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Accuracy of Risk Assessment Tool in Predicting Pneumonia's Outcome among Egyptian Children: Hospital Based Study

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Authors' contributions

This work was carried out in collaboration between all authors. Author HM designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author JRL managed the literature searches, data collection and the analyses of the study. All authors read and approved the final manuscript.

Research Article

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ABSTRACT

Aim: To determine possible factors associated with lethal outcome of pneumonia and to assess the accuracy of Pneumonia Severity Index (PSI) and Pediatric Risk of Mortality (PRISM) score in predicting mortality from pneumonia.
Study Design: A retrospective analytical study
Place and Duration of the Study: Pediatric Emergency Department (PED) of the pediatric hospital (Abu El-Reesh) Egypt, during a period from April 2010 to April 2012.
Methodology: Children ≤5 years admitted to the PED diagnosed having pneumonia were included in the study (n=236). Data were retrieved from the electronic records and consisted of; hospital data, personal data, provisional and definite diagnosis, presenting clinical symptoms and signs, outcome and measurements of blood counts and serum biochemical markers.
Results: Non-survivors constituted 26.7% of the studied group. Non-survivors significantly had a higher median PRISM score (18; IQR 11 for non-survivors compared to 8; IQR 6 for survivors, *P* =.000), have a longer median length of stay (8 days; IQR; 1 day for non-survivors compared to 4 days; IQR 2 days for survivors, *P* =.000), higher PSI

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score (61; IQR 39 for non-survivors compared to 41; IQR 20 for survivors, *P* =.000).Only longer LOS, higher PRISM score were independently associated with mortality. ROC curve analysis revealed area under the curve (AUC) of 0.857 for PRISM score (95% CI 0.80–0.91) and 0.73.6 for PSI score (95% CI 0.66–0.81). A PRISM score ≥ 12.5 is 81.4% sensitive and 73.3% specific in predicting mortality.

Conclusion: Case fatality rate is quite high. PRISM scoring is accurate in predicting mortality among pneumonia pediatric patients and thus useful in decision making concerning management of these cases.

Keywords: Under-5 year children; pneumonia severity; risk of mortality.

1. INTRODUCTION

Acute respiratory infections (ARI) kill more children aged less than five years than any other infectious disease accounting annually for almost 2 million deaths among them. Most of these deaths (>95%) occur in developing countries [1]. Pneumonia accounts for almost one in five deaths in children under the age of five years worldwide each year, the largest from a single disease [2]. Thus many clinicians are concerned about the severity of pneumonia and its associated complications and mortality [3]. Hospital length of stay is long especially among severe pneumonia cases requiring advanced life support measures [4]. Clinical judgment has often been proved inadequate to the task of assessing severity in pneumonia and there is some evidence and good reason to believe that a combination of prediction models and clinical judgment is superior to either alone [5]. Prognostic scores have been developed to assess pneumonia severity in order to validate clinical judgment and to guide decisions about treatment settings and to identify low-risk patients who can be discharged from the emergency department [6,7].The Pneumonia Severity Index (PSI) is a widely used scoring system that involves a two- step algorithm to divide patients into five classes based on the risk of death within 30 days [8]. It has been shown to perform consistently well as a predictor of mortality in pneumonia [9], however its accuracy has been challenged, as it potentially overemphasizes the importance of age [3]. The Pediatric Risk of Mortality (PRISM) score is another prognostic scoring system that has been have been developed and carefully validated in tertiary pediatric intensive care units aiming at assessment of the severity of illness and mortality risk adjustment in an objective manner, enabling conversion of numbers into a numerical mortality risk based on logistic regression analysis [10,11]. The criticism for these prognostic scores includes being complex and difficult to implement in routine clinical practice and that inter-observer and intra-observer variability in estimation of these scores may exist [12].

2. AIM OF WORK

To determine possible factors associated with lethal outcome of pneumonia and to assess the accuracy of PSI score and PRISM score in predicting mortality from pneumonia.

