Journal of Medicine and Medical Sciences Vol. 5(5) pp. 113-120, May 2014
DOI: http:/dx.doi.org/10.14303/jmms.2014.085
Available online http://www.interesjournals.org/JMMS

Full Length Research Paper

Factors Predicting Mortality in Pediatric Intensive Care Unit in a Tertiary Care Center Southwest Region, Saudi Arabia

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Abstract

Pediatric intensive care units (PICU) aim at promoting qualified care with the objective of achieving the best results and better progress for critically ill children. Mortality is the most frequently assessed outcome in PICU. This study was carried out to assess the factors contributing to the patient mortality in our PICU, including PRISM III and other predicting factors. This is a retrospective medical record review study. We reviewed and analyzed all files for pediatric patients who were admitted to the PICU at Aseer Central Hospital (ACH), during the period from January 2006 till December 2008. A total of 171 patients fulfilled the eligible criteria for inclusion. During the study period 171 patients were admitted to the PICU, of whom 64 (37.4%) died. In multivariate logistic regression analysis, considering those who did not need mechanical ventilation as a reference category, those who needed mechanical ventilation were almost three times more likely to die in the ICU (adjusted OR: 3.44, 95% CI: 1.01-11.69). Children who had total parenteral nutrition were almost three-folded more likely to die in the ICU than those who had no total parenteral nutrition (adjusted OR: 2.87, 95% CI: 1.06-7.74). Those with higher PRISM III scores were more likely to die and this probability of dying increase steadily with increase of PRISM III score. High PRISM III score, application of mechanical ventilator and total parenteral nutrition were significantly associated with higher mortality rate in PICU.

Keywords: PICU, PRISM-III, Mortality.

INTRODUCTION

The practice of pediatric critical care is dynamic and evolving. Whether adult or pediatrics, severities of illness, assessments are critical for wide range of ICU management and administration (Pollack et al., 1987; Pollack et al., 1985; Yeh et al., 1984). Risk-adjustment tools that predict death in PICUs have become established in the past 20 years (Anthony et al., 2006). During the early 90s, the focus has shifted from the more traditional quality assurance methods and mortality risk prediction, to another aspect of outcome analysis, which is to identify faulty processes or risk factors that produce poor outcomes. Attempts to address and subsequently eliminate, if not attenuate such factors would lead to an improvement of care. Scarce resources can also be channeled into areas where the greatest amount of benefits could be seen (Tan et al., 1998).

Mortality is the most frequently assessed outcome. For pediatric intensive care, various methods are available for mortality prediction, including the Pediatric Risk of Mortality (PRISM, PRISM III) and the Pediatric Index of Mortality (PIM and PIM2) (Pollack et al., 1988; Shann et al., 1997; Slater et al., 2003). PRISM III, an updated second generation scoring system, included over 11,000 consecutive admissions in 32 PICUs which have 5-fold more patients than the previous studies, has been validated for use in the United States (Pollack et al., 1996). PRISM III is a widely accepted and is a standard against which other scores are compared. However there are some limitations with the use of PRISM III; a lot of information is needed to calculate it and many units do

not calculate it routinely, worst reading of 12/24h is used and a lot of deaths occur (in one study over 40%) within first 24hrs, so the score may be diagnosing death rather predicting it, there may be blurring of differences of two units as patient in a good unit may recover rapidly and score maybe lower and the same patient in a bad unit might have had higher score due to poor management or limited resources. The high mortality of bad unit may be interpreted as due to sicker patients, the time spent in the hospital before coming to ICU could improve the PRISM score and predict lower than actual mortality (lead time bias) and etiology and natural history of disease are not considered. For an example: DKA and Acute Gastroenteritis with severe dehydration where looking at sub scores and daily assessment may help, severe on day of admission and rapid improvement on intervention Vs H1N1 pneumonia which has low scores on Day1 and may progress to ARDS later showing low PRISM scores leading to death (Wells et al., 1996; Karambelkar et al., 2004). So, it is very important to look for other predicting factors of PICU mortality rather than PRISM-III score.

