Original Article

Indications and Outcome of Different Dialysis Modalities in Critically Ill Children.

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ABSTRACT

Introduction: Dialysis is one of therapeutic interventions used for critically ill children .Dialysis modalities include peritoneal dialysis (PD), intermittent hemodialysis (IHD) and continuous renal replacement therapy (CRRT).

Aim of the study: is to describe the use of different dialysis modalities in pediatric intensive care units (PICUs) regarding their indications and outcome.

Methods: The prospective descriptive study included all patients admitted to PICUs over a period of six months from November 2017 to April 2018, we obtained the indications of dialysis, type of dialysis modality received, dialysis prescription, and outcome.

Results: Out of 977 patients admitted to the PICU during the study period, 44 patients (4.5%) required dialysis. Peritoneal dialysis was the most common dialysis modality used in this study (72.8%, n=32/44), CRRT was done for six patients (13.6%), and IHD was done for six patients (13.6%).The main indications of dialysis in the study group were azotemia in 25 cases (56.8%) PD was significantly less successful than IHD (p-value: 0.023), but there was no significant difference in success of CRRT over PD or IHD. The total mortality rate was (40.9% n=18), it was the highest with PD (94.4%, n= 17) and no mortality in IHD group during patients´ stay in the PICU.

Conclusion: PD is the most commonly used dialysis modality in the PICU, but it has poor outcome. CRRT can improve outcome but it may be underutilized, because of the cost and the experience required. IHD is very successful in critically ill-children especially who were previously on regular HD.

Key words: Dialysis modalities, Volume overload, AKI, CKD, and PICU.

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INTRODUCTION

Critically ill patients occasionally require dialysis and it has been reported and implemented in nearly 5% of ICU patients [1]. The indications of dialysis in pediatric patients are metabolic and electrolyte disturbances, azotemia, volume overload, encephalopathy, and intoxication [2].

Dialysis modalities are acute peritoneal dialysis (PD), intermittent hemodialysis (IHD), and continuous renal replacement therapy (CRRT). In pediatric patients, peritoneal dialysis (PD) is considered the most widely used modality [3], but over time, CRRT has become the preferred modality to manage AKI and fluid overload in critically ill children as it provides toxins and metabolite clearance over an extended period of time as well as slow and predictable fluid removal [4].This is despite the fact that CRRT is a resource-intensive therapy [1]. Acute HD is a fast and efficient method of removing toxins from the body, but it needs good vascular access and might not be suitable for hemodynamically unstable patients [5].

The choice of dialysis modality depends on several factors; for example, hemodynamic stability of the patient, indications of RRT (metabolite clearance or fluid removal or both, and time required for replacement), availability of equipment, and expert personnel.The need for dialysis is usually associated with poor outcome in critically ill patients [6]. This study's goal is to assess the different modalities of dialysis employed in critically ill children admitted to the PICU.

METHODS

This was a prospective descriptive observational study that included all patients admitted to PICU at tertiary care University based Children's Hospital over a period of 6 months (from November, 2017 to April, 2018) and received dialysis. Neonates and children older than 12 years were excluded. The study was approved by the pediatric department ethical committee of Cairo University. Informed consent was obtained from the children's care givers prior to inclusion in the study. All procedures followed were in accordance with the Helsinki Declaration of 1964. The choice of dialysis modality and prescription was made by the attending consultant. The following data were obtained:

Demographic data (the body weight was expressed in kilograms, not percentiles, to assess the relationship between the body weight and the choice of dialysis modality regardless of the patient's age), pre-existing conditions, indications of PICU admission, and indications of dialysis (azotemia, intractable metabolic acidosis, and volume overload). Some patients had more than one indication, but we used the main indication of the dialysis in our study. The volume overload was diagnosed by the calculation of cumulative fluid overload. If it is more than 20%, it is an indication that you should start dialysis. High central venous pressure, pulmonary crepitation, chest radiography (if it shows pulmonary congestion) and ultrasonography (thoracic ultrasonography) to detect fluid-filled alveoli a measurement of inferior venacava diameter if 2.5cm is considered volume overload) [7].

