

# Mortality Patterns among Critically Ill Children in a Pediatric Intensive Care Unit of a Sanglah Hospital

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**Abstract:** **Background:** The pediatric intensive care unit (PICU) is a part of the hospital where critically ill pediatric patients who require advanced airway, respiratory, and hemodynamic supports. In intensive care unit (ICU) results can be assessed on the basis of outcomes such as death or survival by means of indicators such as mortality rates. The mortality in a PICU can reflect a hospital health care quality and effective management on handling with critical ill patients. **Objective:** To determine mortality profile of the children admitted at PICU Sanglah Hospital. **Methods:** A total of 100 subjects were analyzed in this study. The median age of treated subjects was 1 year with the youngest 1 month and the oldest 14 years, and the greatest age group was the 1 month-11 months age group (40%). The most subjects treated were male (55%) and 54% subjects with mild malnutrition condition. The subjects predominantly were referral patients from hospitals or other health service facilities. The average length of stay of these subjects from admission to death in PICU was 7.98 days, with length of stay of more than 3 days being higher in proportion. Of the 100 subjects, 85% were on a ventilator, 47% used central venous access and 21% received parenteral nutrition. The mean procalcitonin level was 28.64 ng/mL. The most common cause of death was sepsis (61%). Among the subjects with sepsis, Pelod score 7-10 and inotropic score  $\geq 20$  were the greatest in proportion. **Conclusion:** Sepsis had a higher predisposition of higher mortality rate in PICU. So the source of infection either hospital acquired or community acquired should be identified and managed aggressively.

**Keywords:** children, pediatric intensive care unit, mortality, sepsis

## 1. Background

Intensive care has become very important in the management of critically ill children. The pediatric intensive care unit (PICU) is a part of the hospital where critically ill pediatric patients who require advanced airway, respiratory, and hemodynamic supports are usually admitted with the aim of achieving an outcome better than if the patients were admitted into other parts of the hospital.<sup>1</sup> The care of critically ill children remains one of the most demanding and challenging aspects of the field of pediatrics. The main purpose of the PICU is to prevent mortality by intensively monitoring and treating critically ill children who are considered at high risk of mortality. This, however, comes at a huge cost to all the parties involved the hospital, the personnel, and the caregivers of patients. It is usually only offered to patients whose condition is potentially reversible and who have a good chance of surviving with intensive care support.<sup>2</sup>

Since these patients are critically ill, the outcome of intervention is sometimes difficult to predict. In critical care medicine, intensive care unit (ICU) results can be assessed on the basis of outcomes such as "death" or "survival" by means of indicators such as mortality rates.<sup>3</sup> Evaluation of the outcomes of medical interventions can assess the efficacy of treatment, making it possible to take better decisions, to further improve quality of care, to standardize conduct, and to ensure effective management of the high-

level resources needed to deliver intensive care services thereby optimizing resource utilization.<sup>4</sup> Although mortality in patients depends on many factors such as demographic and clinical characteristic of population, infrastructure and non-medical factors (management and organization), and admission practice, it is also affected by ICU performance.<sup>5</sup>

The mortality in a PICU can reflect a hospital's health care quality and efficiency on handling with critical ill patients, and reduce the mortality in PICU will be the key to reduce the overall mortality in a children's hospital. The studies that investigate mortality and risk factors for death can give information to improve the clinical practices and provide public health strategies to improve the outcomes of ICU care. The outcome measures of PICU include mortality, length of stay (LOS), long-term result such as health status, disability and morbidity. Studies carried out in different countries show that source of patient admission is associated with death in Intensive Care Units (ICU). Patients transferred from wards within the same hospital show a greater ICU mortality when compared with those coming from other sources.<sup>6</sup>

