Evaluation of Patients Followed in he Third Level Pediatric Intensive Care Unit: Single Center Experience

Ali Ateş[1*], Nur Aycan[1], Kabil Shermatov[2]

[1]Department of Pediatrics, Yuzuncu Yil University, Van, Turkiye
[2]Department of Pediatrics, Harran University, Sanlıurfa, Turkiye

ABSTRACT

Pediatric intensive care practices have undergone great changes in the last 30 years. Our knowledge about the pathophysiology of life-threatening processes and the follow-up and treatment of pediatric patients with life-threatening diseases continues to expand in this process. In this study, the outcomes, treatment modalities, treatment responses and clinical characteristics of patients hospitalized in the pediatric intensive care unit (PICU) were evaluated.

497 patients who were hospitalized and followed up in Harran University Faculty of Medicine, PICU between January 2016 and December 2016 were evaluated.

There were 276 (55.5%) male and 221 (44.5%) female patients in our study. The median age and median PICU stay of the patients were 23 months (1-212 months) and 7 days (1-134 days), respectively. The reasons for admission to the intensive care unit were respiratory system diseases in 171 patients (34.4%), poisonings in 88 patients (17.7%), neurological diseases in 71 patients (14.3%), gastrointestinal system diseases in 59 (11.9%) patients, 42 (4%) patients were admitted to the intensive care unit. The need for mechanical ventilation developed in 35.6% of the patients. 49.3% (n=245) of the patients had comorbid disease. Of the patients, 74.7% (n=371) were discharged from the PICU, 6.4% (n=32) were referred to another center, and 18.9% (n=94) died.

Some factors affecting clinical outcomes and mortality were identified. As a result of the regression analyses of these factors, mechanical ventilation requirement (OR=192.8), multi-organ failure (OR=21.2), disseminated intravascular coagulation (OR=9.6), thrombocytopenia (OR=2.4) and positive inotropic drug requirement (OR= 2.3) were associated with mortality.

The clinical results of the patients in the PICU were similar to the results of other PICUs in our country. Our findings showed that there are some factors affecting clinical outcomes. Mechanical ventilation requirement, multiple organ failure, disseminated intravascular coagulation, thrombocytopenia, and need for positive inotropic drugs were found to be effective on mortality.

Keywords: Pediatric intensive care, mortality, life-threatening diseases

Introduction

Pediatric intensive care units are clinics that provide uninterrupted service, care, and treatment of infants, infants, and adolescents whose vital signs are under threat due to one or more organ failures that require a multidisciplinary approach or due to the operations they have undergone, where their vital signs are monitored and supported. The services in these special units, which require more personnel and equipment than other clinics, include supporting vital functions and treating the underlying disease (1,2). The primary aim is to protect and regulate vital functions before the main causes of the disease, and the treatment principles of intensive care, which is carried out together with the treatment of the underlying disease, are basically the same (3).

The first PICU in the world was established at Gothenburg Children's Hospital in Sweden in 1955. Afterwards, PICUs were established in Europe, Australia, and North America, respectively, in the 1960s (4). In our country, especially Hacettepe Children's Hospital, in some of our hospitals in the 1980s-1990s, the practice of bringing children in need of intensive care together in clinics and being treated was started, but there was no permanent physician or team who received special training in these areas. The first PICU was established within the scope of Istanbul University Istanbul Faculty of Medicine in 1994 within the Pediatric Emergency Service, with a responsible physician trained in this field as the team leader. This unit is accepted as the first PICU in our

country (5).

In developed countries, the number of children in need of intensive care has been reported as 1.2-2.3/1000. In our country, child mortality rates have not yet been brought to the desired level, and interest in the field of pediatric intensive care has increased in recent years (5). For this reason, it is necessary to expand the accessibility of intensive care services for children and to increase their quality (6). According to the data of the General Directorate of Health Services for 2020, the number of beds in the PICU was reported to be 1956 in total (1138, 651, 167, respectively) in state, university, and private hospitals (7).

In this study, we retrospectively analyzed the patients who were hospitalized and treated in the PICU of the Harran Medical Faculty Research and Application Hospital. Our aim is to evaluate the patient's length of stay in the intensive care unit, the need for mechanical ventilation (MV), developing complications, mortality, and risk factors affecting mortality by examining the one-year data of the PICU.

Material and Method

Harran University Faculty of Medicine PICU started to serve with 14 beds (12+2 isolation rooms) and 14 mechanical ventilators under the guidance of current and evidence-based treatment guidelines. Admission of patients to the unit is guided by the recommendations of the American Pediatric Intensive Care Association (8).

