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Community acquired infections in elderly population

Research Article

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Abstract: In geriatric practice, data regarding infections including the epidemiology, morbidity, and mortality are lacking. Our aim was to evaluate the frequency, location, microbiological and laboratory characteristics of infectious diseases in elderly population admitted to a training hospital. The patients were included total of 330 patients, aged over 65 with infection, seen between January 1, 2005 and January 1, 2006. In the result, of patients 136 (41%) had respiratory system infection, 90 (27%) urinary system infection, 39 (12%) gastrointestinal system infection, 34 (10%) bloodstream infections, 17 (5%) soft tissue infection, 8 (2%) central nervous system infections, and 6 (2%) others. Average length of hospitalization was 8.6 ± 7.7 days. Mortality rate from all causes was 57 (17%). The most common infections in elderly patients were respiratory tract and urinary system infections, and there were no fever, leukocytes and high CRP levels in approximately 1/3 of cases. Infectious diseases may occur even in the absence of such infection indicators as fever, raised WBC count and high CRP level in the elderly population.

Keywords: Elderly • Fever • Infection • C-reactive protein • Leukocyte

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1. Introduction

Infection is a common problem in elderly patients. In geriatric practice, infection is most frequently seen in combination with many other problems. Data regarding infections in this population including the epidemiology, morbidity, and mortality are lacking. The elderly have defective host defenses that compromise their ability to ward off infectious agents; factors influencing immunocompetence include the following: immune senescence, changes in nonadaptive immunity, chronic diseases, medications, malnutrition, and functional impairments. T-lymphocyte production and proliferation decline with age, resulting in decreased

cell-mediated immunity and decreased antibody production to new antigens [1-3]. Thinning skin, enlarged prostate, diminished cough reflex, and other anatomic or physiologic accompaniments of aging are the changes in nonadaptive immunity that render the elderly more vulnerable to infection. Chronic diseases (such as cancer, atherosclerosis, diabetes mellitus, dementia, etc,) predispose the elderly to certain types of infection. Medications such as sedatives, narcotics, anticholinergics, and gastric acid suppressants may further suppress innate defenses. Malnutrition, which reduces cell-mediated immunity, is common in nursing home residents [2] and may be more common in the geriatric community at large than is generally

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Table 1. Study characteristics of the overall study population.

	RSI	USI	GSI	BSI	STI	CNSI	Other	Total
Patient	136(41%)	90(27%)	39(12%)	34(10%)	17(5%)	8(2%)	6(2%)	330(58
numbers								Female;172
								Male
LOH	9.1±7.1	7.8±5.8	4.0 ± 3.3	16.3±19.6	10.1±8.5	10.5±7.1	8.4±6.6	8.6 ± 7.7
Mortality	27 (20%)	10 (11%)	1 (3 %)	13 (38%)	2 (12%)	3 (37%)	1	57 (17%)
Isolated	82/25(18%)	181/68(75%)	26/5(13%)	99/32(94%)	13/4 (23%)	10/2(25%)	-	477/139
causative								(42%)
organism								

STI:Soft tissue infection, BSI: Bloodstream infection CNSI: Central nervous system infection, USI:Urinary system infection, RSI: Respiratory system, GSI: Gastrointestinal and hepatobiliary system infection, LOH Length of hospitalization

realized [4]. Functional impairments (e.g., immobility, incontinence, dysphagia) can complicate aging and enhance susceptibility to infection.

Age-related functional losses in geriatric patients with multiple morbidities also constitute a risk factor for fever. Infection, collagen tissue diseases, malignancies and drug interactions play significant roles in the underlying diseases found in this age group. It is important to recognize the presentation of the geriatric infections and not to miss the diagnosis.

There was a strong association between leukocytosis and high fever in elderly cases. However, the absence of fever and leukocytosis, made it hard for us to decide whether there was an infection or not [5].

In the present study our aim was to evaluate the incidence and origins of community acquired infections and to evaluate the relationships between the factors such as, fever, white blood cell (WBC) counts, C-reactive protein (CRP) levels, age, gender and the presence of underlying chronic diseases as compared to the length of stay in elderly patients not living in a nursing home.

2. Material and Methods

We conducted this study in GATA Haydarpasa Training Hospital in Turkey as a retrospective research covering a 1-year period between January 2005 and January 2006.