The cumulative percentage of fluid overload was calculated by the following formula [8].

$$\frac{[(\text{fluid input in liters})-(\text{fluid output in liters})] \times 100}{\text{PICU admission weight (kgs)}}$$

In PD, acute peritoneal catheters were inserted by the nephrology physician and the dialysis was performed manually using peritoneal dialysis fluids with dextrose concentrations of 1.7% or 4.25% (in cases of volume overload). In both IHD or CRRT, double-lumen central venous catheters were inserted by PICU or nephrology physicians and IHD was done by conventional low flux HD machines (Fresenius) using polysulfone hollow fiber dialyzers with bicarbonate containing dialysate, while CRRT was done by Baxter Prismaflex CRRT Machine, using filters (M60 or M150 according to the patients' weight).

Dialysis prescription: Standardized ultrafiltration calculation (48 hours of CRRT, or PD, or one HD session). It was calculated by the following formula: (Predialysis weight - post dialysis weight [milliliters]) / Delivered treatment time (hours) / post dialysis weight (kilograms)) **[9].**

Outcome: including patient outcome, dialysis outcome (successful dialysis means correction of the indication of dialysis as well as achievement of normovolumic status, improvement of serum creatinine, serum Na, and correction of metabolic acidosis) **[10]** and dialysis complications were reported.

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 25. Data was summarized using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were done using the non-parametric Mann-Whitney test (Chan, 2003a). For comparing categorical data, Chi square test was performed. Exact test was used instead when the expected frequency is less than 5 (Chan, 2003b). P-values less than 0.05 were considered as statistically significant.

RESULTS

Out of 977 patients admitted to the PICU during the study period, 44 patients (4.5%) required dialysis, 27 of them (61.4%) were males. The median (IQR) age was 24 (6 - 72) months and the median (IQR) weight was 11(7-18.5) Kg. Peritoneal dialysis (PD) was the most common used dialysis modality in this study (72.8%, n=32/44), CRRT was done for six patients (13.6%), two of them had HDF (hemodiafiltration) and 4 patients had CVVH (Continuous Veno-Venous Hemofiltration) and IHD was received by six patients (13.6%) **(Figure 1)**.

Indications of dialysis in the study group were azotemia in 25 cases (56.8%), volume overload in 13 cases (29.6%) and intractable metabolic acidosis in 6 cases (13.6%) as shown in **(Table 1)**. While the original disease of the study group and indications of PICU admission are shown in **(Table 2)** and **(Figure 2)** respectively. Overall six patients (13.6%) had pre-existing ESRD on regular HD, 14 patients (31.8%) had pre-existing CKD not on dialysis, and 10 patients (22.7 %) were admitted with AKI and high serum creatinine.

Fourteen patients (31.8%) had normal kidney functions on admission of whom eleven patients (25%) developed rising chemistry associated with AKI after PICU admission. However three cases (6.8%) required dialysis despite normal serum creatinine (two cases of gastroenteritis with intractable hypernatremia and one case of methylmalonic acidemia with intractable acidosis) **(Figure 3).**

The demographic data of the patients subjected to different dialysis modalities are shown in **(Table 3)**. Patients receiving PD were significantly younger age and lower weight (p-value: 0.01and 0.002) respectively. All patients receiving IHD had ESRD on regular HD prior to PICU admission. Prescription of dialysis modalities are shown in **(Table 4)**. The body weight was expressed in kilograms, not percentiles, to assess the relationship between the body weight and the choice of dialysis modality regardless of the patient's age.

Regarding the outcomes, dialysis was successful in 27 cases (61.3%) [All IHD group (n=6/6), most, CRRT group (n=5/6), and 50 % of PD group (n=16/32)], while in 17cases (38.6%) was not successful .As shown in **(Table 5)**, PD was less successful than IHD (p-value: 0.023), while the difference is not significant regarding CRRT. Similarly, survival was significantly better with IHD than PD (p-value: 0.016), also the survival was better in CRRT group than PD group, but it was not significant. The total mortality rate was (40.9% n=18), it was the highest with PD (94.4%, n= 17) and no mortality in IHD group. The causes of death were due to multisystem organ failure (MSOF) in 72.2% of cases (n=13), pneumonia (22.2%, n=4) and DIC (5.6%, n=1). There were no major dialysis complications apart from one patient was on CRRT stopped dialysis and shifted to PD due filter clotting.

