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A Study of Community Acquired Pneumonia in Elderly Diabetics Admitted To a Rural Hospital in South India

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Abstract: This study aimed to find any difference in the clinical presentation, causative organisms, antimicrobial susceptibility pattern of the isolated bacteria and short term outcome in elderly diabetic and elderly non-diabetic patients admitted with community acquired pneumonia (CAP)**.** In this prospective observational study, 45 elderly diabetic and 45 elderly non-diabetic hospitalized patients with CAP were enrolled. Base line demographic data, detailed clinical and laboratory examination were done. Microbiological examinations of sputum samples were conducted. Immediate outcome was assessed in all patients. Frequency of atypical presentation, pleural effusion with multilobar infiltration and CURB-65 score were significantly higher in elderly diabetics. Renal impairment in the form of raised BUN (50.36±18.40mg/dl) was more in diabetics when compared to non diabetics (16.02±4.80) which was statistically significant (P=0.002361). More than one bacteria (polymicrobial) growth, 48.8% was seen in culture of sputum from elderly diabetics with CAP, whereas Streptococcus pneumoniae 48.8% was the most common culture isolate from sputum in elderly non Diabetics with CAP. Streptococcus pneumoniae (42.2%), Klebsiella pneumoniae (35.5%), Staphylococcus aureus (13.3%), E. coli (17.7%) and Pseudomonas aeruginosa (15.5%) and Acinetobacter (6.6%) were frequently isolated from sputum of elderly diabetics with CAP. Isolates of streptococcus, Staphylococcus, pseudomonas, Escherichia coli, Acinetobacter from diabetic patients with CAP were resistant to Co-Amoxyclav (100%), Levofloxacin (100%), Clarithromycin (100%).Significantly higher mortality rate 48.8% is seen in Elderly Diabetics with CAP, while only 6.6% is the mortality among Elderly Non Diabetics with CAP. P=0.003. Elderly diabetic patients with CAP have frequent atypical presentations; higher CURB-65 score, increased pulmonary complications and mortality. Infections are caused by more than one organism in majority of elderly diabetic males. Drug resistance to commonly used first line drugs for CAP is significantly high in elderly DM patients than NDM patients. In conclusion elderly DM patients with CAP require intensive monitoring and selection of appropriate therapeutic regimen based on anti-microbial drug susceptibility testing.
Keywords: Elderly Diabetics, CAP-Community acquired pneumonia, polymicrobial growth, and complications.

INTRODUCTION

Pneumonia is the second most frequent illness requiring hospitalization in older adults, being surpassed only by congestive heart failure [1]. Older patients are hospitalized more often and have increased mortality compared to younger population due to associated co morbid conditions like diabetes mellitus (DM), heart failure, chronic kidney disease, and decreased immunity [2]. The increased mortality among patients with pneumonia having diabetes mellitus may be due to alterations in host defence, impairment of ciliary motility and pulmonary microangiopathy [3]. However a Canadian study[4] found that history of diabetes did not prognosticate mortality in patients with pneumonia. Due to these controversies regarding association of diabetes and pneumonia, and the paucity of information regarding pneumonia in elderly population we intended to do a comparative study among diabetic and non diabetic patients admitted with pneumonia.

MATERIALS AND METHODS

This prospective observational study was carried out in the Intensive Care Unit (ICU) and Medical wards of PESIMSR, Kuppam, Andhra Pradesh between September

2013 & October 2015. The study was approved by the Ethical Review Committee of PESIMSR. Informed consent was obtained from all participants in the study. Elderly age was defined as per United Nations as more than 60 years of age. Among patients hospitalized with pneumonia, 45 elderly diabetic (EDM) and 45 elderly non-diabetic (ENDM) patients were enrolled in the study. Patients under the age of 60 years, patients having Acid Fast Bacilli (AFB) in sputum, were excluded. Demographic details of all patients were collected as per performa prepared. A detailed clinical examination was done in all study subjects. Complete blood count, biochemical tests, chest radiograph and sputum gram stain, AFB and culture & sensitivity examination were done. Community Acquired Pneumonia (CAP) was defined as the presence of an acute illness with two or more of the symptoms and signs of lower respiratory tract infection: fever, new or increasing cough or sputum production, dyspnoea, chest pain and new focal sign on chest examination and presence of infiltration in the chest radiograph on or within 48 hours of admission that was consistent with acute infection [5]. DM status was determined on the basis of current or previous biochemical diagnosis of DM according to WHO definition [6] with or without treatment with antidiabetic agents. Validated CAP severity index, CURB-65 scoring was done on admission [4]. The presence of co morbid conditions was determined by patient's reports and medical records reviews.

