



## Evaluation of Patients Admitted to the Emergency Medicine Department with Symptoms of Central Nervous System Infection

Santral Sinir Sistemi Enfeksiyonu Semptomları ile Acil Servise Başvuran Hastaların Değerlendirilmesi

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### ABSTRACT

**Aim:** We aimed to investigate the demographic data, diagnoses and predictive factors for infection in patients admitted to the emergency department with central nervous system (CNS) symptoms and signs.

**Material and Method:** We retrospectively analyzed 88 cases admitted to the emergency department of a tertiary care university training and research hospital with central nervous system symptoms in terms of demographic data, examination findings, hospitalization status, cerebrospinal fluid (CSF) culture growth and mortality. The cases were analyzed in 3 groups as central nervous system infection, non-infectious central nervous system pathologies and pathologies other than central nervous system.

**Results:** Out of 88 patients, 17 (19.3%) had central nervous system infection. Purulent meningitis was diagnosed in 11 (64.7%) and encephalitis in 6 (35.2%) of these cases. Complaints of vomiting, CSF culture collection rate, Kernig sign positivity, nuchal rigidity and hospitalization rate were significantly higher in the CNS infection group compared to the other two groups. There was no difference between the groups in terms of mortality. In cases of purulent meningitis, CSF cultures were collected from 9 of 11 patients and growth was observed in 2 samples (22.2%). *Klebsiella pneumoniae* and *Haemophilus influenzae* were grown in CSF in 1 patient with a shunt.

**Conclusion:** CNS infections are a cause of morbidity and mortality and patients presenting to the emergency department with signs and symptoms of CNS infection require rapid and careful evaluation. Non-CNS pathologies and non-infectious CNS pathologies should also be considered in these cases.

**Keywords:** Emergency department, central nervous system infection, meningitis, encephalitis.

### ÖZ

**Amaç:** Merkezi sinir sistemi (MSS) semptom ve bulguları ile acil servise başvuran hastalarda demografik verileri, tanıları ve enfeksiyon için prediktif faktörleri araştırmayı amaçladık.

**Gereç ve Yöntem:** Üçüncü basamak bir üniversite eğitim ve araştırma hastanesinin acil servisine santral sinir sistemi semptomları ile başvuran 88 olgu demografik verileri, muayene bulguları, hastanede yatış durumu, beyin omurilik sıvısı (BOS) kültürü üremesi ve mortalitesi açısından retrospektif olarak incelendi. Olgular merkezi sinir sistemi enfeksiyonu, enfeksiyöz olmayan merkezi sinir sistemi patolojileri ve merkezi sinir sistemi dışındaki patolojiler olarak 3 grupta incelendi.

**Bulgular:** 88 hastanın 17'sinde (%19,3) merkezi sinir sistemi enfeksiyonu vardı. Bu olguların 11'inde (%64,7) pürülan menenjit, 6'sında (%35,2) ensefalit saptandı. Kusma şikayetleri, BOS kültürü alınma oranı, Kernig işareti pozitifliği, ense sertliği ve hastaneye yatış oranları MSS enfeksiyonlu grupta diğer iki gruba göre anlamlı olarak yüksekti. Mortalite açısından gruplar arasında fark yoktu. Pürülan menenjit olgularında 11 hastanın 9'undan BOS kültürü alındı ve 2 örnekte (%22,2) üreme görüldü. Şanlı 1 hastada BOS'ta *Klebsiella pneumoniae* ve *Haemophilus influenzae* üredi.

**Sonuç:** MSS enfeksiyonları bir morbidite ve mortalite nedenidir ve acil servise MSS enfeksiyonu belirti ve semptomları ile başvuran hastaların hızlı ve dikkatli bir şekilde değerlendirilmesi gerekir. Bu vakalarda MSS dışı patolojiler ve enfeksiyöz olmayan MSS patolojileri de düşünülmalıdır.

