

The effect of sociodemographic and clinical features on mortality in patients with diagnosis of aspiration pneumonia

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ABSTRACT

OBJECTIVE: The aim of this study was to evaluate the sociodemographic and clinical characteristics of patients hospitalized with aspiration pneumonia in internal medicine clinics, and to determine the incidence and parameters of mortality among these patients.

METHODS: Patients over the age of 18 years who were hospitalized in clinics of internal medicine between January 1, 2010 and January 1, 2013 (115 male, 89 female; mean age: 77±13 years; patients aged 65 years and over, 88.2%; average duration of hospitalization, 11±9 days) were evaluated retrospectively and consecutively. The incidence of mortality, nutritional status at admission, comorbidity frequency, haematological and biochemical data and their relationship with mortality were evaluated.

RESULTS: At admission, 85% of the patients were fed through oral route, while 15% of them were fed through PEG. There was no relation between nutritional status of the patients (oral, nasogastric tube or PEG) at admission, and development of aspiration pneumonia. Commonly seen comorbidities were dementia (49%), hypertension (43%), cerebrovascular accident (42%), and diabetes mellitus (31%) respectively. The mortality rate was 24.5% (in first three days, 56%). A correlation was found between mortality and increase in neutrophil/lymphocyte ratio (NLR) and increased uric acid rate (for both $p<0.05$).

CONCLUSION: In this study, the mortality rates among patients diagnosed with aspiration pneumonia was found to be increased. The high number of geriatric patients and comorbidities might have played a role in this situation. Neutrophil/lymphocyte ratio (NLR) and uric acid levels in patients with aspiration pneumonia might be evaluated as factors related to mortality.

Key words: Aspiration pneumonia; comorbidity; internal medicine clinic; mortality.

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Aspiration pneumonia is an alveolar infection stemming from inhalation of the pathogenic material in the oropharynx [1]. Demographic factors as advanced age, male gender, comorbidities as dysphagia, diabetes mellitus, severe dementia, deletion of angiotensin -converting enzyme-1, genotype, bad oral hygiene, Parkinson's disease, malnutrition medications as antipsychotics, proton pump inhibitors, and ACE-inhibitors have been demonstrated as risk factors for aspiration pneumonia [2].

Aspiration pneumonia constitutes 5-15% of community-acquired pneumonia, and it is still responsible for 20% of community-acquired pneumonia among elder people, and ranks second among the most frequently seen nosocomial infections after urinary tract infections [1, 3, 4]. Actual incidence of aspiration pneumonia may be higher. As observed by many authors, indeed 50% of healthy individuals, and 70% of the elder population have aspirated something during their sleep [5, 6]. Aspiration pneumonia is one of the most important causes of hospitalization especially of elder people, those with neurological problems or individuals staying in nursing homes.

In the community, the number of geriatric patients increase in parallel with prolongation of mean life span. In addition, higher incidence of comorbidities as dementia, stroke, Alzheimer's disease, diabetes, and hypertension also increases rates of hospitalization. The objective of this study was to evaluate mortality, nutritional status, sociodemographic characteristics, and factors effective on mortality.

MATERIALS AND METHODS

Medical files of the patients aged 18 and over who were hospitalized in the Clinics of Internal Medicine of Istanbul Medeniyet University Goztepe Training and Research Hospital between January 1, 2010, and January 1, 2013 with the diagnosis of pneumonia were retrieved from otomation system, and patients' archives of the hospital and analyzed, and included in the study. The approval (date: January 24, 2013; decision #: 30/H) of the Ethics Committee of Istanbul Medeniyet University Goztepe Training and Research Hospital was obtained.

During the study period, principles of Helsinki Declaration were taken into consideration.

