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Research Article

Could ANP be used as a Predictive Biomarker in Children with acute respiratory distress syndrome?

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Abstract

Background: A hormone generated from the heart, atrial natriuretic peptide (ANP) controls fluid balance and vascular tone by being released in response to atrial stretch and volume overload. ANP levels may increase in children with acute respiratory distress syndrome (ARDS) as a result of cardiac workload, pulmonary hypertension, and abnormal hemodynamics.

Objectives: The purpose of this study was to measure the levels of atrial natriuretic peptide in the plasma of paediatric patients suffering from acute respiratory distress syndrome.

Methods: In this study, 50 healthy children of the same age and sex served as the control group, and 100 children with ARDS were hospitalized to the pediatric intensive care unit (PICU). The study was carried out at Al-Azhar University Hospital between January 2025 and January 2026.

Results: The ANP levels discovered may have predictive power in children with acute respiratory distress syndrome, according to ROC curve analysis, with an area under the curve of 0.903 (95% CI 0.832–1.432, p=0.001). Children with acute respiratory distress syndrome were predicted with 97.88% sensitivity and 90.4% specificity using a cut-off of <511.22 pg/ml.

Conclusions: Elevated atrial natriuretic peptide concentrations increased cardiopulmonary stress and altered fluid dynamics are all possible in children with acute respiratory distress syndrome. In pediatric ARDS, ANP may be useful as a biomarker of disease severity and hemodynamic burden.

Keywords: Acute respiratory distress syndrome, Atrial natriuretic peptide, Alveolar; Cardiopulmonary, Mechanical ventilation, Pulmonary inflammation.

Introduction

The abrupt breakdown of the respiratory system is known as acute respiratory distress syndrome (ARDS). Any seriously ill person above the age of one may experience it. Since the significant fluid accumulation in both lungs, ARDS can be fatal since normal gas exchange is disrupted. Low blood oxygen levels, fast breathing, and trouble getting enough air into the lungs are the hallmarks of the condition. Severe inflammation and diffuse alveolar injury brought on by a range of harmful insults are linked to ARDS. [1].

Because there are many different causes, clinical signs, and criteria used to characterize ARDS, it has been challenging to establish its occurrence. According to a 2007 National Heart, Lung, and Blood Institute estimate, ARDS affects about 190,000 Americans each year. [2]. ARDS's pathogenesis is not fully known. First, inflammatory mediators are thought to proliferate in response to a direct pulmonary or indirect extrapulmonary insult, which encourages neutrophil accumulation in the lung's microcirculation. Large numbers of these neutrophils travel and activate over the surfaces of the alveolar epithelium and vascular endothelium, producing cytokines, reactive oxygen species, and proteases. [3].

Pathologic vascular permeability, holes in the alveolar epithelial barrier, and type I and II alveolar cell necrosis are the results of this movement and mediator release. This ultimately results in the development of hyaline membranes, pulmonary edema, and surfactant depletion, which reduce pulmonary compliance and complicate air exchange. [4]. Patients who are already severely ill due to shock, infection, or other trauma are typically diagnosed with acute respiratory distress syndrome. When there are diffuse abnormalities on x-rays and trouble supplying enough oxygenation, the diagnosis is determined. [5].

In an intensive care unit, supportive care is used to treat ARDS. Additional oxygen and mechanical ventilation are part of the treatment, as is close monitoring of fluid balance and the supportive breathing technique known as positive end expiratory pressure (PEEP). These are coupled with ongoing care for the underlying disease or injury. [6]. The purpose of artificial ventilation is to assist the patient in breathing while the lungs heal. Mechanical ventilation is undergoing new developments. According to preliminary findings from a National Heart, Lung, and Blood Institute study, getting little, as opposed to large, breaths of air from a mechanical ventilator increased the number of days without ventilator usage and decreased the number of deaths by 22%. [7].