A total of 1210 elderly patients were admitted to the relevant departments (internal medicine, infectious diseases, pulmonary diseases) during the study period, of whom 455 (38%) were considered to be eligible for our study.

2.1. Eligibility criteria

Inclusion criteria for participation were the following: age≥65 years; written informed consent to study; patients with fever or who were thought to be suffering from

infectious diseases in the light of physical examination findings; initial laboratory or radiological findings at their first examination; and who have the ability to understand and to answer the posed questions Exclusion criteria from participation were the following: a medical history of primary malignant disease; a previous history of thrombophlebitis or thromboembolic disease;, active chronic inflammatory diseases; or severe cognitive impairment. Hospital acquired infections were not included in the study.

One hundred and twenty-five patients were excluded for reasons such as rheumatic disease activation, malignity or thromboembolic events. Three hundred and thirty (27%) patients were available for analysis. The patients were subdivided into 7 groups based on localization of their infections (Table 1). Infections were classified according to origin, provided with the following listings: respiratory system infection (RSI), urinary system infection (USI), gastrointestinal system infection (GSI), bloodstream infections (BSI), soft tissue infection (STI), central nervous system infections (CNSI), and other infections.

Medical history and systemic physical examination findings of all patients presenting with fever were recorded. Appropriate culture specimens were taken before the empirical antibacterial therapy.

2.2. Diagnostic criteria of the infections 2.2.1. Community-acquired pneumonia (CAP)

CAP was defined as an acute illness associated with 1 or more of the following respiratory signs and symptoms: new cough with or without sputum production, pleuritic chest pain, dyspnea, fever or hypothermia, altered breath sounds on auscultation, and the presence of a new infiltrate on a chest radiograph. *Progressive respiratory failure* was defined as increasing oxygen requirements or the necessity of mechanical ventilation during follow-up. Patients in need of mechanical ventilation on hospital admission whose condition improved at assessment were not considered early failures [6].

2.2.2. Urinary system infections

A level of >10⁵ cfu/mL in two separate urine specimens taken from asymptomatic female patients for USI, >10³ cfu/mL for male patients and >10⁵ cfu/mL for reproduction from urinary samples taken once from patients symptomatic involving dysuria, frequency, urgency, and occasionally suprapubic tenderness of *Enterobacteriaceae* group bacterial reproduction were regarded as significant. However, this level was amended to >10⁴-10⁵ cfu/mL for Gram-positive bacteria, fungi and slower reproducing bacteria [7.8].

2.2.3. Bloodstream infections

At least two blood samples were taken from patients thought to have bacteraemia-sepsis, using antiseptic techniques and from two different extremities, with an interval of at least 30 min. Primary BSI (Bloodstream Infection) was defined by the association between a sepsis syndrome (fever > 38 °C, or rigor or shock) and a positive blood culture for pathogenic microorganisms or two positive blood cultures for non pathogenic microorganisms without any infection at another locations [9].

2.2.4. Soft tissue infections

Soft tissue infection is a rare but very severe type of bacterial infection that can destroy the muscles, skin, and underlying tissue. Diagnostic spectrum of the soft tissue infection include vesicles, bullae, crusted lesions, folliculitis, papulary and nodulary lesions, ulcers with or without eschars erysipelas, cellulitis necrotizing myositis and myonecrosis.

2.2.5. Central nervous system infections

The diagnosis of definite bacterial infection of the central nervous system, including bacterial meningitis, were performed by isolation of the pathogen from the cerebrospinal fluid or other significant clinical site such as surgical tissue, an implanted device, or blood. Probable bacterial infection was defined by the association of a compatible clinical syndrome or cerebrospinal fluid changes associated with bacterial meningitis or other central nervous system infection, and confirmed as an anatomically defined infection by imaging or surgery, in association with positive blood cultures or bacterial antigen from cerebrospinal fluid. Possible bacterial meningitis was defined as a compatible clinical syndrome with predefined cerebrospinal fluid changes in the absence of a confirmatory culture or antigen test from any site [10].

2.3. Microbiological Procedures

All the samples were carried out for all the eligible patients. Culture samples were immediately forwarded by courier to the designated microbiology laboratory for incubation, and identification. Quantification was applied to all urine cultures and tissue cultures cultures. Identification was performed by classical biochemical methods and APIU (bioMérioux, France) identification products [11]. The antimicrobial susceptibility of bacteria was determined using the disc diffusion method as described by the CLSI criteria, formerly known as NCCLS [12]. Muller Hinton Agar and antibiotic discs were obtained from Oxoid Limited (Basingstoke, UK). Disc strengths, zone diameter breakpoints, and corresponding MIC (Minimum Inhibitory Concentration) breakpoints were published in the interim report [13]. In the case of mixed culture, all the bacteria were tested separately.

