

## Predictive Factors of Influenza Outcome in Pediatric Patients by Pediatric Risk of Mortality (PRISM) III

\*Nemat Bilan<sup>1</sup>, Farinaz Amirikar<sup>2</sup>, Shamsi Ghaffari<sup>3</sup>

<sup>1</sup>Pediatric Pulmonologist, Pediatric Health Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

<sup>2</sup>Pediatric Pulmonology Fellowship, Pediatric Health Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

<sup>3</sup>Pediatric Cardiologist, Pediatric Health Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

### Abstract

#### Background

Influenza viral infections lead to a wide range of respiratory diseases which have an annual pattern and are responsible for significant morbidity and mortality among children. It was found that influenza among children has significant rates of mortality and morbidity. We aimed to evaluate the diagnostic value of Pediatric Risk of Mortality (PRISM) III scoring system in children with influenza for clinical outcomes of patients.

#### Materials and Methods

In this cross-sectional study, 50 children referred to the Children's Hospital of Tabriz (Iran) with flu symptoms who were admitted to the ward or pediatric intensive care unit (PICU) were evaluated through the PRISM III model.

#### Results

In this study, 50 children (48% female and 52% male) with a mean age range of  $70.28 \pm 22.46$  months with the flu were studied. The mean PICU of patients' hospitalization was  $34.2 \pm 36.5$  days and the mortality rate was 16%. There was no statistically significant relationship between patient mortality and the variables of age, gender, length of hospitalization in PICU and the length of general hospitalization ( $P < 0.05$ ). However, only a statistically significant inverse relationship was observed between blood urea nitrogen (BUN) level and patient mortality among other variables evaluated in the PRISM III model ( $p = 0.016$ ). In addition, there was a statistically significant relationship between PRISM III model score and mortality in the studied patients ( $p = 0.002$ ).

#### Conclusion

In the present study, considering the cut-off point 14, the sensitivity and specificity of the PRISM III model in estimating the mortality of children with influenza are equal to 87.5% and 85.7%, respectively; so the PRISM III model had excellent diagnostic and estimation power.

**Key Words:** Children, Flu, Mortality, PRISM III.

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#### \*Corresponding Author:

Nemat Bilan, Professor, Pediatric Pulmonologist, Pediatric Health Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

Email: bilannemat@yahoo.co.uk

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## 1- INTRODUCTION

Influenza viral infections result in a wide range of respiratory diseases which have an annual pattern and are responsible for significant morbidity and mortality among children. Influenza with its high penetrability is considered as one of the potential causes of global pandemics (1). Influenza viruses are RNA-related viruses which are divided into three A, B, and C types. Influenza and its complications result in high morbidity in the United States, affecting more than 10 million children annually, leading to the hospitalization of 40,000 children (2).

Nearly 90 million children under the age of 5 worldwide are annually infected with the flu (3). Influenza infection leads to a range of physiological effects such as mild upper respiratory tract symptoms to serious problems such as acute respiratory distress syndrome and septic shock which require hospitalization in the PICU (4). The effect of influenza on PICU capacity was observed during the H1N1 pandemic in 2009 such that the rate of mortality and morbidity among children was much higher than that of seasonal flu (5, 6). In addition, many observational studies indicated that the risk of hospitalization in PICU is higher due to influenza in children with chronic underlying diseases (7).

Today, various scoring systems are used to assess the children's condition in intensive care units, which are classified into three general organ-specific mechanisms of injury and pediatric-dependent categories (8). The PRISM (Pediatric Risk of Mortality) model was first proposed by Pollack et al. (9), which is a modified model of the PSI (Physiologic Stability Index) that measures the severity of the disease in a population of children. The third version of this model (PRISM III) is used to compare the performance and how the resources of different intensive care units are used. This system is based on 17 physiological variables which are divided

into 26 smaller ranges. Further, the patient's previous medical history, especially chronic diseases and previous hospitalization days in the pediatric intensive care unit were evaluated (8). It was found that influenza has significant mortality and morbidity among children. In addition, a high rate of hospitalizations due to influenza is related to children and adults over 65 years old (10). For this purpose, this study aimed to evaluate the diagnostic value of PRISM III scoring system in children with influenza for clinical outcomes of patients.