From each patient, sputum was collected in a wide mouth container, cultured in blood agar and MacConkey's agar media in the Microbiology Laboratory of PESIMSR Hospital. Positive growth was identified by colony characteristics and biochemical tests. Antimicrobial susceptibility pattern was determined by disc diffusion (Kirby-Bauer) method, if cultures were positive [7]. Standardized commercially available antibiotic discs of Co Amoxyclav, ceftriaxone, ceftazidime, clarithromycin, levofloxacin, meropenem and imipenem were used.

In the present study immediate or short outcome was assessed, which is defined as improvement, referral to ICU, development of complications or mortality during stay in the hospital. Improvement of the patient meant clinical wellbeing, improvement of blood chemistry & radiological improvement.

Statistical analysis was conducted using SPSS version 11 for Windows software. Parametric data were expressed in mean ± SD. Parametric data were evaluated by independent sample "t" test and categorical data were evaluated by Chi-square test as needed. Level of significance for all analytical tests was set as 0.05 and $p \leq 0.05$ was considered significant.

RESULTS

A total of 90 patients with CAP were studied over a period of 2 years. Among them, 45 were elderly diabetics and 45 were elderly non-diabetics. Mean age (±SD) of the diabetic and elderly non diabetic groups was 70.13(±11.83) years and 66.04 (±9.71) years respectively, (P=0.003018) (Table 1). Patients who were tachypnoeic (respiratory rate ≥30/min) at the time of admission were more in number in diabetic group (84.4%) than in non-diabetic group (53.3%) (p<0.001434). Hypotension was noted in more than half of the patients of diabetic group (62%) but only in 17.7% in non-diabetic group (P=0.000017). Pleural effusion (80.0%) & multilobar consolidation (84.4%) in the lungs was higher in elderly diabetics. (P<0.05) (Table I). Elevated blood urea nitrogen (BUN) & Total leucocyte count (TLC), hypothermia, tachycardia and higher CURB-65 score (86.6%) were more common in elderly diabetic patients with CAP when compared to elderly non diabetics (P<0.05) (Table 1).

Table-1: Clinical and laboratory findings in elderly diabetics and elderly non diabetics with CAP

Characteristics	Elderly diabetics	Elderly non diabetics	P value
Mean age(±SD)years	66.04(±9.71)	70.13(±11.83)	0.003018
Gender	Males 20(44%)	24(53%)	-
	Females 25(56%)	21(47%)	-
Tachypnea (RR>30)	38(84.4%)	24(53.3%)	0.001434
Hypotension	28(62.2%)	8(17.8%)	0.000017
Multilobar involvement (clinical & radiological)	38(84.4%)	8(17.8%)	<0.05
Synpneumonic effusion	36(80%)	15(33.3%)	0.00008
Atypical presentations	36 (80)	4 (9)	<0.05
Temperature (mean±SD)	96.12 ± 1^0F	101.46 ± 1^0F	<0.05
Pulse rate/min (mean±SD)	122±4	84±4	<0.05
TLC(mean)cells/cu.mm	17,000	11,260	<0.05
BUN(mean±SD)mg/dl	50.36±18.40	16.02±2.01	<0.05
CURB-65 high risk (2-5)	39(86.6%)	13(28.8%)	<0.05

P value <0.05= significant. TLC= Total leucocyte count, BUN= Blood urea nitrogen
RR= respiratory rate

Streptococcus pneumoniae was the most commonly isolated organism from sputum sample in elderly diabetics (42.2%) and elderly non diabetic patients (48.8%) with CAP. In EDM patients other causative organisms were Klebsiella pneumoniae (35.5%), Staphylococcus aureus (13.3%), E. coli (17.7%) and Pseudomonas aeruginosa (15.5%). Polymicrobial growth was noted in 48.8% of sputum cultures of EDM subjects. (Table 2).

Table-2: Isolates from sputum culture in elderly diabetics and elderly non diabetics

ORGANISMS	Diabetic	NonDiabetic
Streptococcus pneumonia	42.2%	48.8%
Klebsiella pneumonia	35.5%	6.6%
Staphylococcus Aureus	13.3%	6.6%
Acinetobacter	6.6%	2.2%
Polymicrobial	48.8%	6.6%
Escherichia .coli	17.7%	13.3%
Pseudomonas .aeruginosa	15.5%	13.3%

It was observed that in all the 22 isolates (42.2%) of Streptococcus pneumoniae the most common isolate from elderly non-diabetic patients with CAP, were sensitive to Co-amoxiclav, Ceftriaxone, Ceftazidime, Imipenem & Meropenem but only 77.8% of isolates were sensitive to Clarithromycin and Levofloxacin. (Table 3)

