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# BMJ Open

**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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3 **1 Incidence and predictors of mortality among children admitted to the pediatric intensive**  
4 **care unit at the University of Gondar comprehensive specialized hospital, northwest**  
5  
6 **2**  
7 **3 Ethiopia: A prospective observational cohort study**

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## 15 Abstract

16 **Objective:** To determine the incidence and predictors of mortality among children admitted to the  
17 pediatric intensive care unit at the University of Gondar comprehensive specialized hospital,  
18 northwest Ethiopia

19 **Design:** An institution based prospective observational cohort study

20 **Participants:** All pediatric age group children admitted to the intensive care unit of university of  
21 Gondar comprehensive specialized hospital from February 2018 to July 2019 were the study  
22 population.

23 **Measurements:** Data were collected using structured interviewer-administered questionnaire,  
24 physical examination and patient document review. Clinical characteristics like, SBP, pupillary  
25 light reflex, SaO<sub>2</sub> need of mechanical ventilator was assessed and documented within the first hour  
26 and entered into an electronic App to calculate pediatrics index mortality 2 (PIM2) score. Cox-  
27 proportional hazard model was fitted to identify factors associated with mortality.

28 **Result:** Based on the 10<sup>th</sup> version of international classifications of disease (ICD) of WHO,  
29 neurologic disorders (22.7%) infectious disease (18.8%) and environmental hazards (11.8%)  
30 account for the top three diagnoses. The median observation time was 3 days with IQR of 1 to 6  
31 days. Of the total of 313 participants, 102 (32.6%) died during the follow-up time. This gives the  
32 incidence of mortality of 6.9 deaths per 100 person day observation. Caregivers' occupation of  
33 government-employed (AHR=0.35, 95%CI: 0.14, 0.89), weekend admission (AHR=1.63, 95%CI:  
34 1.02, 2.62), critical illness (AHR=1.79, 95%CI: 1.13, 2.85) Mechanical ventilation AHR=2.36,  
35 95%CI: 1.39, 4.01) and PIM2 score (AHR=1.53, 95%CI: 1.36, 1.72) were predictors of mortality  
36 in the pediatric ICU.

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3 37 **Conclusion:** Neurologic disorders were the leading causes of admission followed by infectious  
4  
5 38 diseases, and environmental hazards. Rate of mortality was high and admission over weekends,  
6  
7 39 caregivers' occupation, mechanical ventilation, critical illness diagnosis, and higher PIM2 scores were  
8  
9 40 found to be significant and independent predictors of mortality at the PICU. This suggests that ICU  
10  
11 41 medical equipment and interventions should be available up to the standard.

### 14 42 **Strength and limitation of the study**

- 16 43 ➤ This study has used prospective cohort study and better statistical function like survival  
17 44 analysis for better estimation and description
- 18 45 ➤ In resource limited setting like Ethiopia this study could help clinicians and health care  
19 46 planners for evidence based interventions
- 20 47 ➤ Some factors like caregivers income which would have association with mortality was not  
21 48 assessed
- 22 49 ➤ The PIM2 scoring was based on 9 out of 11 parameters as there was no Arterial blood gas  
23 50 analyzer in our PICU during the study period which could introduce misclassifications

## 63 **Introduction**

64 Patients treated by pediatric health professionals exhibit a broad spectrum and frequency of  
65 medical and surgical complaints ranging from mild illnesses that can be reassured to those  
66 requiring pharmacologic and device-related vital function support in the pediatric intensive care  
67 units (PICU).

68 The range, severity, and response for the treatment of illness is dependent on the age of the patient,  
69 biologic, socio-demographic variations, time and place. As per the report of WHO, in low-income  
70 countries like Bangladesh, Dominican Republic, Ethiopia, and Indonesia, 90% of children had  
71 severe forms of common infectious diseases, especially pneumonia, diarrhea, sepsis, malaria, and  
72 meningitis, often complicated with chronic malnutrition [1].

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

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

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3 85 Care in the PICU tremendously improves the success in saving patients having a potentially life-  
4  
5 86 endangering illness but the proportion of survivors with disabilities increased significantly [5]. Its  
6  
7 87 outcome can be measured by standardized mortality ratio (SMR), length of hospital stay,  
8  
9 88 unplanned readmission rate, pain assessment, medication safety practice, and central venous  
10  
11 89 catheter infection prevention practice adoption. Mortality is the most studied outcome measure  
12  
13 90 though data in developing countries is scarce [2]. The mortality rate in the PICU at GUCSH is  
14  
15 91 significantly higher than that of developed countries as to the monthly Mortality-morbidity report.  
16  
17 92 Published data on pediatric critical care in low-income countries remains sparse yet is much  
18  
19 93 needed. This paucity of data makes practice modification and outcome improvement difficult(6).  
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21  
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23  
24 94 Most studies done on determinant factors of mortality in the PICU are from western countries and  
25  
26 95 are dependent on clinical and laboratory indices [5]. The few studies that considered epidemiologic  
27  
28 96 and socio-demographic factors are retrospective cross-sectional studies and most did not consider  
29  
30 97 the severity of illness as a factor as they don't apply severity score in retrospective studies [6]. The  
31  
32 98 ICU equipment and set up in developing countries is not well studied [2, 7]. Hence, this study  
33  
34 99 aimed to determine the incidence and predictors of mortality among children admitted to a  
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36 100 pediatric intensive care unit at the University of Gondar comprehensive specialized hospital.  
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39 101 Findings from this study could help clinicians and case managers for proper management of the  
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41 102 diseases.  
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## 45 103 **Methods**

### 46 104 **Study design, period and setting**



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3 105 An institution-based observation prospective follow up study was conducted among children who  
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5 106 aged 1 months to 18 years and admitted to pediatric intensive care unit of the University of Gondar  
6  
7 107 comprehensive specialized hospital from February 1, 2018, to July 30, 2019.

8  
9  
10 108 The hospital is located in Gondar city, in Amhara Region, 741 km Northwest of Addis Ababa, It  
11  
12 109 is a comprehensive specialized teaching and referral hospital, with a total of 641 beds and 96 beds  
13  
14 110 in the pediatrics side, where a multidisciplinary team of diverse professionals provide a range of  
15  
16 111 health care services for approximately 2806 inpatient and 11986 outpatient children beyond the  
17  
18 112 neonatal age coming from the northwest part of the country including the neighboring  
19  
20 113 administrative regions. The major causes of pediatric admission to the hospital are pneumonia,  
21  
22 114 malaria, neonatal infections, tuberculosis, heart failure, meningitis and other various types of  
23  
24 115 metabolic and organ system-based emergencies according to hospital statistics. On average there  
25  
26 116 are about 25 pediatric critical care admissions per month. The PICU was established in 2013 it has  
27  
28 117 six beds with electronic monitors and one mechanical ventilators. The organizational detail of the  
29  
30 118 PICU in this hospital is lacking. Team composition is often limited to a general pediatrician,  
31  
32 119 resident, interns and a handful of senior-level nurses. Pediatric intensivists, respiratory therapists,  
33  
34 120 pharmacists, and dieticians are not available.  
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### 41 121 **Population and sample**

42  
43 122 The patients aged 1 month to 18 years admitted to pediatric intensive care unit and stayed more  
44  
45 123 than two hours in the hospital were included in the study. Cases having incomplete data and  
46  
47 124 surgical patients admitted only for recovery purposes was excluded from the study.

48  
49  
50 125 The sample size for this study was determined using a single population proportion of  $P=21\%$ ,  
51  
52 126 from previous Bangladesh study [4] 5% margin of error the sample size becomes 254 and after  
53  
54 127 adding 10% contingency, the sample size will be 279. A total of 395 patients were admitted to the  
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3 128 PICU from February 1 2018 to July 30 2019. Data was collected from 327 patients who fulfilled  
4  
5 129 the inclusion criteria, whereas fourteen patients were excluded from the study due to incomplete  
6  
7  
8 130 baseline data.

### 9 10 131 **Data collection procedure**

11  
12 132 Data was collected by treating physicians using standardized questionnaire after taking consent  
13  
14 133 from caretakers. Clinical characteristics like, SBP, pupillary light reflex, SaO<sub>2</sub> need of mechanical  
15  
16 134 ventilator was assessed and documented within the first hour and entered into an electronic App  
17  
18 135 to calculate pediatrics index mortality 2 (PIM2) score. The PIM2 was used in our research because  
19  
20 136 it doesn't need extensive laboratory investigation and it is not affected by subsequent interventions  
21  
22 137 since it is scored within one hour of admission. Socio-demographic data and medical history were  
23  
24 138 taken by interview. Diagnosis, laboratory indices, and courses in the hospital were filled by chart  
25  
26 139 review at discharge. We used the WHO International Classification of Diseases 10<sup>th</sup> version for  
27  
28 140 disease category and only the primary diagnosis was used for ICD-10 assignment in patients  
29  
30 141 having multiple diagnoses. The collected data were double-checked by the data collector and the  
31  
32 142 principal investigator. There were orientations and training about data collection and the objective  
33  
34 143 of the study every three months and demonstration every Monday for treating physicians and data  
35  
36 144 collectors. The principal investigators supervised the overall process and check completeness of  
37  
38 145 questionnaires every day.

### 39 40 146 **Variable of the study and operational definitions**

41  
42 147 The main dependent variable was time to death (event), whereas socio demographic characteristics  
43  
44 148 (age, sex, relation with the caregiver, care giver's educational status, occupation Hospital arrival  
45  
46 149 and admission related factors (duration of illness before admission, time- day and month of  
47  
48 150 admission, source of admission, staff level at admission) clinical characteristics and management-

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3 151 related factors (diagnosis, admission vital signs, comorbidity, nutritional status, vaccination status,  
4  
5 152 interventions given in the ICU and before admission, PIM2 score, MODS, Complications) were  
6  
7  
8 153 the independent variables.  
9

10  
11 154 Event (death): is defined as a patient who died in the hospital during the course of treatment  
12

13 155 Censored: discharged alive from the ICU  
14

15 156 LOS: refers to the duration of stay in a number of days from the date of admission to the date of  
16  
17  
18 157 discharge  
19

20 158 Short term outcome: the outcome of the patient until s/he leaves the hospital  
21

## 22 159 **Data processing and analysis**

23  
24

25 160 After the data were checked for its consistency and completeness, it was entered into EpiData  
26  
27 161 version 3.1 exported to STATA version 14 for cleaning and analysis. Descriptive statistics like  
28  
29 162 mean, median, proportions were carried out to summarize baseline characteristics and pattern of  
30  
31 163 admission. In addition, summary statistics like life table, log-rank test and Kaplan-Meier curves  
32  
33 164 computed was used to determine the incidence rate (IR) of death and to compare survival curves  
34  
35 165 between the different categories of the explanatory variables.  
36  
37

38 166 Both bivariate and multivariate Cox proportional hazard models were used to identify the  
39  
40 167 predictors. Variables with p-value < 0.2 in the bivariate analysis were entered into the multivariate  
41  
42 168 proportional hazard model. Ninety-five percent confidence interval (95% CI) of hazard ratio was  
43  
44 169 computed and variable having p-value < 0.05 in the multivariate Cox proportional hazards model  
45  
46 170 was considered as significantly and independently associated with the dependent variable. Cox  
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48 171 proportional hazard model fitness was checked using the Schoenfeld residuals test.  
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## 172 **Ethical approval and consent to participate**

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

## 178 **Patient and public involvement**

179 Patients were not involved in the study

## 180 **Result**

### 181 **Socio-demographic characteristics**

182 A total of 313 patients out of 376 patients admitted during the eighteen-month study period were  
 183 included in the final analysis. The median age at admission was 48 months with interquartile range  
 184 (IQR) of 12 to 122 months, about 28.1% were infants followed by adolescents (21.4%). More than  
 185 half (59.7%) were males, more than three-fourth (77.3%) were from rural areas and parents were  
 186 the commonest caregivers for the majority (93%) of children. The majority of caregivers had no  
 187 formal education (77.6%) and 71.2% were farmers, most patients were admitted in the spring  
 188 season (38.3%) followed by winter (27.2%) (Table 1).

189 Table 1: Socio-demographic characteristics of children and caregivers who were admitted to the  
 190 pediatric intensive care unit at the University of Gondar comprehensive specialized hospital, from  
 191 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
<b>Sex</b>		
Male	187	59.7
Female	126	40.3
<b>Residence</b>		
Urban	71	22.7
Rural	242	73.3
<b>Caregivers</b>		
Parents	291	93
Grand parents	8	2.6
Siblings	8	2.6
Others	6	1.9
<b>Caregiver level of education</b>		
No formal education	242	77.6
Primary school	32	10.2
Secondary school	17	5.4
College and above	21	6.7
<b>Caregivers occupation</b>		
Farmers	223	71.2
Merchants and private	32	10.2
Government employee	31	9.9
Unemployed	27	8.6
<b>Season of admission</b>		
Summer	63	20.1
Spring	45	14.4
Winter	85	27.2
Autumn	120	38.3

192

193 **Patterns and causes of admission**

194 More than three-fourth (77%) of patients were admitted over weekdays and about 41.5% in the  
 195 night shift. Emergency room (60.4%), wards (13.1%) and referrals from other facilities (11.8%)  
 196 were the commonest sources of admissions to the pediatric intensive care unit. One resident and  
 197 three nurses were available during 85.6% of admissions and the median number of patients in the  
 198 ICU was 4 (IQR: 3 to 5 patients). The median duration of illness before any health facility visit  
 199 and admission to PICU was 3 (IQR: 1 to 7) and 6 (IQR: 3 to 13) days, respectively. The major  
 200 reason for PICU admission were altered mental status (46.3%), respiratory failure (26.5%), sepsis  
 201 (18.8%), shock (17.6%), seizure (14.7), DKA (7.7%) and AKI (7.7%). One patient could have  
 202 more than one reason for the admission. Based on summarized 10<sup>th</sup> version of ICD of WHO,  
 203 neurologic disorders (22.7%) infectious disease (18.8%) and environmental hazards (11.8%)  
 204 account for the top three diagnoses (Table 2).

205 Table 2: patterns and causes of admission among children and caregivers who were admitted to  
 206 the pediatric intensive care unit at the University of Gondar comprehensive specialized hospital,  
 207 from February 1, 2018 to July 30, 2019, northwest Ethiopia (n=313)

Characteristics	Frequency	Percentages (%)
<b>Duration of illness before any health facility visit in days</b>		
≤3days	118	37.7
>3days	195	62.3
<b>Duration of illness before PICU admission in days</b>		
≤6 days	71	22.7
>6 days	242	77.7
<b>Day of admission</b>		
Weekday	241	77
Weekend	72	23
<b>Time of admission</b>		
Dayshift	183	58.5
Nightshift	130	41.5
<b>Sources of admission</b>		
Home	36	11.5
Other facilities	37	11.8

Emergency room	189	60.4
Wards and Operating rooms	51	16.3
<b>Vaccination status</b>		
Complete	203	64.9
Incomplete	110	35.1
<b>Comorbid illness</b>		
Yes	43	13.7
No	270	86.3
<b>Comorbidities (n=43)</b>		
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
<b>Reasons for ICU admission</b>		
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
<b>Interventions given before ICU admission (n=206)</b>		
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

208

### 209 **Clinical characteristics**

210 Only 64.5% of patients were fully vaccinated, 31.9% and 16% of patients had severe and moderate  
 211 acute malnutrition, respectively. Forty-three (13.7%) patients had at least one comorbid illnesses,  
 212 of which congenital malformations and genetic disorders (27.9%), cerebral palsy with or without

213 seizure disorders (25.6%), CKD (16.3%) and HIV/AIDS (14%) are the commonest illnesses.  
 214 Almost all (98.4%) of patients have vital sign derangement of which 53.4% had more than three  
 215 vital sign derangements. Summarized based on the 10<sup>th</sup> version of ICD of WHO, neurologic  
 216 disorders (22.7%) infectious disease (18.8%) and environmental hazards (11.8%) account for the  
 217 top three diagnoses.

218 The baseline severity of diseases was assessed based on the PIM2 score calculated from an android  
 219 medical app QxMD within one hour after admission. The minimum score was -6.46(with predicted  
 220 mortality rate = 0.2%) and the maximum score was 2.47(predicted mortality rate =92.2%). The  
 221 mean predicted mortality rate based on the PIM2 score was 11.14% which gave the standard  
 222 mortality ratio (SMR) of 2.94. One-third of patients had critical illness diagnosis of which (41%)  
 223 had sepsis, (47%) septic shock and the remaining (12%) had ARDS. About a third of patients  
 224 (30.7%) had multiple organ dysfunction syndrome (MODS). Renal failure (57.3%),  
 225 encephalopathy (49%), cardiac failure (46.9%), respiratory failure (41.7%) were the most common  
 226 MODS (Table 3).

227 Table 3: clinical characteristics of children and caregivers who were admitted to the pediatric  
 228 intensive care unit at the University of Gondar comprehensive specialized hospital, from February  
 229 1, 2018 to July 30, 2019, northwest Ethiopia (n=313)

Characteristics	Frequency	Percentages
<b>ICD 10 category</b>		
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
<b>MODS(n=96)</b>		
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
<b>Critical illness Dx(n=100)</b>		
Sepsis	32	32
Severe sepsis	9	9
Septic shock	47	47
ARDS	12	12
<b>Complications in the PICU(n=56)</b>		
HAS	26	46.4
HAP	10	17.9
Ventilator associated complication	6	10.7
Drug reaction	4	7.1
Other complications	10	17.9
<b>Interventions in the PICU</b>		
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
<b>Vaccination status</b>		
Complete	203	64.9
Incomplete	110	35.1
<b>Comorbid illness</b>		
Yes	43	13.7
No	270	86.3
<b>Comorbidities (n=43)</b>		
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

### 230 **Intensive care unit outcomes and the incidence of mortality**

231 Nearly one-third of patients (32.6%) were died at discharge from the PICU. Severe sepsis/MOF  
 232 (41.2%) was the leading immediate cause of death in the PICU followed by respiratory failure  
 233 (23.5%) and brain herniation (21.6%). Cardiac arrest accounts for 12.7% of immediate causes of  
 234 deaths and others accounted to nearly 1%.