## 2- MATERIALS AND METHODS

### 2-1. Study design and duration

In this cross-sectional study, 50 children referred to the Children's Hospital of Tabriz (Iran) with flu symptoms who were admitted to the ward or PICU were evaluated through the PRISM III model (2019-2020).

### 2-2. Study population and inclusion criteria

The data were collected by consecutive sampling method. Children with the poor general condition and flu symptoms ranging from 1 month to 12 years of age admitted to the ward or PICU were included in the study. In addition, the informed consent form was obtained from the patients' parents.

### 2-3. Exclusion criteria

The exclusion criteria included death within the first 10 hours of hospitalization in PICU, discharge in less than 24 hours from the beginning of hospitalization in PICU, patients with elective hospitalization in PICU, infants less than 1-month-old and patients older than 12 years, and being affected by any malignancy or congenital malformations.

### 2-4. Instrument

After hospitalization of patients, the data related to the patients during the first 24

hours of hospitalization in PICU were extracted through the standard PRISM III form and the score of each patient was calculated. The results obtained from the patients' short-term follow-up (during hospitalization) such as survived and deceased were identified. According to the PRISM III score, patients were divided into four groups: 1-9 points, 10-19 points, 20-29 points and greater or equal to 30 points (greater score reveals higher risk of mortality). Finally, age, sex, and duration of PICU hospitalization were recorded.

### 2-5. Statistical analysis

The data were analyzed by SPSS software version 18 (IBM, Armonk, NY). The quantitative variables such as weight, age and duration of PICU hospitalization and qualitative variables were reported as mean  $\pm$  standard deviation and frequency

(percentage), respectively. Student t-test and Chi-square tests were used to compare the relationship between study variables. Further, ROC Curve (receiver operating characteristics) was plotted to evaluate the sensitivity and specificity of PRISM III. Hosmer-Lemeshow goodness-of-fit Chi-square test was used to evaluate the suitability of the PRISM III model in the study. A p-value of less than 0.05 was considered as significant.

## 3- RESULTS

### 3-1. Demographic data

First, 50 children (48% female and 52% male) with a mean age of 70.28  $\pm$  22.46 months with influenza were studied. **Table.1** indicates the characteristics of the studied patients.

**Table-1:** Baseline characteristics of the participants.

Variables	Number (%)	P-value
Gender		0.095
Males	24 (48%)	-
Females	26 (52%)	-
Mean age (months)	46.22 $\pm$ 28.70	0.074
Median age (months)	37	0.307
PICU admission (yes)	22 (44%)	-
Mean PICU stay (Days)	5.36 $\pm$ 2.34	0.538
Mean Hospitalization (Days)	12.18 $\pm$ 3.84	0.804
Outcome		-
Survived	42 (84%)	-
Expired	8 (16%)	-
P-value shows the association of the variables with mortality outcome. PICU: pediatric intensive care unit		

### 3-2. Mortality and variables

Among the 50 studied patients, 22 (44%) were hospitalized for PICU. The overall mortality rate in the studied patients was 16%. There was no statistically significant relationship between patient mortality and age, gender, duration of hospitalization in PICU and duration of hospitalization (0.074, 0.095, 0.538, and  $p = 0.804$ , respectively). Among the other variables evaluated in the PRISM III model, only a

