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#### RESEARCH

## IS THE DISTRIBUTION OF GERIATRIC INFECTIONS DIFFERENT IN EASTERN TURKEY? RETROSPECTIVE EVALUATION OF GERIATRIC INFECTIONS

### ABSTRACT

**Introduction:** Infections are one of the most important reasons for hospitalization, morbidity and mortality among geriatric patients.

**Materials and Method:** Between June 2016 and December 2017, patients aged 65 and older who were hospitalized for treatment were retrospectively evaluated at the infectious diseases and clinical microbiology department of Firat University Hospital.

**Results:** In total, 900 patients were admitted to our clinic. Of these, 350 (38.8%) of these patients were over 65 years old; 218 (62.3%) were male and 132 (37.7%) were female. The most common reasons for hospitalization were pyelonephritis in 109 patients (31.5%), pneumonia in 78 (22.2%), cystitis in 72 (20.6%) and skin and soft-tissue infection in 32 (9.3%). Extrapulmonary tuberculosis, brucellosis, Crimean Congo haemorrhagic fever, fascioliasis and cutaneous leishmaniasis were the prominent causes of hospitalization. Hypertension and diabetes mellitus were the most common comorbidities. Combination antibiotics were administered to 95 (27.4%) patients, whereas 251 patients received a single antibiotic. Of 245 (70%) patients who required consultation with various departments, 77 (20%) consulted with neurology, 68 (19.4%) with urology and 44 (12.5%) with chest diseases departments. Radiological imaging, most commonly abdominal ultrasound, was performed in 228 (65.1%) patients. Blood infection was detected in 31 patients.

**Conclusion:** In areas such as our region, where many infectious diseases are endemic, diseases, such as tuberculosis, brucellosis, parasitic diseases, or Crimean Congo haemorrhagic fever, can occur in elderly individuals. Therefore, a multidisciplinary approach is essential to evaluate geriatric infections and a radiologist should be included in this multidisciplinary team.

**Keywords:** Infection; Geriatrics; Tuberculosis; Referral and consultation

#### ARAŞTIRMA

## TÜRKİYE'NİN DOĞU BÖLGESİNDE GERİATRİK İNFEKSİYONLARIN DAĞILIMI FARKLI MI? GERİATRİK İNFEKSİYONLARIN RETROSPEKTİF DEĞERLENDİRİLMESİ

### Öz

**Giriş:** Enfeksiyon geriatric hastalarda en önemli hastaneye yatış, mortalite ve morbidite sebeplerinden biridir.

**Gereç ve Yöntem:** Haziran 2016-Aralık 2017 yılları arasında Firat Üniversitesi Hastanesi enfeksiyon hastalıkları ve klinik mikrobiyoloji bölümünde tedavi gören 65 yaş ve üzeri hastalar retrospektif olarak incelendi.

**Bulgular:** On sekiz aylık zaman diliminde kliniğimize 900 hasta yatırıldı. Bu hastaların 350 (%38.8)'si 65 yaş üstü idi. Hastaların 218 (%62.3)'i erkek, 132 (%37.7)'si kadındı. En sık hastaneye yatış sebebi piyelonefrit 109 (%31.5), pnömoni 78 (%22.2), sistit 72 (%20.6), deri ve yumuşak doku enfeksiyonu 32 (%9.3) idi. Ekstrapulmoner tüberküloz, bruselloz, kırım kongo kanamalı ateşi, fascioliasis, cutaneous leishmaniasis dikkat çeken hospitalizasyon sebeplerindendi. En sık eşlik eden kronik hastalık diyabet, hipertansiyon ve serebrovasküler hastalıktı. Doksan beş (%27.4) hastada kombine antibiyoterapi uygulandı. İki yüz elli bir hastada ise tekli antibiyotik ile tedaviye başlandı. 245 (%70) hasta çeşitli bölümler ile konsülte edildi. Hastaların 71 (%20)'i nöroloji, 68 (%19.4)'i üroloji, 44 (%12.5)'ü göğüs hastalıkları ile konsülte edildi. Hastaların 228 (%65,1)'ine radyolojik görüntüleme istendi. En sık yapılan görüntüleme batın ultrasonografisiydi. 31 hastada kan dolaşım enfeksiyonu saptandı.