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

240 Study subjects were followed for different periods which gave a total of 1473 person-day  
 241 observations (49.1person-months). The median observation time was 3days with IQR of 1 to 6  
 242 days. Of the total of 313 participants, 102 (32.6%) died during the follow-up time that gives the

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3 243 incidence of mortality of 6.9 deaths per 100 person day observations. Of deaths reported more than  
4  
5 244 half (53.9%) died within 24 hours, 13(12.7%) died between 24 and 48 hours and the remaining  
6  
7  
8 245 died after 48 hours of admission. Differences in all variables at baseline between strata were  
9  
10 246 determined using the log-rank ( $\chi^2$ ) test, and the equality of hazard was assessed for the different  
11  
12 247 explanatory variables. Mechanical ventilation (P-value=0.039) and critical illness (P-value=  
13  
14 248 0.0001) (Figure 1) and (Figure 2).

### 17 249 **Predictors of mortality in the ICU**

19 250 The total follow up time in the intensive care unit were 1473 person day observation (49.1person  
20  
21 251 month) with the median observation time was 3 days with IQR of 1 to 6 days. Of the total of 313  
22  
23 252 participants, 102 (32.6%) died during the follow-up time, which gives the incidence of mortality  
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26 253 6.9 deaths per 100 person-day observation with (95%CI: 5.34 to 8.34 deaths per 100 person-day).  
27  
28  
29 254 From bivariable and multivariable cox proportional hazard model caregivers' occupation, day's  
30  
31 255 admission to ICU, critically illnesses, PIM2 score, and mechanical ventilation were predictors of  
32  
33 256 mortality in the PICU. Thus, caregivers of a child whose occupation of government employees the  
34  
35  
36 257 hazard of mortality was decreased by 65% compared to those farmer caregivers (AHR=0.35,  
37  
38 258 95%CI: 0.14, 0.89). Whereas those children who were admitted to ICU during the weekend the  
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40 259 hazard of mortality was 1.63 times higher compared to weekdays (AHR=1.63, 95%CI: 1.02, 2.60).  
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43 260 Those patients who had critical illness diagnosis the hazard of mortality were 1.79 times higher  
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45 261 compared to those who had such diagnosis(AHR=95%CI:1.13, 2.85). Similarly, a unit increased  
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47 262 in the PIM2 score of a child at admission the hazard of mortality was increased by 1.53 times  
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50 263 keeping other variables constant (AHR=1.53,95%CI:1.36, 1.72). In addition, those patient who  
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52 264 were on mechanical ventilation the hazard of mortality were 2.36 times higher compared to those  
53  
54 265 who were not MV(AHR=2.36,95%CI:1.39, 4.01) (Table 4)

266 Table 4: Bivariate and multivariable Cox proportional hazard model to identify predictors of  
 267 mortality among patients admitted at the pediatric intensive care unit of University of Gondar  
 268 comprehensive specialized hospital, northwest Ethiopia, 2019

Variables	Status		CHR (95% CI)	AHR (95% CI)
	Event	Censored		
Age				
≤12	28	60	1	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	1
Rural	74	168	0.73(0.47,1.13)	0.63(0.37,1.05)
Caregiver' level of education				
No formal education	96	195	1	1
Primary and above	6	16	0.78(0.34, 1.80)	1.26(0.51,3.13)
Caregivers' occupation				
Farmers	72	151	1	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	1
Weekend	31	41	1.47(0.96,2.26)	1.63(1.02,2.60)**
Source of admission				
Home	9	27	1	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	1
≥6 days	63	104	1.43(0.96,2.12)	0.97(0.62,1.54)
Comorbidities				
No	85	185	1	1
Yes	17	26	1.31(0.78 2.21)	0.66(0.36 1.23)
Critical illness DX				
No	53	160	1	1
Yes	49	51	2.05(1.39,3.04)	1.79(1.13, 2.85)**
Nutritional status, Z score				
Normal	45	118	1	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		1.51(1.37,1.67)	1.53(1.36,1.72)**
Mechanical ventilation				
No	79	197	1	1
Yes	23	14	1.93(1.20,3.10)	2.36(1.39,4.01)**
Complications in the PICU				
No	86	190	1	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	1
Yes	58	106	1.24(0.83 1.84)	0.92(0.59 1.44)

269 \* show statistical significance at a p-value of 0.05

## 270 Discussion

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

278 Neurologic disorders accounted for nearly a quarter of the total admissions followed by infectious  
 279 diseases, and environmental hazards. This finding is in line with findings in other studies where  
 280 neurologic disorder was consistently among the top three causes of admission to PICU [5, 11, 12].  
 281 More than half of patients were transferred from the pediatric emergency room which is a  
 282 consistent finding with studies done in Mekelle, Ethiopia [7], USA [13], Iran [14] and Pakistan  
 283 [11].

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3 284 The maximum possible advanced life support interventions given were mechanical ventilation and  
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5 285 vasoactive agent infusion. Blood and blood products, antimicrobials, anticonvulsants, Mannitol,  
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7 286 steroids, antihypertensive, and insulin were the other commonly used drugs in the PICU.

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10 287 The median LOS in this study was comparable with the findings of the multi-center study in  
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12 288 Europe and USA [15], Japan [16] and South Africa [17], but the proportion of LSP in our study is  
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14 289 lower than findings in these studies. But the fact that the proportion of LSP is significantly lower  
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16 290 than the findings in these studies could be due to a higher proportion of early deaths and LAMAs  
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18 291 on the verge of death there are no life sustain interventions like ECMO in our setting. LOS is not  
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20 292 a good indicator of PICU outcome and quality of care as it may vary based on the admission and  
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22 293 discharge protocol of each institution. LOS might be short due to increased early mortality or  
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24 294 improved quality of care.

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30 295 This study revealed that the incidence rate of mortality was 6.92deaths (95% CI: 5.68, 8.34) per  
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32 296 100 person-day observations. The cumulative probability of death at the end of the first day was  
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34 297 18.4%, and at the end of the fourth day, the cumulative probability of death was 34.2%. On the  
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36 298 other hand, proportion of death in our PICU was 32.6% (95% CI: 27.4,37.8) which is consistent  
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38 299 with a retrospective cross-sectional study done in the same PICU from 2013 to 2016(30.9%)[10],  
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40 300 Egypt (33.1%)[18], Nigeria (36.1%) [19] and Saudi Arabia (37.4%)[20]. The proportion of  
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42 301 mortality in our PICU is lower than the finding of a retrospective cross-sectional study done in  
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44 302 Jimma-Ethiopia (40%)[9]. The difference could be attributed to the higher proportion of trauma  
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46 303 patients admitted in their PICU as compared to ours. The other possible reason could be that the  
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48 304 higher proportion of LAMAs in our study might underestimate the mortality rate in our study.

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53 305 However, it is higher than the mortality rates in studies done in Pakistan (14%)[11], the average  
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55 306 of Latin American countries (13.29%) [21], India (10.58%)[14] and European countries (5%)[22].

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3 307 The possible explanation the observed discrepancies might be due to a suboptimal care inadequacy  
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5 308 of both diagnostic, interventional facilities in our PICU.

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8 309 In this study, admission over weekends, admission from other facility and emergency room,  
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10 310 presence of more than one resident at admission, presence of severe acute malnutrition, MODS,  
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12 311 mechanical ventilation, and higher PIM2 scores were found to be significant and independent  
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14 312 predictors of mortality at the PICU.

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17 313 Children who were admitted over weekends had nearly twice an increased risk of mortality than  
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19 314 those admitted over weekdays which is consistent with the findings of studies done in Canada,  
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21 315 Finland, and Austria [22-24]. This might be due to failure to early recognize deteriorations at wards  
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23 316 and other sources as a result of reduced staffing ratios. Access to diagnostic services is also limited  
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25 317 in weekends which limits the likelihood of putting correct diagnoses, there could be unrecognized  
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27 318 deteriorations during handover round times and delays in giving interventions. The fact that duty  
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29 319 teams come from other wards during weekends may contribute to the increased mortality over  
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31 320 weekends. But our finding was not supported by three American studies, and studies done in the  
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33 321 United Kingdom and the Republic of Ireland [25, 26]. This could be explained by the better  
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35 322 standard of care they have and 24 hours around the clock full staffing. This study also reviewed  
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37 323 that caregiver occupation of government-employed associated with lower risk mortality compared  
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39 324 to caregivers of peasants. This could be explained by differences in health-seeking behavior and  
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41 325 early identification and notice of dangers conditions of their children.

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43 326 The child whose critical illness diagnosis had increased risk of mortality compared to those who  
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45 327 had no such history. This could be due to the fact that critical illnesses are associated with an  
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47 328 increased probability of death.

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3 329 Amongst many baseline disease severity assessment tools, we used PIM2 as it doesn't need  
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5 330 extensive laboratory investigation and it is not affected by subsequent interventions since it is  
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7 331 scored within one hour of admission. Accordingly, A unit increment in PIM2 score had doubled  
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9 332 the hazard of mortality and discriminated well between survival and death at our PICU with Area  
10  
11 333 under the curve AUROC of 76.4%. Which shows the score is sensitive in detecting mortality. This  
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13 334 scoring system is also validated and applicable in many PICUs across the world [27-31]. As to our  
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15 335 finding the high observed mortality rate than predicted mortality by PIM2 score cannot be  
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17 336 attributed to the severity of illness at admission. It indicates the poor quality of intensive care in  
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19 337 our setting. PIM2 Score was found to be nondiscriminatory for the risk of death in studies done in  
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21 338 Addis Ababa and India [29, 32].

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26 339 Patients who were mechanically ventilated had more than two times increased hazard of death.  
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28 340 This is in line with the findings of studies[33, 34]. This might be due to the fact that patients who  
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30 341 need mechanical ventilation are in advanced stages of the disease. The other explanation for this  
31  
32 342 could be ventilator-associated complications.

### 343 **Strength and limitations of the study**

344 This study has used prospective cohort study and better statistical function like survival analysis  
345 for better estimation and description were strengths of the study. However, the income of  
346 caregivers was not assessed because it was difficult to ascertain because the majority of admissions  
347 were from a rural area and they usually underreport the assets they have. PIM2 scoring was based  
348 on 9 out of 11 parameters as there was no Arterial blood gas analyzer in our PICU during the study  
349 period. Availability of medical equipment and PICU quality of care and their impact on survival  
350 was not fully assessed using standard parameters. Pediatric critical care is not just about saving



351 lives, so the degree of physiologic function retained at discharge should have been assessed using  
352 a standard checklist for all of the patients discharged.

## 353 **Conclusion**

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

## 360 **List of abbreviations**

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

## 369 **Declaration**

370 **stcox i.ADRESS i.criticalillnes i.DURICUIL\_rec i.sourceadmission i.occupation\_recoded**  
371 **i.CAREGIVErecoded i.age\_categorized PIM2SCOR i.COMPLICA i.COMORBID i.FLUID**  
372 **i.DAYOFADM i.MV i.ZSCORE**

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3 **373 Ethics approval and consent to participate**  
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6 374 Ethical clearance was obtained from the Institutional Ethical Review Board of College of Medicine  
7  
8 375 and Health Sciences, University of Gondar (ref.no 20/12/2018). Assent and informed written  
9  
10 376 consent was obtained from the care takers. The name or any other identifying information was not  
11  
12 377 recorded on the questionnaire and all information taken from the chart was kept strictly for  
13  
14 378 confidential and in a safe place. The information retrieved was used only for the study purpose.

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17 **379 Consent for publication**  
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19  
20 380 Not applicable  
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22 **381 Availability of data and material**  
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24  
25 382 Data is available from the corresponding author upon reasonable request.  
26

27 **383 Competing interests**  
28

29  
30 384 The authors declare that they have no competing interests.  
31  
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35

36  
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38  
39 387 data collection and analysis, interpretation of data, decision to publish, or preparation of the  
40  
41 388 manuscript.  
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44 **389 Authors' contributions**  
45

46  
47 390 NWT, ATA, and KST participated to design the study, performed data analysis, visualization,  
48  
49 391 validation the whole work and prepared the manuscript. NWT took part in funding acquisition,  
50  
51 392 data collection, supervision and software and other resources. All authors read and approved the  
52  
53 393 final manuscript.  
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5  
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7  
8 396 the University of Gondar Comprehensive specialized hospital. In addition we would like to  
9  
10 397 acknowledge the department of pediatrics and child health.  
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12  
13 398 **Figures and legends**  
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15 399 **Figure 1:** Kaplan-Meier failure (death) estimates curves by days of admission among children  
16  
17 400 treated in the pediatric intensive care unit of University of Gondar comprehensive specialized  
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19 401 hospital from February 1/2018 to July 30/2019  
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21 402 **Figure 2:** Kaplan-Meier failure (death) estimates curves by children critical illness admitted to  
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23 403 pediatric intensive care unit of University of Gondar comprehensive specialized hospital from  
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25 404 February 1/2018 to July 30/2019  
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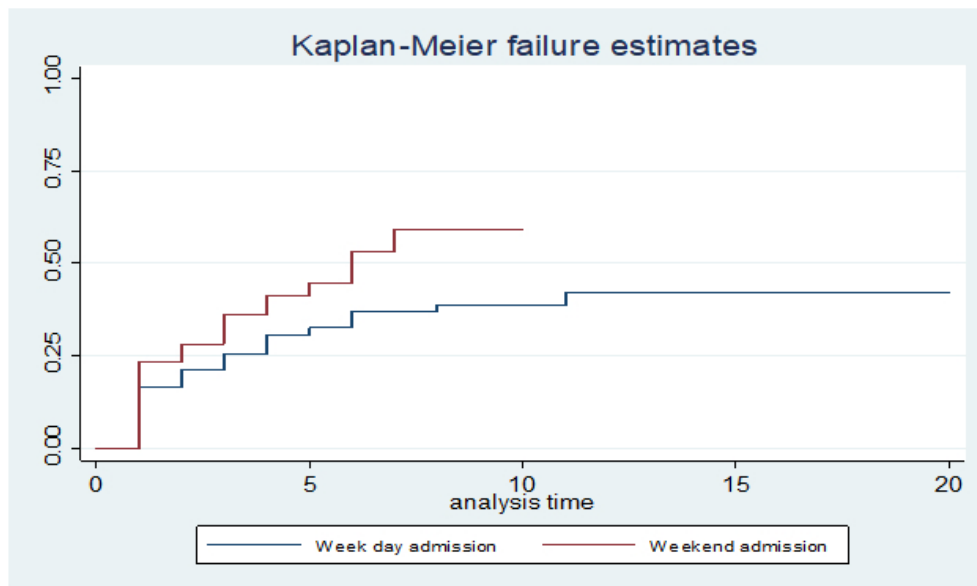
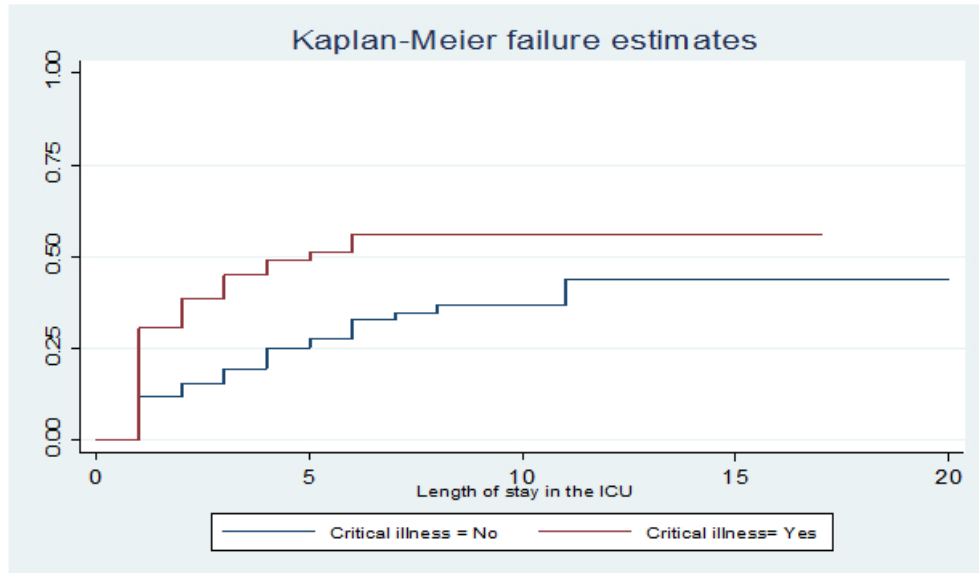


Figure 1: Kaplan-Meier failure (death) estimates curves by days of admission among children treated in the pediatric intensive care unit of University of Gondar comprehensive specialized hospital from February 1/2018 to July 30/2019

168x100mm (96 x 96 DPI)



26 Figure 2: Kaplan-Meier failure (death) estimates curves by children critical illness admitted to pediatric  
27 intensive care unit of University of Gondar comprehensive specialized hospital from February 1/2018 to July  
28 30/2019

29 164x96mm (96 x 96 DPI)

## STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
<b>Title and abstract</b>	1	Indicate the study's design with a commonly used term in the title or the abstract <i>The title describes the study design as "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". Page 1</i>
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found <i>The abstract describes the method used and Main findings. page 2, line 19-31</i>
<b>Introduction</b>		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported <i>The background and rationale are described in the Background, paragraphs 1, 2, 3, 4, 5 and 6. Page 4-5, Line 64-102</i>
Objectives	3	State specific objectives, including any pre specified hypotheses <i>The specific aims of the study are stated in the Background, paragraphs 6, page 5, line 94-104</i>
<b>Methods</b>		
Study design	4	Present key elements of study design early in the paper <i>The study design is discussed in paragraphs 1 of the Methods section, page 6, line 105-107</i>
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection <i>The institutional setting is described in paragraphs 2 line 108-120 of the Methods section. Study locations are described in paragraph 1 and 2 of the Methods section; and study timing is discussed in paragraphs of the Methods section. Participant recruitment is mentioned in population and sample section. Page 6</i>
Participants	6	<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants <i>Selection of the sample is discussed in paragraph 1 and 2 line 121-130, of population and sample subsection of the Methods section. page 6-7</i>
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable

		<p>Outcomes are discussed in the Outcomes subsection (paragraphs 3 of the Methods section).</p> <p>Data was collected by treating physicians using standardized questionnaire after taking consent from caretakers. Clinical characteristics like, SBP, pupillary light reflex, SaO<sub>2</sub> 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.</p> <p><b>Mentioned in the method section of 131-158, page 7-8</b></p>
	8*	<p>For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group</p> <p><b>Measurement of the outcomes are discussed in the data collection and measurement of variables subsection. Page 8</b></p>
Bias	9	<p>Describe any efforts to address potential sources of bias</p> <p><b>Mentioned in the method section of variable of the study and operational definitions Page 7-8</b></p>
Study size	10	<p>Explain how the study size was arrived at</p> <p><b>Sample size determination was discussed at method, population and sample section. Page 6</b></p>
Quantitative variables	11	<p>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why</p> <p><b>Use of variables is discussed in the data management and analysis subsection. Page 8</b></p>
Statistical methods	12	<p>(a) Describe all statistical methods, including those used to control for confounding</p> <p><b>Statistical methods are discussed in the data management and analysis subsection. Page 8 line 160-178</b></p>
		<p>(b) Describe any methods used to examine subgroups and interactions</p> <p>Described in in the data management and analysis subsection.</p> <p><b>Results are analysed by socio-demographic and personal attributes like age place of residence .</b></p>
		<p>(c) Explain how missing data were addressed</p> <p><b>None</b></p>
		<p>(e) Describe any sensitivity analyses</p> <p><b>None</b></p>

Continued on next page

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## Results

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed <i>At paragraph 1 of result section, page 9</i> (b) Give reasons for non-participation at each stage <i>None</i> (c) Consider use of a flow diagram <i>None</i>
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Provider characteristics are presented in Table 1, Table 2, and Table 3. (b) Indicate number of participants with missing data for each variable of interest <i>None</i>
Outcome data	15*	<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures Both numbers and percentages/proportions are reported throughout the <b>Results Section. Page 15-16 line 230-248</b>
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included <b>Adjusted results are presented for all outcomes. Page 16-17, table 4</b> (b) Report category boundaries when continuous variables were categorized <i>Not applicable</i> (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period <i>Not applicable.</i>
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses <i>None</i>
<b>Discussion</b>		
Key results	18	Summarise key results with reference to study objectives <b>Results are summarized in paragraphs, 1, and 2 of the Discussion section. Page 18, line 271-283</b>
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias <b>Strength and limitations are discussed in paragraphs 21, line 344-352</b>
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence <b>Discussed in discussion and conclusion sub section. 18-22</b>
Generalizability	21	<b>Discuss the generalizability (external validity) of the study results</b> <b>The representativeness of the sample is discussed in the final paragraph of the limitations subsection.</b>



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60**Other information**

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Funding 22 Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based  
*Not applicable*

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

# BMJ Open

**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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Date Submitted by the Author:	26-Mar-2020
Complete List of Authors:	Teshager, Nahom; Department of Pediatrics and Child Health, School of Medicine, College of Medicine and Health ScienceS, University of Gondar, Gondar, Ethiopia Amare, Ashenafi; University of Gondar College of Medicine and Health Sciences; Tamirat, koku; University of Gondar, Epidemiology and Biostatistics
<b>Primary Subject Heading</b>:	Intensive care
Secondary Subject Heading:	Emergency medicine
Keywords:	Paediatric intensive & critical care < ANAESTHETICS, ACCIDENT & EMERGENCY MEDICINE, INTENSIVE & CRITICAL CARE

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3 **1 Incidence and predictors of mortality among children admitted to the pediatric intensive**  
4 **care unit at the University of Gondar comprehensive specialized hospital, northwest**  
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7 **3 Ethiopia: A prospective observational cohort study**

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## 15 Abstract

16 **Objective:** To determine the incidence and predictors of mortality among children admitted to the  
17 pediatric intensive care unit at the University of Gondar comprehensive specialized hospital,  
18 northwest Ethiopia

19 **Design:** An institution-based prospective observational cohort study

20 **Participants:** A total of 313 children admitted to the intensive care unit of the University of  
21 Gondar Comprehensive specialized hospital during one year period were the study population.

22 **Measurements:** Data were collected using standard case record form, physical examination, and  
23 patient document review. Clinical characteristics like systolic blood pressure, pupillary light  
24 reflex, oxygen saturation, and need for mechanical ventilation was assessed and documented  
25 within the first hour of admission and entered into an electronic application to calculate the  
26 pediatrics index of mortality 2 (PIM 2) score. We fitted the cox-proportional hazard model to  
27 identify factors associated with mortality.

28 **Result:** The median age at admission was 48 months with interquartile range (IQR: 12 to 122),  
29 28.1% were infants followed by adolescents (21.4%), and 59.7% were males. The median  
30 observation time was 3days with (IQR: 1 to 6 days). One hundred two (32.6%) children died during  
31 the follow-up time, and the incidence of mortality was 6.9 deaths per 100 person-day observation.  
32 Weekend admission [Adjusted Hazard Ratio (AHR) =1.63, 95%CI: 1.02, 2.62], critical illness  
33 (AHR=1.79, 95%CI: 1.13, 2.85), need of mechanical ventilation ( AHR=2.36, 95%CI: 1.39, 4.01)  
34 and PIM2 score (AHR=1.53, 95%CI: 1.36, 1.72) were predictors of mortality.

35 **Conclusion:** Rate of mortality in the ICU was high, admission over weekends, need for  
36 mechanical ventilation, critical illness diagnoses, and higher PIM 2 scores were significant and  
37 independent predictors of mortality at the PICU.

## 38 **Strength and limitation of the study**

- 39 ➤ This study is a prospective cohort study and has used better statistical functions ( survival  
40 analysis) for better estimation and description.
- 41 ➤ In a resource-limited setting like Ethiopia, this study could help clinicians and health care  
42 planners practice evidence-based medicine.
- 43 ➤ The PIM2 scoring was based on 9 out of 11 parameters as there was no arterial blood gas  
44 analyzer in our PICU during the study period which could introduce misclassifications

## 45 **Introduction**

46 Patients having one or more failing vital function with a reasonable chance of recovery and  
47 postoperative patients requiring frequent monitoring are candidates for care in the intensive care  
48 unit (ICU). Children with acute neurological deterioration, respiratory distress, cardiovascular  
49 compromise, severe infections, and accidental poisoning constitute primary admissions in  
50 pediatric intensive care units [1].

51 Intensive care units (PICU) tremendously saves the life of patients who had potentially  
52 endangering illnesses, but the proportion of survivors with disabilities increased significantly [2].

53 The outcome of ICU care often measured by standardized mortality ratio (SMR), length of hospital  
54 stay, unplanned readmission rate, pain assessment, medication safety practice, and central venous  
55 catheter-associated infection prevention practice adoption. Mortality is the most studied outcome  
56 measure, though data in developing countries is scarce [3]. The mortality rate in the PICU in  
57 Ethiopian hospitals is significantly higher than that of developed countries' health facilities based  
58 on annual health sector morbidity and mortality reports. Published data on pediatric critical care  
59 in low-income countries remains sparse yet is much needed. This paucity of data makes practice  
60 modification and outcome improvement difficult (6).

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3 61 Most studies done on determinant factors of mortality in the PICU are from western countries and  
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5 62 are dependent on clinical and laboratory indices [2]. The few studies that considered epidemiologic  
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7 63 and socio-demographic factors were retrospective and cross-sectional studies and most did not  
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9 64 consider the severity of illness as a factor as they do not apply severity score in retrospective  
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11 65 studies [4]. The ICU equipment and set up in developing countries are not well studied [3, 5].  
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14 66 Hence, this study aimed to determine the incidence and predictors of mortality among children  
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16 67 admitted to a pediatric intensive care unit at the University of Gondar comprehensive specialized  
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18 68 hospital. Findings from this study could help clinicians and case managers for the proper  
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20 69 management of cases. This study could also serve as an entry point for the evaluation of pediatric  
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22 70 critical care and assist program planners in evidence-based decision making.  
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## 27 **Methods**

### 28 29 30 72 **Study design, period and setting**

31  
32 73 An institution-based prospective observational follow-up study was conducted among children age  
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34 74 1month to 18 years and admitted to the pediatric intensive care unit at the University of Gondar  
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36 75 comprehensive specialized hospital from February 1, 2018, to July 30, 2019.

37  
38 76 The PICU has six beds with electronic monitors and one mechanical ventilator; on average, there  
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40 77 are about 25 pediatric critical care admissions per month. The organizational detail of the PICU in  
41  
42 78 this hospital is lacking. Team composition is often limited to a general pediatrician, resident,  
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44 79 interns, and a handful of senior-level nurses, but there are no pediatric intensivists, respiratory  
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46 80 therapists, pharmacists, and dieticians in the team.  
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### 51 81 **Population and sample**

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3 82 The patients aged one month to 18 years admitted to the pediatric intensive care unit and stayed  
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5 83 for more than two hours in the hospital were included in the study. We excluded cases having  
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7 84 incomplete data, and surgical patients admitted only for recovery purposes from the study.  
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10 85 The sample size for this study was determined using a single population proportion of  $P=21\%$ ,  
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12 86 from previous Bangladesh study [1] with a 5% margin of error the sample size becomes 254 and  
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14 87 after adding 10% contingency, the sample became 279. A total of 376 patients were admitted to  
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16 88 the PICU from February 1, 2018, to July 30, 2019. We collected data from 327 patients who  
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18 89 fulfilled the inclusion criteria. Fourteen patients were excluded from the study due to incomplete  
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20 90 data.  
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### 23 91 **Data collection procedure**

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26 92 Data was collected by treating physicians using standard case record form after taking consent  
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28 93 from caretakers. Clinical characteristics like systolic blood pressure (SBO), pupillary light reflex,  
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30 94 the saturation of oxygen, and need for mechanical ventilation was assessed and documented within  
31  
32 95 the first hour and entered into an electronic application to calculate the pediatrics index of mortality  
33  
34 96 2 (PIM2) score. We took socio-demographic data and medical history by interview; and diagnosis,  
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36 97 laboratory indices, and courses in the hospital by chart review at discharge. We used the WHO  
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38 98 International Classification of Diseases 10<sup>th</sup> version for a disease category, and only the primary  
39  
40 99 diagnoses were used for ICD-10 assignment in patients having multiple diagnoses. The collected  
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42 100 data were double-checked by the data collector and the principal investigator. There were  
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44 101 orientations and training about data collection and the objective of the study every three months  
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46 102 and demonstration every Monday for treating physicians and data collectors. The principal  
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48 103 investigator supervised the overall process and checked the completeness of case record forms  
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50 104 every day.  
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## 105 **Variable of the study and operational definitions**

106 The primary dependent variable was time to death (event). In contrast, socio-demographic  
107 characteristics (age, sex, relation with the caregiver, care giver's educational status, occupation)  
108 and clinical characteristics (duration of illness before admission, source of admission, critical  
109 illness diagnosis, comorbidity, nutritional status, vaccination status, interventions given in the ICU  
110 and before admissions like fluid resuscitation, PIM2 score, multi-organ dysfunction  
111 syndrome(MODS ), and complications) were the independent variables.

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

113 Censored: refers to patients who were discharged alive from the ICU or those with no event of  
114 interest

115 length of stay(LOS): refers to the duration of stay in days from the date of admission to the date  
116 of discharge

117 Short term outcome: the outcome of the patient until he or she leaves the hospital

118 Critical illness: refers to the presence of sepsis, severe sepsis or septic shock within 24hours of  
119 admission or acute respiratory distress syndrome during ICU admission

120 MODS: refers to a potentially reversible physiologic derangement in two or more organ systems

## 121 **Data processing and analysis**

122 After we checked the data for its consistency and completeness, we entered it into EpiData version  
123 3.1 and exported to STATA version 14 for cleaning and analysis. Descriptive statistics like mean,  
124 median, proportions were carried out to summarize baseline characteristics and patterns of  
125 admission. Also, summary statistics like life table, log-rank test, and Kaplan-Meir curves were  
126 computed to determine the incidence rate (IR) of death and to compare survival curves between  
127 the different categories of the explanatory variables.

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3 128 Both bivariate and multivariate Cox proportional hazard models were used to identify the  
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5 129 predictors. Variables with p-value < 0.2 in the bivariate analysis were entered into the multivariate  
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7 130 proportional hazard model. Ninety-five percent confidence interval (95% CI) of hazard ratio was  
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9 131 computed, and variable having p-value < 0.05 in the multivariate cox-proportional hazards model  
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11 132 was considered as significantly and independently associated with the dependent variable. Cox-  
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13 133 proportional hazard model fitness was checked using the Schoenfeld residuals test.

### 14 15 16 17 134 **Ethical approval and consent to participate**

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19 135 Ethical clearance was obtained from the Institutional Ethical Review Board of the College of  
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21 136 Medicine and Health Sciences, the University of Gondar. Informed verbal consent was obtained  
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23 137 from the caretakers. The name or any other identifying information was not recorded on the data  
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25 138 collection form, and all information is taken from the chart was kept strictly confidential and in a  
26  
27 139 safe place. The information retrieved was used only for the study purpose.

### 30 31 140 **Patient and public involvement**

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33 141 Patients were not involved in the study

## 34 35 36 142 **Result**

### 37 38 39 143 **Socio-demographic characteristics**

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42 144 A total of 313 patients out of 376 patients admitted during the eighteen-month study period were  
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44 145 included in the final analysis. The median age at admission was 48 months with interquartile range  
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46 146 (IQR) of 12 to 122 months, about 28.1% were infants, followed by adolescents (21.4%). More  
47  
48 147 than half (59.7%) were males, more than three-fourth (77.3%) were from rural areas, and parents  
49  
50 148 were the commonest caregivers for the majority (93%) of children. The majority of caregivers had  
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149 no formal education (77.6%), and 71.2% were farmers, most patients were admitted in the spring  
 150 season (38.3%) followed by winter (27.2%) (Table 1).

151 Table 1: Socio-demographic characteristics of children and caregivers (n=313)

Characteristics	Frequency	Percentages (%)
<b>Age in months</b>		
≤ 12	88	28.1
13-24	29	9.3
25-60	66	21.1
61-132	63	20.1
>132	67	21.4
<b>Caregivers</b>		
Parents	291	
Grandparentsnts	8	2.6
Siblings	8	2.6
Others	6	1.9
<b>Caregiver level of education</b>		
No formal education	242	77.6
Primary school	32	10.2
Secondary school	17	5.4
College and above	21	6.7
<b>Caregivers occupation</b>		
Farmers	223	71.2
Merchants and private	32	10.2
Government employee	31	9.9
Unemployed	27	8.6
<b>Season of admission</b>		
Summer	63	20.1
Spring	45	14.4
Winter	85	27.2
Autumn	120	38.3

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### 153 **The clinical condition of admitted children**

154 More than three-fourth (77%) of patients were admitted over weekdays, 41.5% in the night shift,  
 155 and emergency room (60.4%), wards (13.1%) and referrals from other facilities (11.8%) were the  
 156 primary sources of admissions to the pediatric intensive care unit. The median duration of illness  
 157 before any health facility visit and admission to PICU was 3 (IQR: 1 to 7) and 6 (IQR: 3 to 13)  
 158 days, respectively. Forty-three (13.7%) patients had at least one comorbid illnesses, of which,  
 159 congenital malformations and genetic disorders (27.9%), cerebral palsy with or without seizure  
 160 disorders (25.6%), CKD (16.3%) and HIV/AIDS (14%) were the comorbid illnesses. One-third of  
 161 patients had critical illness diagnoses, of which (41%) had sepsis, (47%) septic shock and the  
 162 remaining (12%) had ARDS. About a third of patients (30.7%) had multiple organ dysfunction  
 163 syndromes (MODS).

164 The baseline severity of disease was assessed based on the PIM2 score calculated from an android  
 165 medical application QxMD within one hour after admission. The minimum score was -6.46 (with  
 166 predicted mortality rate = 0.2%), and the maximum score was 2.47 (predicted mortality rate  
 167 =92.2%). The mean predicted mortality rate based on the PIM2 score was 11.14%, which gave the  
 168 standard mortality ratio (SMR) of 2.94 (Table 2).

169 Table 2: The clinical condition of children admitted to the pediatric intensive care unit (n=313)

Characteristics	Frequency	Percentages (%)
<b>Critical illness diagnosis</b>		
Yes	100	31.9
No	213	68.1
<b>Duration of illness before PICU admission in days</b>		
≤Six days	71	22.7
>6 days	242	77.7
<b>Day of admission</b>		
Weekday	241	77
Weekend	72	23

<b>MODS</b>		
Yes	96	30.6
No	217	69.4
<b>Sources of admission</b>		
Home	36	11.5
Other facilities	37	11.8
Emergency room	189	60.4
Wards and Operating rooms	51	16.3
<b>Vaccination status</b>		
Complete	203	64.9
Incomplete	110	35.1
<b>Need mechanical ventilation</b>		
Yes	37	11.8
No	276	88.2
<b>Nutritional status, Z score</b>		
Normal	163	52.1
MAM	50	16
SAM	100	31.9
<b>Reasons for ICU admission</b>		
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
<b>Fluid resuscitation before ICU admission</b>		
Yes	164	52.4
No	149	47.6

#### 170 **Intensive care unit outcomes and the incidence of mortality**

171 Nearly one-third of patients (32.6%) died in the PICU, severe sepsis or multi-organ failure (MOF)  
 172 (41.2%) was the leading immediate cause of death in the PICU followed by respiratory failure  
 173 (23.5%), brain herniation (21.6%) and cardiac arrest accounts 12.7% of deaths.