3. MATERIALS AND METHODS

3.1 Subjects and Setting

The study included all children under -5 years of age consecutively admitted to the Pediatric Emergency Department (PED) in the pediatric hospital (Abu El-Reesh) affiliated to the

faculty of medicine, Cairo University, Egypt. Subjects were definitely diagnosed with pneumonia during a period of 2 years (from April 2010 to April 2012). Inclusion criteria were: under 5 year child, definite diagnosis of pneumonia as presented with a radiographic infiltrate, and showed at least two compatible clinical symptoms of lower respiratory infections (e.g., body temperature > 38°C, productive cough, chest pain, shortness of breath, crackles on auscultation). Out of the retrieved records during the period of the study (from April 2010 to April 2012) (n=261), 236 had completed records and were included in the study. Records with missing or unavailable data such as the arterial partial pressure of oxygen (PO_2), carbon dioxide (PCO_2) measurements, were excluded from the study.

3.2 Study Design

This is a retrospective analytical study.

3.3 Data Collection

Data were retrieved from the electronic records of patients definitely diagnosed with pneumonia, consecutively admitted to the PED during the study period. These consisted of hospital data (patient hospital number, date of admission and date of discharge from the PED), Personal data (name, age, sex, vaccination status), provisional and definite diagnosis, presenting clinical symptoms and signs, outcome when discharged from the PED being discharged alive or referred to another department or died. The outcome was collapsed in statistical analysis into survivor (I.e. discharged alive from the PED) or non-survivor (died during stay in the PED). Measurements of blood counts and serum biochemical markers (i.e., blood urea nitrogen, albumin, glucose, creatinine, sodium, C-reactive protein); blood glucose level and blood electrolytes, which were performed immediately after venous blood sampling on admission and laboratory processed according to routine protocols in the PED, were retrieved from records as well.

3.4 Outcome Measures

Pneumonia Severity Index (PSI) score and class and PRISM scores were calculated for all patients using an online software PSI calculator [13] and PRISM calculator [14]. PSI is a tool that uses a two- step algorithm to divide patients into five classes based on the risk of death within 30 days. It includes patient characteristics, comorbid illnesses, and physical examination data on admission, radiographic findings, and laboratory results [9]. The PRISM score incorporates 14 physiological and laboratory parameters with 34 variables (according to the age and severity) including: systolic and diastolic blood pressure, heart and respiratory rate, pupillary reaction, Glasgow coma scale, arterial partial pressure of oxygen (PO_2) and carbon dioxide (PCO_2), prothrombin time (PT) and partial thromboplastin time (PTT), blood glucose and bicarbonate deficit; and serum concentrations of calcium, potassium and total bilirubin [10]. In case of presence of two readings for the same variable within 24 hours on admission, only the worst was included. Each admission and discharge for a pneumonia case was considered as one observation unit. The outcome of interest is in-PED mortality among under- 5 years children definitely diagnosed with pneumonia. An official permission was sought from the PED administrative authority prior to conducting the study. Consequently, patients' electronic records, being secured, were transferred by means of the responsible database management official in the department to Excel and then delivered to the researchers.

3.5 Statistical Analysis

Statistical analysis was performed using SPSS version 17. Data were expressed as percentages for categorical variables. For quantitative variables, testing for normality was performed using histogram plotting and Kolmogorov-Smirnov test for age, LOS, PSI score and PRISM score, serum albumin, creatinine, blood glucose, which were not normally distributed. Accordingly, measures of central tendency (median) and measures of dispersion (interquartile range; IQR including 25^{th} and 75^{th} percentiles) were used to summarize continuous variables. Univariate analysis of the factors associated with non-survival of pneumonia cases was performed using the nonparametric Mann-Whitney U test for continuous variables and Chi squared test for categorical variables. Multivariate logistic regression analysis using (ENTER) method was performed to assess the independent association between independent predictors and non-survival outcome. Only variables significantly associated with non-survival in univariate analysis were considered in the multivariate analysis. For categorical variables, namely the age groups and PSI class, the reference group was the first group. Results were expressed as OR and 95% confidence intervals (95% CI). Analysis of a Receiver-Operating Characteristic (ROC) curve was performed to identify the discriminatory ability of both PRISM scoring and PSI scoring to correctly pick up non- survivors and survivors and to find optimal cut-off point to least misclassify non-survivors and survivors with sensitivity and specificity calculated. A probability (*P*) value equal or less than 0.05 is considered to be statistically significant.