In our study, 582 patients followed in the PICU of Harran University Faculty of Medicine between January 2016 and December 2016 were evaluated retrospectively. Patients aged 1-18 years, with complete data and followed in the intensive care unit for more than 24 hours, were included in the study. Patients who were not in the relevant age range, had missing records in their data, and were hospitalized in the PICU for less than 24 hours were excluded from the study. Of these patients, 45 patients with missing data records in the hospital archives and 40 patients who did not meet the inclusion criteria were excluded from the study. The remaining 497 patients were included in the study. Informed consent for participation in the study was obtained from the parents of the patients included in the study. The study was approved by the Harran University Faculty of Medicine Scientific Research Ethics Committee with the decision dated 09.03.2017 and numbered 17.03.43.

The socio-demographic characteristics of the patients admitted to the PICU, from which services or external centers they were referred, and the indications for admission to the PICU were analyzed. The relationship between the reasons for admission to the intensive care unit and the age of the patients, the comorbid chronic diseases of the admitted patients, the total length of stay in the PICU, and the parameters that affect the length of stay were evaluated. Raw mortality rate, which is one of the main criteria of intensive care units, and socio-demographic characteristics of patients above this rate, comorbid diseases, treatments given and procedures performed, and complications were analyzed. In addition, the relationship between laboratory data and mortality was examined. The last hospitalization information of the patients who had a history of staying in the PICU was taken into account.

Statistical Analysis: Statistical analyses were performed using the SPSS (ver. 20.0) package program. Descriptive statistics are summarized as a number, percentage, median, minimum-maximum value, mean, and standard deviation. While numerical variables that did not show normal distribution were compared using the Mann-Whitney U test or Kruskal Wallis Test. The chi-square test was used to determine the relationship between categorical variables. Continuous or categorical variables that were effective on mortality were evaluated in the Binary Logistic Regression Model. After finding the best model fit, the effect of the variables on mortality was evaluated. In the statistical analyses of the study, comparisons with a p-value below 0.05 were considered statistically significant.

Results

In our study, 582 patients followed in the PICU of Harran University Faculty of Medicine between January 2016 and December 2016 were evaluated retrospectively. According to the inclusion and exclusion criteria, 276 (55.5%) of the 497 patients who participated in the study and whose files were examined were male and 221 (44.5%) were female. While 85.5% of the patients were citizens of the Republic of Turkiye, 14.5% were citizens of the Syrian Arab Republic.

The mean age of the children was 53.7±62.4 (min-max:1-212; median:23) months. Of the patients admitted to the PICU, 41.9% were admitted from the emergency department, 34.6% by referral from external centers, and 23.5% from other inpatient services.

Reasons for admission of patients to the intensive care unit: 171(34.4%) respiratory system diseases, 88(17.7%) poisonings, 71(14.3%) neurological

Table 1. Length of Stay In The Intensive Care Unit By Age Groups of The Patients

age	mean ± stdev	median	min-max	p-value
1-12 month	10.1 ± 16.9a	5.0	1-134	
13-48 month	6.2 ± 11.2b	3.0	1-123	0.030*
49-96 ay month	10.1 ± 13.6ab	4.0	1-64	
>96 ay month	5.1 ± 6.2b	2.0	1-31	

*Kruskal Wallis test was preferred. Mann Whitney U test was used for pairwise comparisons. There is no statistical significance between the ones with the same letter, there is statistical significance between different letters

Table 2. Factors Affecting Mortality

Factors		exitus N(%)	alive N(%)	p-value
chronic disease	+	75 (30.6)	170(69.4)	<0.001*
	-	19 (7.5)	233 (92.5)	
MV	+	93 (52.5)	84 (47.5)	<0.001*
	-	1 (0.3)	319 (99.7)	
MV complication	+	34 (73.9)	12 (26.1)	<0.001*
	-	60(13.3)	391 (86.7)	
central venous catheter	+	43 (48.3)	46 (51.7)	<0.001*
	-	51 (12.5)	357 (87.5)	
multiple organ failure	+	20 (95.2)	1 (4.8)	<0.001*
	-	74 (15.5)	402 (84.5)	
DIC	+	38 (88.4)	5 (11.6)	<0.001*
	-	56 (12.3)	398 (87.7)	
blood culture positivity	+	24 (42.9)	32 (57.1)	<0.001*
	-	7 (15.9)	371 (84.1)	
urine culture positivity	+	3 (25.0)	9 (75.0)	0.586
	-	91 (18.8)	394 (81.2)	
CSF culture positivity	+	6 (40.0)	9 (60.0)	0.034*
	-	88 (18.3)	394 (81.7)	
sex	male	55 (19.9)	221 (80.1)	0.519
	female	39 (17.6)	182 (82.4)	
ethnic	Turkish	79 (18.6)	346 (81.4)	0.870
	Syrian	15 (20.8)	57 (79.2)	

*Chi square

diseases, 59(11.9%) gastrointestinal system diseases, 42(8.5%) infections, 38(7.6%) accidents, 9(1.8%) cardiac diseases, 8(1.6%) metabolic and endocrinological diseases, and 6(1.2%) hematological and oncological diseases.