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3 174 Fifty-six patients (17.9%) had developed complications during their stay in the PICU, of which  
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5 175 hospital-acquired sepsis (46.4%), followed by hospital-acquired pneumonia (17.9%), and  
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7 176 mechanical ventilator-associated complications (10.7%) were the most common complications.  
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10 177 Study subjects were followed for a different period, which gave a total of 1473 person-day  
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12 178 observations (49.1person-months), and the median length of stay in the ICU was 3 (IQR:1 to 6)  
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14 179 days. Of the total of 313 participants, 102 (32.6%) died during the follow-up time that gives the  
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16 180 incidence of mortality of 6.9 deaths per 100 person day observations (95%CI: 5.34 to 8.34 deaths  
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18 181 per 100 person-day). Of deaths reported, more than half (53.9%) died within 24 hours, 13(12.7%)  
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20 182 died between 24 and 48 hours, and the remaining died after 48 hours of admission. Differences in  
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22 183 all variables at baseline between strata were determined using the log-rank ( $\chi^2$ ) test, and the  
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24 184 equality of hazard was assessed for the different explanatory variables. Mechanical ventilation (P-  
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26 185 value=0.039) and critical illness (P-value= 0.0001) (Figure 1) and (Figure 2).  
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### 30 186 **Predictors of mortality in the ICU**

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32 187 The cox-proportional hazard model was fitted to identify predictors of mortality. Thus, caregivers'  
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34 188 occupation, weekend admission, critical illness diagnoses, PIM2 score, and need for mechanical  
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36 189 ventilation were predictors of mortality. Thus, government employee caregivers' associated with  
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38 190 a 65% lower risk of child mortality in the ICU compared to those farmers (AHR=0.35, 95%CI:  
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40 191 0.14, 0.89). Whereas, admission in the weekend and critical illness, the hazard of mortality was  
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42 192 1.63 (AHR=1.63, 95%CI: 1.02, 2.60) and 1.79 (AHR=1.79, 95%CI: 1.13, 2.85) times higher  
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44 193 compared to weekday admission and those with critical illness diagnosis, respectively. Similarly,  
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46 194 a unit increased in the PIM 2 score of a child at admission, the hazard of mortality was 1.53 times  
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48 195 increased, keeping other variables constant (AHR=1.53,95%CI:1.36, 1.72). Also, those patients  
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50 196 who need mechanical ventilation (MV), the hazard of mortality was 2.36 times higher compared  
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52 197 to those who did not need MV (AHR=2.36, 95%CI: 1.39, 4.01) (Table 3).  
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198 Table 3: Bivariate and multivariable Cox proportional hazard model to identify predictors of  
 199 mortality (n=313)

Variables	Status		CHR (95% CI)	AHR (95% CI)
	Event	Censored		
<b>Age</b>				
≤12	28	60	1	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)
<b>Address</b>				
Urban	28	43	1	1
Rural	74	168	0.73(0.47,1.13)	0.63(0.37,1.05)
<b>Caregiver' level of education</b>				
No formal education	96	195	1	1
Primary and above	6	16	0.78(0.34, 1.80)	1.26(0.51,3.13)
<b>Caregivers' occupation</b>				
Farmers	72	151	1	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)
<b>Day of admission</b>				
Weekday	71	170	1	1
Weekend	31	41	1.47(0.96,2.26)	1.63(1.02,2.60)**
<b>Source of admission</b>				
Home	9	27	1	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)
<b>Duration of illness before PICU admission</b>				
<6 days	39	107	1	1
≥6 days	63	104	1.43(0.96,2.12)	0.97(0.62,1.54)
<b>Comorbidities</b>				
No	85	185	1	1
Yes	17	26	1.31(0.78 2.21)	0.66(0.36 1.23)
<b>Critical illness diagnosis</b>				
No	53	160	1	1
Yes	49	51	2.05(1.39,3.04)	1.79(1.13, 2.85)**
<b>Nutritional status, Z score</b>				
Normal	45	118	1	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)
<b>PIM2 score</b>	-3.22±1.81		1.51(1.37,1.67)	1.53(1.36,1.72)**
<b>Mechanical ventilation need</b>				
No	79	197	1	1
Yes	23	14	1.93(1.20,3.10)	2.36(1.39,4.01)**
<b>Complications in the PICU</b>				
No	86	190	1	1
Yes	16	21	2.39(1.20,4.73)	1.62(0.79,3.31)
<b>Fluid resuscitation intervention before ICU admission</b>				
No	44	105	1	1
Yes	58	106	1.24(0.83 1.84)	0.92(0.59 1.44)

200 \* show statistical significance at a p-value of 0.05

## 201 Discussion

202 This study revealed that 32.6% of patients died with a rate of 6.92 deaths per 100 person-day  
 203 observations. Weekend admission, critical illness diagnosis, pediatrics index of mortality (PIM 2),  
 204 and need for mechanical ventilation were predictors of child mortality in the ICU. The proportion  
 205 of mortality in this study was consistent with retrospective cross-sectional studies done in the same  
 206 PICU from 2013 to 2016(30.9%)[6], Egypt (33.1%)[7], Nigeria (36.1%) [8] and Saudi Arabia  
 207 (37.4%)[9]. The proportion of mortality in our PICU is lower than the finding of a retrospective  
 208 cross-sectional study done in Jimma-Ethiopia (40%)[10]. The difference could be attributed to the  
 209 higher proportion of trauma patients admitted in their PICU as compared to ours. The other  
 210 possible reason could be that the higher proportion of left against medical advice (LAMAs) in our  
 211 study might underestimate the mortality rate in our study. However, it is higher than the mortality  
 212 rates in studies done in Pakistan (14%)[11], the average of Latin American countries (13.29%)  
 213 [12], India (10.58%)[13] and European countries (5%)[14]. The possible explanation for the  
 214 observed discrepancies might be due to suboptimal care, the inadequacy of both diagnostic, and  
 215 interventional facilities in our PICU.

216 Children who were admitted over the weekends had nearly twice an increased risk of mortality  
 217 than those admitted over weekdays, which is consistent with the findings of studies done in



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3 218 Canada, Finland, and Austria [14-16]. This increased mortality over weekends might be due to  
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5 219 failure to early recognize deteriorations at wards and other sources as a result of reduced staffing  
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8 220 ratios. Access to diagnostic services is limited at weekends, which limits the likelihood of putting  
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10 221 correct diagnoses, there could be unrecognized deteriorations during handover round times and  
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12 222 delays in giving interventions. The fact that duty teams come from other wards during weekends  
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14 223 may contribute to the increased mortality over weekends. However, our finding was not supported  
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17 224 by three American studies and studies done in the United Kingdom and the Republic of Ireland  
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19 225 [17, 18]. This discrepancy could be explained by the better standard of care they have and 24 hours  
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21 226 around the clock full staffing.

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24 227 This study also reviewed that caregiver occupation of government-employed associated with lower  
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26 228 risk mortality compared to caregivers of peasants. This finding could be explained by differences  
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28 229 in health-seeking behavior and early identification of danger signs between these groups.

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31 230 The child who had critical illness diagnosis had an increased risk of mortality compared to those  
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33 231 who had not. This difference could be because patients with critical illnesses have a low reserve  
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35 232 of physiologic function. This finding was consistent with other studies.

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38 233 Amongst many disease severity assessment tools at baseline, we used PIM2 as it does not need  
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40 234 extensive laboratory investigation, and it is not affected by subsequent interventions since it is  
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42 235 scored within one hour of admission. A unit increment in the PIM2 score had doubled the hazard  
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44 236 of mortality, which shows the score is sensitive in detecting mortality, and this scoring system is  
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47 237 also validated and applicable in many PICUs across the world [19-23]. The higher observed  
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49 238 mortality rate than the predicted one by PIM2 score in our study indicates the poor quality of  
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51 239 intensive care in our setting. PIM 2 Score was found to be nondiscriminatory for the risk of death  
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53 240 in studies done in Addis Ababa and India [21, 24].

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3 241 Patients who needed mechanical ventilation had increased mortality compared to those who did  
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5 242 not need it. This finding is in line with the findings of other studies [25, 26]. The explanation for  
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7 243 this might be because patients who need mechanical ventilation tend to have advanced disease  
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9 244 stages. This can also be attributed to a limited number of mechanical ventilators we had. There  
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11 245 might also be unrecognized ventilator-associated complications.  
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### 16 246 **Strength and limitations of the study**

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18 247 This study is a prospective cohort study with a better statistical function (survival analysis). The  
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20 248 PIM2 scoring was based on 9 out of 11 parameters as there was no Arterial blood gas analyzer in  
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22 249 our PICU during the study period. The availability of medical equipment and PICU quality of care  
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24 250 and their impact on patient survival was not adequately assessed using standard parameters.  
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26 251 Pediatric critical care is not just about saving lives, so the degree of physiologic function retained  
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28 252 at discharge should have been assessed using a standard checklist for all of the patients discharged.  
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### 32 253 **Conclusion**

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35 254 Rate of mortality in the ICU was high, admission over weekends, need for mechanical ventilation,  
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37 255 critical illness diagnoses, and higher PIM 2 score were found to be significant and independent  
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39 256 predictors of mortality at the PICU. Availing mechanical ventilators up to the standard, intensivist,  
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41 257 and full staffing around the clock, including weekends and paying due attention for critical illness  
42  
43 258 and critical illness diagnoses tailored care, may improve PICU outcome. Using PIM 2 score to  
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45 259 prognosticate outcomes and tunnel resources to the most in need patients and council caregivers  
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47 260 might be advisable.  
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### 51 261 **List of abbreviations**

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3 262 AHR: Adjusted Hazard Ratio, AKI: Acute Kidney Injury, CI: Confidence Intervals, CHR: Crude  
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5 263 Hazard Ratio, HAS: Hospital-Acquired Sepsis, HAP: Hospital-Acquired Pneumonia, ICD:  
6  
7 264 International Classifications of Disease, ICU: Intensive Care Unit, IQR: Interquartile Range, IR:  
8  
9 265 Incidence Rate, LAMA: Left Against Medical Advice, LOS: Length of Hospital stay, MAM:  
10  
11 266 Moderate Acute Malnutrition, MODS: Multiple Organ Dysfunction Syndrome, MV: Mechanical  
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13 267 Ventilation, PI: Principal Investigator, PICU: Pediatric Intensive Care Unit, PIM: Pediatrics Index  
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15 268 Mortality, SAM: Severe Acute Malnutrition, OR: Operation Room, USA: the United States of  
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17 269 America, WHO, World Health Organization  
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## 22 270 **Declaration**

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24 271 **stcox i.ADRESS i.criticalillnes i.DURICUIL\_rec i.sourceadmission i.occupation\_recoded**  
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26 272 **i.CAREGIVerecoded i.age\_categorized PIM2SCOR i.COMPLICA i.COMORBID i.FLUID**  
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28 273 **i.DAYOFADM i.MV i.Z SCORE**  
29

## 30 274 **Ethics approval and consent to participate**

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32  
33 275 Ethical clearance was obtained from the Institutional Ethical Review Board of College of Medicine  
34  
35 276 and Health Sciences, University of Gondar. Assent and informed written consent were obtained  
36  
37 277 from the caretakers. The name or any other identifying information was not recorded on the data  
38  
39 278 collection form. All information taken from the chart was kept strictly confidential in a safe place.  
40  
41  
42 279 The information retrieved was used only for the study purpose.  
43

## 44 280 **Consent for publication**

45  
46  
47 281 Not applicable  
48

## 49 282 **Availability of data and material**

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51  
52 283 Data is available from the corresponding author upon reasonable request.  
53  
54  
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## 284 **Competing interests**

285 The authors declare that they have no competing interests.

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288 design, data collection, and analysis, interpretation of data, the decision to publish, or preparation  
289 of the manuscript.

## 290 **Authors' contributions**

291 NWT, ATA, and KST participated in designing the study, performed data analysis, visualization,  
292 validation of the whole work, and prepared the manuscript. NWT took part in funding acquisition,  
293 data collection, supervision and software, and other resources. All authors read and approved the  
294 final manuscript.

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297 the University of Gondar Comprehensive specialized hospital. We also would like to acknowledge  
298 the department of pediatrics and child health.

## 299 **Figures and legends**

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

303 **Figure 2:** Kaplan-Meier failure (death) estimates curves by children critical illness admitted to the  
304 pediatric intensive care unit of University of Gondar comprehensive specialized hospital from  
305 February 1/2018 to July 30/2019

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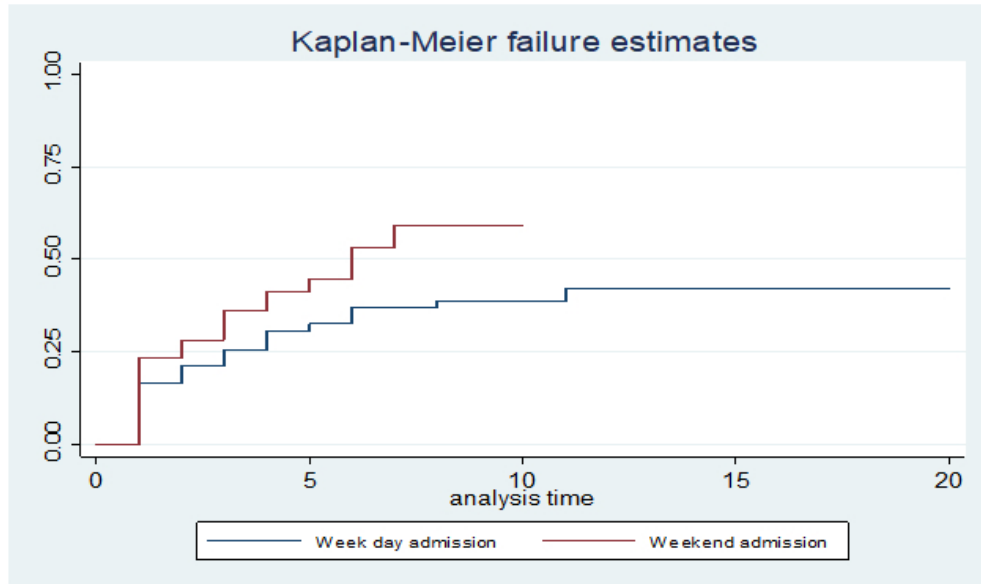


Figure 1: Kaplan-Meier failure (death) estimates curves by days of admission among children treated in the pediatric intensive care unit of University of Gondar comprehensive specialized hospital from February 1/2018 to July 30/2019

168x100mm (96 x 96 DPI)

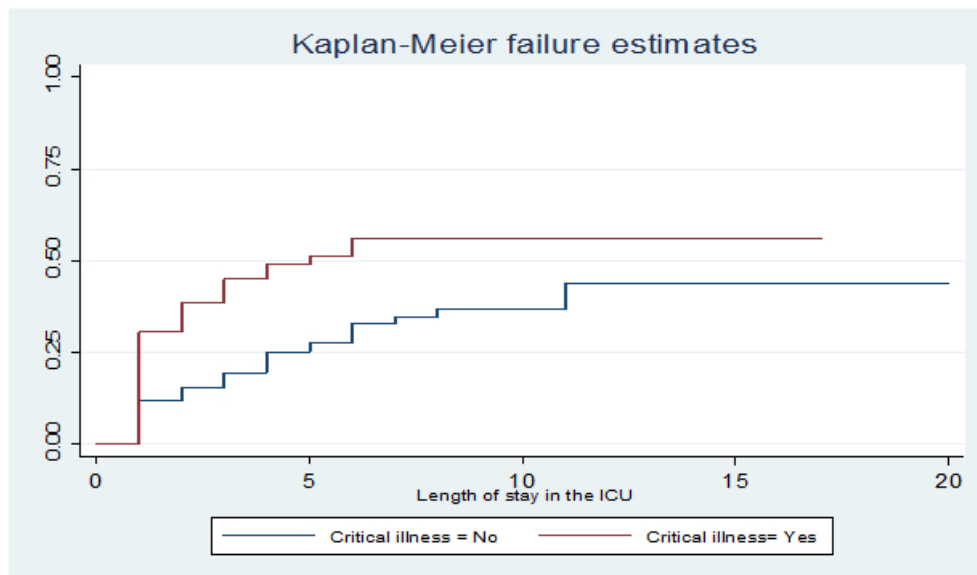


Figure 2: Kaplan-Meier failure (death) estimates curves by children critical illness admitted to pediatric intensive care unit of University of Gondar comprehensive specialized hospital from February 1/2018 to July 30/2019

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## STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	Indicate the study's design with a commonly used term in the title or the abstract <i>The title describes the study design as "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". Page 1</i>
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found <i>The abstract describes the method used and Main findings. page 2, line 19-31</i>
<b>Introduction</b>		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported <i>The background and rationale are described in the Background, paragraphs 1, 2, 3, 4, 5 and 6. Page 4-5, Line 64-102</i>
Objectives	3	State specific objectives, including any pre specified hypotheses <i>The specific aims of the study are stated in the Background, paragraphs 6, page 5, line 94-104</i>
<b>Methods</b>		
Study design	4	Present key elements of study design early in the paper <i>The study design is discussed in paragraphs 1 of the Methods section, page 6, line 105-107</i>
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection <i>The institutional setting is described in paragraphs 2 line 108-120 of the Methods section. Study locations are described in paragraph 1 and 2 of the Methods section; and study timing is discussed in paragraphs of the Methods section. Participant recruitment is mentioned in in population and sample section. Page 6</i>
Participants	6	<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants <i>Selection of the sample is discussed in paragraph 1 and 2 line 121-130, of population and sample subsection of the Methods section. page 6-7</i>
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable

		<p>Outcomes are discussed in the Outcomes subsection (paragraphs 3 of the Methods section).</p> <p>Data was collected by treating physicians using standardized questionnaire after taking consent from caretakers. Clinical characteristics like, SBP, pupillary light reflex, SaO<sub>2</sub> 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.</p> <p><b>Mentioned in the method section of 131-158, page 7-8</b></p>
	8*	<p>For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group</p> <p><b>Measurement of the outcomes are discussed in the data collection and measurement of variables subsection. Page 8</b></p>
Bias	9	<p>Describe any efforts to address potential sources of bias</p> <p><b>Mentioned in the method section of variable of the study and operational definitions Page 7-8</b></p>
Study size	10	<p>Explain how the study size was arrived at</p> <p><b>Sample size determination was discussed at method, population and sample section. Page 6</b></p>
Quantitative variables	11	<p>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why</p> <p><b>Use of variables is discussed in the data management and analysis subsection. Page 8</b></p>
Statistical methods	12	<p>(a) Describe all statistical methods, including those used to control for confounding</p> <p><b>Statistical methods are discussed in the data management and analysis subsection. Page 8 line 160-178</b></p>
		<p>(b) Describe any methods used to examine subgroups and interactions</p> <p>Described in in the data management and analysis subsection.</p> <p><b>Results are analysed by socio-demographic and personal attributes like age place of residence .</b></p>
		<p>(c) Explain how missing data were addressed</p> <p><b>None</b></p>
		<p>(e) Describe any sensitivity analyses</p> <p><b>None</b></p>

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60**Results**

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed <i>At paragraph 1 of result section, page 9</i> (b) Give reasons for non-participation at each stage <i>None</i> (c) Consider use of a flow diagram <i>None</i>
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Provider characteristics are presented in Table 1, Table 2, and Table 3. (b) Indicate number of participants with missing data for each variable of interest <i>None</i>
Outcome data	15*	<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures Both numbers and percentages/proportions are reported throughout the <b>Results Section. Page 15-16 line 230-248</b>
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included <b>Adjusted results are presented for all outcomes. Page 16-17, table 4</b> (b) Report category boundaries when continuous variables were categorized <i>Not applicable</i> (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period <i>Not applicable.</i>
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses <i>None</i>
<b>Discussion</b>		
Key results	18	Summarise key results with reference to study objectives <b>Results are summarized in paragraphs, 1, and 2 of the Discussion section. Page 18, line 271-283</b>
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias <b>Strength and limitations are discussed in paragraphs 21, line 344-352</b>
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence <b>Discussed in discussion and conclusion sub section. 18-22</b>
Generalizability	21	<b>Discuss the generalizability (external validity) of the study results The representativeness of the sample is discussed in the final paragraph of the limitations subsection.</b>

**Other information**

---

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based
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*Not applicable*

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

# BMJ Open

**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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Article Type:	Original research
Date Submitted by the Author:	18-Jun-2020
Complete List of Authors:	Teshager, Nahom; Department of Pediatrics and Child Health, School of Medicine, College of Medicine and Health ScienceS, University of Gondar, Gondar, Ethiopia Amare, Ashenafi; University of Gondar College of Medicine and Health Sciences; Tamirat, koku; University of Gondar, Epidemiology and Biostatistics
<b>Primary Subject Heading</b>:	Intensive care
Secondary Subject Heading:	Emergency medicine
Keywords:	Paediatric intensive & critical care < ANAESTHETICS, ACCIDENT & EMERGENCY MEDICINE, INTENSIVE & CRITICAL CARE

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7 **3 Ethiopia: A prospective observational cohort study**

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3 **15 Abstract**  
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5 **16 Objective:** To determine the incidence and predictors of mortality among children admitted to the  
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7 pediatric intensive care unit at the University of Gondar comprehensive specialized hospital,  
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9 northwest Ethiopia  
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12 **19 Design:** A single-center prospective observational cohort study  
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15 **20 Participants:** A total of 313 children admitted to the intensive care unit of the University of  
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17 Gondar comprehensive specialized hospital during one-and-a-half-year period.  
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20 **22 Measurements:** Data were collected using standard case record form, physical examination, and  
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22 patient document review. Clinical characteristics like systolic blood pressure, pupillary light  
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24 reflex, oxygen saturation, and need for mechanical ventilation were assessed and documented  
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26 within the first hour of admission and entered into an electronic application to calculate the  
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28 Pediatric Index of Mortality 2 (PIM 2) score. We fitted the Cox proportional hazards model to  
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30 identify predictors of mortality.  
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34 **28 Result:** The median age at admission was 48 months with interquartile range (IQR: 12 to 122),  
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36 28.1% were infants, and adolescents accounted for 21.4%. Of the total patients studied, 59.7%  
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38 were males. The median observation time was three days with (IQR: 1 to 6). One hundred two  
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40 (32.6%) children died during the follow-up time, and the incidence of mortality was 6.9 deaths per  
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42 100 person-day observation. Weekend admission [Adjusted Hazard Ratio (AHR) =1.63, 95%CI:  
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44 1.02, 2.62], critical illness diagnoses (AHR=1.79, 95%CI: 1.13, 2.85), need for mechanical  
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46 ventilation (AHR=2.36, 95%CI: 1.39, 4.01) and PIM 2 score (AHR=1.53, 95%CI: 1.36, 1.72) were  
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48 the predictors of mortality.  
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36 **Conclusion:** The rate of mortality in the Pediatric intensive care unit (PICU) was high, admission  
37 over weekends, need for mechanical ventilation, critical illness diagnoses, and higher Pediatric  
38 Index of Mortality 2 scores were significant and independent predictors of mortality.

### 39 **Strength and limitation of the study**

- 40 ➤ This study was a prospective cohort study and had used better statistical functions (survival  
41 analysis) for better estimation and prediction of mortality.
- 42 ➤ This study could help clinicians and health care planners practice evidence-based medicine  
43 in a resource-limited setting like ours.
- 44 ➤ The PIM 2 scoring was done based on 9 out of 11 parameters as there was no arterial blood  
45 gas analyzer in our set up during the study period that might result in misclassification.

### 46 **Introduction**

47 Pediatric intensive care units (PICUs) are essential areas of service to save the lives of children  
48 with life-threatening conditions. Children with acute neurological deterioration, respiratory  
49 distress, cardiovascular compromise, severe infections, and accidental poisoning constitute  
50 primary admissions in PICUs [1].

51 Children admitted to the PICU may die or survive with or without permanent sequelae, and the  
52 proportion of survivors with disabilities has increased significantly [2]. It is essential to prioritize  
53 and tunnel resources to the most fruitful practice based on the prediction of patient outcomes,  
54 especially in resource-limited setups.

55 The outcome of intensive care is often measured by standardized mortality ratio (SMR), length of  
56 hospital stays, unplanned readmission rate, pain assessment, medication safety practice, and  
57 central venous catheter-associated infection prevention practice adoption.

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3 58 Mortality is the most studied outcome measure within PICUs, though data from developing  
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5 59 countries are scarce [3]. The mortality rate among PICUs in Ethiopian hospitals is thought to be  
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7 60 significantly higher than in developed countries based on annual health sector morbidity and  
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9 61 mortality reports. Published data on pediatric critical care in low-income countries remains sparse.  
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11 62 This paucity of data makes practice modification and outcome improvement difficult. Also, most  
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13 63 studies done on predictors of mortality in the PICUs are from high-income countries and are  
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15 64 dependent on clinical and laboratory indices, which are not readily available in low-income  
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17 65 countries [2]. The few studies that considered epidemiologic and sociodemographic factors were  
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19 66 retrospective and cross-sectional, and most did not consider important parameters[4].  
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22 67 This study aimed to determine the incidence and predictors of mortality among children admitted  
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24 68 to a pediatric intensive care unit at the University of Gondar comprehensive specialized hospital.  
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26 69 It might add to the knowledge of mortality and its predictors, thereby hoping to plan the most  
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28 70 efficient method of intervention for those at higher mortality risk, thus contributing to recovery as  
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30 71 well as making the assessment of the performance of the services delivered.  
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## 38 73 **Methods**

### 39 74 **Study design, period and setting**

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41 75 A single-center prospective cohort study was conducted among children aged one month to 18  
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43 76 years admitted to the PICU at the University of Gondar comprehensive specialized hospital from  
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45 77 February 1, 2018, to July 30, 2019.

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47 78 The PICU has six beds with electronic monitors and one mechanical ventilator; on average, there  
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49 79 are about 25 pediatric critical care admissions per month. The organizational detail of the PICU in  
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51 80 this hospital is lacking. Team composition is often limited to a general pediatrician, resident,  
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3 81 interns, and a handful of senior-level nurses, but there are no pediatric intensivists, respiratory  
4  
5 82 therapists, pharmacists, and dieticians in the team.  
6  
7

### 8 83 **Population and sample**

9  
10 84 Patients who stayed for more than two hours in the hospital were included in the study. We  
11  
12  
13 85 excluded patients having incomplete data, and surgical patients admitted only for recovery  
14  
15 86 purposes from the study.

16  
17 87 The sample size for this study was determined using a single population proportion of  $P=21\%$ ,  
18  
19 88 from previous Bangladesh study [1] with a 5% margin of error; the sample size became 254, and  
20  
21  
22 89 after adding 10% contingency, the sample became 279. A total of 376 patients were admitted to  
23  
24 90 the PICU during the study period. We collected data from 327 patients who fulfilled the inclusion  
25  
26  
27 91 criteria. Fourteen patients were excluded from the study due to incomplete data.  
28

### 29 92 **Data collection procedure**

30  
31 93 Data was collected by treating physicians using standard case record form after receiving consent  
32  
33  
34 94 from caretakers. Clinical characteristics like systolic blood pressure (SBP), pupillary light reflex,  
35  
36 95 the saturation of oxygen, and need for mechanical ventilation was assessed and documented within  
37  
38 96 the first hour and entered into an electronic application to calculate the Pediatric Index of Mortality  
39  
40  
41 97 2 (PIM 2) score. We took sociodemographic data and medical history by interview; and diagnosis,  
42  
43 98 laboratory indices, and the clinical course during the hospital by chart review at discharge. We  
44  
45 99 used the World Health Organization (WHO) International Classification of Diseases 10<sup>th</sup> version  
46  
47  
48 100 (ICD-10) for disease category, and only the primary diagnoses were used for ICD-10 assignment  
49  
50 101 in patients having multiple diagnoses. The collected data were double-checked by the data  
51  
52 102 collector and the principal investigator. There were orientations and training about data collection  
53  
54  
55 103 and the objective of the study every three months and demonstration every Monday for treating  
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3 104 physicians and data collectors. The principal investigator supervised the overall process and  
4  
5 105 checked the completeness of case record forms every day. No direct patient care was provided by  
6  
7  
8 106 investigators, who only accessed patients' records.  
9

### 10 107 **Variable of the study and operational definitions**

11  
12  
13 108 The primary dependent variable was time to death (event). In contrast, sociodemographic  
14  
15 109 characteristics included age, sex, relation with the caregiver, caregiver's educational status, and  
16  
17  
18 110 occupation. Clinical characteristics included duration of illness before admission, source of  
19  
20  
21 111 admission, critical illness diagnosis, comorbidity, nutritional status, vaccination status,  
22  
23 112 interventions given in the PICU, and before admissions like fluid resuscitation, PIM 2 score, multi-  
24  
25 113 organ dysfunction syndrome (MODS), and complications.  
26

27  
28 114 Event (death): is defined as a patient who died in the hospital during treatment.  
29

30  
31 115 Censored: refers to patients who were discharged alive from the PICU or those with no event of  
32  
33 116 interest.  
34

35 117 Length of stay (LOS): refers to the duration of stay in days from the date of admission to the date  
36  
37 118 of discharge.  
38

39  
40 119 Short term outcome: the outcome of the patient until he or she leaves the hospital  
41

42 120 Critical illness: refers to the presence of sepsis, severe sepsis or septic shock within 24 hours of  
43  
44 121 admission or acute respiratory distress syndrome during PICU admission  
45

46 122 MODS: refers to a potentially reversible physiologic derangement in two or more organ systems  
47  
48

### 49 123 **Data processing and analysis**

50  
51 124 After we checked the data for its consistency and completeness, we entered data into EpiData  
52  
53  
54 125 version 3.1 and exported to STATA version 14 for cleaning and analysis. Descriptive statistics like  
55  
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2  
3 126 mean, median, and proportions were carried out to summarize baseline characteristics and patterns  
4  
5 127 of admission. Also, summary statistics like life table, log-rank test, and Kaplan-Meier curves were  
6  
7  
8 128 computed to determine the incidence rate (IR) of death and to compare survival curves between  
9  
10 129 the different categories of the explanatory variables.

11  
12 130 Both bivariate and multivariate Cox proportional hazards models were used to identify the  
13  
14 131 predictors. Variables with p-value < 0.2 in the bivariate analysis were entered into the multivariate  
15  
16 132 proportional hazard model. Ninety-five percent confidence intervals (95% CI) of hazard ratio were  
17  
18 133 computed, and variables having p-value < 0.05 in the multivariate Cox proportional hazards model  
19  
20 134 were considered as significantly and independently associated with the dependent variable. Cox  
21  
22 135 proportional hazards model fitness was checked using the Schoenfeld residuals test.

### 23 24 136 **Ethical approval and consent to participate**

25  
26  
27 137 Ethical clearance was obtained from the Institutional Ethical Review Board of the University of  
28  
29 138 Gondar's College of Medicine and Health Sciences. Informed verbal consent was obtained from  
30  
31 139 the caretakers. The name or any other identifying information was not recorded on the data  
32  
33 140 collection form, and all information taken from the chart was kept strictly confidential and in a  
34  
35 141 safe place. The information retrieved was used only for the study purpose.

### 36 37 38 142 **Patient and public involvement**

39  
40  
41 143 There was no direct patient contact, and investigators accessed only patient records.

## 42 43 144 **Result**

### 44 45 145 **Sociodemographic characteristics**

46  
47 146 A total of 313 patients out of 376 admitted during the 18-month study period were included in the  
48  
49 147 final analysis. The median age at admission was 48 months with interquartile range (IQR: 12 to  
50  
51 148 122), with a male to female ratio of 1.7:1, as shown in Table 1. The majority of caregivers (92.9%)

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2  
3 149 were parents. More than three-fourth (77.6%) of caregivers had no formal education, and 71.2%  
4  
5 150 were farmers. Most patients were admitted in the spring season (38.3%), followed by winter  
6  
7  
8 151 (27.2%) (Table 1).  
9

10 152 **Table 1:** Sociodemographic characteristics of patients  
11

Characteristics	Frequency	Percentages (%)
<b>Age in months</b>		
≤ 12	88	28.1
13-24	29	9.3
25-60	66	21.1
61-132	63	20.1
>132	67	21.4
<b>Sex</b>		
Male	188	59.7
Female	125	39.3
<b>Season of admission</b>		
Summer	63	20.1
Spring	45	14.4
Winter	85	27.2
Autumn	120	38.3
<b>Vaccination status</b>		
Complete	203	64.9
Incomplete/unvaccinated	110	35.1
<b>Comorbid illness (n=43)</b>		
Congenital malformations/genetic disorders	12	27.9
Cerebral palsy with or without seizure disorders	11	25.6
Chronic kidney disease	7	16.3
HIV/AIDS	6	14
Others	7	16.3

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51 153 HIV/AIDS: Human immunodeficiency virus infection and acquired immune deficiency syndrome  
52

53 154 **The clinical condition of admitted children**  
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155 The primary source of admissions in the PICU was the emergency room (60.4%), inpatient  
 156 pediatrics wards (13.1%), and referrals from other facilities (11.8%). More than three-fourth (77%)  
 157 of patients were admitted over weekdays and 41.5% in the night shift. The median duration of  
 158 illness before any health facility visit and admission to PICU was 3 (IQR: 1 to 7) and 6 (IQR: 3 to  
 159 13) days, respectively.

160 One-third of patients had critical illness diagnoses, of which (41%) had sepsis, (47%) septic shock,  
 161 and the remaining (12%) had acute respiratory distress syndrome. About one-third of patients  
 162 (30.7%) had multiple organ dysfunction syndromes (MODS).

163 The minimum PIM 2score was -6.46 (with predicted mortality rate = 0.2%), and the maximum  
 164 score was 2.47 (predicted mortality rate =92.2%). The mean predicted mortality rate based on the  
 165 PIM 2 score was 11.14%, which gave the standard mortality ratio (SMR) of 2.94 (Table 2).

