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Bacterial pneumonia: comparison between diabetics and non-diabetics

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Abstract To determine the causative organisms, antimicrobial susceptibility, and outcome of community- and hospital-acquired pneumonia in diabetics and to compare this with non-diabetics, sputum cultures done at King Abdulaziz University Hospital in the period between January 1998 and December 1999 were reviewed. A total of 354 cases were studied, of which 125 (35%) were diabetics. Diabetic patients were older with a male predominance compared to non-diabetics. *H. influenza* was the commonest pathogen in community-acquired pneumonia (CAP) in both diabetics and non-diabetics, but there was a predominance of *Staphylococcus aureus* in diabetics compared to non-diabetics. Gram-negative bacilli were the commonest pathogens in hospital-acquired pneumonia (HAP) in both diabetics and non-diabetics. Ampicillin, co-amoxyclav, flouroquinolones, second-generation cephalosporins and erythromycin were used empirically in CAP while aminoglycosides, fluoroquinolones and imipenem were used in HAP in both diabetics and non-diabetics. No significant difference in mortality was found between diabetics and non-diabetics, for either CAP or HAP

Key words Pneumonia · Diabetics · Microorganism · Mortality · Treatment

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Introduction

Diabetes mellitus (DM) is often identified as an independent risk factor for developing respiratory tract infections. Diabetic patients are predisposed to colonization and pneumonia because of disease-associated impairment in host defensive functions [1, 2]. Also, they are more liable to develop complications such as bacteremia, delayed resolution, and recurrent pneumonia [3]. Pneumonia is the leading cause of hospitalization and mortality [4]. Several studies have shown that the use of appropriate antimicrobial therapy can improve outcome with survival rate reaching 70%–80% [2]. The aim of this study was to determine the causative organisms, antimicrobial susceptibility, and mortality of community- and hospital-acquired pneumonia in diabetics, and to report on any difference between them and non-diabetics.

Patients and methods

King Abdulaziz University Hospital (KAUH) is a 400-bed teaching hospital in Jeddah, the western province of Saudi Arabia. For this study, I reviewed sputum cultures of patients above the age of 14 years, performed in the period between January 1998 and December 1999. Sputum cultures positive for bacteria were analyzed, although those positive for acid-fast bacilli were excluded.

Sputum samples were processed by gram stain and culture. Only samples showing greater than 25 polymorphonuclear leucocytes and less than 10 squamous epithelial cells per low-power field were cultured [5]. Cultures were performed on 5% sheep blood agar (oxoid) and chocolate agar. The plates were incubated at 37° C for 24 h in 5% CO2 atmosphere. Bacteria isolated from sputum culture were considered presumptive etiologic pathogens if they were compatible with the predominant organisms present on gram stain and if cultured in abundant growth or in pure growth. The isolated organisms were identi-

fied using a standard method [6]. Gram negative aerobes were identified using API 20 E (Analytab, Biomeriuex, France). Pneumonia was diagnosed according to the American Thoracic Society criteria [7].

Cases were classified into hospital-acquired pneumonia (HAP) if the sputum culture was first positive more than 72 h after admission, excluding any infection that was incubating at the time of admission. Community-acquired pneumonia (CAP) was defined by a positive sputum culture less than 72 h after admission or by a positive culture performed as outpatient.

For each patient with pneumonia, I recorded age, gender, outcome, type of organisms isolated and their antimicrobial susceptibility, empiric use of antimicrobial agents, presence of DM (diagnosed according to WHO criteria [8]), treatment regimen for DM, and degree of control (good control was defined as a glycated hemoglobin (HbA1c) <7%).

The in vivo antibacterial susceptibility of the isolated bacteria was determined by the disk diffusion method according to the guidelines of the National Committee for Clinical Laboratory Standards (NCCLS) [9]. Briefly, 5 representative colonies taken from the purity plates were suspended in sterile saline and diluted to a no. 5 McFarland turbidity standard. A sterile cotton swab dipped into this inoculum was used to streak Mueller-Hinton agar supplemented with 5% sheep blood and chocolate agar (Baltimore Biological Laboratories). The antibiotic disks were then applied onto the surface of the agar plates using a disk dispencer. The inoculum agar plates were incubated at 37° C for 24 h; after incubation the diameter of the zone of inhibition was measured and the results were interpreted in accordance with the criteria recommended by NCCLS.

Patients were divided into two groups according to the presence or absence of DM. Statistical analysis was done using Statistical Package for Social Sciences (SPSS) computer software and p values less than 0.05 were considered significant.