**Sonuç:** Bölgemiz gibi bir çok enfeksiyon hastalığı için endemik olan yerlerde, tüberküloz, bruselloz, paraziter hastalıklar, kırım kongo kanamalı ateşi gibi hastalıkların yaşlı bireylerde de görülebileceği akılda bulundurulmalıdır. Geriatric enfeksiyonlar değerlendirilirken multidisipliner yaklaşım şarttır ve bu ekibin içinde radyolog bulunmalıdır.

**Anahtar sözcükler:** Enfeksiyon; Geriatri; Tüberküloz; Konsültasyon



## INTRODUCTION

Aging is a continuous and universal process occurring in all organisms. It causes a decrease in all functions and describes the entirety of the gradual irreversible structural and functional changes at all levels. The geriatric population (aged  $\geq 65$  years) constituted 6.2% of the world population in 1992 and is expected to reach 20% by 2050 (1). The number and proportion of elderly people is continually rising in Turkey and worldwide as the death and birth rates decrease (2). Infections are one of the most important reasons for hospitalization, morbidity and mortality among geriatric patients.

Many infectious diseases are more common in the eastern than in the western part of Turkey, including classical infectious diseases, such as brucellosis or tuberculosis. A multidisciplinary approach is required because of the excessive presence of comorbidity in geriatric patients. Consultation support is often needed during the follow-up of patients. In addition, auxiliary diagnostic methods are more frequently needed for elderly patients because of the atypical course of diseases. Radiological imaging is one of the most prominent techniques among these supportive diagnostic methods.

Our hospital is in the eastern part of Turkey. It provides tertiary healthcare services and the patients from the all provinces of the region are transferred to there. In this study, we assessed the epidemiological characteristics, diagnosis and follow-up, required imagings, and consultation distributions of patients over 65 years old who were treated in the infection diseases and clinical microbiology clinic within 18 months. The aim of the study was to evaluate the epidemiological differences in our region in terms of geriatric infections by comparing them with the other regions of Turkey.

## MATERIALS AND METHOD

This retrospective study has been conducted in accordance with the principles of the Helsinki Declaration and approved by the local Institutional Review Board (5.1.2018/ Decision number 1/ 3). The consent of patients could not be taken because of retrospective study.

Between June 2016 and December 2017, patients aged 65 years and over were retrospectively evaluated at the infectious diseases clinic. For the study, a form is filled in which consists of a patient's demographic characteristics, laboratory and clinical findings, desired consultation and radiological examinations. The data of the patients were obtained by examining the files and epicrisis reports. Direct radiographic images were excluded from the study. In patients with recurrent hospitalizations, their first hospitalization was included in the study.

### Statistical analysis

Data were analyzed using the IBM Statistical Package for Social Sciences v22 (SPSS, Inc., Chicago, IL, USA). Descriptive statistics, such as frequencies or percentages for categorical variables and mean ( $\pm$  standard deviation) and median+interquartile range for continuous variables, were used to describe baseline demographic data and clinical characteristics. The variables were investigated using visual (histograms, probability plots) and analytic (Shapiro-Wilk's test) methods to determine whether they were normally distributed. In addition, the differences in variables were analysed using the analysis of variance or the Kruskal-Wallis tests. *P* values of  $<0.05$  were considered statistically significant for all analysis.

## RESULTS

Of the 900 patients admitted to our clinic during an 18-month period, 350 (38.8%; 218 (62.3%) were

male, 132 (37.7%) were female; median age, 77 (interquartile range, 73.7–84) were aged over 65 years. The diagnoses of patients admitted to the infectious diseases clinic are shown in Table 1. Two-infection focuses occurred at the same time in 32 (9.1%) patients, including pneumonia + cystitis in 16 (4.6%), pneumonia + pyelonephritis in 7 (2%), spondylitis + cystitis in 3 (0.8%), cellulite + cystitis in 3 (0.8%), mucormycosis+pyelonephritis in 1 (0.3%) and wound infection + liver abscess in 2 (0.6%) patients.

