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Pediatric organ donation: retrospective study in five centers in Argentina

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ABSTRACT

Introduction. Advances in medicine have made organ and tissue transplantation a feasible therapeutic option. However, the shortage of pediatric donors leads to deaths among children on the organ waiting list in Argentina. The objective of this study was to identify variables related to the donation process that may offer opportunities to improve the pediatric donation rate.

Population and methods. This was a retrospective observational study conducted in five institutions. Data were obtained from the medical records of patients aged 0 to 18 years who met the clinical criteria for death based on neurological criteria (DNC) in pediatric intensive care units (PICUs), emergency departments, and cardiovascular intensive care units between January 1, 2018, and December 31, 2022.

Results. Among the participating centers, three were pediatric and two were general hospitals. A total of 124 patients with clinical DNC were included (1.3% of PICU admissions, 23% of deaths). Of these, 21 (17%) were donors. An 83% rate of missed donation opportunities was identified; the main areas for improvement were detection, diagnosis, and evaluation.

Conclusion. DNC is an uncommon condition in pediatrics. This study identifies key areas for action to optimize the evaluation, detection, and management of potential donors—necessary steps to reduce deaths among children on transplant waiting lists.

Keywords: organ and tissue procurement; pediatrics; brain death; organ waiting lists.

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INTRODUCTION

The organ donation rate in Argentina has gradually increased over the past few years; however, there remains a challenge in improving access to transplantation among the pediatric population. A rapid search of the Central Registry of the National Procurement and Transplant Information System of the Argentine Republic (SINTRA), managed by the National Central Institute for the Coordination of Ablation and Implantation (INCUCAI), shows that a total of 1961 individuals under 18 years of age were registered on the transplant waiting list over the past ten years (2015–2024). During that period, 164 (8.4%) of them died while waiting for an organ; 24% received an organ from a living donor, and only 57% received one from a deceased donor.1 Given that indications for transplantation and living donation are limited, the survival of children on the waiting list depends largely on improving the stages of the deceased donation process.2,3

The deceased donation process begins with the detection of a neurocritical patient with a poor prognosis, followed by identification of the clinical signs of brain death, certification of death based on neurological criteria (DNC) using the national protocol, family interview, judicial authorization (in cases of violent death), and management of the potential donor until organ and tissue procurement. Multiple factors are associated with these initial stages. Modifiable factors include deficiencies in detection, delays in death certification, cardiopulmonary arrest (CPA), and family refusal. Non-modifiable factors include donor comorbidities, cause of death, and donorrecipient anthropometric compatibility. Institutions that care for critically ill patients under 18 years of age, along with the professionals responsible for their care, play a fundamental role in all these factors.4

The objective of this study was to identify variables related to the donation process that offer opportunities to improve the pediatric donation rate.

POPULATION AND METHODS

This was a multicenter, descriptive, retrospective observational study conducted in five high-complexity hospitals in Argentina: Hospital General de Niños "Ricardo Gutiérrez" (HGNRG) and Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garrahan" (HPJPG) in the Autonomous City of Buenos Aires; Hospital

Descentralizado "Dr. Guillermo Rawson" (HGR) in San Juan; Hospital Regional de Comodoro Rivadavia "Dr. Víctor Manuel Sanguinetti" (HRCR) in Chubut; and Hospital Pediátrico "Dr. Humberto Notti" (HPHN) in Mendoza.

Participating centers

Institutions were characterized according to the population they serve (pediatric or general adults and pediatric inpatients), annual pediatric hospital admissions, annual pediatric hospital mortality, performance of transplants at the institution, presence of a hospital transplant coordinator (HTC), existence of a pediatric intensive care unit (PICU), availability of pediatric intensive care and neurosurgery staff on active 24-hour call. In each center, the PICU, emergency department, and cardiovascular recovery unit were evaluated, recording the number of pediatric admissions to critical care areas per year; the percentage of neurocritical patients (neurological injury as the main cause of admission) per year; and mortality in critical care areas per year.

