

Evaluation of Pediatric Brain Death and Organ Donation: 10-Year Experience in a Pediatric Intensive Care Unit in Turkey

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What is already known on this topic?

- Worldwide, hundreds of people are currently waiting for a life-saving organ transplantation. Unfortunately, organs donated by living donors are insufficient to meet all demand.
- Pediatric BD is a highly complex and sensitive issue in the pediatric practice for clinicians.
- Early diagnosis and good donor care after diagnosis may enhance the chance of OD in pediatric cases.

What this study adds on this topic?

- The pediatric donor rate in our study cohort was 20.8%, which reflects the relatively low cadaveric OD rates in our country, in comparison with the developed European and American countries.
- We report more complication rates in pediatric BD patients. Hyperglycemia, diabetes insipidus (DI), and hemodynamic instability were observed in over 50% of the patients. It should be remembered that these complications can be a severe barrier to OD, and therefore need to be diagnosed and managed immediately.
- We could not find any statistically significant difference between the donors and non-donors in terms of the interval between BD and its diagnosis, but multicenter national studies investigating pediatric BD and factors affecting OD should be conducted, to test our results.

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ABSTRACT

Objective: We aimed to investigate the rate of brain death (BD) determinations and organ donations (OD) in our tertiary pediatric intensive care unit (PICU), and to report the data on the demographic pattern and supplementary descriptive data on BD declarations.

Methods: The study was designed as a retrospective, single-center, descriptive cohort study. We evaluated all children who were determined to meet the criteria for BD in our tertiary PICU between January 2011 and December 2020.

Results: During study period, BD was identified in 24 patients among 225 total deaths (10.7%). Their median age was 85 months (8–214) and the male-to-female ratio was 1 : 1. The most common diagnosis was meningoencephalitis in 25%, followed by traumatic intracranial hemorrhage (16.7%). The median time from admission to PICU until BD diagnosis was 6.5 days. The time from the first BD physical examination to the declaration of BD was 27.5 hours. There was no statistically important difference between donors and non-donors. The apnea test (AT) was the most performed ancillary method (100%), followed by electroencephalogram (EEG) (66.7%), and magnetic resonance angiography or computed tomography angiography (MRA/CTA) (54.2%). Hyperglycemia developed in 79.2% of the cases, and 70.8% developed diabetes insipidus (DI). Five patients (20.8%) were organ donors in study group. In the study, 13 solid organ and 4 tissue transplantations were performed after OD.

Conclusion: Awareness of the incidence and etiology may contribute to the timely diagnosis and declaration of brain death, and with the help of good donor care, may help in increasing OD rates in the pediatric population.

Keywords: Apnea test, brain death, organ donation, organ transplantation, pediatrics, pediatric intensive care

INTRODUCTION

Brain death (BD), resulting from increased intracranial pressure, is a clinical condition defined as the complete and irreversible loss of consciousness and all brainstem functions that are needed to sustain vital functions, including respiratory activity.^{1,2} During BD, some pathophysiological changes take place in the cardiovascular, respiratory, and endocrine systems in the body, and these changes cause metabolic and hormonal abnormalities that invariably end with the loss of vital functions, cardiac arrest, and finally, somatic death. Brain death is accepted as a medical and legal criterion of death in a majority of countries, including our country.^{3,4} Traumatic brain injury and hypoxic-anoxic encephalopathy are the most common causes of BD in children.⁵

Pediatric intensive care unit (PICUs) are the most common locations for pediatric mortalities, and a percentage of these are, unfortunately, BD. The early diagnosis of BD, the maintenance

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of vital functions, and correction of pathologic changes make it possible to delay somatic death, which may create an opportunity for organ donations (OD). Worldwide, hundreds of people are currently on the waiting list for a lifesaving organ transplant. Organs donated by living donors are insufficient to meet all demand, and therefore a considerable portion of these people on the waiting lists die because of the lack of appropriate cadaveric donors and worsening organ failure during this period. The pediatric age group accounts for approximately 2% of patients in the waiting lists of the United Kingdom and 1.5% in the United States of America.⁶ In Turkey, there are currently over 26 000 patients on waiting lists for organ transplants, according to the 2020 data of the Turkish Ministry of Health. Pediatric patients, no less than the rates reported in the United States and United Kingdom, are, unfortunately, an important part of these waiting lists.