The principal objective of pediatric critical care is not only to decrease the mortality but also to restore the child who is suffering from a life-threatening condition to health with a minimum pain anxiety and complications and to provide comfort and guidance to the child's family. The World Health Organization (WHO) estimates that 10 million

children die annually worldwide and that 99% of these deaths occur in developing countries. Many of these children are at risk for multiple organ dysfunction syndrome (MODS), which is a major cause of death in the intensive care unit (ICU).<sup>7</sup> Under-five mortality according to data provided by UNICEF is 39.4 deaths/1000 live births in 2018. Diarrheal diseases, pneumonia, and other infectious diseases are leading causes of death among the children below 5 years of age in developing countries. In the United States, 55 000 infants and children die annually, mostly in neonatal or pediatric intensive care units (NICUs and PICUs). Previous literature has documented the overall mortality rate in pediatric intensive care units (PICUs) at U. S. teaching hospitals at around 5 percent, well below that in adult critical care.<sup>8</sup> Published data reveal that more than half of all pediatric hospital deaths involve care in the PICU (BURN) Previous reports from European countries show cardiovascular and neuromuscular diseases as the most frequent causes of death in critically ill paediatric patients in PICUs or intensive care.<sup>9</sup> However, little is known about profile of mortality among children admitted at intensive care in Indonesia especially at Sanglah Hospital as teaching hospital. This study will add to the knowledge mortality profile of the children admitted at PICU Sanglah Hospital, also can help in better decision-making, improving quality of care, and modifying future management.

## 2. Methods

This research was a retrospective study that reported mortality pattern among critically ill children admitted to the PICU over a period of 1 year. Data were drawn from medical record of pediatric patients who were treated in the PICU room at Sanglah Hospital Denpasar which was recorded during January 2018–December 2018. The inclusion criteria were all pediatric patients who were treated and died at PICU whereas patients with incomplete medical records according to the study questionnaire were excluded. The sample size is obtained by calculating the sample size using the formula for a single proportion sample with 10% precision, a minimum sample size of 95 samples is obtained. The data of this study include baseline data during treatment at the PICU, organ involvement that causes patients to require PICU treatment and causes of death for children admitted to PICU. Baseline data includes age, sex, nutritional status, referral status, length of stay, surgery, parenteral nutrition, inotropic score, pelod score and level of procalcitonin. Causes of death include sepsis, acute respiratory distress syndrome (ARDS), heart failure and intracranial processes. Referral status of the patient explains where the patient comes from, whether referral from another hospital or patient came by self to hospital. The calculation of Vasoactive Inotropes Score (VIS) was done for first 48 hours in PICU. The maximum VIS was calculated from hourly recorded inotropes on PICU sheets. Divided into two group based on the cut-off value of 20. The length of stay in the PICU defined as the length of stay at the PICU for initial treatment until the patient died. Length of stay is written in days. Procalcitonin levels described the procalcitonin levels that are checked in patients with infection categories.

All appropriate data is then collected and processed using a computer program. Categorical variables are described in

terms of number (n) and percentage (%). Processed data is presented in the form of tables, diagrams and narration. This research has received permission from the ethical committee of the Faculty of Medicine, Udayana University with the ethical clearance number 2019.02.1.1416.

## 3. Results

A total of 100 children who died in the PICU room at Sanglah Hospital were analyzed in this study. The median age of treated subjects was 1 year with the youngest 1 month and the oldest 14 years with the largest age group was the 1 month-11 months age group (40%).

**Table 1:** Characteristics of subjects

Variable	N = 100 subjects
Age	Median 11 months (range 1 months -14 years)
1-11 months, n (%)	40 (40)
1-4 years, n (%)	27 (27)
5-9 years, n (%)	22 (22)
10-18 years, n (%)	11 (11)
Male, n, %	55 (55)
Nutritional status	
Well Nourished	33 (33)
Mild Malnutrition	54 (54)
Severe Malnutrition	13 (13)
Referral patients, n, %	65 (65)
Length of stay, n (%)	
< 3 Days	33 (33)
≥ 3 Days	67 (67)
Surgery	18 (18)
Ventilator, n, %	85 (85)
≤28 days	78 (78)
>28 days	7 (7)
Central venous catheter, n, %	47 (47)
Parenteral nutrition, n, %	21 (21)
Inotropic score, n, %	
< 20	48(48)
≥ 20	52(52)
Pelod score, n, %	
< 7	47(47)
7-10	42(42)
≥ 11	11(11)
Level of procalcitonin, mean, ng/mL	44,19

Based on gender, the most people treated were male (55%) with 54% subjects had mild malnutrition condition. As many as 65% of the subjects were referral patients from hospitals or other health service facilities.