Population

Patients aged between 1 month and 18 years who died with clinical signs consistent with DNC between January 1, 2018, and December 31, 2022, in the evaluated critical care areas were included. The clinical diagnosis of brain death (deep apneic coma, absence of brainstem reflexes, and generalized flaccid hypotonia) was identified by the investigators through a review of the medical records of all deceased patients.⁵ Neonatal intensive care unit deaths were excluded.^{6,7} Data obtained from the medical records were compared with those recorded in SINTRA, the national system for the management, oversight, and consultation of organ, tissue, and cell procurement and transplantation activities.

Age, weight, sex, and Glasgow Coma Scale score at PICU admission were recorded. Preexisting comorbidities were categorized as neuromuscular, oncologic, cardiovascular, immunologic/hematologic, congenital/genetic, gastrointestinal, metabolic, respiratory, renal, or none.

Disease severity upon admission was assessed using the Pediatric Index of Mortality 3 (PIM3).8 Causes of death were classified as anoxic, traumatic, neurologic, infectious, oncologic, or other.

The Provincial Ablation and Implant Agency (OPAI), representing INCUCAI in each jurisdiction,

is responsible for assessing notified potential donors, collaborating with the referring hospital in the diagnosis of DNC and donor management, among other functions. In patients evaluated by OPAI, the following were recorded:

- Time 1: Number of days in the PICU from admission until OPAI notification of a patient with clinical DNC (reflecting the time from catastrophic neurological injury to DNC, delays in identification of DNC by the treating team, and fulfillment of national protocol prerequisites).^{9,10}
- Time 2: Number of days in the PICU from admission until completion of DNC certification according to the national protocol (including Time 1, observation period, instrumental testing, and neurological or neurosurgical evaluation).¹¹

In addition, medical and legal contraindications for donation, family consent, number of actual (procured) donors, and documentation of the process in the medical record were collected. Deceased patients with clinical DNC were categorized as certified DNC (DNCc) or noncertified DNC (DNCnc) depending on whether or not legal certification was completed by OPAI.

Statistical analysis

Data were analyzed using Infostat software. Continuous variables were expressed as median and interquartile range (IQR) or as mean and standard deviation (SD), depending on whether their distribution was nonparametric or normal, determined by the Kolmogorov–Smirnov test. Categorical data were expressed as frequencies and percentages. Quantitative variables across hospitals were compared using Student's t test for normally distributed data or Kruskal–Wallis/Friedman tests for nonparametric distributions. Categorical variables were compared using the chi-square test. A p value <0.05 was considered statistically significant.

Ethical considerations

This study did not affect the type or quality of care provided, and there were no risks inherent to participation. The protocol was approved by the INCUCAI Health Research Ethics Committee on December 26, 2022 (GEDO No. IF-2022-139668037-APN-INCUCAI#MS). Patient data confidentiality was ensured, and information was used solely for research purposes, in accordance with National Law 25.326 on Personal Data Protection.

RESULTS

Hospital characteristics

Data are summarized in *Table 1*. Both general hospitals and two of the pediatric hospitals had a hospital transplant coordinator (HTC). The HPHN only had an HTC during 2018 and 2019.

Patient characteristics

During the study period, 297 157 patients were admitted to the participating hospitals; 9800 were admitted to critical care areas, 15.4% of whom were neurocritical patients. Of these, 124 patients were included in this study (1.3% of PICU admissions and 23% of deaths) (*Figure 1*).

Patient characteristics are described in Table 2. Comorbidities and causes of death are shown in *Tables 3* and 4. Among all patients with clinical signs of brain death, 8 (6%) from pediatric hospitals were not identified by the treating team as potential donors. The remaining 116 began the DNC certification process through OPAI, with a median Time 1 of 3 days (IQR 1–6); in 22% of cases, it exceeded 5 days.

Patients with certified DNC (DNCc) were 74 (60% of those clinically diagnosed with DNC and 54% of total PICU deaths), with a median Time 2 of 3 days (IQR 2–6). Of these, 21 (28%) became actual donors, 29 (39%) had medical contraindications (*Figure* 2), and 24 (32%) involved family refusal to donate. The difference between Times 1 and 2 was statistically significant (p < 0.001).