Results

From a total of 2880 sputum cultures done during the study period, 354 (12%) cases with a positive culture were included in the study. Of these, 125 (35%) were diabetics, having a mean age of 59.4±14.0 years vs 53.7±20.6 years

Table 1 Pathogens isolated 26 diabetics and 59 non-diabetics with community-acquired pneumonia

Pathogen	Diabetics n (%)	Non-diabetics n (%)	p value
Streptococcus pneumoniae	1 (4)	3 (5)	0.3
Staphylococcus aureus	6 (23)	6 (10)	0.02
Haemophilus influenzae	13 (50)	31 (53)	0.8
Moraxella catarrhalis	2 (8)	8 (14)	0.6
Pseudomonas spp.	3 (12)	5 (8)	0.7
Klebsiella spp.	1 (4)	3 (5)	0.6
Enterobacter spp.	–	1 (2)	0.5
Acinetobacter spp.	–	1 (2)	0.5
Streptococcus viridans	–	1 (2)	0.5

Table 2 Pathogens isolated from 99 diabetics and 170 non-diabetics with hospital-acquired pneumonia

Pathogen	Diabetics n (%)	Non-diabetics n (%)	p value
Streptococcus pneumoniae	3 (3)	1 (1)	0.1
Staphylococcus aureus	14 (14)	27 (16)	0.6
Haemophilus influenzae	13 (13)	26 (15)	0.9
Moraxella catarrhalis	6 (6)	9 (5)	0.4
Pseudomonas spp.	30 (30)	43 (25)	0.5
Klebsiella spp.	6 (6)	15 (9)	0.5
Enterobacter spp.	9 (9)	14 (8)	0.4
Proteus spp.	2 (2)	3 (2)	0.7
Escherichia coli	2 (2)	8 (5)	0.4
Enterococci	1 (1)	–	0.1
Citrobacter spp.	1 (1)	3 (2)	0.7
Acinetobacter spp.	6 (6)	7 (4)	0.2
Others[a]	6 (6)	14 (8)	0.3

Table 3 Antibiotic sensitivity of some isolates in community and hospital acquired pneumonia

Antimicrobial agent	Pathogens, n (%)											
	Community acquired						Hospital acquired					
	S. pneumoniae		*H. influenzae*		*Moraxella catarrhalis*		*S. aureus*		*Pseudomonas* spp.		*Enterobacter* spp.	
	D n=1	ND n=3	D n=13	ND n=31	D n=2	ND n=8	D n=14	ND n=27	D n=30	ND n=43	D n=9	ND n=14
Penicillin	–	1 (33)	–	–	1 (50)	1 (13)	–	4 (15)	–	–	6 (67)	2 (18)
Ampicillin	1 (100)	3 (100)	9 (70)	23 (74)	1 (50)	8 (100)	2 (14)	–	2 (7)	–	–	1 (7)
Co-amoxyclav	1 (100)	3 (100)	9 (70)	23 (74)	2 (100)	8 (100)	2 (14)	–	2 (7)	1 (2)	2 (22)	1 (7)
Ciprofloxacin	–	–	10 (77)	26 (84)	1 (50)	8 (100)	2 (14)	–	24 (79)	30 (70)	7 (78)	11 (79)
Cefuroxim	1 (100)	3 (100)	12 (92)	30 (97)	1 (50)	8 (100)	2 (14)	–	1 (4)	–	2 (22)	2 (14)
Erythromycin	1 (100)	3 (100)	6 (46)	19 (60)	2 (100)	7 (86)	5 (36)	18 (67)	–	1 (2)	4 (44)	3 (21)
Oxacillin	1 (100)	3 (100)	–	–	–	–	9 (64)	22 (81)	–	–	–	–
Vancomycin	–	3 (100)	–	1 (3)	–	–	12 (86)	18 (67)	–	–	–	2 (14)
Azterionam	–	1 (33)	4 (31)	17 (55)	–	–	–	–	20 (67)	25 (59)	2 (22)	7 (50)
Ceftazidim	–	–	1 (8)	–	–	–	–	–	21 (71)	29 (68)	2 (22)	2 (14)
Ceftriaxon	–	3 (100)	10 (77)	27 (87)	–	1 (13)	–	–	8 (27)	9 (21)	2 (22)	7 (50)
Gentamycin	–	1 (33)	–	1 (3)	–	–	2 (14)	8 (30)	27 (79)	36 (84)	7 (78)	7 (50)
Amikacin	–	–	–	–	–	–	–	–	25 (82)	36 (85)	9 (100)	14 (100)
Imepenum	–	–	1 (8)	2 (6)	–	–	–	–	15 (50)	29 (68)	9 (100)	13 (93)
Pipracillin	–	–	–	–	–	–	–	–	22 (73)	30 (70)	2 (22)	7 (50)

D, Diabetics; *ND*, Non-diabetics; *co-amoxyclav*, a combination of amoxycillin and clavulanica acid

for the non-diabetics (p=0.006). Male predominance was noticed in the diabetic group: the male:female ratio was 3:1 vs 1.2:1 for non-diabetics (p<0.001). Most of the diabetic patients were using oral hypoglycemia agents for blood glucose control (n=75, 60%); of the remainder, 38 (30%) were on insulin, 7 (6%) on diet, and 5 (4%) on combination therapy. There were 86 (69%) diabetics who were poorly controlled.

Of the 354 patients with a positive sputum culture, 85 (24%) were diagnosed as having CAP, while the remaining 269 patients (76%) had HAP. Among the patients diagnosed with CAP, 26 (31%) were diabetics while among those with HAP there were 99 diabetics (37%).