The main objective of this study is to assess the risk factors contributing to the increased mortality in our PICU, including PRISM III, route of admission and other predicting factors.

SUBJECTS AND METHODS

This is a retrospective medical record review study which was approved by the ethical committee of Asser Central Hospital. We reviewed and analyzed all files for pediatric patients who were admitted to the Pediatric Intensive Care Unit at Aseer Central Hospital (ACH), Southwest Region, Saudi Arabia, during the period from January 2006 till December 2008. It is a tertiary referral hospital which receives patients from 20 peripheral hospitals. It is a 7-bed medical and surgical pediatric intensive care unit (PICU), in a tertiary care hospital 570 total bed capacity with 50 beds pediatric department. This study included the inclusion criteria were children from 1 month till 12 years and who stayed in pediatric intensive care unit more than 6 hours. We excluded patients with burn as well as traumatic patients with *Glasgow Coma Scale* (GCS) less than 5/15.

A total of 171 patients fulfilled the eligible criteria for inclusion. Our institutional review board approved the project and waived the need for consent. The initial vital signs and basic laboratory investigations were recorded. Respiratory distress was defined according to the World Health Organization age-related tachypnea as follows; younger than two months: >60 breaths/min, two to 12 months: >50 breaths/min, one to 5 years: >40 breaths/min and ≥5 years: >20 breaths/min (World Health Organization, 1995; Russell, 2001).

The pediatric risk of mortality (PRISM-III) scoring scale was applied for 142 children out of the included patient in his/her first 24h of PICU admission, their calculated score recorded and then the patients' hospital course followed to determine the early outcome of his/her acute sickness (as dead or survived) (Pollack et al., 1996).

Following parameters were covered as determined by PRISM-III system for scoring:

- Cardiovascular system: including systolic blood pressure and heart rate
- Nervous system: including pupils' light reflex and level of consciousness
- Blood tests: including arterial blood gas (pH, total CO2,PaO2 and PaCO2), serum levels of sugar, BUN and creatinine, platelet and white blood cell counts, prothrombin time and partial thromboplastin time
- Body temperature

Data collected was entered in an Online PRISM III calculator available online at www.medal.org (Svirbely, 1999). No patient was imposed by any excessive cost or hazard for mere study. In addition to PRISM-III scores; age, sex, nationality, route of admission, duration of PICU and total hospital admission of every patient, involved system, respiratory distress, renal failure, heart failure, mechanical ventilation, central line, peritoneal dialysis, total parenteral nutrition and inotropic support were recorded. Studied patients were classified into 5 groups according to their PRISM-III scores: 0-5, 6-10, 11-15, 16-20and 20 or more. PRISM III total score and sub scores were calculated as follows (Karambelkar et al., 2004):

- Cardiovascular and Neurologic sub-score = (points for systolic pressure) + (points for temperature) + (points for mental status) + (points for heart rate) + (points for pupillary reflex)Max=30 & Min=0
- Acid-base and Blood gas sub-score = (points for acidosis) + (points for pH) + (points for PaCO2) +(points for total CO2) + (points for PaO2)Max=22 & Min=0
- Chemistry sub-score = (points for glucose) + (points for potassium) + (points for creatinine) + (points for blood urea nitrogen)Max=10 & Min=0
- Hematology sub-score = (points for WBC count) +(points for platelet count) + (points for PT and PTT testing)Max=12 & Min=0

Total PRISM III score = (cardiovascular and neurologic subscore) + (acid base and blood gas subscore) +(chemistry subscore) + (hematology subscore)Max=74 & Min=0

Statistical Package for Social Sciences SPSSTM version 20and Microsoft Office Excel® 2007 were used for statistical analysis of recorded data. Categorical (qualitative) variables were sorted in Contingency Tables and compared by Chi-square test or Fisher's exact test. Quantitative variables were assessed by student t-test. Multivariate logistic regression analysis was performed including significant variables in bivariate analysis in order to control for confounding. Results were considered to be statistically significant if there was $P \leq 0.05$.