Among the 50 non-certified DNC (DNCnc) patients, all evolved to cardiopulmonary arrest (CPA); 80% of these had medical contraindications to donation (23 due to severe hemodynamic instability and multiorgan failure, 17 due to other causes), and 4% (2 patients) had judicial refusal. In cases without donation potential, the treating team decided to withdraw life support as part of the adjustment of therapeutic effort, since OPAI did not certify DNC and the hospital lacked the necessary means to complete the national protocol requirements.

In 10 patients, the cause of CPA was not recorded. Three families were interviewed and refused tissue donation; in two cases there was judicial refusal. The remaining five patients did not undergo interviews, and no tissue donors were identified among those who died following CPA.

The DNC certification process was documented in the medical record in 46 (40%) of the 116 cases in which it was initiated; in the remaining cases, it was recorded only in SINTRA.

Table 1. Characterization of the participating centers in the study

Variables Participating centers					
	HGNRG	HPJPG	HGR	HRCR	HPHN
Province where it is located	CABA	CABA	San Juan	Chubut	Mendoza
Population served by the hospital	Children	Children	Children and adults	Children and adults	Children
Pediatric hospital admissions/year (N)	9907 ± 1103	23 580 ± 5457	7177 ± 2039	6504 ± 331	14 774 ± 2896
Admissions to pediatric critical care units/year (N)	348 ± 79	671 ± 90	433 ± 71	128 ± 45	440 ± 73
Admissions of pediatric neurocritical patients/year (%	6) 20.7 ± 4.6	10.3 ± 5.8	10.6 ± 0.9	12.7 ± 5	21 ± 7.7
Pediatric hospital mortality/year (%)	1 ± 0.3	1 ± 0.4	0.4 ± 0.3	0.3 ± 0.2	0.6 ± 0.1
Mortality in critical pediatric areas/year (%)	9.8 ± 1.9	2.4 ± 0.58	6.3 ± 2.1	3.1 ± 2.2	6.6 ± 1.8
Hospital transplant coordinator	5/5 years	2/5 years	5/5 years	5/5 years	2/5 years
Transplants at the institution	Organs and tissues	Organs and tissues	Organs and tissues	No	Tissues
Pediatric intensive care	Yes	Yes	Yes	Yes	Yes
Training in pediatric intensive care	Yes	Yes	Yes	Yes	Yes
24-hour neurosurgery on call	Yes	Yes	Yes	No	No

CABA: Autonomous City of Buenos Aires (by its Spanish acronym), HGNRG: Ricardo Gutiérrez General Children's Hospital, HPJPG: Prof. Dr. Juan P. Garrahan Pediatric Hospital, HGR: Dr. Guillermo Rawson Decentralized Hospital, HRCR: Dr. Guillermo Sanguinetti Regional Hospital of Comodoro Rivadavia, HPHN: Dr. Humberto Notti Pediatric Hospital.

The data are summarized as the mean and standard deviation of the annual values from 2018 to 2022.

DISCUSSION

Several factors were identified as targets for improving the donor rate. Regarding detection, 6% of patients were not identified by the treating team as potential donors. In other countries, failure to detect such cases accounts for up to 16% of missed donation opportunities. 12 Incorporating organ procurement training into professional education programs could help address this deficiency.

The mortality rate in PICUs due to DNC was 1.3% of total admissions, similar to that reported in other multicenter Argentine studies (0.8%-1.4%). 11,13 Kirschen described a linear association of four DNC cases per year for every 1000 PICU discharges,14 corresponding to an annual mortality of 0.4% of admissions in the United States, comparable to the 0.3% reported in Spain.¹⁵ The lower mortality in developed countries may be related to better quality of care or a lower incidence of neurocritical patients, among other factors. Nevertheless, pediatric donors represent 6% and 3% of total annual donors in those countries, respectively, 16,17 while in Argentina they reach 8%.1 This may represent an opportunity related to demographic distribution.