The mean length of stay of these subjects from admission to death in PICU was 7.98 days. Of 100 death, mortality pattern mostly occurred after 3 days of admission (67%). Use of mechanical ventilation proportion was 85%, central venous access was 47%, and received parenteral nutrition was 21%. Score inotropic ≥ 20 (52%) and Pelod score <7 (47%) were the highest in each group respectively. The mean procalcitonin level was 44.19 ng /mL. The baseline characteristics were shown in Table 1.

A higher proportion mortality in subject who stayed more than three days in the PICU regarding of age, surgical case and pelod score were shown in Table 2.

Most of the children died with a sepsis or sepsis-related diagnosis (61%) followed by ARDS (18%), intracranial process (11%) and heart failure (10%) (Table 3).

Among the sepsis subject, pelod score 7-10 and inotropic score  $\geq 20$  was the highest proportion (Table 4).

**Table 2:** Length of stay based on age category, surgical case and pelod score group

Variable	Length of stay Total= 100 subjects	
	< 3 days N=33, n(%)	$\geq 3$ days N=67, n(%)
Age,n(%)		
1-11 months	11 (33.3)	29 (43.3)
1-4 years	11 (33.3)	16 (23.8)
5-9 years	9 (27.3)	13 (19.4)
10-14 years	2(6)	9 (13.4)
Surgical case	6 (18.2)	18 (26.8)
Pelod score		
< 7	19 (57.6)	28 (41.8)
7-10	8 (24.2)	34 (50.7)
$\geq 11$	6 (18.2)	5 (7.5)

**Table 3:** Cause of death in PICU

Cause of death	N = 100 (%)
Sepsis	61
ARDS	18
Heart failure	10
Intracranial process	11

**Table 4:** Proportion of Pelod score and Inotropic score among sepsis subjects

Variable	N=61 n (%)
<b>Pelodscore, n (%)</b>	
< 7	9 (14.7)
7-10	41 (67.2)
$\geq 11$	11 (18)
<b>Inotropic score, n (%)</b>	
<20	21 (34.4)
$\geq 20$	40 (65.5)

#### 4. Discussion

The intensive care unit is very important in the management of critical patients. The Pediatric Intensive Care Unit (PICU) is part of a hospital where pediatric patients are critically ill who need respiratory assistance and hemodynamic support with the aim of achieving better outcomes. With the critical condition of the children, the characteristics of death as an outcome for patients who are treated at the PICU are very important to be studied further in an effort to achieve optimal outcomes for patients.

This study describes the characteristics of subjects who died in the PICU of Sanglah Hospital during the period 2018. Of the 100 subjects who were included as research subjects, it was found that most of the subjects were male with a median age of 11 months, and the largest age group was 1-11 months. The results of this study were similar to those reported by Siddique, where the greatest number of child deaths ranged from 0.8 to 3.1 years and the most were in the age group under 1 year. This can be explained by the numerous factors that affect the stages of child development. For children less than 1 year of age, will potentially expose

the child to malnutrition and infectious diseases due to lack of breastfeeding and maternal care. In the present study, we observed that most of the deaths (40%) were below 1 year of age which is comparable to other studies by Shashikala *et al.* and Ramnarayan *et al* that found mortality rate at younger age is higher than at older age.<sup>10</sup>

In this study, the proportion of male sex was higher than women with a ratio of 1.2:1. Similar results were reported by Siddique where the male: female mortality ratio was 1.3:1.<sup>10</sup> This difference in mortality ratio may be due to hormonal influence on infection response, presence of comorbid, or source of infection. Differences in cardiovascular responses, possibly related to endothelial cell sex hormone receptors, may lead to the lower rate of hemodynamic instability and high severity of illness on presentation males. X-linked genetic differences between the genders may be a factor, although it unlikely plays a large role. Children with comorbidities, particularly oncologic diseases, are at increased risk for mortality including from sepsis. The relationships among gender, comorbidity type, and mortality merit further investigation.<sup>11</sup>

This study also showed that 65% of patients who needed PICU care and died in the PICU were referred from outside the hospital. Distance to referral hospital and type of health service were not studied in this study. In some studies, reference of patients from faraway cities and transfer of patients from other hospitals are considered as risk factors for increased mortality.<sup>12</sup> In comparison with direct admissions, transfer admissions were younger on average, and inter-PICU transfer admissions had significantly longer average length of PICU and hospital stay within each stratum of disease severity. Furthermore, both PICU and hospital mortality were higher for inter-PICU transfers, relative to patients directly admitted, in all but the greatest stratum of mortality risk inter-PICU transfer admissions had the greatest unadjusted mortality and longest hospital stay.<sup>13</sup>