Study design: On patient registration forms, age, gender, diagnosis of admission in the Service of Internal Medicine, nutritional status, duration of hospitalization, clinical, and laboratory information, and prognoses (rates of discharge or exitus), comorbidities (chronic obstructive pulmonary disease, diabetes mellitus, heart failure, hypertension, chronic renal disease, chronic ischemic heart disease, atrial fibrillation, dementia, Parkinson's disease, and cerebrovascular disease) were recorded. Mortality rates, nutritional status, frequency of comorbidities, hematological, and biochemical data, and their relation with mortality were evaluated. Data of the patients discharged, and exited were also compared.

Diagnosis of aspiration pneumonia: Despite lack of defined, and precise diagnostic criteria diagnosis of aspiration pneumonia was made based on witnessed event of aspiration or strong evidence of suspect aspiration (abnormal swallowing function, and dysphagia) and confirmation of findings of pulmonary inflammation [1].

Laboratory parametres: From patients' files, whole blood counts, biochemical data (glucose, urea, uric acid, creatinine, sodium, potassium, phosphorus, aspartate aminotransferase, alanine transferase, total bilirubin, indirect bilirubin, gamma glutamyl transferase, alkaline transferase, lactate dehydrogenase, cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol, creatinine kinase, CK-MB, iron, iron-binding capacity, amilase, lipase, protein, albumin, sedimentation rate, C-reactive protein, aPTT, INR, HbA1c, TSH, freeT3, free T4, ferritin, folic acid, and vitamin B12) were recorded.

Statistical analyses were performed using SPSS for Windows V.21.0 program. Before analyses, fitness of variables to normal distribution pattern was analyzed using Kolmogorov- Smirnov test. Continuous variables were expressed as mean $\pm$ SD. Classified and numerical data were analyzed using chi-square test, Student's t test, and Mann-Whitney U test, respectively. Independent factors effective on mortality, and results of logistic regression analysis were expressed as levels of significance, and

estimated relative risks (odds ratio-OR), and 95% confidence intervals (95% CI) Results at a level of significance of $p < 0.05$ within 95% confidence interval were accepted as statistically significant values.

RESULTS

A total of 204 (115 male, and 89 female) patients diagnosed as aspiration pneumonia with a mean age of 77 ± 13 years, and duration of hospitalization of 11 ± 9 days were included in the study. Median mortality rate was 24.5 percent. Eighty-eight percent of the patients were older than 65 years of age. Nearly 56% of the deaths occurred within the first 3 days. At first admission, the patients were receiving their nutrients through oral route ($n=174$; 85%) or percutaneous endoscopic gastrostomy (PEG) ($n=30$; 15%). Distribution of demographic data, and comorbidities are given in Table 1. The most frequently associated comorbidities were dementia (49%), hypertension (43%), cerebrovascular events (42%), and diabetes mellitus (31%). Hospitalization rates were higher in discharged patients when compared with exited patients ($p=0.001$).

Laboratory data are given in Tables 2, and 3.

When compared with survived patients, in exited patients neutrophil/lymphocyte ratio, urea, uric acid, ALP, LDH, phosphorus, prothrombin time were relatively higher (for all, $p < 0.05$), while TSH, and free T3 levels were lower (for all, $p < 0.05$).

In a multivariate logistic regression analysis where factors effective on mortality were evaluated, increased uric acid levels, and neutrophil/lymphocyte ratios predicted mortality. In these patients uric acid levels, and neutrophil/lymphocyte ratios were higher in exited patients when compared with those discharged. Uric acid levels higher than 5.35 mg/dL (AUC=0.620) have 61.3% sensitivity, and 62% specificity in predicting mortality, however neutrophil/lymphocyte ratios over 10.63 (AUC=0.608) have 44% sensitivity, and 74% specificity in predicting mortality.

