Incidence and predictors of mortality among children admitted to the pediatric intensive care unit at the University of Gondar comprehensive specialized hospital, northwest Ethiopia: A prospective observational cohort study

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Abstract

Background
Pediatric intensive care unit (PICU) tremendously improves the success of saving patients having potentially life-threatening illness. An accurate estimate of lives saved through pediatric critical care intervention is important to evaluate the quality of the health care system. Data on pediatric critical care in developing countries remain scarce yet is much needed to improve clinical practices and outcomes. This study aimed to determine the incidence and predictors of mortality in the pediatric intensive care unit in the study setting.

Method
An institution based prospective cohort study was conducted from February 2018 to July 2019. We collected data by interview, chart and registration book review. Life table was used to estimate the cumulative survival of patients and Log rank test was used to compare survival curves between different categories of the explanatory variables. Survival trend over the follow up time was described using the Kaplan Meier graph. Bivariate and multivariate Cox proportional hazard model were used to identify predictors.

Result
Based on the 10th version of international classifications of disease (ICD) of WHO, neurologic disorders (22.7%) infectious disease (18.8%) and environmental hazards (11.8%) account for the top three diagnoses. The median observation time was 3 days with IQR of 1 to 6 days. Of the total of 313 participants, 102 (32.6%) died during the follow-up time. This gives the incidence of mortality of 6.9 deaths per 100 person day observation. Caregivers’ occupation of government-employed (AHR=0.35, 95%CI: 0.14, 0.89), weekend admission (AHR=1.63, 95%CI: 1.02, 2.62), critical illness (AHR=1.79, 95%CI: 1.13, 2.85) Mechanical ventilation AHR=2.36, 95%CI: 1.39, 4.01)and PIM2 score (AHR=1.53, 95%CI: 1.36, 1.72) were predictors of mortality in the pediatric ICU.

Conclusion
Neurologic disorder was the leading causes of admission followed by infectious diseases, and environmental hazards. Rate of mortality was high and admission over weekends, caregivers’
occupation, mechanical ventilation, critical illness diagnosis, and higher PIM2 scores were found to be significant and independent predictors of mortality at the PICU. This suggests that ICU medical equipment, diagnostics, and interventions should be available up to the standard. Intensivist and full staffing around the clock has to be available in the PICU.

**Background**

Patients treated by pediatric health professionals exhibit a broad spectrum and frequency of medical and surgical complaints ranging from mild illnesses that can be reassured to those requiring pharmacologic and device-related vital function support in the pediatric intensive care units (PICU). The range, severity, and response for the treatment of illness is dependent on the age of the patient, biologic, socio-demographic variations, time and place. As per the report of WHO, in low-income countries like Bangladesh, Dominican Republic, Ethiopia, and Indonesia, 90% of children had severe forms of common infectious diseases, especially pneumonia, diarrhea, sepsis, malaria, and meningitis, often complicated with chronic malnutrition [1].

The PICU is a distinct organizational and geographic entity designed for monitoring and support of failing vital functions. It ideally has to be established in an area where an integral medical, surgical, anesthesiologic and radiologic intervention is possible. It is a well-staffed and technologically well-equipped than other wards in the hospital. The professional to patient ratio in the ICU is higher considering the severity of illness. There are three levels of care in the PICU ranging from the most intensive Level III where patients have two or more organ failures and require pharmacologic or device interventions that are required to the mildest level I [2, 3].

Patients having one or more failing vital function with a reasonable chance of meaningful recovery and postoperative patients requiring frequent monitoring are candidates for care in the ICU. Children having acute neurological deterioration, respiratory distress, cardiovascular compromise, severe infections, and accidental poisoning constitute the major admission in a pediatric intensive care unit [4].

Care in the PICU tremendously improves the success in saving patients having a potentially life-endangering illness but the proportion of survivors with disabilities increased significantly [5]. Its
outcome can be measured by standardized mortality ratio (SMR), length of hospital stay, unplanned readmission rate, pain assessment, medication safety practice, and central venous catheter infection prevention practice adoption. Mortality is the most studied outcome measure though data in developing countries is scarce [2]. The mortality rate in the PICU at GUCSH is significantly higher than that of developed countries as to the monthly Mortality-morbidity report. Published data on pediatric critical care in low-income countries remains sparse yet is much needed. This paucity of data makes practice modification and outcome improvement difficult (6).

