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**Study of Predictive Value of Pediatric Risk of Mortality
(PRISM) Score in Children with End Stage Liver Disease**

THESIS
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IN
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BY

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ABSTRACT

Introduction: The Pediatric Risk of Mortality (PRISM) score is a physiology based scoring system used to quantify risk of mortality in pediatric intensive care unit (PICU) populations.

The aim of this study: was to evaluate the use of the PRISM score to predict the outcome of patients with end stage liver disease (ESLD) and fulminant hepatic failure (FHF).

Patients and methods: This present study included 30 patients with ESLD and FHF, whose ages ranged from 2 to 108 months, who were admitted to the Emergency room (ER) and the Hepatology department of Cairo University Pediatric Hospital (tertiary referral hospital) during the period from May to November 2008. Surviving patients were followed up for 6 months till May 2009.

Results: Deceased patients compared with survivors were significantly younger (median age 7 vs 24 months). The median PRISM Score was 10. Deceased patients showed higher PRISM Score than survivors (15 vs 9). The GCS ($p = 0.002$) and the systolic blood pressure ($p = 0.001$) showed high statistical difference between survivors and deceased patients. The diastolic blood pressure ($p = 0.015$), respiratory rate ($p = 0.033$), PCO₂ ($p = 0.018$) and the pupillary response ($p = 0.052$) were statistically different between them. Other laboratory tests including tests of liver function such as serum bilirubin ($p = 1.00$), PT and PTT ($p = 0.961$) did not show any statistical significance.

The PRISM score was not significantly different within the different ESLD and FHF etiologies ($p = 0.385$). Neither the PELD score ($p = 0.2$), nor the Child-Pugh score ($p = 0.4$) was associated with mortality

Conclusion: The PRISM score is a good means of severity assessment & mortality prediction in pediatric ESLD and FHF patients, with a cut-off point of 9.5, 70.6% sensitivity and 61% specificity. A death probability higher than 5.95 had a 70.6 % sensitivity and 85% specificity.

Keywords: End stage liver disease, fulminant hepatic failure, PRISM score, pediatric intensive care units.

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LIST OF ABBREVIATIONS

AIH	Autoimmune Hepatitis
AJCC	American Joint Committee on Cancer
ALF	Acute Liver Failure
ALT	Alanine Aminotransferase
AMA	Antimiochondrial Antibodies
ANA	Antinuclear Antibodies
Anti-LKM	Anti Liver- Kidney Microsomal antibodies
ASMA	Anti smooth muscle Antibodies
AST	Aspartate Aminotransferase
CMV	Cytomegalovirus
CPAP	Continuous positive airway pressure
CPR	Cardiopulmonary resuscitation
CTP	Child-Turcotte-Pugh
CVP	Central venous pressure
DKA	Diabetic ketoacidosis
EBV	Epstein Barr virus
ECG	Electrocardiogram
EDTA	Ethylene diamine tetra acetic acid
EEG	Electroencephalogram
EHBA	Extra hepatic biliary atresia
ER	Emergency Room
ESLD	End Stage Liver Disease
FFP	Fresh Frozen Plasma
FHF	Fulminant Hepatic Failure

FIO ₂	Fractional inspired oxygen
GCS	Glasgow Coma Scale
GGT	Gamma Glutamyl Transpeptidase
GI	Gastro-Intestinal
HAV	Hepatitis A virus
HBsAg	Hepatitis B surface Antigen
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HDV	Hepatitis D virus
HE	Hepatic Encephalopathy
HIV	Human Immunodeficiency virus
HRS	Hepato renal syndrome
HSV	Herpes Simplex virus
ICP	Intracranial pressure
ICU	Intensive Care Unit
INR	International Normalized Ratio
LOS	Length of stay
LT	Liver Transplantation
MEGX	Monoethyl-glycine xylidide
MRI	Magnetic Resonance Imaging
NICU	Neonatal Intensive Care Unit
NIs	Nosocomial Infections
OLT	Orthotropic Liver Transplantation
PaCO ₂	Partial pressure of Carbon dioxide in arterial blood

PALF	Pediatric Acute Liver Failure
PaO ₂	Partial pressure of Oxygen in arterial blood
PCWP	Pulmonary Capillary Wedge Pressure
PDR	Predicted death rate
PELD	Pediatric End-Stage Liver Disease
PICU	Pediatric Intensive Care Unit
PIM	Pediatric Index of Mortality
PRISM	Pediatric Risk of Mortality
PSI	Physiological Stability Index
PT	Prothrombin Time
PTLD	Post transplantation Lymphoproliferative disease
PTT	Partial Thromboplastin Time
ROC	Receiver operating characteristic
RRR	Rounded Regular Reactive
SBP	Spontaneous bacterial peritonitis
SSU	Short Stay Unit
TGF-beta1	Transforming growth factor beta1
TIBC	Total iron binding capacity
TIPS	Transjugular intrahepatic portosystemic shunt
TISS	Therapeutic Intervention Scoring System