The primary objective of this study is to analyze the causes of BD, the ancillary tests used to diagnose BD, the duration of hospitalization before declaration of BD, the duration of survival after diagnosis, the time to BD declaration (from first physical examination to BD declaration), the complications observed during hospitalization, and apnea test (AT) results. We also discuss the OD rates in pediatric and adult patients during the study period, and compare our results with those in existing literature.

METHODS

Study Design, Population, and Setting

The study was designed as a retrospective, single-center, descriptive cohort study. We evaluated all children who were determined to meet the criteria for pediatric BD in our tertiary PICU between January 2011 and December 2020. The Çukurova University Hospital provides a 13-bed tertiary care PICU facility for children aged from 1 month to 18 years. Both medical, general surgical, and cardiothoracic patients are treated, including trauma patients. This study was ethically approved by the Çukurova University Institutional Research Ethics Committee (Date: May21, 2021, Number: 111). The need for informed consent for participation was waived, as this was a retrospective confidential medical record review.

Institutional BD Evaluation Policy

The study included 2 distinct time periods: between 2011 and 2014, and after 2014. In 2011–2014, 4 specialist physicians were consulted for the diagnosis of BD, from the anesthesiology, cardiology, neurology, and neurosurgery departments. BD is now diagnosed by 2 physicians (a neurologist or neurosurgeon, and an anesthesiologist or intensive care specialist) since 2014, in accordance with the rules of evidence-based medicine.

Data Collection

We screened all hospitalizations and deaths that occurred in the PICU of our hospital over a 10-year period (2011–2020). Patients were eligible if they were aged between 1 month and 18 years. BD was diagnosed in accordance with the conditions outlined in the applicable law, and the criteria specified in the guidelines.^{5,7,8} The records of 24 patients diagnosed with BD during the study period were reviewed retrospectively. The medical records, BD determination reports, and other data were obtained from our institutional database along with the

medical reports of the patients and the reports of the organ transplant coordination. The following data were recorded: age, gender, diagnosis, the time from admission to PICU until declaration of BD, time from BD declaration to cardiac arrest, duration of BD diagnosis (time from first BD physical examination to declaration of BD), total hospital and PICU length of stay, ancillary tests used to support BD determination (apnea test (AT), electroencephalogram (EEG), brainstem evoked potential and imaging studies to determine cerebral blood flow), and the complications of BD (such as diabetes insipidus (DI), hypothermia, hyperglycemia, coagulopathy, hemodynamic instability, and multiple organ failure).

The main causes of BD were grouped into the following categories: traumatic brain injury, non-traumatic intracranial hemorrhage, central nervous system (CNS) infections, hypoxic ischemic injury from a known cardiac arrest, intoxications, CNS malignancies, CNS infarction, metabolic encephalopathy, and other reasons (such as sepsis, status epilepticus).

Ancillary tests and radiologic methods were carried out for some patients, and an AT was performed on all patients. It was considered positive when the patient did not show any respiratory effort, despite PaCO₂ levels of ≥ 60 mmHg and an increase of ≥ 20 mmHg compared to the baseline value. AT was performed in all patients, and the test results and parameters in blood gas analyses before and after the test were also recorded. The cerebral blood flow was measured by computerized tomography angiography (CTA), magnetic resonance angiography (MRA), or transcranial Doppler ultrasound (TCD), and the results were considered positive when an absence of blood flow was identified.

The complications that occurred during BD were also analyzed, such as coagulopathy, hypothermia ($<35^{\circ}\text{C}$), hyperglycemia (blood glucose >180 mg/dL), DI, hemodynamic dysfunction, and multiple organ failure after BD determination. The rate of OD by the families, the potential reasons for unwillingness to being a donor, the organs removed, and their number were determined using data obtained from the department of organ transplant coordination.