**Anahtar Kelimeler:** Acil servis, santral sinir sistemi enfeksiyonu, menenjit, ensefalit.

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## INTRODUCTION

In patients presenting to the emergency department with symptoms and signs of meningitis, sepsis and neutropenic fever, rapid evaluation of clinical findings and initiation of antibiotherapy within the first hour after collecting the appropriate samples is life-saving. Among these pathologies, although they are not common among emergency department presentations, central nervous system infections are very important and are the highest cause of mortality among infectious diseases. Patients in this group present to the emergency department with fever, headache, nuchal rigidity, and/or altered mental status. The causative agents of central nervous system infection can be bacteria, viruses, fungi, mycobacteria, and parasites. The causative agent profile is determined by the patient's age, region of residence, vaccination status, history of head trauma and cranial operations, accessibility to diagnostic tests, previous hospitalization history, and immune status. The most common community-acquired bacterial agents are *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Listeria monocytogenes*, *Haemophilus influenzae*, and gram-negative bacilli (1). Central nervous system infections may show an acute or chronic course.

Particularly in acute bacterial meningitis presenting to the emergency department, if there is no contraindication for lumbar puncture (when there is proof of no intracranial space-occupying lesions by radiologic imaging methods or no signs of increased intracranial pressure detected on ophthalmoscopy), lumbar puncture should be performed rapidly within the first hour, (CSF) should be collected and antibiotherapy and other treatments should be started after CSF and blood culture are sent for evaluation. Otherwise, a mortal course may be observed (2,3,4,5). While mortality in bacterial meningitis was 100% in the pre-antibiotic era, bacterial clearance from CSF is achieved with effective antibiotherapy, but the disease still continues to be a cause of morbidity and mortality worldwide. In a study conducted in 2016, the number of deaths due to meningitis in the world was reported as 318,000 and the annual disability-adjusted life years were reported as 21,866,000 (6). While the mortality rate is 30%, particularly in pneumococcal meningitis, this rate is reported to be 5-10% in meningococcal meningitis (7,8). These rates decrease with the initiation of emergency antibiotherapy (9,10,11). In addition, *Streptococcus pneumoniae*, *Haemophilus influenzae* type B, and *Neisseria meningitidis* vaccinations decrease the frequency of the disease. There are few studies in the literature on patients presenting to the emergency department with signs and symptoms of CNS infection. Our primary aim in this study is to retrospectively evaluate the cases admitted to the emergency department of a tertiary university training and research hospital with suspicion of central nervous system infection. Our secondary aim is to determine in

what proportion of patients with central nervous system infection in the emergency department this preliminary diagnosis is correct.

## MATERIAL AND METHOD

The Ethical Approval for the study was obtained from the Non-Interventional Ethics Committee of Katip Çelebi University Atatürk Training and Research Hospital on 24.11.2023 with the number 0555.

### Study Design

We conducted this observational retrospective study in the emergency department of a tertiary care university training and research hospital between December 1, 2021, and December 1, 2022, by analyzing 88 patients admitted to the emergency department with symptoms and signs of fever, headache, confusion, nausea, and vomiting, which may suggest a central nervous system infection.

In addition to demographic data, by reviewing the hospital records, we retrospectively evaluated the comorbid factors, emergency department diagnosis, hospitalization rate, and outcome information. Patients were divided and compared into 3 groups; non-central nervous system pathologies, central nervous system infection, and non-infectious central nervous system pathologies.

### Study Population

In this study, we included patients over the age of 18 years, who presented to the emergency department with central nervous system infection findings and were consulted by the infectious diseases department with a preliminary diagnosis of central nervous system infection. We excluded patients under 18 years of age, patients with suspected foci of infection other than the central nervous system, patients whose information could not be reached, and patients with missing laboratory data.

### Data collection

We collected the patients data included in the study via the hospital's data management system and vital parameters, demographic data, and laboratory test results of the patients were recorded on patient forms created for statistical analysis. We noted down the information on admission status to the ward and intensive care units, as well as information on exitus and discharge.

### Statistical Analysis

The data were evaluated using the statistical package program IBM SPSS Statistics Standard Concurrent User V 26 (IBM Corp., Armonk, New York, USA). The descriptive statistics were presented as the number of units (n), percentage (%), and mean  $\pm$  standard deviation ( $\bar{x} \pm sd$ )

values. The normal distribution of the data of numerical variables was evaluated by the Shapiro-Wilk normality test. The "One-way ANOVA" test was used to evaluate the differences between the three groups, since the data were normally distributed.

