Morbidity Pattern With Treatment Outcome and Predictors of Mortality of Children Admitted to Pediatric Intensive Care Unit in a Peripheral Medical College in India

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Abstract- To capture lapses in management, active surveillance of pediatric intensive care unit **(**PICU) admissions should consider as an essential tool to bring a better outcome with available resources, while there is a scarcity of data from comparatively newly set up peripheral PICU in developing countries. An observational record-based cross-sectional study was conducted in a peripheral medical college PICU over one year to evaluate morbidity pattern, outcome, and predictors of mortality. Binomial logistic regression (SPSS version-25) was used for analysis. The confidence interval (CI) of Odd's ratio was used to report the strength of association between dependent and independent variables. Pneumonia was the major cause of admission (27%), followed by septicemia (25.5%), congenital heart diseases (12.2%), bronchiolitis (6.6%), seizure disorders (8.6%), encephalitis (5%), and meningitis (4%). 51.7% were discharged, 14.6 %were referred, 3.2% were left against medical advice, and 30.4% were expired. Pneumonia (46.44%) was the most common cause of death, followed by sepsis (42.07%), congenital heart disease (15.3%), and bronchiolitis (6.01%). The mean duration of stay in PICU was five days (range 1-31 days). Patients who required ventilation (40%) or Inotropes (55.6%) had increased risk of mortality by 14 and 8 times, respectively. Age below one year, presence of bronchiolitis, pneumonia, ARDS, encephalitis, anemia, sepsis, dyselectrolytemia, and requirement of inotropes or ventilation were statistically significant risk factors for mortality (P<0.05). These predictors of morality will help to identify severe cases, prioritize resources and focus on the preventable methods in the public such as a vaccine, creating awareness about diseases, and proper referral.

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Keywords: Morbidity; Mortality; Mortality predictors; Outcome; Peripheral medical college; Pediatric intensive care unit **(**PICU)

Introduction

A pediatric intensive care unit (PICU) is a designated corner in a hospital with special equipment and trained staff for the management of pediatric patients with life-threatening illnesses (1). According to World Health Organization (WHO), the major causes of mortality in under-five children are preventable and curable with proper interventions in developing countries (2,3). Intensive care could reduce mortality rates by 15-60% when it is well-equipped and staffed with intensivists (2,4). Regional disparities in the availability of resources, the quality of pediatric critical care services play a major role in the outcome of critically ill children.

Demographic profile and outcome of PICU patients can vary widely in different studies, while there is a scarcity of data from comparatively newly set up PICU from a peripheral government medical college in India. Many new medical colleges were opened at the district level in the last few years throughout India to strengthen

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our health system. The knowledge of the clinical profile and outcome of critically ill children from such a peripheral newly established medical college will help in planning health policies. The aim of the present study was to describe the demographic profile and the outcome of our patients, to find out the relationship of the outcome to diagnostic categories and treatment characteristics, and to assess the predictors of mortality among patients admitted to PICU.

