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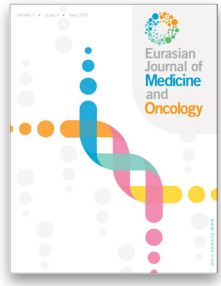

Research Article

Pneumonia in Patients with Diabetes Mellitus: A Single-Center Experience

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Abstract

Objectives: The rate of infection and hospitalization due to infection as well as the risk of mortality are greater in patients with diabetes mellitus (DM). The aim of the present study was to determine the frequency of pneumonia, length of hospital stay, rate of patients requiring hospitalization in the intensive care unit (ICU), and rates of discharge or mortality among patients hospitalized due to DM in internal medicine inpatient clinics.

Methods: A total of 399 patients with DM (170 males and 229 females) were enrolled in the study. The frequency of pneumonia in the group was determined, and the length of hospital stay, rate of patients requiring hospitalization in ICU, discharge rate, mortality, and factors related to mortality were evaluated, comparing those with pneumonia and DM and those with DM alone.

Results: The frequency of pneumonia among the DM patients was 12% (48 cases). Hypertension was the most common comorbidity in the 2 groups (31.8% and 32.8%, respectively, among those with pneumonia and DM and those with DM alone). The rate of discharge, mortality, and the rate of patients transferred to the ICU was 92% (367 cases), 4% (16 cases), and 4% (16 cases). The length of hospital stay, discharge rate, mortality, and the rate of patients transferred to the ICU was similar between the patients with and without pneumonia ($p>0.05$ for each), but the length of hospital stay and the rate of patients transferred to the ICU was higher among patients with pneumonia ($p<0.05$ for each).

Conclusion: About 10% of diabetic patients were treated for pneumonia. Infection in patients with DM leads to a longer hospital stay and fewer hospital discharges. The Infection-related disease burden leads to serious morbidity in patients with DM, and therefore, longer hospital stay and more patients transferred to ICU.

Keywords: Diabetes mellitus, morbidity, mortality, pneumonia

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Patients with diabetes mellitus (DM) have an increased propensity to develop infections. It is a known fact that the risk of hospitalization and mortality is greater in diabetic patients. Factors such as an impaired immune response, vascular insufficiency, sensory peripheral neuropathy, autonomic neuropathy, serious infections, community-acquired pneumonia (CAP), urinary tract infection, inclination to necrotizing bacterial or fungal skin and mucosal colonization, and surgical wound infections render diabetic patients more sensitive to infection related to hyperglycemia.[1] Hospitalization risk due to pneumonia has been reported to be 26% higher in diabetic cases than in control cases, and the risk increases even more in patients with longer duration of diabetes and in patients with poor glycemic control.[2] There is a dramatic increase in the frequency of diabetes in parallel with the increase

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in obesity and metabolic syndrome, which are considered to be a global epidemic. This leads to an increase in the frequency of other infections, particularly pneumonia, in the diabetic population, which is already susceptible to infection. The primary outcome of this study was a determination of the frequency of pneumonia in diabetic patients admitted to internal medicine clinics and a comparison with literature information. A secondary outcome was an analysis of the relationship between diabetes and variables such as mortality, duration of hospitalization, and intensive care need.

Methods

Study Patients

Patients aged 18 and over who were admitted to the Internal Medicine Department of the Ministry of Health İstanbul Medeniyet University Göztepe Training and Research Hospital with a diagnosis of diabetes between June 2009 and June 2013 were included in the study consecutively and retrospectively. Approval of institutional ethics committee was received for the study (date: June 25, 2013; approval no.: 2013/0010). The principles of the Declaration of Helsinki were observed during the study. Inclusion criteria were a diagnosis of diabetes and pneumonia, respectively, according to the International Classification of Diseases code in the patient file. Exclusion criteria from the study were as follows: aspiration pneumonia, possibility of ventilator-associated pneumonia, administration of immunosuppressive therapy, presence of immunosuppressive disease (asplenia, AIDS, organ transplantation, hematological malignancies), and pregnancy.

Study Design

This study was a retrospective descriptive case series study. Patient data regarding age, sex, smoking and alcohol usage, duration of hospital stay, presence of diabetes, treatment received for diabetes (oral antidiabetics and/or insulin), and diagnosis of comorbid diseases (hypertension, chronic obstructive pulmonary disease, chronic renal disease, cardiac insufficiency, dementia, chronic stroke, neoplasia, asthma, peripheral artery disease), as well as clinical, radiological, and laboratory data and outcomes (discharge, referral to intensive care, death) of all participants were recorded from their files. The study's primary outcome was a determination of the frequency of pneumonia in diabetic patients. Furthermore, the mean duration of hospitalization; rates of discharge, mortality, and referral to the intensive care unit (ICU); and the frequency of comorbidities and infections in patients hospitalized with diagnosis of diabetes were determined.