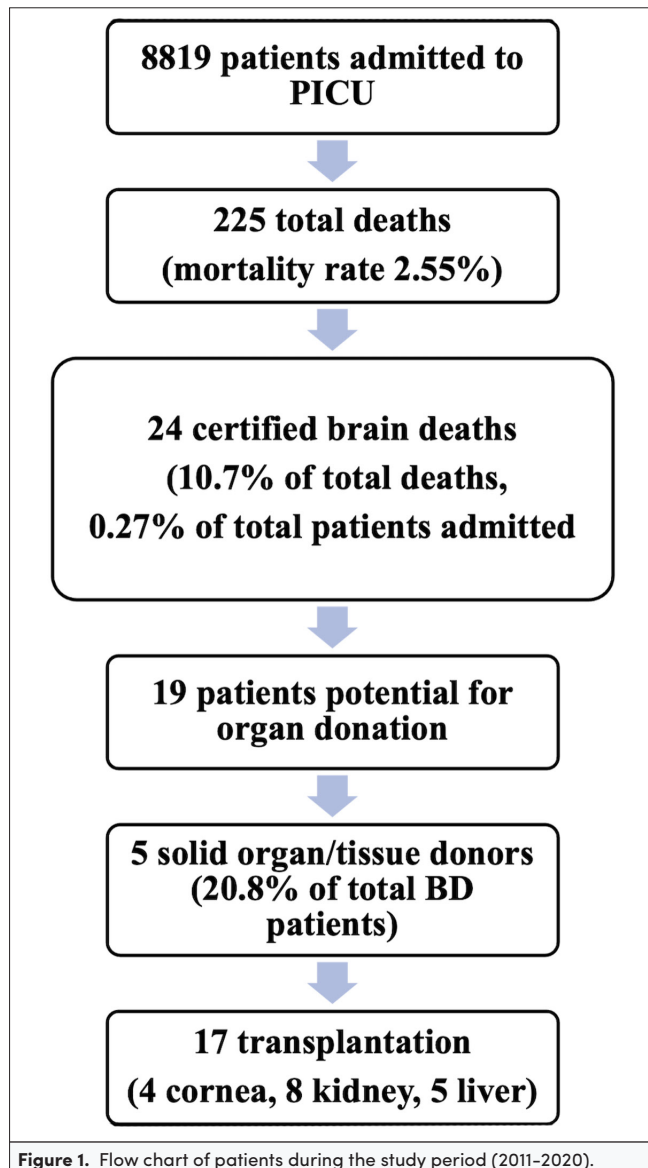
We completed the results section with the manuscripts published in Turkey about pediatric BD.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) version 26.0 (IBM SPSS Corp.; Armonk, NY, USA) was used for statistical analysis. The results were analyzed with descriptive statistics for categorical data, percentages for continuous data, mean (standard deviation) if normally distributed, and median (range) if not normally distributed. The Shapiro–Wilk test was used to test the normal distribution of variables. Data with non-normal distribution were compared using the Mann–Whitney *U*-test. A *P* value $\leq .05$ was considered statistically significant.

RESULTS

During the study period, a total of 8819 admissions were recorded at the PICU, with an overall mortality of 2.55% ($N = 225$). BD was identified in 24 patients (10.7%) among 225 total deaths (Figure 1). Their median age was 85 months (8–214), and the



male-to-female ratio was 1 : 1. The most common diagnoses were meningoencephalitis ($n = 6$, 25%), traumatic intracranial hemorrhage ($n = 4$, 16.7%) and non-traumatic intracranial hemorrhage ($n = 4$, 16.7%) (Table 1).

Among the patients with certified BD, the total length of stay in the hospital and in the PICU were a median 13 and 11 days, respectively. The median time from admission to PICU until BD diagnosis was 6.5 days (2-36 days), whereas the median time between BD diagnosis and cardiac arrest was 2 days (1-9 days). The time from the first physical examination for BD to the declaration of BD was 27.5 hours, and there was no statistically important difference between the donors and non-donors.