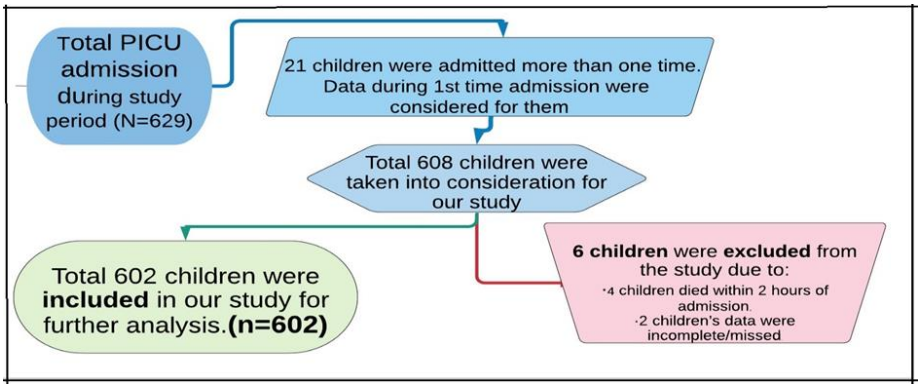
Materials and Methods

This study was a retrospective record based cross sectional analytical study conducted in PICU of a tertiary care government teaching hospital Midnapore Medical College, West Bengal, India. This newly established PICU started functioning since 2016. The patients seeking treatment in this hospital belong to the urban area of small twin cities and surrounding rural districts of West Bengal. This study was conducted in a PICU with eight beds and four stepdown beds facility from November 2018 to October 2019. The patient care was delivered by pediatric MD junior residents, nursing staffs with a few of them critical care trained and critical care technicians under supervision of attending consultants. But our unit was lacking of any formal trained pediatric intensivist or any round the clock dedicated pediatric senior resident and optimal nurse-to-patient ratio. As it is a comparatively newly established set up, all logistic facilities like bed side ultrasound, echocardiography, EEG, central venous pressure monitoring were not available like a fully functional urban metro city-based PICU. This data was obtained from the PICU register, record books, and patient treatment charts.

Inclusion and exclusion criteria: (Flowchart 1)

1. Children aged more than 28 days to 12 years admitted to the PICU during that period were included in this study.
2. In case of readmission, we included the information recorded only during the first admission.
3. We excluded those patients whose data were incomplete or missed.
4. Patients who died on arrival (within 2 hours of admission), not gave sufficient time to give optimal ICU care were also being excluded from the study.

Due to the observational retrospective character of the study, which didn't require any deviation from routine medical care, institutional review board approval was waived, and informed consent was not required. We took permission from a higher authority to retrieve our information. The outcome was categorized as transfers to the main pediatric ward and discharged, later on, left against medical advice (LAMA), referred to specialized centers for further management and death. Due to the lack of clear legal guidelines in our country, withdrawal of life supports was not practiced.



Flowchart 1

Study variable

1. Dependent variable- Outcome.
2. Independent variable -Age, sex, length of stay, diagnosis, need for a mechanical ventilator, inotropes use at admission.

Data collection

The following clinico-demographic data were collected retrospectively from the PICU record book and patient treatment chart: age, gender, diagnosis, presence of comorbidities, the need for mechanical ventilation (MV) and inotropes, length of stay (LOS), and final

outcome. Relevant investigations including complete blood count, ESR, C-Reactive protein, electrolytes, liver function test, kidney function test, blood glucose, blood culture, arterial blood gas, coagulation profile, X-ray were done at admission and repeated subsequently as per requirements. In patients with suspected central nervous system infections or inflammations, cerebrospinal fluid analysis was done. As per the protocol, treatment was started and was modified accordingly. Whenever necessary, antibiotics were changed depending upon the cultureand sensitivity pattern. For the management of patients with shock or poor perfusion,a vasopressor was used. Mechanical Ventilators (MVs) were used to give cardio-pulmonary supports. Both patients with suspected sepsis (Systemic Inflammatory Response syndrome [SIRS] with culture-negative) and proven sepsis with culture-positive body fluid or positive viral marker were included in infectious disease. Patients admitted due to various tropical diseases with complications (malaria/typhoid/dengue/scrub typhus) were also included in this group.

Data analysis

Data was entered into Microsoft excel sheet and SPSS software (version 25) was used for data analysis. The binomial logistic regression model was fitted to the data. A parameter was considered statistically significantfor the patient outcome if the *P*-value was found to be <0.05. 95% Confidence interval (CI) of Odd's ratio was used to report the strength of association between dependent and independent variables.

Results

Out of 602 patients admitted during the study period, 327 were male (M), and 275 were female (F) [M: F=1.2:1]. The average age of admission was 38.87 (~39) months. The most common age group was between 1-month to 1-year (46.7%), and a total of 429 children (71.3%) were below five years of age. The most common disease categories admitted were respiratory (41%), infectious diseases including septicemia (26.9%), cardiological (18.0%), hematological system (8.8%), and central nervous system diseases (6.4%) (Table 1).

Table 1. Age, sex, and system-wise distribution ofpatients admitted in PICU

Age Gr	Sex	RS	Infectious	CNS	CVS	Hematological	Renal	GI	Endocrinal	other
<1 year	Female	85	54	12	33	4	1	5	2	13
	Male	93	41	16	36	5	1	3	5	8
	Total	178	95	28	69	9	2	8	7	21
1 to 5 years	Female	17	13	21	10	11	1	1	1	9
	Male	25	17	29	10	9	7	5	3	15
	Total	42	30	50	20	20	8	6	4	24
>5 years	Female	14	16	32	10	7	5	5	5	13
	Male	13	21	35	12	17	11	5	3	19
	Total	27	37	67	22	24	16	10	8	32
Total	Female	116	83	65	53	22	7	11	8	35
	Male	131	79	80	58	31	19	13	11	42
	Total	247	162	145	111	53	26	24	19	77