Most studies done on determinant factors of mortality in the PICU are from western countries and are dependent on clinical and laboratory indices [5]. The few studies that considered epidemiologic and socio-demographic factors are retrospective cross-sectional studies and most did not consider the severity of illness as a factor as they don’t apply severity score in retrospective studies [6]. The ICU equipment and set up in developing countries is not well studied [2, 7]. Hence, this study aimed to determine the incidence and predictors of mortality among children admitted to a pediatric intensive care unit at the University of Gondar comprehensive specialized hospital. Findings from this study could help clinicians and case managers for proper management of the diseases.

Methods
Study design, period and setting

An institution-based observation prospective follow up study was conducted among children who aged 1 months to 18 years and admitted to pediatric intensive care unit of the University of Gondar comprehensive specialized hospital from February 1, 2018, to July 30, 2019.

The hospital is located in Gondar city, in Amhara Region, 741 km Northwest of Addis Ababa, It is a comprehensive specialized teaching and referral hospital, with a total of 641 beds and 96 beds in the pediatrics side, where a multidisciplinary team of diverse professionals provide a range of health care services for approximately 2806 inpatient and 11986 outpatient children beyond the neonatal age coming from the northwest part of the country including the neighboring administrative regions. The major causes of pediatric admission to the hospital are pneumonia, malaria, neonatal infections, tuberculosis, heart failure, meningitis and other various types of metabolic and organ system-based
emergencies according to hospital statistics. On average there are about 25 pediatric critical care admissions per month. The PICU was established in 2013 it has six beds with electronic monitors and one mechanical ventilators. The organizational detail of the PICU in this hospital is lacking. Team composition is often limited to a general pediatrician, resident, interns and a handful of senior-level nurses. Pediatric intensivists, respiratory therapists, pharmacists, and dieticians are not available.

Population and sample
The patients aged 1 month to 18 years admitted to pediatric intensive care unit and stayed more than two hours in the hospital were included in the study. Cases having incomplete data and surgical patients admitted only for recovery purposes was excluded from the study.

The sample size for this study was determined using a single population proportion of $P = 21\%$, from previous Bangladesh study [4] 5% margin of error the sample size becomes 254 and after adding 10% contingency, the sample size will be 279. A total of 395 patients were admitted to the PICU from February 1 2018 to July 30 2019. Data was collected from 327 patients who fulfilled the inclusion criteria, whereas fourteen patients were excluded from the study due to incomplete baseline data.

Data collection procedure
Data was collected by treating physicians using standardized questionnaire after taking consent from caretakers. Clinical characteristics like, SBP, pupillary light reflex, $\text{SaO}_2$ need of mechanical ventilator was assessed and documented within the first hour and entered into an electronic App to calculate pediatrics index mortality 2 (PIM2) score. The PIM2 was used in our research because it doesn't need extensive laboratory investigation and it is not affected by subsequent interventions since it is scored within one hour of admission. Sociodemographic data and medical history were taken by interview. Diagnosis, laboratory indices, and courses in the hospital were filled by chart review at discharge. We used the WHO International Classification of Diseases 10th version for disease category and only the primary diagnosis was used for ICD-10 assignment in patients having multiple diagnoses. The collected data were double-checked by the data collector and the principal investigator. There were orientations and training about data collection and the objective of the study every three months and demonstration every Monday for treating physicians and data collectors. The principal
investigators surevised the overall process and check completeness of questionaires everyday.

Variable of the study and operational definitions

The main dependent variable was time to death (event), whereas sociodemographic characteristics (age, sex, relation with the caregiver, care giver’s educational status, occupation Hospital arrival and admission related factors (duration of illness before admission, time- day and month of admission, source of admission, staff level at admission) clinical characteristics and management-related factors (diagnosis, admission vital signs, comorbidity, nutritional status, vaccination status, interventions given in the ICU and before admission, PIM2 score, MODS, Complications) were the independent variables.

Event (death): is defined as a patient who died in the hospital during the course of treatment

Censored: discharged alive from the ICU

LOS: refers to the duration of stay in a number of days from the date of admission to the date of discharge

Short term outcome: the outcome of the patient until s/he leaves the hospital

Data processing and analysis

After the data were checked for its consistency and completeness, it was entered into EpiData version 3.1 exported to STATA version 14 for cleaning and analysis. Descriptive statistics like mean, median, proportions were carried out to to summarize baseline characteristics and pattern of admission. In addition, summary statistics like life table, log-rank test and Kaplan-meir curves computed was used to detremimne the incidence rate (IR) of death and to compare survival curves between the different categories of the explanatory variables.