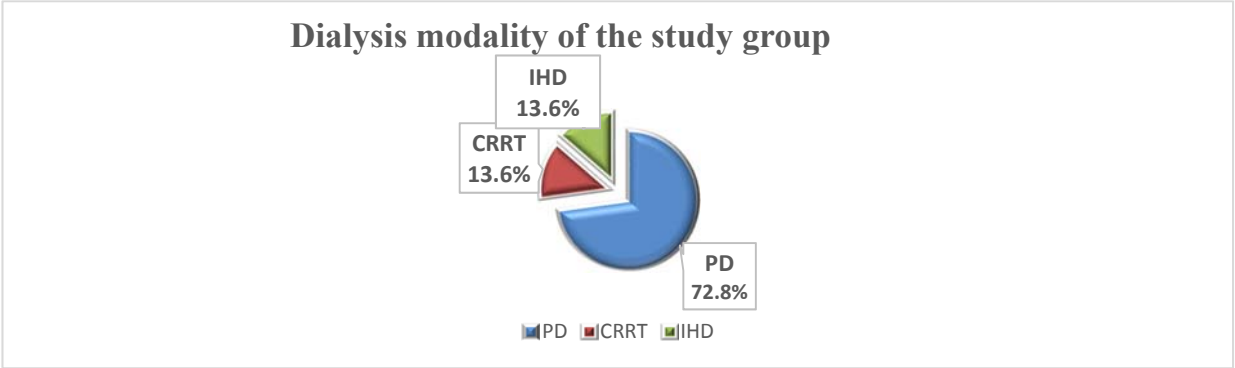

Figure 1: Dialysis modality of the study group
* PD: Peritoneal dialysis, CRRT: Continuous renal replacement therapy, IHD: Intermittent hemodialysis

Table 1: Indications of dialysis in the study group

Indication of dialysis	CRRT (n=6)	PD (n=32)	IHD (n=6)	P-value
Azotemia	3(50 %)	20(62.6%)	2(33.3%)	0.390
Volume overload	3(50%)	6(18.7%)	4(66.6%)	0.031
Intractable metabolic acidosis	0	6(18.7%)	0	0.272

* PD: Peritoneal dialysis, CRRT: Continuous renal replacement therapy, IHD: Intermittent hemodialysis

Table 2: The original disease of the study group

The original disease of the study group	
Renal (59%)	**Non-renal (41%)**
HUS (25%)	Septic shock (18.20%)
Nephrotic syndrome (18.20%)	Bronchopneumonia (11.30%)
CAKUT (11.40%)	Gastroenteritis (4.50%)
Lupus nephritis (2.30%)	DKA (2.30%)
Nephrocalcinosis (2.30%)	Severe burn (2.30%)
	MMA (2.30%)

* HUS: Hemolytic uremic syndrome, CAKUT: congenital anomalies of the kidney and urinary tract, DKA: Diabetic ketoacidosis, MMA: Methylmalonic academia.

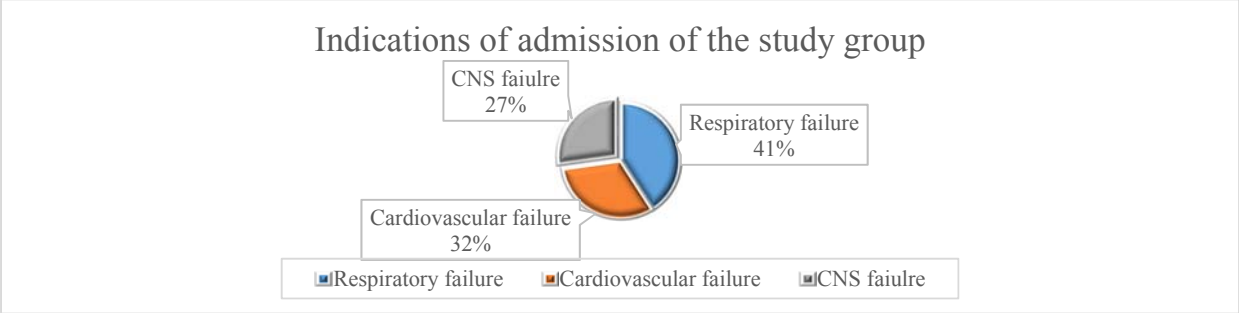

Figure 2: Indications of PICU admission of the patients

* Respiratory failure (40.9%, n=18) mainly due to bronchopneumonia and pulmonary edema, Cardiovascular failure (31.8%, n=14) which was mainly due to septic shock, CNS failure and encephalopathy (27.2%, n=12) which was mainly due to azotemia and hypertension.