RS= Respiratory system, CVS= Cardiovascular system, CNS= Central Nervous System, GI= Gastrointestinal System

Pneumonia was the major cause of admission (27%), followed by septicemia (25.5%), congenital heart diseases (CHD) (12.2%), bronchiolitis (6.6%), seizure disorders (8.6%), encephalitis (5%), and meningitis (4%). Most of the patients admitted with pneumonia, sepsis, CHD were under five years of age. Out of total admission, 51.7% were shifted out to the pediatric ward and later discharged, 14.6%were referred to specialized centers for further management, 3.2% were left against medical advice (LAMA), and 30.4% were expired. Mortality analysis showed respiratory and cardiology were the most common primary system involved, constituting more than two third of the total death. Pneumonia (46.44%) was the most common cause of death, followed by sepsis (42.07%), CHD (15.3%), and bronchiolitis (6.01%) (Figure 1).

The overall median PICU stay was five days (range 1-31 days), with a majority (78.4%) of them staying for 1 to 7days. The median number of days stayed in PICU was significantly low for expired patients (2 days, range

1-23 days) as compared to those patients who were discharged (median 7days, range 2-31 days) (Table 2). 52 (28.57% of total expired) patients died on the first dayof admission, the majority of them having pneumonia (31, 59.6%), bronchiolitis (5, 9.6%), CHD (10, 19.2%), septicemia (20, 38.4%), seizure disorders (4, 7.7%) with several overlaps.

In our study 241(40%) patients were candidate for mechanical ventilator, 156 (64.7%) of them expired. Inotropic support was started in 335(55.6%) patients only after full fluids resuscitation was performed according to international guidelines. From study participants on inotropes, 49.6% (166/335) patients were expired. We found statistically significant correlation between patient's outcome and use of inotropes or mechanical ventilator (Figure 2). Patients who required inotropes support had almost 8 times increased risk of mortality than those who did not need any inotrope [AOR-7.979 (range 4.341-14.653)]. Regarding use of mechanical ventilator, patient who were on MV had 14 times higher risk of mortality than those who did not need MV [AOR-14.051 (range 8.380-23.560)].

Binomial logistic regression model was fitted to the data with outcome as the dependent variable [having 2 major categories- death and survival (discharge+ LAMA+ transferred)] and age, sex, diagnosis, length of PICU stay, the requirement of inotrope/ventilator,*etc*. as independent variables. Variables with $P<0.05$ were considered statistically significant.

For patients who expired - age under 1-year [AOR-2.33 (range 1.282-4.246)], presence of respiratory morbidities like- bronchiolitis [AOR-3.088 (range 1.174-8.125)],pneumonia [AOR8.174 (range 4.292-15.566)],ARDS [AOR-46.051 (range 7.254-292.349)], CNS morbidity like encephalitis [AOR-6.244 (range 1.980-19.687)], haematological morbidity like anaemia [AOR3.453 (range 1.146-10.400)], sepsis [AOR-3.990 (range 2.315-6.877)], electrolyte abnormalities [(AOR-3.538 (range 1.319-9.494)] , use of inotropes and MV were found to be statistically significant(Table 3).

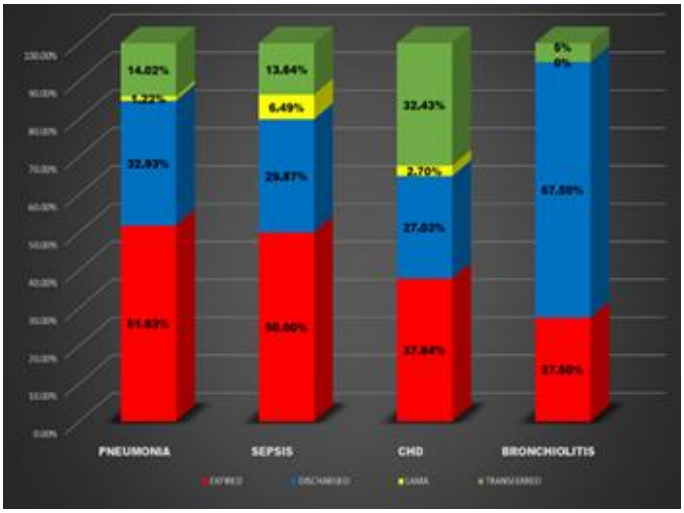


Figure 1. Showing outcome among common causes ofdiagnostic categories.(CHD= Congenital Heart Diseases, LAMA= Left Against Medical Advice)