All the urine samples were classified as negative or positive according to the guidelines for testing issued by the Infectious Diseases Society of America (IDSA) [14]. A urine sample containing between ≥10³ and <10⁵ cfu/mL and positive for the presence of pyuria or a sample containing ≥10⁵ cfu/ml irrespective of the presence of pyuria was defined as positive. Pyuria was defined as 'trace' or more as determined with the Multistix 2 system (Bayer Corporation, Diagnostics, Division, Elkhart, IN, USA).

The age, gender, comorbid diseases, diagnosis, fever, WBC counts, CRP levels, duration of hospitalization and mortality results of all patients were recorded.

2.4. Statistical Analysis

Qualitative variables were analysed using the chisquare test of homogeneity or Fisher Exact tests, and quantitative variables were compared using Student's t-test or Wilcoxon ranked sum test, when appropriate. Statistical analyses were performed with a PC compatible statistics program (SPSS, v.13, Chicago, IL). A P-value less than 0.05 was considered astatistically significant.

3. Results

During the 1-year study period, 330 patients over 65 years were included in this study. Patients had a mean age \pm standard deviation (SD) of 76 \pm 12 years. Of these, 163 (50%) patients were aged 65 to 74 years, and 167 (50%) patients were aged \geq 75 years. There were 158 (48%) female patients and 172 (52%) male patients.

In terms of infectious diseases, the diagnosis distribution was 136 cases (41%) of RSI, 90 (27%) cases of USI, 39 (12%) cases of GSI,34 (10%) cases of

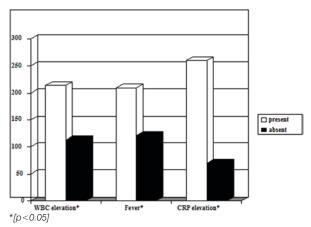
Table 2. Normal body temperature, normal C-reactive protein (CRP) levels and white blood cells (WBC) count rates of total and subgroup population.

	STI(n=17)	BSI(n=34)	CNSI(n=8)	USI(n=90)	RSI(n=136)	GSI(n=39)	Other (n=6)	Total (n=330)
Normal WBC	7 (41%)	5 (12%)	2 (25%)	33 (37%)	49 (36%)	16 (41%)	2	113 (34%)
р	NS	0.0001*	NS	0.01*	0.0001*	NS	NS	0.0001*
Normal body								
temperature	8 (47%)	7 (21%)	2 (25%)	28 (31%)	56 (42%)	17 (44%)	3	121 (37%)
p	NS	0.0001*	NS	0.0001*	0.04*	NS	NS	0.0001*
Normal CRP								
levels (<6 mg/dl)	4 (24%)	1 (3%)	4 (50%)	15 (17%)	26 (19%)	18 (46%)	2 (34%)	70 (21%)
p	0.029*	0.0001*	NS	0.0001*	0.0001*	NS	NS	0.0001*

*Statistically significant; NS, non-significant

STI:Soft tissue infection, BSI: Bloodstream infection CNSI: Central nervous system infection, USI:Urinary system infection, RSI: Respiratory system, GSI: Gastrointestinal and hepatobiliary system

Figure 1. High leucocyt, CRP and fever rates in elderly patients with infectious disease.

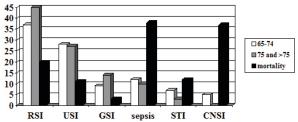


BSI, 17 (5%) cases of STI, and 8 (2%) cases CNSI, and 6 cases (2%) of other infection, (please see Table 1). The rate of respiratory infections was higher in males than in females, while females had a higher rate of urinary infections than males, but the difference was not statistically significant (p>0.05). Average length of hospitalization was 8.6 ± 7.7 days. Sepsis cases remained hospitalized the longest time (16.3 ± 19.6 days) and GSI cases for the shortest time (16.3 ± 19.6 days). Normal body temperature, normal C-reactive protein (CRP) levels and white blood cells (WBC) count rates of total and subgroup population are displayed in Table 2.