Both bivariate and multivariate Cox proportional hazard models were used to identify the predictors. Variables with p-value < 0.2 in the bivariate analysis were entered into the multivariate proportional hazard model. Ninety-five percent confidence interval (95% CI) of hazard ratio was computed and variable having p-value < 0.05 in the multivariate Cox proportional hazards model was considered as significantly and independently associated with the dependent variable. Cox proportional hazard model fitness was checked using the Schoenfeld residuals test.
Ethical approval and consent to participate

Ethical clearance was obtained from the Institutional Ethical Review Board of College of Medicine and Health Sciences, University of Gondar (ref.no 20/12/2018). Informed verbal consent was obtained from the caretakers. The name or any other identifying information was not recorded on the questionnaire and all information is taken from the chart was kept strictly for confidential and in a safe place. The information retrieved was used only for the study purpose.

Result

Socio-demographic characteristics

A total of 313 patients out of 376 patients admitted during the eighteen-month study period were included in the final analysis. The median age at admission was 48 months with interquartile range (IQR) of 12 to 122 months, about 28.1% were infants followed by adolescents (21.4%). More than half (59.7%) were males, more than three-fourth (77.3%) were from rural areas and parents were the commonest caregivers for the majority (93%) of children. The majority of caregivers had no formal education (77.6%) and 71.2% were farmers, most patients were admitted in the Tseday season (38.3%) followed by Bega (27.2%) (Table 1).
Table 1
Socio-demographic characteristics of children and caregivers who were admitted to the pediatric intensive care unit at the University of Gondar comprehensive specialized hospital, from February 1/2018 to July 30/2019, northwest Ethiopia (n = 313)

| Characteristics                        | Frequency | Percentages (%) |
|----------------------------------------|-----------|-----------------|
| Age in months                          |           |                 |
| ≤ 12                                   | 88        | 28.1            |
| 13–24                                  | 29        | 9.3             |
| 25–60                                  | 66        | 21.1            |
| 61–132                                 | 63        | 20.1            |
| > 132                                  | 67        | 21.4            |
| Sex                                    |           |                 |
| Male                                   | 187       | 59.7            |
| Female                                 | 126       | 40.3            |
| Residence                              |           |                 |
| Urban                                  | 71        | 22.7            |
| Rural                                  | 242       | 73.3            |
| Caregivers                             |           |                 |
| Parents                                | 291       | 93              |
| Grand parents                          | 8         | 2.6             |
| Siblings                               | 8         | 2.6             |
| Others                                 | 6         | 1.9             |
| Caregiver level of education           |           |                 |
| No formal education                    | 242       | 77.6            |
| Primary school                         | 32        | 10.2            |
| Secondary school                       | 17        | 5.4             |
| College and above                      | 21        | 6.7             |
| Caregivers occupation                  |           |                 |
| Farmers                                | 223       | 71.2            |
| Merchants and private                  | 32        | 10.2            |
| Government employee                    | 31        | 9.9             |
| Unemployed                             | 27        | 8.6             |
| Season of admission                    |           |                 |
| Summer                                 | 63        | 20.1            |
| Spring                                 | 45        | 14.4            |
| Winter                                 | 85        | 27.2            |
| Autumn                                 | 120       | 38.3            |
patterns and causes of admission among children and caregivers who were admitted to the pediatric intensive care unit at the University of Gondar comprehensive specialized hospital, from February 1/2018 to July 30/2019, northwest Ethiopia (n = 313)

