RESEARCH ARTICLE

A relation between serum albumin level and prognosis of critically ill children admitted to the paediatric Intensive Care Unit

Murtaza Ali Gowa,[1] Usman Tauseef,[2] Syed Habib Ahmed[3]

Abstract

Objective: To determine the frequency of hypoalbuminaemia in critically ill children, and to assess the association of low serum albumin with clinical deterioration and outcome.

Method: The prospective, descriptive study was conducted from September 1, 2020, to October 31, 2021, at the National Institute of Child Health, Karachi, and comprised critically ill children of either gender aged between 3 months and 16 years admitted to the paediatric intensive care unit. Serum albumin values were documented at 2 hours post-admission and at 24 hours. Paediatric Index of Mortality 2 score, Vasoactive Inotropic Score, and Paediatric Sequential Organ Failure Assessment scores were calculated. Hypoalbuminaemia was defined as serum albumin ≤3.3gdl. Data was analysed using SPSS 27.

Results: Of the 110 patients, 70(63.6%) were boys and 40(36.4%) were girls. The overall mean age was 46.72±43.28 months. Hypoalbuminaemia at 24 hours was found in 74(67.3%) subjects compared to 60(54.5%) at 2 hours, and mean serum albumin was lower at 24 hours compared to 2 hours post-admission ($p<0.05$). Patients with hypoalbuminaemia had significant relation with Paediatric Index of Mortality 2 score, Vasoactive Inotropic Score, Paediatric Sequential Organ Failure Assessment score, and outcome ($p<0.05$). The risk of mortality was 4.1 times higher in patients with hypoalbuminaemia ($p=0.001$).

Conclusion: The incidence of hypoalbuminaemia was found to be higher in children in intensive care settings, and hypoalbuminaemia was a significant independent predictor of mortality in a critically ill child.

Key Words: hypoalbuminaemia, Serum albumin, Critically ill, Children, PICU, Prognosis.

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Introduction

Albumin is the most abundant serum protein. In addition to its physiological role of maintaining the colloid osmotic pressure and preventing fluid leaking into the extravascular space, albumin acts as a low-affinity, high-capacity carrier for many exogenous and endogenous compounds. Albumin maintains the storage and intravascular transportation of hormones, like cortisol, thyroxin and testosterone. It is also a carrier for noxious compounds, like bilirubin, bile acids, fatty acids, cations like Fe+2, Ca+2, Cu+2, and Zn+2, and several drugs. Albumin can bind toxins, and, quantitatively, it is the primary extracellular antioxidant which constitutes three-fourths of the plasma antioxidant capacity. Besides, albumin acts as a plasma buffer and helps maintain the acid-base balance in the blood. Albumin is synthesised exclusively in the liver hepatocytes as pre-proalbumin and proalbumin, which is converted to albumin by the Golgi apparatus. The final product secretes into circulation at a rate of about 10-15gm per day. About 40% of the albumin remains in circulation, while a fraction moves to the interstitial space. Factors that stimulate albumin synthesis include the action of hormones, such as insulin and growth hormone. Most of the clearance of albumin occurs by catabolism (84%) and the remaining through gastrointestinal (10%) and renal clearance (6%)[1,2].

The average plasma albumin value range varies with age. At birth, it ranges from 1.8-3.0g/dl in premature babies on the first day of life, 2.5-3.4g/dl at <6 days in a full-term case, and its usual range is 1.9-4.9g/dl in infants <1 year. After the first year of life, the normal range of albumin is 3.4-4.2g/dl for a child <3 years and 3.5-5.6g/dl in children aged 4-19 years. But beyond infancy, any value of plasma albumin <3.3g/dl is considered hypoalbuminaemia irrespective of age[3, 4].

hypoalbuminaemia can be caused by physiological states, like growth, menstruation, second and third trimester of pregnancy, lactation, or female gender. Pathologically, it can be a result of decreased intake as in

[1]Department of Pediatric Critical Care Medicine, National Institute of Child Health, Karachi, Pakistan, [2]Department of Pediatric Medicine, National Institute of Child Health, Karachi, Pakistan, [3]Department of Pediatric Oncology, National Institute of Child Health, Karachi, Pakistan.