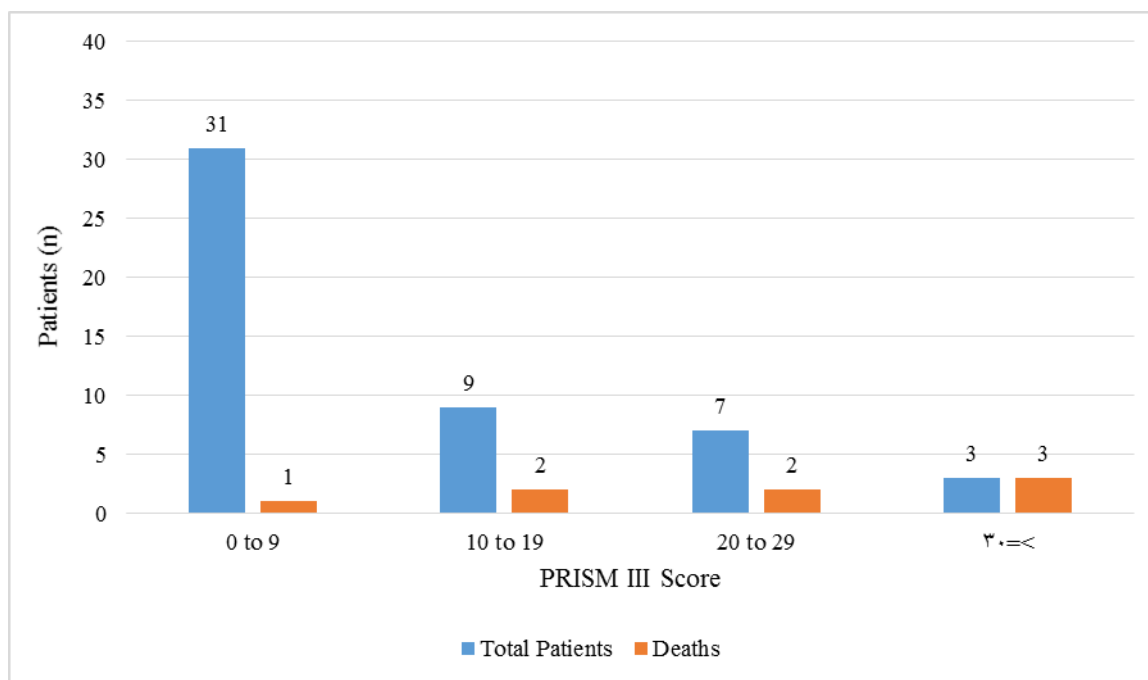
statistically significant inverse relationship was observed between BUN serum level and patient mortality ( $p = 0.016$ ).

### 3-3. PRISM III score and mortality

There was a statistically significant relationship between the PRISM III score and mortality in the studied patients ( $p = 0.002$ ). The mean score of PRISM III model was 44.9  $\pm$  12.10 with a median of 6.5. 31 patients (62%) had a PRISM III score below 10 of the 50 studied patients

and the mortality rate in this group of patients was 3.2%. Among nine patients with a score of 10-19, 77.8% were alive and 22.2% were died. In addition, the mortality rate was 100% in patients with a

score of 30 and above. **Figure. 1** shows the mortality distribution in the studied patients based on the PRISM III score division.



**Fig 1:** Distribution of mortality according to PRISM III score.

### 3-4. Goodness of prediction of PRISM III

The mortality rate estimated by the PRISM III model based on Binary Logistic Regression analysis was consistent with the observed actual mortality values, the results of which are displayed in **Table.2**. In addition, the Hosmer-Lemeshow goodness-of-fit Chi-square test was used to

assess the goodness of prediction, the mortality rate of which was estimated as 16.88%. No statistically significant relationship was observed between actual and estimated mortality values ( $p = 0.893$ ). It was found that p-value higher than 0.05 indicates better test appropriateness.

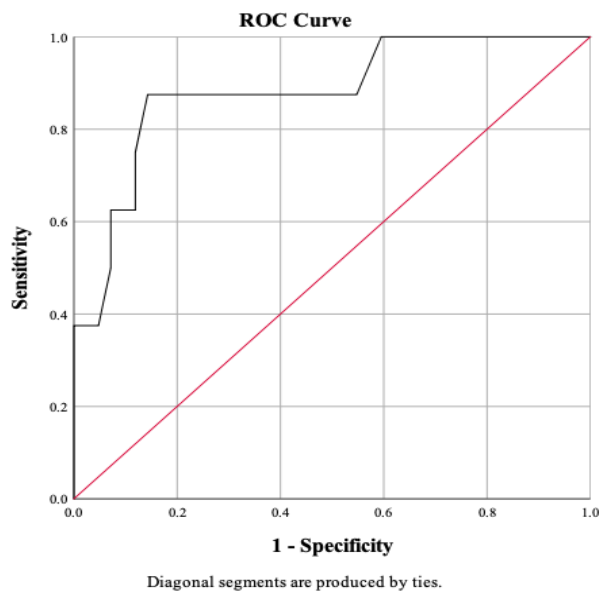
**Table-2:** Goodness of the predictive model by the Hosmer-Lemeshow Chi-square test.