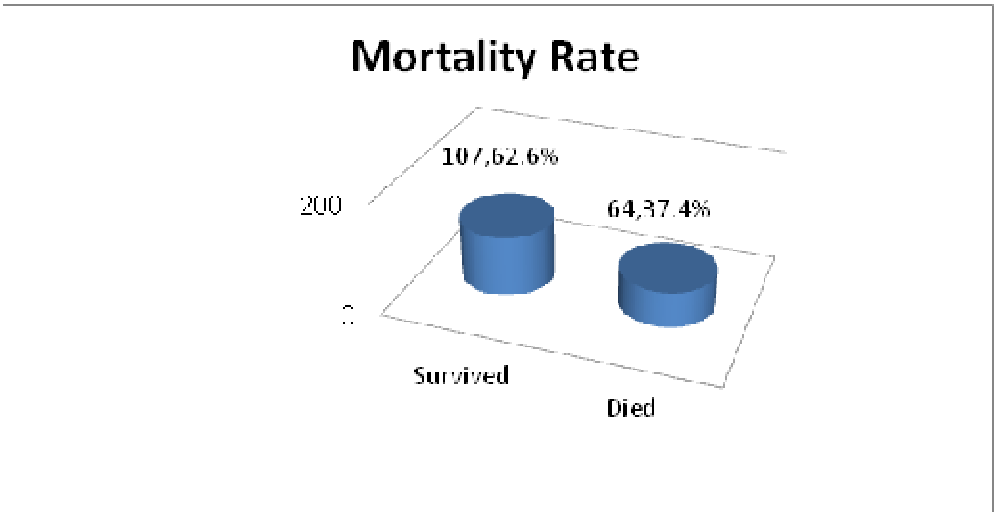

Figure 1. Mortality rate in pediatric ICU, Aseer Central Hospital (ACH), Southwest Region, Saudi Arabia during the period January 2006 -December 2008.

RESULTS

During the study period 171 patients were admitted to the PICU, of whom 64 (37.4%) died (figure 1). More than half (55.6%) of children admitted to the ICU during the study period were one year or younger. Table 1 presents the factors that could contribute to the death on children admitted to the ICU. Younger children reported higher significant death rate ($p<0.05$) compared to older children (45.6 and 48.5% for children aged less than 6 months and between 6 and 12 months, respectively compared to 16.7% among those aged over 60 months).

Regarding route of admission, children referred from other hospitals or those transferred from pediatric department reported higher mortality rate than those referred from ER department (48.5 and 48.6% versus 29.7% respectively, $p<0.05$). Almost two thirds (61.1%) of children who had central line died in the pediatric ICU whereas mortality rate among those who hadn't central line was 26.5%, $p<0.001$. Similarly, 64.2% of children who had total parenteral nutrition died in the pediatric ICU compared to 25.4% among those who hadn't total parenteral nutrition, $p<0.001$. More than half (55.4%) of children who had inotropic support compared to only 23.7% of those who hadn`t inotropic support died in the pediatric ICU. This difference was statistically significant ($p<0.001$). Similarly, more than half (53.2%) of children who needed mechanical ventilation compared to only 9.7% of those who did not need mechanical ventilation died in the pediatric ICU. This difference was statistically significant ($p<0.001$).

Children who stayed in the hospital, including pediatric ICU for more than 4 weeks reported higher mortality rate opposed to those stayed for less than one week (50% versus 30.2%). However, this difference was not statistically significant, $p=0.084$.

Other studied factors (gender, nationality, involved system, respiratory distress, CNS deficit, renal failure, heart failure and peritoneal dialysis) were not significantly associated with mortality of children in pediatric ICU.