Correspondence: Usman Tauseef. Email: usman.tauseef.dr@gmail.com

ORCID ID. 0000-0002-9545-9505

protein-calorie malnutrition, kwashiorkor, decreased production as in liver diseases, increased loss in the urine as in nephrotic syndrome, or in the stool as in protein-losing enteropathy, vascular endothelial growth factor (VEGF) up regulation as in cancers, or secondary to the more complex mechanisms, like trauma, surgery, infection or mono-organ failure[5,6].

Albumin production may be inhibited by pro-inflammatory mediators, such as interleukin-6 (IL-6), IL-1, and tumour necrosis factor (TNF). So, it is considered a marker of nutritional status and disease severity, particularly in chronic and critically ill patients. Lower serum albumin levels are linked pathologically to inflammation in several aspects. Inflammation increases capillary permeability due to the release of inflammatory cytokines, such as TNF-alpha and IL-6, chemokines, and the action of prostaglandins, and complement components as well as endotoxins from gram-negative bacteria also cause escape and redistribution of albumin from vascular to interstitial space, leading to expansion of interstitial space and increasing the distribution volume of albumin. The rate of synthesis is also decreased in inflammation as a consequence of the increase in gene transcription for positive acute-phase proteins, such as C-reactive protein (CRP), and a decrease in the rate of transcription of albumin messenger ribonucleic acid (mRNA). On the other hand, albumin has a short half-life, and all of these factors lead to lower albumin levels despite increased fractional synthesis rates in the plasma[5,7].

The incidence of hypoalbuminaemia in critically ill children is reported to be >50%, and a significant relationship between lower albumin levels and mortality risk in children with critical illness has been established[4,8]. Low serum albumin levels with a persisting positive fluid balance are associated with increased mortality and prolonged illness course in a critically ill or severely septic patient, and a shift to a negative fluid balance (polyuria) with rising serum albumin levels herald recovery in a critically ill child[4, 5, 9, 10].

Hypoalbuminaemia on admission was found to be associated with prolonged paediatric intensive care unit (PICU) stay, higher Paediatric Risk of Mortality scores, more need for assisted respiratory support in the form of mechanical ventilation, higher progression to multi-organ dysfunction, and remarkably higher morbidity and mortality [11-14].

However, data from local studies is still scanty in this regard. The current study was planned to document the incidence of hypoalbuminaemia in critically ill children, and to find out its correlation with clinical deterioration and outcome.

Patients and Methods

The prospective, descriptive, cross-sectional, analytical study was conducted from September 1, 2020, to October 31, 2021, at the National Institute of Child Health (NICH), Karachi, which is a tertiary care hospital and a regional referral site. After approval of the institutional ethics review committee (ERC), the sample size was calculated using OpenEpi[15] with 99% confidence interval (CI) while assuming the prevalence of hypoalbuminaemia on admission to be 56.7%[4]. The probability simple random sampling technique was used. Those included were critically ill children of either gender aged between 3 months and 16 years admitted to the 13-bed NICH PICU. Patients diagnosed with nephrotic or nephritic syndrome or protein-losing enteropathy, cardiac failure, or patients who were there after cardiac surgery and those who came with burns were excluded. Also excluded were patients who received albumin solution at any time during the admission or were on total parenteral nutrition (TPN).

A proforma (Appendix 1) was used as the data-collection instrument filled out by the researchers. Socio-demographic characteristics of the patients, hospital registration number, age, gender, weight, height and the diagnosis were recorded. Serum albumin levels at 2 hours and 24 hours post-admission were noted. Quantitative measurement of serum albumin was performed by photometric colour test (Beckman Coulter analyser). Hypoalbuminaemia was defined as serum albumin ≤3.3g/dl.

In addition, mortality risk assessed by calculating Paediatric Index of Mortality 2 (PIM2) score[16], Vasoactive Inotropic Score (VIS)[17,18], and Multiple Organ Dysfunction Score (MODS) Paediatric Sequential Organ Failure Assessment (pSOFA) score[19] (Appendices 2-4). Parameters required for calculating theses scores, like PaO2, FiO2, base excess, SO2, platelet count, bilirubin count, and serum creatinine were recorded. The need of mechanical ventilation (MV), MV duration, and the duration of PICU stay were recorded. The outcome was noted in terms of survived or expired. The institutional ERC waived parental consent as all sampling and monitoring was going on as part of routine management. The anonymity of the patients was, however, maintained throughout the study.

