

“STUDY OF PRO-BRAIN NATRIURETIC PEPTIDE LEVELS IN PATIENTS OF ACUTE RESPIRATORY DISTRESS SYNDROME” Page Title

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ABSTRACT:

Background: Acute Respiratory Distress Syndrome (ARDS) is a life-threatening condition with high morbidity and mortality. Brain Natriuretic Peptide (BNP) and its precursor, Pro-BNP, have been explored as potential biomarkers for predicting outcomes in ARDS, but their clinical significance remains unclear.

Methods: This single-center, prospective study included 96 ARDS patients. Pro-BNP levels were measured at admission and after 72 hours. Patients were categorized based on ARDS severity, ventilatory support, ICU stay duration, and outcomes. Statistical analysis assessed the correlation between Pro-BNP levels and disease severity, oxygenation status (PaO₂/FiO₂ ratio), and prognosis.

Results: The study observed significantly elevated Pro-BNP levels at admission, with a marked decrease at 72 hours ($p < 0.001$), except in non-survivors, where levels increased. Improved PaO₂/FiO₂ ratios were noted over 72 hours, indicating better oxygenation. Higher Pro-BNP levels correlated with severe ARDS, prolonged ICU stays, and increased mortality ($p < 0.0001$). The overall mortality rate was 14.58%, with 85.42% of patients discharged.

Conclusion: Pro-BNP levels serve as a valuable prognostic marker in ARDS, correlating with disease severity and outcomes. Its decreasing trend over time suggests clinical improvement, while persistently high levels indicate poor prognosis.

Keywords: Acute Respiratory Distress Syndrome, Pro-Brain Natriuretic Peptide, ARDS severity, ventilatory support, biomarker, patient outcomes.

INTRODUCTION: -

Acute Respiratory Distress Syndrome (ARDS) is a life-threatening condition marked by severe hypoxemia and lung stiffness, where mechanical ventilation is often the only lifeline. ⁽¹⁾ It arises from various insults, including pneumonia, sepsis, trauma, burns, inhalational injuries, acute pancreatitis, and elective surgery. ⁽²⁾

The pathophysiology involves alveolar-capillary damage, increased permeability, and a cascade of inflammatory responses, ultimately progressing to a fibro-proliferative phase. ⁽³⁾