Table-3: Resistance pattern of isolated bacteria from sputum culture of diabetic and non diabetic elderly CAP patients to different antimicrobial agents (in %)

organism	Streptococcus		Polymicrobial		Staph aureus		Pseudomonas		E.coli		Klebsiella		Acinetobacter	
Drug	DM n=19	NDM n=22	DM n=22	NDM n=3	DM n=6	NDM n=3	DM n=7	NDM n=6	DM n=8	NDM n=6	DM n=16	NDM n=3	DM n=3	NDM n=1
CAX	100	0	100	0	100	0	100	0	100	0	100	0	100	0
CTY	100	22.2	100	0	50	0	100	0	100	0	56.2	0	100	0
LFX	100	22.2	100	0	50	0	100	0	100	0	68.7	0	100	0
CTX	57	0	57	0	0	0	0	0	50	0	12.5	0	0	0
CTZ	57	0	57	0	50	0	100	0	0	0	12.5	0	0	0
IMP	0	0	0	0	0	0	0	0	0	0	0	0	0	0
MRP	0	0	0	0	0	0	0	0	0	0	0	0	0	0

CAX=Coamoxiclav, CTY=Clarithromycin, LFX=levofloxacin, CTX=ceftriaxone, CTZ=Ceftazidime, IMP=Imipenem, MRP=meropenem, DM= diabetic, NDM= Non Diabetic.

Isolates of Klebsiella pneumoniae (35.5%) from diabetic patients with CAP were resistant to Co-Amoxyclav (100%), Levofloxacin (66.7%), Clarithromycin (55.6%), Ceftriaxone and Ceftazidime (11.1%). Among non-diabetic patients with CAP in whom Klebsiella was isolated (6.6%), the organisms were sensitive to Co-amoxiclav, Ceftriaxone and Ceftazidime.

Isolates of *Staphylococcus aureus* (13.3%) from diabetic patients with CAP were sensitive to Ceftriaxone, Imipenem and Meropenem and 50% sensitive to Ceftazidime, Clarithromycin and Levofloxacin. All isolates tested were resistant to Co Amoxyclav.

Eight *E. coli* isolates (17.7%) from diabetic patients were sensitive to Ceftazidime, Imipenem and Meropenem, 50% were sensitive to Ceftriaxone and Levofloxacin and all were resistant to Co-Amoxyclav.

The *Pseudomonas aeruginosa* isolates (15.5%) from diabetic patients with CAP were sensitive to Ceftazidime, Imipenem and Meropenem and were resistant to Co-Amoxyclav, Ceftriaxone, Clarithromycin and Levofloxacin.

Three isolates of Acinetobacter from diabetic patients were sensitive to Ceftazidime, Ceftriaxone, Imipenem and Meropenem and resistant to Co-amoxiclav, Clarithromycin and Levofloxacin.

Polymicrobial growth was isolated from the sputum of 22 (48.8%) of diabetic patient with CAP. This group of organisms were 100% resistant to Co-amoxiclav, Clarithromycin, levofloxacin and 57% resistant to Ceftriaxone and Ceftazidime but all (100%) were sensitive to Meropenem and Imipenem, 42% sensitive to Ceftriaxone and Ceftazidime.

Outcome was determined in terms of duration of hospital stay, improvement and mortality (Table 4). Mean duration of hospital stay was higher in elderly diabetics (12.3±4.98days) than in elderly non-diabetics (9.10±5.24days), which was statistically significant ($P<0.05$). Table 4 also presented the immediate outcome of two groups of study subjects. It was observed that in terms of improvement, 52.2% and 94.4% patients improved & were discharged in elderly diabetics and elderly non-diabetic groups respectively. ICU transfer in elderly diabetic patients was higher than that of elderly

non diabetic patients with CAP (73.3% vs 35.6%). The complications (62.2%) like empyema, abscess formation and mortality (48.8%) were higher in diabetic (DM) group with CAP when compared to non-diabetic (NDM) group with CAP.

Table-4: Course and outcome of CAP in elderly diabetics & elderly non diabetics

Parameter	Elderly diabetics n, (%)	Elderly non diabetics n, (%)	P value
Improved and discharged from hospital	23(52.2%)	42(94.4%)	0.000008
ICU transfer	33(73.3%)	12(35.6%)	P=0.0001
Complications	28(62.2%)	5(11.1%)	P<0.05
Mean duration of hospital stay	12.3±4.98	9.10±5.24	
Mortality	22(48.8%)	3(6.6%)	0.000008

DISCUSSION

Community acquired pneumonia is a significant health problem among the elderly. Numerous factors associated with aging, presence of comorbities, poor nutrition have been implicated for increasing incidence of pneumonia in the elderly [8]. This study was done to find difference in clinical features, etiology and outcome between DM and NDM elderly patients.