Fever of unknown aetiology (FUE) was diagnosed in 4 patients and was related to infections in 2 (50%). Overall, 2 patients were diagnosed with liver abscess, 1 with non-Hodgkin's lymphoma and 1 with multiple myeloma.

In addition, among patients diagnosed with extrapulmonary tuberculosis, 3 (0.9%)

had tuberculosis lymphadenitis, 3 (0.9%) had tuberculosis spondylitis, 1 had tuberculosis endometritis, 1 had tuberculous fasciitis, 1 had tuberculous osteomyelitis and 1 had tuberculosis-related brain abscess.

In total, 54 (15.4%), 119 (34%), 65 (18.6%) and 112 (32%) patients had no, 1, 2 and 3 or more associated comorbid diseases, respectively (Table 2).

Antibiotics were administered to 346 (98.9%) patients. Four patients who did not receive treatment had hepatitis B and C. Combination antibiotics were administered to 95 (27.4%) patients, whereas 251 patients were treated with a single antibiotic. Initial antibiotic therapies according to the diagnosis are presented in Table 3.

**Table 1.** The distribution of patients according to their diagnosis for hospitalization.

Diagnosis	n (%)	Diagnosis	n (%)
Urinary tract infection	188 (53.7)	Diabetic foot infection	5 (1.4)
Pneumonia	78 (22.2)	Fever of unknown origin	4 (1.1)
Skin and soft-tissue infection	32 (9.3)	Brucellosis	2 (0.6)
Extrapulmonary tuberculosis	10 (2.85)	Crimean_Congo Hemorrhagic Fever	3 (0.9)
Gastroenteritis	17 (4.9)	Abscess (in various organs)	7 (2.0)
Spondylodiscitis	10 (2.85)	Fascioliasis	1 (0.3)
Urosepsis	7 (2.0)	Mucormycosis	1 (0.3)
Meningoencephalitis	6 (1.7)	Bloodstream infection	5 (1.5)
Cutaneous Leishmaniasis	1 (0.3)	*Others	11(3.2)

\*: Hepatitis B, Hepatitis C, Osteomyelitis, Prosthetic joint infection, Septic arthritis



**Table 2.** Distribution of comorbid diseases.

Chronic Diseases	n (%)
Diabetes Mellitus	114 (32.6)
Hypertension	109 (31.1)
Cerebrovascular attack	36 (10.3)
Malignity	35 (10.0)
Chronic kidney failure	45 (12.8)
Benign prostatic hyperplasia	59 (16.8)
Cardiovascular disease	60 (17.1)
Chronic obstructive pulmonary disease	40 (11.4)
*Others	34 (9.7)

\*: Cirrhosis, organ transplantation, nephrolithiasis, spinal disc hernia, gout

**Table 3.** Initial antibiotic regimens according to diagnosis.

Diagnosis	Used Antibiotics n (%)
Pneumonia	Beta-lactam + quinolone 37 (47.4)
	Beta-lactam + macrolide 8 (10.3)
	Carbapenem 14 (13.4)
	Piperacillin Tazobactam 10 (12.8)
	Ceftriaxone + moxifloxacin+ Oseltamivir 3 (3.8)
	Moxifloxacin 3 (3.8)
	Beta-lactam +linezolid 3(3.8)
Urinary tract infection	Piperacillin Tazobactam 49 (25)
	Ciprofloksasin 2 (1)
	Carbapenem 110 (56)
	Vancomycin 3 (1.5)
	Linezolid 2 (1)
	Ceftriaxone 30 (15.3)
Gastroenteritis	Ciprofloxacin + Metronidazole 7 (41.2)
	Ciprofloxacin 4 (23.5)
	Ceftriaxone 6 (35.3)
Skin and soft-tissue infection	Piperacillin Tazobactam 9 (28.1)
	Ampicillin sulbactam 9 (28.1)
	Carbapenem 5 (15.6)
	Carbapenem +Linezolid 3 (9.4)
	Tigecycline 3 (9.4)
	Cefazolin 3 (9.4)