Empiric antimicrobial treatment was in use at the time of specimen collection in 81 (95%) of patients with CAP vs. 231 (86%) of patients with HAP (p=0.2). Most of the patients were started on two empiric antimicrobial agents: 72 of 81 (85%) in CAP and 212 of 231 (92%) in HAP (p=0.09). *Haemophilus influenzae* was the commonest cause of CAP in both diabetics and non-diabetics (Table 1). There was a predominance of infections by *Staphylococcus aureus* among diabetics with CAP compared to non-diabetics. Gram-negative bacilli were the commonest cause of HAP in both diabetics and non-diabetics (Table 2). Ampicillin, co-amoxyclav (a combination of amoxycillin and clavulanica acid), flouroquinolone, second-generation cephalosporins and erythromicin were used empirically in CAP, while aminoglycosides, flouroquinolones and impenem were used in HAP in both diabetics and non-diabetics (Table 3).

There were 159 reported deaths among the pneumonia patients. No significant difference in mortality was found between diabetics and non-diabetics for either type of pneumonia (Table 4).

Discussion

Pneumonia is one of the most common infectious diseases and it is the sixth leading cause of death in the United States [10]. It is clear from our study that almost one-third of the cases admitted with bacterial pneumonia were diabetics. Diabetics have alterations of pulmonary host defenses [11] which make them more susceptible to infection. Advanced age is also associated with immune changes that increase the risk of pneumonia [12]. In this study, diabetics were older than non-diabetics; therefore they were at increased risk for pneumonia also for their age.

Several studies have shown that *S. pneumoniae* is the most common pathogen isolated in CAP [13–15]. Other organisms isolated in CAP include *H. influenzae*, atypical bacteria, *Moraxella catarrhalis*, *S. aureus*, and gram-negative bacilli [16–18]. Interestingly, this study showed that *H. influenzae* was the commonest pathogen isolated in CAP in both diabetics and non-diabetics, while *S. pneumoniae* was isolated in a smaller percentage. Some studies have found that sputum cultures were negative in about 50% of patients with pneumococcal bacteremia, and that the rate of isolation increases when more invasive methods are used for obtaining specimens, such as transtracheal aspiration which eliminates contaminating oropharyngeal flora [16, 19]. Due to the retrospective design of this study, invasive methods for obtaining sputum specimens were not used for all the cases. Another possible reason for the low isolation rate of S. Pneumoniae is the use of antimicrobial agents at the time of specimen collection [20]. The majority of these patients were started on empiric antimicrobial agents.

Table 4 Mortality among patients diagnosed with pneumonia in the 2-years period 1998–1999, according to comorbidity with diabetes mellitus

	Patients, n	Mortality, n (%)
CAP		
Diabetics	26	8 (31)*
Non-diabetics	59	12 (20)
HAP		
Diabetics	99	53 (54)**
Non-diabetics	170	86 (51)
Total	354	159 (45)

CAP, community-acquired pneumonia; *HAP*, hospital-acquired pneumonia

S. aureus is a major pathogen of CAP in diabetics compared to non-diabetics. This observation can be attributed to the high nasal carriage rate of *S. aureus* in diabetics where it reached 30% compared to 11% in healthy individuals [21], The rate of nasal carriage of *S. aureus* is directly related to the glycosylated hemoglobin (HbA_{1c}) level [21].

The prevalence of atypical pathogens was not identified in this study because results were reviewed retrospectively. According to the American Thoracic Society (ATS) [22], testing for atypical pathogens should be performed in selected settings which were not possible in the present study.

Garibaldi [10] reported a mortality of 25% among patients with CAP requiring hospitalization. This is not far from that found in the present study, with no significant difference between diabetics and non-diabetics. For every 1000 hospital admissions, there are 5–10 cases of HAP, and the incidence increases as much as 6- to 20-fold in patients who are mechanically ventilated [1, 2]. The bacterial pathogens most frequently associated with HAP are gram-negative bacilli and *S. aureus* [23–25]. HAP is the leading cause of death among all hospital-acquired infections, with a mortality rate of 20%–50% [1, 25]. In the present study, mortality due to HAP was 54% in diabetics and 51% in non-diabetics.

The ATS recommends to use empiric treatment for pneumonia as pathogen identification can be difficult [26]. We found that co-amoxyclav, ampicillin, flouroquinolones, second-generation cephalosporins, and erythromycin were used empirically to treat CAP in both diabetics and non-diabetics, while in severe cases of CAP (especially in poorly controlled diabetics Staphylococcus can be combatted with cloxacillin or vancomycin. In HAP, aminoglycosides, flouroquinolones, and imipenem were used in both diabetics and non-diabetics, which is in agreement with what has been reccommended by others [10, 27–31].

One of the limitations of microbiological diagnosis of pneumonia is the lower prevalence of positive sputum cultures due to either the use of empiric antimicrobial agents at the time of specimen collection or the failure to use of invasive methods for obtaining sputum specimens. Due to the retrospective design of this study, these limitations could not be avoided. Prospective studies are needed in this regard, as the proper use of antimicrobial agents will decrease mortality in both diabetics and non-diabetics.

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