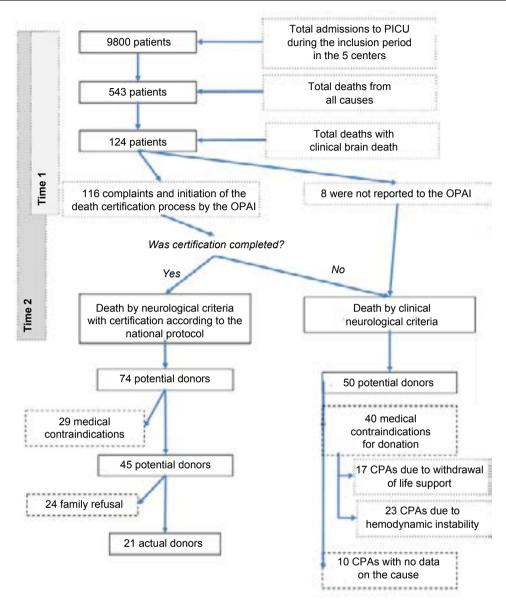
Furthermore, 75% of the included patients had a Glasgow score of 3 upon PICU admission. Although the national program recommends notifying OPAI when patients have a Glasgow score below 7, regardless of age, the specificity

of this criterion for the pediatric population could be reassessed.

In relation to diagnosis, DNC was certified in 60% of clinically deceased patients, while the remaining 40% experienced CPA before completing the national protocol. The Argentine procedure for DNC certification has advantages over other Latin American countries, ¹⁸ but the mandatory use of instrumental methods hinders autonomous certification by hospitals and has been questioned in other nations. ¹⁹ The causes of CPA among non-certified DNC patients suggest that this outcome could be avoided through improved training and provision of resources for healthcare teams.

With regard to evaluation, the median Time 1 was three days (IQR 1-6). Although specific causes of delay (e.g., late notification to OPAI, delayed clinical detection, or unmet prerequisites such as normothermia or hemodynamic stability) were not recorded, previous studies have reported times from severe brain injury to DNC ranging from 0.7 to 6.5 days. 10,20 Median Time 2 was also three days, with some cases reaching up to ten days. Similar values have been reported in Argentina,¹¹ Mexico,²¹ and the United States.²²In contrast, a Spanish center that does not require instrumental testing reported shorter times (median 1.4 days, IQR 3 hours-12 days).23 The significant difference observed between Times 1 and 2 in this study suggests that execution

FIGURE 1. Flowchart of patients included



PICU: pediatric intensive care unit. CPA: cardiopulmonary arrest. Time 1: days of hospitalization from the patient's admission to the PICU until the start of the evaluation by the OPAI. Time 2: days of hospitalization from admission to the PICU until completion of death certification by neurological criteria.

of the national protocol contributes to delays in certification. Future research could explore barriers to its implementation in pediatric settings.

Medical contraindications accounted for 39% of potential donors in this series, mainly due to hemodynamic instability and multiorgan failure. Other studies have reported medical contraindication rates between 20% and 59%. 11,12 Multiorgan dysfunction in pediatric brain-dead patients is often more severe than in adults but may improve within 36-48 hours after brain

death.²⁴ Recent studies have even documented successful transplantation from donors with multiorgan failure.²⁵ Establishing specific pediatric criteria for medical contraindications to donation could increase the number of viable donors.

Regarding family interviews, 53% resulted in refusal. A similar outcome in Turkey highlighted the importance of hospital transplant coordinators (HTCs) for effective communication.²⁶ Likewise, in Spain, a 91.7% family consent rate has been attributed to the presence of trained hospital

Table 2. Characterization of patients included according to the hospital of origin