"Pearson" and "Fisher exact" tests were used to compare categorical variables with each other.  $p < 0.05$  was considered statistically significant.

## RESULTS

We included 88 patients in the study and 48 of them were female (54.5%). The mean age was  $58.15 \pm 21.10$  years. While confirming the diagnosis of central nervous system infection in 17 patients (19.3%) (purulent meningitis in 11 patients (64.7%), encephalitis in 6 patients (35.2%), we detected non-infectious central pathologies in 11 patients (cerebrovascular event (CVE) in 8 patients, intracranial hemorrhage in 2 patients, metabolic encephalopathy in 1 patient) and non-central nervous system pathologies in 60 patients. The comparison of these 3 groups according to demographic data, history of hospitalization in the last 3 months, history of neurosurgical operation, presence of EVD catheter, fever, vomiting, and CSF culture are given in **Table 1**.

While comparing all 3 groups with each other in terms of general characteristics, we observed that the hospitalization history in the last 3 months was higher in the group with non-infectious CNS pathology compared to the other 2 groups ( $p=0.030$ ). The presence

of vomiting complaints and CSF culture rate were significantly higher in the group with CNS infection compared to the other 2 groups ( $p=0.040$ ,  $p=0.005$ , respectively).

Kernig, Brudzinski's sign positivity, nuchal rigidity, clouding of consciousness, presence of localized motor findings and EMV score evaluation in the 3 groups analyzed in the study are given in **Table 2**.

While comparing all 3 groups with each other, we observed that Kernig positivity and nuchal rigidity were higher in the group with CNS infection compared to the other two groups ( $p=0.049$ ,  $p=0.001$ , respectively). While evaluating in terms of localized motor findings and clouding of consciousness, we observed that there was a statistically significant increase in the group with non-infectious CNS pathology ( $p=0.003$ ,  $p < 0.001$ ).

The 3 groups included in the study were evaluated in terms of hospitalization rate and a summary of the findings is given in **Table 3**.

While comparing all 3 groups in terms of hospitalization, we observed that there was a statistically significant difference ( $p=0.005$ ). We observed that patients with central nervous system infections were indicated for hospitalization except for 1 case (this case was referred to an external center due to lack of space). Non-central nervous system pathologies resulted in significantly more emergency department discharges.

The results of statistical analysis in terms of mortality in the three groups are given in **Table 4**.

**Table 1: The comparison of general characteristics according to patient groups**

	Diagnosis			Test Statistics	
	Non-CNS pathologies	CNS Infection	Non-infectious CNS Pathologies	Test value	p value
Age $\bar{x} \pm sd$	56,13 $\pm$ 20,38	55,94 $\pm$ 22,13	72,63 $\pm$ 19,40	F=3,100	0,050
Gender				$\chi^2=1,814$	0,430
Female	23 (60,5)	9 (27,3)	6 (15,8)		
Male	37 (74,0)	8 (16,0)	5 (10,0)		
Hospitalization in the Last 3 Months				$\chi^2=5,997$	0,030
No	55 (72,4)	14 (18,4)	7 (9,2)		
Yes	5 (41,7)	3 (25,0)	4 (33,3)		
Neurosurgical Operation				$\chi^2=2,165$	0,378
No	55 (68,8)	14 (17,5)	11 (13,8)		
Yes	5 (62,5)	3 (37,5)	0 (0,0)		
EVD Catheter				$\chi^2=0,633$	>0,999
No	58 (67,4)	17 (19,8)	11 (12,8)		
Yes	2 (100,0)	0 (0,0)	0 (0,0)		
Fever $\bar{x} \pm sd$	36,96 $\pm$ 0,95	37,34 $\pm$ 1,10	37,07 $\pm$ 0,64	F=1,060	0,351
Vomiting				$\chi^2=5,963$	0,040
No	54 (72,0)	11 (14,7)	10 (13,3)		
Yes	6 (46,2)	6 (42,6)	1 (7,7)		
CSF Culture				$\chi^2=9,353$	0,005
No	53 (74,6)	9 (12,7)	9 (12,7)		
Yes	7 (41,2)	8 (47,1)	2 (11,8)		