Table 2. Outcome and length of stay (LOS) in days for patients admitted to a pediatric intensive care unit.(LAMA= Left Against Medical Advice)

OUTCOME		No. of cases	Median LOS (in days)	Minimum LOS (in days)	Maximum LOS (in days)	Standard Deviation (SD)
EXPIRED		183	2	1	23	2.887
SURVIVED	**Discharged**	312	7	2	31	5.110
	LAMA	19	5	2	22	4.819
	Transfer	88	6	1	28	4.580
	TOTAL	602	5	1	31	5.005

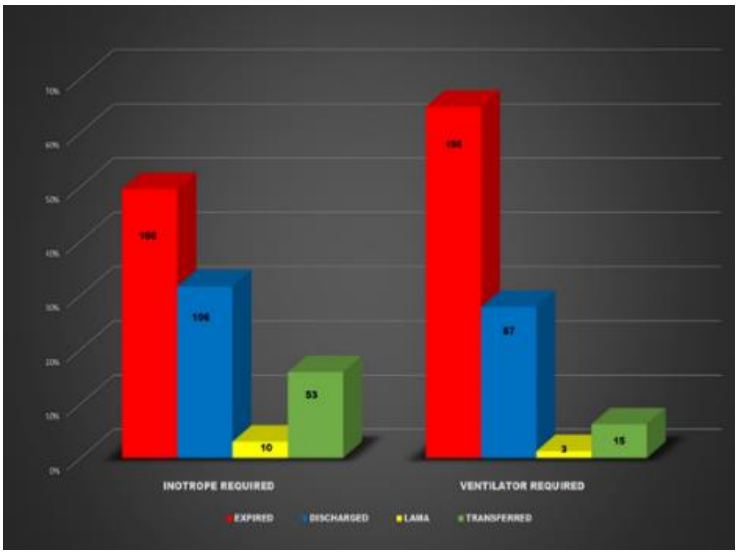


Figure 2. Divided column diagram of outcome based on the requirement of inotropes and ventilator. (LAMA= Left Against Medical Advice)

Table 3. Logistic Regression analysis of predictors associated with mortality in PICU

Independent Variables		Wald (*df=1*)	*P*	AOR	95% C.I.
Age Group	**Under 1 year**	7.688	0.006	2.333	1.282 - 4.246
	1-5 years	0.359	0.549	0.821	0.431-1.565
	Above 5 years			1.000	
Sex	**Female**	0.559	0.455	1.168	0.778-1.753
	Male			1.000	
Respiratory morbidities	**Bronchiolitis**	5.218	0.022	3.088	1.174-8.125
	Pneumonia	40.862	<0.001	8.174	4.292-15.556
	ARDS	16.495	<0.001	46.051	7.254-292.34
	Other respiratory morbidities	3.582	0.058	2.585	0.967-6.911
	nil			1.000	
Cardiological morbidities	**CHD**	0.097	0.755	0.905	0.483-1.696
	other cardiac morbidities	2.177	0.140	1.982	0.799-4.916
	nil			1.000	
CNS morbidities	**Meningitis**	0.866	0.352	1.958	0.476-8.059
	Encephalitis	9.772	0.002	6.244	1.980-19.687
	other CNS morbidities	0.297	0.585	1.272	0.536-3.018
	nil			1.000	
GIT morbidities	**Hepatic encephalopathy**	1.894	0.169	2.673	0.659-10.842
	GI haemorrhage	2.611	0.106	3.105	0.786-12.272
	nil			1.000	
Haematological morbidities	**Anemia**	4.851	0.028	3.453	1.146-10.400
	other	9.544	0.002	5.062	1.809-14.164
	nil			1.000	
Nephrological morbidities	**Nephrotic syndrome**	1.228	0.268	0.279	0.029-2.663
	AKI/RF	3.425	0.064	8.320	0.882-78.452
	other	0.057	0.811	0.730	0.055-9.628
	nil			1.000	
Infection	**Sepsis**	24.832	0.002	3.990	2.315-6.877
	Infection (others/nil)			1.000	
Endocrinal morbidities	**DKA**	3.025	0.082	3.978	0.839-18.854
	others	0.102	0.749	0.753	0.132-4.301
	nil			1.000	
Miscellaneous morbidities	**Poison/bite**	0.313	0.576	0.538	0.061-4.716
	Electrolyte abnormalities	6.298	0.012	3.538	1.319-9.494
	others	2.052	0.152	2.383	0.726-7.816
	nil			1.000	
Inotrope requirement (YES)		44.767	<0.001	7.976	4.341-14.653
Ventilator requirement (YES)		100.426	<0.001	14.051	8.380-23.560
Length of PICU Stay	**Under 1 week**	7.098	0.008	8.837	1.779-43.899
	1-2 weeks	0.101	0.751	0.740	0.115-4.748
	Above 2 weeks			1.000	