At least 1 ancillary method to certify BD was performed in all patients. AT was the most performed ancillary method, and it was performed in all patients. Since the first AT could not be tolerated in 2 patients, the test was repeated after the patient became stable, and was completed successfully. All ATs

Table 1. Demographic and Clinical Characteristics of 24 Pediatric Brain Dead Patients

Demographic and Clinical Characteristics	Results
Age (months), median (range)	85 (8-214)
Gender	
Male	12 (50%)
Total hospitalization (days), median (range)	13 (3-38)
Total hospitalization in PICU (days), median (range)	11 (3-38)
BD declaration (days), median (range)	6.5 (2-36)
Non-donors, median (range)	6 (2-34)
Donors, median (range)	11 (3-36)
BD to cardiac arrest (days), median (range)	2 (1-9)
Non-donors, median (range)	2 (1-9)
Donors, median (range)	1(1-3)
BD diagnosis interval (hours) (from first examination to declaration of brain death) median (range)	27.5 (22-50)
Non-donors, median (range)	27 (22-48)
Donors, median (range)	30 (22-50)
Primary diagnosis (%)	
Meningoencephalitis	6 (25%)
Traumatic intracranial hemorrhage	4 (16.7%)
Non-traumatic intracranial hemorrhage	4 (16.7%)
Hypoxic ischemic injury	3 (12.5%)
Intoxication	2 (8.3%)
Metabolic encephalopathy	2 (8.3%)
Central nervous system tumors	1 (4.2%)
Central nervous system infarction	1 (4.2%)
Other	1 (4.2%)
Ancillary tests for BD diagnosis	
Apnea test	24 (100%)
EEG	16 (66.7%)
Transcranial Doppler ultrasound	1 (4.2%)
MRA/CTA	13 (54.2%)
Other (direct angiography, brainstem evoked potentials)	0
Ancillary test combinations	
Only 1 test	1 (4.2%)
2 tests	16 (66.7%)
3 tests	7 (29.1%)
4 tests	0
Complications of BD	
Hyperglycemia	19 (79.2%)
Diabetes insipidus	17 (70.8%)
Hemodynamic instability	15 (62.5%)
Hypothermia	12 (50%)
Coagulopathy	5 (20.8%)
Multiple organ failure	4 (16.4%)

PICU, pediatric intensive care unit; BD, brain death; EEG; electroencephalogram; MRA, magnetic resonance angiography; CTA, computerized tomography angiography.

performed were evaluated as positive. The AT was followed by an EEG (16 of 24 patients, 66.7%) and MRA/CTA (13 out of 24 patients, 54.2%), respectively (Table 1). The most common combination of ancillary methods was AT plus EEG, which was performed in 9 patients (37.5%).

Regarding the complications that follow BD, there were 72 complications in 24 patients, which corresponded to 3 complications per patient. All patients had at least 1 complication after BD diagnosis. Hyperglycemia (79.2%), DI (70.8%), hemodynamic instability (62.5%), and hypothermia (50%) were the most common complications, and they were observed in over 50% of all patients (Table 1).

Of the 24 patients diagnosed with BD, 19 (79.2%) were considered eligible for OD. The remaining 5 patients were not found suitable for OD due to organ failure, malignancy, or serious infection. Five patients (20.8%) were organ donors in the study group, whereas family refusal for OD was 73.7% among the patients suitable for OD. In the study, 13 solid organ and 4 tissue transplantations were performed after OD, which is equal to 0.7 transplantations per BD patient and 3.4 transplantations per donor.

During the whole study period, there were a total of 138 BDs in our hospital, including both pediatric and adult patients. Of the 138, 28 were pediatric patients (20.3%). The total organ donors were 27 patients (19.6% of total BDs), of which 5 were pediatric patients. The organ donation rates in adults and pediatric patients were 20% and 17.9%, respectively. During the study period, 102 organ transplantations were performed in 27 donors. The rates of transplantation per donor in the pediatric and adult patients were 3.4 and 3.9, respectively.

Studies including data about pediatric BD in Turkey are shown in Table 2.