According to the age of the patients, the most common reasons for admission to the intensive care unit were respiratory system diseases between 1-12 months, 13-48 months, and 49-96 months (50.8%, 26.2%, 31.0%, respectively), and poisoning (41.9%) after 96 months. While 94 (18.9%) of 497 patients admitted to the intensive care unit died.

The mean duration of hospitalization was 7.8±13.1 days (median: 23, min-max: 1-134 days). In terms of the length of stay in the intensive care unit, it was observed that the patients between 1-12 months stayed in the PICU longer than the patients between 13-48 months ($p<0.05$) and patients older than 96 months ($p<0.05$) (Table1).

While 177 (35.6%) of the patients needed MV, the mean need for MV of the patients was 2.0±6.3 days (min-max:0-103 days). Complications developed in 46(25.9%) of 177 patients followed up with MV. These complications were 19(10.7%) atelectasis, 17(9.6%) ventilator associated pneumonia (VAP)+atelectasis, 7(3.9%) VAP, 3(1.6%) pneumothorax.

Mortality rates were higher in patients with chronic disease, central venous catheter, MV need and complications under MV support, multiple organ

Table 3. Other Factors Affecting Mortality

		exitus		alive		p value
		N	%	N	%	
erythrocyte transfusion	+	35	59.3	24	40.7	<0.001
	-	59	13.5	379	86.5	
platelet transfusion	+	8	80.0	2	20	<0.001
	-	86	17.7	401	82.3	
FFP transfusion	+	40	83.3	8	16.7	<0.001
	-	54	12.0	395	88.0	
positive inotropic therapy	+	84	47.2	94	52.8	<0.001
	-	10	3.1	309	96.9	
Total parenteral nutrition	+	26	37.1	44	62.9	<0.001
	-	68	15.9	359	84.1	
anemia	+	35	52.2	32	47.8	<0.001
	-	59	13.7	371	86.3	
thrombocytopenia	+	50	54.9	41	45.1	<0.001
	-	44	10.8	362	89.2	
CRP value	+	86	29.5	206	70.5	<0.001
	-	8	3.9	197	96.1	
blood glucose level	normoglycemia	53	14.0	325	86.0	
	hypoglycemia	26	55.3	21	44.7	<0.001
	hyperglycemia	15	20.8	57	79.2	

*Chi-square

failure, DIC, and blood and CSF culture positivity. ($p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$, $p<0.05$, respectively) (Table 2).

The mortality rates of the patients who received blood product transfusions and cardiological supportive treatment (Table 3). The mean age of exitus patients (32.4±45.9 months) was significantly lower than that of living patients (58.6±64.7 months) (p<0.001). The mean length of stay in the intensive care unit of patients who died (15.8±25.0) was significantly higher than that of patients who survived (5.9±7.1) (p<0.001).

A logistic regression model was created by determining the factors that may have an effect on mortality. It was seen that the best model was provided with positive inotrope requirement, MV requirement, DIC, multi-organ failure, and thrombocytopenia. The probability of determining mortality in this model was approximately 70% (Nagelkerke R square=0.702). According to the logistic regression model created, the need for MV increased the mortality risk 192 times, multi-organ failure 21 times, DIC 9 times, thrombocytopenia and positive inotrope need two times. The most prominent variable on mortality was MV (Table 4).

Discussion

Pediatric intensive care units are specialized units that provide uninterrupted service and serve patients aged 1 month to 18 years. The patients it serves consist of critically ill patients who require a multidisciplinary approach, often have accompanying complications, develop one or more organ system failures, and whose mortality can be expected.

The aim of PICU is to treat children whose health and survival are in danger with minimum pain, anxiety, and complications, to increase their quality of life, and to provide necessary guidance to their parents. With the establishment of PICU and the increase in their number and quality, a decrease in the preventable child mortality rate has been achieved (9). Patients in need of intensive care generally close follow-up, invasive catheterization and monitoring, commonly use sedation and analgesia, and frequently require MV (1). Multi-faceted care and the implementation of various equipment in patients who require emergency treatment or who are difficult to treat have given birth to the concept of intensive care and ensured the determination of intensive care goals, methods, and targets (4).