(ARDS= Acute Respiratory Distress Syndrome, CHD= Congenital Heart Disease, CNS= Central Nervous System, GIT= Gastrointestinal Tract, AKI= Acute Kidney Injury, RF= Renal Failure, DKA= Diabetic Keto Acidosis)

Discussion

Admission criteria for PICU are institution dependent, based on the available facilities, bed strength, and draining area with medical facilities. Auditing the ICU is an integral component of health planning and improvement of intensive care (5), because many new medical colleges with PICU facilities either started or planned to be started in rural India.

In this study, a total of 602 children in the age group of more than 28 days to 12 years were admitted to the pediatric intensive care unit of Midnapore Medical college and hospital over one year. We found 429 (71.3%) children below the age of 5 years out of them, 281 (46.7%) cases belonged to the age group between 28 days and one year. Below one-year age group was an important predictor of mortality in our study. This is comparable to a study published by Abhulimhen-Iyoha BI *et al.*, (6) showed 72.4% and 50.7% of patients in the above-mentioned age groupand Haque A *et al.*, (7) from Pakistan, where 62.5 % were under five years of age. However, the mean age of our admitted patients was 39 months, similar to other studies in India (40.01±45.79 months) and in Greece (54.26±49.93 months) (6,8). Our study showed a male to female ratio of 1.2:1 similar to Abhulimhen-Iyoha BI *et al.*, (6) (male: female 1.49:1.5) and Haque A *et al.*, (7) where the majority were male (60.9%).

Infectious diseases were major contributors to admission in the past, especially in developing countries like India. But recently, non-communicable diseases and surgical causes of admission are predominant. In this study, most of the cases admitted in PICU belonged to respiratory system disorders, which constituted 41% cases, followed by infectious diseases including septicemia (26.9%), cardiological (18.0%), and central nervous system diseases (6.4%). It was similar to the study done by Earan SK *et al*., (9) in South India, where disease involving the respiratory system was the commonest system (40.2%), followed by infectious disease (19.5%). Our study was in contrast to the study by Haque *et al.*, (7), which showed a morbidity pattern of neurological (28%), followed by cardiovascular and post-cardiac surgery. However, cardiovascular disease entity was the most common (41.1%), followed by neurological (12%) as reported by Abhulimhen-Iyoha *et al*., (6). We had a smaller number of patients with cardiovascular complaints as we lack a full-fledged cardiovascular and any cardiothoracic surgery unit in our center. Infectious diseases like scrub typhus, complicated typhoid, bacterial (mainly with E. coli, Klebsiella, Pseudomonas, Proteus along with a few multidrug-resistant coagulase-positive and coagulase-negative staph aureus), and fungal (predominantly with Candida Albicans) sepsis constituted the next major cases (26.9%) in our study like Kapil *et al*., (10) where septicemia was not an isolated entity, might be associated with other systemic diseases like respiratory tract infection, CNS infection and multiorgan failure.

We analyzed the length of stay (LOS) in our study. The median PICU stay was five days (range 1-31 days) with a majority (78.4%) of them staying for 1 to 7 days. The median length of stay was 2.0 days for those expired in this study. This reflects either an early death in PICU following treatment failure or severity of illness of cardio respiratory aetiology associated with septicemia. The duration of stay in the PICU is an index of severity of morbidity, although this cannot be interpreted in isolation. This is contrast to the study by AdrianPlunkett *et al*., (11) in UK. They showed increased length of stay in non-survivor by advances in pediatric critical care andhealth care delivery. But long stay patients were associated with increased mortality and unfavourable outcome in follow up as evidenced by Japanese study (12).