**Table 4.** The distribution of microorganisms in blood culture according to the infection focus.

Microorganism	n (%)	Infection focus n (%)
<i>E.coli</i>	20 (64.5)	Pyelonephritis 15 (75) Urosepsis 2 (10) Pneumonia 3 (15)
<i>Staphylococcus aureus</i>	4 (12.9)	Primary bloodstream infection 1(25) Catheter-related bloodstream infection 3 (75)
<i>Klebsiella spp</i>	3 (9.7)	Pyelonephritis 1 (33.3) Urosepsis 2 (66.7)
<i>Enterococcus spp.</i>	2 (6.5)	Pyelonephritis 1 (50) Spondylodiscitis 1 (50)
<i>Pseudomonas aeruginosa</i>	1 (3.2)	Urosepsis 1 (100)
<b>Coagulase- negative Staphylococci</b>	1 (3.2)	Catheter-related bloodstream infection 1(100)

**Table 5.** Various laboratory test values on the admission day of patients according to their diagnosis.

Median (interquartile range)	Pyelonephritis	Pneumonia	Urosepsis	Skin and soft-tissue infection	Gastroenteritis	p
<b>WBC (mm<sup>3</sup>)</b>	14400 (10900-22000)	11250 (8230-15340)	9300 (8690-23330)	10465 (7712-14865)	8500 (5660-10785)	>0.05
<b>Neutrophil</b>	11200 (9000-19000)	8540 (6000-13000)	8030 (5590-20400)	7580 (4835-0337)	6790 (4190-9790)	>0.05
<b>CRP (mg/L)</b>	104 (64-190)	91 (31-138)	73 (25-209)	103 (43-169)	43 (22-105)	>0.05
<b>ESR (mm/h)</b>	54 (46-92)	39 (19-52)	35 (24-81)	42 (24-70)	28 (19-52)	>0.05
<b>Albumin (g/dl)</b>	2.9 (2.6-3.7)	3.6 (3.2-4)	3.2 (2.9-3.3)	3.9 (3.3-4.1)	3.9 (3.3-4.3)	<0.05

WBC: White blood cell, CRP: C reactive protein, ESR: Erythrocyte sedimentation rate, WBC: 3800-8600 mm<sup>3</sup>, C-reactive protein: 0-5 mg/L, Erythrocyte sedimentation rate: 0-20, Albumin: 3.5-5.3 g/dl, Neutrofile: 2100-6100. p<0.05 significant



In total, 245 (70%) patients consulted with various departments: 1 department in 67 (27.3%), 2 in 58 (23.7%) and 3 or more in 120 (49%). Consultations were requested from neurology, urology, chest diseases, endocrine, cardiology, dermatology, nephrology, otolaryngology, gastroenterology and psychiatry departments in 71 (29%), 68 (27.2%), 44 (18%), 40 (16%), 35 (14%), 33 (13.4%), 24 (9.8%), 19 (7.7%), 18 (7.3%) and 18 (7.3%) patients, respectively. Consultations were requested from other internal and surgical units as well.

Radiological imaging was performed in 228 (65.1%) patients (1, 2 and 3 or more images in 134 (58.7%), 54 (23.6%) and 40 (14.4%), respectively). Abdominal ultrasonography (US) was the most frequently performed radiological imaging technique (n =145, 63.5%), whereas 38 patients (16.6%) underwent lower extremity venous Doppler US, 34 (14.9%) underwent computed tomography (CT) of the brain, 22 (9.6%) underwent superficial soft tissue US, 22 (9.6%) underwent thorax CT, 21 (9.2%) underwent brain magnetic resonance imaging and 17 (7.45%) underwent abdominal CT.

In total, 300 (85.7%) patients were healed and discharged, 21 (6%) were transferred to intensive care unit, 5 (1.4%) were transferred to other clinics, 21 (6%) were discharged with their current medical status, and 3 (0.9%) died.

Blood infection was detected in 31 patients. The distribution of microorganisms in blood culture according to the infection focus is presented in Table 4.

The medians of the various laboratory values according to the diagnosis at admission are presented in Table 5. Although there was a statistically significant difference in the albumin levels among urosepsis patients compared with other diagnostic groups, there was no significant difference in the values of white blood cell (WBC), sedimentation, C-reactive protein (CRP) and neutrophils ( $p > 0.05$ ).