Data was analysed using SPSS 27. Data normality was assessed using Shapiro-Wilks test, and serum albumin values were found to be normally distributed at all points (coefficient 0.98, p=0.48). Mean and standard deviations

were calculated for quantitative data, while frequencies and percentages were calculated for qualitative data. Comparison of mean values was done using dependent and independent t-test, as appropriate. Pearson's coefficient of correlation was applied for determining the relationship among quantitative variables, and Chi-square/Fischer Exact test were utilised, as appropriate, for qualitative variables. McNemar's test was applied to check the proportion difference at two different time frames. The odds ratio (OR) was calculated by univariate and multivariate binary logistic regression. P<0.05 was considered statistically significant.

Results

Of the 110 patients, 70(63.6%) were boys and 40(36.4%) were girls. The overall mean age was 46.72±43.28 months. Hypoalbuminaemia at 24 hours was found in 74(67.3%) subjects compared to 60(54.5%) at 2 hours (p=0.007). Of the total, 96(87.3%) patients required MV and 62(56.4%) required inotropic support. There were 48(43.6%) deaths; 40(36.4%) among those with hypoalbuminaemia, and 8(7.3%) among those with normal albumin level (Table 1).

Table-1: Data comparison between hypoalbuminemia and normal albumin groups

Variable	Hypoalbuminemia group (n=74)	Normal Albumin group (n=36)	Total (n=110)
Serum albumin, mean±SD, g/dl	2.72±0.39	3.61±0.22	3.01±0.54
Age, mean±SD, months	44.61±44.02	51.06±41.98	46.72±43.28
Weight, mean±SD, kg	12.48±7.96	13.81±6.62	12.91±7.54
PIM2[1] Score, mean±SD, % Risk of mortality	13.35±12.75	6.92±8.97	11.24±11.99
VIS[2] score, mean±SD	12.15±14.57	6.69±10.20	10.36±13.49
pSOFA[3] score, mean±SD	8.04±4.01	6.00±3.15	7.37±3.86
MAP[a], mean±SD, mmHg	78.04±14.27	83.14±16.06	79.71±15.00
Length of Mechanical ventilation, mean±SD, days	10.16±7.73	7.50±7.43	9.29±7.70
Length of PICU stay, mean±SD, days	12.22±7.78	12.72±8.53	12.38±8.00
Outcome (Expired) n(% of Total, n=110)	40(36.4%)	8(7.3%)	48(43.6%)

[1] PIM: Paediatric index of mortality, [2] VIS: Vasoactive inotropic score, [3] pSOFA: Paediatric Sequential Organ Failure Assessment score, [a] MAP: Mean arterial pressure, PICU: Paediatric intensive care unit, SD: Standard deviation

Mean serum albumin was lower at 24 hours 3.20±0.54g/dl compared to 2 hours post-admission 3.31±0.57g/dl (p<0.05).

Patients with hypoalbuminaemia had significant relation with PIM2, VIS, pSOFA scores, and outcome (p<0.05). The risk of mortality was 4.1 times higher in patients with hypoalbuminaemia (p=0.001) Patients aged <60 months were 1.17 times more likely to have hypoalbuminaemia than patients aged >60 months (Table 2).(Page-70)

Discussion

The incidence of hypoalbuminaemia in children admitted to PICU (67.3%) was higher than reported earlier in a study (56.7%)[4].

The pathophysiology of hypoalbuminaemia in a sick child is multifactorial, and this can occur as a consequence of decreased production by the liver during critical illness or due to malnutrition, or it can occur because of increased degradation and altered distribution caused by increased catabolism or capillary leakage and an altered distribution of albumin during inflammation and illness[4].