166 **Table 2:** Clinical condition of patients

Characteristics	Frequency	Percentages (%)
<b>Critical illness diagnosis</b>		
Yes	100	31.9
No	213	68.1
<b>Duration of illness before PICU admission in days</b>		
≤6 days	71	22.7
>6 days	242	77.7
<b>Day of admission</b>		
Weekday	241	77
Weekend	72	23
<b>Multi-organ dysfunction syndrome</b>		
Yes	96	30.6
No	217	69.4
<b>Sources of admission</b>		
Home	36	11.5
Other facilities	37	11.8
Emergency room	189	60.4
Wards and Operating rooms	51	16.3
<b>Need for mechanical ventilation</b>		
Yes	37	11.8

No	276	88.2
<b>Nutritional status, Z score</b>		
Normal	163	52.1
Moderate acute malnutrition	50	16
Severe acute malnutrition	100	31.9
<b>Reasons for PICU admission</b>		
Altered mental status	145	46.3
Respiratory failure	82	26.5
Sepsis	59	18.8
Shock	55	17.6
Seizure	46	14.7
Diabetic ketoacidosis	24	7
Acute kidney injury	24	7
Congestive heart failure	21	6.7
Hemorrhage	14	4.5
Trauma	6	1.9
Others	23	7.3
<b>Fluid resuscitation before PICU admission</b>		
Yes	164	52.4
No	149	47.6

167 PICU: Pediatric intensive care unit

### 168 **Intensive care unit outcomes and the incidence of mortality**

169 Nearly one-third of patients (32.6%) died in the PICU. Severe sepsis or multi-organ failure (MOF)  
 170 (41.2%) was the leading immediate cause of death in the PICU followed by respiratory failure  
 171 (23.5%), brain herniation (21.6%), and cardiac arrest (12.7%).

172 Fifty-six patients (17.9%) developed complications during their stay in the PICU, including  
 173 hospital-acquired sepsis (46.4%), hospital-acquired pneumonia (17.9%), and mechanical  
 174 ventilator-associated complications (10.7%).

175 Study subjects were followed during the study period, which gave a total of 1473 person-day  
 176 observations (49.1 person-months), and the median length of stay in the ICU was 3 (IQR:1 to 6)  
 177 days. Of the total of 313 participants, 102 (32.6%) died during the follow-up time. The incidence  
 178 of mortality was 6.9 deaths per 100-person day observations (95%CI: 5.34 to 8.34 deaths per 100



179 person-day). Among deaths reported, more than half (53.9%) died within 24 hours, 13 (12.7%)  
 180 died between 24 and 48 hours, and the remaining died after 48 hours of admission. Differences in  
 181 all variables at baseline between strata were determined using the log-rank ( $\chi^2$ ) test, and the  
 182 equality of hazard was assessed for the different explanatory variables. Kaplan Meir failure curve  
 183 was plotted for weekend admission (P-value=0.039) and critical illness (P-value= 0.0001) shows  
 184 significant difference. (Figure 1) and (Figure 2).

### 185 Predictors of mortality in the PICU

186 The Cox proportional hazards model was fitted to identify predictors of mortality. From the  
 187 multivariate analysis, caregivers' occupation, weekend admission, critical illness diagnoses, PIM  
 188 2 score, and need for mechanical ventilation were predictors of mortality. Mortality was 65% lower  
 189 for those whose caregivers were government employees compared to farmers (AHR=0.35, 95%CI:  
 190 0.14, 0.89). The hazard of mortality was 1.63 times higher for patients admitted over weekends  
 191 (AHR=1.63, 95%CI: 1.02, 2.60) and 1.79 times higher in patients who had critical illness  
 192 diagnoses(AHR=1.79, 95%CI: 1.13, 2.85) compared to weekday admission and those without  
 193 critical illness diagnosis, respectively. Similarly, each one-unit increase in the PIM 2 score  
 194 increased the hazard of mortality 1.53 times, keeping other variables constant (AHR=1.53,  
 195 95%CI:1.36, 1.72). Also, those patients who met the criteria for mechanical ventilation (MV), the  
 196 hazard of mortality was 2.36 times higher compared to those who did not need MV (AHR=2.36,  
 197 95%CI: 1.39, 4.01) (Table 3).

198 **Table 3:** Bivariate and multivariate Cox proportional hazard model Fit for different independent  
 199 variables

Variables	Status		CHR (95% CI)	AHR (95% CI)
	Event	Censored		
<b>Age (months)</b>				
≤12	28	60	1	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)
<b>Address</b>				
Urban	28	43	1	1
Rural	74	168	0.73(0.47,1.13)	0.63(0.37,1.05)
<b>Caregiver' level of education</b>				
No formal education	96	195	1	1
Primary and above	6	16	0.78(0.34, 1.80)	1.26(0.51,3.13)
<b>Caregivers' occupation</b>				
Farmers	72	151	1	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)
<b>Day of admission</b>				
Weekday	71	170	1	1
Weekend	31	41	1.47(0.96,2.26)	1.63(1.02,2.60) *
<b>Source of admission</b>				
Home	9	27	1	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)
<b>Duration of illness before PICU admission</b>				
<6 days	39	107	1	1
≥6 days	63	104	1.43(0.96,2.12)	0.97(0.62,1.54)
<b>Comorbidities</b>				
No	85	185	1	1
Yes	17	26	1.31(0.78 ,2.21)	0.66(0.36, 1.23)
<b>Critical illness diagnosis</b>				
No	53	160	1	1
Yes	49	51	2.05(1.39,3.04)	1.79(1.13, 2.85) *
<b>Nutritional status, Z score</b>				
Normal	45	118	1	1
Moderate acute malnutrition	15	35	1.19(0.66,2.14)	1.49(0.79,2.82)
Severe acute malnutrition	42	58	1.67(1.09,2.55)	1.69(0.94,2.61)
Pediatric Index of Mortality 2	-3.22±1.81		1.51(1.37,1.67)	1.53(1.36,1.72) *
<b>Mechanical ventilation need</b>				
No	79	197	1	1
Yes	23	14	1.93(1.20,3.10)	2.36(1.39,4.01) *
<b>Complications in the PICU</b>				
No	86	190	1	1
Yes	16	21	2.39(1.20,4.73)	1.62(0.79,3.31)
<b>Fluid resuscitation intervention before PICU admission</b>				

No	44	105	1	1
Yes	58	106	1.24(0.83, 1.84)	0.92(0.59, 1.44)

\* Shows statistical significance at a p-value of 0.05, AHR: Adjusted hazard ratio, CHR: Crude hazard ratio

PICU: Pediatric intensive care unit

## Discussion

Our study is the first report from a prospective study from PICU in Ethiopia that demonstrates the mortality is high. Our analysis demonstrated that lack of appropriate human resources (weekend admission), critical illness diagnosis, and need for mechanical ventilation were important risk factors for death.

The proportion of mortality( 32.6%) in this study with a rate of 6.92 deaths per 100 person-day observation was consistent with retrospective cross-sectional studies done in same PICU from 2013 to 2016 (30.9%)[5], and other countries like Egypt (33.1%)[6], Nigeria (36.1%) [7] and Saudi Arabia (37.4%)[8]. However, it 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. When we compare it with other lower and middle-income countries the mortality rate in our PICU is higher than the mortality rates in studies done in Pakistan (14%)[10], the average of Latin American countries (13.29%) [11], and India (10.58%)[12]. The possible explanation for the observed discrepancies might be due to suboptimal care, the inadequacy of both diagnostic, and interventional facilities in our PICU.

Children who were admitted over the 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 [13-15]. This increased mortality over weekends might be due to failure to promptly recognize deteriorations among patients in the wards and other sources as a result of reduced staffing ratios. Access to diagnostic services is limited during weekends, which

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3 223 limits the likelihood of arriving at diagnoses. Furthermore, there could be unrecognized  
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5 224 deteriorations during handoff and round times and delays in administering interventions. However,  
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8 225 our finding was not supported by three American studies and studies done in the United Kingdom  
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10 226 and the Republic of Ireland [16, 17]. This discrepancy could be explained by the better standard  
11  
12 227 of care they have and 24 hours around the clock staffing.

13  
14 228 This study also highlighted how being a caregiver who is a government employee was associated  
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16 229 with lower risk mortality compared to caregivers of peasants. This finding could be explained by  
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18 230 differences in health-seeking behavior, access to funds for transportation, and early identification  
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20 231 of danger signs between these groups.

21  
22 232 The child who had a critical illness diagnosis had an increased risk of mortality compared to those  
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24 233 who had not. This difference could be because patients with critical illnesses have a low reserve  
25  
26 234 of physiologic function. This finding was consistent with other studies [18, 19].

27  
28 235 Amongst many disease severity assessment tools at baseline, PIM 2 does not need extensive  
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30 236 laboratory investigation, and it is not affected by subsequent interventions since it is scored within  
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32 237 one hour of admission resulting in early identification of the severity of illness and stratification of  
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34 238 children for necessary intervention [20], which in turn helps in counseling caregivers of sick children. A  
35  
36 239 unit increment in the PIM 2 score doubled the hazard of mortality, which shows the score is  
37  
38 240 sensitive in detecting mortality, and this scoring system is also validated and applicable in many  
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40 241 PICUs across the world [21-25]. The higher observed mortality rate than the predicted one by PIM  
41  
42 242 2 score in our study indicates the poor quality of intensive care in our setting.

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44 243 Patients who had respiratory failure, and those who met the criteria for mechanical ventilation had  
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46 244 increased mortality compared to those who did not have indications for ventilation. This finding  
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48 245 is consistent with the findings from other studies [26, 27]. Patients who need mechanical  
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3 246 ventilation tend to have advanced disease stages. This finding can also be attributed to a limited  
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5 247 number of mechanical ventilators in our PICU. There might also be unrecognized ventilator-  
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7  
8 248 associated complications in those who were placed on a mechanical ventilator.  
9

### 10 249 **Strength and limitations of the study**

11 250 This study is a prospective cohort study with a better statistical function (survival analysis). The  
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13  
14 251 PIM 2 scoring was based on 9 out of 11 parameters as there was no arterial blood gas analyzer in  
15  
16 252 our PICU during the study period. The availability of medical equipment and PICU quality of care  
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18 253 and their impact on patient survival was not adequately assessed using standard parameters.  
19  
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21 254 Pediatric critical care is not just about saving lives, so the degree of physiologic function retained  
22  
23 255 at discharge should have been assessed using a standard checklist for all discharged patients.  
24

### 25 256 **Conclusion**

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28 257 Rate of mortality in the PICU was high, and admission during weekends, need for mechanical  
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31 258 ventilation, critical illness diagnoses, and higher PIM 2 score were significant and independent  
32  
33 259 predictors of mortality. Availing mechanical ventilators, providing care by intensivists, full  
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35 260 staffing around the clock, and paying due attention for early signs of critical illness may improve  
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37  
38 261 intensive care outcomes. Using the PIM 2 score to prognosticate outcomes and tunnel resources to  
39  
40 262 the most in need patients and counseling of caregivers might be advisable.  
41

### 42 263 **List of abbreviations**

43  
44  
45 264 AHR: Adjusted Hazard Ratio, AKI: Acute Kidney Injury, CI: Confidence Intervals, CHR: Crude  
46  
47 265 Hazard Ratio, HAS: Hospital-Acquired Sepsis, HAP: Hospital-Acquired Pneumonia, ICD:  
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49  
50 266 International Classifications of Disease, ICU: Intensive Care Unit, IQR: Interquartile Range, IR:  
51  
52 267 Incidence Rate, LAMA: Left Against Medical Advice, LOS: Length of Hospital stay, MAM:  
53  
54 268 Moderate Acute Malnutrition, MODS: Multiple Organ Dysfunction Syndrome, MV: Mechanical  
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3 269 Ventilation, PI: Principal Investigator, PICU: Pediatric Intensive Care Unit, PIM 2: Pediatrics  
4  
5 270 Index of Mortality 2, SAM: Severe Acute Malnutrition, OR: Operation Room, USA: the United  
6  
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8 271 States of America, WHO: World Health Organization  
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## 11 272 **Declaration**

### 12 273 **Ethical approval and consent to participate**

13  
14  
15 274 Ethical clearance was obtained from the Institutional Ethical Review Board of College of Medicine  
16  
17 275 and Health Sciences, University of Gondar. Assent and informed written consent were obtained  
18  
19  
20 276 from the caretakers. The name or any other identifying information was not recorded on the data  
21  
22 277 collection form. All information taken from the chart was kept strictly confidential in a safe place.  
23  
24  
25 278 The information retrieved was used only for the study purpose.

### 26 279 **Consent for publication**

27  
28  
29 280 Not applicable  
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31

### 32 281 **Availability of data and material**

33  
34 282 Data is available from the corresponding author upon reasonable request.  
35  
36

### 37 283 **Competing interests**

38  
39  
40 284 The authors declare that they have no competing interests.  
41  
42  
43

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47  
48 287 design, data collection, and analysis, interpretation of data, the decision to publish, or preparation  
49  
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51 288 of the manuscript.  
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## 289 Authors' contributions

290 NWT, ATA, and KST participated in designing the study, performing data analysis and  
291 visualization, validating the work, and preparing the manuscript. NWT took part in funding  
292 acquisition, data collection, supervision and software, and other resources. All authors read and  
293 approved the final manuscript.

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## 298 Figures and legends

299 **Figure 1:** Kaplan-Meier failure (death) estimates curves by days of admission

300 **Figure 2:** Kaplan-Meier failure (death) estimates curves by critical illness

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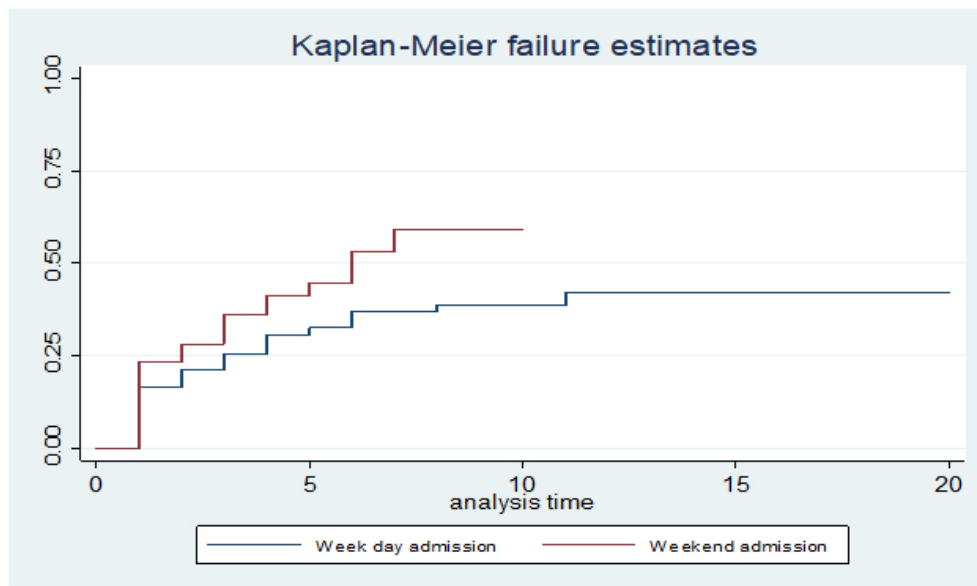


Figure 1: Kaplan-Meier failure (death) estimates curves by days of admission among children treated in the pediatric intensive care unit of University of Gondar comprehensive specialized hospital from February 1/2018 to July 30/2019

168x100mm (96 x 96 DPI)

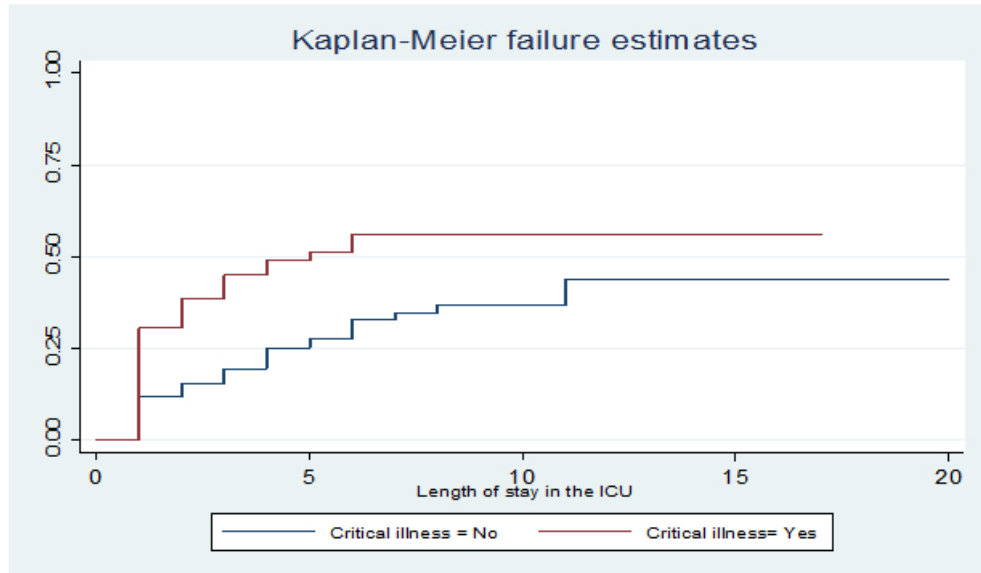


Figure 2: Kaplan-Meier failure (death) estimates curves by children critical illness admitted to pediatric intensive care unit of University of Gondar comprehensive specialized hospital from February 1/2018 to July 30/2019

164x96mm (96 x 96 DPI)

## STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
<b>Title and abstract</b>	1	<p>Indicate the study's design with a commonly used term in the title or the abstract  <i>The title describes the study design as "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". Page 1</i></p> <p>(b) Provide in the abstract an informative and balanced summary of what was done and what was found  <i>The abstract describes the method used and Main findings. page 2, line 19-31</i></p>
<b>Introduction</b>		
Background/rationale	2	<p>Explain the scientific background and rationale for the investigation being reported  <i>The background and rationale are described in the Background, paragraphs 1, 2, 3, 4, 5 and 6. Page 4-5, Line 64-102</i></p>
Objectives	3	<p>State specific objectives, including any pre specified hypotheses  <i>The specific aims of the study are stated in the Background, paragraphs 6, page 5, line 94-104</i></p>
<b>Methods</b>		
Study design	4	<p>Present key elements of study design early in the paper  <i>The study design is discussed in paragraphs 1 of the Methods section, page 6, line 105-107</i></p>
Setting	5	<p>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection  <i>The institutional setting is described in paragraphs 2 line 108-120 of the Methods section.  Study locations are described in paragraph 1 and 2 of the Methods section; and study timing is discussed in paragraphs of the Methods section. Participant recruitment is mentioned in in population and sample section. Page 6</i></p>
Participants	6	<p><i>Cross-sectional study</i>—Give the eligibility criteria, and the sources and methods of selection of participants  <i>Selection of the sample is discussed in paragraph 1 and 2 line 121-130, of population and sample subsection of the Methods section. page 6-7</i></p>
Variables	7	<p>Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable</p>