When all infection cases/facts were evaluated, the leukocytes, fever and CRP levels were found significant (p<0.0001), (Figure 1). When it is evaluated according to the localizations of infection, leukocytes, fever and CRP levels in BSI, USI, and RSI, STI level were particularly found significant. There was no relation between infection locations and age (Figure 2).

Overall hospital mortality of the study group was 57 (17%) patients. The highest mortality rates were observed in the BSI (38 %) and CNSI (37%) groups.

Figure 2. Infection rates between two age groups* and mortality in all groups.



p<0.05 in all body system

STI: Soft tissue infection, CNSI: Central nervous system infection, USI: Urinary system infection , RSI: Respiratory system, GSI: Gastrointestinal and hepatobiliary system

Accompanying diseases in order of prevalence were 140 (42%) cases of hypertension, 96 (29%) of diabetes, 82 (25 %) of chronic obstructive pulmonary disease (COPD) and 75 of coronary artery disease. The rate of the elderly patients having 2 or more chronic diseases was 63% in our study.

A total of 427 culture specimens were investigated and 139 culture specimens were positive. Overall gram negative bacilli accounted for 43.1% of the culture isolates, gram positive for 33.8%, anaerobes for 7.9% and fungal agents for 10%. Gram negative bacilli caused 50.6% of all identified infection and was significantly more frequent in age group>75. Distribution of microorganisms by age group was shown in Table 3. The isolated strains listed in reducing frequency were Escherichia coli in 35 cases (29 urine, 5 blood), coagulase-negative staphylococcus in 23 cases (13 blood, 5 urine), Candida spp. in 14 cases (9 urine, 3 sputum), Pseudomonas aeruginosa in 10 (7 urine) Enterococcus faecalis in 9, Streptococcus pneumoniae in 9 Klebsiella oxytoca in 8 cases, M. Tuberculosis in 7 cases and others in 24 cases.

Table 3. Distribution of microorganisms by age group.

Organism	Age 65-74	Age ≥ 75	Total
Gram positive	26 (40.6)	21 (28)	47 (33.8)
Staph. aureus	12	11	23
Enterecoccus faecalis	4	5	9
Strep. pneumonia	6	3	9
Others	4	2	6
Gram negative	22 (34.3)	38 (50.6)*	60 (43.1)
E. coli	10	25	35
Ps. aeruginosa	4	6	10
Klebsiella sp.	3	5	8
Others	5	2	7
Fungal agents	6 (9.3)	8 (10.6)	14 (10)
Anaerobes	5	6	11 (7.9)
Bacteroides fragillis	3	4	7
Clostridium difficile	2	2	4
MiscellousM. tuberculosis	5	2	7
	64	75	139

p < 0.001 between age groups.

4. Discussion

In geriatric practice, infection is most frequently seen in combination with many other problems. It is important to recognize this presentation and not to miss the diagnosis. The presence of pathophysiological changes and organ involvement, together with fever, raised WBC count, or elevated ESR, are strongly supportive of a diagnosis of infection.

It was seen in this study that the leukocytes, fever and CRP levels in elderly in bloodstream, urinary and respiratory system infections were significantly high. The frequency of respiratory and urinary system infections was higher, whereas in central nervous system and bloodstream infections, mortality was higher. There was no observed difference in the frequency of the infection localizations in elderly under and above 75 and in male—female gender. In a recent study it ws shown that Serum CRP at admission is an independent predictor of mortality in hospitalized patients, particularly in the elderly. Admission CRP higher than 120 mg/l was associated with increased probability of in-hospital death (three fold in the overall population and five fold in the elderly subgroup) compared with lower levels [15].

In the elderly generally reduced thermoregulatory system functional deficiency and fever response may lead to insufficient pyrogenic response. In 34% of the cases in our study no high leukocytes was observed, neither high fever in 37%, nor high CRP in 21%. Mouton et al. reported that while 60 percent of older adults with serious infections develop leukocytosis, its absence

does not rule its existence an infectious process [16]. Avkan and co-workers reported that there was a strong association between leukocytosis and high fever in elderly cases [5]. However, the absence of fever and leukocytosis in 78 (32.5%) of their cases, made it hard for them to decide whether there was an infection or not [5]. These results suggest that if other symptoms and findings support infection, infectious disease must not be excluded even if there is no fever and leukocytosis in the elderly population.