$\bar{x}$ : Mean, sd: Standard deviation,  $\chi^2$ : Chi-squared test statistic obtained by Exact method, F: ANOVA test

**Table 2: The comparison of examination findings according to patient groups**

	Diagnosis			Test Statistics	
	Non-CNS pathologies	CNS Infection	Non-infectious CNS Pathologies	Test value	p value
Kernig				$\chi^2=5,765$	0,049
No	60 (69,8)	15 (17,4)	11 (12,8)		
Yes	0 (0,0)	2 (100,0)	0 (0,0)		
Brudzinski				$\chi^2=3,501$	0,131
No	59 (69,4)	15 (17,6)	11 (12,9)		
Yes	1 (33,3)	2 (66,7)	0 (0,0)		
Nuchal Rigidity				$\chi^2=13,601$	0,001
No	54 (74,0)	8 (11,0)	11 (15,1)		
Yes	6 (42,9)	8 (57,1)	0 (0,0)		
Clouding of Consciousness				$\chi^2=19,445$	<0,001
No	51 (82,3)	8 (12,9)	3 (4,8)		
Yes	9 (34,6)	9 (34,6)	8 (30,8)		
Localized Motor Finding				$\chi^2=11,366$	0,003
No	57 (73,1)	15 (19,2)	6 (7,7)		
Yes	3 (30,0)	2 (20,0)	5 (50,0)		
EMV Score $\bar{x}\pm sd$	14,83 $\pm$ 1,66	13,76 $\pm$ 2,35	14,45 $\pm$ 1,80	F=1,045	0,356

$\bar{x}$ : Mean, sd: Standard deviation,  $\chi^2$ : Chi-squared test statistic obtained by Exact method, F: ANOVA test

**Table 3: The comparison of hospitalization status according to patient groups**

	Diagnosis			Test Statistics	
	Non-CNS pathologies	CNS Infection	Non-infectious CNS Pathologies	$\chi^2$ value	p value
Hospitalization				13,508	0,005
Ward	23 (57,5)	12 (30,0)	5 (12,5)		
Intensive Care	6 (50,0)	4 (33,3)	2 (16,7)		
Discharged	31 (86,1)	1 (2,8)	4 (11,1)		

$\chi^2$ : Chi-squared test statistic obtained by Exact method

**Table 4: The comparison of mortality status according to patient groups**

	Diagnosis			Test Statistics	
	Non-CNS pathologies	CNS Infection	Non-infectious CNS Pathologies	$\chi^2$ value	p value
Mortality				1,388	0,541
Surviver	55 (67,1)	17 (20,7)	10 (12,2)		
Exitus	5 (83,3)	0 (0,0)	1 (16,7)		

$\chi^2$ : Chi-squared test statistic obtained by Exact method

While comparing all 3 groups in terms of mortality, we observed that no statistically significant difference was found between them ( $p=0.541$ ). Patients with a prediagnosis of central nervous system infection in the emergency department had similar outcomes in terms of mortality, even if the final diagnosis was not an infection.

Of the 17 patients with central nervous system infection, 11 were diagnosed with meningitis and 6 were diagnosed with encephalitis. While CSF sampling and culture were collected from 14 patients in the emergency department, CSF culture could not be collected because 2 patients refused the lumbar puncture procedure and although the procedure was attempted on one patient, the culture was not successfully obtained. Of the 9 patients who were diagnosed with meningitis and in whom CSF samples were collected, culture positivity was found only in 2 patients; *Klebsiella pneumoniae* was grown in a patient with a shunt and *Haemophilus influenzae* in another patient. No growth was detected in the bacterial cultures of 5 encephalitis patients.