Infants, children aged <6 years and malnourished children were more prone to develop hypoalbuminaemia compared to older and good-weight children in the current study. The mean serum albumin in patients who expired was lower (2.81g/dl) compared to those who survived (3.17g/dl). In contrast, a study reported that means albumin levels were similar between non-survivors and survivors[4].

The current findings related to PIM2 and MODS pSOFA were consistent with earlier reports[11, 20].

Mean Arterial Pressure (MAP) had no significant correlation with serum albumin (r=0.052), but the hypoalbuminaemia group had a slightly lower average MAP (78.04mHg) compared to the normoalbuminaemia group (83.14mmHg). The finding explains that hypoalbuminaemia is not the solitary culprit causing hypotension in a critically ill child, and a fall in MAP in such patients is multifactorial. There was a moderate negative correlation between serum albumin and VIS (r=-0.30, p=0.05). The mean VIS was higher in the hypoalbuminaemia group than in patients with normal albumin (12.15 vs. 6.69), and the odds of having VIS score >10 were 2.3 times higher in patients with hypoalbuminaemia than patients with normal albumin (p=0.07). The patients who needed inotropic support had low serum albumin, indicating the importance of intravascular albumin in maintaining blood pressure. Theoretically, albumin infusion as a volume expander should increase blood pressure, but the evidence of albumin infusion for hypotension is still lacking. In a double-blind Saline vs. Albumin Fluid Evaluation (DAFE) trial, the albumin infusion given to treat hypotension in adult patients failed to reduce mortality and morbidity in critical adult patients[21,22]. As such, it more research is needed in this regard, especially in the paediatric population.

Patients with hypoalbuminaemia were more likely to

Table-2: Association of hypoalbuminemia with study variables.

Variables	Serum Albumin (g/dl) Comparison of Means[1] Mean±SD		Association with Hypoalbuminemia with variables[2] n (%)		Odds Ratio for Hypoalbuminemia[3] OR (95% CI)	Correlation of Serum Albumin(g/dl) r[5]
Mortality Risk <20%	3.060±0.557		54(73)	33(91.7)	1	-0.32**
Mortality Risk <20%	2.865±0.459		20(27)	3(8.3)	4.07 (1.12-14.77)	
PIM2 Score *(p-value)*	**(0.12)**		**(0.02)**		**(0.03)**	
Low <10	3.112±0.532		47(63.5)	29(80.6)	1	-0.30**
High ≥10	2.812±0.513		27(36.5)	7(19.4)	2.38(0.91-6.16)	
VIS Score (p-value)	**(0.00)**		**(0.07)**		**(0.07)**	
Mortality Risk <50%	3.158±0.510		62(83.8)	36(100)		-0.33**
Mortality Risk >50%	3.093±0.581		12(16.2)	0(0)		
pSOFA Score *(p-value)*	**(0.00)**		**(0.00)**		**NA**	
Yes	2.979±0.541		7(9.5)	7(19.4)	2.3(0.74-7.14)	-0.19*
No	3.293±0.485		67(90.5)	29(80.6)	1	
MVδ required *(p-value)*	**(0.04)**		**(0.22)**		**(0.14)**	
Yes	2.918±0.548		45(60.8)	17(47.2)	1.734(0.776-3.874)	0.21*
No	3.150±0.51	1	29(39.2)	19(52.8)	1	
Inotropic support required *(p-value)*	**(0.02)**		**(0.18)**		**(0.17)**	
<7 days	3.128±0.616		59(79.7)	26(72.2)	1	-0.10
≥7 days	2.987±0.518		15(20.3)	10(27.8)	1.51(0.60-3.81)	
Hospital stay *(p-value)*	**(0.25)**		**(0.38)**		**(0.38)**	
Survived	3.179±0.490		59(79.7)	26(72.2)	1	-0.33**
Expired	2.812±0.541		15(20.3)	10(27.8	) 4.11 (1.65-10.22)	
Outcome *(p-value)*	**(0.00)**		**(0.00)**		**(0.00)**	

[1]Independent t-test, [2]Chi-square test, [3]Univariate and multivariate binary logistic regression

PIM: Paediatric index of mortality, VIS: Vasoactive inotropic score, pSOFA: Paediatric Sequential Organ Failure Assessment, MV: Mechanical ventilation, SD: Standard deviation, CI: Confidence interval.