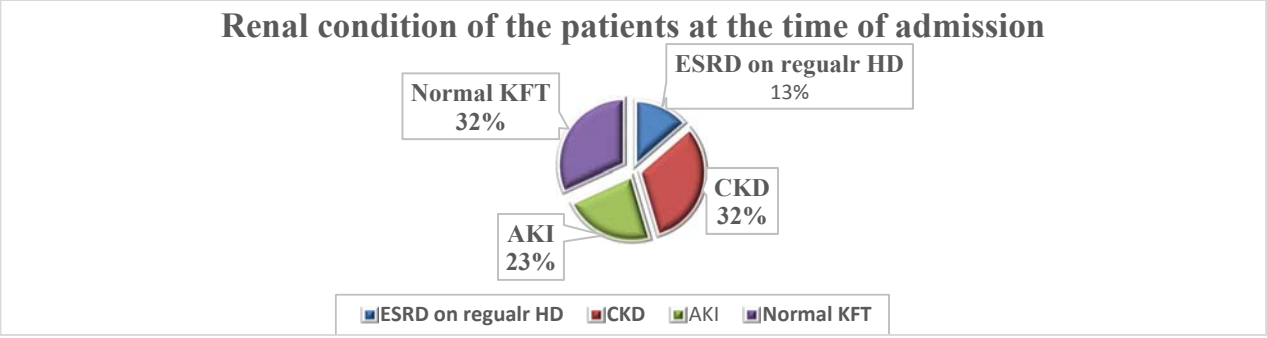

Figure 3 :Renal condition of the patients at the time of PICU admission

*ESRD :End stage renal disease ,HD:Hemodialysis.CKD :Chronic kidney disease on conservative treatment, AKI:Acute kidney injury , KFT: Kidney function tests.

Table 3: Demographic data of patients subjected to different dialysis modalities

		CRRT (n=6)	PD (n=32)	IHD (n=6)	Total (n=44)	P-value
Sex	**Females**	3 (50.0%)	13 (40.6%)	1 (16.7%)	17 (38.6%)	0.449
	Males	3 (50.0%)	19 (59.4%)	5 (83.3%)	27 (61.4%)	
Age (months)	**Median (IQR)**	84 (11 – 144)	12 (5.5 – 30)	72 (54 – 102)	24 (7.5 – 78)	**0.010***
	Range	9 – 144	2 – 144	48 – 108	2-144	
Weight (kg)	**Median (IQR)**	18 (10 – 41.5)	9.25 (6 – 12)	21.5 (18 – 26.3)	11 (7 – 19)	**0.002***
	Range	8 – 47	2.9 – 26	13 – 37.2	2.9 – 47	

PD: Peritoneal dialysis, CRRT: Continuous renal replacement therapy, IHD: Intermittent hemodialysis, IQR: Interquartile range.

*post-hoc analysis shows significant lower body weight for PD vs each of CRRT (p-value: 0.030) and IHD (p-value: 0.002).

NB: The body weight was expressed in kilograms, not percentiles, to assess the relationship between the body weight and the choice of dialysis modality regardless of the patient's age.

Table 4: Dialysis prescription in the three modalities (PD, CRRT, and HD)

	Median	IQR	Minimum	Maximum
PD (n=32)				
*** 2 sessions in 4 cases**				
Total runs	59	51.25	70.5	125
Total dialysate (L/Kg)	2.34	0.95	2.82	5.4
Dialysate/ session (L/Kg)	2.32	1.9	2.59	3.7
Total UF (mL/Kg)	145	80	228	408
UF/session (mL/Kg)	121	68	198	314
**** Standardized UF (mL/Kg)**	82	62	142	208
HD (n=6)				
No of sessions	3	1.5	3.75	5
Max. session UF (mL/Kg)	76	57	78	92
CRRT (n=6)				
Duration (h)	86	36	96	120
UF/session (mL/Kg)	76	50	130	668
***** Standardized UF (mL/Kg)**	51	13	87	186

PD: Peritoneal dialysis, CRRT: Continuous renal replacement therapy, IHD: Intermittent hemodialysis.
* The session lasts 12 to 24 hours. ** Standardized ultrafiltration (48 hours of CRRT, or PD, or one HD session)
*** Standardized ultrafiltration was not significantly different between dialysis modalities (p-value: 0.26 for HD vs PD, 0.31 for CRRT vs PD, and 0.69 for CRRT vs HD).
NB: PD (n=32) refers to the number of patients who were received PD, not the number of sessions, but when we calculated the UF it was calculated for all sessions received by 32 patients, including the extra-sessions.