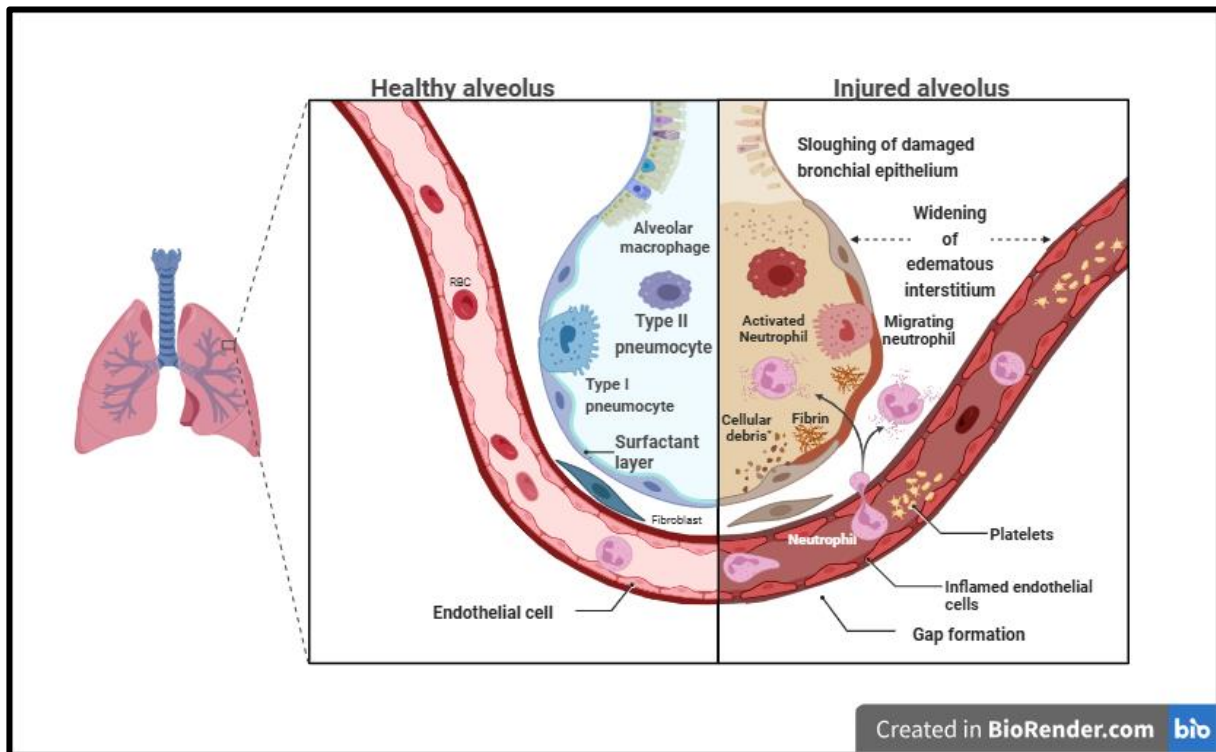


Figure no:1:- Crucial mechanism involved in ADRS.

In India, ARDS incidence rates vary with age, increasing from 16 per 100,000 person-years in younger populations to over 300 per 100,000 in the elderly. ⁽⁴⁻⁵⁾ Prognostic markers such as interleukin-18 and angiotensin peptides have been studied but are rarely used in clinical practice. ⁽⁶⁾ Early identification of high-risk patients is crucial for optimizing treatment and improving survival.

Brain Natriuretic Peptide (BNP) and its precursor, NT-proBNP, are primarily secreted in response to myocardial wall stress. ⁽⁷⁾ While traditionally linked to heart failure, elevated levels can also result from non-cardiac conditions, including ARDS. It is suggested that Pro-BNP could serve as a potential prognostic biomarker, helping to predict ICU outcomes and mortality in ARDS patients. ⁽⁸⁾ However, clinical evidence remains scarce, leaving a crucial gap in understanding its true significance. Unraveling this connection could be a game-changer in refining prognostic strategies and enhancing patient management in the ICU. Thus, our present analysis aims to investigate the role of pro-brain natriuretic peptide levels in patients of ARDS.

Aim and Objectives

Aim:

To study the levels of Pro-Brain Natriuretic Peptide in patients with Acute Respiratory Distress Syndrome (ARDS).

Objectives:

- To assess the levels of Pro-Brain Natriuretic Peptide in patients with Acute Respiratory Distress Syndrome.
- To evaluate the association of Pro-BNP levels with ICU stay duration, morbidity, and mortality.
- To determine the significance of Pro-Brain Natriuretic Peptide in the severity of Acute Respiratory Distress Syndrome.

MATERIAL AND METHOD

The present study was a single-center, prospective, cross-sectional, and analytical investigation conducted at MGM Medical College and Hospital, Aurangabad, over two years. A total of 96 patients diagnosed with Acute Respiratory Distress Syndrome (ARDS), as per the Berlin Definition, were included in the study. Patients were thoroughly screened based on specific inclusion and exclusion criteria to ensure appropriate selection. The inclusion criteria encompassed all patients aged 18 years and older who met the ARDS definition, while those with congestive cardiac failure, rheumatic valvular heart disease, chronic kidney disease, acute coronary syndrome, or chronic liver parenchymal disease were excluded.

The primary objective of the study was to assess the levels of Pro-Brain Natriuretic Peptide (Pro-BNP) in patients with ARDS. Laboratory parameters were analyzed at predetermined time intervals, with routine investigations

conducted and recorded upon admission. Additionally, specific laboratory parameters, particularly Pro-BNP levels, were measured both at admission and 72 hours later. Arterial blood gas (ABG) analysis was performed to calculate the $\text{PaO}_2/\text{FiO}_2$ ratio, which was used to assess the severity of ARDS.

Demographic details, clinical presentations, and disease manifestations were systematically documented in case record forms. The study also maintained a comprehensive record of patient outcomes, including morbidity, mortality, and ICU stay duration, which were analyzed about disease severity. The collected data were subjected to statistical analysis to determine their significance, and the results were interpreted to draw meaningful conclusions regarding the role of Pro-BNP in ARDS.