| Characteristics                                           | Frequency | Percentages (%) |
|-----------------------------------------------------------|-----------|-----------------|
| Duration of illness before any health facility visit in days |           |                 |
| ≤3 days                                                   | 118       | 37.7            |
| >3 days                                                   | 195       | 62.3            |
| Duration of illness before PICU admission in days         |           |                 |
| ≤6 days                                                   | 71        | 22.7            |
| >6 days                                                   | 242       | 77.7            |
| Day of admission                                          |           |                 |
| Weekday                                                   | 241       | 77              |
| Weekend                                                   | 72        | 23              |
| Time of admission                                         |           |                 |
| Dayshift                                                  | 183       | 58.5            |
| Nightshift                                                | 130       | 41.5            |
| Sources of admission                                      |           |                 |
| Home                                                      | 36        | 11.5            |
| Other facilities                                          | 37        | 11.8            |
| Emergency room                                            | 189       | 60.4            |
| Wards and Operating rooms                                 | 51        | 16.3            |
| Vaccination status                                        |           |                 |
| Complete                                                  | 203       | 64.9            |
| Incomplete                                                | 110       | 35.1            |
| Comorbid illness                                          |           |                 |
| Yes                                                       | 43        | 13.7            |
| No                                                        | 270       | 86.3            |
| Comorbidities (n = 43)                                    |           |                 |
| Congenital malformations and genetic disorders            | 23        | 53.4            |
| Cerebral palsy and epilepsy                               | 11        | 25.8            |
| Chronic kidney disease                                    | 7         | 16.3            |
| HIV/AIDS                                                  | 6         | 14              |
| Reasons for ICU admission                                 |           |                 |
| Altered mental status                                     | 145       | 46.3            |
| Respiratory failure                                       | 82        | 26.5            |
| Sepsis                                                    | 59        | 18.8            |
| Shock                                                     | 55        | 17.6            |
| Seizure                                                   | 46        | 14.7            |
| DKA                                                       | 24        | 7               |
| AKI                                                       | 24        | 7               |
| CHF                                                       | 21        | 6.7             |
| Hemorrhage                                                | 14        | 4.5             |
| Trauma                                                    | 6         | 1.9             |
| Others                                                    | 23        | 7.3             |
| Interventions given before ICU admission (n = 206)         |           |                 |
| Intranasal oxygen                                         | 206       | 100             |
| Herbal medications                                        | 23        | 11.2            |
| Fluid resuscitation                                       | 164       | 79.6            |
| Dextrose                                                  | 35        | 17              |
| Blood transfusion                                          | 30        | 14.6            |
| Antibiotics                                               | 206       | 100             |

Patterns and causes of admission

More than three-fourth (77%) of patients were admitted over weekdays and about 41.5% in the night shift. Emergency room (60.4%), wards (13.1%) and referrals from other facilities (11.8%) were the commonest sources of admissions to the pediatric intensive care unit. One resident and three nurses
were available during 85.6% of admissions and the median number of patients in the ICU was 4 (IQR: 3 to 5 patients). The median duration of illness before any health facility visit and admission to PICU was 3 (IQR: 1 to 7) and 6 (IQR: 3 to 13) days, respectively. The major reason for PICU admission were altered mental status (46.3%), respiratory failure (26.5%), sepsis (18.8%), shock (17.6%), seizure (14.7), DKA (7.7%) and AKI (7.7%). One patient could have more than one reason for the admission. Based on summarized 10th version of ICD of WHO, neurologic disorders (22.7%) infectious disease (18.8%) and environmental hazards (11.8%) account for the top three diagnoses.

Clinical characteristics

Only 64.5% of patients were fully vaccinated, 31.9% and 16% of patients had severe and moderate acute malnutrition, respectively. Forty-three (13.7%) patients had at least one comorbid illnesses, of which congenital malformations and genetic disorders (27.9%), cerebral palsy with or without seizure disorders (25.6%), CKD (16.3%) and HIV/AIDS (14%) are the commonest illnesses. Almost all (98.4%) of patients have vital sign derangement of which 53.4% had more than three vital sign derangements. Summarized based on the 10th version of ICD of WHO, neurologic disorders (22.7%) infectious disease (18.8%) and environmental hazards (11.8%) account for the top three diagnoses.

The baseline severity of diseases was assessed based on the PIM2 score calculated from an android medical app QxMD within one hour after admission. The minimum score was \(-6.46\) (with predicted mortality rate = 0.2%) and the maximum score was 2.47 (predicted mortality rate = 92.2%). The mean predicted mortality rate based on the PIM2 score was 11.14% which gave the standard mortality ratio (SMR) of 2.94. One-third of patients had critical illness diagnosis of which (41%) had sepsis, (47%) septic shock and the remaining (12%) had ARDS. About a third of patients (30.7%) had multiple organ dysfunction syndrome (MODS). Renal failure (57.3%), encephalopathy (49%), cardiac failure (46.9%), respiratory failure (41.7%) were the most common MODS (Table 3).
Table 3
clinical characteristics of children and caregivers who were admitted to the pediatric intensive care unit at the University of Gondar comprehensive specialized hospital, from February 1/2018 to July 30/2019, northwest Ethiopia (n = 313)