DISCUSSION

In this study, 88.2% of the cases with aspiration pneumonia were over 65 years of age, and at admission the patients were fed via oral (85%) route or PEG (15%). Development of aspiration pneumonia had no effect on the patients' nutritional

TABLE 1. Demographic characteristics and comorbidities of the patients

	Total (n=204)		Discharged (n=154)		Exited (n=50)		p
	n	%	n	%	n	%	
Age, years	77±13		78±13		75±16		NS
Gender, M/F	115/89		89/65		26/24		NS
Duration of hospitalization, days	11±9		12±7		7±12		0.001
Comorbidities							
Renal diseases	14	6.6	8	4	6	3	NS
Diabetes mellitus	64	31	42	21	32	15	NS
Hypertension	91	45	65	33	26	13	NS
Congestive heart failure	27	13	19	9	18	5	NS
Atrial fibrillatiion	26	12	14	7	12	6	NS
Chronic ischemic heart disease	34	17	24	12	10	5	NS
Dementia	104	49	83	42	21	11	NS
Parkinsonism	20	10	18	9	2	1	NS
Cerebrovascular disease	89	42	69	35	20	10	NS

TABLE 2. Hematological parameters of patients with aspiration pneumonia

	Total (n=204)	Discharged (n=154)	Exited (n=50)	p
Hematocrit (%)	34.5±7.5	34.7±8.1	33.8±5.5	NS
Platelet (10 ³ /mm ³)	284±140	292±142	258±126	NS
Leukocyte (10 ³ /mm ³)	13447±6180	13200±6150	14200±6275	NS
Neutrophil (10 ³ /mm ³)	11380±7670	11196±8160	11950±5960	NS
Lymphocyte (10 ³ /mm ³)	1300 (900-1800)	1300 (900-1800)	800 (700-1400)	0.02
Neutrophil/Lymphocyte	7.6 (4.3-12.3)	7.1 (3.8-11.4)	8.7 (4.5-19.7)	0.05
Neutrophil/Leukocyte	0.82 (0.74-0.88)	0.82 (0.75-0.87)	0.82 (0.76-0.91)	NS
Lymphocyte/Leukocyte	0.13±0.08	0.13±0.058	0.11±0.08	NS
MCV ¹ (fL)	88 (84-94)	88 (84-93)	84 (82-95)	NS
RDW ² (%)	15.5±2.5	15.3±2.2	15.7±3.1	NS
MPV ³ (fL)	9.8±6.9	9.9±7.9	9.4±1.3	NS
PDW ⁴ (GSD)	16.3 (15.6-17.5)	16.3 (15.6-17.5)	16.3 (15.8-17.5)	NS
Iron (µgr/dL)	23 (14-37)	23 (14-35)	40 (18-48)	NS
Folate (pg/ml)	8.1±5.5	8.1±5.6	7.9±5.2	NS
Vitamin B12 (pg/ml)	320 (198-520)	316 (198-542)	542 (270-970)	0.05

MCV¹: Mean corpuscular volume; RDW²: Erythrocyte distribution width (%); MPV³: Mean platelet volume; PDW⁴: Platelet distribution width.

status (oral, nasogastric tube or PEG). The most frequently seen comorbidities were dementia, hypertension, cerebrovascular event, and diabetes mellitus. Mortality rate was 24.5% (56% within the first 3 days). Increase in neutrophil/lymphocyte ratios (NLRs), and uric acid levels were found to be related to mortality (for both, $p < 0.05$).

Demographic characteristics as advanced age, and male gender were known to be risk factors for aspiration pneumonia. In a study where mortality rates in inpatients with aspiration pneumonia were investigated, median age of the patients, and percentage of male patients were reported as 76.7 years, and 50.2%, respectively [7]. In a prospective study on 62 cases performed by Tokuyasu et al. median age of the patients was 86.6 years, and male patients constituted 56.8% of the study population [8]. In their retrospective study by Fidan et al. on 31 cases with aspiration pneumonia, median age of their study population was 61 years, while 55% of their patients consisted of male patients [9]. In our study median age of 204 patients diagnosed as aspiration pneumonia in the clinics of internal medi-

cine was 77 years, and 56% of the study population comprised of male patients. Similar to the literature findings, distribution of aspiration pneumonia was nearly the same in both genders, and median age of the patients was similar to that encountered during literature reviews.