From table 2, it is clear that Pediatric risk of mortality score was significantly higher among children who died in the ICU than among those who survived (17.2±6.73 versus 7.90±4.74, $p<0.001$). Considering categorization of Total PRISM III score, figure 2 demonstrates that high Total PRISM III score (>20) was accompanied by a mortality rate of 85% whereas Total PRISM III scores of 0-5 and 6-10 were accompanied with mortality rates of 4.2% and 22.2%, respectively, $p<0.001$.

In multivariate logistic regression analysis (table 3), considering those who didn`t need mechanical ventilation as a reference category, those who needed mechanical ventilation were almost three times more likely to die in the ICU (adjusted OR:3.44, 95% CI: 1.01-11.69). Children who had total parenteral nutrition were almost three-folded more likely to die in the ICU than those who hadn`t total parenteral nutrition (adjusted OR: 2.87, 95% CI:1.06-7.74). Taking PRISM III score 0-5 as a reference category, those with higher scores were more likely to die and this probability of dying increase steadily with increase of PRISM III score. Patients with PRISM III scores of 11-15, 16-20 and > 20 were at almost 23 (adjusted OR: 22.91, 95% CI: 2.56-204.45), 174 (adjusted OR: 174.35, 95% CI: 13.45-2259.1) and 80 (adjusted OR: 80.43, 95% CI: 7.08-913.61) folded higher risk of death in the ICU opposed to those with PRISM III score of 0-5.

Table 1. Factors associated with mortality in pediatric ICU, Aseer Central Hospital (ACH), Southwest Region, Saudi Arabia.

	Survived N=107 N (%)	**Died** N=64 N (%)	Chi-square value	P-value
Age				
less than 6 months (n=57)	31(54.4)	26 (45.6)		
6-12 months (n=33)	17 (51.5)	16 (48.5)		
>12-60 months (n=51)	34 (66.7)	17 (33.3)		
more than 60 months (n=30)	25 (83.3)	5 (16.7)	9.24	0.026
Gender				
male (n=95)	63 (66.3)	32 (33.7)		
female (n=76)	44 (57.9)	32 (42.1)	1.28	0.270
Nationality				
Citizen (n=159)	97 (61.0)	62 (39.0)		
Non-citizen (n=12)	10 (83.3)	2 (16.7)		0.106*
Route of admission				
Emergency room (n=101)	71 (70.3)	30 (29.7)		
Referral from other hospitals (n=33)	17 (51.5)	16 (48.5)		
Transferred from pediatric department (n=37)	19 (51.4)	18 (48.6)	6.29	0.043
Length of hospital stay				
Less than 7 days (n=96)	67 (69.8)	29 (30.2)		
8-28 days (n=61)	33 (54.1)	28 (45.9)		
More than 28 days (n=14)	7 (50.0)	7 (50.0)	4.95	0.084
Involved system				
Central nervous system “CNS” (n=31)	22 (71.0)	9 (29.0)		
Respiratory system (n=29)	19 (65.5)	10 (34.5)		
Gastrointestinal tract (n=15)	8 (53.3)	7 (46.7)		
Endocrinology/genetic/metabolic (n=22)	12 (54.4)	10 (45.5)		
Cardiovascular system (n=25)	12 (48.0)	13 (52.0)		
Surgical cases (n=18)	11 (61.1)	7 (38.8)		
Others (n=31)	23 (74.2)	8 (25.8)	6.26	0.394
Respiratory distress				
No (n=91)	62 (68.1)	29 (31.9)		
Yes (n=80)	45 (56.2)	35 (43.8)	2.57	0.109
CNS deficit				
No (n=148)	93 (62.8)	55 (37.2)		
Yes (n=23)	14 (60.9)	9 (39.1)	0.03	0.856
Renal failure				
No (n=159)	98 (61.6)	61 (38.4)		
Yes (n=12)	9 (75.0)	3 (25.0)		0.538*
Heart failure				
No (n=146)	92 (63.0)	54 (37.0)		
Yes (n=25)	15 (60.0)	10 (40.0)	0.08	0.774
Mechanical ventilation				
No (n=62)	56 (90.3)	6 (9.7)		
Yes (109)	51 (46.8)	58 (53.2)	31.98	<0.001
Central line				
No (n=117)	86 (73.5)	31 (26.5)		
Yes (n=54)	21 (38.9)	33 (61.1)	18.90	<0.001
Peritoneal dialysis				
No (n=166)	104 (62.7)	62 (37.3)		
Yes (n=5)	3 (60.0)	2 (40.0)		0.620*
Total parenteral nutrition				
No (n=118)	88 (74.6)	30 (25.4)		
Yes (n=53)	19 (35.8)	34 (64.2)	23.42	<0.001
Inotropic support				
No (n=97)	74 (76.3)	23 (23.7)		
Yes (n=74)	33 (44.6)	41 (55.4)	18.01	<0.001