DISCUSSION

In the study, our mortality rate, including a 10-year period, was 2.55%. Different mortality rates have been reported in PICUs of different countries. Burns et al.⁹ reported that BD was diagnosed in 16% of total deaths in a multicenter study conducted in the USA.⁹ The incidence of certified BD in our study was 0.27% of all PICU admissions, which accounts for 10.7% of the total deaths observed during the study period. Our BD ratio was very similar to that published by Althabe et al.,¹⁰ reporting 11% BD among the total deaths in a very comprehensive multicenter study, including 16 PICUs in Argentina.¹⁰ In a multicenter study including 4 PICUs in Canada, Joffe et al.¹¹ reported BD in 15% of the total deaths during the study period.¹¹ A single-center report from Turkey established that BD cases accounted for 17% of the total deaths.¹² In our study, the percentage of patients with BD among the total deaths was slightly lower, but comparable to the numbers of patients with BD in these reports.

In our study, meningoenitis was the most common cause of BD in children ($n = 6$, 25%), followed by traumatic brain injury ($n = 4$, 25%), and non-traumatic cerebral hemorrhage ($n = 4$, 25%). Lago et al.¹³ reported that intracranial hemorrhage was the most frequent cause of BD (31%), in their study, carried out in 7 Brazilian PICUs.¹³ In most of the multicenter studies evaluating pediatric BD, multiple trauma and traumatic brain injury, hypoxic ischemic injury resulting from cardiac arrest, and intracranial hemorrhages were found to be the leading causes of BD in the pediatric population.^{11,14-16} The reason for this difference in etiologies between our study and most of the existing literature, may be that some pediatric cases with BD

that occurred after traumatic brain injury had been admitted to the neurosurgical intensive care unit or other departments in our hospital, and therefore they were excluded from our study. The median age in our study was about 7 years, similar to that reported by Gündüz and Joffe.^{11,17}

In our country, ancillary tests are mandatory for BD declaration, but a physical examination is enough for BD declaration in the USA, Canada, and some European countries.⁵ In our study, AT was performed in all cases. EEG was performed in 16 patients (67%), whereas MRA/CTA was performed in 13 patients (54%). Bonetto et al.¹⁴ reported that EEG was the most commonly performed ancillary test (93.2%) to diagnose BD, and AT was performed in 69% of the whole cohort. CTA or MRA was much lower, at 10%, in comparison with our study. They also revealed that the combination of EEG and AT was the most used ancillary method, in about 65% of their study cohort, like the observation in our study.¹⁴ Aslan et al.¹⁸ from Turkey reported similarly high rates of ancillary tests in their study group, including 20 pediatric BD cases. In their report, they showed that they routinely use EEG and AT in 19 out of 20 patients, whereas CTA/MRA was applied to 8 patients (40%).¹⁸ A study comparing pediatric and adult BD patients report that AT was performed in 83% of adults and 90% of the pediatric population. The same study reveals that the percentages of ancillary tests performed in adult and pediatric patients were 42% and 58%, respectively. These data show us that when it comes to pediatric patients, clinicians tend to use more ATs and additional imaging methods to show the absence of cerebral blood flow.¹⁹ That may be the reason for the high percentage of MRA/BTA in our study cohort, and we think that this dilemma should be the subject of another study, evaluating the pediatricians' reasons and the need for more complex imaging modalities to diagnose pediatric BD.

As a result of irreversible loss of brain functions, some regulatory mechanisms, such as the hypothalamic-pituitary-adrenocortical regulation and thermoregulation are disrupted. As a result, DI, hypothermia, myocardial dysfunction, and hyperglycemia can be observed during and after BD diagnosis. Antidiuretic hormone deficiency occurs in approximately 65–90% of the patients with BD, due to neurohypophysis damage.²⁰ In our study, we found that at least 1 complication was observed after BD declaration in all patients, with a mean of 3 complications in the whole cohort. Hyperglycemia (79%), DI (71%), hemodynamic instability (62.5%), and hypothermia (50%) were the most common complications, and they were observed in over 50% of all patients. Özmert et al.²¹ reported that hypothermia ($<36^{\circ}\text{C}$) was observed in 78.2%, and DI was observed in 47.8% of the cases.²¹ A review, evaluating DI incidence in BD patients, reported an incidence of 49% DI in both pediatric and adult patients, with a range between 9% and 100%. It also stated that for the pediatric population, 5 studies collectively report that 145 (52%) of 279 had DI.²²