4. RESULTS

A total of 236 under-5 years of age children definitely diagnosed having pneumonia and admitted to the PED were included. Table 1 demonstrates that 69.9% of cases were males and that 47% of them are aged ≤ 12 months and 31.8% are aged from 13 to ≤ 24 months. Non-survivors represent 26.7% of the group and associated co-morbidities such as heart diseases and congenital anomalies are diagnosed in 22.5% of the cases. The studied group has low vaccination coverage for childhood compulsory vaccinations particularly for MMR vaccine (19.1%). Half of included cases were classified in PSI class 1 and nearly third of them were in PSI class 2. A comparison of characteristics between survivors and non-survivors shows that non-survivors were significantly more likely to have a lower median weight, a lower median height and to be classified into PSI class 3 and class 4, to have a higher PRISM score and a higher PSI score and to have a longer median LOS in the PED.

Table 2 illustrates clinical signs and Laboratory markers comparisons between survivors and non-survivors. Non survivors had significantly higher serum creatinine levels and lower serum albumin levels and lower platelet count compared to surviving patients. Conversely, clinical signs such as systolic blood pressure, heart rate, respiratory rate and temperature were insignificantly associated with mortality.

Table 1. Description of the studied group and comparison of characteristics between survivors and non-survivors

Variable		Total		Survivors		Non-survivors		OR	95% CI		*P*
		n=236	%	n=173	%	n=63	%		Lower	Upper	
Outcome	Survivors	173	73.3								
	Non-survivors	63	26.7								
Age groups (months)	≤12	111	47	75	43.4	36	57.1	1.74	.97	3.12	.06
	13 - 24	75	31.8	55	31.8	20	31.7	.99	.53	1.85	1
	25 - 36	29	12.3	26	15	3	4.8	.28	.08	.96	.042*
	37 - 48	11	4.7	8	4.6	3	4.8	1.03	.26	4.01	.60
	49 -60	10	4.2	9	5.2	1	1.6	2.94	.036	2.36	.202
Sex	Male	165	69.9	123	71.1	42	66.7	.81	.43	1.50	.511
	Female	71	30.1	50	28.9	21	33.3				
Associated comorbidities		53	22.5	35	20.2	18	28.6	1.57	.81	3.05	.174
PSI class	Class 1	118	50	102	59	16	25.4	.237	.125	.451	0.000*
	Class 2	79	33.5	57	32.9	22	34.9	1.09	.59	2.00	0.446
	Class 3	28	11.9	10	5.8	18	28.6	6.52	2.81	15.11	0.00*
	Class 4	11	4.7	4	2.3	7	11.1	5.28	1.49	18.71	0.009*
Vaccination	BCG	88	37.3	61	35.3	27	42.9	1.37	.765	2.48	.18
	Polio	71	30.1	47	27.2	24	38.1	1.65	.89	3.03	.07
	DPT+HBV	59	25	42	24.3	17	27	1.15	.59	2.22	.67
	MMR	45	19.1	29	16.8	16	25.4	1.69	.84	3.38	.13