| Characteristics                        | Frequency | Percentages |
|----------------------------------------|-----------|-------------|
| ICD 10 category                        |           |             |
| Neurology                              | 71        | 26.7        |
| Infectious disease                     | 59        | 18.8        |
| Trauma and environmental               | 37        | 11.8        |
| Metabolic diseases                     | 28        | 8.9         |
| Congenital malformation                | 23        | 7.4         |
| Cardiovascular disease                 | 21        | 6.7         |
| Gastrointestinal                       | 20        | 6.4         |
| Renal diseases                         | 20        | 6.4         |
| Respiratory diseases                   | 18        | 5.7         |
| Neoplasm                               | 18        | 5.7         |
| Hematology                             | 3         | 1           |
| MODS (n = 96)                           |           |             |
| Renal failure                          | 55        | 57.3        |
| Encephalopathy                         | 47        | 49          |
| Cardiac failure                        | 45        | 46.3        |
| Respiratory failure                    | 40        | 41.7        |
| Hepatic failure                        | 26        | 27.1        |
| Hematologic failure                    | 18        | 18.8        |
| Metabolic failure                      | 10        | 10.4        |
| Critical illness Dx (n = 100)          |           |             |
| Sepsis                                 | 32        | 32          |
| Severe sepsis                          | 9         | 9           |
| Septic shock                           | 47        | 47          |
| ARDS                                   | 12        | 12          |
| Complications in the PICU (n = 56)     |           |             |
| HAS                                    | 26        | 46.4        |
| HAP                                    | 10        | 17.9        |
| Ventilator associated complication    | 6         | 10.7        |
| Drug reaction                          | 4         | 7.1         |
| Other complications                    | 10        | 17.9        |
| Interventions in the PICU              |           |             |
| Mechanical ventilation                 | 36        | 11.5        |
| Inotropes                              | 60        | 19.2        |
| Blood/ blood products                  | 73        | 23.3        |
| RRT                                    | 0         | 0           |
| Antibiotics                            | 308       | 98.4        |
| Surgery                                | 9         | 2.9         |
| Vaccination status                     |           |             |
| Complete                               | 203       | 64.9        |
| Incomplete                             | 110       | 35.1        |
| Comorbid illness                       |           |             |
| Yes                                    | 43        | 13.7        |
| No                                     | 270       | 86.3        |
| Comorbidities (n = 43)                 |           |             |
| Congenital malformations and genetic disorders | 23  | 53.4        |
| Cerebral palsy and epilepsy            | 11        | 25.8        |
| Chronic kidney disease                 | 7         | 16.3        |
| HIV/AIDS                               | 6         | 14          |

Intensive care unit outcomes and the incidence of mortality

Nearly one-third of patients (32.6%) were died at discharge from the PICU. Severe sepsis/MOF (41.2%) was the leading immediate cause of death in the PICU followed by respiratory failure (23.5%) and brain herniation (21.6%). Cardiac arrest accounts for 12.7% of immediate causes of deaths and others
accounted to nearly 1%.

Of the survivors 13.3% were discharged improved home, 20.9% left against medical advice (LAMA) and 62.1% were transferred towards, and 3.3% were transferred to other centers. Fifty-six patients (17.9%) had developed complications during their stay in the PICU, of which hospital-acquired sepsis (46.4%), followed by hospital-acquired pneumonia (17.9%), and mechanical ventilator-associated complications (10.7%) were the most common complications.

Study subjects were followed for different periods which gave a total of 1473 person-day observationS (49.1person-months). The median observation time was 3 days with IQR of 1 to 6 days. Of the total of 313 participants, 102 (32.6%) died during the follow-up time that gives the incidence of mortality of 6.9 deaths per 100 person day observations. Of deaths reported more than half (53.9%) died within 24 hours, 13 (12.7%) died between 24 and 48 hours and the remaining died after 48 hours of admission. Differences in all variables at baseline between strata were determined using the log-rank (χ2) test, and the equality of hazard was assessed for the different explanatory variables. Mechanical ventilation (P-value = 0.039) and critical illness (P-value = 0.0001) (Fig. 1) and (Fig. 2).

Predictors of mortality

The total follow up time in the intensive care unit were 1473 person day observation (49.1person month) with the median observation time was 3 days with IQR of 1 to 6 days. Of the total of 313 participants, 102 (32.6%) died during the follow-up time, which gives the incidence of mortality 6.9 deaths per 100 person-day observation with (95%CI: 5.34 to 8.34 deaths per 100 person-day).