We found that the median time from admission to BD declaration was 6.5 days, and from BD declaration to cardiac arrest was 2 days. The time to BD varies due to some factors such as age, the primary diagnosis leading to BD, and the number of physical examinations and ancillary tests needed to diagnose BD according to public laws. Sari et al.²³ reported that the time to BD in their study group was in a range between 1 and

Table 2. Studies Including Data About Pediatric Brain Death in Turkey

Study	Gündüz et al. ¹⁷ 2014	Gençpinar et al. ³¹ 2015	Öztürk et al. ³² 2016	Sarı et al. ²³ 2018	Sucu et al. ¹⁹ 2018	Yener et al. ³³ 2018
Study period	2009-2012	2007-2013	2012-2014	2016-2017	2015-2016	2012-2016
Number of BD cases	20	28	10	11	14	37
BD/total deaths	NA	NA	NA	NA	14/83 (17%)	37/341 (10.8%)
Age (years)	Mean: 6.2 ± 5.3 Median: 3.8 (0.8-17.5)	Mean: 7.8 ± 5.9 Median: 3 (0.8-17.5)	Mean: 7.2 ± 3 Median: 7 (2-12)	Mean: 6.18 ± 1.3 Median: 2.4 (1-16.9)	Mean: 6.96 ± 5.53 Median: 7.5 (0.6-16)	Median: 6
Male : Female	1.85 : 1	2.5 : 1	1.5 : 1	1.2 : 1	1.3 : 1	1.05 : 1
Primary diagnosis	1-TBI (55%) 2-Intracranial hemorrhage (20%) 3-Intracranial infection (15%)	1-Asphyxia (46%) 2-CNS hemorrhage (36%) 3-Increase in ICP (11%)	1-Trauma (70%) 2-Post-arrest (30%)	1-Trauma (73%) 2-Post-arrest (27%)	1-Hypoxia-asphyxia (29%) 2-Malignancy (29%)	1-Post-arrest (24.3%) 2-Head trauma (21.6%) 3-Drowning (10.8%)
Admission to BD declaration (days)	Mean: 4.2 ± 5 Median: 2 (1-20)	NA	Mean: 10.2 ± 8.2 Median: 7(2-27)	Mean: 4.6 ± 8.8 Median: 3 (1-21)	NA	Median: 7
BD declaration to cardiac arrest (days)	Mean: 5.8 ± 7.5 Median: 2.5 (1-28)	NA	NA	Mean: 3.3 ± 3.8 Median: 2 (0-11)	NA	NA
BD diagnosis duration (days)	NA	NA	Median: 3 (1-4.7)	NA	Mean: 2,14 ± 1,16 Median: 2 (1-5)	Median: 3
Apnea test	100%	100% (could not be completed in 3 cases)	100%	100%	100% (Could not be completed in 64%)	NA
Other ancillary tests	1-EEG (90%) 2-MRA/CTA (10%)	1-TCd (64%) 2-SPECT (40%)	1-TCd (90%) 2-CTA (10%)	1-CTA (36%)	1-TCd (78.6%)	1-TCd (100%)
BD complications	1-Hyperglycemia (65%) 2-DI (35%)	1-DI (75%) 2-Hypothermia (50%)	NA	1-Hemodynamic instability (82%) 2-Hyperglycemia (46%) 3-DI (27%)	NA	1-DI (89%)
Donor/total BD	5/20 (25%)	13/28 (46%)	2/10 (20%)	3/11 (27%)	0	6/37 (16%)
Family refusal of organ donation	75%	46%	80%	73%	100%	81%
Study	Aslan et al.¹⁸ 2019	Aydin et al.¹⁸ 2019	Özmerit et al.²¹ 2019	Duyu et al.³⁴ 2020	Our Study, 2021	
Study period	2010-2017	2001-2016	2009-2016	2015-2019	2011-2020	
Number of BD cases	20	42	23	23	24	
BD/total deaths	NA	NA	NA	23/121 (19%)	24/225 (10.7%)	
Age (years)	Mean: 8.45 ± 5.93 Median: 9 (1-17)	Mean: 9.7 ± 6.1	Mean: 6.8 ± 5.5 Median: 6 (0.6-17)	Mean: 5.5 ± 4.9 Median: 3 (0.4-15)	Mean: 8.9 ± 5.8 Median 7.1 (0.7-17.8)	
Male : Female	1.2 : 1	1.6 : 1	1.1 : 1	1.9 : 1	1 : 1	