	Total		Survivors		Non-survivors		*P*
	Median	IQR (25^{th} -75^{th} percentiles)	Median	IQR ($25^{th}$$75^{th}$ percentiles)	Median	IQR (25^{th} 75^{th} percentiles)	
Age (months)	14	17	15	18.5(6-24.5)	11	12 (6-18)	.09
Weight (KG)	5.5	4 (4 – 8)	6	5 (4 – 9)	5	3 (3.95 – 7)	.05*
Height (cm)	60	26 (52.25-78)	65	25 (55 -80)	60	23 (50 – 72.75)	.04*
LOS(days)	4	4.7 (3 – 7.7)	4	2 (2 - 4)	8	1 (7 – 8)	.000*
PRISM score	10	8 (6 – 14)	8	6 (5 – 11)	18	11 (12 – 23)	.000*
PSI score	50.5	30 (31 -61)	41	20 (31 – 51)	61	39 (46 – 80)	.000*

**P≤ 0.05 is statistically significant.*

Table 2. Comparison of clinical and laboratory markers between survivors and non-survivors

Variable	Survivors				Non survivors				*P*
	n	Median	IQR	(25^{th} -75^{th} percentiles)	n	Median	IQR	(25^{th} -75^{th} percentiles)	
Systolic blood pressure(mm Hg)	173	99.5	28.5	(84.75 - 113.25)	63	93.5	27.25	(79 -106.25)	.19
Heart rate (beat / minute	173	140	32	(123 -155)	63	140	30	(122.75 – 153)	.93
Respiratory Rate / minute	173	33	12	(27 -39)	63	33	9	(28.5 – 37.78)	.49
Temperature (°C)	173	37	1	(37 – 37.5)	63	37	1	(37 – 37.5)	.99
Albumin (g / dL)	106	3.7	1.3	(3 – 4.32)	45	2.85	1	(2.45 – 3.40)	.000*
Blood urea nitrogen (mg / dL)	149	11	9.8	(8 – 17.75)	63	14	14.2	(9- 23.2)	.08
Creatinine (mg / dL)	150	.40	.50	(.20 - .70)	62	.50	.6	(.30 - .50)	.03*
Glucose (mg / dL)	112	122	126	(86.5 – 212.5)	60	127.5	177.25	(88.75 – 266)	.25
Hemoglobin % (g/dL)	149	10.74	2.79	(9.31 – 12.1)	63	11	3.50	(9.40 – 14.50)	.49
Blood K level	139	4.4	1.1	(3.80 – 4.40)	60	4.1	1.75	(3.20 – 4.95)	.09
Platelet count ($\times 10^3$ / mm^3)	138	313	271	(180.5 – 451.5)	63	187	246	(72 – 318)	.000*
White blood cell count ($\times 10^3/mm^3$)	147	11.3	8.94	(7.78 – 16.72)	63	10.7	13.4	(4.8 – 18.2)	.40

**P≤ 0.05 is statistically significant.*

The results of multivariate analysis for non-survival are shown in Table 3. Predictors of mortality were only longer LOS in the PED (OR 1.511, 95% CI 1.18-1.93, *P* = 0.000), and higher PRISM score (OR 1.179, 95% CI 1.063-1.306, *P* = 0.008). Conversely, there was no significant independent association between the PSI score, serum albumin levels, blood creatinine, subject's weight and height and risk of non-survival among pneumonic patients, (Nagelkerke R square model summary is equal to 0.70).

Table 3. Multivariate analysis for predictors of non-survival among under 5 year patients diagnosed with pneumonia.