Table 5: Outcome of the three dialysis modalities during the patients' stay in the PICU

Out come		Total (n=44)	CRRT (n=6)	PD (n=32)	IHD (n=6)	P-value
		No. (%)	No. (%)	No. (%)	No. (%)	
Patient Outcome **	**Died**	18 (40.9%)	1 (16.7%)	17 (53.1%)	0 (0.0%)	0.023
	Survived	26 (59.09%)	5 (83.3%)	15 (46.9%)	6 (100.0%)	
Renal outcome of survived patients	**CKD/ESRD from the start**	20 (45.4%)	1 (16.6%)	13 (40.6%)	6 (100.0%)	0.094
	New CKD/ESRD	16 (36.3%)	2 (33.3%)	14 (43.7%)	0 (0.0%)	
	Normal KFT	8 (18.1%)	3 (50%)	5 (15.6%)	0	
Dialysis Outcome **	**Successful**	27 (61.3%)	5 (83.3%)	16 (50.0%)	6 (100.0%)	0.034
	Non-successful	17 (38.6%)	1 (16.7%)	16 (50.0%)	0 (0.0%)	

* PD: Peritoneal dialysis, CRRT: Continuous renal replacement therapy, IHD: Intermittent hemodialysis, CKD: Chronic kidney disease, ESRD: End Stage Renal Disease, KFT: Kidney functions test.
**post-hoc analysis shows significant difference in Patient outcome and dialysis outcome (p-value: 0.016 for PD vs IHD patient outcome, 0.023 for PD vs IHD dialysis outcome), but difference was not significant in CRRT vs PD and CRRT vs IHD.

DISCUSSION

Dialysis may be required in critically ill children for correction of volume overload, uremia and other metabolic disturbances [11]. PD was considered the most frequently used dialysis modality in children, but it may not be optimal, especially in cases with severe fluid overload and abdominal surgery [12]. Over time, CRRT has become the preferred modality to manage AKI and fluid overload in critically ill children. However, some limitations are present, such as experienced personnel, cost, and anticoagulant use [4].

In the present study, we aimed to assess the choice, indications and the outcome of the different of dialysis modalities employed in critically ill children admitted to PICU. Out of 977 pediatric PICU patients in tertiary university based children hospital over a period of 6 months 44 children (4.5%)

required dialysis, and this is consistent with a study that showed nearly 5% of PICU patients required dialysis [1], but Vasudevan and others found that 10–30% of patients admitted to PICU required dialysis [13].

The children were divided into three groups: group 1 included children who underwent PD, which included 32 (72.8%) patients; group 2, which included six (13.6%) patients who underwent CRRT; and group 3, which included six (13.6%) patients who underwent IHD. As regards this number, we found that PD had the upper hand and this is consistent with the study done in India by Mishra et al. who showed that PD is the most commonly used form of dialysis in children worldwide, especially in developing countries, owing to cost and ease of use [14]. But this is in contrast to a study done in the United Kingdom that revealed CRRT is used more frequently than PD in critically ill children [15].

In this study we noticed that patients receiving PD had significantly younger age and lower weight (p-value: 0.01and 0.002) respectively. Which is due to technical difficulties and vascular access insertion required for HD and CRRT in those patients.

We noticed in this study, that volume overload as an indication of dialysis was more in HD than PD (p-value: 0.014), but we found that the patients who received IHD, they were on regular HD before PICU admission. In the present study, volume overload as an indication of dialysis was present in 50% (n = 3) of CRRT patients, and this is consistent with a study done on 63 pediatric critically ill patients that showed that the main indication of CRRT was volume overload in 31.7% of cases [16].

