

# Frequency of Brain Death in Children and Donation Rate

## Çocuklarda Beyin Ölümü Sıklığı ve Donasyon Oranı

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### ABSTRACT

**Objective:** The aim of this study was to determine the frequency of patients diagnosed with brain death after admission to the pediatric intensive care unit and the organ donation rate.

**Material and Methods:** The study was carried out as a retrospective analysis. Patients diagnosed with brain death in the pediatric intensive care unit of the Ankara City Hospital were recorded in the patient form. The study was limited to patients admitted to the hospital between 1 December 2019 and 1 December 2021.

**Results:** The data of the patients who died in the PICU (n= 325) were evaluated. A total of 17 (5.2%) of these patients were diagnosed with brain death (BD). The underlying diseases of brain death in 7 (42%) patients was central nervous system disorders (cerebral palsy, meningocoele, hydrocephalus, etc.), head trauma (such as traffic accidents and falls) in 5 others (29%), and hypoxic-ischemic injury owing to cardiopulmonary arrest in the remaining 5 (29%) patients. Cranial CT angiography was performed to all patients as an ancillary test. Six (35%) patients with hypernatremia were diagnosed with Central Diabetes Insipidus (DI). Only one patient became an organ donor.

**Conclusion:** The diagnosis of brain death should be made more frequently. People should be informed about organ donation, Many attempts should be made to influence public opinion about the benefits of the organ transplantation.

**Key Words:** Brain death, Central diabetes insipidus, Children, Organ transplantation

### ÖZ

**Amaç:** Bu çalışmanın amacı, çocuk yoğun bakıma yattıktan sonra beyin ölümü tanısı alan hastaların sıklığını ve donasyon oranını tespit etmektir.

**Gereç ve Yöntemler:** Geriye dönük bir çalışma olarak yapıldı. Otuz iki yataklı Ankara Şehir Hastanesi Çocuk Yoğun Bakım Ünitesi'nde beyin ölümü tanısı konan hastalar hasta formuna kaydedildi. 01.12.2019 ile 01.12.2021 tarihleri arasında beyin ölümü tanısı almış hastalar dahil edildi.

**Bulgular:** Çocuk yoğun bakım ünitesinde (n= 325) ölen hastalar tarandı. Bu ölen hastalardan 17 (%5.2)'sında beyin Ölümü (BÖ) tanısı kondu. Beyin ölümüne neden olan altta yatan hastalıklar, 7 (%42) hastada santral sinir sistemi patolojileri (serebral palsy, meningocoele, hidrosefali vb.) olan hastalardı, 5 (%29)'inde kafa travması (trafik kazaları ve düşme gibi nedenler), 5 (%29) hasta kardiyopulmoner arrest sonrası olmasıdır. Tüm hastalara ek test olarak Kranial BT anjiyo uygulandı. Hipernatremi olan 6 (%35) hasta Santral Diyabetes Insipidus (DI) tanısı aldı. BÖ tanısı konan hastalardan sadece biri (%6) donör olmayı kabul etti.



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**Sonuç:** Beyin ölümü tanısı daha sık konulmalıdır. Organ bağıışı için halk bilgilendirilmelidir. Organ nakli için kamuoyu oluşturulmalıdır.

**Anahtar Sözcükler:** Beyin ölümü, Santral diabetes İnsipidus, Çocuklar, Organ nakli

## INTRODUCTION

The brain death (BD) status is defined as an irreversible coma in which the brain and brain stem lose all functions, apnea persists, and there is a loss of supraspinal reflexes. Patient with BD does not show any reflexes and there is no spontaneous respiratory effort during a 3-minute disconnection from the ventilator, the patient is completely unresponsive. Patients diagnosed with brain death are considered clinically and legally dead (1). The organ donation rate in Turkey is lower than in other countries (2). Majority of the pediatric patients waiting for an organ transplant succumb to their sickness due to the insufficient organ donation. Therefore, it is crucial to diagnose BD and the care of the patients who donate organs is important.

The most remarkable sign of brain death is central diabetes insipidus (CDI). CDI is characterized by polyuria, hypernatremia and hyperosmolar dehydration due to antidiuretic hormone deficiency (3). Intoxication (alcohol), drugs including central nervous system (CNS) depressant muscle relaxants, primary hypothermia, hypovolemic shock, as well as metabolic and endocrine disorders should be excluded before diagnosing BD. Hypernatremia and high blood sugar levels are consequences rather than causes of brain death (4). The clinical diagnosis of brain death should be made in three steps: Establishing the etiology; excluding potentially reversible syndromes that may produce symptoms similar to brain death; and detecting clinical signs of brain death, including coma, brain stem areflexia, and apnea (1-3,5).