Statistical Analysis

Statistical analyses were conducted using SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was employed to determine if the distribution of variables was appropriate prior to analysis. Continuous variables were expressed as mean±SD. Classifiable data were analyzed by using the chi-square test, and numerical data were analyzed using Student's t-test and the Mann-Whitney U test. Independent factors affecting mortality were demonstrated in logistic regression analysis and significance levels, in addition to estimated relative risk (odds ratio [OR] and 95% confidence interval [CI]) values. Results obtained with $p<0.05$ in 95% CI were accepted as meaningful in terms of statistical significance.

Results

A total of 399 patients (170 males constituting 42.6% and 229 females constituting 57.4%) were included and evaluated in the study. Pneumonia was detected in 12% of these patients. The mean age of all of the patients was 68 years (range: 56–78 years), while the mean age of those with pneumonia was 73 years (range: 68–81 years), and the mean age of non-pneumonia patients was 67 years (range: 54–76 years). The mean age of the diabetic patients with pneumonia was significantly higher ($p=0.001$). The mean length of stay in hospital was 6 days (range: 4–9 days); there was no significant difference between the patients with and without pneumonia ($p>0.05$). About 4% of diabetic patients admitted to the ICU for any reason died, while 4% were referred to ICU and 92% were discharged. The demographic characteristics, outcomes, and infections of diabetic patients are provided in Table 1. Glycated hemoglobin (HbA1c) level in those who died was 6.9±1.5%, while HbA1c in cases referred to ICU was 6.6±1.3% and level was 9.6±3.2% in the discharged group. HbA1c level in cases of death and referral to ICU was statistically significantly lower compared to discharged patients ($p=0.009$). The most frequent infection observed in diabetic patients in the internal medicine clinics was pneumonia, with a rate of 12%. This was followed by urinary tract infection, with a rate of 6.8%. Concomitant comorbidities in diabetic patients are provided in Table 2. The most frequent comorbidity observed in diabetic patients was essential hypertension, with 131 patients (32.8%). The intensive care referral rate was significantly higher in diabetic pneumonia patients ($p<0.05$); however, the mortality rate was similar between patients with diabetic pneumonia and those without diabetic pneumonia ($p>0.05$). The discharge rate was lower

Table 1. Demographic and clinical characteristics of study subjects

	Discharged	Death	ICU	p
Age, year	63±16	67±8	70±12	0.07
Gender (%)				
Male	157 (40)	5 (1.3)	8 (2)	0.54
Female	210 (53)	11 (2.8)	8 (2)	
Length of hospital stay, days	7.5±6.5	4.4±3.7	4.1±2	**0.001**
HbA1c (%)	9.6±3.2	6.9±1.5	6.6±1.3	0.009
Infectious disease				
Pneumonia	36 (34)	2 (1.9)	6 (5.7)	0.31
Urinary tract infection	24 (22.6)	1 (0.9)	2 (1.9)	0.56
Diabetic ulcer	9 (10.2)	0	0	0.36
Celulitis	5 (4.7)	0	0	0.38
COPD exacerbation	4 (4.5)	0	0	0.65
Diarrhea	5 (4.7)	0	1 (0.9)	0.65
Sepsis	2 (1.9)	5 (4.7)	1 (0.9)	**0.001**
Acute cholangitis	1 (0.9)	0	0	0.98
Acute peritonitis	2 (1.9)	0	0	0.81

COPD: Chronic obstructive pulmonary disease; HbA1c: glycated hemoglobin; ICU: intensive care unit.

Table 2. Comorbidites of diabetes mellitus patients

	n	%
Hypertension	131	32.8
COPD	32	8
Coronary artery disease	55	13.8
Congestive heart failure	25	6.3
Chronic renal failure	47	11.8
Cerebrovscular disease	6	1.5
Chronic liver disease	4	1

COPD: Chronic obstructive pulmonary disease

in patients with diabetic pneumonia (p<0.05) (Table 3). Factors that were not revealed to be significant in multivariate analysis were age, gender, presence chronic renal failure (CRF), level of urea, aspartate aminotransferase (AST), alanine aminotransferase (ALT), HbA1C, and C-reactive protein (CRP) (p>0.05).