The ANP is a member of a recently discovered family of heart hormones that control salt and water balance. It has strong natriuretic and diuretic effects in addition to reducing blood pressure. ANP can be regarded as an endogenous antagonist of the antidiuretic hormone and the renin-angiotensin-aldosterone pathway. ANP helps the body avoid fluid overload by reducing intravascular fluid volume, which in turn reduces

the amount of ANP secreted by the heart. [8].

There is significant variation in the reported pharmacokinetic properties of ANP. ANP's effects have prompted attempts to employ this peptide hormone in the treatment of several illnesses, including hypertension and other conditions that impact electrolyte and water balance. Additionally, attempts to use this hormone in the study and regulation of certain disorders have been prompted by variations in plasma ANP concentrations in different diseases. [9]. Atrial natriuretic peptide release has been shown in prior research to be associated with increases in atrial pressure and/or strain, as well as with pressor medications at levels that raise arterial pressure. [10].

Patients and Methods

Study design and study group

In this study, 50 healthy children of the same age and sex served as the control group, whereas 100 children with acute respiratory distress syndrome were hospitalized to the pediatric intensive care unit (PICU). The study was carried out at Al-Azhar University Hospitals between January 2024 and September 2025.

The study included two groups

Group (I): 100 children admitted to PICU with ARDS.

Group (II): 50 healthy children matched age and sex serving as the control group.

Ethical consideration status

Every procedure was completed in accordance with the institutional committee's ethical guidelines. The study was approved by the Al-Azhar University Faculty of Medicine's Ethical Committee (RESEARCH/AZ.AST./phy003/5/210/3/2025). Parents of study participants were informed of the study's purpose and procedures, and all parents provided written informed consent following an explanation of the study's nature and scope.

Inclusion criteria: Children who have respiratory distress syndrome with an immediate onset are admitted to the intensive care unit. The PALICC criteria for pediatrics were used to diagnose ARDS.

Exclusion criteria: Children with metabolic disorders, chronic conditions such as chest, kidney, and secondary brain injury, as well as suspected inborn flaws.

All children included in this study were subjected to the following

Age, sex, residency, family history, social history, medication history, and a thorough history of chest disease (fever, cough, and dyspnea) were all part of the complete history

taking. Body mass index (kg/m²), height in cm, and weight in kg are examples of anthropometric measures. A comprehensive clinical assessment comprised: general examination (blood pressure, heart rate, respiration rate, temperature, and pulse). Local analysis comprised: Chest form, scars, apical pulsation, intercostal gaps, chest movement, and breathing pattern are all examined. Palpation involves apical beat palpation and chest expansion for equal and symmetrical movements during inspiration and expiration. Using percussion to identify hyper-resonance or dullness. The quality of the sounds and any additional sounds, such as wheeze, stridor, coarse crackles, and fine end-inspiratory crackles, are compared between the two sides using auscultation. Oxygen saturation and oxygen saturation index (OSI) are examples of oxygenation status and mechanical ventilation. Tidal volume (VT), respiratory rate (RR), percentage of inspired oxygen (FiO₂), positive end-expiratory pressure (PEEP), and trigger sensitivity are examples of mechanical ventilation characteristics. CT or chest x-ray, standard tests such as CBC, ESR, liver and kidney function, and serum electrolytes including calcium, potassium, and salt. For both ARDS cases upon admission to the pediatric intensive care unit and the control groups upon study enrollment, serum ANP was tested once in the laboratory.

Statistical Analysis

Serum ANP was measured by Enzyme linked immuno sorbent assay (ELISA) Kit. IBM compatible personal computer running the Statistical Package for the Social Sciences (SPSS) version 25 (SPSS Inc., 2015) was used to gather, tabulate, and statistically analyze the data. The programs MEDCALC V.19.6.1 and IBM SPSS statistics for Windows, version 25.0, Armonk, NY: IBM Corp., displayed qualitative data as numbers (N) and percentages (%), while quantitative data was displayed as mean, standard deviation (SD), median, and range. The following tests are part of analytical statistics: Chi-Squared (χ^2), the Kruskal Wallis test (H), and the Mann-Whitney U test. A P value of less than 0.05 is regarded as significant.