The mean age of the patients in our study was 53.7±62.4 months (median 23; min-max: 1-212

Table 4. Regression Model of Factors Affecting Mortality

	B	p	OR	%95 CI	
				min	max
MV	5.262	0.001	192.8	23.3	1591.6
multiple organ failure	3.056	0.027	21.2	0.9	5035.8
DIC	2.263	0.012	9.6	1.6	56.5
thrombocytopenia	0.912	0.033	2.4	1.0	5.7
positive inotrope	0.856	0.044	2.3	1.0	5.4

* Binary Logistic Regression Model

months). Similar age ranges have been reported in other studies conducted in different centers. The median was 30 months in the study of Kristensen et al. (11), and 22 months in the study of Namachivayam et al. (12).

The reasons for hospitalization of the patients in the intensive care unit were respiratory system diseases in 34.4%, poisoning in 17.7%, neurological diseases in 14.3%, accidents in 7.6%, and 1.8% cardiac diseases. In the study of Aşılıoğlu et al. (13), the diagnosis was poisoning in 22.5% of the patients, and in the study conducted by Bayrakçı et al., the diagnoses of the patients were respiratory system diseases in 29% (14). The reason for the differences observed between the studies may be that they were performed at different times, in different patient populations, in hospitals at different stages, and that these units use different criteria for patient admission. However, there is more consensus that the patients most frequently admitted to PICU are respiratory system diseases, neurological diseases, infections and trauma (15-18). Especially neurological diseases and complications have been defined as risk factors for readmission to the intensive care unit (19). It changes the diagnosis of patients admitted to PICU due to the development level of the countries. In a study conducted in the Netherlands (12), 41% of the patients were admitted due to cardiovascular diseases, 27% due to respiratory system diseases, 8% for neurological diseases. In our study, respiratory system diseases were the most common reason for admission.

In our study, 49.3% of the patients had one or more concomitant chronic diseases. The most common comorbid diseases were neurological (65.7%), gastrointestinal system (10.2%), and respiratory system (7.3%). Kristensen et al. (11) reported the rate of chronic disease in patients hospitalized in the intensive care unit as 44%, Kılıç et al. (19) as 46.9%, and Poyrazoğlu et al. (20) as 47.2%. Kılıç et al. (19) and Poyrazoğlu et al. (20) confirmed that neurological diseases are the most common comorbidity seen in PICU. There is ample evidence that existing comorbidities will adversely affect patient outcomes

and increase mortality (21-25). These results are in line with our findings and indicate that patients admitted to the PICU will have a high risk of complications and a high mortality rate.

In our study, in which the findings of 497 patients were evaluated, 65.4% of the patients were referred from the hospital (41.9% from the emergency department, 23.5% from other services) and 34.6% from the PICU of external centers. El Halal et al. (26) reported this rate was 34.7% (26) while it was 12.1% in the study of Ülgen et al. (10). The reason may be related with the development level of the countries and the different patients referral procedures.

The mean duration of treatment in the PICU was 7.8±13.1 days (min-max=1-134 days). This period was longer in patients aged 1-12 months (10.1±16.9 days) and in patients with chronic disease (11.4±17 days). Kılıç et al. (19) reported that the presence of chronic disease prolongs the length of stay in the intensive care unit up to approximately 6 days and is also effective on mortality. The median length of stay in the PICU was determined by Aslıoğlu et al. (13) median 3 days, and Asembergiene et al. (27) study reported 6.1 days. In a comprehensive study conducted by Bayrakçı et al. in 2014, the length of stay in the PICU was found to be 0-2 days in 23% of the patients, 3-7 days in 25%, 8-14 days in 15%, and 14 days or more in 37% (14). In our study, the length of stay in the intensive care unit was consistent with the length of stay reported from other PICU in our country.

MV is one of the frequently required therapeutic options in intensive care units; its usage rates vary according to accessibility and patient presentations. MV was applied for an average of 2.0±6.3 days. Complications related to MV developed in 46% of the patients. Özdemir et al. (28) reported this rate as 40.9% and 31.7% in the study of Asembergiene et al. (27). In the study of Kılıç et al., atelectasis (33%), pneumothorax (23%) and VAP (23%) were reported as the most common MV complications with a rate of 29.5% (19). Similarly, in our study, the most common atelectasis (10.7%), VAP (9.6%) and pneumothorax

(1.6%) were seen, respectively.