Mechanical ventilation usage (40%) in our study was in the upper reference values of 31.5-67% according to other study (8,13,14). Those required MV and inotropic support in our study, had poor outcome similar to other studies (4,8).

We referred 14.6% of patients, most of them had complex congenital heart diseases, arrhythmias, surgical cases who required advanced investigations and interventions like electrophysiology (EP) study and radiofrequency ablation, hematological malignancies to specialized centres for further management. Most of them survived because of proper referral to our higher referral centre with telephonic communication.

In our study 3.2% patients left against medical advice. There were many common reasons identified to be financial constraints, domestic problems, overall poor prognosis, wishing to continue treatment elsewhere, dissatisfaction and feeling better. All of these factors are well recognized in literature (15). The limitations of our study included its retrospective study design, which necessitated a dependence on patient records. Due to this we are unable to include those patients in our follow-up who might have presented to or been admitted at another hospital following their LAMA.

Mortality is proportional to the underlying nature of

the disease, physiological status in arrival, admission criteria, and the quality of care. Overall mortality in our study was 30.4%. This is comparable to the mortality rate (28%) of a PICU in a medical college in South India by AK Jyoti *et al*., (16) and Haque A *et al.*, (7) in Pakistan. Various studies reported mortality in the range of 2.6-35% (17-21). This high mortality is related to inadequate resources similar to other developing countries (19). Different studies have proved that full-time trained critical care specialists in pediatric ICUs improve the quality of care and are associated with lower mortality and morbidity rates (20). Limitation of logistics and trained manpower which was appointed and sometimes transferred by the government is part of our health system. But now a day's government's initiatives regarding critical care will improve the system in the coming future.

A study by Kaur G *et al.*, (21) showed sepsis contributes to almost two-third of admission to PICU with a high mortality rate of 42%, similar to our study. We sent blood cultures of pneumonia and septicemic patients, but previously used antibiotics and lack of good microbiological backup did not evaluate organisms in all cases. This relatively high mortality rate in our study may be due to varied reasons, the severity of illness associated with sepsis, delayed referral of complicated pneumonia, bronchiolitis, congenital heart diseases and encephalitis cases from many newly established super-specialty government hospitals, treatment by local quacks, use of irrational combinations of antibiotics and routine use of steroids by few untrained local practitioners could be one of the many reasons.

We used the binomial logistic regression model to determine the strength of association between several clinicodemographic factors and disease outcomes. This study revealed that factors including age below one year, diseases like bronchiolitis, pneumonia, ARDS, encephalitis, anemia, sepsis, and dyselectrolytemia were found to be significant factors associated with mortality. There were some studies done by Gauri S *et al*., (22) and others (4,8,11,19,21) showed different factors of disease outcomes, but this is one of the first kind of study on predictors of mortality from a newly setup PICU of a peripheral government medical college to help future critical care strategy.

Prediction of patient outcomes at admission to PICU is essential not only for counseling parents about the prognosis but also for the optimum utilization of limited resources, evaluating therapies, controlling, and matching the severity of illness in clinical studies.

Our study is one of the first to provide clinicodemographic data and predictors of mortality for critically ill children in the rural population from a newly established peripheral medical college PICU. The demographic profile of our patients showed that although age, sex and comorbidities follow the general pattern of PICU patients in developing countries, there are major differences in overlaps of comorbidity and the severity of the diseases which was supported by less median PICU stay with high uses of inotropes and mechanical ventilations. Outcome analysis showed that mortality rate (30.4%) was high in accordance with the underlying morbidity, its severity and inadequate resources. The statistically significant predictors of mortality in this study were: the presence of comorbid illness, sepsis, anemia, dyselectrolytemia, need for mechanical ventilation, inotropes, and duration of ICU stay. It will help to identify severe cases, prioritize resources and focus on the preventable methods in the public such as vaccine, creating awareness about diseases and proper referral.

This study had some limitations; a retrospective analysis of admitted patients who were not assessed by any proper severity scoring tools like Pediatric Risk of Mortality (PRISM) and Pediatric Index of Mortality (PIM) at the time of admission. The Medical College at the time of study did not have all subspecialty treatment facility and therefore patients were referred. The population is not truly representative of the existing social demographics as it is a rural medical college hospital. However, larger multicentre prospective studies should be done on morbidity and outcome analysis among peripheral medical colleges in India for a better conclusion.

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