[5]Pearson's coefficient of correlation was applied. Interpretation: perfect: if the coefficient value is near ±1, high degree/strong correlation: if coefficient value lies between ±0.50 and ±1, moderate degree/medium correlation: if value lies between ±0.30±0.49, low degree/small correlation: when the value lies below +0.29

* Correlation is significance at 0.05 levels (2-tailed).

** Correlation is significance at 0.01 levels (2-tailed)

require MV than patients with normal albumin in the current study (p=0.14). MV duration was also higher in the hypoalbuminaemia group, which is consistent with literature[8,22].

The average PICU stay was almost similar in both groups (p=0.38) in the current study, which was in contrast to Tiwari et al[8].

Finally, there was also a significant relation between hypoalbuminaemia and patient outcome (p=0.001), and the mean serum albumin was lower in non-survivors than the survivors (p=0.001), which is contrary to the findings of Durward et al[4], who reported that mean serum albumin was similar in both groups. The overall risk of mortality was 4.1 times higher in patients with hypoalbuminaemia in the current study, highlighting low serum albumin as a crucial independent predictor of mortality in critically ill children. The finding is also in contrast to that of Durward et al[4].

The major limitation of the current study was that it did not look for the response of albumin infusion in increasing blood pressure and decreasing mortality and morbidity. In terms of strength, the current study is the first to establish a relation between serum albumin level and MODS pSOFA score.

Conclusion

The findings provided supportive evidence to the literature about the frequent incidence of hypoalbuminaemia among critically ill patients. A significant relationship between low serum albumin was established with mortality and morbidity.

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Appendix 1: The study proforma

PROFORMA Date: _____

BIODATA:

Name(optional): _____ Age: _____ Gender: M/F Height: _____cm Weight: _____Kg

Provisional Diagnosis: _____ Hospital Registration No: _____

Date of Admission: _____ Date of Discharge/Death: _____ Final Diagnosis:_____

Serum Albumin levels:

At 2 hours: _____ At 24 hours: _____

PIM 2 (Pediatric Index of Mortality 2) Score(Error! Reference source not found.): _____

Systolic BP: _____ mmHg PaO2: _____ mmHg FIO2 at the time of PaO2: _____ Base excess: _____ mmol/l

Pupillary reactions to bright light: >3 mm and both fixed/other/unknown

Mechanical ventilation at any time during the first hour in ICU: No/Yes Elective admission to ICU: No/Yes

Recovery from surgery or a procedure is the main reason for ICU admission: No/Yes

Admitted following cardiac bypass No/Yes High risk diagnosis:

Vasoactive Inotropic Score(VIS)(Error! Reference source not found.): _____

Dopamine dose: _____ (µg/kg/min) Dobutamine dose: _____ (µg/kg/min) Epinephrine dose: _____(µg/kg/min) Milrinone dose: _____(µg/kg/min)

Vasopressin dose: _____(U/kg/min) Norepinephrine dose: _____ (µg/kg/min)

Length of PICU stay: _____ days

Length of Mechanical Ventilation: _____ days

MODS(pSOFA-Pediatric Sequential Organ Failure Assessment Score)(Error! Reference source not found.): _____

PO2: _____ FiO2: _____ P/F ratio: _____ SO2: _____ S/F Ratio: _____

Platelet count: _____ x 10^5uL Bilirubin levels: _____mg/dl Creatinine: _____ mg/dL

Mean Arterial Pressure: _____mmHg Inotropic Support: _____ at dose : _____

Glasgow Coma Score : _____

Outcome: survived/expired/LAMA/Step Down/Discharge/other: _____

Remarks: _____

Appendix 2: Paediatric Index Of Mortality Score

Paediatric Index of Mortality 2 (PIM 2)

1. Systolic blood pressure, mmHg (unknown =120)1

2. Pupillary reactions to bright light (>3 mm and both fixed =1, other or unknown =0)2

3. PaO2, mmHg (unknown =0)

FIO2 at the time of PaO2 if oxygen via ETT or headbox (unknown =0)