Results

A population flow chart for the 113 children who were admitted to Al-Azhar University Hospitals' pediatric intensive care unit (PICU) with acute respiratory distress syndrome between January 2025 and January 2026. 100 children took part in the trial and were split into two groups: 50 healthy children and 100 children with acute respiratory distress syndrome. 13 patients were excluded from the study (5 patients denied consent and 8 did not match the inclusion criteria). (Fig1).

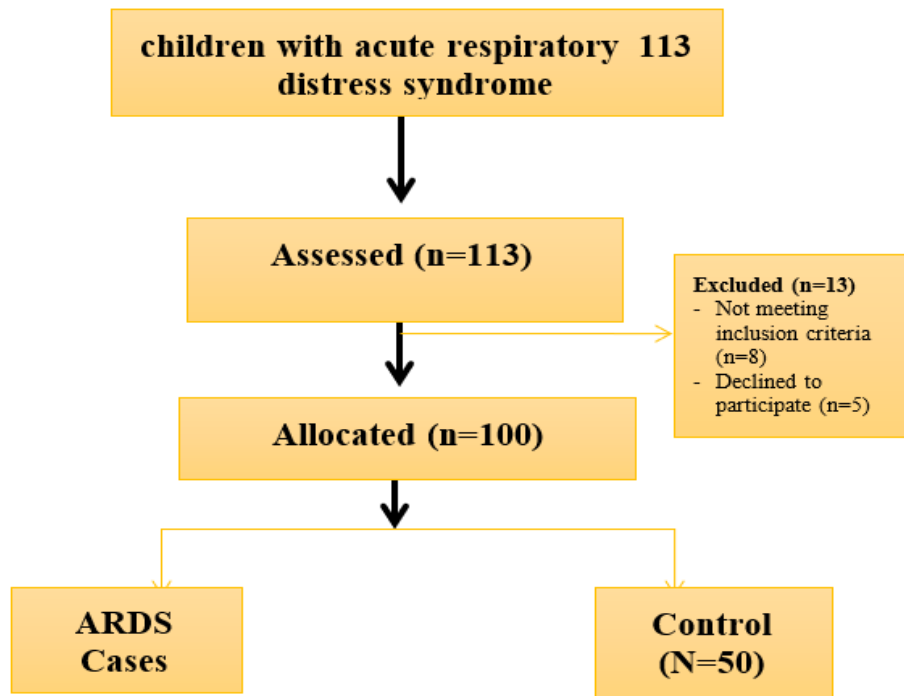


Figure 1. Flowchart of the studied groups

Age, sex, and place of residence did not significantly differ among the groups under study ($P>0.05$), (Table 1). Additionally, Hb, RBCs, renal and liver function tests, sodium, potassium, and calcium levels did not differ statistically significant-

ly between ARDS cases and controls ($p>0.05$). However, ARDS cases have significantly greater WBCs than controls ($p=0.007$), and ARDS cases have much lower PLT than controls ($p=0.001$), (Table 2).

	ARDS Cases (N=100)		Control (N=50)		X2	P-value
Age (years) Mean ± SD	9.66±4.18		9.67±3.88		t=0.565	0.624
Sex, n (%)						
Male	58	58.0	25	50.0	0.863	0.353
Female	42	42.0	25	50.0		

X2: Chi square, t: Independent t test

Table 1. Demographic data among the groups studied.