* Fisher exact test

Table 2. Association of pediatric risk of mortality score with mortality of children in the PICU, Aseer Central Hospital (ACH), Southwest Region, Saudi Arabia.

	Survived N=107 mean±SD	**Died** N=64 mean±SD	t-test value	P-value
Pediatric risk of mortality score**	7.90±4.74	17.20±6.73	9.64	<0.001

* Fisher exact test
** Available for 142 patients (78 survived and 64 died)

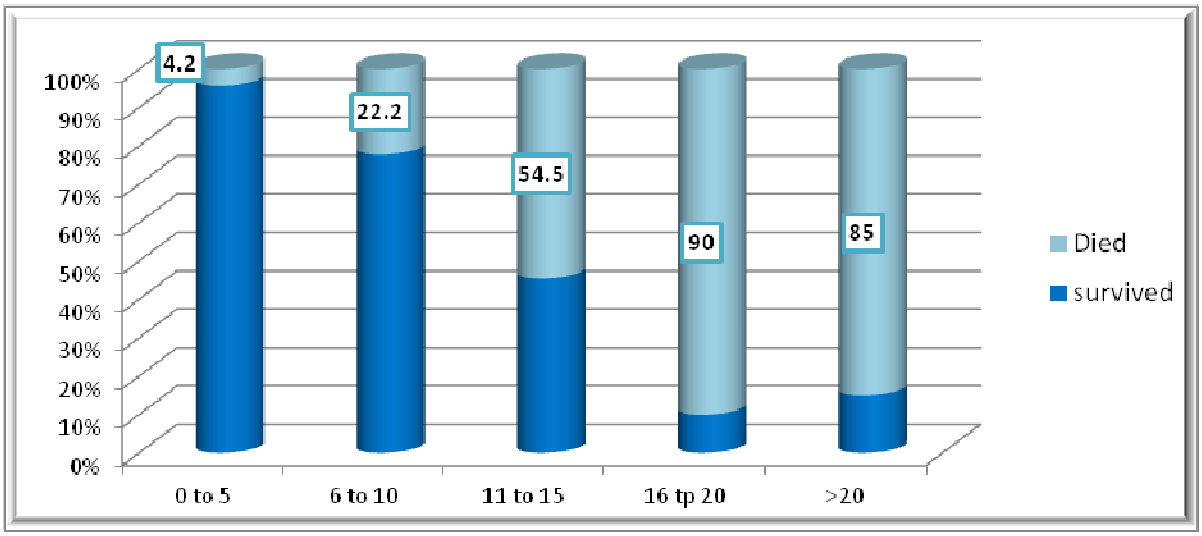

Figure 2. Mortality in the pediatric ICU according to level of pediatric risk of mortality score.

Table 3. Predictors of mortality in the pediatric ICU, Aseer Central Hospital (ACH), Southwest Region, Saudi Arabia: Results of multivariate logistic regression analysis.