From bivariable and multivariable cox proportional hazard model caregivers occupation, days admission to ICU, critically illnesses, PIM2 score, and mechanical ventilation were predictors of mortality in the PICU. Thus, caregivers of a child whose occupation of government employees the hazard of mortality was decreased by 65% compared to those farmer caregivers (AHR = 0.35, 95%CI:0.14, 0.89). whereas those children who were admitted to ICU during the weekend the hazard of mortality was 1.63 times higher compared to weekdays (AHR = 1.63,95%CI:1.02, 2.60). Those patients who had critical illness diagnosis the hazard of mortality were 1.79 times higher compared to those who had such diagnosis(AHR = 95%CI:1.13, 2.85). Similarly, a unit increased in the PIM2 score
of a child at admission the hazard of mortality was increased by 1.53 times keeping other
variables constant (AHR = 1.53, 95% CI: 1.36, 1.72). In addition, those patient who were on mechanical
ventilation the hazard of morality were 2.36 times higher compared to those who were not MV (AHR =
2.36, 95% CI: 1.39, 4.01) (Table 4)
Table 4
Bivariate and multivariable Cox proportional hazard model to identify predictors of mortality among patients admitted at the pediatric intensive care unit of University of Gondar comprehensive specialized hospital, northwest Ethiopia, 2019

| Variables                               | Status                        | CHR (95% CI)     | AHR (95% CI)     |
|-----------------------------------------|-------------------------------|------------------|------------------|
|                                         | Event                        | Censored         |                  |
| Age                                     |                               |                  |                  |
| ≤ 12                                    | 28                            | 60               | 1                |
| 13–24                                   | 10                            | 19               | 0.98 (0.47, 2.12) | 1.40 (0.65, 3.04) |
| 25–60                                   | 26                            | 40               | 1.30 (0.75, 2.23) | 1.15 (0.63, 2.08) |
| 61–132                                  | 20                            | 43               | 1.07 (0.60, 1.90) | 1.20 (0.65, 2.21) |
| > 132                                   | 18                            | 49               | 0.92 (0.50, 1.67) | 1.61 (0.84, 3.08) |
| Address                                 |                               |                  |                  |
| Urban                                   | 28                            | 43               | 1                |
| Rural                                   | 74                            | 168              | 0.73 (0.47, 1.13) | 0.63 (0.37, 1.05) |
| Caregiver’s level of education          |                               |                  |                  |
| No formal education                     | 96                            | 195              | 1                |
| Primary and above                       | 6                             | 16               | 0.78 (0.34, 1.80) | 1.26 (0.51, 3.13) |
| Caregiver’s occupation                  |                               |                  |                  |
| Farmers                                 | 72                            | 151              | 1                |
| Merchants and private                   | 9                             | 23               | 0.82 (0.41, 1.64) | 1.06 (0.47, 2.35) |
| Government employee                     | 7                             | 24               | 0.50 (0.22, 1.16) | 0.35 (0.14, 0.89)* |
| Unemployed                              | 14                            | 13               | 1.61 (0.91, 2.86) | 1.11 (0.55, 2.24) |
| Day of admission                        |                               |                  |                  |
| Week day                                | 71                            | 170              | 1                |
| Weekend                                 | 31                            | 41               | 1.47 (0.96, 2.26) | 1.63 (1.02, 2.60)** |
| Source of admission                     |                               |                  |                  |
| Home                                    | 9                             | 27               | 1                |
| Other facilities                        | 14                            | 23               | 1.66 (0.72, 3.86) | 1.90 (0.76, 4.76) |
| Emergency room                          | 55                            | 134              | 1.13 (0.56, 2.29) | 1.59 (0.72, 3.48) |
| Wards and OR                            | 24                            | 27               | 2.11 (0.98, 4.56) | 2.07 (0.86, 4.99) |
| Duration of illness before PICU admission |                               |                  |                  |
| <6 days                                 | 39                            | 107              | 1                |
| ≥6 days                                 | 63                            | 104              | 1.43 (0.96, 2.12) | 0.97 (0.62, 1.54) |
| Comorbidities                           |                               |                  |                  |
| No                                      | 85                            | 185              | 1                |
| Yes                                     | 17                            | 26               | 1.31 (0.78, 2.21) | 0.66 (0.36 1.23) |
| Critical illness DX                     |                               |                  |                  |
| No                                      | 53                            | 160              | 1                |
| Yes                                     | 49                            | 51               | 2.05 (1.39, 3.04) | 1.79 (1.13, 2.85)** |
| Nutritional status, Z score             |                               |                  |                  |
| Normal                                  | 45                            | 118              | 1                |
| MAM                                     | 15                            | 35               | 1.19 (0.66, 2.14) | 1.49 (0.79, 2.82) |
| SAM                                     | 42                            | 58               | 1.67 (1.09, 2.55) | 1.69 (0.94, 2.61) |
| PIM2 score                              | -3.22 ± 1.81                  |                  |                  |
| Mechanical ventilation                  |                               |                  |                  |
| No                                      | 79                            | 197              | 1                |
| Yes                                     | 23                            | 14               | 1.93 (1.20, 3.10) | 2.36 (1.39, 4.01)** |
| Complications in the PICU               |                               |                  |                  |
| No                                      | 86                            | 190              | 1                |
| Yes                                     | 16                            | 21               | 2.39 (1.20, 4.73) | 1.62 (0.79, 3.31) |
| Fluid resuscitation intervention before ICU admission | | | |
| No                                      | 44                            | 105              | 1                |
| Yes                                     | 58                            | 106              | 1.24 (0.83, 1.84) | 0.92 (0.59, 1.44) |