Variable	ARDS Cases N=100 Mean ±SD	Controls N=50 Mean ±SD	t	P-value
Hb	10.12±2.34	12.15±2.67	0.876	0.365
WBCs	17.65±3.12	8.76±5.19	3.67	0.007*
RBCs	3.82±1.14	4.43±0.71	0.760	0.542
PLT	134±15.10	349.12±63.09	8.100	0.001*
Urea(mg/dl)	43.23±18.66	27.88±13.45	2.11	0.059
Creatinine (mg/dl)	1.95±0.45	0.47±0.21	1.87	0.083
ALT (lu/L)	42.11±19.04	29.10±13.09	2.03	0.061
AST(lu/L)	48.90±21.35	26.09±16.82	2.17	0.058
Sodium (mmol/L)	138.5±2.8	139.9±2.6	0.768	0.450
Potassium (mmol/L)	4.3±0.4	4.8±0.4	0.260	0.915
Calcium (mmol/L)	11.45±5.0	10.45±3.0	1.802	0.511

t: Independent test, *Significant

Table 2. Laboratory investigations among the studied groups.

Additionally, ANP was substantially greater in ARDS cases than in controls, with median values of 513.21 ± 259.44 pg/ml and 185.99 ± 66.32 pg/ml, respectively (P<0.001), (Fig 2). Additionally, among the cases under study, there is no significant correlation between ANP levels and either sex (p=0.807) or age (p=0.067). On the other hand, patients with O2 saturation ≤ 90 had considerably higher ANP levels (762.11 ± 429.10). Additionally, non-survivor patients had a considerably higher score (714.87 ± 210.50) than survivors (582.11±179.22) (P=0.004), (Fig 3).

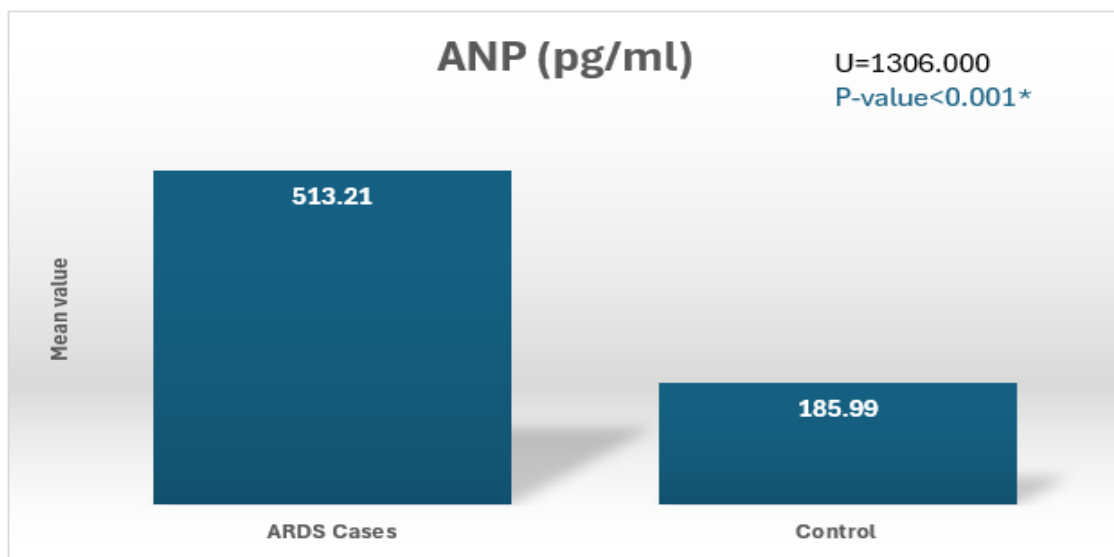


Figure2. Comparison of ANP measurements between the study groups. ANP: Atrial natriuretic peptide, U: Mann Whitney u test, *Significant



Figure 3. ANP concerning different variables among the cases studied. ANP: Atrial natriuretic peptide, U: Mann Whitney u test, *Significant

Furthermore, ROC curve analysis revealed that the ANP levels at the area under the curve of 0.903 (95% confidence interval of 0.832–1.432, $p=0.001$) may be predictive in children with acute respiratory distress syndrome. Children with

acute respiratory distress syndrome were predicted with 97.88% sensitivity and 90.4% specificity using a cut-off of <511.22 pg/ml. (Fig 4).