There is a greater likelihood of these aspirations ending with colonization in the lower respiratory passages in old people. However, as well as age, this colonization is also known to be linked to other factors such as hospitalization, cigarette smoking, malnutrition, antibiotherapy, endotracheal intubation, surgery and therapies for reducing gastric acidity. It has been demonstrated that up to 35% of the elderly have significantly low levels of food intake and low mineral/vitamin levels [17]. Low serum albumin, body-mass index and arm muscle mass have been reported to be linked to a decrease in delayed hypersensitivity [18]. The level of death from pneumonia may be 2-3 times higher in such cases.

One study analyzed class I and II community acquired pneumonia (CAP) [19], ninety-nine percent of cases recovered, while 3 patients (1%) died. However, in Class III and IV geriatric CAP cases the picture is less encouraging. Twenty-seven (20%) of the 136 cases of CAP in our study ended in mortality. Because in our cases the average age was 76, there had been comorbid diseases (65%) and 55% were class III or IV CAP.

The most common respiratory pathogen was H. influenza (26.86%), followed by *S. pneumoniae* (21.16%). *Moraxella catarrhalis* accounted for 6.90% [20]. In one study reported from Taiwan, *S. pneumoniae*, *M. pneumoniae* and *C. pneumoniae* were described as the most frequently observed agents [21]. *S. Pneumonia* was also observed as the most coincided respiratory pathogen in our study.

Acinetobacter baumanii is an uncommon but important cause of CAP with high mortality. Factors associated with the higher mortality in the CAP-Acinetobacter baumanii group included the presence of an Acinetobacter baumanii bacteremia platelet count of <120000 cells/µl, pH < 7.35 on presentation and the presence of DIC [22]. We determined one case of Acinetobacter baumanii-related CAP and this case presented with low platelet count and DIC.

Routine laboratory testing is considered to have little value in determining the etiology of pneumonia. However, it may have prognostic significance in patients 60 years and older and, therefore, is recommended for

them. The value of a Gram stain and routine bacterial cultures of sputum from patients with pneumonia are debated, and obtaining adequate sputum specimens in frail, older adults may be particularly difficult [23].

Regardless of age, bacterial causes of pneumonia can only be identified in 20 to 50 percent of patients [24]. Eighteen percent of the cases those had respiratory infection were being able to diagnosed bacteriologically in our study.

An elderly patient with USI may have no fever, and in these diseases infection may follow a course with only a change in mental state. In our study, there was no development of leukocytes in 37%, of fever in 31%, and of CRP in 27% in the cases of urinary infection. Therefore, the possibility of infectious diseases must not be forgotten during the investigation of neurological pathology in patients with an altered mental state. USIs are the most frequent bacterial infection and the most common source of bacteremia in older adults [25]. The results we acquired confirm this. Seventy-three percent of urinary pathogens we assigned were *E. Coli* and 19% of those led to bloodstream infections.

Factors that predispose older adults to USIs include the use of urethral or condom catheters, and neurogenic bladders with increased residual urine. Contributing factors specific to gender include prostate enlargement in men, an increase in vaginal pH, vaginal atrophy that is due to post menopausal estrogen depletion, and incomplete emptying of the bladder in women [26].

After E. coli the most frequently encountered agents in non-complicated USI in elderly patients aged 70 and above are Proteus and Klebsiella pneumonia. P. aeruginosa and E. faecalis are the most isolated in complicated USI [27,28]. The most frequently isolated agents in our cases were E. coli, Candida sp., Pseudomonas sp. and Klebsiella sp.. In these cases, mortality was 25%, although 50% of cases were aged over 75 and a co morbid state of two or more conditions was determined in 80%. The effect of diabetes on uropathogen distribution was analyzed in Bonadio's study and the prevalence of agents in diabetic and non-diabetic groups, respectively, of E. coli at 54.1% vs. 58.2%, Enterococcus sp. at 8.3% vs. 6.5%, and Pseudomonas sp. at 3.9 vs. 4.7% was determined to have no significant effect [29]. In our study the prevalence of these agents was 47%, 5% and 15%, respectively (diabetics and nondiabetics).

In one study, USI was diagnosed in only in 40% of positive urine cultures from elderly patients [30]. However the rate was higher in our study. It was possible to assign the accountable pathogen in 68 urine cultures out of 181 in USI, our rate to diagnose by the culture was 75% (68/90).