Discussion
Data from 313 patients admitted during 18 months of study period was analyzed, of which under-five children outnumber any other age groups, which is supported by other studies in India and Brazil [6, 8] but different from a retrospective study done in our PICU and a general PICU in Ethiopia which shows that above fives outnumber the under-five children [9, 10], which show that admission patterns vary among different regions of the globe, settings of the same country, and even it could be different in time in the same set up. This tells us important information that PICU resource allocation and protocol preparation should be based on settings and revised timely.

Neurologic disorders accounted for nearly a quarter of the total admissions followed by infectious diseases, and environmental hazards. This finding is in line with findings in other studies where neurologic disorder was consistently among the top three causes of admission to PICU [5, 11, 12].

More than half of patients were transferred from the pediatric emergency room which is a consistent finding with studies done in Mekelle, Ethiopia [7], USA [13], Iran [14] and Pakistan [11]. The maximum possible advanced life support interventions given were mechanical ventilation and vasoactive agent infusion. Blood and blood products, antimicrobials, anticonvulsants, mannitol, steroids, antihypertensive, and insulin were the other commonly used drugs in the PICU.

The median LOS in this study was comparable with the findings of the multi-center study in Europe and USA [15], Japan [16] and South Africa [17], but the proportion of LSP in our study is lower than findings in this studies. But the fact that the proportion of LSP is significantly lower than the findings in these studies could be due to a higher proportion of early deaths and LAMAs on the verge of death there are no life sustain interventions like ECMO in our setting. LOS is not a good indicator of PICU outcome and quality of care as it may vary based on the admission and discharge protocol of each institution. LOS might be short due to increased early mortality or improved quality of care.

This study revealed that the incidence rate of mortality was 6.92 deaths (95% CI: 5.68, 8.34) per 100 person-day observations. The cumulative probability of death at the end of the first day was 18.4%, and at the end of the fourth day, the cumulative probability of death was 34.2%. On the other hand, proportion of death in our PICU was 32.6% (95% CI: 27.4, 37.8) which is consistent with a retrospective cross-sectional study done in the same PICU from 2013 to 2016 (30.9%) [10], Egypt
(33.1%)[18], Nigeria (36.1%) [19] and Saudi Arabia (37.4%)[20]. The proportion of mortality in our PICU is lower than the finding of a retrospective cross-sectional study done in Jimma-Ethiopia (40%) [9]. The difference could be attributed to the higher proportion of trauma patients admitted in their PICU as compared to ours. The other possible reason could be that the higher proportion of LAMAs in our study might underestimate the mortality rate in our study.

However, it is higher than the mortality rates in studies done in Pakistan (14%)[11], the average of Latin American countries (13.29%) [21], India (10.58%)[14] and European countries (5%)[22]. The possible explanation the observed discrepancies might be due to a suboptimal care inadequacy of both diagnostic, interventional facilities in our PICU.

In this study, admission over weekends, admission from other facility and emergency room, presence of more than one resident at admission, presence of severe acute malnutrition, MODS, mechanical ventilation, and higher PIM2 scores were found to be significant and independent predictors of mortality at the PICU.

Children who were admitted over weekends had nearly twice an increased risk of mortality than those admitted over weekdays which is consistent with the findings of studies done in Canada, Finland, and Austria [22–24]. This might be due to failure to early recognize deteriorations at wards and other sources as a result of reduced staffing ratios. Access to diagnostic services is also limited in weekends which limits the likelihood of putting correct diagnoses, there could be unrecognized deteriorations during handover round times and delays in giving interventions. The fact that duty teams come from other wards during weekends may contribute to the increased mortality over weekends. But our finding was not supported by three American studies, and studies done in the United Kingdom and the Republic of Ireland [25, 26]. This could be explained by the better standard of care they have and 24 hours around the clock full staffing. This study also reviewed that caregiver occupation of government-employed associated with lower risk mortality compared to caregivers of peasants. This could be explained by differences in health-seeking behavior and early identification and notice of dangers conditions of their children.