The mean length of stay in this study was 7.98 days with the greatest proportion in the group length of stay of more than 3 days. This length of stay is still longer than previous studies from Abhulimhen-lyoha *et al.* 2013<sup>14</sup> and Rashma *et al.* 2018<sup>15</sup> with mean length of stay to death is 3-4.5 days. Plunkett *et al.* 2016 is said its to be related to the ability to control predictor factors and the risk of death in patients who are admitted and treated at PICU.<sup>16</sup> Burn *et al.* in 2014 conducted a study on the epidemiology of mortality in PICU at 5 teaching hospitals in the United States. In the report says death in the PICU follows two differing profiles based on length of hospitalization. Those dying within the first 3 days tend to have new onset illnesses or injuries and are more likely to die following unsuccessful cardiopulmonary resuscitation or the diagnosis of brain death. Those dying later in the PICU stay are more likely to have pre-existing diagnoses, to be technology dependent prior to admission, and more likely to die following the withdrawal of life-sustaining treatment. These findings have implications for future quality improvement initiatives, especially around palliative care, end-of-life decision making, and organ donation.<sup>17</sup>

The use of mechanical ventilation (MV) and central venous access are frequent and important life supporting device in the care of pediatric patients in the PICU. MV is invasive technology of intensive care unit, to mimic the respiratory physiological function at the time of either impending or acute respiratory failure. Intubated patients on arrival at the ICU is a significant risk factor for mortality and therefore, it is necessary to pay attention to the transfer of these patients to prevent further hypoxemia and other complications of uncontrolled ventilation, such as pneumothorax formation.<sup>18</sup>

The use of venous access is significantly helpful, especially in terms of administering hemodynamic support drugs, monitoring hemodynamics and providing parenteral nutrition. However, despite the advantages given, the use of MV and central venous access is one of the factors that need to be controlled in the mortality rate in the PICU. This study found that, of the 100 subjects who died in the PICU, 85% were on a ventilator and 47% had central venous access during their admit in the PICU. Mukhtar et al.<sup>15</sup> 2014 found that 30.3% of the deaths in the PICU were children who were on a ventilator for more than 24 hours, with 35.8% due to decreased consciousness.<sup>18</sup> The study by Stocco et al. 16 2010 reported the results that the use of central venous access in the intensive care unit of infants and children found that increased mortality was associated with infectious complications arising from the use of central venous access used for drug administration, postoperative cardiac and parenteral nutrition.<sup>19</sup>

Based on parenteral nutrition, our study found that 21% of 100 subjects died using parenteral nutrition during PICU treatment. Khajavi et al. 17 2017 and Mehta et al. 18 2012 report their study which found that the use of parenteral nutrition was associated with increased mortality with dysglycemia due to parenteral nutrition as the strongest predictor of mortality.<sup>20</sup>

Vasoactive and inotropic drugs are hemodynamic support drugs that are often used in the care of critical pediatric patients in PICU. These drugs are standardly used to treat hypotension and cardiovascular dysfunction in patients with sepsis or in patients after undergoing cardiac surgery. The vasoactive-inotropic score (VIS) is an assessment used by adding up the dosage of drugs such as dobutamine, dopamine, epinephrine, milrinone, vasopressin, and norepinephrine are translated in a scoring system. The use of these drugs with a high score is said to be associated with an increase in mortality. Our study found that there are three types of drugs used in the treatment of pediatric patients in PICU, namely dobutamine, epinephrine and milrinone. Epinephrine is the type of drug that is most often used (56%) with the greatest proportion VIS score  $\geq 20$ . This score should be assessed within 6, 12, 24, and 48 hours after entering the PICU. On the other hand, the study of Gaies dk.<sup>22</sup> 2014 report that the relationship between total inotropic score and mortality rate in PICU patients. It is said that VIS  $> 20$  is significantly associated with poor outcome thus increasing morbidity and even mortality.<sup>21</sup>