Variables	Hospitals included							
	TOTAL	HGNRG	HPJPG	HGR	HRCR	HPHN	p*	
Clinical DNC (n, %)	124 (100%)	30 (24%)	34 (27%)	31 (25%)	4 (3%)	25 (20%)	0.01	
Age, years (m, IQR)	6 (1-12)	6.5 (2-13)	6 (1-13)	4 (1-13)	7 (1-9)	6 (1-11)	0.92	
Weight, kg (m, IQR)	19 (12-40)	14 (10-34)	20 (9-40)	18 (13-52)	20 (10-40)	20 (14-40)	0.65	
Female (n, %)	55 (44%)	14 (47%)	14 (41%)	14 (45%)	2 (50%)	11 (44%)	0.99	
Glasgow Coma Scale sca	ore							
on admission (m, IQR)	3 (3-3)	3 (3-3)	3 (3-3)	3 (3-3)	3 (3-3)	3 (3-6)	0.11	
PIM at admission,								
% mortality (m, CI)	43 (11-9)	10.5 (6-32)	52.5 (5-86)	87.7 (17-96)	7.2 (0-8)	46 (27-92)	0.01	
Comorbidities (n, %)	46 (37%)	17 (57%)	18 (53%)	31 (23%)	0 (0%)	25 (16%)	0.001	
Judicial intervention								
(n, %)	26 (21%)	1 (3%)	3 (9%)	4 (13%)	1 (25%)	10 (40%)	0.01	
Cardiorespiratory arrest								
(n, %)	50 (40%)	9 (30%)	13 (38%)	21 (70%)	1 (25%)	7 (28%)	0.008	
Time until the first OPAI								
assessment,								
days (m, IQR)	3 (1-6)	3 (1-5)	2 (2-6)	4 (2-6)	5 (1-6)	3 (1-6)	0.29	
Time until								
DNC certified,								
days (m, IQR)	3 (2-6)	4 (2-6)	3 (2-6)	6 (3-6)	5 (1-6)	3 (2-6)	0.46	
Certified DNC (n, %)	74 (60%)	21 (70%)	22 (65%)	10 (32%)	3 (75%)	18 (72%)	0.001	
Medical contraindication								
for donation (n, %)	29 (39%)	14 (67%)	6 (27%)	3 (30%)	0 (0%)	6 (33%)	0.03	
Family refusal								
to donate (n, %) #	24 (53%)	2 (25%)	9 (56%)	4 (57%)	2 (67%)	7 (58%)	0.09	
Actual donor (n, %)	21 (28%)	5 (24%)	7 (32%)	3 (30%)	1 (33%)	5 (28%)	0.76	

HGNRG: Ricardo Gutiérrez General Children's Hospital, HPJPG: Prof. Dr. Juan P. Garrahan Pediatric Hospital, HGR: Dr. Guillermo Rawson Decentralized Hospital, HRCR: Dr. Guillermo Sanguinetti Regional Hospital of Comodoro Rivadavia, HPHN: Dr. Humberto Notti Pediatric Hospital.

PIM: pediatric mortality index, DNC: death by neurological criteria, OPAI: Provincial Organ Transplant and Ablation Agency (by its Spanish acronym), m: median, IQR: interquartile range.

transplant and bereavement management teams.²³ In cases of pediatric trauma, where emotional burden and judicial intervention may complicate donation, the presence of HTCs is particularly crucial.²⁷ In the present study, pediatric hospitals with HTCs (HGNRG and HPJPG) achieved the highest consent rates (75% and 44%, respectively).

In terms of donor management, a low percentage of certified DNC patients who suffer CPA before procurement is considered an indicator of good hospital performance. In our cohort, no patient experienced CPA after certification. However, during the same period, SINTRA reported that 6% (42 of 684) of pediatric DNC-certified patients nationwide died from

CPA before procurement.¹ Training in donor management could help prevent this loss of potential donors.

There were also two cases of judicial refusal and a 60% absence of documentation of the donation process in medical records, underscoring the need for greater legal awareness within both the healthcare and judicial systems.^{28,29}

Finally, 17% of patients in this study became actual donors, a rate comparable to that reported in an Argentine multicenter study including seven PICUs (25%) and higher than that observed in Brazil (10%)³⁰ and Colombia (1%).³¹ In contrast, the United States reported a 50% donor rate in a large series involving 150 PICUs.¹⁴ The existence of national consensus guidelines on the diagnosis

^{*} Chi-square comparison of the summary values for the 5 years in the hospitals included; a p-value <0.05 is statistically significant.