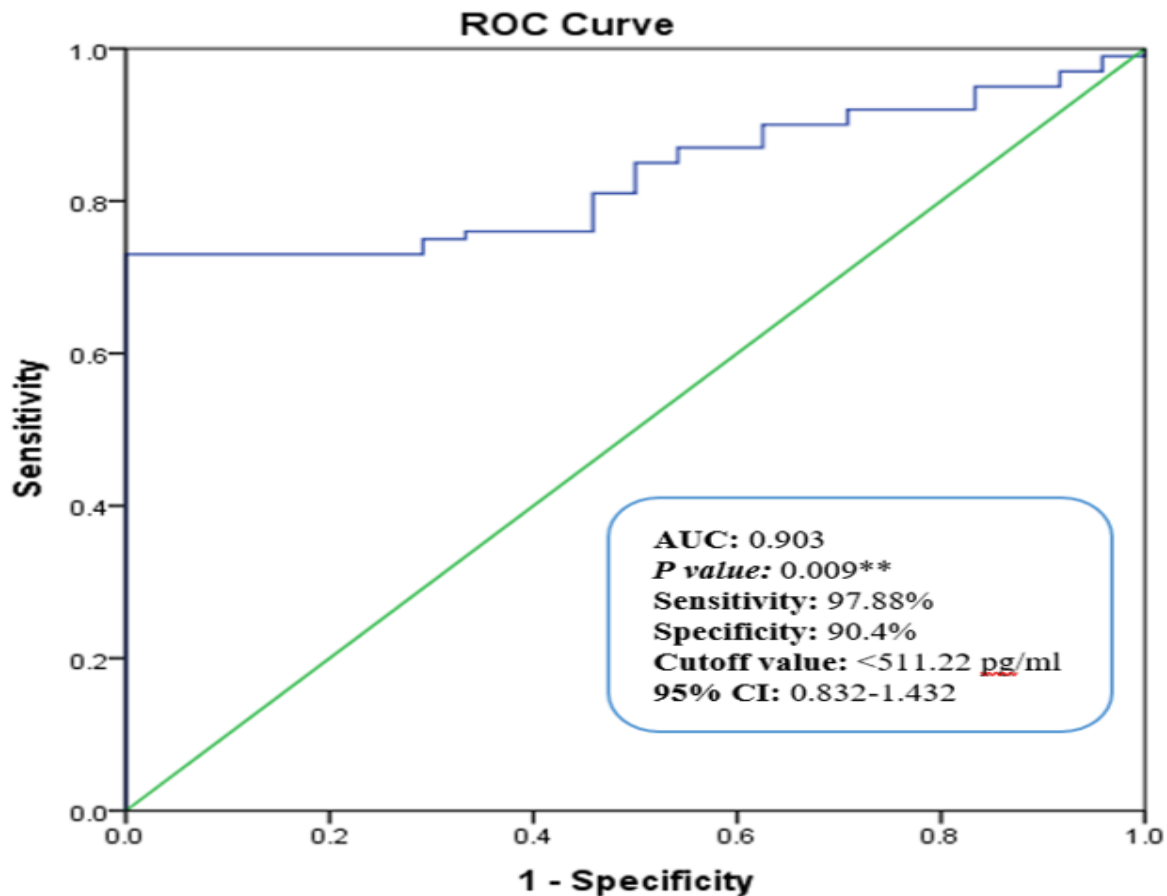


Figure 4. ROC curve of ANP as a marker of in children with ARDS. AUC: area under the curve, CI: Confidence Interval, *: Significant.