In our study, most of elderly diabetics had atypical presentations of pneumonia (80%), altered mental status and a high CURB- 65 score in comparison to elderly NDM patients. A study done by Saibal *et al*.[9] found clinical signs like tachypnoea(85%) and hypotension(46.8%) were more in elderly DM patients. Simonetti *et al*.[8] found that the clinical presentation in elderly patients with CAP is subtle and they may be afebrile.

In the present study, Streptococcus pneumonia was the most common organism isolated in both DM and NDM patients. This is in correlation with other studies [10, 8]. However Smith *et al*.[11] found that incidence of Streptococcus pneumonia is in decreasing trend due to effective vaccination, which reduces the risk of more severe and invasive disease.

Klebsiella pneumonia was isolated from 35.5% of DM patients and 6.6% of NDM patients. Klebsiella was the most common organism isolated in diabetic patients with CAP in studies done from Bangladesh [9,12]. A study by Simonetti *et al*.[8]. found increasing incidence of gram negative bacteria in CAP in elderly. In diabetics, the increasing trend of gram negative organisms in CAP may be due to reduced clearance of respiratory secretions, increased rate of colonization, adherences of gram negative bacteria and diabetic gastroparesis leading to aspiration of these bacteria to lungs [13].

Staphylococcus aureus was isolated in 13.3% of diabetic and 6.6% of nondiabetic patients. The presence of nasal carriage state of staphylococcus in diabetic patients (30%) predisposes them to pneumonia [14]. Diabetics with staphylococcal pneumonia are at an increased risk of complications including mortality [13].

In our study, more than one organism (polymicrobial) was isolated in 48.8% of elderly DM patients as compared to 6.6% in NDM patients. Presence of chronic hyperglycemia, changes in healthy micro circulation, abnormalities in ciliary motility, alteration in host defense in diabetic patients predisposes them to polymicrobial infections [13].

The gram negative bacteria isolated in our study were Escherichia coli, Pseudomonas and Acinetobacter. Aspiration of the pathogen from the colonized pharynx along with hematogenous spread accounts for gram negative organisms causing CAP. Gram negative aerobes account for approximately 10-20% of CAP and 60-80% of nosocomial pneumonia. In diabetic patients Acinetobacter pneumonia has a high rate of mortality [13].

In our study antibiotic sensitivity patterns of isolated organisms was studied. Among elderly diabetic patients the rate of resistances among all strains isolated (both gram positive and negative) showed high degree of resistance to Coamoxiclav, Clarithromycin, and levofloxacin. A study done by Rawat *et al*. [15] had similar findings and detected high antibiotic resistance rates; Amp C beta lactamases producers (32.5%), extended spectrum beta lactamases producers (40%) and metallo beta lactamases positivity (37.5%) in gram negative bacteria. In an Indian study [16] 70% of antibiotic resistant bacteria were isolated from DM patients. In diabetic patients with polymicrobial infections, it becomes a therapeutic challenge. Studies done in Kuwait [17] showed majority of isolates from mixed infections in diabetics were multidrug resistant.

In the present study, microorganisms isolated from both diabetic and non diabetic patients with CAP remained uniformly sensitive to Carbapenems. Similar findings have been noted by Saibal *et al*.[9] Carbapenems have a broad antibacterial spectrum and its usage should be limited to prevent acquisition of drug resistance. American thoracic society and infectious disease society of America do not

recommend Carbapenems as a first line of drugs in CAP [18, 19].

In our study, all patients were observed during hospital stay for development of any complications till discharge or death. Elderly diabetics had increased incidence of transfer to ICU, increased mean duration of hospital stay and mortality as compared to non diabetics. Martin *et al*. [20] found patients with diabetes had a longer duration of hospital stay and increased mortality than those without diabetes. Kornum *et al*. [3] also found type 2 diabetes mellitus and presence of hyperglycemia at admission predicted increased mortality in patients with CAP.

CONCLUSIONS

Elderly diabetic patients with CAP have frequent atypical presentations; higher CURB-65 score, increased pulmonary complications and mortality. Infections are caused by more than one organism in majority of elderly diabetic males. Drug resistance to commonly used first line drugs for CAP is significantly high in elderly DM patients than NDM patients. In conclusion elderly DM patients with CAP require intensive monitoring and selection of appropriate therapeutic regimen based on anti microbial drug susceptibility testing

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