The raw mortality of the patients examined in our study was measured as 18.9%. It was 22.6% in the study of Özdemir et al. (28), 17.2% in the study of Aşılıoğlu et al. (13), and 6.7% in the study of Khilnani et al. (18). In studies reporting lower mortality rates, the underlying reasons for this situation are: the low number of patients with multi-organ failure and the relatively high rate of patients presenting with the diagnosis of poisoning. On the other hand, the differences in the developed levels of the countries affect the effectiveness of PICU and therefore mortality rates. Mortality rates were reported between 2.9% and 5.6% in two studies conducted in the United States (29,30). In another study conducted in Lithuania (27), the mortality rate was reported as 3.4%. In a study conducted by Namachivayam et al. (12) in the Netherlands, covering 30 years, the effect of development level on mortality was comprehensively demonstrated. In this study, mortality was 15.2% in the 80s, 7.8% in the 90s, and 5.1% in the 2005-2006 years. In a study conducted in Africa, PICU were evaluated over a 25-year period (31) and the mortality rate was reported as 35.4%.

In order to reduce mortality rates, scales that can be used to determine survival have been developed. PRISM (Pediatric Risk of Mortality) (32), APACHE II (Acute Physiology and Chronic Health Evaluation II) (33) and SAPSII (Simplified Acute Physiology Score II) (34), PELOD (Paediatric Logistic Organ Dysfunction) (35), PIM II (Pediatric Index of Mortality II) (36) are scales developed for this purpose. In this way, it is possible to take precautions and be ready for possible problems by identifying high-risk patients and high-risk factors. In our study, the presence of additional disease, MV need, insertion of central venous catheter, multi-organ failure status, DIC, positivity of blood culture, high CRP, need for positive inotropic support, anemia, thrombocytopenia, were among the clinical and laboratory variables associated with mortality in our study. Konca et al. associated the need for MV, multiple organ failure, and the presence of comorbid disease with mortality (15). In addition, they reported that the mortality rate was higher in patients with hematologic-oncologic disease.

It can be predicted that mortality will be higher in patients who frequently need vasoactive agents and positive inotropic support to keep the systemic blood pressure above a certain level in the PICU. Kılıç et al. (19), Abraham et al. (37), and Krishnan et al. (38) stated that starting positive inotropic therapy increases mortality significantly (up to 4 times). In our unit, 47.2% of the patients who were given positive inotropic drugs died, while only 3.1% of the patients

who could not be given died.

Blood and blood products have been used less and less in PICU. Dallman et al., in their study in 2013, stated that the need for blood products increases in respiratory failure, metabolic acidosis and multi-organ failure (39). In our patients, mortality rates were found to be higher in those who received erythrocyte, thrombocyte or FFP transfusion compared to those who did not. Similarly, Duke et al. reported that mortality was higher in intensive care patients who received blood transfusions (40). For this reason, the profit-loss ratio should be considered in the use of blood and blood products.

When the factors that increase mortality are investigated, MV 192 times, multi-organ failure 21 times, DIC development 9.6 times, thrombocytopenia and the need for positive inotropic support increased mortality approximately 2.5 times. In the study of Kılıç et al. (19), it was reported that the need for MV increased 12 times, the need for transfusion 6 times, the need for vasoactive drugs 4 times, and the presence of chronic disease 2.7 times. Mortality rates can be reduced by improving MV application methods, preventing and/or intensive treatment of MV-related complications, and providing adequate tissue perfusion and oxygenation as soon as possible.

Our research had some limitations. Our retrospective study includes all the limitations of such studies. Since it is a retrospective and descriptive study, the cause/effect relationship cannot be fully reached. On the other hand, generally accepted, evidence-based scoring systems such as PRISM, PIM or PELOD, which have recently become widespread, were not evaluated in our study. Our findings can be confirmed with additional prospective, multicenter studies, and data such as mortality rate as well as morbidity rates can be investigated with more precise accuracy.

Pediatric intensive care units, which are very limited in number in our country, have great importance in preventing child deaths. For this reason, although the information obtained in our study is limited, we believe that it has increased our knowledge about the work and problems of intensive care units. In the light of these data, we can say that increasing the number of pediatric intensivists and trained technical personnel for more efficient operation of PICU can provide better service to patients with increasing knowledge and experience about pediatric intensive care. When we analyzed the one-year data of Harran University PICU, we saw that the conditions affecting mortality and morbidity were

compatible with the literature, and we think that it can guide multicenter or more detailed studies.

PICU: Pediatric intensive care unit

MV: Mechanical ventilation

VAP: Ventilator-associated pneumonia

FFP: Fresh frozen plasma

DIC: Disseminated Intravascular Coagulation

PRISM: Pediatric Risk of Mortality Score

CRP: C reactive protein

CSF: Cerebrospinal Fluid

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