To declaration of brain death, the following should be assessed: presence of irreversible coma and absence of spontaneous breathing confirmed by apnea tests; absence of pupillary light reflexes, corneal reflexes, doll's eye movements, gag reflex, cough reflex (tracheal), eye movements on bilateral caloric test, motor response in any cranial nerve distribution, and absence of motor response upon facial/limb/trunk stimulation. Hypotension, hypothermia, and metabolic disorders should be corrected before an assessment of brain death in infants and children. Although the diagnosis of brain death is clear, there is still no consensus on the follow-up of the patients.

The aim of this study was to define the demographic and clinical characteristics of patients that were diagnosed with brain death and to determine the frequency of organ donation.

## MATERIALS and METHODS

This retrospective study was carried out in the 32-bed capacity tertiary pediatric intensive care unit of the Ankara City Hospital.

The hospital database was used to collect data. All deaths in the PICU during the 2-year period between December 2019 and December 2021 were screened. Patients aged one month to 18 years old that were diagnosed with BD were identified and evaluated. Demographic information, cause of BP, evaluation of BP, and length of hospital stay were included in the study. The diagnosis of BD requires confirmation of a known, irreversible cause of coma with apnea, brain stem areflexia and cerebral unresponsiveness, and a lack of clinical functions of the brain as assessed by an ancillary test for children. Two examinations are required, each separated by an observation period, including the apnea test. In the diagnostic criteria of infants and children, an observation period of 48 hours for babies under 2 months old, 24 hours for those between 2 months and 1 year of age, and 12 hours for children between 1 and 18 years old is required. A known cause of irreversible coma was combined with an ancillary test in children and the diagnosis of BD was finally made, with brain stem areflexia and cerebral unresponsiveness. The final decision regarding a diagnosis of BD had to be approved by a group of doctors. The determination of BD was then explained by the PICU physician to the relatives of the patient. The organ donation request was made by the hospital's organ donation coordinator. Cranial CT angiography was used as an ancillary test in all patients. Tests were repeated by a pediatric neurologist until brain stem reflexes and supraspinal reflexes were coherent with brain death.

CDI, polyuria (urine output > 4 mL/kg/hr for children, 300 mL/hr for adults  $\geq$  70 kg for adults) for at least two consecutive hours, hypernatremia (Serum Na > 145 mmol/L), high serum osmolality (> 300 mOsm/kg) and low urine osmolality (< 300 mOsm/kg) at the time of diagnosis were taken as diagnostic criteria (6,7).

The study was approved by the Ankara City Hospital No. 2 Clinical Research Ethics Committee (E2-22-1244 /1244).

## Statistical analysis and method

First, the descriptive properties (mean, median, number, and percentage) of the variables were determined. The numeric variables were checked for fit with normal distribution. While comparing the two groups, the Student's t-test was used for numeric variables with normal distribution. The Mann-Whitney U test was performed for numeric variables not normally distributed. The chi-square test was performed to compare categorical variables. A p-value < 0.05 was considered statistically significant. Statistical Package for the Social Sciences (SPSS) version 17 (Chicago, Illinois, USA) software was used to analyze the results.

## RESULTS

The data of the patients who died in the PICU (n= 325) between December 2019 and December 2021 were screened. BD was diagnosed in 17 (5.2%) of these patients. Among the patients diagnosed with BD, 9 (53%) patients were male and 8 (47%) were female. The median age of the patients was 10.5 years (IQR: 3-16). The primary cause of brain death in 7 (42%) patients was central nervous system disorders (cerebral palsy, meningocele, hydrocephalus, etc.), head trauma (such as traffic accidents and falls) in 5 (29%), and hypoxic-ischemic injury owing to cardiopulmonary arrest in the remaining 5 (29%) patients. In one of the patients, the COVID-19 test was positive during screening. The median length of hospital stay was 12.5 days (IQR: 7-19.75). The median time for brain death assessment was 3 days (IQR: 2-7). Demographic data and laboratory findings of patients with brain death are given in Table I.

Cranial CT angiography was applied to all patients as an ancillary test. These were interpreted by an experienced radiologist and were evaluated as congruent with BD. Cranial CT angiography was repeated twice at one-week intervals in 3 (18%) patients, and the diagnosis was made. The first cranial CT angiography was not congruent even though it was clinically congruent with BD

The apnea test was applied to all patients. It supported BD diagnosis in only 9 (53%) patients. In the other 8 (47%) patients, the test was terminated because bradycardia and hypotension occurred.