Procalcitonin is a predictive marker of infection used in diagnosing and evaluating infectious conditions in patients and includes predicting mortality.<sup>22</sup> In our study it was found that the mean procalcitonin level was 44.19 ng/mL. This is

consistent with the findings of Aygun 2018 in his research which describes the relationship that the higher the procalcitonin value the higher the risk of death. It is said that procalcitonin levels  $> 20$  ng / mL are associated with the need for inotropic drug administration and accelerated death.<sup>23</sup> However, it is different from the findings of Ismy et al. 2015 which actually found that procalcitonin levels were not associated with mortality predictions.<sup>24</sup>

In our study, younger age was the greatest proportion prolong PICU stay. Study from Miura et al reported that age was identified as an influential factor regarding prolong PICU stay, consistent with some studies such as Pollack et al. 2018<sup>25</sup> and Marcin et al. 2001 studies.<sup>26</sup> Patients requiring medical or surgical treatments during the early stage of life may be more likely to suffer from severe diseases and comorbidities. In addition, young children often require prolonged recovery time.<sup>27</sup>

Nearly all patients treated in PICU in this study had medical emergency; only 33% subject were surgical patients. Leteurtre et al, reported that as many as 49% of patients were surgical patients. Study from Arafah YF et al reported that surgical procedures significantly increased the risk of prolonged PICU stay. Children admitted to PICU with sepsis in our study tended to have shorter length of stay. This might be because among those who had sepsis might develop septic shock and the mortality was high. The different results of this study might be caused by the different population of patients in various PICU and the utilization frequency of facilities.<sup>28</sup>

Study PELOD scoring system was not used to estimate the length of stay in PICU. Among patients with high PELOD scores ( $>20$ ), the numbers of survivors left were lessened by the extended length of stay in PICU. Yet, it was not significantly different ( $P=0.15$ ), between survivors at high and low PELOD scores, related to the length of stay in PICU. It was because patients with high PELOD scores died after a short time period of treatment in PICU or survived but were treated for quite long in PICU.<sup>29</sup>

In terms of the etiology of death, this study shows that the most common cause is sepsis (61%). Sageeth in his research reported that the greatest cause of death in PICU patients is infection.<sup>30</sup> Kapil and Bagga reported that septicemia was the most common cause of death followed by congenital heart disease.<sup>31</sup> Shah et al reported that pneumonia was the leading cause of death. In children under 5 years, infection is 58.9% cause of death.<sup>32</sup> Morris et al. reported 60% of deaths were due to infection.<sup>33</sup> Shukla et al. reported that infectious diseases are still one of the most common causes of inclusion in PICU and cause of death. A study by Epstein D in the United States reported that infectious diseases or oncological diseases have a higher risk of death. Similar results were reported by Rashma et al. 12 2018 where the category of infection as a predilection for increased mortality in PICU.<sup>15</sup>

Patients experiencing septic shock have risk of organ system dysfunction. Astu et al reported in the study that high PELOD score is associated with higher risk of death in children with sepsis. Patients who had PELOD score 20

have higher risk of death compared to those with PELOD score <20. In this study among sepsis subject, Pelod score 7-10 was the greatest proportion.

In this study also found  $VIS \geq 20$  was the greatest proportion among sepsis subject. Inotrope and vasoactive agents are routinely employed in children with septic shock to maintain cardiovascular support for oxygen delivery and tissue perfusion. The Vasoactive-Inotropic Score (VIS) is an objective clinical tool that is used to quantify the need of cardiovascular support in children with septic shock, and used as a predictor of morbidity and mortality. Study from Haque et al results demonstrate that there is a strong correlation between high VIS and mortality in children with fluid-refractory septic shock.<sup>34</sup> Jat, *et al.* also reported similar mortality rate (50%) in their cohort of children with septic shock.<sup>35</sup>

There were several limitations in this study. First, it is a retrospective study which may have some recall and interpretation bias that could lead to incomplete data. Second, this study might represent the reality in just one tertiary care center and, therefore, other studies are necessary to assess mortality pattern in the PICUs all over the country.

## 5. Conclusion

Sepsis have a higher predisposition on higher mortality rate in PICU. So the source of infection either hospital acquired or community acquired should be identified and managed aggressively

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