OBSERVATION AND RESULTS

The study on pro-brain natriuretic peptide levels in patients with acute respiratory distress syndrome reveals a diverse patient demographic. The mean age of the participants is 47.15 years, with the largest group being between 31-50 years (48.96%), followed by 51-70 years (29.17%), 10-30 years (15.63%), and 71-90 years (6.25%). Gender distribution shows a higher proportion of males (60.42%) compared to females (39.58%). The most common chief complaints include fever, chest pain, and productive cough (26.04%), followed by fever, chest pain, and non-productive cough (18.75%). Diagnosis-wise, viral pneumonitis is the most prevalent (40.63%), followed by pneumonia (27.08%), acute pancreatitis (8.33%), and road traffic accidents (7.29%). Other less frequent diagnoses include blunt trauma, surgical complications, and pulmonary conditions. The data on ICU duration shows that most patients (52.08%) stayed in the ICU for 1-3 days, with fewer patients having longer stays: 33.33% stayed for 3-5 days, 11.46% stayed 5-7 days, and 3.13% stayed 7-9 days, indicating that the majority of ICU stays were within the 1-3 day range.

Table 1: Distribution of study population according to severity of ARDS

Severity of ARDS	no. of cases	%
Mild ARDS	41	42.71%
Moderate ARDS	34	35.42%
Severe ARDS	21	21.88%
Total	96	100.00%

The severity of ARDS among 96 cases showed that most of the cases were mild, with 41 cases (42.71%). Moderate ARDS was observed in 34 cases (35.42%), and severe ARDS was present in 21 cases (21.88%). This distribution indicates that most ARDS cases were either mild or moderate in severity.

Table 2: Distribution according to type of ventilatory support

Type OF Ventilatory Support	No. of cases	%
High-Flow Nasal Cannula	7	7.29%
Non-Invasive Ventilation	32	33.33%
Oxygen Support	34	35.42%
Pressure Control Ventilation	23	23.96%
Total	96	100.00%

The above data showed that, the type of ventilatory support among 96 cases reveals that oxygen support is the most commonly used method, accounting for 34 cases (35.42%). Non-invasive ventilation is also prevalent, with 32 cases (33.33%). Pressure control ventilation is used in 23 cases (23.96%), and high flow nasal cannula is the least common, used in 7 cases (7.29%).

Table 3 Distribution according to PaO_2 : FiO_2 ratio and Pro-BNP levels at the time of admission and PaO_2 : FiO_2 after 72 hours of admission

FiO2 after 72 hours of admission		
PaO2:FiO2 ratio	Mean ± SD	P value
PaO2:FiO2 @ Admission	192.18 ± 71.67	<0.001
PaO2: FiO2 @ 72 hours	269.64 ± 97.14	
Pro-BNP levels		
Pro-BNP levels @ Admission	1970.59 ± 1797.81	<0.001
Pro-BNP levels @ 72 Hours	1372.04 ± 1992.67	

The findings showed a significant improvement in the PaO_2 : FiO_2 ratio, increasing from 192.18 $\pm$ 71.67 at admission to 269.64 $\pm$ 97.14 at 72 hours ($p < 0.001$), indicating a positive response to treatment. Similarly, a significant decrease was observed in Pro-BNP levels, from 1970.59 $\pm$ 1797.81 at admission to 1372.04 $\pm$ 1992.67 at 72 hours ($p < 0.001$), suggesting a clinical improvement or response to therapy.

Table 4: Distribution according to Pro-BNP levels at the time of admission and Pro-BNP levels after 72 Hours with Severity of ARDS

Severity of ARDS	Pro-BNP levels @ Admission	Pro-BNP levels @ 72 Hours	p-value
Mild ARDS	465.0243	217.82926	<0.0001
Moderate ARDS	2236.2647	854.2058	<0.0001
Severe ARDS	4479.9047	4463.904	<0.0001

The above table shows that in mild ARDS cases, Pro-BNP levels drop from 465.02 to 217.83, in moderate ARDS from 2236.26 to 854.21, and in severe ARDS from 4479.90 to 4463.90. All changes are highly significant with p-values < 0.0001.

Table 5: Distribution according to Pro-BNP levels at the time of admission and after 72 Hours with outcome of the patient

Outcome	Pro-BNP levels @ Admission	Pro-BNP levels @ 72 Hours	p-value
Death	3862.28 ± 1413.52	5609.5 ± 1575.40	<0.0001
Discharge	1647.62 ± 1657.09	648.5731 ± 790.78	<0.0001

Significant changes were observed in Pro-BNP levels from admission to 72 hours in patients who died and those who were discharged. Patients who died had a notable increase in Pro-BNP levels (3862.3 ± 1413.5 to 5609.5 ± 1575.4, $p < 0.0001$), while discharged patients exhibited a significant decrease (1647.6 ± 1657.1 to 648.6 ± 790.8, $p < 0.0001$).