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RECOMMENDATIONS

- 1) Mortality risk scoring systems are integral part of PICUs care.
- 2) Patients with ESLD and FHF should have the priority on the waiting list for LT according to their severity of illness.
- 3) The PRISM score may be repeated during admission to show the progress in the patient's condition whether it is deteriorating or regressing and also before discharge.
- 4) More wide application of the PRISM score in a larger group of patients; as our study included only 30 patients, also separation of patients with ESLD from patients with FHF may add new findings.
- 5) Application of other numeric scores in patients with ESLD and FHF to assess their discriminative power in mortality prediction and choose the most ideal one with more stress on scores including different ranges for variables that are closely related to impairment of liver functions such as bilirubin level which is an important prognostic indicator in patients with chronic liver disease, albumin level which indicates chronicity of liver illness, coagulation time, etc.
- 6) Physicians should not be guided only by scoring systems.
- 7) Numeric scoring systems should be always updated and validated for use. A PRISM score with ranges of variables based on data collected from Egyptian PICUs is recommended.

INTRODUCTION AND AIM OF THE WORK

Introduction

End-stage liver disease (ESLD) in children presents a challenging array of medical and psychosocial problems for the health care delivery team. Many of these problems are similar to those encountered by caregivers of adults with ESLD, such as the development of complications of cirrhosis, including ascites, spontaneous bacterial peritonitis (SBP), and esophageal variceal hemorrhage. However, the natural history of disease progression in children and their responses to medical therapy can differ significantly from that of their adult counterparts (**Leonis and Balistreri, 2008**).

A primary obstacle to early diagnosis and treatment of ESLD is the lack of a well- validated, standardized assessment method (**Tarek et al., 2006**).

The pediatric risk of mortality (PRISM) score was published in **1988a** by **Pollack et al.** and exhibited an excellent discriminatory and predictive performance. The PRISM score is a second-generation physiology-based predictor for pediatric intensive care unit (PICU) patients (**Wells et al., 1996**).

It is still the most widely known and used at the PICU and used in clinical trials as a standard prognostic score for evaluation of disease severity in pediatric patients (**Gemke and Van, 2002**). The PRISM score was developed from the Physiologic Stability Index (PSI) to reduce the number of physiologic variables required for PICU mortality risk assessment and to obtain an objective weighing of the remaining variables (**Apostopoulou et al., 2005**).

The relationship between physiologic status and mortality risk may change as new treatment protocols, therapeutic interventions and monitoring strategies are introduced (**Jacques and Jacques, 2005**).

The use of PRISM score or other scoring systems in the PICU is of great importance for evaluating the efficacy and efficiency of a particular PICU. However, the PRISM score was developed and validated in the United States and subsequently validated in Europe, but has not been evaluated in a less affluent society (**William et al., 2004**).

The PRISM score was used for assessing the severity of pediatric fulminant hepatic failure (FHF) and had proved to be an accurate means of severity assessment (Tissieres *et al.*, 2003).

Aim of work

The aim of this work was to study the predictive value of the PRISM score in admitted patients with ESLD and FHF to the Emergency Room (ER) and the Pediatric Hepatology Unit at Cairo University Pediatric Hospital (tertiary referral hospital) during a period of 6 months. Survivors were followed up for another 6 months.

SEVERITY SCORES IN PICUs

Scoring systems to measure the severity of illness in patients in the intensive care unit (ICU) have evolved significantly over the past decade and are gaining widespread acceptance among health care providers and institutions (**Markovitz, 1999**).

Health care providers have long sought methods to objectively describe the severity of illness of patients and groups of patients. Many disease or organ-specific systems, eg, the Apgar score for newborns, the Glasgow Coma Scale (GCS) for head-injured patients, and the New York Heart Association Functional Classification for patients with heart disease, have gained widespread acceptance over time. New tools that may offer better predictive ability, identifying pertinent variables using the modern techniques of regression analysis, are being developed (**Combes et al., 1996**).

Severity scores were first developed for adult ICUs and subsequently, in 1988, the first specific pediatric score was published: the PRISM score (**Pollack et al., 1988a**). Severity scoring systems currently available can be divided into four categories: injury scores, severity of illness (case mix adjustment), intervention scores, and workload scores. Severity of illness scores are abundant (**El-Nawawy, 2003**). In the PICU, the PRISM score is the most relevant and best known (**Russell, 1999**).

The first scoring system in PICU was the Therapeutic Intervention Scoring System (TISS). The basis of this system is that therapeutic intensity defines severity of illness. A score of one to four points is awarded to each of 70 nursing and medical procedure. However, the system does not take into account the variability in clinical practice which may occur between ICUs and between different countries. It is however a useful system for assessing expenditure and has been extensively used for this purpose (**Bion, 1992**).

The first physiology based scoring system to assess severity of acute illness in the total population of infants and children admitted to the pediatric ICU was PSI. It