The child whose critical illness diagnosis had increased risk of mortality compared to those who had
no such history. This could be due to the fact that critical illnesses are associated with an increased probability of death.

Amongst many baseline disease severity assessment tools, we used PIM2 as it doesn’t need extensive laboratory investigation and it is not affected by subsequent interventions since it is scored within one hour of admission. Accordingly, A unit increment in PIM2 score had doubled the hazard of mortality and discriminated well between survival and death at our PICU with Area under the curve AUROC of 76.4%. Which shows the score is sensitive in detecting morality. This scoring system is also validated and applicable in many PICUs across the world [27–31]. As to our finding the high observed mortality rate than predicted mortality by PIM2 score cannot be attributed to the severity of illness at admission. It indicates the poor quality of intensive care in our setting. PIM2 Score was found to be nondiscriminatory for the risk of death in studies done in Addis Ababa and India [29, 32].

Patients who were mechanically ventilated had more than two times increased hazard of death. This is in line with the findings of studies[33, 34]. This might be due to the fact that patients who need mechanical ventilation are in advanced stages of the disease. The other explanation for this could be ventilator-associated complications.

Limitation of the study
The income of careGivers was not assessed because it was difficult to ascertain because the majority of admissions were from a rural area and they usually underreport the assets they have. PIM2 scoring was based on 9 out of 11 parameters as there was no Arterial blood gas analyzer in our PICU during the study period. Availability of medical equipment and PICU quality of care and their impact on survival was not fully assessed using standard parameters. Pediatric critical care is not just about saving lives, so the degree of physiologic function retained at discharge should have been assessed using a standard checklist for all of the patients discharged.

Conclusion
Neurologic disorders were the leading causes of admission followed by infectious diseases, and environmental hazards. Rate of mortality was high and admission over weekends, caregivers’ occupation, mechanical ventilation, critical illness diagnosis, and higher PIM2 scores were found to be
significant and independent predictors of mortality at the PICU. This suggests that ICU medical equipment, diagnostics, and interventions should be available up to the standard. Intensivist and full staffing around the clock has to be available in the PICU.

Abbreviations
AUROC: Area Under the Receiver Operating Curve, AHR: Adjusted Hazard Ratio, AKI: Acute Kidney Injury, CI: Confidence Intervals, CHR: Crude Hazard Ratio, HAS: Hospital Acquired Sepsis, HAP: Hospital Acquired Pneumonia, ICD: International Classifications of Disease, ICU: Intensive Care Unit, IQR: Interquartile Range, IR: Incidence Rate, LAMA: Left Against Medical Advice, LOS: Length of Hospital stay, MAM: Moderate Acute Malnutrition, MODS: Multiple Organ Dysfunction Syndrome, MV: Mechanical Ventilation, PI: Principal Investigator, PICU: Pediatric Intensive Care Unit, PIM: Pediatrics Index Mortality, SAM: Sever Acute Malnutrition, OR: Operation Room, USA: United States of America, WHO, World Health Organization

Declarations

Ethics approval and consent to participate
Ethical clearance was obtained from the Institutional Ethical Review Board of College of Medicine and Health Sciences, University of Gondar (ref.no 20/12/2018). Assent and informed written consent was obtained from the care takers. The name or any other identifying information was not recorded on the questionnaire and all information taken from the chart was kept strictly for confidential and in a safe place. The information retrieved was used only for the study purpose.

Consent for publication
Not applicable

Availability of data and material
Data is available from the corresponding author upon reasonable request.

Competing interests
The authors declare that they have no competing interests.

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Authors' contributions
NWT, ATA, and KST participated to design the study, performed data analysis, visualization, validation
the whole work and prepared the manuscript. NWT took part in funding acquisition, data collection, supervision and software and other resources. All authors read and approved the final manuscript.

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Figures

Figure 1

Kaplan-Meier failure (death) estimates curves by days of admission among children treated in the pediatric intensive care unit of University of Gondar comprehensive specialized hospital from February 1/2018 to July 30/2019
Figure 2

Kaplan-Meier failure (death) estimates curves by children critical illness admitted to pediatric intensive care unit of University of Gondar comprehensive specialized hospital from February 1/2018 to July 30/2019