Table 6: Distribution according to outcome of patient

Outcome of patient	No. of cases	%
Discharge	82	85.42%
Death	14	14.58%
Total	96	100.00%

The outcomes for 96 patients indicate that the majority were discharged, with 82 cases (85.42%) resulting in discharge. In contrast, 14 cases (14.58%) ended in death. This suggests a high discharge rate among the patients.

DISCUSSION

In the present study, elevated Pro-BNP levels were observed in ARDS patients, with significantly higher levels in non-survivors, aligning with findings from **Determann et al.** who reported similar trends in NT-ProBNP levels. **Sun et al.** also demonstrated that ARDS non-survivors had markedly increased BNP levels, reinforcing the association between BNP and mortality risk. ⁽⁹⁻¹⁰⁾ Furthermore, **Karpaliotis et al.** and **Lin et al.** established a graded correlation between BNP levels and death, consistent with our study's findings that Pro-BNP levels significantly declined over 72 hours, reflecting a positive response to treatment. ⁽¹¹⁻¹²⁾

Demographically, our study showed a higher prevalence of ARDS among males (60.42%), comparable to the observations of **Tolossa T, et al.** and **Vahdatpour CA et al.**, where males constituted the majority of cases. The age distribution in our study (mean age: 47.15 years) also aligns with **Determann et al.**, who reported a mean age of 61 ± 16 years, and **Tolossa T, et al.**, who noted a mean age of 54.29 years. The ARDS severity classification in our study, with most cases being mild to moderate (42.71% and 35.42%, respectively), is consistent with **Tolossa T, et al.**, though **Vahdatpour CA et al.** reported a higher proportion of severe cases. ^(13-14,9)

The present study observed an improvement in PaO₂/FiO₂ ratios from 192.18 ± 71.67 to 269.64 ± 97.14 at 72 hours, with a significant P-value (<0.001), indicating improved oxygenation. This is in line with **Tolossa T, et al.**, who reported that severe ARDS cases had poorer outcomes, emphasizing the importance of oxygenation parameters. Additionally, our study's ICU stay duration (1–3 days for most patients) contrasts with **Tolossa T, et al.** and **Vahdatpour CA et al.**, where median ICU stays ranged between 10–16 days. ⁽¹³⁻¹⁴⁾

With an 85.42% discharge rate and 14.58% mortality, our findings demonstrate a relatively favorable outcome compared to **Sun et al.**, where the survival rate was 41 out of 59 patients. ⁽¹⁰⁾

However, several studies have demonstrated that elevated Pro-BNP levels in ARDS are primarily a consequence of increased strain on the right ventricle due to heightened pulmonary vascular resistance. In a study by **MekontsoDessap et al.** (2005), patients with ARDS exhibited elevated BNP levels, which correlated with right ventricular overload and high positive end-expiratory pressure (PEEP), even in the absence of left ventricular dysfunction. ⁽¹⁵⁾ Similarly, **Mitaka et al.** (2006) reported that NT-proBNP levels were significantly raised in ARDS patients, correlating positively with right atrial pressure and pulmonary artery pressures, thereby confirming that NT-proBNP acts as a marker of right heart strain in ARDS rather than reflecting primary left heart failure. ⁽¹⁶⁾

These findings support the hypothesis that Pro-BNP elevation in ARDS reflects pulmonary-induced right ventricular stress. Thus, this highlights a controversy regarding the effect of Pro-BNP in ARDS. The present study not only corroborates previous findings linking elevated Pro-BNP levels with right ventricular strain in ARDS but also provides novel insight by demonstrating a significant decline in Pro-BNP levels over 72 hours, suggesting its potential utility in monitoring therapeutic response, an aspect that has been less explored in earlier studies.

CONCLUSION

This study highlights the significance of Pro-BNP in ARDS, demonstrating its correlation with disease severity and patient outcomes. While initially elevated, Pro-BNP levels showed a significant decline at 72 hours, reflecting potential cardiac strain reduction and clinical improvement. The findings suggest that Pro-BNP trends could help predict ICU stay duration and patient prognosis. However, as a single-center study, further research is needed to establish its role in ARDS management.

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