Variables	OR	95% CI		*P*
		Lower	Upper	
LOS	1.511	1.182	1.931	0.001*
PRISM score	1.179	1.063	1.306	0.002*
PSI class 1	.700	.06	8.10	.775
PSI class 3	4.41	,374	52.109	.239
PSI class 4	6.99	.180	271.67	.298
PSI score	.994	.914	1.78	.880
Serum albumin	0.664	0.276	1.600	.362
Serum Creatinine	1.476	.790	2.758	.222
Platelet Count	0.999	0.995	1.003	.640
Weight (kg)	1.103	.791	1.539	.563
Height (cm)	.948	.894	1.005	.071

**P≤ 0.05 is statistically significant.*

Results of the ROC curve analysis for predicting non-survival from pneumonia are shown in Fig. 1. The area under the curve (AUC) is 0.857 (95 CI .800 - .915) for PRISM score and 0.736 (.661 - .812) for PSI score. Thus the PRISM score is superior to PSI score in predicting non-survival of pneumonia patients. At a cut-off level of PRISM score ≥ 12.5 is 74.6% sensitive and 83.8% specific in predicting non-survival of pneumonia children aged ≤5 years. Regarding PSI score, a cut-off level ≥ 56 is 60.3% sensitive and 78.6% specific in predicting mortality.

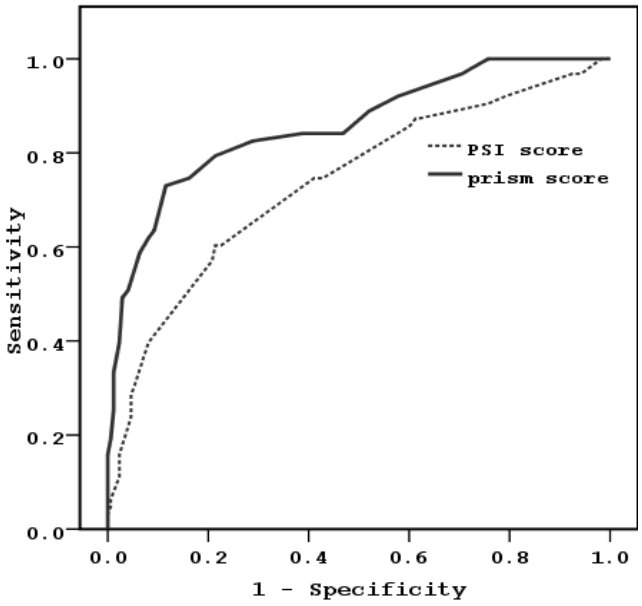

Fig. 1. Analysis of receiver-operating characteristics curve for predicting mortality. The area under the curve is 0.857 for PRISM score, 0.73 for PSI score.

5. DISCUSSION

Pneumonia affects all pediatric age groups, though the highest incidence is among those under- 5 years particularly in the first year of life [15], which is in agreement with the findings of the present study where half of the subjects are aged ≤12 months. The percent of males admitted to the PED in the current study is higher than the females, consistent with sex-specific data for pneumonia incidence which is higher in boys than in girls [16], but these differences in age and sex between survivors and non survivors are statistically insignificant except for children aged 25-36 months who showed significantly higher survival. The percent of immunized children (for compulsory childhood immunizations) included in the present study is low particularly for MMR. Considering that lack of measles immunization (within the first 12 months of life) is a definite risk factor for pneumonia among under 5 years children and that immunization against measles and possibly tuberculosis have contributed substantially to decreasing the pneumonia burden worldwide [17,18], thus, healthcare providers must emphasize upon compulsory immunizations for children admitted to the PED in the future for the sake of general wellbeing of under 5 year children.

The pneumonia case fatality rate in the current study (26.7%) is quite higher than in other similar studies such as the case fatality rate of 8.7% reported among 6202 under-five year children having pneumonia emergently admitted to 2 district hospitals in Malawi [19] and of only 4% among under-5 year children having pneumonia admitted to emergency units in 2 teaching hospitals in Sudan [20]. High mortalities in the present study could be attributed to delayed referral of needy cases to the intensive care as beds in the later setting are nearly 100% occupied all year round and this is a permanent complaint in these settings. In consistent with that, it was observed that all patients referred to the PICU in Alexandria University pediatric hospital in Egypt had delayed transfer and that the total in - PICU mortality rate is as high as 50% [21]. Further research is required to reveal factors of

increased mortality among children with pneumonia admitted to the emergency units particularly the long waiting time for referral to the intensive care.