4. Base excess in arterial or capillary blood, mmol/l (unknown =0)

5. Mechanical ventilation at any time during the first hour in ICU (no=0, yes=1)3

6. Elective admission to ICU (no=0, yes=1)4

7. Recovery from surgery or a procedure is the main reason for ICU admission (no =0, yes =1)5

8. Admitted following cardiac bypass (no =0, yes =1)6

9. High risk diagnosis. Record the number in brackets. If in doubt record 0.

[0] None

[1] Cardiac arrest preceding ICU admission7

[2] Severe combined immune deficiency

[3] Leukaemia or lymphoma after first induction

[4] Spontaneous cerebral haemorrhage8

[5] Cardiomyopathy or myocarditis

[6] Hypoplastic left heart syndrome9

[7] HIV infection

[8] Liver failure is the main reason for ICU admission10

[9] Neuro-degenerative disorder1

10. Low risk diagnosis. Record the number in brackets. If in doubt record 0.

[0] None

[1] Asthma is the main reason for ICU admission

[2] Bronchiolitis is the main reason for ICU admission12

[3] Croup is the main reason for ICU admission

[4] Obstructive sleep apnoea is the main reason for ICU admission13

[5] Diabetic keto-acidosis is the main reason for ICU admission

Coding rules. These rules must be followed carefully for PIM2 to perform reliably:

1.Record SBP as 0 if the patient is in cardiac arrest, record 30 if the patient is shocked and the blood pressure is so low that it cannot be measured.

2.Pupillary reactions to bright light are used as an index of brain function. Do not record an abnormal finding if this is due to drugs, toxins or local eye injury.

3.Mechanical ventilation includes mask or nasal CPAP or BiPAP or negative pressure ventilation.

4.Elective admission. Include admission after elective surgery or admission for an elective procedure (e.g. insertion of a central line), or elective monitoring, or review of home ventilation. An ICU admission or an operation is considered elective if it could be postponed for more than 6 h without adverse effect.

5.Recovery from surgery or procedure includes a radiology procedure or cardiac catheter. Do not include patients admitted from the operating theatre where recovery from surgery is not the main reason for ICU admission (e.g. a patient with a head injury who is admitted from theatre after insertion of an ICP monitor; in this patient the main reason for ICU admission is the head injury).

6.Cardiac bypass. These patients must also be coded as recovery from surgery.

7.Cardiac arrest preceding ICU admission includes both in-hospital and out-of-hospital arrests. Requires either documented absent pulse or the requirement for external cardiac compression. Do not include past history of cardiac arrest.

8.Cerebral haemorrhage must be spontaneous (e.g. from aneurysm or AV malformation). Do not include traumatic cerebral haemorrhage or intracranial haemorrhage that is not intracerebral (e.g. subdural haemorrhage).

9.Hypoplastic left heart syndrome. Any age, but include only cases where a Norwood procedure or equivalent is or was required in the neonatal period to sustain life.

10.Liver failure acute or chronic must be the main reason for ICU admission. Include patients admitted for recovery following liver transplantation for acute or chronic liver failure.