		<p>Outcomes are discussed in the Outcomes subsection (paragraphs 3 of the Methods section).</p> <p>Data was collected by treating physicians using standardized questionnaire after taking consent from caretakers. Clinical characteristics like, SBP, pupillary light reflex, SaO<sub>2</sub> 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.</p> <p><b>Mentioned in the method section of 131-158, page 7-8</b></p>
	8*	<p>For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group</p> <p><b>Measurement of the outcomes are discussed in the data collection and measurement of variables subsection. Page 8</b></p>
Bias	9	<p>Describe any efforts to address potential sources of bias</p> <p><b>Mentioned in the method section of variable of the study and operational definitions Page 7-8</b></p>
Study size	10	<p>Explain how the study size was arrived at</p> <p><b>Sample size determination was discussed at method, population and sample section. Page 6</b></p>
Quantitative variables	11	<p>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why</p> <p><b>Use of variables is discussed in the data management and analysis subsection. Page 8</b></p>
Statistical methods	12	<p>(a) Describe all statistical methods, including those used to control for confounding</p> <p><b>Statistical methods are discussed in the data management and analysis subsection. Page 8 line 160-178</b></p>
		<p>(b) Describe any methods used to examine subgroups and interactions</p> <p>Described in in the data management and analysis subsection.</p> <p><b>Results are analysed by socio-demographic and personal attributes like age place of residence .</b></p>
		<p>(c) Explain how missing data were addressed</p> <p><b>None</b></p>
		<p>(e) Describe any sensitivity analyses</p> <p><b>None</b></p>

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60**Results**

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed <i>At paragraph 1 of result section, page 9</i> (b) Give reasons for non-participation at each stage <i>None</i> (c) Consider use of a flow diagram <i>None</i>
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Provider characteristics are presented in Table 1, Table 2, and Table 3. (b) Indicate number of participants with missing data for each variable of interest <i>None</i>
Outcome data	15*	<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures Both numbers and percentages/proportions are reported throughout the <b>Results Section. Page 15-16 line 230-248</b>
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included <b>Adjusted results are presented for all outcomes. Page 16-17, table 4</b> (b) Report category boundaries when continuous variables were categorized <i>Not applicable</i> (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period <i>Not applicable.</i>
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses <i>None</i>
<b>Discussion</b>		
Key results	18	Summarise key results with reference to study objectives <b>Results are summarized in paragraphs, 1, and 2 of the Discussion section. Page 18, line 271-283</b>
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias <b>Strength and limitations are discussed in paragraphs 21, line 344-352</b>
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence <b>Discussed in discussion and conclusion sub section. 18-22</b>
Generalizability	21	<b>Discuss the generalizability (external validity) of the study results</b> <b>The representativeness of the sample is discussed in the final paragraph of the limitations subsection.</b>

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60**Other information**

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Funding 22 Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based  
*Not applicable*

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

# BMJ Open

**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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<b>Primary Subject Heading</b>:	Intensive care
Secondary Subject Heading:	Emergency medicine
Keywords:	Paediatric intensive & critical care < ANAESTHETICS, ACCIDENT & EMERGENCY MEDICINE, INTENSIVE & CRITICAL CARE

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4 **care unit at the University of Gondar comprehensive specialized hospital, northwest**  
5 **Ethiopia: A prospective observational cohort study.**  
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## Abstract

**Objective:** To determine the incidence and predictors of mortality among children admitted to the pediatric intensive care unit at the University of Gondar comprehensive specialized hospital, northwest Ethiopia

**Design:** A single-center prospective observational cohort study

**Participants:** A total of 313 children admitted to the intensive care unit of the University of Gondar comprehensive specialized hospital during a one-and-a-half-year period.

**Measurements:** Data were collected using standard case record form, physical examination, and patient document review. Clinical characteristics like systolic blood pressure, pupillary light reflex, oxygen saturation, and need for mechanical ventilation were assessed and documented within the first hour of admission and entered into an electronic application to calculate the modified Pediatric Index of Mortality 2 (PIM 2) score. We fitted the Cox proportional hazards model to identify predictors of mortality.

**Result:** The median age at admission was 48 months with interquartile range (IQR: 12 to 122), 28.1% were infants, and adolescents accounted for 21.4%. Of the total patients studied, 59.7% were males. The median observation time was three days with (IQR: 1 to 6). One hundred two (32.6%) children died during the follow-up time, and the incidence of mortality was 6.9 deaths per 100 person-day observation. Weekend admission [Adjusted Hazard Ratio (AHR) =1.63, 95%CI: 1.02, 2.62], critical illness diagnoses (AHR=1.79, 95%CI: 1.13, 2.85), need for mechanical ventilation (AHR=2.36, 95%CI: 1.39, 4.01) and modified PIM 2 score (AHR=1.53, 95%CI: 1.36, 1.72) were the predictors of mortality.

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3 **Conclusion:** The rate of mortality in the Pediatric intensive care unit (PICU) was high, admission  
4 over weekends, need for mechanical ventilation, critical illness diagnoses, and higher Pediatric  
5 Index of Mortality 2 scores were significant and independent predictors of mortality.  
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### 10 **Strength and limitation of the study**

- 12 ➤ This study was a prospective cohort study and had used better statistical functions (survival  
13 analysis) for better estimation and prediction of mortality.
- 14 ➤ This study could help clinicians and health care planners practice evidence-based medicine  
15 in a resource-limited setting like ours.
- 16 ➤ The PIM 2 scoring was done based on 9 out of 11 parameters as there was no arterial blood  
17 gas analyzer in our set up during the study period that might result in misclassification.  
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### 27 **Introduction**

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30 Though pediatric intensive care units (PICUs) are essential areas of service to save the lives of  
31 children with acute neurological deterioration, respiratory distress, cardiovascular compromise,  
32 severe infections, accidental poisoning, and other life-threatening conditions; organizational  
33 details of pediatric ICUs in low-income settings are lacking [1, 2].  
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Published data on pediatric critical care in low-income countries remains sparse, making practice  
modification and outcome improvement difficult. Also, most studies done on predictors of  
mortality in the PICUs are from high-income countries and are dependent on clinical and  
laboratory indices, which are not readily available in low-income countries [3]. The few studies  
that considered epidemiologic and sociodemographic factors were retrospective and cross-  
sectional, and most did not consider essential parameters [4]. Determining the risk factors of  
mortality among children admitted to the pediatric intensive care will be crucial to prioritize and

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3 tunnel resources to the most fruitful practice based on the prediction of patient outcomes,  
4 especially in resource-limited setups like ours.  
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8 This study aimed to determine the incidence and predictors of mortality among children admitted  
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10 to a pediatric intensive care unit at the University of Gondar comprehensive specialized hospital.  
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12 It will add to the knowledge of mortality and its predictors, thereby hoping to plan the most  
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14 efficient method of intervention for those at higher mortality risk, thus contributing to recovery as  
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16 well as making the assessment of the performance of the services delivered.  
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## 19 **Methods**

### 20 **Study design, period and setting**

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22 A single-center prospective cohort study was conducted among children aged one month to 18  
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24 years admitted to the PICU at the University of Gondar comprehensive specialized hospital from  
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26 February 1, 2018, to July 30, 2019.  
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31 The PICU has six beds with electronic monitors and one mechanical ventilator; on average, there  
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33 are about 25 pediatric critical care admissions per month. The organizational detail of the PICU in  
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35 this hospital is lacking. Team composition is often limited to a general pediatrician, resident,  
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37 interns, and a handful of senior-level nurses, but there are no pediatric intensivists, respiratory  
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39 therapists, pharmacists, and dieticians.  
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### 44 **Population and sample**

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46 Patients who stayed for more than two hours in the hospital were included in the study. We  
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48 excluded patients having incomplete data, and surgical patients admitted only for recovery  
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50 purposes from the study.  
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54 The sample size for this study was determined using a single population proportion of  $P=21\%$ ,  
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56 from previous Bangladesh study [2] with a 5% margin of error; the sample size became 254, and  
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3 after adding 10% contingency, the sample became 279. A total of 376 patients were admitted to  
4 the PICU during the study period. We collected data from 327 patients who fulfilled the inclusion  
5 criteria. Fourteen patients were excluded from the study due to incomplete data.  
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### 8 9 10 **Data collection procedure**

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12 Data was collected by treating physicians using standard case record form after receiving consent  
13 from caretakers. Clinical characteristics like systolic blood pressure (SBP), pupillary light reflex,  
14 oxygen saturation, and need for mechanical ventilation were assessed and documented within the  
15 first hour and entered into an electronic application to calculate the modified Pediatric Index of  
16 Mortality 2 (PIM 2) score. We took sociodemographic data and medical history by interview; and  
17 diagnosis, laboratory indices, and the clinical course during the hospital by chart review at  
18 discharge. We used the World Health Organization (WHO) International Classification of Diseases  
19 10<sup>th</sup> version (ICD-10) for disease category, and only the primary diagnoses were used for ICD-10  
20 assignment in patients having multiple diagnoses. The collected data were double-checked by the  
21 data collector and the principal investigator. There were orientations and training about data  
22 collection and the study's objective every three months and demonstration every Monday for  
23 treating physicians and data collectors. The principal investigator supervised the overall process  
24 and checked the completeness of case record forms every day. No direct patient care was provided  
25 by investigators, who only accessed patients' records.  
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### 45 **Variable of the study and operational definitions**

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48 The primary dependent variable was time to death (event). In contrast, sociodemographic  
49 characteristics included age, sex, relation with the caregiver, caregiver's educational status, and  
50 occupation. Clinical characteristics included duration of illness before admission, source of  
51 admission, critical illness diagnosis, comorbidity, nutritional status, vaccination status,  
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3 interventions given in the PICU, and before admissions like fluid resuscitation, modified PIM 2  
4 score, multi-organ dysfunction syndrome (MODS), and complications.  
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8 Event (death): is defined as a patient who died in the hospital during treatment.  
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10 Censored: refers to patients who were discharged alive from the PICU or those with no event of  
11 interest.  
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15 Length of stay (LOS): refers to the duration of stay in days from the date of admission to the date  
16 of discharge.  
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19 Short term outcome: the outcome of the patient until he or she leaves the hospital  
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22 Critical illness: refers to sepsis, severe sepsis, or septic shock within 24 hours of admission or  
23 acute respiratory distress syndrome during PICU admission.  
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27 MODS: refers to a potentially reversible physiologic derangement in two or more organ systems  
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### 29 **Data processing and analysis**

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31 After we checked the data for its consistency and completeness, we entered data into EpiData  
32 version 3.1 and exported to STATA version 14 for cleaning and analysis. Descriptive statistics like  
33 mean, median, and proportions were carried out to summarize baseline characteristics and  
34 admission patterns. Also, summary statistics like life table, log-rank test, and Kaplan-Meier curves  
35 were computed to determine the incidence rate (IR) of death and to compare survival curves  
36 between the different categories of the explanatory variables.  
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41 Both bivariate and multivariate Cox proportional hazards models were used to identify the  
42 predictors. Variables with p-value < 0.2 in the bivariate analysis were entered into the multivariate  
43 proportional hazard model. Ninety-five percent confidence intervals (95% CI) of hazard ratios  
44 were computed, and variables with p-value < 0.05 in the multivariate Cox proportional hazards  
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model were considered significantly and independently associated with the dependent variable. Cox proportional hazards 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 the University of Gondar's College of Medicine and Health Sciences. Informed verbal consent was obtained from the caretakers. The name or any other identifying information was not recorded on the data collection form, and all information taken from the chart was kept strictly confidential and in a safe place. The information retrieved was used only for the study purpose.

### **Patient and public involvement**

There was no direct patient contact, and investigators accessed only patient records.

## **Result**

### **Sociodemographic characteristics**

A total of 313 patients out of 376 admitted during the 18-month study period were included in the final analysis. The median age at admission was 48 months with interquartile range (IQR: 12 to 122), with a male to female ratio of 1.7:1, as shown in Table 1. The majority of caregivers (92.9%) were parents. More than three-fourth (77.6%) of caregivers had no formal education, and 71.2% were farmers. Most patients were admitted in the spring season (38.3%), followed by winter (27.2%) (Table 1).

**Table 1:** Sociodemographic characteristics of patients

<b>Characteristics</b>	<b>Frequency</b>	<b>Percentages (%)</b>
<b>Age in months</b>		
≤ 12	88	28.1
13-24	29	9.3
25-60	66	21.1
61-132	63	20.1

>132	67	21.4
<b>Sex</b>		
Male	188	59.7
<b>Vaccination status</b>		
Complete	203	64.9
Incomplete/unvaccinated	110	35.1
<b>Comorbid illness (n=43)</b>		
Congenital malformations/genetic disorders	12	27.9
Cerebral palsy with or without seizure disorders	11	25.6
Chronic kidney disease	7	16.3
HIV/AIDS	6	14
Others	7	16.3

HIV/AIDS: Human immunodeficiency virus infection and acquired immune deficiency syndrome

### The clinical condition of admitted children

The primary source of admissions in the PICU was the emergency room (60.4%), inpatient pediatrics wards (13.1%), and referrals from other facilities (11.8%). More than three-fourth (77%) of patients were admitted over weekdays and 41.5% in the night shift. 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. One-third of patients had critical illness diagnoses, of which (41%) had sepsis, (47%) septic shock, and the remaining (12%) had acute respiratory distress syndrome. About one-third of patients (30.7%) had multiple organ dysfunction syndromes (MODS). The minimum modified PIM 2 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 modified PIM 2 score was 11.14%, which gave the standard mortality ratio (SMR) of 2.94 (Table 2).

**Table 2:** Clinical condition of patients

Characteristics	Frequency	Percentages (%)
<b>Duration of illness before PICU admission in days</b>		
≤6 days	71	22.7
>6 days	242	77.7



<b>Multi-organ dysfunction syndrome</b>		
Yes	96	30.6
No	217	69.4
<b>Sources of admission</b>		
Home	36	11.5
Other facilities	37	11.8
Emergency room	189	60.4
Wards and Operating rooms	51	16.3
<b>Need for mechanical ventilation</b>		
Yes	37	11.8
No	276	88.2
<b>Nutritional status, Z score</b>		
Normal	163	52.1
Moderate acute malnutrition	50	16
Severe acute malnutrition	100	31.9
<b>Reasons for PICU admission</b>		
Altered mental status	145	46.3
Respiratory failure	82	26.5
Sepsis	59	18.8
Shock	55	17.6
Seizure	46	14.7
Diabetic ketoacidosis	24	7
Acute kidney injury	24	7
Congestive heart failure	21	6.7
Hemorrhage	14	4.5
Trauma	6	1.9
Others	23	7.3

PICU: Pediatric intensive care unit

### **Intensive care unit outcomes and the incidence of mortality**

Nearly one-third of patients (32.6%) died in the PICU. Severe sepsis or multi-organ failure (MOF) (41.2%) was the leading immediate cause of death in the PICU followed by respiratory failure (23.5%), brain herniation (21.6%), and cardiac arrest (12.7%). Fifty-six patients (17.9%) developed complications during their stay in the PICU, including hospital-acquired sepsis (46.4%), hospital-acquired pneumonia (17.9%), and mechanical ventilator-associated complications (10.7%).

