronic Obstructive Pulmonary Disease was present in 14.3% of the total patients. Previous studies also have established that COPD is common comorbidity in CAP patients. The prevalence ranges from 15% to 42% in various studies.^{15,16}

COPD however did not have any significant association with mortality in my study. This also is in agreement with previous studies. In a study by Liapikou et al CAP in COPD though was associated with worse clinical features had comparable mortality with general population.¹⁷ The same was the result of another study by Snijders et al.¹⁸

Chronic Kidney Disease (CKD) was present in 17.9%. The rate of CKD among hospitalized patients with CAP is 5-10% according to previous studies.¹⁹ The high rate in the present study may be explained by the fact that Diabetic patients are more prone to develop renal diseases. CKD was a predictor of mortality in the present study. This finding is also in congruence with previous studies in this regard.^{20, 21}

In the study 53.6% where hypertensive and 35.7% had coexisting ischemic heart disease. Neither of them did have a statistically significant association with mortality.

Clinical Features: 11.7% of the patients did not have fever at presentation. This is in accordance in with other studies regarding CAP. Studies show that fever was absent in 9 to 33% of CAP cases.^{22,23} The lack of fever has been found to be a poor prognostic marker in elderly in some studies. However, no such association was found in our study.

Cough and sputum production were present in 96.4% and 89.3% of the patients respectively. This is also in concordance with previous studies on CAP.^{22, 23,24,25,26}

Chest pain was present in 53.6% and breathlessness in 57.1%. Of the presenting symptoms only breathlessness was a significant predictor of mortality.

Among the physical signs tachycardia, hypotension, tachypnoea and altered sensorium where associated with mortality, the associations being statistically significant. The presence of crepitations, cyanosis or bronchial breathing did not have any statistically significant association with mortality. These factors are well established predictors of mortality in CAP according to large previous studies.^{27,28}

Blood Components: Most patients had a blood count more than 11000/mm³ (71.4%). Only 1.2% had a count less than 4000/mm.³ Though previous studies.^{29,30} Have found association between very high or low total count and mortality in CAP no such association was found in my study.

However, a low platelet count ($<1,50,000/\text{mm}^3$) had significant association with mortality in the current study. In a study by Mirsaedi et al both thrombocytopenia and thrombocytosis was associated with increased mortality in patients with CAP.³¹

Blood Chemistry: Among the blood chemical parameters both elevated Blood Urea Nitrogen ($>30\text{mg/dl}$) and serum creatinine ($>1.6\text{mg/dl}$) was associated with increases risk of mortality, the association being significant. This is also in accordance with multiple studies in the past. CKD is a known predictor of mortality in CAP patients as discussed. Acute Kidney Injury in CAP is also associated with high mortality, as is evident in previous studies.^{32,33} In the current study however no attempt was made to separate between CKD and AKI in assessing the association with mortality with reference to elevated renal function parameters.

Hyponatremia was present in 27.4% while 19.4% had hypokalaemia. Neither of them were associated significantly with mortality. Previous studies have found significant association between hyponatremia and mortality.³⁴

Hypoalbuminemia was present in 28.6% and elevated ALT levels in 48.8% of the patients. Neither had any significant association with mortality.

Glycaemic Status: Neither a high random blood sugar at presentation ($>200\text{mg/dl}$) nor a high fasting blood sugar had a significant association with mortality. This finding differs from what was observed in previous larger studies. It has been found that for diabetic patients admitted with pneumonia hyperglycaemia was independently associated with mortality.³⁵

Aetiology: Etiological agents could be isolated in 16 of the 84 cases (19%). All the isolations were made from sputum alone and none from blood. The sensitivity of sputum culture for the isolation of etiological organisms is very low. In a study by Taylor et al showed that Sputum culture results served as the basis for the assignment of an etiological diagnosis of the pneumonia by investigators in 67% of cases.³⁶ The rate of isolation in Indian studies which used sputum culture alone is still low. In a study by Acharya et al the isolation rate was 39% while it was only 29% in another study by Shah et al.^{6,7}

Among the organisms isolated gram negative organisms predominated (56%). *Klebsiella pneumoniae* was the most common isolated organism followed by *Streptococcus pneumoniae*. Worldwide *Streptococcus pneumoniae* is considered to be the most common bacterial agent associated with Community Acquired Pneumonia.^{37,38,19} However the frequency at which *S pneumoniae* has been implicated in CAP has declined.³⁹ Other commonly encountered bacteria include *Haemophilus influenzae*, *Staphylococcus aureus*, *Moraxella catarrhalis*, *Pseudomonas aeruginosa*, and other gram-negative bacilli.^{40,41} The exact etiological profile of CAP in India is unclear. In a study from Jammu and Kashmir *P. aeruginosa* was *K pneumoniae* the most common isolated organism.⁶ In another study from

Karnataka *Streptococcus pneumoniae* (31%) was the most common agent isolated followed by, *Pseudomonas pyrogens* (15%), *Klebsiella pneumoniae* (13%).⁷ There is insufficient data regarding the etiological agents of CAP in diabetic patients. While in one study there were no differences in the etiological agents (*S. pneumoniae* being the commonest organism)⁴² Two other studies found differences in the most common etiological agents. Of these the first study from Saudi Arabia which compared the etiological agents of CAP among diabetics and non-diabetics it was found that *H influenzae* was the most common organism in both Diabetics and non-diabetics, but Diabetic patients had a preponderance for *Staphylococcal pneumoniae*.⁴³ In a similar study from Bangladesh was the most common isolated pathogen among Diabetic patients while it was *S pneumoniae* in non-diabetic patients.⁴⁴

CONCLUSIONS: In conclusion, the yield of causative organisms of Community Acquired pneumonia by routine sputum cultures is low. Among the organisms isolated gram negative organisms predominated. Tuberculosis accounted for 6% of the total CAP cases. Among the presenting symptoms breathlessness at presentation had significant association with mortality, whereas presence or absence of fever, cough or sputum production did not have any significant association with mortality. Among physical signs at examination tachycardia, tachypnoea, hypotension and altered sensorium had significant association with mortality. A low platelet count and impaired renal function was also associated with mortality. However, a high blood sugar value at presentation did not have any significant association with mortality.

The results of the study, thus calls for alternative diagnostic tests like serology for determining the etiological agents in CAP. Also, Tuberculosis should be considered as a differential diagnosis in CAP especially in diabetics.

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