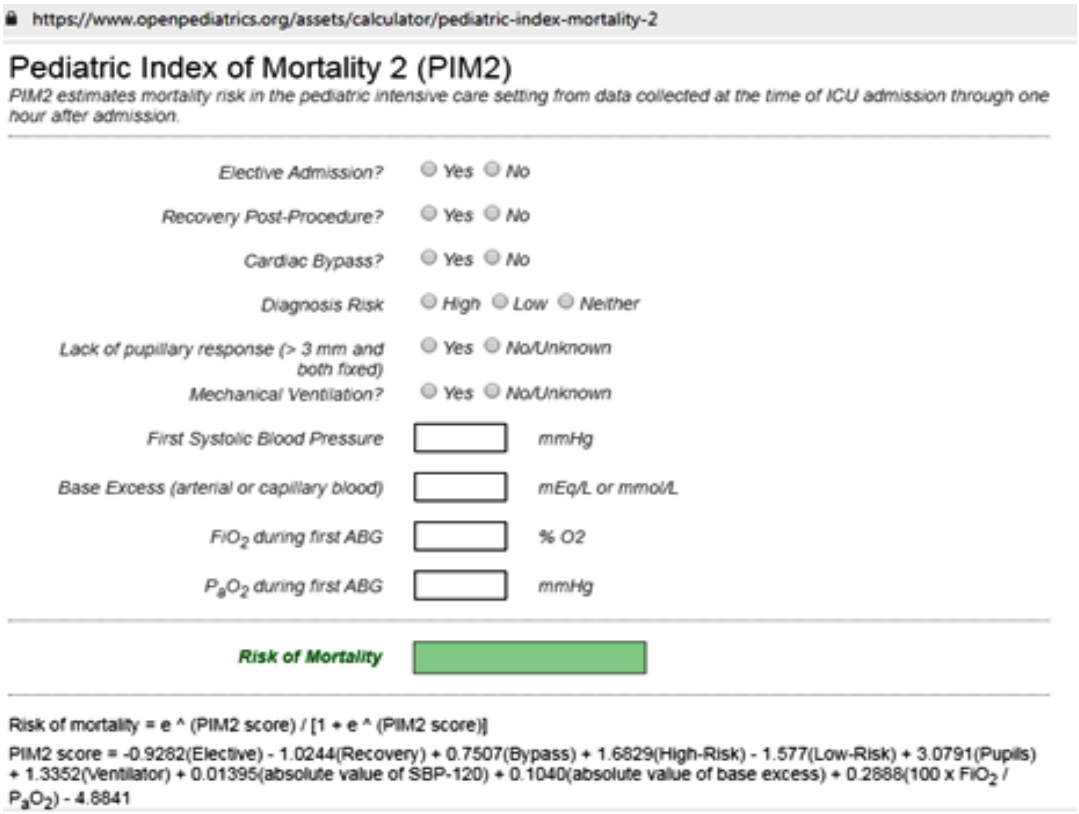
11.Neuro-degenerative disorder. Requires a history of progressive loss of milestones or a diagnosis where this will inevitably occur.

12.Bronchiolitis. Include children who present either with respiratory distress or central apnoea where the clinical diagnosis is bronchiolitis.

13.Obstructive sleep apnea. Include patients admitted following adenoidectomy and/or tonsillectomy in whom obstructive sleep apnoea is the main reason for ICU admission (and code as recovery from surgery).

Note: For the sake of convenience PIM 2 score will be calculated using online calculator available at OPENPediatrics https://www.openpediatrics.org/assets/calculator/pediatric-index-mortality-2

Appendix 3: Vasoactive Inotropic Score (VIS)



https://www.openpediatrics.org/assets/calculator/pediatric-index-mortality-2

Pediatric Index of Mortality 2 (PIM2)

PIM2 estimates mortality risk in the pediatric intensive care setting from data collected at the time of ICU admission through one hour after admission.

Elective Admission?	○ *Yes* ○ *No*
Recovery Post-Procedure?	○ *Yes* ○ *No*
Cardiac Bypass?	○ *Yes* ○ *No*
Diagnosis Risk	○ *High* ○ *Low* ○ *Neither*
Lack of pupillary response (> 3 mm and both fixed)	○ *Yes* ○ *No/Unknown*
Mechanical Ventilation?	○ *Yes* ○ *No/Unknown*
First Systolic Blood Pressure	[ ] *mmHg*
Base Excess (arterial or capillary blood)	[ ] *mEq/L or mmol/L*
FiO_2 during first ABG	[ ] *% O2*
P_aO_2 during first ABG	[ ] *mmHg*
Risk of Mortality	[ ]

Risk of mortality = e ^ (PIM2 score) / [1 + e ^ (PIM2 score)]

PIM2 score = -0.9282(Elective) - 1.0244(Recovery) + 0.7507(Bypass) + 1.6829(High-Risk) - 1.577(Low-Risk) + 3.0791(Pupils) + 1.3352(Ventilator) + 0.01395(absolute value of SBP-120) + 0.1040(absolute value of base excess) + 0.2888(100 x FiO_2 / P_aO_2) - 4.8841