^{*} The percentage was calculated based on the total number of interviews conducted, which was 45 in total: 8 at HGNRG, 16 at HPJPG, 7 at HGR, 3 at HRCR, and 12 at HPHN.

Table 3. Comorbidities of the 124 patients who died with clinical brain death

Comorbidities before admission to the PICU		N	%	
None		78	62.9	
Neuromuscular	Cerebral palsyEpilepsySpinal cord atrophy	17	13.7	
Oncological	Leukemia Solid tumors	9	7.2	
Cardiovascular	Congenital heart diseaseHigh blood pressure	6	4.8	
Immunological/hematological	LupusAnemiasCoagulopathy	4	3.2	
Congenital/genetic	 Malformations Chromosomal syndromes Prematurity	4	3.2	
Gastrointestinal	Celiac diseaseMalabsorption	2	1.6	
Metabolic	DiabetesFabry disease	2	1.6	
Respiratory	 Asthma 	1	8.0	
Renal	 Kidney failure 	1	0.8	

Table 4. Causes of brain death

Type of pathology		N	% of total	% of total per group
Anoxia	Cardiorespiratory arrest	36	29.0	39.5
	Respiratory failure	5	4.0	
	Carbon monoxide poisoning	3	2.4	
	Hanging	2	1.6	
	Asphyxiation by immersion	2	1.6	
	Airway obstruction by a foreign body	1	0.8	
Trauma	Traumatic brain injury due to a traffic accident	11	8.8	16.9
	Traumatic brain injury due to a fall from height	3	2.4	
	Electrocution	3	2.4	
	Gunshot wound	2	1.6	
	Traumatic brain injury due to child abuse	1	0.8	
	Crushing	1	0.8	
Neurological	Hemorrhagic stroke	18	14.5	25.8
	Ischemic stroke	12	9.7	
	Ventricular shunt valve dysfunction	2	1.6	
Infectious	Primary (meningitis, encephalitis)	10	8.0	11.4
	Secondary (embolisms/septic shock)	4	3.2	
Oncological	Primary tumor of the central nervous system	4	3.2	3.2
Others	Leukodystrophy, diabetic ketoacidosis, polymyositis, chronic renal failure	4	3.2	3.2

and management of potential donors may explain these better results.³²

LIMITATIONS

The retrospective design limited data collection to information available in medical records and in the SINTRA database. The exact moment

of clinical suspicion of DNC and other causes of delay during Time 1 were not available. In addition, auxiliary diagnostic methods used for DNC certification were not analyzed, so potential barriers in these stages could not be identified.

Moreover, hospitals were selected by convenience and all belonged to the public sector.

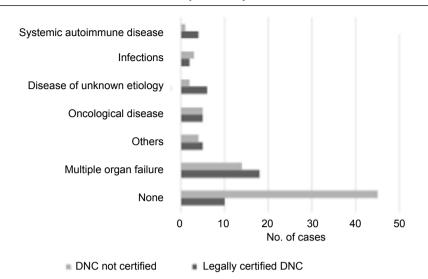


FIGURE 2. Medical contraindications for donation in potential pediatric donors

Infections include human immunodeficiency virus, active tuberculosis, and SARS-CoV-2, among others. Multiple organ failure includes hemodynamic instability and sepsis. "Others" include genetic syndromes, metabolic disorders, and severe burns, among others.

The bars show the total number of medical contraindications (55%, n = 69) in the potential pediatric donors included (n = 124). In each series, the bars are divided between patients who completed the DNC diagnosis according to the national protocol (n = 74) and those who died from PCR without completing DNC certification (n = 50). DNC: death by neurological criteria.

Previous studies have reported differences in the donation process between public and private institutions,³³ which may limit the generalizability of these findings.

CONCLUSION

DNC is an uncommon condition in pediatrics. An 83% rate of missed donation opportunities was identified. The main targets for improvement include detection, diagnosis, and evaluation. In addition, a 60% lack of documentation of the donation process in medical records was observed.

This study highlights key areas for optimizing the assessment, detection, and management of potential donors—essential steps to reduce mortality among children on transplant waiting lists.

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