

Inborn Errors of Metabolism in Pediatric Intensive Care Unit: Much More to Understand

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We read with interest the recently published article titled “Inborn Errors of Metabolism in a Tertiary Pediatric Intensive Care Unit” by Lipari et al¹ and want to make few important comments. Authors enrolled 65 cases of inborn errors of metabolism (IEMs) with 88 admission to a pediatric intensive care unit (PICU) in Portugal over a period 11 years (2009–2019) accounting for 2% of PICU admissions. The children with intoxication disorders, energy metabolism defects, complex molecules, and other disorders accounted for 35.4% ($n = 23$), 32.3% ($n = 21$), 26.2% ($n = 17$), and 6.1% ($n = 4$), respectively. The median age at admission to PICU was 3 years (range: 3 days–21 years) and 70.4% ($n = 62$) admissions were for metabolic decompensation and 29.5% ($n = 26$) were elective/scheduled surgery/procedure admissions. The reasons for decompensation included infections (55.4%, $n = 36$) and metabolic stress during neonatal period (18.7%, $n = 12$). The common clinical presentations were respiratory failure (34.1%, 30/88) and neurological deterioration (29.5%, 26/88). The treatment included mechanical ventilation ($n = 30$), continuous venovenous hemodiafiltration (CVVHDF) ($n = 16$), specific nutritional management, and supportive care. The median duration of PICU stay was 3.6 days (range: 3 hours–35 days) and mortality was 12.3% ($n = 8$). The comparison of cases with intoxication disorders, energy metabolism defects, and complex molecules disorders is depicted in ►Table 1. Children with intoxication disorders constituted one-third of cases (35.4%), diagnosed early (median: 6 days of life), and had lowest median age at PICU admission (1.5 years). Although one-third cases with intoxication disorders had neonatal diagnosis (32.2%), only 65.2% were diagnosed before PICU admission and among 34.8% cases, the diagnosis was made after PICU admission. The higher proportion of children with intoxication disorders presented with coma (30.3%), required mechanical ventila-

tion (9/31), CVVHDF ($n = 14$) ($p < 0.0001$), had longest PICU stay, and highest mortality (17.3%, $n = 4$) ($p < 0.0001$).

Authors did a commendable job in highlighting the intensive care course and outcome of children with IEMs.¹ We would like to highlight few points pertinent to our setting. In developing countries like India, there is lack of universal neonatal testing for IEMs. In addition, the testing facilities for IEMs (tandem mass spectrometry, gas chromatography mass spectrometry, and molecular tests) are not available at all the cities and centers. A general understanding among pediatricians and physicians that the IEMs are rare compounded the issue of missed opportunity for diagnosis, inappropriate treatment, and poor outcome. Also, there is lack of well-designed large-scale studies from PICUs in India highlighting the intensive care needs and outcome of children with IEMs. A few small studies highlighted the profile and outcome of children with IEMs admitted to PICUs.^{2,3} These studies showed that children with IEMs constituted 0.9 to 2.6% of PICU admissions. The median age at presentation was 7 to 15 months. In one study, diagnosis was established in 80% cases before admission to PICU,³ whereas in another study, none of the cases had diagnosis prior to the PICU admission.² This highlights the lack of universal neonatal testing for IEMs in India. The mortality was 33 to 36%^{2,3} that is much higher than the study by Lipari et al¹ highlighting late presentation, late diagnosis, and possibly lack of extracorporeal therapies in Indian PICUs.

The diagnosis of IEMs is not rare and IEMs contribute significantly to the global child mortality and morbidity.^{4,5} There is need to adopt universal neonatal screening program for common IEMs, facilities to diagnose IEMs at major centers, prenatal diagnosis, and specialized units to manage these cases to limit the burden of IEMs. In majority of infants and children, the diagnosis is usually not established prior to

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Table 1 Clinical characteristics, complications, treatment, and outcome among patients in different groups of IEMs admitted to a PICU

Characteristics	Total cases	Intoxication disorders	Energy metabolism defects	Complex molecules disorders
Number of cases	65	23 (35.4%)	21 (32.3%)	17 (26.2%)
Number of admissions	88	31		
Neonatal diagnosis	20/65 (30.7%)	10/23 (43.5%)	6/21 (28.6%)	–
Median age at diagnosis	3 mo (3 d–9 y)	6 d	12 mo (6 d–3.5 y)	21 months (1 mo–2.5 y)
Diagnosed before PICU admission	54/65 (83.1%)	15/23 (65.2%)	19/21 (90.4%)	15/17 (88.2%)
Neonatal admissions	14/88 (15.9%)	10/31 (32.2%)	2/21 (9.5%)	0
Median age at PICU admission	3 y (3 d–21 y)	1.5 y (3 d–12 mo)	3 y (14d–21 y)	3 y (3.5 mo–16 y)
Males	33			
Admission reasons				
Metabolic decompensation	62/88 (70.4%)			
Elective (elective or scheduled surgery)	26/88 (29.5%)			
Reason of decompensation				
Infection	36 (55.4%)	13/31 (41.9%)	11/21 (52.4%)	11/17 (64.7%)
Metabolic stress during neonatal period	12 (18.5%)	11/31 (35.5%)	1 (4.3%)	0
Presentation				
Respiratory failure	30/88 (34.1%)	4/31 (12.9%)	4/21 (19%)	12/17 (70.6%)
Neurological deterioration	26/88 (29.5%)			
Coma	15 (23.1%)	10/31 (30.3%)	4/21 (19%)	1/17 (5.9%)
Lethargy with or without dehydration	10 (15.4%)	5 (21.7%)	5 (23.8%)	0
Complications				
Neurological repercussions		7/31		
Seizures	12 (18.5%)	4 (17.4%)	2 (9.5%)	6 (35.3%)
Abnormal neuroimaging		5/31		2
Coagulopathy		5/31	2	
Cardiac abnormalities		1	3	7
Treatment				
Concentrated dextrose			21 (100%)	
Respiratory support		11/31		
Invasive mechanical ventilation	30	9/31	5	11
Parenteral nutrition	6	–	–	–
CVVHDF	16	14	1	0
Mortality	8 (12.3%)	4/23 (17.3%)	1/21 (4.8%)	2/17 (11.8%)
PICU stay	3.6 d (3 h–35 d)	2 (1–16) d	1 (1–19) d	1 (1–35) d

Abbreviations: CVVHDF, continuous venovenous hemodiafiltration; IEM, inborn errors of metabolism; PICU, pediatric intensive care unit.

PICU admission in Indian setting. Therefore, to diagnose IEMs in PICU, intensivists should keep a high index of suspicion. Children admitted to PICU with IEMs require aggressive treatment in form of mechanical ventilation, extracorporeal therapies, nutritional modifications, and supportive care. In view of paucity of literature from developing countries, there

is need of large multicentric studies on the profile, intensive care needs, and outcomes in children with IEM admitted to PICUs.

Conflict of Interest
None declared.

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