(Continued)

Table 2. Studies Including Data About Pediatric Brain Death in Turkey (Continued)

Study	Aslan et al. ¹⁸ 2019	Aydin et al. ¹⁹ 2019	Özmerter et al. ²¹ 2019	Duyu et al. ³⁴ 2020	Our Study, 2021
Primary diagnosis	1-Fulminan hepatitis (35%) 2-Sepsis (15%) 3-Trauma (15%)	1-TBI (42.9%) 2-Anoxic brain injury (14.3%) 3-Other (14.3%)	1-Intracranial hemorrhage (30.4%) 2-Hypoxic brain damage (26%) 3-Intracranial infection (17.3%)	1-TBI (39.3%) 2-Malignancy (13%) 3-Post-arrest (13%)	1-Meningoencephalitis (25%) 2-Traumatic intracranial hemorrhage (16.7%) 3-Non-traumatic hemorrhage (16.7%)
Admission to BD declaration (days)	Mean: 11.1 ± 8.94 Median: 9 (2-33)	Mean: 5.8 ± 5.1	Mean: 5.9 ± 6.2 days Median: 3 (1-26)	Mean 5.6 ± 5.5 Median: 3 (1-24)	Mean: 12 ± 10.9 Median: 6.5 (2-36)
BD declaration to cardiac arrest (days)	Mean: 5.6 ± 6.05 Median: 3 (1-25)	NA	Mean: 6.9 ± 7.4 Median: 4 (0.2-25)	Mean: 13.1 ± 21.6 Median: 5 (1-95)	Mean: 2.9 ± 2.2 Median: 2 (1-9)
BD diagnosis duration	NA	NA	NA	Mean: 1.6 ± 0.7 Median: 1 (1-3)	Mean: 1.3 ± 0.4 Median: 1.1 (0.9-2.1)
Apnea test	100%	90.5%	100% (could not be completed in 1 case)	100% (Could not be completed in 4 cases)	100%
Other ancillary tests	1-EEG (100%) 2-MRA/CTA (40%) 3-TCD (15%)	1-EEG (41.7%) 2-TCD (33.3%) 3-CTA (16.7%)	1-EEG (100%) 2-CTA/MRA (39%)	1-CTA (82.6%) 2-CTA+TCD (13%) 3-TCD (4.4%)	1-EEG (66.7%) 2-MRA/CTA (54.2%) 3-TCD (4.2%)
BD complications	1-Hypermotremia (65%) 2-DI (45%)	NA	1-Hypothermia +DI (43.4%) 2-hypothermia (34.7%) 3-DI (4.3%)	1-DI (56.5%) 2-Hypothermia (52.2%) 3-Hyperglycemia (39.1%)	1-Hyperglycemia (79%) 2-DI (70.8%) 3-Hemodynamic instability (62.5%)
Donor/total BD	2/20 (10%)	12/42 (28.6%)	3/23 (13%)	4/23 (17.4%)	5/23 (20.8%)
Family refusal for organ donation	NA	59.5%	82.6%	NA	58%

BD, brain death; NA, not applicable; EEG, electroencephalogram; MRA, magnetic resonance angiography; CTA, computerized tomography angiography; TCD, transcranial Doppler ultrasound; DI, diabetes insipidus; TBI, traumatic brain injury; CNS, central nervous system.

21 days, with a median of 3 days.²³ Aslan et al.¹⁸ reported a wider interval, with a range between 2 and 33 days and a mean of 11.1 days.¹⁸ Özmert et al.²¹ reported that the time from BD declaration to cardiac arrest was a mean 6.9 days (0.2-25 days).²¹ In an adult study including 60 BD patients, the mean time from the diagnosis of brain death to somatic death was 2.4 ± 0.3 days in the non-donor group, and from 1.08 ± 0.2 days in the donor group.²⁴ In our study, the median results in the donor and non-donor groups were 1 and 2 days, respectively.