VIS = [IS] + 10 X Milrinone dose (µg/kg/min) +10,000 × Vasopressin dose (U/kg/min) + 100 × Norepinephrine dose (µg/kg/min)
[Wernowsky IS] = [Dopamine dose (µg/kg/min) + Dobutamine dose (µg/kg/min) +100 × epinephrine dose (µg/kg/min)]
A score of < 10 will be assigned as low, 10-20 as moderate and >20 as high

Appendix 4: Paediatric Sequential Organ Failure Assessment (pSOFA) Score

Table 1. Pediatric Sequential Organ Failure Assessment Score

Variables	Score[a] 0	1	2	3	4
Respiratory					
Pao_2:Fio_2[b] or Spo_2:Fio_2[c]	≥400	300-399	200-299	100-199 With respiratory support	<100 With respiratory support
	≥292	264-291	221-264	148-220 With respiratory support	<148 With respiratory support
Coagulation					
Platelet count, $\times 10^3/\mu L$	≥150	100-149	50-99	20-49	<20
Hepatic					
Bilirubin, mg/dL	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
Cardiovascular					
MAP by age group or vasoactive infusion, mm Hg or μg/kg/min[d]					
<1 mo	≥46	<46	Dopamine hydrochloride ≤5 or dobutamine hydrochloride (any)	Dopamine hydrochloride >5 or epinephrine ≤0.1 or norepinephrine bitartrate ≤0.1	Dopamine hydrochloride >15 or epinephrine >0.1 or norepinephrine bitartrate >0.1
1-11 mo	≥55	<55			
12-23 mo	≥60	<60			
24-59 mo	≥62	<62			
60-143 mo	≥65	<65			
144-216 mo	≥67	<67			
>216 mo[e]	≥70	<70			
Neurologic					
Glasgow Coma Score[f]	15	13-14	10-12	6-9	<6
Renal					
Creatinine by age group, mg/dL					
<1 mo	<0.8	0.8-0.9	1.0-1.1	1.2-1.5	≥1.6
1-11 mo	<0.3	0.3-0.4	0.5-0.7	0.8-1.1	≥1.2
12-23 mo	<0.4	0.4-0.5	0.6-1.0	1.1-1.4	≥1.5
24-59 mo	<0.6	0.6-0.8	0.9-1.5	1.6-2.2	≥2.3
60-143 mo	<0.7	0.7-1.0	1.1-1.7	1.8-2.5	≥2.6
144-216 mo	<1.0	1.0-1.6	1.7-2.8	2.9-4.1	≥4.2
>216 mo[e]	<1.2	1.2-1.9	2.0-3.4	3.5-4.9	≥5

Abbreviations: Fio_2, fraction of inspired oxygen; MAP, mean arterial pressure; pSOFA, pediatric Sequential Organ Failure Assessment; Spo_2, peripheral oxygen saturation.

SI conversion factors: To convert bilirubin to micromoles per liter, multiply by 17.104; creatinine to micromoles per liter, multiply by 88.4; and platelet count to $\times 10^9$/L, multiply by 1.

[a] The pSOFA score was calculated for every 24-hour period. The worst value for every variable in each 24-hour period was used to calculate the subscore for each of the 6 organ systems. If a variable was not recorded in a given 24-hour period, it was assumed to be normal and a score of 0 was used. Daily pSOFA score was the sum of the 6 subscores (range, 0-24 points; higher scores indicate a worse outcome).

[b] Pao_2 was measured in millimeters of mercury.

[c] Only Spo_2 measurements of 97% or lower were used in the calculation.

[d] MAP (measured in millimeters of mercury) was used for scores 0 and 1; vasoactive infusion (measured in micrograms per kilogram per minute), for scores 2 to 4. Maximum continuous vasoactive infusion was administered for at least 1 hour.

[e] Cutoffs for patients older than 18 years (216 months) were identical to the original SOFA score.

[f] Glasgow Coma Scale was calculated using the pediatric scale.

The sum of sub-scores will result in pSOFA score (ranging from 0-24 points; higher scores indicate a worse outcome. Risk of mortality interpreted from pSOFA score of 0-6 is <10%, 7-9 is 15-20%, 10-12 is 40-50%, 13-14 is 50-60%, 15 is >80% and 15-24 is > 90% respectively.