The vast majority of elderly patients with bacteriuria do not have urinary symptoms; when symptoms are present, they are difficult to be interpreted, because uninfected elderly subjects commonly experience dysuria urgent urination, frequent urination and incontinence. Clinical findings and a urinalysis are usually sufficient for diagnosis in older adults; however, a urine Gram stain and culture should be considered to direct therapy.

It was found out that in the cases suffering blood infection, hospitalization time was the longest. The 4 factors delaying discharge are sepsis, lack of condition, lack of social support and cardiovasculary events. It is believed that the early provision of social support may play a role in early discharge [31]. There were 33 cases of BSI in our series, of which 8 (24%) followed a fatal course. In Gavazzi's study [31], it was reported that the rate of gram negative pathogens being accountable increases by the increase in age and in 14% overall mortality rate. Gram negative pathogens were more frequently seen in onward age group in our study. However this difference does not originate in blood infections, but in the abundance of gram negative factor in urinary system. The reason for our mortality rate being high may be in relation with the high level of comorbidity.

As people age they experience more illnesses, and this applies in particular to skin infections. Pathogenic states that provide the milieu for infection are more common in the elderly. Infections that occur more commonly in the elderly include Gram-positive bacterial infections of the skin, intertriginous infections, herpes zoster/shingles and onychomycosis [32]. STI was determined in 17 of our cases (infected diabetic foot, infected head wound, lymphangitis, cellulites, herpes etc.). The mortality rate was 12%.

An estimated 50%-75% of cases of rhino cerebral mucurmycosis occur in patients with diabetes, including elderly individuals [33]. Several complicated skin and soft tissue infections occur more frequently in individual with diabetes than in the general population. Because of peripheral neuropathy, trauma and peripheral vascular diseases, mixed anaerobic soft tissue infections (synergistic narcotizing cellulites, narcotizing fasciitis, Fourier gangrene, foot ulcers). Infection with herpes zoster caused by a reactivation of varicella virus dormant in dorsal root ganglia is also common in older adults. As cellular immunity wanes with advancing age, clinical reactivation of the virus may occur.

Acute cholangitis is more common in older people, and increasing age is a determinant of morbidity and mortality. The most common symptom at presentation was abdominal pain (81%), followed by jaundice (55%). These symptoms were no less common in older patients.

Overall mortality was 10%, and the incidence of septic shock was similar in both groups. Given the greater difficulty in assessing jaundice in older people and the confounding effect of falls, incontinence and confusion, a routine policy of liver function tests, with further investigation of abnormal results in such presentations, may reduce delays in diagnosing and treating acute cholangitis [34]. Diarrhea in the elderly population is one disease that needs special attention in treatment and management, especially in acuteand long-term care residents, because of their multiple comorbidities, immunosenescence, frailty, and poor nutritional status. When the diarrhea is chronic and all stool testings and serologies have been performed, the patient may benefit from endoscopy and colonoscopy for biopsy. Attentive and vigilant nursing staff is crucial in the timely diagnosis and treatment of diarrheal diseases to improve quality of life and reduce mortality [35].

Infectious diseases are some of the most significant diseases observed in the elderly population and necessitating hospitalization. Studies have reported high rates of mortality and length of hospitalization in the elderly population due to infection induced pneumonia in particular [3,4]. Despite advances in antibiotic therapy, infectious diseases continue to be the major cause of mortality in older adults. The diagnostic and

therapeutic nuances of managing infections in older adults create special challenges for physicians. Between 1980 and 1992, the infectious disease mortality rate in patients 65 years and older actually rose 25 percent. That comparative mortality rate is nine times the rate in patients between 25 and 44 years of age [36]. Frequently seen in the elderly, diabetes mellitus, renal deficiency, cancer, COPD, neurological impairments, gastrointestinal diseases, renal deficiency, surgery or inhalation therapy with trauma, adjunctive pathologies such as malnutrition and being bed-ridden increase the risk of pneumonia and death there from. Coughing, fever and dyspnoea have been determined in 56% of elderly pneumonia patients [37]. Fever was determined in 53% of patients in our study. The majority of these cases (55%) were aged above 75, and 77% were males.

In conclusion, this study determined that infectious diseases were those most frequently requiring hospitalization in the elderly population, as well as the need not to exclude infectious diseases even in the absence of such infection indicators as fever, raised WBC count and high CRP level. Approaches to elderly patients need to be determined in the light of widerranging studies on the subject.

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