PRISM III score	Total	Survival		Expired	
		Observed	Expected	Observed	Expected
0-9	31	30	30.12	1	1.01
10-19	9	7	7.19	2	2.12
20-29	7	5	5.13	2	2.17
≥30	3	0	0	3	3.14
Total	50	42	42.32	8	8.44

### 3-5. Accuracy of prediction of PRISM III

The results indicated that the PRISM III model in the study therapeutic center has high diagnostic power and differentiation for mortality of children with influenza with the area under the curve of 0.881 (Figure. 2). In addition, considering the cut-off point 14, the sensitivity and specificity of the PRISM III model in estimating the mortality of children with influenza are equal to 87.5% and 85.7%,

respectively. The mortality estimation models provide excellent visibility of disease progression for medical staff such that the obtained results are significantly effective for making the decision by the medical staff and the patient. In addition, children with a mean age of 46.22 months who were admitted to Tabriz Children's Hospital with a diagnosis of influenza were examined for short-term outcome based on the PRISM III model.



**Fig. 2:** ROC curve for PRISM III score.

[Area under the curve is  $0.881 \pm 0.069$  ( $p < 0.001$ , 95% CI: 0.746-1.000)].

## 4- DISCUSSION

Numerous models were used to estimate mortality in patients admitted to PICU such as PRISM and PIM (Pediatric Index of Mortality) (5, 9, 11). Although the PRISM III model is commonly used worldwide in PICU wards, this study aimed to assess the diagnostic value of this model in patients diagnosed with influenza. Since the models mentioned in the PICU sections were used in general and were not specifically examined in a specific diagnosis (patients with

influenza), it is essential that the diagnostic value of this model be measured before routine use in these patients. Generally, it was found that the mortality rate estimated by PRISM III model in children with influenza is in line with the actual observed value and this model with a cut-off point of 14 points has a sensitivity and specificity of 87.5% and 85.7%, respectively, in estimating the mortality of children with influenza. The mortality observed in the current study was 16%, which is consistent with other studies in

developing countries which examined the mortality rate in the PICU (12-14). The present results indicated the proper use and high skill of the medical staff. In addition, a direct and significant relationship was observed between PRISM III score and mortality rate. In fact, an increase in the PRISM III score leads to an increase in the mortality rate, which is in line with the results of other studies conducted in India (12), Hong Kong (15), and the United Kingdom (16). The gender distribution of patients in the current study is in line with those conducted in the surrounding countries; however, no statistically significant relationship was observed between gender and mortality of patients (14, 17). Further, the results are inconsistent with those conducted in the PICU ward in Brazil and Nepal (13, 18).

On the contrary, Aragao et al. reported that the mortality rates are significantly higher in males in PICU wards (19). The PRISM III model has 17 physiological variables, all of which are involved in the result; however, the relationship between systolic blood pressure, heart rate, pupillary reflex, and blood pH were examined in recent studies. No relationship was observed between the above variables and mortality rate. In the study conducted by Varma et al., no relationship was observed between heart rate and mortality, although the relationship between mortality and the desired variable was significant in other variables (12). Ana Lilia et al. found a statistically significant relationship between pupil reflex and blood pH with patient mortality in PICU (20).

Scoring models are considered as excellent for estimating a particular situation with the differentiation power above 0.90. In addition, models with a score of 0.80 to 0.89 and 0.70 to 0.79 are considered good and relatively appropriate, respectively (21, 22). Further, the estimation property of a model is evaluated by the ROC curve with the area under the curve close to 1.

The PRISM III model was a good model in estimating mortality in children with influenza with a surface area below the 0.881 curve. Similarly, the area under curve in the PRISM III model in estimating mortality in PICU was 0.885 and 0.780, respectively, in the study performed by Siddique et al. and Quereshi et al. (14, 17). This value was reported as 0.910 in the study of Choi et al. (15). The studies conducted in Iran and India reported high diagnostic power for the PRISM III model in PICU, where the area under the observed curve was 0.8 and 0.86, respectively (12, 23).

## 5- CONCLUSION

From the result, considering the cut-off point 14, the sensitivity and specificity of the PRISM III model in estimating the mortality of children with influenza are equal to 87.5% and 85.7%, respectively; so the PRISM III model had excellent diagnostic and estimation power. This study has several limitations such as low sample size and retrospectives. In addition, the PRISM III model had excellent diagnostic and estimation power. In the conditions with limited facilities, using patient status assessment models is helpful in clinical decisions. However, it is recommended that clinical examination, para-clinical tests and other diagnostic protocols be used along with the use of these models.

## 6- ACKNOWLEDGMENTS

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**7- CONFLICT OF INTEREST:** None.

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