HD was very successful, but this cannot be generalized as the patients who received IHD were on regular HD before PICU admission and critically ill patients were mostly unfit for conventional HD. Prolonged intermittent renal replacement therapy (PIRRT) can be beneficial in children with small body weight where there is a specific need to reduce the hemodynamic instability associated with traditional IHD or the increased clotting and blood loss associated with CRRT, as PIRRT combines the slow sustained modality of continuous venovenous hemodialysis, ensuring hemodynamic stability and better biochemical clearance along with the cost effectiveness of conventional IHD, but its limited use as it requires expert personnel [17,18].

In the present study, the survival rate during the patient' stay in the PICU was higher among IHD than in PD (p-value = 0.016) and in CRRT was higher than PD, but with no significant difference. Beltamo and others found that lower mortality was associated with IHD and PD than that in CRRT which is mostly due to the better general condition of the patients who underwent HD than those who received CRRT [19].

PD is not always successful, HD is the most efficient in stable patients especially with volume overload, CRRT has a role but limited due to technical and personnel considerations. CRRT is only offered to children at tertiary pediatric hospitals and is more expensive than other forms of dialysis. CRRT requires personnel who are trained in the initiation of the therapy as well as the continued maintenance of the machine. CRRT requires reliable vascular access, which can be difficult to obtain in neonates and infants [20].

The limitation of the use of conventional HD in PICU patients is the aggravation of hypotension in those hemodynamically unstable patients [21]. In the present study, it was noticed that patients who are stable and on regular HD when admitted to the PICU, especially with volume overload, HD is still an option for dialysis and cannot be excluded. In other less stable patients, we used PD, although it has a poor outcome and higher mortality. We could have a potential improvement in outcome if we used CRRT in those patients.

CONCLUSION

Dialysis is an essential therapy in the setting of AKI and fluid overload, not only this but can be required for other conditions such as inborn error of metabolism and refractory hypernatremia.

Peritoneal dialysis is the most commonly used dialysis modality in the PICU. In patients who are stable and are already on regular hemodialysis when they admitted in the PICU due to volume overload HD is still an option of dialysis. PD has poor outcome mostly due to its use in unstable patients. So, dialysis modalities should be an individualized decision and different modalities should be available in the PICU to optimize the management of critically ill patient. PD is easier but not always sufficiently efficient, therefore if the patient is unfit for hemodialysis, CRRT may be utilized, however its use may be limited by the cost and experience requirements.

ABBREVIATIONS

AKI	Acute kidney injury	**IHD**	Intermittent hemodialysis
CAKUT	Congenital anomalies of the kidney and urinary tract	**IQR**	Interquartile range
CKD	Chronic kidney disease on conservative treatment	**KFT**	Kidney function tests
CRRT	Continuous renal replacement therapy	**MMA**	Methylmalonic academia
CVVH	Continuous Veno-Venous Hemofiltration	**PD**	Peritoneal dialysis
DKA	Diabetic ketoacidosis	**PICUs**	Pediatric intensive care units
ESRD	End stage renal disease	**PIRRT**	Prolonged intermittent renal replacement therapy
HD	Hemodialysis		
HDF	Hemodiafiltration	**UF**	Ultrafiltration
HUS	Hemolytic uremic syndrome		

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AUTHORS' CONTRIBUTIONS

The submitted manuscript is the work of the author & co-author.
All authors have contributed to authorship, have read and approved the manuscript.
Conception and design of study: Hafez Mahmoud Bazaraa
Acquisition of data: Ayman Soliman
Analysis and/or interpretation of data: Eman Abobakr and Khaled Amin
Drafting the manuscript: Eman Abobakr
Revising the manuscript critically for important intellectual content: Hafez Mahmoud Bazaraa
Approval of the version of the manuscript to be published: All authors.

STATEMENTS

Ethics approval and consent to participate
This study was approved by the Research Ethics committee of Cairo University, Egypt. The ethical committee approval number is I-

050414.Written informed consent to participate in this study was provided by the participants' legal guardians. All procedures used in this study adhere to the tenets of the Declaration of Helsinki 1967.

Consent for publication

Informed consent was obtained and documented for all participants.

Availability of data and material

All data will be available upon request from the corresponding author after all authors' approval.

Conflict of interest

The authors declare that there is no conflict of interests.

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