Aspiration can cause serious problems especially in patients with dementia. In a study by Feinberg et al. the authors performed a study in nursing home patients using modified videofluoroscopy guided swallowing test with barium, and detected events of major, and minor aspiration in 24, and 50% of the patients, respectively [10]. In a study by Metan et al. the most frequent comorbidity in their patients with aspiration pneumonia was neurological diseases (78%) which were detected in 20% of the patients with dementia [11]. Still in our study, great majority of the patients with aspiration pneumonia had a neurological disease (cerebrovascular disease, dementia, Parkinson's disease), and 49% of the study population consisted of patients with dementia.

Relationship between enteral nutrition, and complication of aspiration is already acknowledged.

TABLE 3. Biochemical parameters of the patients

	Total (n=204)	Exited (n=50)	Discharged (n=154)	p
Glucose (mg/dL)	109 (82-162)	149 (85-178)	108 (82-145)	0.02
Urea (mg/dL)	61 (41-113)	79 (46-156)	56 (38-101)	0.002
Uric acid (mg/dL)	5 (3.5-6.5)	5.9 (4.1-8.2)	4.9 (3.4-5.9)	0.003
Creatinine (mg/dL)	0.9 (0.6-1.4)	1.3 (0.7-2.6)	0.9 (0.6-1.2)	0.015
Sodium (mEq/L) (Mean±SD)	141±10	140±10	141±10	NS
Potassium (mEq/L) (Mean±SD)	4.2 (3.7-4.5)	4.3 (3.9-4.9)	4.1 (3.6-4.4)	NS
AST ¹ (U/L)	26 (18-49)	30 (22-69)	25 (18-42)	0.02
ALT ² (U/L)	20 (13-35)	25 (13-41)	20 (13-32)	0.04
T bilirubin ³ (mg/dL)	0.56 (0.37-0.8)	0.64 (0.47-0.89)	0.53 (0.36-0.88)	0.02
I Bilirubin ⁴ (mg/dL)	0.41 (0.28-0.6)	0.45 (0.23-0.65)	0.41 (0.27-0.62)	0.05
GGT ⁵ (U/L)	29 (16-62)	48 (16-98)	27 (17-53)	0.01
ALP ⁶ (U/L)	79 (64-100)	92 (73-114)	76 (61-93)	0.003
LDH ⁷ (U/L)	244 (211-329)	262 (227-367)	246 (207-288)	0.007
Cholesterol (mg/dL) (Mean±SD)	136±45	142±64	134±39	NS
Triglyceride (mg/dL) (Mean±SD)	115±70	129±65	111±73	NS
HDL-C ⁸ (mg/dL) (Mean±SD)	33±15	32±18	33±14	NS
LDL-C ⁹ (mg/dL) (Mean±SD)	83±37	85±49	82±33	NS
CK ¹⁰ (U/L)	106 (47-224)	77 (29-109)	122 (52-227)	NS
Protein (g/dL) (Mean±SD)	6.1±0.8	6.1±0.7	6.2±0.8	NS
HbA1c ¹¹ (%)	5.8 (5.5-6.7)	5.8 (5.6-7)	5.7 (5.5-6.6)	NS
Phosphorus (mEq/L)	3.3 (2.8-4)	4 (3.2-4.7)	3.2 (2.7-3.7)	<0.001
INR ¹² (%)	1.25 (1.18-1.36)	1.32 (1.25-1.45)	1.23 (1.16-1.3)	0.008
TSH ¹³ (uIU/mL)	1.12 (0.66-2.26)	0.99 (0.33-1.91)	1.33 (0.69-2.34)	0.059
FreeT3 ¹⁴ (pgr/mL)	2.06 (1.74-2.30)	1.85 (1.59-2.15)	2.12 (1.81-2.33)	0.005
FreeT4 ¹⁵ (ng/dL)	1.06 (0.87-1.23)	1.08 (0.89-1.23)	1.06 (0.87-1.23)	NS