	Survived N=107 N (%)	**Died** N=64 N (%)	Adjusted OR	P-value	95% CI
Mechanical ventilation					
No (n=62)®	56 (90.3)	6 (9.7)	1.0	------	
Yes (109)	51 (46.8)	58 (53.2)	3.44	0.048	1.01-11.69
Total parenteral nutrition					
No (n=118)®	88 (74.6)	30 (25.4)	1.0	------	
Yes (n=53)	19 (35.8)	34 (64.2)	2.87	0.037	1.06-7.74
Pediatric risk of mortality score (n=142)					
0-5 (n=24)®	23 (95.8)	1 (4.2)	1.0	------	
6-10 (n=45)	35(77.8)	10 (22.2)	4.66	0.167	0.52-41.45
11-15 (n=33)	15 (45.5)	18 (54.5)	22.91	0.005	2.56-204.45
16-20 (n=20)	2 (10.0)	18 (90.0)	174.35	<0.001	13.45-2259.1
>20 (n=20)	3 (15.0)	17 (85.0)	80.43	<0.001	7.08-913.61

OR: Odds Ratio CI: Confidence interval
® Reference category
Variables of age, route of admission, central line and inotropic support were removed from the final logistic regression model (insignificant)

DISCUSSION

The overall mortality rate at our PICU (37.4%) is higher than mortality rates reported at PICUs in North and South America and Europe (4.4-16.2%) [16-20].This finding could be attributed partially to the high percentage of infants in our cohort (>55% were under one year of age) with higher mortality rate compared to older children. In addition It could reflect many factors which participate in higher mortality rates, especially in infancy period.

The clinical judgment of the severity of a disease process is not uniform and is related to the experience and clinical ability of physician. Prediction of patient outcome is important for the patients and family and is relevant for policy formulation and resource allocation; the optimum usage of ICU beds will obviously allow maximum utilization of limited resources (Bhadoria and Bhagwat, 2008; Wells et al., 1996).

Because of the shortage of available beds in PICUs (Ballot et al., 1995) and the cost of critical care borne by the families, the selection of patients has always been a factor determining patient care. Factors such as availability of beds and cost frequently delay the hospitalization and transfer of patients (Flabouris, 1999) and delay the use of diagnostic procedures and therapeutic measures as clearly noticed in peripheral hospitals. Together, these factors may increase the length of stay, cause the patient's condition to deteriorate, increase the risk of adverse events, and increase hospital costs and finally increase the mortality rate in PICU.

This study confirms many previous observations about deaths within a PICU, and adds some details of value. In this study, 36.3% of admitted patients underwent mechanical ventilation for 24 hours or more. This finding agrees with that described by others (da Silva et al., 2009; Farias et al., 2004; Randolph et al., 2003; Fedora et al., 2005). Patients ventilated for less than 24 hours were usually of immediate postoperative status, those who had low level of consciousness that was rapidly reversed, and those who died within 24 hours after PICU admission. The current study proved that patients who underwent mechanical ventilation were more likely to die in the PICU.

The adverse sequelae associated with TPN result from the combined detrimental effects of not directly feeding the bowel, as well as the metabolic, immunological, endocrine, and infective complications associated with infusing a synthetic "nutrient cocktail" into a patients` systemic venous system (Marik and Pinsky, 2003).The gastrointestinal mucosa is metabolically highly active, and enteral nutrition increases mucosal blood flow and provides a direct source of nutrients. Lack of enteral feeding results in gastrointestinal mucosal atrophy, bacterial overgrowth, increased intestinal permeability, and translocation of bacteria and/or bacterial products into the portal circulation (Hadfield et al., 1995; Nakasaki et al., 1998).