Discussion

Age, sex, and place of residence did not significantly differ among the groups under investigation in this study. Likewise, [11] showed that the demographic information for the two groups did not differ significantly. However, [12] found a statistically significant correlation between an increased prevalence of ARDS and male sex. Males experienced ARDS at a higher rate than females (53 [66.3%] versus 27 [33.7%]). The vital signs of the patients and control groups in the current investigation differed significantly. Compared to the controls, the patients' temperatures, pulses, and respiration rates were all noticeably greater. In contrast to controls, oxygen saturation is noticeably lower. According to [13], the degree of respiratory distress was correlated with an increase in heart rate and breathing frequency. Across all respiratory distress levels, there was a substantial difference in the frequency of breathing. Except for comparing participants with moderate and severe respiratory distress, there was a significant difference in heart rate across all levels of respiratory distress. The correlation coefficients between distress and heart rate, breathing frequency, and SpO₂ were -0.25, 0.42, and 0.25, respectively. Furthermore, [11] found that

more ARDS patients utilized midazolam and norepinephrine, and that their systolic blood pressure and respiratory rates were considerably greater than those of the control group. According to arterial blood gas research, ARDS patients had significantly greater PaCO₂ but significantly lower PaO₂ and PaO₂/FIO₂ than control patients. In terms of ventilator settings, ARDS patients required considerably higher positive end-expiratory pressure (PEEP) and higher FIO₂ than the non-ARDS patients, but inspiratory pressure (P_{insp}) and inspiratory time did not change significantly across groups. Hb, RBCs, renal and liver function tests, sodium, potassium, and calcium levels did not differ statistically significantly between ARDS cases and controls in the current investigation. However, ARDS cases had much greater WBCs than controls, while ARDS cases have significantly lower PLT than controls. These hematologic changes are consistent with [14], which demonstrated that sepsis from either pulmonary or extrapulmonary causes frequently triggers the systemic inflammatory response linked to ARDS. According to the literature, ARDS is frequently linked to abnormalities that are secondary to the underlying illness, especially sepsis,

although it is not distinguished by a single diagnostic test marker. Tumor necrosis factor- α , interleukins (IL-1, IL-6, and IL-8), soluble intracellular adhesion molecules, and E-selectin are examples of inflammatory mediators that are higher in septic patients and are linked to the pathophysiology of ARDS.

These conclusions are corroborated by earlier research that found hematologic abnormalities, specifically leukocytosis or, on the other hand, leukopenia and lymphopenia, as well as thrombocytopenia, to be common among ARDS patients. In research comparing patients with and without ARDS, [15] found that 85.1% of ARDS patients had lymphocyte counts below 1,000/mm³ and 22.4% of ARDS patients had platelet counts below 100,000/mm³. However, we did not observe statistically significant variations in liver function tests between the groups, which suggests that hepatic involvement may depend on certain etiologic factors or may not be a consistent feature throughout ARDS populations.

These results were consistent with previous research showing the hematologic and inflammatory abnormalities frequently seen in ARDS. Elevated leukocyte counts and thrombocytopenia may be indicative of systemic inflammation, endothelial damage, and coagulopathy linked to the pathogenesis of ARDS, as demonstrated by [16]. However, decreased platelets and increased WBCs seem to be statistically significant characteristics that set our ARDS group apart from non-ARDS controls. These results are in line with the development of respiratory acidosis as ventilation-perfusion mismatch deteriorates and dead space rises, following initial respiratory alkalosis brought on by compensatory hyperventilation.

According to a different study by [17], children with upper respiratory tract infections had the highest frequency of hyponatremia (44.1%). Acute bronchitis had the highest rate (10.5%), followed by interstitial pneumonia (13.4%), segmental and lobar pneumonia (16.7%), and acute bronchiolitis (9.7%). Furthermore, children with hyponatremia had significantly higher serum blood urea nitrogen (BUN) levels and significantly lower serum potassium and calcium levels than children without the condition. Bicarbonate and potassium were linked to mortality outcomes in a study by [18]. There was no statistical significance in other factors. Serum potassium levels were lower in survivors than in non-survivors. On Day 0, non-survivors' 24-hour urine output was noticeably less than survivors'. Additionally, a study by [19] discovered that children with respiratory tract infections had a higher prevalence of hyponatremia when the inflammatory areas in the respiratory tract were deeper.