AST¹: Acid transferase; ALT²: Alkaline transferase; T. bilirubin³: Total bilirubin; I. Bilirubin⁴: Indirect bilirubin; GGT⁵: Gamma glutamyl transferase; ALP⁶: Alkaline phosphatase; LDH⁷: Lactate dehydrogenase; HDL-C⁸: High-density lipoprotein cholesterol; LDL-C⁹: Low-density lipoprotein cholesterol; CK¹⁰: Creatinine kinase; HbA1c¹¹: Hemoglobin A1c; INR¹²: International normalized ratio; TSH¹³: Thyroid stimulating hormone; Free T3¹⁴: Triiodothyronine; FreeT4¹⁵: Thyroxine.

In patients on tube feeding, and those dependent on others for oral hygiene, the risk of aspiration was observedly 20-fold higher when compared with healthy individuals [12, 13]. Nakajoh et al. investigated one-year incidence of aspiration pneumonia in patients who experienced a cerebrovascular event, and observed its incidence as 54.3% in dysphagic patients on oral intake which was higher than dysphagic cases on tube feeding (13.2%). The incidence of aspiration pneumonia was 64.3% in bedridden patients fed through nasogastric tube [14]. Our patients were fed via PEG (15%) or through oral

route (85%) at admission. This finding suggests that aspiration pneumonia is more frequently seen in elder patients fed through oral route, and alimentation through PEG has not any prophylactic effect in these cases.

Though mortality rates of aspiration pneumonia ranged between 20, and 50%, in some studies higher rates up to 80% have been reported [15, 16, 17, 18]. In our study median rate of mortality was found as 24.5% in compliance with the literature findings. In cases with aspiration pneumonia, disparities between mortality rates can be attributed to the lack

of definitive diagnostic criteria defined for aspiration pneumonia, and higher mortality rates can be associated with advanced age of these patients, and concomitant diseases.

In recent years an index which reflects both acute inflammation, and lymphopenia developing after acute physiologic stress has been started to be used. This index is a neutrophil/lymphocyte ratio which has been reported to be a good marker of the inflammatory state [19]. Duffy et al. divided 1046 patients into 3 groups (mean NLR 1.7 ± 0.5 ; 3.2 ± 0.6 ; 11.2 ± 12.9) before percutaneous coronary intervention, and followed them for postoperative 32 months. They reported 144 cases of death, and in patients with increased neutrophil/lymphocyte ratios, higher mortality rates were detected [20]. In a study performed on non-small cell lung cancer patients who had undergone complete resection, Sarraf et al. detected higher mortality rates in patients with increased neutrophil/lymphocyte ratios [21]. Uthamalingam et al. divided 1212 patients with diagnosis of acute decompensated heart disease according to their neutrophil/lymphocyte ratios, and found a positive correlation between mortality, and neutrophil/lymphocyte ratios during a median follow-up period of 26 months [22]. In our study, we also found a correlation between mortality, and neutrophil/leukocyte ratios in patients with aspiration pneumonia which suggests that this parametre can be used as an easily available, simple, and cost-effective marker.

Uric acid is considered as a cardiovascular risk marker [23]. In a study performed by Tomita et al. the authors reported higher risk of all-cause death (from coronary heart disease, stroke, liver disease and/or renal failure) in 49413 patients aged between 25, and 60 years with uric acid levels over 8.5 mg/dl during a median follow-up period of 5.5 years when compared with those with uric acid levels at 5-6.4 mg/dl [24]. In our study relationship between uric acid levels, and mortality supports their outcome.

In conclusion, in this study we found increased mortality rates in patients hospitalized with the diagnosis of aspiration pneumonia. Higher number of geriatric patients, and also higher incidence rates of comorbidities may be responsible for higher mor-

tality rates. Neutrophil/lymphocyte ratios (NLR), and uric acid levels can be evaluated as mortality-related factors in cases with aspiration pneumonia.

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