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3 Study subjects were followed during the study period, which gave a total of 1473 person-day  
4 observations (49.1 person-months), and the median length of stay in the ICU was 3 (IQR:1 to 6)  
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6 of mortality was 6.9 deaths per 100-person day observations (95%CI: 5.34 to 8.34 deaths per 100  
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8 days. Of the total of 313 participants, 102 (32.6%) died during the follow-up time. The incidence  
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10 of mortality was 6.9 deaths per 100-person day observations (95%CI: 5.34 to 8.34 deaths per 100  
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12 person-day). Among deaths reported, more than half (53.9%) died within 24 hours, 13 (12.7%)  
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14 died between 24 and 48 hours, and the remaining died after 48 hours of admission. Differences in  
15  
16 all variables at baseline between strata were determined using the log-rank ( $\chi^2$ ) test, and the  
17  
18 equality of hazard was assessed for the different explanatory variables. Kaplan Meier failure curve  
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20 was plotted for weekend admission (P-value=0.039), and critical illness (P-value= 0.0001) shows  
21  
22 a significant difference (Figure 1) and (Figure 2).  
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### 25 26 **Predictors of mortality in the PICU**

27  
28 The Cox proportional hazards model was fitted to identify predictors of mortality. From the  
29  
30 multivariate analysis, caregivers' occupation, weekend admission, critical illness diagnoses, PIM  
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32 2 score, and need for mechanical ventilation were predictors of mortality. Mortality was 65% lower  
33  
34 for those whose caregivers were government employees than farmers (AHR=0.35, 95%CI: 0.14,  
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36 0.89). The hazard of mortality was 1.63 times higher for patients admitted over weekends  
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38 (AHR=1.63, 95%CI: 1.02, 2.60) and 1.79 times higher in patients who had critical illness  
39  
40 diagnoses (AHR=1.79, 95%CI: 1.13, 2.85) compared to weekday admission and those without  
41  
42 critical illness diagnosis, respectively. Similarly, each one-unit increase in the modified PIM 2  
43  
44 score increased the hazard of mortality 1.53 times, keeping other variables constant (AHR=1.53,  
45  
46 95%CI:1.36, 1.72). Also, those patients who met the criteria for mechanical ventilation (MV), the  
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48 hazard of mortality was 2.36 times higher compared to those who did not need MV (AHR=2.36,  
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50 95%CI: 1.39, 4.01) (Table 3).  
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**Table 3:** Bivariate and multivariate Cox proportional hazard model Fit for different independent variables

Variables	Status		CHR (95% CI)	AHR (95% CI)
	Event	Censored		
<b>Age (months)</b>				
≤12	28	60	1	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)
<b>Address</b>				
Urban	28	43	1	1
Rural	74	168	0.73(0.47, 1.13)	0.63(0.37, 1.05)
<b>Caregiver' level of education</b>				
No formal education	96	195	1	1
Primary and above	6	16	0.78(0.34, 1.80)	1.26(0.51, 3.13)
<b>Caregivers' occupation</b>				
Farmers	72	151	1	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)
<b>Day of admission</b>				
Weekday	71	170	1	1
Weekend	31	41	1.47(0.96, 2.26)	1.63(1.02, 2.60) *
<b>Source of admission</b>				
Home	9	27	1	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)
<b>Duration of illness before PICU admission</b>				
<6 days	39	107	1	1
≥6 days	63	104	1.43(0.96, 2.12)	0.97(0.62, 1.54)
<b>Comorbidities</b>				
No	85	185	1	1
Yes	17	26	1.31(0.78, 2.21)	0.66(0.36, 1.23)
<b>Critical illness diagnosis</b>				
No	53	160	1	1
Yes	49	51	2.05(1.39, 3.04)	1.79(1.13, 2.85) *
<b>Nutritional status, Z score</b>				
Normal	45	118	1	1
Moderate acute malnutrition	15	35	1.19(0.66, 2.14)	1.49(0.79, 2.82)
Severe acute malnutrition	42	58	1.67(1.09, 2.55)	1.69(0.94, 2.61)

Modified Pediatric Index of Mortality 2	-3.22±1.81		1.51(1.37,1.67)	1.53(1.36,1.72) *
<b>Mechanical ventilation need</b>				
No	79	197	1	1
Yes	23	14	1.93(1.20,3.10)	2.36(1.39,4.01) *
<b>Complications in the PICU</b>				
No	86	190	1	1
Yes	16	21	2.39(1.20,4.73)	1.62(0.79,3.31)
<b>Fluid resuscitation intervention before PICU admission</b>				
No	44	105	1	1
Yes	58	106	1.24(0.83, 1.84)	0.92(0.59 ,1.44)

\* Shows statistical significance at a p-value of 0.05, AHR: Adjusted hazard ratio, CHR: Crude hazard ratio  
PICU: Pediatric intensive care unit

## Discussion

Our study is the first report from a prospective study in a PICU in Ethiopia that demonstrates the mortality is high and identified predictors of mortality like lack of appropriate human resources (weekend admission), critical illness diagnosis, and need for mechanical ventilation. These findings help clinicians, and health care planners practice evidence-based medicine in a resource-limited setting and effective prognosis tailored care and resource utilization.

The proportion of mortality( 32.6%) in this study with a rate of 6.92 deaths per 100 person-day observation was consistent with the mortality rate in retrospective cross-sectional studies done in the same PICU from 2013 to 2016 (30.9%) [5], and other studies in low-income countries in Africa which ranged from 25% in Mozambique to 50% in Rwanda [6-8]. However, it 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 compared to ours. When we compare it with other lower and middle-income countries, the mortality rate in our PICU is higher than the mortality rates in studies done in Pakistan (14%)[10] and India (10.58%)[11]. The possible explanation for the observed discrepancies might be suboptimal care, the inadequacy of diagnostic and interventional facilities in our PICU.

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3 Children admitted over the weekends had nearly twice increased risk of mortality than those  
4 admitted over weekdays, consistent with the findings of studies done in Canada, Finland, and  
5 Austria [12-14]. This increased mortality over weekends might be due to failure to promptly  
6 recognize deteriorations among patients in the wards and other sources as a result of reduced  
7 staffing ratios. Access to diagnostic services is limited during weekends, which limits the  
8 likelihood of arriving at diagnoses. Furthermore, there could be unrecognized deteriorations during  
9 handoff and round times and delays in administering interventions. However, our finding was not  
10 supported by three American studies and studies done in the United Kingdom and the Republic of  
11 Ireland [15, 16]. This discrepancy could be explained by the better standard of care they have and  
12 24 hours around the clock staffing. Better weekend coverage and full hour staffing is recommended for  
13 a better critical care delivery.  
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28 This study also highlighted how being a caregiver who is a government employee was associated  
29 with lower risk mortality compared to caregivers of peasants. This finding could be explained by  
30 differences in health-seeking behavior, access to funds for transportation, and early identification  
31 of danger signs between them.  
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38 The child who had a critical illness diagnosis had an increased risk of mortality than those who  
39 had not. This difference could be because patients with critical illnesses have a low reserve of  
40 physiologic function. This finding was consistent with other studies [17, 18].  
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44 Amongst many disease severity assessment tools at baseline, PIM 2 does not need extensive  
45 laboratory investigation, and it is not affected by subsequent interventions since it is scored within  
46 one hour of admission resulting in early identification of the severity of illness and stratification of  
47 children for necessary intervention [19], which in turn helps in counseling caregivers of sick children. We  
48 used a modified PIM2 score as there was no arterial blood gas analyzer in our PICU during the study period.  
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55 A unit increment in the modified PIM 2 score doubled the hazard of mortality, which shows the  
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3 score is sensitive in detecting mortality, and this scoring system is also validated and applicable in  
4 many PICUs across the world [20-24]. The higher observed mortality rate than the predicted ones  
5 by the modified PIM 2 score in our study indicates the poor quality of intensive care in our setting.  
6  
7 Using the modified PIM 2 score to focus the care on those with dangerous modified PIM2 scores,  
8 prognosticate outcomes, and tunnel resources to the most in need patients will improve the critical  
9 care outcome in low-income settings.

10  
11 Patients who had respiratory failure, and those who met the criteria for mechanical ventilation had  
12 increased mortality than those who did not have indications for ventilation. This finding is  
13 consistent with the findings from other studies [25, 26]. Patients who need mechanical ventilation  
14 tend to have advanced disease stages. This finding can also be attributed to a limited number of  
15 mechanical ventilators in our PICU. There might also be unrecognized ventilator-associated  
16 complications in those who were placed on a mechanical ventilator.

### 30 **Strength and limitations of the study**

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32 This study is a prospective cohort study with a better statistical function (survival analysis). The  
33 PIM 2 scoring was based on 9 out of 11 parameters as there was no arterial blood gas analyzer in  
34 our PICU during the study period. The availability of medical equipment and PICU quality of care  
35 and their impact on patient survival was not adequately assessed using standard parameters.  
36  
37 Pediatric critical care is not just about saving lives, so the degree of physiologic function retained  
38 at discharge should have been assessed using a standard checklist for all discharged patients.

### 46 **Conclusion**

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48 Rate of mortality in the PICU was high, and admission during weekends, need for mechanical  
49 ventilation, critical illness diagnoses, and higher modified PIM 2 score were significant and  
50 independent predictors of mortality. Full staffing around the clock including better weekend  
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3 coverages, and paying due attention for early signs of critical illness may improve intensive care  
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5 outcomes. Using the modified PIM 2 score to focus the care on those with risky scores, and tunnel  
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7 resources to the most in need patients and counseling of caregivers might be advisable.  
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### 10 **List of abbreviations**

11  
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13 AHR: Adjusted Hazard Ratio, AKI: Acute Kidney Injury, CI: Confidence Intervals, CHR: Crude  
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15 Hazard Ratio, HAS: Hospital-Acquired Sepsis, HAP: Hospital-Acquired Pneumonia, ICD:  
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17 International Classifications of Disease, ICU: Intensive Care Unit, IQR: Interquartile Range, IR:  
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19 Incidence Rate, LAMA: Left Against Medical Advice, LOS: Length of Hospital stay, MAM:  
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21 Moderate Acute Malnutrition, MODS: Multiple Organ Dysfunction Syndrome, MV: Mechanical  
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23 Ventilation, PI: Principal Investigator, PICU: Pediatric Intensive Care Unit, PIM 2: Pediatrics  
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25 Index of Mortality 2, SAM: Severe Acute Malnutrition, OR: Operation Room, USA: the United  
26  
27 States of America, WHO: World Health Organization  
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### 32 **Declaration**

#### 33 **Ethical approval and consent to participate**

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37 Ethical clearance was obtained from the Institutional Ethical Review Board of College of Medicine  
38  
39 and Health Sciences, University of Gondar. Assent and informed written consent were obtained  
40  
41 from the caretakers. The name or any other identifying information was not recorded on the data  
42  
43 collection form. All information taken from the chart was kept strictly confidential in a safe place.  
44  
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46 The information retrieved was used only for the study purpose.  
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#### 48 **Consent for publication**

49  
50  
51 Not applicable  
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#### 53 **Availability of data and material**

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56 Data is available from the corresponding author upon reasonable request.  
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## Competing interests

None declared

## Funding

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## Authors' contributions

NWT, ATA, and KST participated in designing the study, performing data analysis and visualization, validating the work, and preparing 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 and legends

**Figure 1:** Kaplan-Meier failure (death) estimates curves by days of admission

**Figure 2:** Kaplan-Meier failure (death) estimates curves by critical illness

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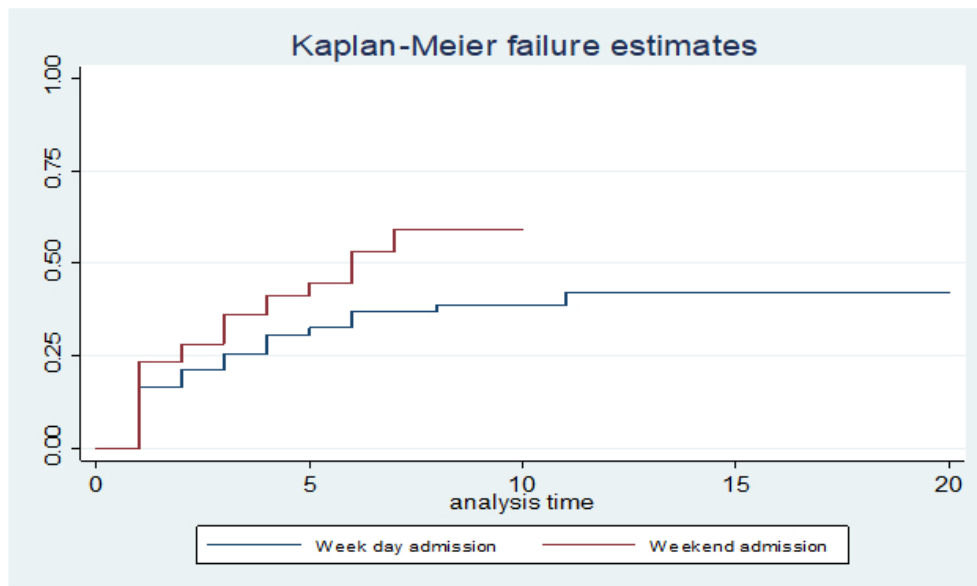


Figure 1: Kaplan-Meier failure (death) estimates curves by days of admission among children treated in the pediatric intensive care unit of University of Gondar comprehensive specialized hospital from February 1/2018 to July 30/2019

53x32mm (300 x 300 DPI)

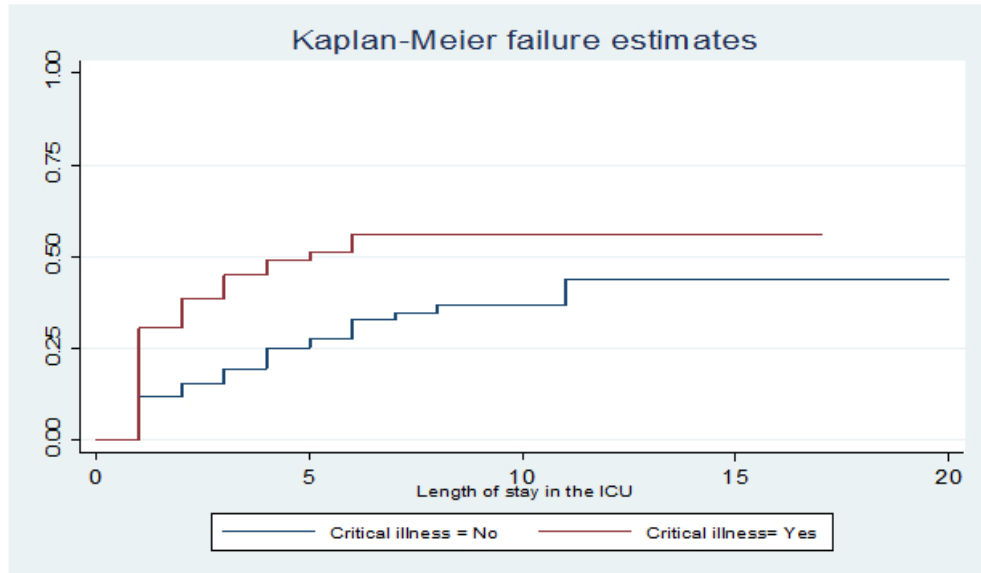


Figure 2: Kaplan-Meier failure (death) estimates curves by children critical illness admitted to pediatric intensive care unit of University of Gondar comprehensive specialized hospital from February 1/2018 to July 30/2019

52x30mm (300 x 300 DPI)

## STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
<b>Title and abstract</b>	1	<p>Indicate the study's design with a commonly used term in the title or the abstract  <i>The title describes the study design as "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". Page 1</i></p> <p>(b) Provide in the abstract an informative and balanced summary of what was done and what was found  <i>The abstract describes the method used and Main findings. page 2, line 19-31</i></p>
<b>Introduction</b>		
Background/rationale	2	<p>Explain the scientific background and rationale for the investigation being reported  <i>The background and rationale are described in the Background, paragraphs 1, 2, 3, 4, 5 and 6. Page 4-5, Line 64-102</i></p>
Objectives	3	<p>State specific objectives, including any pre specified hypotheses  <i>The specific aims of the study are stated in the Background, paragraphs 6, page 5, line 94-104</i></p>
<b>Methods</b>		
Study design	4	<p>Present key elements of study design early in the paper  <i>The study design is discussed in paragraphs 1 of the Methods section, page 6, line 105-107</i></p>
Setting	5	<p>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection  <i>The institutional setting is described in paragraphs 2 line 108-120 of the Methods section.  Study locations are described in paragraph 1 and 2 of the Methods section; and study timing is discussed in paragraphs of the Methods section. Participant recruitment is mentioned in in population and sample section. Page 6</i></p>
Participants	6	<p><i>Cross-sectional study</i>—Give the eligibility criteria, and the sources and methods of selection of participants  <i>Selection of the sample is discussed in paragraph 1 and 2 line 121-130, of population and sample subsection of the Methods section. page 6-7</i></p>
Variables	7	<p>Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable</p>

		<p>Outcomes are discussed in the Outcomes subsection (paragraphs 3 of the Methods section).</p> <p>Data was collected by treating physicians using standardized questionnaire after taking consent from caretakers. Clinical characteristics like, SBP, pupillary light reflex, SaO<sub>2</sub> 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.</p> <p><b>Mentioned in the method section of 131-158, page 7-8</b></p>
	8*	<p>For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group</p> <p><b>Measurement of the outcomes are discussed in the data collection and measurement of variables subsection. Page 8</b></p>
Bias	9	<p>Describe any efforts to address potential sources of bias</p> <p><b>Mentioned in the method section of variable of the study and operational definitions Page 7-8</b></p>
Study size	10	<p>Explain how the study size was arrived at</p> <p><b>Sample size determination was discussed at method, population and sample section. Page 6</b></p>
Quantitative variables	11	<p>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why</p> <p><b>Use of variables is discussed in the data management and analysis subsection. Page 8</b></p>
Statistical methods	12	<p>(a) Describe all statistical methods, including those used to control for confounding</p> <p><b>Statistical methods are discussed in the data management and analysis subsection. Page 8 line 160-178</b></p>
		<p>(b) Describe any methods used to examine subgroups and interactions</p> <p>Described in in the data management and analysis subsection.</p> <p><b>Results are analysed by socio-demographic and personal attributes like age place of residence .</b></p>
		<p>(c) Explain how missing data were addressed</p> <p><b>None</b></p>
		<p>(e) Describe any sensitivity analyses</p> <p><b>None</b></p>

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60**Results**

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed <i>At paragraph 1 of result section, page 9</i> (b) Give reasons for non-participation at each stage <i>None</i> (c) Consider use of a flow diagram <i>None</i>
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Provider characteristics are presented in Table 1, Table 2, and Table 3. (b) Indicate number of participants with missing data for each variable of interest <i>None</i>
Outcome data	15*	<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures Both numbers and percentages/proportions are reported throughout the <b>Results Section. Page 15-16 line 230-248</b>
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included <b>Adjusted results are presented for all outcomes. Page 16-17, table 4</b> (b) Report category boundaries when continuous variables were categorized <i>Not applicable</i> (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period <i>Not applicable.</i>
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses <i>None</i>
<b>Discussion</b>		
Key results	18	Summarise key results with reference to study objectives <b>Results are summarized in paragraphs, 1, and 2 of the Discussion section. Page 18, line 271-283</b>
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias <b>Strength and limitations are discussed in paragraphs 21, line 344-352</b>
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence <b>Discussed in discussion and conclusion sub section. 18-22</b>
Generalizability	21	<b>Discuss the generalizability (external validity) of the study results</b> <b>The representativeness of the sample is discussed in the final paragraph of the limitations subsection.</b>

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60**Other information**

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Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based
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*Not applicable*

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).