## DISCUSSION

Infections are among the top 10 causes of hospitalization and the top 5 causes of mortality for individuals aged over 65 years (3). Overall, 38.8% of the patients hospitalized at our clinic were over 65 years old. This rate has been reported as 28.6%, 13.5%, 33.1% and 40% in different studies from our country (3–6). These studies show that the geriatric patient population tends to increase in infection diseases clinics over years. This may be explained by the increase in the elderly population as well as the widespread use of interference and immunosuppressive drugs. Recent advances in technology mean that it is now possible for the patients to survive for extended periods with diseases that were once fatal.

Concomitant chronic diseases are precipitating factors for infections (7). The concomitant disease rate was 84.6%. Ozen et al. (6) and Temel and Akcam (8) reported chronic diseases in 86.2% and 89% of their patients, respectively. Therefore, comorbid conditions increase the risk of infection in elderly people.

The increased rates of admission of the elderly people to hospitals and additional interventions increase the risk of infection with resistant microorganisms. Therefore, elderly patients with developing infections should be hospitalized. This may be the reason for the excess of comorbid conditions in patients at the infectious diseases clinic.

The patients admitted to our clinic most frequently had urinary tract infection, pneumonia and skin and soft-tissue infections. In the study by Ulug et al. (4), sepsis, pneumonia and acute gastroenteritis were most frequently detected. Ozen et al. (6) reported pneumonia, urinary tract infections and skin and soft-tissue infections most frequently. Internal intensive care units have been established at many hospitals. In the first stage, patients with sepsis are usually monitored in

intensive care units. Therefore, in recent studies, the rate of sepsis might be lower.

Tuberculosis is a common infectious disease in endemic areas, especially among elderly people, and its incidence rate can reach up to 46% (9). The use of immunosuppressive drugs and chronic diseases, such as diabetes mellitus, chronic renal failure, cancer and malnutrition, are factors that trigger tuberculosis reactivation (10). Approximately, 75% of tuberculosis cases comprise active pulmonary tuberculosis. At our clinic, only cases of extrapulmonary tuberculosis were observed and pulmonary tuberculosis was not detected.

Various organ involvements of extrapulmonary tuberculosis were noted in our study. In a recent study involving 853 patients examined in Ankara, only 3 were diagnosed with tuberculosis (6). The study of Ulug et al. (4) in Diyarbakir, where is in the same region with our province, reported that the rate of tuberculosis was found as 2.6%, which is similar to our study. This shows that tuberculosis is still an important problem in the east of Turkey. Tuberculosis can occur in all organs and tissues. As in our study, rare involvement sites can be seen in elderly patients. In geriatric individuals, the cellular immunity and specific cytokines (interleukin (IL)-2) decreases, and the vulnerability to infections due to intracellular pathogens increases. In addition, the sensitivity of tuberculin skin test, which helps for diagnosis, decreased in elderly patients. This makes the diagnosis even more difficult.

Tuberculosis should be considered in the differential diagnosis, especially in endemic areas.

In geriatric patients, the cause of unknown fever is due to infections with a rate of 30% (11). In our study, 4 patients were followed up with a diagnosis of unknown fever: liver abscess was found in 2 and haematological malignancy in 2 patients. Fasciolosis is a zoonotic disease caused by the *Fasciola* species in humans. Kaplan et al. reported the rate of fasciolosis as 2.77% in our province (12). One of our patients had fasciolosis.

Cutaneous leishmaniasis is a parasitic disease caused by the leishmania protozoa *Phlebotomus*, in which infection occurs during the process of blood extraction from the skin (13). Our patient had a nose wound. Promastigotes were observed in the Tzanck smear of the serous fluid from an ulcer at the lesion site.

Mucormycosis is a rare and fatal opportunistic fungal infection that is seen especially in cases where the immune system is suppressed (14). Diabetes is the most common risk factor. Our patient with mucormycosis was diabetic and was transferred to intensive care unit for follow-up.