**Table 5: The cultures of patients with CNS infections**

Diagnosis	Number of patients	CSF Culture		Growth in culture	
		Collected	Not Collected	Yes	No
Meningitis	11	9	2	2	7
Encephalitis	6	5	1	0	5
Total	17	14	3	2	12

## DISCUSSION

Central nervous system infections are relatively rare compared to other infections presenting to the emergency department, but are very important because of their morbid and mortal course. Therefore, rapid differential diagnosis and initiation of antibacterial treatment within the first hour after presentation, particularly in patients with acute purulent meningitis, is life-saving. In this study, we analyzed 88 patients admitted to the emergency department of a tertiary care university training and research hospital with signs and symptoms of central nervous system infection.

The hospitalization rate in the last 3 months was higher in the group with non-infectious CNS pathology compared to the other two groups ( $p=0.030$ ). Since diseases involving different systems were included in this disease group, we thought that recent hospitalization might trigger CNS disease. The presence of vomiting complaints and CSF culture rate were significantly higher in the group with CNS infection compared to the other 2 groups ( $p=0.040$ ,  $p=0.005$ , respectively). Vomiting, which is one finding of increased intracranial pressure in CNS infections, is an expected symptom and CSF examination and culture are procedures that should be performed routinely in the prediagnosis of meningitis.

While comparing all 3 groups with each other, we observed that Kernig positivity and the presence of nuchal rigidity were higher in the group with CNS infection compared to the other two groups ( $p=0.049$ ,  $p=0.001$ , respectively). In terms of localized motor findings and clouding of consciousness, there was a statistically significant increase in the group with non-infectious CNS pathology ( $p=0.003$ ,  $p<0.001$ ). While reviewing the literature, we concluded that Kernig positivity and nuchal rigidity may be good markers in differentiating central nervous system infections.

While evaluating the cases in the three groups in terms of hospitalization, we observed that patients with central nervous system infections mostly required hospitalization. Non-CNS pathologies resulted in significantly more emergency department discharges. This may be explained by the fact that the course of CNS infections is serious and pathologies other than CNS, especially those related to metabolic conditions, respond rapidly to supportive treatment in the emergency department.

There was no statistically significant difference in mortality between the 3 groups. Patients with a prediagnosis of central nervous system infection in the emergency department had similar outcomes in terms of mortality even if the final diagnosis was not an infection. Due to limitations such as the retrospective, single-center, and small sample size of this study, we thought that the mortality rate was similar between the 3 groups.

The culture negativity rate was 77.7% in the patients who were included in the study and diagnosed with bacterial meningitis, which is similar to the literature, and 87.2% of CSF culture negativity was found in the study by Altunal et al. (12). In the study by Yücel et al, the rate of isolation of the causative agent in 55 CSF samples collected in the emergency department was reported as 7%, culture negativity was reported as 93%, and *Klebsiella pneumoniae* was found among the causative agents similar to our study (13). The low rate of growth in culture may be attributed to prior antibiotic use and

possible problems in the transportation of cultures collected in emergency department conditions to the laboratory.

It is very important to start management and treatment within the first hour for central nervous system infections such as bacterial meningitis and encephalitis, which are morbid and mortal in patients presenting to the emergency department with symptoms and signs of nausea, vomiting, neck stiffness, fever, and clouding of consciousness. In this study, the rate of central nervous system infection was 19.3% and the rate of meningitis was 12.5% in patients with a prediagnosis of central nervous system infection presenting with these symptoms. In our study, pathologies other than CNS infection were found in 69% of the patients who presented to the emergency department with complaints suggestive of CNS pathology.

## CONCLUSION

Since CNS infections may have a morbid and mortal course, the necessary investigations must be planned, the diagnosis made, and empirical treatment initiated without delay in emergency department conditions. In addition, pathologies other than CNS infection and infectious diseases due to foci outside the CNS should also be considered in patients presenting to the emergency department with findings suggestive of CNS pathology.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The Ethical Approval for the study was obtained from the Non-Interventional Ethics Committee of Katip Çelebi University Atatürk Training and Research Hospital on 24.11.2023 with the number 0555.

**Informed Consent:** Informed consent form did not obtained from the participants due to the nature of the study.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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