Some studies indicate that the short duration of BD diagnosis is associated with increased OD rates.²⁵ We found that the BD diagnosis interval (from the first physical examination to the declaration of BD) was a median of 27.5 hours (22-50 hours), and we could not find any statistical significance between the donors and the non-donors in terms of BD diagnosis interval.

In our series, 5 out of 24 BD patients were donors (20.8%). Five patients were found to be unsuitable for OD for several reasons. The families of 14 patients refused to be donors, and that accounts for approximately 60% of the total cases. In many studies, family refusal is the main reason for BD patients being non-donors, and our results indicate the same. Relevant literature suggests that 20-40% of the families of these patients refuse organ donation.²⁶ Lago et al.¹³ from Brazil reported only 6 ODs among 61 pediatric BD cases.¹³ Morris et al.,²⁷ from the UK, reported that nearly 50% of children with BD resulting from severe TBI, go on to OD, and this is one of the highest percentages in pediatric BD studies.²⁷ Bonetto et al.¹⁴ reported that 25% of their BD patients became donors, and 72 solid organs were transplanted into suitable patients. The recipient-to-donor ratio (solid organs) in their study was close to 4.¹⁴ This ratio was 2 : 5 in Briery's study.²⁸ In our study, the recipient-to-donor ratio was found to be 2 : 6 (13 solid organs per 5 donors), which is comparable to the existing literature.

Since the diagnosis of pediatric BD and organ donor status is an issue that needs to be evaluated more precisely compared to adults, more comprehensive and multicenter studies are needed, especially in pediatric patients. The problem of organ donation is still an important barrier for organ transplantation in our country, and the cadaveric donation rate per million population is much lower than in European countries.²⁹ A pediatric study from Turkey revealed that the most important reasons relevant to parents' refusal for organ donation were the parents' low level of education and insufficient information about BD and OD.³⁰ In our study and other pediatric studies conducted in our country, we also observed that family refusal is the main problem for OD among pediatric BD patients, and that the refusal rates are much higher than in the USA, Canada, and most European countries. Table 2 shows the pediatric BD studies conducted in our country, including our study results. It shows that trauma and associated brain injury are the leading causes of BD in a majority of the studies. The ancillary tests vary by centers, but the EEG seems to be the most commonly used ancillary method, followed by TCD or MRA/CTA. Family refusal rates vary over a wide range (46-100%).

This study has several limitations. First, it was performed at a single institution, and therefore, the number of the cases is low

in comparison with multicenter studies, and our results may not comprehensively reflect situation across our country. Second, because of the study's retrospective design, we were not able to find out the detailed reasons for family members' reluctance to consent to OD. Third, we could not analyze factors affecting OD in pediatric cases due to the low number of cases. However, the present study has significant strengths. It yields important and detailed information about pediatric BD in a tertiary university hospital over a relatively long time period, and this is the first pediatric study on this issue at our institution.

CONCLUSIONS

Pediatric BD is a highly complex and yet sensitive issue in pediatric practice for clinicians. In recent years, the number of pediatric patients with organ failure and awaiting suitable transplantation has increased all over the world. Thus, increasing the importance and sensitivity of this issue once more is necessary. In our study cohort, OD among BD patients was 20.8%, reflecting relatively low donation rates in comparison with the European and developed American countries. The complications of BD were observed at higher rates in our study. Therefore, multicenter national studies investigating pediatric BD, the factors affecting OD, and the causes of family rejection need to be investigated. Accordingly, a nationwide study to evaluate the incidence and characteristics of pediatric BD should be conducted in the future.

Ethical Committee Approval: Ethics committee approval was received from the ethics committee of Çukurova University Faculty of Medicine Ethics Committee (Date: May 21, 2021; Number: 111).

Informed Consent: Informed consent was not obtained due to the retrospective design of this study.

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