Discussion

Approximately 1 of 10 of patients admitted to the internal medicine clinic with diabetes in this study was treated for pneumonia. It was revealed, however, that pneumonia did not have an effect on mortality, although it does lead to longer hospitalization and increased referral to ICU. It is known that the incidence of infection is greater in diabetic patients. Diabetes is a significant risk-raising factor for lower respiratory tract, urinary tract, and bacterial skin and mucous membrane infections.[3] Shah et al. observed that diabetes increased the risk of pneumonia in a cohort study performed in Canada.[4] Pneumonia was detected in 12% of 399 diabetic patients in our study. It was followed by urinary tract infection at a rate of 6.8%. Type 2 diabetes increased the risk of hospitalization for pneumonia by 1.23 times, while type 1 diabetes increased the risk of hospitalization for pneumonia by 4.43 times, compared with a control group.[2]

Data regarding the effect of diabetes on the duration of pneumonia are conflicting.[5–7] Patients among the diabetic group with pneumonia in our study had a significantly longer hospitalization time and greater rate of referral to the ICU compared with patients without pneumonia (p<0.05). However, there was no difference with respect to mortality rate (p>0.05). These results may have been due to the

Table 3. Clinical outcome of patients

	All (n=399)		Pneumonia (+) (n=48)		Pneumonia (-) (n=351)		p
	n	%	n	%	n	%	
Discharged	367	92	40	83.3	327	93.2	**0.02**
Death	16	4	2	4.2	14	4	0.95
ICU	16	4	6	12.5	10	2.8	**0.001**

ICU: Intensive care unit

fact that the average age of the patients with pneumonia was higher. We found that factors affecting mortality in diabetic patients such as age, gender, presence of CRF, and level of urea, AST, ALT, CRP and HbA1c were not statistically significant. On the other hand, in numerous studies examining etiology, clinical features, outcomes of CAP in diabetic patients, age, presence of gram-negative pneumonia, septic shock table result upon admission, and bacteremia mortality have been found to be associated in multivariate analysis.[7] Chronic pulmonary disease, chronic heart disease, hypertension, male gender, CRP and urea level were found to be factors affecting mortality in multivariate analysis in our study. However, the presence of diabetes was not found to be associated with mortality. It has been reported that diabetes history does not predict mortality in hospital, though hyperglycemia prolongs stay in hospital, and increases likelihood of morbidity, mortality.[8] Umpierrez et al. found that that glucose level is a more important prognostic factor than DM.[9] Similarly, a comprehensive study of the prognosis of CAP found that plasma glucose was an independent risk factor for mortality, while diabetes was not.[10] Moreover, a correlation between the severity of pneumonia and non-diabetic hyperglycemia was detected.[11] No statistically significant difference was found in death rate when non-diabetic patients were compared with diabetic patients in our study. This may indicate that hyperglycemia level is more important than the presence of diabetes. HbA1c percentage in patients who died, were referred to the ICU, and those discharged, was found to be 6.9±1.5, 6.6±1.3, and 9.6±3.2, respectively, in this study population. HbA1c level in patients who died and those referred to the ICU were statistically significantly lower compared with discharged patients. This may be related to the fact that intense control of blood glucose level increases the frequency of hypoglycemia, as well as increased mortality.[12–14]

There are several limitations to our study. First and foremost, it is a retrospective study and does not include data such as duration of the presence of diabetes or organ damage of the patients, which may have had an effect on mortality. Furthermore, diabetes subtypes, namely type 1 DM and type 2 DM, were not differentiated and no association was made between mechanisms such as insulin resistance to infection or metabolic syndrome and pneumonia. In addition, there was no differentiation made between patients with diabetes who received a pneumococcal vaccine and those who did not.

In conclusion, the incidence of pneumonia in patients with diabetes (399 cases), was 12% (48 cases). Sixteen (4%) of 399 diabetic patients died, and 16 patients (4%) were referred to intensive care. It was observed that the duration of hospitalization was longer for diabetic pneumonia patients. Similarly, the rate of diabetic pneumonia patients referred to intensive care was significantly higher compared to non-diabetic pneumonia patients. However, mortality rates were similar. More extensive and prospective studies and more consistent information are required with regard to the presence of diabetes in the clinical course of infectious diseases.

Disclosures

Ethics Committee Approval: The study was approved by the Local Ethics Committee (date: June 25, 2013; approval no.: 2013/0010).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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