Hypernatremia (over 145meq/L) was present in 14 (82%) of the patients with a clinical diagnosis of BD, 2 (12%) had normonatremia (135-145 meq/L), and 1 (6%) had hyponatremia. A total of 6 (35%) patients with hypernatremia were diagnosed with Central Diabetes Insipidus (DI) and all of them were given desmopressin and their polyuria and sodium levels improved.

**Table I: Demographic data and laboratory findings of patients with brain death.**

Demographic data	n (%) or Median (IQR)
Brain Death (%)	(5.2%)
Age (years)	10.5 (3-16)
Sex (male)	9 (53%)
Hospital stay duration	12.5 days (7-19.75)
Median duration of BD assessment	3 (2-7)
Hypernatremia	164.5 meq/L (158.0-174.0)
Central DI	6 (35%)
Organ Transplant	1 (6%)
Hospital Admission Diagnosis	
Central nervous system pathologies	7 (42%)
Head trauma	5 (29%)
Cardiopulmonary arrest	5 (29%)

After the PICU doctor declare the BD diagnosis with the family, the organ donation team gave information and let the family choose whether or not to donate. Only one family (6%) approved the donation of their child's organs. The heart, liver and kidney of this donor patient were used for organ transplantation.

## DISCUSSION

In this study, the frequency of brain death was found to be 5.2%. This frequency rate varies between 10-37% in the literature (8-10). Also religious reasons may play a role in the low level of donation rates. Additionally, the transport of these patients for radiologic ancillary tests may not be suitable due to the unstable status of the patients.

In the this study, the most important causes of BD were central nervous system , disorders, head trauma, and hypoxic-ischemic injury owing to cardiopulmonary arrest. Brain injuries leading to brain death can be precipitated by extracranial or intracranial events. The main extracranial event leading to brain death is delayed or inadequate cardiopulmonary resuscitation following cardiopulmonary arrest, resulting in prolonged and severe disruption of blood flow to the brain. Following this, hypoxia and ischemia cause disruption in cellular osmoregulation, which leads to increased water entry into the brain parenchyma and causes cerebral edema. Since the brain is surrounded by a rigid skull, this swelling will eventually cause blood flow disturbances and more hypoxia, resulting in increased edema. The detrimental result of this ongoing edema of the brain, if high enough, will compress the entire brain and brain stem or cause herniation or complete cessation of cerebral circulation, aseptic necrosis of brain tissue, and eventually brain death with increased intracranial pressure. Hypoxic ischemic brain damage occurs when oxygen and nutrients do not reach the brain tissue as a result of impaired circulation. Brain edema develops and brain death occurs when brain stem functions are lost (11).

Five studies published exclusively on pediatric patients showed that collectively 145 (52%) of 279 patients had CDI (12-16). In the present study, 6 (35%) patients with hypernatremia were diagnosed with Central Diabetes Insipidus (DI), and all of them were given DDAVP. Their polyuria and sodium levels improved. Hypernatremia (over 145mg/dl) was present in 14 (82%) of the patients, but 8 of these patients were not diagnosed with CDI since they received 3% NaCl treatment. After the 3% NaCl treatment was discontinued, their sodium values returned to normal. The reason why some patients do not develop CDI may be due to the functioning of the hypothalamic osmoregulation system.

An absence of cerebral circulation is an important confirmatory test for brain death. In cases of brain death, cerebral angiography usually shows a lack of blood flow at the carotid bifurcation or the Circle of Willis or beyond. There should be no intracerebral filling at the level of the skull entrance of the carotid or vertebral

artery. Conventional 4-vessel cerebral angiography remains the “gold standard” imaging method and is widely used as an ancillary test for brain death (17). In Turkey, the law requires an additional test to be performed together with the apnea test for the diagnosis of BD in children. Cerebral angiography was performed as an additional test in all patients who were clinically diagnosed with BD in our study. This test was repeated until it correlated with BD. In this way, the diagnosis of BD was made.

In this study, only 1 (6%) family donated the child’s organs. In a Canadian study, the approval rate for organ donation was 64%. The organs of 47% of these donors were used (18). The reasons for refusing organ donation were religious reasons (87%) and ethnic origin (13%).

Prejudices can be broken in terms of organ donation by increasing the communication between families and doctors, and providing more information about the patient’s disease. Organ donation can also be promoted through the social media. If necessary, support can be obtained from the religious officials for organ donation in religious matters.

## CONCLUSION

The ability to make a diagnosis of BD is extremely necessary. Families should be informed about organ donation and preliminary preparation ought to be made. The diagnosis should be confirmed quickly with ancillary tests for the patients whose clinical findings are compatible with BD.

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