Furthermore, the absence of enteral nutrition causes liver atrophy with rapid depletion of the liver's antioxidant enzyme systems (Marik and Pinsky, 2003). In addition, TPN is often associated with significant hepatobiliary complications, including hepatosteatosis and hepatocellular injury leading to liver failure (Sandhu et al., 1999) and it is immunosuppressive (Alverdy et al., 1992).

Lin and colleagues (Lin et al., 1996) have demonstrated that TPN, as compared to enteral nutrition, is associated with decreased mobilization of inflammatory cells and decreased production of tumor necrosis factor-α,interleukin-1β, and interferon-γ, with decreased bacterial clearance. Experimental sepsis models have demonstrated a significantly higher mortality in animals receiving parenteral than enteral nutrition (Lin et al., 1996; Kudsk et al., 1981). These data are supported by clinical studies which consistently demonstrate a higher risk of infection in patients receiving TPN than enteral nutrition (Moore et al., 1992; Kalfarentzos et al., 1997; Abou-Assi et al., 2002).

Heyland and colleagues (Heyland et al., 1998) performed a metaanalysis of TPN (compared to no nutritional support) in critically ill patients. They demonstrated that in critically ill patients TPN almost doubles the risk of dying (RR1.78; 95% CI 1.11–2.85). Similarly, using a risk adjusted mortality ratio we have demonstrated that in critically ill ICU patients TPN, as compared to enteral nutrition, doubles the risk of dying (Marik and Karnack, 2001).

In the current, in a multivariate logistic regression analysis, after controlling for confounding, TPN was significantly associated with almost three-folded risk for death in PICU.

Our country is becoming increasingly concerned about the costs and questions of effectiveness and quality of care using high-technology medicine in PICUs. Until the development of the PRISM score for mortality prediction and the subsequent validation by other studies (Bilan et al., 2009), comparing performance of different PICU settings was nearly impossible because of the wide variability in the types and conditions of the patients and the multiple factors influencing their outcomes. The PRISM score is a major step forward in standardizing these conditions.

PRISM III scores have been studied extensively by Karambelkar et al. (2012), Tan et al (1998), Gemke (2002), El-Nawawy in Egypt (2003), Bhatia et al. (2003), Slater et al. (2003), Leteurtre et al. (2004) and Choi et al. (2005). The above-mentioned studies have results that were similar to the present study as we proved that PRISM III is a significant predictor for mortality in pediatric ICU. We concluded that PRISM III is a good tool for prognostication and comparison of PICU practices with respect to outcome, despite that a lot of information is needed to calculate it and many units do not calculate it routinely (Karambelkar et al., 2004) and the time spent

in the hospital before coming to ICU could improve the PRISM score and predict lower than actual mortality (lead time bias) (Wells et al., 1996).

Among limitations of the current report, it was based on retrospective chart reviews. Such studies may suffer from recall and interpretation bias (Keenan et al., 1997). However, the prospective studies in this type of research are exposed to the possibility of "responder bias," as a result of the emotional nature of these encounters and the possibility of recall bias when the main investigator had to interview the staff (Ruttimann, 1994).

CONCLUSION

Mortality rate of Pediatric Intensive Care Unit at Aseer Central Hospital is higher than those reported in other countries. High PRISM III score, application of mechanical ventilator and total parenteral nutrition were significantly associated with higher mortality rate in PICU. Further studies and researches are needed in PICU with availability of modern facilities and high quality services nowadays and to be compared with the previous one.

ACKNOWLEDGEMENT

We gratefully acknowledge the review of the manuscript by Prof. Mohammed Awad Elhaj(Professor of Pediatrics, College of Medicine, King Khalid University) and Dr. Ahmad Al-Barki (Consultant of Pediatric Intensivist, Aseer Central Hospital) for his great effort supervising our work.

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How to cite this article: Alsuheel A.M. and Shati A.A. (2014). Factors Predicting Mortality in Pediatric Intensive Care Unit in a Tertiary Care Center Southwest Region, Saudi Arabia. J. Med. Med. Sci. 5(5):113-120