According to this study, ARDS sufferers had a considerably higher plasma level of ANP than controls, with median values of 637.3 pg/ml and 173.9, respectively. Our findings are in line with those of [20, 21], who found that ARDS patients had a noticeably greater amount of atrial natriuretic peptide than healthy controls. Furthermore, in research conducted by [22,

23]. Children with pulmonary disease had somewhat higher mean plasma atrial natriuretic peptide levels than healthy controls when comparing the levels of this protein between children who were admitted to the hospital with respiratory distress and those who were in good health. Additionally, the potential causes of these neuropeptide increases were described by [24]. In both people and experimental animals, acute hypoxemia increases ANP secretion. Patients with acute respiratory distress syndrome have altered levels of atrial natriuretic peptide, which is released from the ventricles in response to elevated ventricular end-diastolic volume and pressure. Nevertheless, [25] also noted that ARDS patients had reduced atrial natriuretic peptide plasma concentrations. The tiny sample size of his patients could be the cause of this.

ANP levels do not significantly correlate with age or sex among the subjects examined in this study. On the other hand, patients with O₂ saturation ≤ 90 had considerably higher ANP levels (762.11 \pm 429.10). Additionally, non-survivor patients had a considerably higher score (714.87 \pm 210.50) than survivors (582.11 \pm 179.22). ANP has also been demonstrated to decrease pulmonary edema and enhance gas exchange and lung injury scores in patients with acute lung injury receiving mechanical ventilation, according to [26]. This suggests that ANP is both a physiological response marker and a possible therapeutic target. These results support our findings and imply that ANP may be a very sensitive and specific biomarker for early detection of ARDS in pediatric patients, particularly when hypoxia-induced cardiopulmonary stress is present.

Evidence from adult research using various types of natriuretic peptides supports our results that increased plasma ANP levels can be a sensitive and specific predictor of ARDS in children. Higher mid-regional pro-atrial natriuretic peptide (MR-proANP) levels upon admission have been demonstrated to independently correlate with mortality in patients with community-acquired pneumonia (CAP), according to [27]. MR-proANP levels were substantially greater in nonsurvivors (median 293.0 pmol/L) than in survivors (129.0 pmol/L), indicating a strong predictive function for natriuretic peptides in severe respiratory diseases (reference). Furthermore, with 71% sensitivity and 67% specificity at a 214 pmol/L cut-off, the area under the ROC curve (AUC) for MR-proANP in predicting death was higher than that of CRP and equivalent to clinical scoring systems like the PSI, highlighting its diagnostic importance. These results are similar to ours, which showed that ANP at a cut-off of <659.4 pg/mL produced an AUC of 0.832, with 85.9% specificity and 98.9% sensitivity in predicting juvenile ARDS.

Conclusions

In conclusion, children who have acute respiratory distress syndrome may modify fluid dynamics, show higher cardio-

pulmonary stress, and have elevated atrial natriuretic peptide concentrations. In pediatric ARDS, ANP may be useful as a biomarker of disease severity and hemodynamic burden.

Declarations

Data sharing statement: All the information and resources used in this work are accessible.

Consent for publication: All authors read the article, made necessary revisions, and consented to publish it; there were no conflicts of interest.

Authors contributions: Every author contributed significantly to the work reported, whether it was in the idea, study design, execution, data collection, analysis, and interpretation, or all of these areas; they all participated in the article's drafting, revision, or critical review; they all agreed on the journal to which the article was submitted; and they all agreed to take responsibility for every part of the work.

Disclosure: The authors declare no competing interest in this work.

Acknowledgements: Not applicable.

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