In-hospital mortality due to pneumonia is often related to associated co-existing illnesses [22,23], however; in the current study associated co-morbidities were not associated with mortality. Longer LOS in the PED and a higher PRISM scoring (higher than a median score of 17.5) were independently associated with mortality in the current study. As regards PSI class in the present study, nearly half of admitted cases were classified PSI class 1 probably due to inability of the family to provide adequate care or that recurrent pneumonia are considered during admission in this setting as well as worldwide [24].

Some studies have demonstrated that PSI class is a predictor of mortality in pneumonia cases such as a study including 213 adult Japanese patients diagnosed with pneumonia showing that higher PSI class is an independent predictor for mortality (OR= 3.55, 95% CI 1.08–11.66, P = 0.037) [25]. In the current study, class 3 and class 4 were associated with mortality in univariate but not multivariate analysis. A study among children admitted to the Pediatric Intensive Care Unit (PICU) in Alexandria, Egypt, have reported that a shorter length of stay was independently associated with risk of mortality [21], while in the current study the opposite was found. This might be due to dissimilarities in included subjects and study settings as El-Nawawy, 2003 included all admitted patients to the PICU with various diagnoses while in our study we included only pneumonia children less than 5 years of age admitted to the emergency unit. It was observed as well by El-Naway, 2003 that a higher PRISM score was independently associated with risk of mortality [21], in agreement with the findings of the current study, although it was suggested a PRISM score of ≥ 26 as a predictor of mortality [21], we suggest here a much lower PRISM score of ≥ 12.5 of 74.6% sensitivity to pick up children at high risk of mortality from pneumonia and although it is a low scoring, yet it guarantees patient safety putting into consideration that some studies have mentioned that risk scores substantially underestimate observed mortalities and misclassify patients with relevant risks of death and that patients at low risk to die according to these scores still have relevant mortality rates with emphasis on importance of recalibration of these scores in different clinical settings [26]. It is to be said that inter-observer and intra-observer variability in calculation of PRISM score exist in clinical settings [12]. Using online PSI and PRISM score calculators, such as in the current study, is easy, rapid, and accessible in the PED and contributes to decreasing such variability considering that scoring ideally is to be calculated by well-trained dedicated staff members to decrease observers' variability.

Extensive studies present many biomarker tests as prognostic candidates for either 30-day or in-hospital mortality in pneumonia patients [26,27,28,29,30,31]. In the present study, none of the tested laboratory markers showed independent association with lethal outcome of pneumonia. These are namely; platelet count, serum albumin, and serum creatinine. Platelets have been increasingly recognized as an important component of innate and adaptive immunity and play a crucial role in antimicrobial host defenses and the coagulation system. A study among adult patients with community acquired pneumonia (CAP) indicated that thrombocytopenia and thrombocytosis are significantly associated with CAP mortality [32], however in the current study; platelet count did not show independent association with mortality due to pneumonia. Regarding serum albumin, it plays an important role in maintaining physiological homeostasis, including maintenance of normal colloid osmotic pressure, transport of endogenous compounds, and scavenging of oxidizing agents [33]. Ugajin et al, 2012 documented in a study among adult patients with severe pneumonia that low serum albumin level is associated with non-survival of patients with severe pneumonia in

univariate analysis but not in multivariate analysis [25] and this finding is in agreement with the current study.

6. CONCLUSION

It is concluded that the pneumonia case fatality rate of under-five year children is quite high. PRISM scoring is more accurate than PSI scoring in predicting mortality among pneumonia pediatric patients and thus useful in decision making concerning management of these cases. PRISM scoring system although involving many variables, yet could be easily calculated using online calculators, as a routine working situation in daily practice.

CONSENT

Not applicable.

ETHICAL APPROVAL

All authors hereby declare that the study has been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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