Degeneration and chronic diseases in elderly individuals also increase the risk of infection. Chronic diseases increase the susceptibility to infection and cause the disease to appear more severe. These factors increase the need for consultation. Of our patients, 70% required consultation with various departments. Our high consultation rate supports the need for a multidisciplinary approach among geriatric patients. The establishment of geriatrics units at universities and education and service hospitals can achieve a multidisciplinary solution for such complex issues. The establishment of geriatrics hospitals at large centres should also be considered. Our centre has no geriatrics department.

The accompanying problems of geriatric patients, such as malnutrition or dementia, can mask the signs and symptoms of infectious diseases. Classical symptoms and signs of infectious diseases may not be present in elderly patients. Auxiliary diagnostic procedures are needed more frequently because of this atypical course. Radiological imaging methods are the most prominent of these procedures. We applied imaging methods in 228 (65.1%) of our patients.

Many diseases, such as embolism, deep vein thrombosis or cerebrovascular disease, which must be supported with radiology for diagnosis,



are more common in elderly patients than in the younger population. Mass or metastases may be confused with the radiological appearance of many infectious diseases such as tularemia, tuberculosis. An experienced radiologist should be included in the multidisciplinary approach in geriatric patients. As in paediatric radiology, the establishment of geriatric radiology units and increased specificity will significantly contribute to an early diagnosis by clinicians.

The rate of development of infections with bacteraemia is higher in elderly patients than in young patients. Weakness of the immune system, comorbid conditions and more frequent invasive procedures increase the risk of bacteraemia (15). Infectious agents in the blood circulation mainly consist of Gram-positive bacteria (16). Lee et al. (17) found Gram-positive microorganisms in 30.4% and Gram-negative microorganisms in 56.2% of cases. In our study, 77.4% Gram-negative and 22.6% Gram-positive microorganisms were determined in bacteraemia. The high levels of Gram-negative bacteria can be explained by the diagnosis made during the hospitalization of the patients in our clinic. Bacteraemia with pyelonephritis and urosepsis was diagnosed in a significant proportion of inpatients.

In case of infection, the increase in leukocytes in elderly patients may be lower than expected. Studies have shown that 32%–49% of geriatric patients have no increase in WBC despite a serious infection (18). However, despite the normal leukocyte count, the increase in young neutrophils is remarkable (19). In our study, the numbers of leukocytes in 41% of our patients and the CRP values in 8.8% were normal. Current scientific literature supports the use of serum CRP levels to detect systemic infection in hospitalized geriatric patients, especially when clinical examinations and first-level diagnostic tests are negative or misleading. The role of CRP elevation in the diagnosis of localized infections in older patients

also needs further investigation (20). The change in serum albumin levels in elderly patients with an infection indicates an acute phase reaction rather than malnutrition. Changes in cytokine and hormone levels occur as part of the acute response. The increase in tumor necrosis factor (TNF)- $\alpha$  and IL-1 and IL-6 in sepsis inhibits albumin synthesis. The value of albumin was significantly lower in patients with urosepsis ( $p < 0.05$ ). The decrease in the albumin level in patients with sepsis may be explained by severe inflammation.

As a result, human life has been prolonged in parallel with rapid progress in the medical world. Comorbid conditions, frequent admissions to the hospital and medical interventions increase the risk of infection with resistant microorganisms among elderly people. Classical symptoms and signs of infectious diseases may not be present in elderly patients. Auxiliary diagnostic procedures are needed more frequently because of this atypical course. The multidisciplinary approach is essential to evaluate geriatric infections and a radiologist must be included in this team. In areas endemic for infectious diseases, tuberculosis, brucellosis, parasitic diseases and Crimean Congolese haemorrhage fever also can occur in elderly individuals. In this respect, doctors should be more sensitive and sceptical in the evaluation of elderly patients. Travel history should be questioned for elderly patients who are suspected to have an infection. These diseases should be considered in the differential diagnosis of individuals with a history of travel to the endemic regions. The limitations of the present study include its retrospective design and being a single-site study. Prospective and multi-site studies would enable acquisition of more accurate information.

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#### **Conflicts of interest**

The authors have no conflicts of interest to declare.

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